The current evidence of dental care and oral health for achieving healthy longevity in an aging society

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Japan Dental Association

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I Introduction and summary overview

Introduction and summary overview

Kakuhiro Fukai
Japan Dental Association

[Introduction]

As we face the rapid aging of our population, which is proceeding at a rate never before experienced by humankind, many efforts to deal with this problem have been initiated in various fields of academic research as well as in medical, health, welfare, and community settings. In order to realize a society where elderly people can live life in peace and with dignity, it is essential to develop health and medical care systems that provide high-quality healthcare services.

It is inevitable that in old age, people experience a decline in the functions of daily living and become more susceptible to diseases. The aging of the population is a result of decreasing mortality in adulthood and old age, not to mention the neonatal period and early childhood, which has been achieved through the accumulation by humankind of science, technology, and knowledge. However, population aging has also extended the period during which people require care, and it will continue to increase the amount of healthcare needed at the national and community level.

Under the present circumstances, providing sufficient healthcare to all elderly individuals requires adequate human and social resources, a social security system which includes a healthcare system and rests on a solid financial foundation, and the accumulation of scientific evidence. Moreover, it will be necessary to inform the citizenry, policymakers, and healthcare workers regarding the outcomes of the various measures. Another big political issue is how to extend the healthy period during old age.

On the other hand, dental and oral health is an essential element for the maintenance of QOL throughout one's life. Moreover, research has made it clear that dental and oral health has the potential to maintain and improve systemic health status. Therefore, a social system that allows everyone to receive high-quality dental care and oral health services even during old age is necessary. In addition, collaboration between the medical and dental fields and between professionals in both fields toward the development of a more effective healthcare provision system is needed. To this end, it is necessary to accumulate clearer evidence and take specific actions in order to situate dental care and oral health firmly within the social security system and healthcare policy, which in turn will facilitate its contribution to the realization of healthy longevity.

Against this backdrop, this collection of reviews aims to provide the target audience (i.e., policymakers, healthcare professionals, and researchers) with a summary of the present evidence and issues. To this end, I conducted a literature review for each topic based on the hypotheses (II-1 of this collection of reviews, Figure 10) regarding the conceptual pathway linking dental/oral health and the extension of healthy life expectancy, and then the evidence regarding each topics was analyzed The topics covered in this collection of reviews include the relationship of dental and oral health with (1) age-related changes and aging, (2) life expectancy, (3) NCDs as the main causes of death and the risk factors thereof, (4) diseases that cause conditions requiring long-term care, (5) health promotion activities such as exercise, nutrition, and rest, (6) socioeconomic factors, and (7) the effects of dental care. In addition, the particularly important literature is summarized, in some cases in table form, within the review of each topic. Moreover, the strength of the evidence presented in each study is noted by specifying the study design (e.g., observational study, intervention study, data integration study), so that this collection of reviews can be used as an easy-to-understand resource where policymakers as well as the general public can obtain oral health information. At the end of this collection of reviews, we have also provided a commentary regarding the history of Japan's 8020 campaign and the universal health insurance system that was implemented in 1961.

The reviews contained herein were conducted mainly by using Ichushi (the largest database of medical literature in Japan) for Japanese articles and PubMed for English articles to conduct searches of research reported up through 2014. Excerpts of the main findings from the topic-specific reviews by each author are provided below.

[Summary of findings from each topic-specific review]

1. Age-related changes and aging

[Fukai K, Kambara M, Morito M *et al*.]

With regard to aging in the oral area, chewing and swallowing were examined as representative of oral functions. The results confirmed that all oral functions, including occlusion, chewing (mastication), salivation,

articulation, and swallowing, show a decline while influencing each other. Moreover, reduced oral function was closely related to dementia, systemic diseases, and motor function, as well as the functions of daily living.

Age-related changes in the oral cavity due to aging, the oral health status of the elderly in Japan, dental care among the elderly, the daily life of the elderly, and oral health risks among the elderly were examined. The results revealed that organic changes in the oral cavity affect oral function, and that with aging comes specific changes in terms of oral diseases, oral health behaviors, and lifestyle habits; thus, appropriate measures to address these changes are necessary. If we were to address these changes with conventional strategies on a disease-by-disease basis, changes associated with aging must be quantified using appropriate measurement methods, and tailor-made treatment programs would be developed in accordance with established thresholds. However, age-related changes are often subjective. Thus, resident- or patient-based responses should be emphasized in order to address the problem of how best to go about one's daily life, including daily activities and work, rather than simply looking at everything from the perspective of treating diseases and mental or physical disorders.

2. Life expectancy [Fukai K, Anzai T *et al*.]

The association of dental and oral health with mortality was reviewed. With regard to the relationship between the number of teeth and overall mortality, the results of several cohort studies from different countries have provided evidence that the maintenance of higher numbers of teeth contributes to the extension of life expectancy. Meta-analyses have confirmed that vital prognosis is improved due to the use of dentures after tooth loss. A number of reports have also shown an association between tooth number and cardiovascular disease (CVD).

With regard to the effect of masticatory function and occlusal state on life expectancy, individuals with high masticatory function or a stable occlusal state (i.e., able to chew in the molar region) have better health status and significantly lower mortality risk. An association between masticatory function and CVD mortality has also been reported.

The results of investigations regarding the relationship between oral diseases (e.g., dental caries and periodontal disease) and life expectancy revealed that there is currently insufficient evidence to establish a clear relationship. One report, however, did show that people with regular oral care habits have a longer life span.

3. NCDs as primary causes of death and associated risk factors

[Izumi Y, Yoneyama T, Ueno T, Kikutani T, Shimazaki Y *et al*.]

The results of the investigation regarding the association of dental and oral health with main causes of death and NCDs revealed that there exists evidence showing associations with diabetes mellitus, pneumonia, cancer, cardiovascular diseases, and metabolic syndrome, as detailed below. The association of dental and oral health with cerebrovascular diseases, and the effects of maintaining dental and oral health during the perioperative period following cancer surgery will be described in separate sections of this introduction.

Diabetes mellitus affects diseases in the oral cavity, and periodontal diseases in particular are closely associated with diabetes mellitus. For this reason, dentists have a potential role in contributing to the improvement of diabetes mellitus. Moreover, since performing oral health management can potentially result in early detection of diabetes mellitus or provide opportunities to educate patients in the pre-diabetic stage, medical-dental cooperation should be further promoted in the future.

The idea that oral care can help prevent aspiration pneumonia in elderly patients has already gained social support; however, this claim rests primarily on evidence from a single RCT, so further accumulation of evidence from well-planned RCTs is needed. On the other hand, a sufficient level of evidence does exist to support a connection between oral care and the prevention of ventilator-associated pneumonia.

With regard to the association between cancer and oral health, oral adverse events that occur in association with cancer treatment can hinder treatment and sometimes affect patients' vital prognosis. Some evidence suggests that the implementation of proper oral hygiene management before initiating cancer treatment is effective in decreasing the risk of oral adverse events and reducing their severity.

An association between periodontal and cardiovascular diseases has been observed. Moreover, there have been new findings, such as that the risk of cardiovascular disease among people with periodontal disease is higher in people who are 65 years of age or younger, that the association of periodontal disease with acute myocardial infarction is stronger than with chronic coronary heart disease, and that people with periodontal disease accompanied by systemic bacterial infection have a higher risk of coronary heart disease. A few studies have revealed that the treatment of periodontal disease is associated with reduced risk of developing cardiovascular disease or a decrease in serum

antibody titers, but these have not yet been established as causal relationships.

Among reports from various countries regarding the association between metabolic syndrome and oral health, there have been a relatively large number of studies conducted in Japan. Individuals with metabolic syndrome have a high risk of periodontal disease, and some studies have shown that metabolic syndrome is more prevalent among those with periodontal disease; however, the majority of this evidence is from cross-sectional studies. Obesity, which plays a central role in metabolic syndrome, is an important risk factor for diabetes mellitus and arteriosclerotic diseases. Many studies have shown that obesity is also associated with periodontal disease, and in particular, a strong association has been found between visceral fat obesity and periodontitis. Since many aspects of the relationship between metabolic syndrome and oral health, such as the direction and underlying mechanisms of the association, remain unclear, more evidence needs to be accumulated in order to further elucidate this association.

With respect to NCD risk factors, smoking, drinking, exercise, and eating habits have each been found to be associated with oral health problems such as periodontal disease. In particular, smoking clearly affects periodontal health. Although it has been suggested that intake of a large amount of alcohol may affect periodontal health, results have varied among studies. People with good exercise habits and those who consume healthy food and nutrients tend to have better periodontal health. Improved lifestyle habits bring about positive effects for not only systemic health but also oral health, but further evidence is required to justify the inclusion of instruction regarding lifestyle habits (other than smoking) into oral health guidance programs and routines.

4. Diseases which cause conditions necessitating long-term care [Kikutani T, Yamamoto T, Aida J *et al*.]

Predictive factors for the incidence of conditions that necessitate long-term care include old age, cognitive dysfunction, visual impairment, low subjective health, decreased or increased body mass index (BMI), decreased functionality in the extremities, decreased exercise or social interaction, and smoking. In addition to these factors, it has been pointed out that oral health may be related to some of the risk factors associated with the development of a condition requiring long-term care. For example, oral health affects social activities, such as interacting with friends and participating in recreational activities, through conversation, facial appearance and smile, and eating function. For the elderly, social participation has been shown to prevent the occurrence of conditions that necessitate long-term care, thus it is possible that oral health status plays an important role in terms of its effect on social participation.

As for the specific evidence, healthy oral conditions including denture use have been associated with a low incidence of future occurrence of a condition requiring long-term care. In the future, by further disseminating healthcare interventions aimed at maintaining oral health among the elderly, the incidence of conditions requiring long-term care can be reduced.

The leading disease resulting in long-term care among the Japanese people is cerebrovascular disease. Cerebrovascular disease causes movement disorders that affect not only the extremities but also the orofacial area, and it can even cause the deterioration of oral hygienic status. Investigations of the association between oral health status and cerebrovascular diseases have revealed that young people and people with many missing teeth or high CAL and PPD have an increased risk of stroke, as reported in the context of the association between periodontal disease and stroke. Moreover, the association of periodontal disease is stronger with non-hemorrhagic (ischemic) stroke than with hemorrhagic stroke. However, the current evidence regarding the reduced risk of cerebrovascular events associated with periodontal disease is insufficient to establish causality. It will be necessary to conduct follow-up and/or intervention studies in order to address these issues.

The question of whether oral health is associated with the later onset of dementia or cognitive decline was examined based on original articles reporting cross-sectional and/or intervention studies. The majority of the studies examined have reported significant associations. Oral hygiene, periodontal disease, number of teeth, occlusion, mastication, presence of a primary care dental clinic, and dental visitation have been reported as factors that are likely associated with the onset of dementia and cognitive decline.

The question of whether poor oral status increases the risk of future incidence of falls and femoral neck fracture, as well as which oral conditions have associations with falls and fractures, was investigated. Several cohort studies have demonstrated that loss of occlusal support and non-use of dentures after tooth loss are risk factors for subsequent fall events. Moreover, having periodontal disease and fewer teeth have been shown to increase the risk of subsequent femoral neck fracture.

The relationship between oral health and joint diseases was examined based on the results from intervention studies, case-control studies, cross-sectional studies, and

basic studies. The results suggest an association between periodontal disease and rheumatoid arthritis, and that the prevention and treatment of periodontal disease could improve some of the symptoms of rheumatoid arthritis. However, these improvements were limited, and the effectiveness of such improvements is ambiguous in some of the articles; therefore, further investigative research is necessary.

5. Health promotion such as exercise, nutrition, and rest

[Miyazaki H, Hanada N, Ando Y, Naito M *et al*.]

With regard to motor function, the association of dental/oral health with physical fitness and activities of daily living (ADL) was examined. The existing research shows that balance, lower limb muscle strength, and upper limb muscle strength are associated with occlusal support and chewing ability, and that deterioration of occlusal status causes deterioration of balance and lower limb muscle strength over time. However, the interpretation of these results requires that consideration be given to dental treatment interventions as well as sampling bias. Moreover, the relationship between oral health status and ADL is believed to be indirect, i.e., nutritional state and physical strength serve as mediators, meaning that the maintenance of oral health status or recovery of oral function likely prevents reduced ADL through these mediators.

The results of the review of the relationship between dental/oral health and nutrition revealed that tooth loss is associated with a decrease in food consumption, mainly that of vegetables and fruits, and nutrient intake, mainly vitamins with anti-oxidation effects. In addition, tooth loss is associated with obesity or weight loss. This association is affected by factors such as age, sex, and race. Especially among the elderly, associations with a decrease in total energy intake and malnutrition have been observed. Edentulous individuals with full dentures have inferior nutrition intake compared to non-edentulous individuals, but such an association is not observed among those with adequate denture fit who have received regular maintenance. Self-rated oral pain is associated with malnutrition. However, no improvement effects on nutrition intake have been observed as a result of dental prosthesis treatment alone. Improvements in healthy dietary intake and nutritional status, which require behavior modification, are difficult to achieve without nutritional guidance. Based on these findings, it is likely that regular dental maintenance which results in tooth loss prevention and maintenance of denture fit will decrease the risk of NCDs, prevent malnutrition among the elderly, and prevent reduced ADL, ultimately leading to the extension of healthy life expectancy. There is, however, a methodological challenge that must be overcome in future research; namely, that it is difficult to assess causality because observational studies regarding the association between dental/oral health and nutrition have usually relied on a cross-sectional design. Therefore, studies with a higher level of reliability (e.g., cohort studies) need to be conducted in order to accumulate a strong body of evidence that would clarify the nature of this association. It would also be desirable to conduct research that assesses the effects of improved nutrition through collaboration with other professionals, such as nutritionists, in the context of an intervention study.

Concerning the association between oral health and rest, communication, and QOL, the research indicates that oral health and health-related QOL are significantly correlated, and that the maintenance and promotion of oral health contributes to improved QOL. Furthermore, stress and sleep, which are associated with communication and rest, are also associated with oral status. While few reports exist on these factors, rest and communication are thought to be related to survival, ADL, social participation, and QOL, thereby indirectly affecting healthy longevity. The association of stress and amount of sleep with mortality risk has been reported, so research on how oral health is related to these factors would have great public health significance. Therefore, further accumulation of evidence in this area is encouraged.

6. Social determinants

[Aida J *et al*.]

Social determinants of health are "causes of the cause" that inevitably affect the health and behavior of people. A review of systematic reviews and meta-analyses regarding social determinants and dental health inequalities was conducted to examine the existing evidence, both globally and in Japan. It was found that higher income and education level were associated with better oral health conditions and behaviors, confirming the existence of health inequalities. Even among the studies conducted in Japan, where dental treatment is covered by the universal health insurance system, similar health inequalities were observed. Health inequalities arise due to inequalities not only in disease treatment, but also in disease incidence. Accordingly, inequalities are known to exist even if the cost of medical examination is free. Concerted efforts must be made if inequalities in the occurrence and treatment of dental diseases are to be reduced. It is difficult to implement measures that will improve the condition of patients who do not readily change their health behaviors even after

repeated health guidance, or those who do not even come to a medical checkup. In order to improve the health of our entire society, including people who are unwilling to make any effort, it is necessary to come up with an approach that takes into account the health-related social determinants that exist in the background. Clarification of the social determinants that impact health, and then the realization of an environment that promotes the health of everyone in society, are essential.

7. Effects of dental care

[Ueno T, Morito M, Izumi Y, Yamamoto T, Tsuneishi M *et al*.]

Reducing perioperative complications in surgery has important implications not only in terms of improved treatment prognosis but also from the perspective of medical economics. Some postoperative complications occur in the oral environment (hygiene status, dental disease, etc.). Therefore, oral management during the perioperative period helps to reduce the risk of infectious complications such as pneumonia, and it contributes to postoperative recovery by supporting the reinitiation of oral intake after surgery. To date, studies have reported evidence regarding risk reduction for the following specific postoperative complications: 1) postoperative pneumonia, 2) complications during endotracheal intubation (tooth fracture and loss, etc.), 3) infection during cardiovascular surgery, 4) infection during organ transplant surgery, and 5) postoperative complications associated with oropharyngeal and esophageal surgery (respiratory complications, wound infection).

With regard to the effect of dental care on improvement of oral function, our review found evidence for the recovery of mastication due to dental prosthesis treatment after tooth loss, significant contribution of improved chewing ability to systemic problems, and possible improvements resulting from the provision of professional care in patients whose oral function has been reduced to the extent that chewing capacity is hindered.

Many reports have provided evidence that proper continuation of maintenance aimed at preventing the worsening of dental diseases such as dental caries and periodontal disease can help prevent tooth loss. In these studies, the necessary dental treatment is performed before initiating maintenance, and even during the maintenance period it is necessary to carry out early disease detection and treatment procedures. Long-term preservation of teeth can be achieved through proper dental treatment and continued maintenance. Some reports have indicated that putting a complete veneer crown on teeth that have been subjected to root canal treatment decreases the rate of tooth loss. However, overall the abovementioned results show that dental treatment alone does not ensure a sufficient prevention of tooth loss unless maintenance is continued as well.

The degree of effectiveness of health guidance and dental health education, particularly regarding participant behavior modification and oral status improvement, was examined. In addition, paying particular attention to the relationships between risk factors which are common to dental diseases and systemic chronic diseases, a literature search was conducted to examine the possibility of dental health education contributing to the common risk factor approach. Furthermore, in the context of preventive measures in dental health education, the findings regarding the effect of dental caries prevention from the topical application of fluoride were summarized. This analysis revealed that dental health education is effective in promoting knowledge acquisition and attitude change in participants, and somewhat effective in preventing or improving dental caries, plaque deposition, and periodontal disease. However, many of the studies have verified only short-term effects (i.e., those under six months or less), so the long-term effects are still uncertain. Dental healthcare workers should keep in mind that dental health education is likely effective only for a short-term period of up to 6 months, and they should conduct dental health guidance accordingly. Based on the fact that dental caries and periodontal disease have the characteristics of lifestyle-related diseases and that health education has short-term effects, it is important to encourage patients to visit a dentist regularly, at least every six months, and at to provide them with dental health guidance during each visit. In order to efficiently carry out dental health education in the field of clinical and public health, there is a need to consider the cost-effectiveness of various types of dental health education. Among the common risk factors (nutrition, cleanliness, smoking, drinking, stress, and injury), smoking is one for which dental health instruction support is effective. In relation to dental health education and prevention, topical fluoride applications such as fluoride-containing dentifrices and fluoride mouth rinsing have been shown to be effective in preventing dental caries in the primary teeth as well as permanent teeth of young people.

In Japan, dental care has been provided mainly in outpatient settings, so the reality has been that elderly individuals age 75 years old and older often lack access to sufficient dental care. The review of studies on the effects of dental care provided to elderly individuals at home or in a facility in the form of home-visit care services revealed that

the regular provision of such care by dental professionals contributed not only to a decreased bacteria count, but also to improvements in pneumonia incidence, fever length, and cognitive function. However, underlying diseases and oral status differ among elderly individuals requiring long-term care at home or in a facility, and no systematic study regarding on the effect of home-visit dental services alone could be found.

[Conclusions]

Many of the research results showing associations between dental/oral health and systemic health provide strong, reliable evidence. This evidence comes from cohort studies, meta-analyses, and observational studies that examine the causality of the relationship by allocating the subjects and adjusting the data for confounding factors by using methods which incorporate propensity scores (propensity score analysis). With regard to the associations between dental/oral health and life expectancy as well as healthy life expectancy, as shown in this collection of reviews, evidence has already been obtained for some of the individual pathways. However, the mechanisms through which dental and oral health affects systemic health has not yet been clarified. One possible mechanism involves the infections and inflammation that arise due to oral diseases, such as periodontal disease, causing systemic health problems. Another possibility is that there is a relationship between reduced oral function and dietary behavior and/or nutritional state. While the goal of oral health management is to maintain the health of the teeth and the oral cavity, the role of dental care is to recover lost functionality as well as to prevent the progression of dental diseases. Evidence regarding the effect of dental care on improvements of oral function and systemic health should be further accumulated and clarified by conducting well-designed studies.

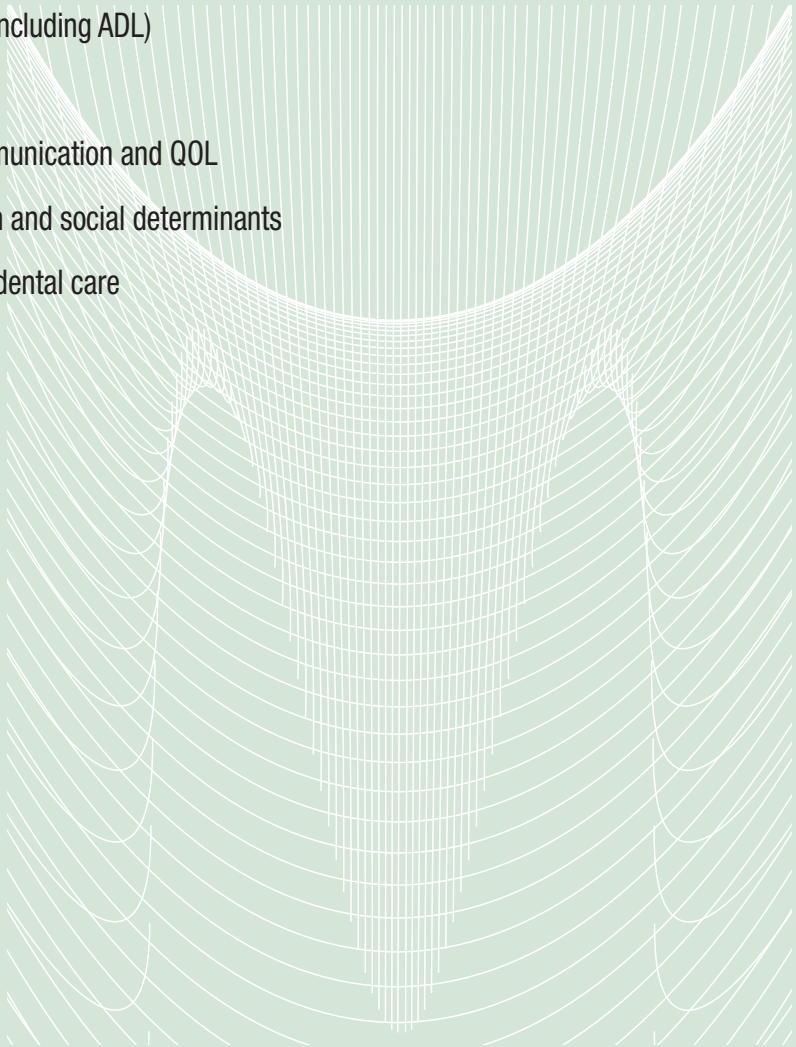
Medical economic analysis on the efficient use of healthcare resources is necessary in order to clearly position dental care and oral health as essential health measures aimed at extending healthy life expectancy. This collection of reviews did not address this point. In the future, the effect of dental and oral health on the extension of healthy longevity needs to be analyzed by estimating its efficiency in terms of healthcare cost reduction, while at the same time accumulating evidence of its effectiveness.

Moreover, with regard to the prevention of NCDs and disease progression, which represent central issues in the current enforcement of healthcare policy, enacting measures that target risk factors which are common to both medical and dental health is an important and efficient approach. However, among lifestyle-related risk factors associated with NCDs, such as smoking, drinking, exercise, and eating habits, smoking is currently the only one where there is sufficient evidence regarding its association with oral health; in other words, ther is not yet enough evidence to justify actively incorporating these factors into clinical and health guidance. In addition to smoking, evidence should be further accumulated regarding the associations between oral health and lifestyle habits such as drinking, exercise, and dietary habits. Furthermore, the practice of common risk diagnosis and handling needs to be systematized across fields.

As shown in this collection of reviews, specific measures to realize healthy longevity in society include (1) extension of life expectancy and prevention of death in early life (prevention of diseases that are main causes of death), (2) prevention of conditions that necessitate long-term care, (3) prevention of a decline in daily living activities, and (4) lifelong health promotion from the viewpoint of a life course approach. The development and implementation of specific practical models, the enactment of health policy to the extent possible, and the accumulation of evidence that demonstrates causal relationships and medical economic effects are required.

II Issue-specific reviews of the evidence

1. Oral health and aging
2. Oral health (tooth condition, mastication, oral diseases, etc.) and life span
3. Oral health and lifestyle-related diseases, non-communicable diseases (NCDs)
4. Association between oral health and main illnesses underlying conditions that necessitate long-term care
5. Exercise (including ADL)
6. Nutrition
7. Rest/communication and QOL
8. Oral health and social determinants
9. Effects of dental care



Ⅱ Issue-specific reviews of the evidence

1. Oral health and aging

1) Oral health in an aging society

2) Oral disease, Tooth number, oral tissue and dietary habit, and aging

3) Mastication (including occlusion), swallowing (including oral dryness)

1. Oral health and aging
1) Oral health in an aging society

Kakuhiro Fukai

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[Abstract]

The unavoidable reality of population aging is affecting our society on a global scale. Biological aging makes elderly people more susceptible to disease and leads to a decline in the bodily functions needed for daily living. Dental and oral health itself is essential for the lifelong maintenance of quality of life (QOL), and research has furthermore established that dental and oral health contributes to the maintenance and improvement of general health. A social system in which anyone can receive high-quality dental care and oral health services during old age needs to be established. To ensure that dental care and oral health maximally contributes to attaining healthy longevity, it is essential to accumulate clear evidence and take the specific actions needed to ensure that dental care and oral health has a secure and established position within an effective and efficient social security system and healthcare policy.

[Introduction]

The demographic shift associated with an altered disease structure and increased average life expectancy is a global phenomenon seen not only in industrialized nations but also in developing countries. Humans have always desired longer lives, and now larger populations and longevity have become a reality due to the accumulation of scientific and medical knowledge and the resulting progress in technology and treatment around the world. However, it is an unavoidable fact that with increased longevity comes a decline in the bodily functions needed for daily living, and that aging makes people more susceptible to disease. For this reason, there are challenges to be addressed in order achieve a society in which all elderly people can live with dignity and security. Such challenges include improving the long-term care system, providing social security as well as effective medicine and healthcare, securing financial resources for these services, and accumulating the research needed for extending health. The aging society of the twenty-first century is therefore now facing the dual realities of longevity on the one hand and the burdens it brings with it on the other[1,2].

Dental and oral functions such as eating and communication are essential for maintaining a person's QOL. For this reason, it is essential that we create and maintain a social system in which people can receive dental care and oral health services over their entire lifetime, irrespective of the region or country in which they live. Moreover, scientific evidence has been accumulating that shows the effectiveness of dental and oral health in preventing illnesses in other organs besides the oral cavity and in maintaining general health. It is therefore generally accepted that dental care and oral health can play a role in solving the problems that our aging society is facing and that achieving this requires maintaining an established position for dental care and oral health within each country's health policies[3,4].

In this paper we attempt to describe the current status of global population aging, not only in industrialized countries such as Japan but also in developing countries, and to postulate a conceptual pathway linking oral care to enhanced general health.

[Objective]

This paper aims to review the literature on population aging and the determinants of health and life expectancy, and to propose a conceptual framework for the role dental care and oral health should play in extending healthy life expectancy.

[Methods]

The results of previous research on human life expectancy, social security systems, dental/oral and general health investigations, and statistical data provided by public institutions were analyzed.

[Results]

1. Changes in the world population and longevity

The world population increased nearly threefold from 2.526 billion in 1950 to 7.162 billion in 2013, and is projected to reach 8.083 billion in 2025 and 9.551 billion in 2050. As shown in Figure 1, the majority of people will be

living in developing countries[5].

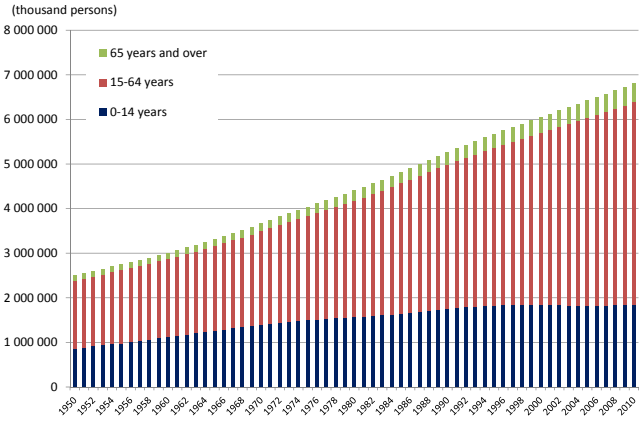
A look at the history of population aging reveals that average life expectancy was around 40 years up to the eighteenth century. As a result of decreases in infection-related deaths, the life expectancy rose to 50 years by the twentieth century, and then rose further to about 80 years from the middle of the twentieth century to the present day[6]. The percentage of people aged 65 years and over, as shown in Figures 2 and 3, increased in developed countries from 7.7% in 1950 to 16.1% in 2010, and also in developing countries from 3.8% to 5.8%[5]. Population aging is occurring in all regions of the world and in countries at various levels of development, and it is progressing at a faster rate in the developing countries.

2. Causes of death and determinants of life expectancy

While acute diseases such as infections and diarrheal diseases are the top causes of death in low-income countries, chronic diseases such as ischemic heart disease, stroke, and cancer are the main causes of death in high-income countries[7]. Developing countries are subject in particular to three types of diseases: chronic diseases, emerging infections, and acute infections (triple burden). As a country's economy improves, the mortality of pregnant women and newborns declines. Beyond this point, contributing factors for the further extension of life expectancy are the prevention of diseases from the early years of adulthood and lowering mortality among the elderly. For this reason, preventing the occurrence and increase of non-communicable diseases (NCDs) such as cardiovascular diseases, cancer, and diabetes mellitus is an important health policy issue in both industrialized countries and developing nations[8].

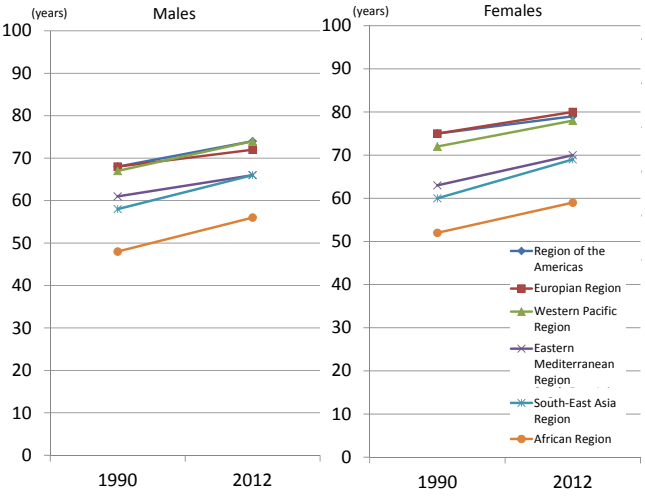
The main causes of death among the Japanese, who have the world's highest life expectancy, are heart disease, pneumonia, and cerebrovascular diseases; these account for approximately 70% of all deaths[9]. In the past 50 years, there has been a great shift in the disease structure and causes of death. Theoretically, if these diseases could be successfully prevented an extension in average life expectancy of around 3 to 4 years would be expected in the case of cancer, around 1.5 years in the case of heart disease, and around 1 year in the case of pneumonia and cerebrovascular diseases[10] (Figures 4 and 5).

Figures 6 and 7 show the number of deaths by age and the survival curve for Japanese people. The survival rate at the age of average life expectancy is approximately 60% for men and 80% for women[10]. The number of deaths peaks at age 85 in men and age 91 in women[9]. Since many Japanese live longer than the average life expectancy, the healthcare system must take this fact into consideration.



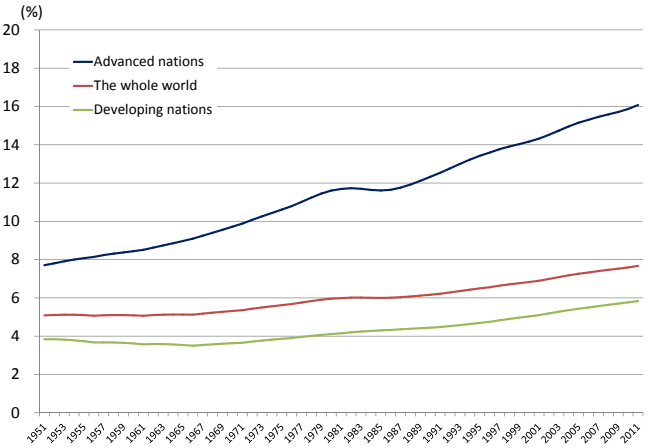
Prepared by Fukai from United Nations World Population Prospects: The 2012 Revision, 2013

Figure 1: Changes in world population and age structure



Prepared by Fukai from United Nations, World Population Prospects: The 2012 Revision, 2013

Figure 2: Annual change in average life expectancy in major countries

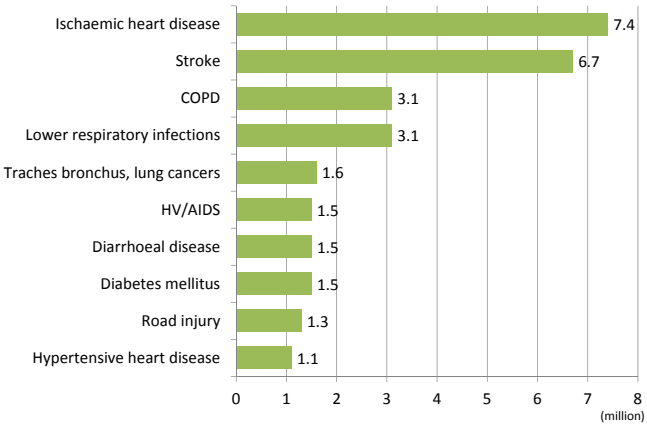


Prepared by Fukai from United Nations, World Population Prospects; The 2012 Revision, 2013.

Figure 3: Change in the percentage of older population (65 years of age and over) in industrialized and developing countries

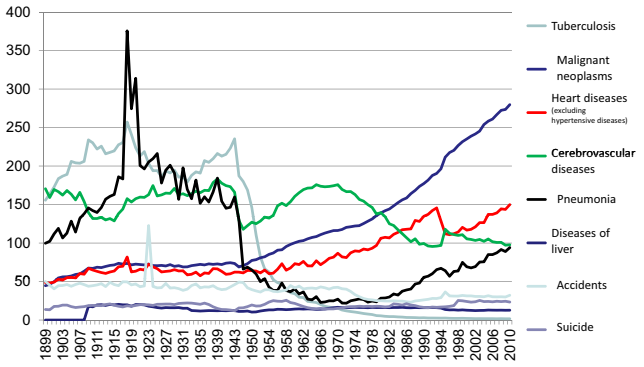
3. Aging and decline in living function

Apart from diseases, other causes of death include aging



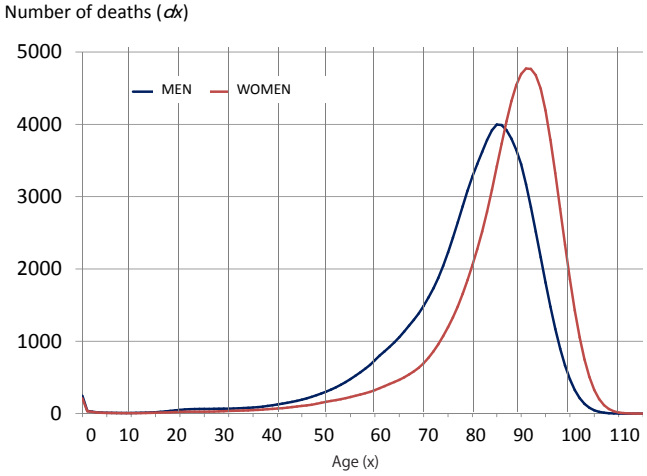
Source: WHO Fact sheet The top 10 causes of death http://www.who.int/mediacentre/factsheets/fs310/en/

Figure 4: Top 10 causes of death in the world(2012)



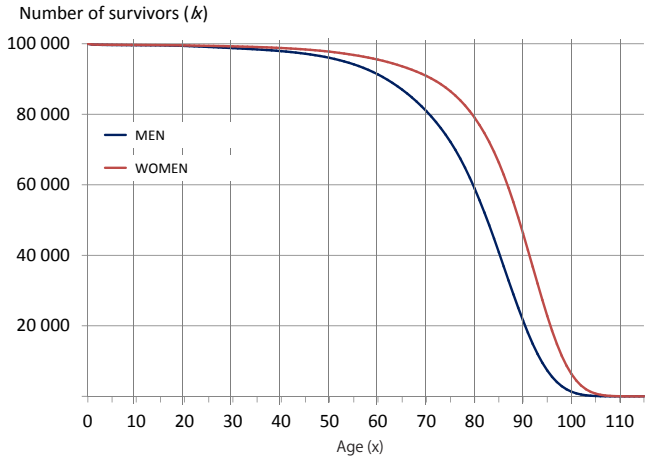
Source: "Vital Statistics", Statistics and Information Department, Minister's Secretariat, MHLW(Note) The figures for 2011 are approximate.

Figure 5: Annual transition in the number of deaths among the Japanese by cause of death (per 100,000 population)



Source: MHLW, 2010 Complete Life Tables

Figure 6: Number of deaths by age among the Japanese

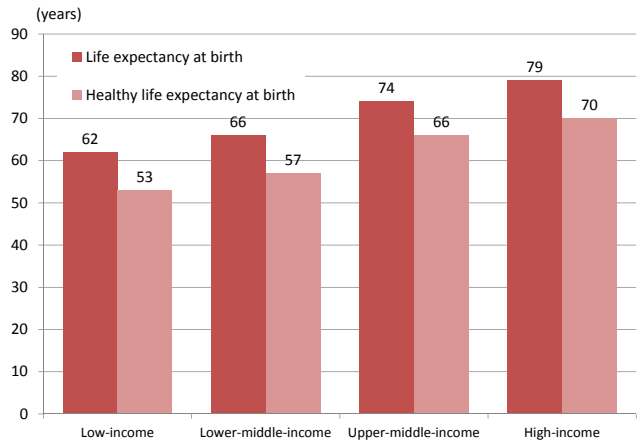


Source: MHLW, 2010 Complete Life Tables
Number of survivors (lx) : The number of survivors is calculated on the assumption that 100,000 children dieaccording to the death rate by age shown on the life table. The median life expectancy [the number of years inwhich half the children (50,000 on the complete life table) are expected to survive] is 82.60 years for men and 89.17years for women.

Figure 7: Survival curve by age among Japanese

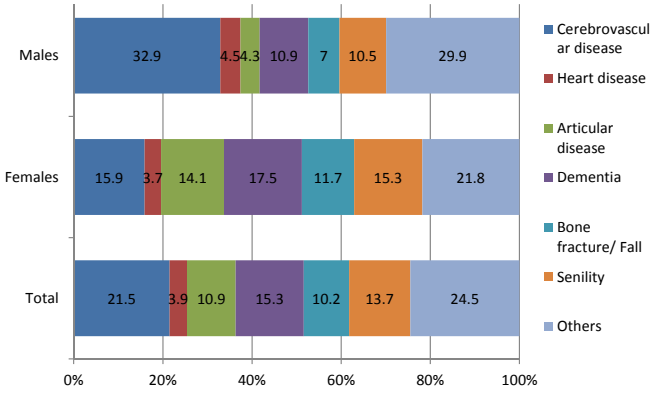
and accidents. For some reason, when cells and organs (which are made up of cell tissue) can no longer function, humans become incapable of maintaining their bodily functions as an individual organism, and this results in death. In fact, looking at the causes of individual deaths reveals that death occurs when any of the organs that are vital for maintaining life, such as the heart, brain, kidney, or various arteries, can no longer function. Moreover, the temporal process leading to death varies depending on the disease that causes this decline in organ function. In terms of the length of time during which one functions autonomously in daily life, activity may be restricted over a long period of time, such as with cerebrovascular diseases, or the restrictions may extend for a relatively short period, such as with cancer[11].

Aging refers to a gradually progressive decline in physical functions that occurs as a person ages. Aging at the organ level can be attributed to damage to cells that have almost no ability to divide, such as brain and nerve cells as well as myocardial cells. In other cases, aging occurs when cells stop dividing after completing about 50 cycles of subdivision, as seen in almost all organs other than the above-mentioned ones[12]. However, all organs age as one gets older, and the aging of organs manifests itself in the form of reduced functionality. This means that muscle strength, nerve conduction velocity, lung capacity, and resistance to disease decline with age, and this decline cannot be avoided in humans. For example, when evaluating changes in grip strength that occur with age in Japanese people, a decrease of about 13kg in men and about 8kg in women has been observed between late-middle age and old age[13]. Moreover, the percentage of functionality remaining at age 80 (age 30 = 100%) in nerve conduction velocity, lung capacity and renal plasma flow (PAH), and maximal voluntary ventilation decreases to about 80%, less than 60%, and about 40%, respectively[14]. Despite such a decline in organ functions due to aging, the organs function together in a complementary manner to maintain a condition where everyday living functions can be performed without any trouble. However, a variety of different causes lead to various physical and



Source: WHO World Health Statistics 2014

Figure 8: Average life expectancy and healthy life expectancy by country economic status



Source: Ministry of Health, Labour and Welfare, 2010

Figure 9: Causes leading to a state requiring care (Japan)

psychological symptoms and to conditions commonly observed in the elderly, which are collectively referred to as geriatric syndrome[15].

4. Average life expectancy and healthy life expectancy

The world's average life expectancy as of 2012 is 68 years in men and 73 years in women, with a mean of 70 years for both sexes combined. In contrast to the average life expectancy of 60 years in men and 63 years in women in low-income countries, the life expectancy in high-income countries reaches 76 years and 82 years, respectively. The average life expectancy of both sexes combined is 62 years in low-income countries, 66 years in low middle income countries, 74 years in high middle income countries, and 79 years in high-income countries, indicating that life expectancy increases with greater economic development. In contrast, healthy life expectancy in those same categories of economic development is 53, 57, 66, and 70 years, respectively. Healthy life expectancy throughout the world as a whole is 62 years[16] (Figure 8). There is approximately an 8-year difference between average life expectancy and healthy life expectancy, and this does not vary with the economic status of the country.

In Japan, healthy life expectancy is defined as extending up to the point at which a person begins to experience restrictions on their daily living activities at or above Care Level 2 under the Long-term Care Insurance System (Level 2 is a state requiring partial care due to a decline in the ability to perform basic self-care tasks and other activities of daily living, or ADL). The healthy life expectancy in Japan is 70.4 years in men and 73.6 years in women, which compared with actual life expectancy is a difference of 9.1 years and 12.7 years, respectively. Of the 30.74 million people aged 65 years and over, 2.942 million are at Care Level 2 or higher, accounting for 9.6% (2012).

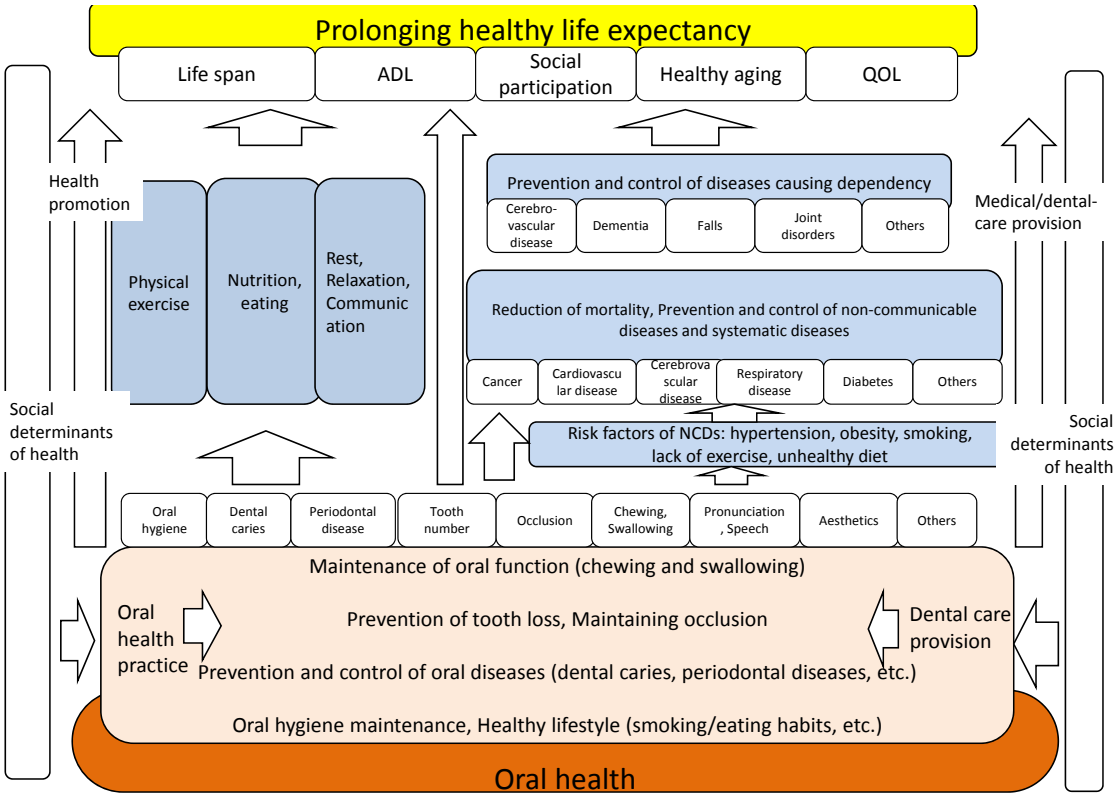
The percentage distribution of the main diseases leading to a condition requiring care, as shown in Figure 9, is 21.5% cerebrovascular diseases, 15.3% dementia, 10.9% joint disorders, and 10.2% fracture/fall[17].

5. Aging society and social security

Improvements in pension, medical insurance, and long-term care insurance programs are essential in order for the elderly to live a secure life. In Japan, which has become the world leader in terms of longevity, a universal national health insurance and pension system was started in 1961 and has been maintained up to the present time. Japan's insurance and pension systems are funded by both insurance fees and tax revenues, and also effectively redistribute income among age groups while improving the health conditions and average life expectancy of the Japanese. Nevertheless, rapid population aging and a falling birth rate pose an enormous financial burden on the country[18].

A look at the current state of population aging in Japan from a generational perspective reveals that when the "baby-boom generation" (born in 1947-1949) turned 65 years old in 2012, the number of people aged 65 years and over reached 30.74 million, topping the 30 million mark for the first time ever. As a result, Japan has become a super-aging society with the percentage of people aged 65 years and over reaching 24.1%, which breaks down to people aged 65-74 years accounting for 12.2%, and those aged 75 years and over accounting for 11.9% of the population. Around 20 years in the future (2035), when this baby-boom generation reaches the current average life expectancy, people aged 65 years and over are projected to make up 33.4% of the population[19].

Meanwhile, social security benefits in Japan reached 107.4950 trillion yen in fiscal 2011, which breaks down to 53.0623 trillion yen for pensions (49.4%), 34.0634 trillion



Fukai K. Future directions for research on the contributions of dental and oral health to a healthy aging society. Health Science and Health Care 2013; 13 (2) 39–42

Figure 10: Conceptual pathway showing the relationship between dental care/oral health and healthy life expectancy

yen for medical care (31.7%), and 7.8881 trillion yen for long-term care (7.3%). These numbers have been increasing since the start of record-keeping in 1950[20]. This is due to the rapid aging of the population accompanied by an improvement in the survival rate, giving rise to issues related to the financial foundation of this system as well as the quality of health care and long-term care.

6. Dental care/oral health and healthy life expectancy

Based on the relationship between dental/oral and general health, the following two factors are involved in the pathway by which dental care and oral health contribute to healthy longevity: (1) prevention of aging and promotion of health including improvements in systemic tolerance or resistance and (2) reduction in diseases and risk of disease. The former includes promotion of health through exercise, nutrition, and rest. The latter includes reducing the risk factors for NCDs and preventing the development and worsening of diseases that lead to death or to a condition requiring care.

Based on the results from previous research, I postulate a conceptual pathway which shows the extent to which dental and oral health as well as the resulting maintenance and recovery of oral functions would lead to the maintenance of QOL and ADL as well as the extension of life expectancy[3,4] (Figure 10). The relationship between oral and general health and life expectancy sometimes reciprocally correlates to the function and condition of each organ, so caution is needed when showing causes and results in a simple diagrammatic form. On the other hand, when providing explanations to policymakers and laypeople, it is necessary to demonstrate a simple and easily understandable concept along with its rationale. This makes it necessary to accumulate individual evidence which supports and/or refines this pathway.

[Discussion]

Population aging occurring at the global level is an unavoidable fact. The issue is how to prolong the healthy period of human life.

The survival curve by gender and age among the Japanese is shown in the Results section of this paper. The survival rate at age 80 years is about 80% for women and about 60% for men. Assuming that 100,000 persons will eventually die in accordance with the death rate shown on the life table, then the number of deaths peaks at age 85 in men and 91 in women (Figure 6). The death rate increases linearly (log plot) with age from about 30 years until reaching old age, and then the rate decreases after reaching about 90 years. This is known as the Gompertz law (1825), which states that the probability of death exponentially increases with age, and that there is a twofold increase in the probability

of death every 8 years from age 30, and that people at 80 years of age are 30 times more likely to die than those at 40 years of age. This law is also used as a definition of aging (aging means increased susceptibility to death). Aging makes humans more susceptible to death and diseases. The world's oldest person on record was a French woman called Calmant, who died at the age of 122 years in 1997. The lifespan limit for human beings is considered to be about 120 years[21]. The survival curve becomes markedly rectangular with age[22]. This is an important point in understanding why an extension in healthy life expectancy is needed to bring the average life expectancy of humans closer to the lifespan limit. To achieve this, preventive measures against the main causes of death and health promotion aimed at the prevention of aging are required. Specifically, to further enhance the health of the population, it is necessary to improve other risk factors such as hyperglycemia, lack of exercise, drinking, excess weight and obesity, and high intake of salt in addition to smoking and high blood pressure[23]. It is also important to clarify the diseases that lead to a condition requiring care and to prevent such diseases.

In terms of social security costs, a system that will effectively and efficiently reduce preventable diseases is needed. The factors that damage health are genetic, lifestyle-related, social security and health system-related, and social determinants. Among these, the genetic factor accounts for about 25 to 30% of all factors that contribute to death[24,25]. In fact, in a well-known follow-up study on Japanese-Americans investigating the prevalence of ischemic heart disease and cerebrovascular disease, the Japanese-Americans (first-generation immigrants) were reported to have a higher risk of ischemic heart disease and a lower risk of cerebrovascular disease than Japanese people living in Japan[26]. When judging disease risks, therefore, lifestyle and social environments are more important than genetic background. From this standpoint, an approach which aims to prevent NCDs by targeting the risk factors thereof should be pursued[27].

In order to create and maintain a society in which elderly people can live with security and dignity, it is important to provide income support for the elderly and to create an environment ensuring their social activity[1]. A system in which elderly people can receive high-quality, effective, efficient healthcare sevices[28] through better collaboration between medical and dental fields is required not only in industrialized countries but also in developing countries.

[Conclusions]

In order to attain a healthy society of longevity based on the relationship between oral and general health, the currently available scientific evidence showing the contributions to general health made by dental care and oral health must be clarified. There is an urgent need to verify the effects of dental care and oral health on various factors impairing health and to prepare new policy proposals for the social security system based on the currently available evidence. In order to realize a healthy society marked by longevity, the following four goals should be our priority: 1) to increase life expectancy and prevent early death, 2) to prevent people from falling into a state of dependency, 3) to prevent the decline in living functions due to aging, and 4) to promote health from the early years of adulthood based on the life course approach.

[Conflict of interest]

There are no items applicable to "conflict of interest" in this article.

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1. Oral health and aging

2) Oral disease, Tooth number, oral tissue and dietary habit, and aging

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[Abstract]

A literature survey was performed in order to determine age-related changes in the oral cavity, in the oral health status of the elderly in Japan, in dental care of the elderly, in daily life, and in oral health risks for the elderly. This work clarified that organic changes in the oral cavity render an effect on oral functions, and the oral diseases, oral care activities and life style are causing specific changes in the elderly, showing that it is essential to take relevant measures depending on the changes.

[Introduction]

All living organisms are constantly aging. Unlike the aging that occurs in the process of growth and development after birth, the aging in the later stages of life, such as the phenomenon of senescence is not easily observed in organisms in the wild but is currently an urgent problem for humans in modern society.

To resolve this problem, an interdisciplinary science called gerontology provides common values for the age-related changes accompanying senescence aimed at "resolving the various problems of individuals and society occurring in an aging society by investigating the mental and physical changes that occur along with aging" [1]. Atchley and Barusch[2] defined that the fields of gerontology are based on the following 4 viewpoints: (i) a biological viewpoint to investigate "the causes of physical function deterioration and treatment methods, and to prevent the diseases and disorders caused by the deterioration", (ii) a psychological viewpoint for "research of emotion and intelligence", (iii) a sociopsychological viewpoint concerning the "mutual relation between individuals and surroundings" and (iv) a sociological viewpoint focusing on "effects of the social system and aging population on the individual".

Among the viewpoints defined above, the biological viewpoint is first of all necessary for the healthcare professionals working in the dental field. The modality of medical care having aimed conventionally at the goal of saving lives and prolonging life now requires a viewpoint on how to support the daily lives of the elderly and how to improve the QOL. In order to secure evidence for methods to prevent and treat various diseases and disorders accompanying senescence, it is necessary to organize the basic points concerning what senescence-related changes occur in human oral cavity. However, as pointed out by Mjör[3] and Russell, Ship *et al*.[4], it is difficult to accurately classify the age-related changes in the teeth and oral cavity into physiological age-related changes and pathological changes. Nevertheless, it seems acceptable to try to understand the characteristic changes often observed with the teeth functioning in the elderly as the age-related changes of teeth. In this article, a review is first performed while focusing on age-related changes of oral cavity accompanying senescence.

Furthermore, from the viewpoint of oral care after age-related changes in the oral cavity, the current status of oral care of the elderly in Japan, dental treatment of the elderly, daily lives of the elderly and risks in oral health of the elderly are reviewed by using the results of various statistical surveys.

[Objective]

The objectives of this study were to perform a literature survey about what senescence-related changes occur in the oral cavity in terms of teeth (enamel, dentin, cement and pulp), periodontal tissues, oral mucosa, salivary gland and saliva to allow a further search of results of various statistical surveys and to organize the information obtained in this way.

[Methods]

This study was performed by way of a literature survey. The literature inclusion criteria were as follows: (i) studies performed focusing on humans, (ii) literature written in English or Japanese and (iii) original articles or para-original articles. In the Internet search, PubMed, Scopus and ICHUSHI were utilized and a manual search was also performed for literature not obtained by Internet search (in

the period from January 1960 to July 2014). In the light of the nature of this study no particular limits were placed on the key words in literature survey.

[Results]

1. Organic changes

1) Age-related changes in enamel

It is well known that the fluoride content in enamel increases with aging. According to the analysis performed by Brudevold *et al*.[5], the fluoride content in surface enamel is lowest in the impacted teeth in the region where the fluoride content in tap water is around 0.1 ppm and increases with aging in the age layer from at least 20 years to 50 years or more. The age-related increase in fluoride content in enamel is caused by exposure to fluoride in the living environment, and this is supported by the following facts: (i) the fluoride content is especially high in the surface enamel[6], (ii) the inner enamel acquires the nature of surface enamel relatively early after exposure to the outside[7], and (iii) the enamel crystal layer is much thicker in the surface layer than in the inner layer, but such difference is not observed in unerupted teeth[8].

In addition to the above change in composition, the changes over the course of a year known as so called "tooth wear" occur in the enamel. According to Lussi *et al*.[9], in the elderly population, acid erosion reaching the dentin was recognized in 13.2% of the buccolabial-side surfaces and 42.6% of the occlusion surfaces. As also clarified in this report, the enamel is subject to physicochemical influences such as acid erosion, occlusal wear and abrasion, and as a result, the composition of enamel such as the fluoride content is affected. Weatherell *et al*.[10] reported that the fluoride content is higher on the cervical side than on the incisal edge / cusp side in the elderly and estimated the reason as follows: the surface part with a high fluoride content is lost due to occlusal wear on the incisal edge side and fluoride incorporation occurs on the cervical side due to plaque deposition, etc.

2) Age-related changes in dentin

Age-related changes in dentin include formation of secondary dentin in the pulp cavity[11] and dentinal tubule obstruction[12]. Along with calcification of peritubular dentin, the dentinal tubule is closed and sclerotic dentin is formed[13]. Due to this sclerosis phenomenon, the durability limit of the dentin decreases in the elderly[14]. In the molar, the secondary dentin is formed mostly at the top and bottom parts of pulp chamber[15]. But, in impacted teeth, the secondary dentin is reported to be thicker in the apical area than in the crown part[16]. In addition, the series of processes in which sclerotic dentin is formed by intratubular dentin deposition starts at the premolar root even in the absence of external factors, starting from the age of about 18 years[17].

Such age-related histological changes render a clinical effect at least at the onset of dentin hyperesthesia and aesthetic tooth color tone. Dentin hyperesthesia occurs in a wide age layer from the early teens and into the 70's[18] but a peak is observed in the age range from 20 years to 40 years[19], showing clearly that the dentinal tubule closure due to age-related changes has the effect of making the dentin perception less sensitive. The color tone of natural teeth is known to darken and become yellowish with aging[20]. Tooth color changes also occur due to an endogenous color change such as tooth discoloration on taking tetracycline, but the change in light refraction index due to the aforementioned histological change of dentin, i.e., dentinal tubule closure is thought to also cause an irreversible effect on the tooth color tone.

3) Age-related changes in cementum

Tooth abrasion occurs when the oral cavity performs its various functions. The cement is absorbed by the mechanical force at this time, and on the other hand new cement formation occurs to supplement the results of abrasion. Cement thickness was reported to increase about 3 times from the age of 10 years to the age of 75 years[21], and the infectivity also increases along with age-related changes[22]. In addition, the amounts of fluoride and magnesium contained in the cement change with aging[23], but it seems that the fluoride concentration in drinking water and the period of exposure to fluoride render a large effect. In any age group, the fluoride content is higher in the cervical part than in the root part, suggesting the tremendous effect rendered from ingested foods and beverages.

4) Age-related changes in dental pulp

The pulp shows various changes that occur along with aging. Well-known age-related changes in pulp are a decrease in pulp cells and an increase in collagen fibers[12]. In addition, the number of arteries entering the pulp from the apical foramen and the number of blood vessel branches decrease[24], causing an apparent age-related decrease in blood flow in the pulp. The specific changes include calcareous degeneration[12]. It was reported that the degree of pulp calcification of dental caries-free teeth is 10 times higher in the elderly than in the young[25]. The secondary dentin is formed on the pulp wall and denticles appear in the crown part pulp, followed by diffuse calcification. As a result, the volume of the pulp cavity declines to about half in the elderly as compared with young people.

5) Age-related changes in periodontal tissues

It was reported that gingival recession is closely related to aging in residents of Western countries who are receiving periodic dental care[26]. There is an increase in gingival recession causing greater attachment loss increases, but the worsening of attachment loss does not necessarily increase the pocket depth[27,28]. In addition, it was also reported that gingivitis progresses more rapidly in the elderly than in the young when the oral prophylaxis status is unfavorable[29]. It was clinically observed that a loss of alveolar bone proceeds with aging but it seems difficult to identify the range of pure age-related loss. However, this alveolar bone regeneration does not indicate a marked age-related change, since it was reported that there were no marked differences in the wound healing process after tooth extraction among either the young or the elderly[30].

6) Age-related changes in oral mucosa

Oral mucosa has been reported to become thinner[31] with aging and the degree of cornification also becomes lower[32] with aging. However in clinical research, the appearance of oral mucosa did not show age-related changes[33], and there were no differences in the size, shape and structure of mucosal epithelial cell either[34]. It was reported that mucosal diseases appear frequently in the elderly[35], but it was also reported, on the other hand that there is no increased risk of mucosal disease in the elderly[36]. As for the tongue, the clinical symptom called "smooth tongue" appears due to the disappearance of filiform papilla, and it is said that the threshold value for sensing a sweet taste lowers.

7) Age-related changes in the salivary gland and saliva

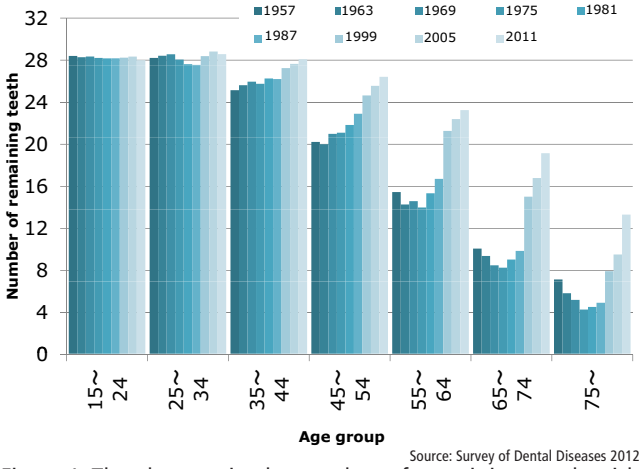
It is widely recognized that about 1.5 liters of saliva is secreted per day from all salivary glands[37]. Also reported is that the number of acinar cells decreases by 30 to 40% in the elderly[38], but it seems that a significant decrease of saliva secretion purely due to aging was not confirmed in the recent reports[39,40].

Concerning the saliva components, it was reported that the sodium and potassium concentrations in the parotid saliva shows no marked age-related changes in the elderly[41]. It was also reported that the protein concentration shows almost no marked age-related changes and no marked age-related changes are seen either in dissolution of calcium into the saliva and maintenance of the antibacterial effect exerted by various saliva proteins.

The aforementioned age-related organic changes are summarized in Table 1.

Table 1: Age-related organic changes in the oral cavity

	Age-related changes		Clinical effects
	Composition and tissues	Morphology	
Enamel	・An increase in fluoride content	・Tooth wear (acid erosion, occlusal wear, and abrasion)	・Change in the color tone and morphology ・A decrease in transparency ・Aesthetic problems ・Effect on mastication
Dentin	・Formation of secondary dentin ・Obstruction of dentinal tubule	・Tooth wear (acid erosion, occlusal wear, and abrasion	・Change in the color tone and morphology ・Aesthetic problem ・Effect on dentin hyperesthesia ・Effect on endodontic therapy ・Effect on mastication
Cement	・An increase in the amounts of fluoride and magnesium content.	・An increase in thickness	
Pulp	・A decrease in pulp cells ・An increase in collagen fibers ・A decrease in blood flow	・A decrease in the volume	・Effect on dentin hyperesthesia ・Effect on endodontic therapy
Periodontal tissues	・Absorption of alveolar-bone ・An increase in collagen fibers	・Gingival recession ・An increase in attachment loss	・Effect on masticatory efficiency ・Aesthetic problems
Oral mucosa	・A decrease in the degree of cornification ・Disappearance of tongue filiform papilla	・Thinning ・A decrease in elasticity	・Effect on taste sensations ・Effect on pronunciation and phonation ・Effect on infectivity
Salivary gland and saliva	・A decrease in acinar cells ・Fat deposition		・Effect on taste sensations ・Effect on pronunciation and phonation ・Effect on mastication



Source: Survey of Dental Diseases 2012

Figure 1: The changes in the number of remaining teeth with year by age groups

2. Oral disease

1) Oral health status in the elderly

a) Number of remaining teeth

The number of remaining teeth in the elderly tends to increase year by year and at present an average of 14 teeth remain by the age of 80 years (Figure 1)[42], or namely a state where half of all the teeth other than the wisdom teeth still remain. The Ministry of Health, Labour and Welfare and the Japan Dental Association are promoting "Campaign 8020" to achieve an average of 20 teeth remaining by the age of 80 years however the current mean level is 8014 (14 teeth remaining at the age of 80 years), and those persons who achieved the 8020 goal account for 35% of the total at present. The goal in 2010 was set at 50%. It is estimated that 8020 goal will be achieved in about 15 years.

b) Tooth decay

In a by-generation cohort analysis using Life Course Epidemiology Approach to results of dental disease actual

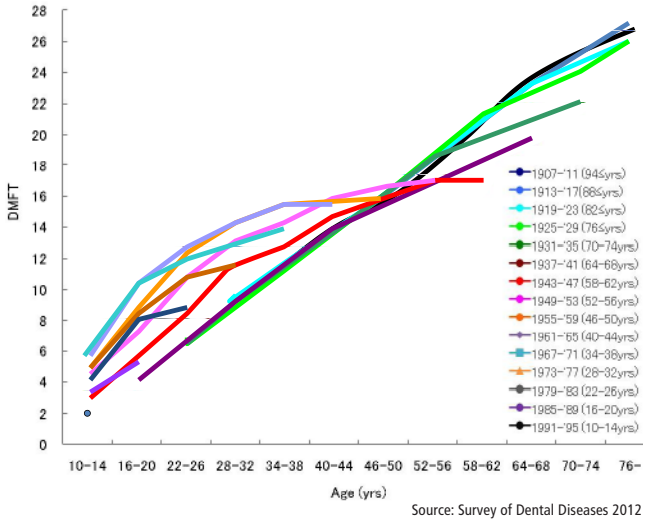
status survey performed 10 times (every 6 years) in the past, the number of DMFT shows an age-related increase in those persons who were born before 1945 (the elderly). The age-related linear increase of DMFT is caused by an aged-related increase in lost teeth. In those persons who were born in the period from 1946 to 1980s (the pre-elderly), DMFT does not increase, since the increase of lost teeth disappears from a certain age. In those persons who were born in 1980s or later (adults), the low DMFT value of 12-year-old children is maintained and the age-related increase rate of DMFT is low (Figure 2).

c) Periodontal disease

Periodontal disease progresses with aging and fewer people exhibit no symptoms of periodontal disease, and other show an increasing degree of severity in gingival bleeding, calculus deposition, attachment loss, and alveolar-bone absorption (Figure 3). However it is difficult to discern whether these changes in periodontal tissues are senescence-related changes or pathological changes. Since the elderly have many remaining teeth recently, the number of elderly patients with periodontal disease tends to increase.

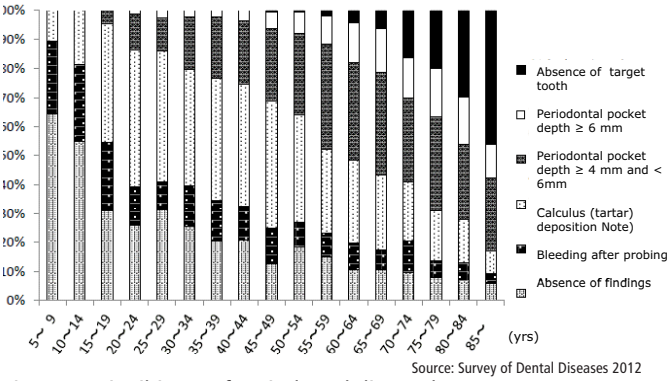
d) Tooth wear

Tooth wear including attrition, abrasions, and abfractions can be seen in teeth remaining in the elderly. The severity is diverse, and in the most severe cases, the enamel is lost and the dentin is exposed.



Source: Survey of Dental Diseases 2012

Figure 2: The number of DMFT according to birth year cohort studies



Source: Survey of Dental Diseases 2012

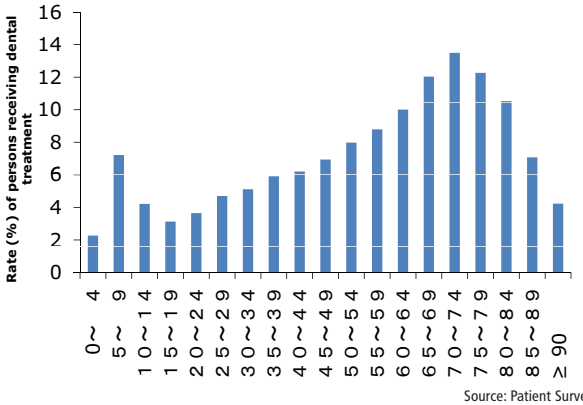
Figure 3: Distrihitron of Periodontal disease by age groups

3. Oral health behavior and daily habits

1) Dental care of the elderly

a) Rate of persons receiving dental treatment

According to the patient survey in 2011[43,44], the dental consultation rate (estimated number of patients / population x 100) in each age layer increases with aging showing a peak in the age layer of 70 to74 years and then decreases (Figure 4). The above trend is different from past trends in which the dental consultation rate had been low in the elderly, and the dental consultation rate pattern has now become similar to that for the medical consultation rate pattern.



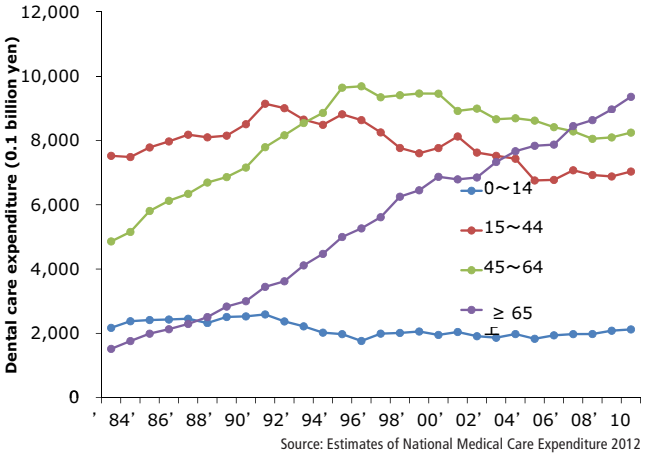
Source: Patient Survey 2011

Figure 4: Rate of persons receiving dental treatment by age groups

b) Dental Insurance (insurance treatment, visiting dental treatment)

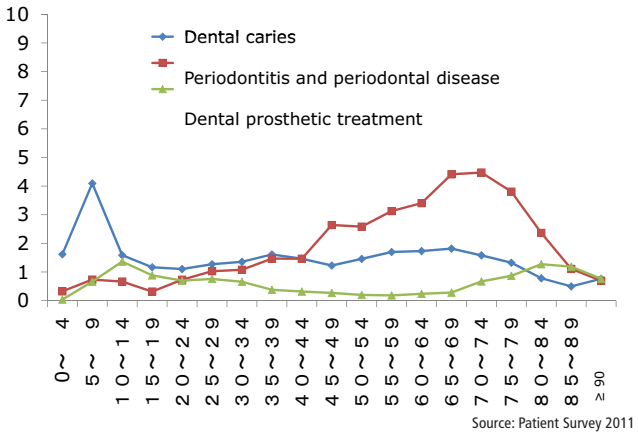
(1)Regular health insurance system and health insurance system for the elderly aged 75 years or over

In regards to dental treatment visits (home dental treatment) to the elderly, the regular health insurance system applies to the elderly aged 65 to 74 years, and the health insurance system for the elderly aged 75 years or over is applied to the elderly aged 75 years or over. In the medical/dental service fee revision in fiscal 2014, for promotion and evaluation of home dental treatment accompanying the increase of the elderly needing dental treatment, the premium for visiting dental clinic and the premiums for dental institution cooperation were newly established. According to the results of survey of medical/dental treatment activity in 2013, the score per day was 627.2 points for the elderly aged up to 64 years, 639.3 points for the elderly aged 65 to 74 years and 696.5 points for the elderly aged 75 years or over, thus being higher with aging, and the rate of "crown restoration and defect prosthesis"



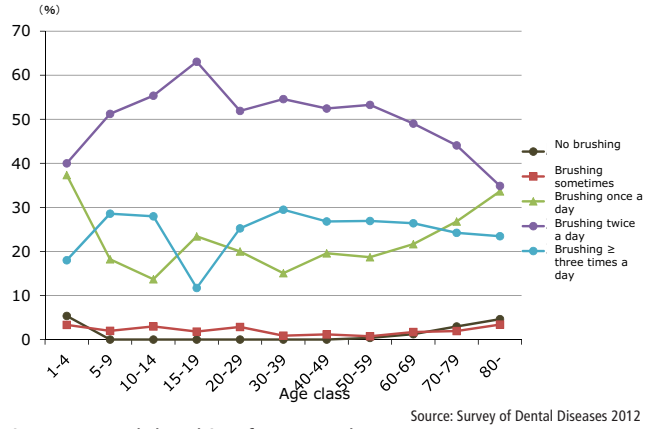
Source: Estimates of National Medical Care Expenditure 2012

Figure 5: Social Security cost of dental care by age groups



Source: Patient Survey 2011

Figure 6: Rate of persons receiving dental treatment by age groups and dental disease



Source: Survey of Dental Diseases 2012

Figure 7: Tooth brushing frequency by age groups

Table 2: Oral health system by generation in Japan

	mother and child	school	adult	the elderly
data from survey	national survey of oral health (every six years)			
	oral examination in 1.6 and 3 year-of-age	statistical survey of health in school		
strategy and goal	Next Healthy Japan 21, New Healthy Frontier Plan			
	Healthy parent and child 21			
health examination	Expectant women and nursing mothers, infants, 1.6 and 3 years of age	At the time of attendance at school, temporary, regularly	Specific medical examination (40～74 years of age), examination for periodontal disease (40・50・60・70 years of old)	
health education and guidance	Expectant women and nursing mothers, infants, 1.6 and 3 years of age	Oral health for educational guideline in elementary school	specific health guidance (40 years of age ～)	
enlightenment and spread	8020 campaign, Week for oral health (4 -10/ Jun), Day of good teeth (8th of Nov)			
	contest of good teeth	school dentistry excellent school commendation		8020 accomplisher commendation
evaluation	Health Japan 21・Healthy parent and child 21 (2010), new healthy frontier (2016)			
country assistance project	specific promotion project for 8020 campaign			
			At-home dental service	

was high and the rate of "treatment" was low. The number of treatments of the elderly by disease was 3,365,113 for "periodontitis, etc." accounting for 70.9% of the total number of treatments of the elderly (4,748,513).

(2) Nursing insurance

The nursing insurance system does not cover dental treatment visits for home-bound patients, however a "home care supervisor fee" calculated for oral health instruction given by dentist or dental hygienist and the "premium for oral function improvement" calculated for instruction on mouth cleaning or ingestion swallowing training given by dental hygienist as a part of care management are approved.

c) Social security cost of dental care

The dental care cost[45] for the elderly was the lowest among the various age layers until 1988 but increased from 1989 and became highest among all the age layers in and after 2007, accounting for about 40% of the entire dental care cost. In the other age layers, the dental care cost remained at nearly the same level from 1995. This tendency is considered likely to become more drastic hereafter due to the increase in the elderly population and an increase in remaining teeth among the elderly (Figure 5).

Examining the treatment content for the elderly based on the results of patient surveys, shows that in the elderly aged 65 to80 years, most patients receive periodontal treatment, followed by tooth decay treatment and prosthesis treatment. In the elderly aged70 years and above, fewer patients received periodontal treatment and tooth decay treatment and those patients receiving prosthesis treatment increased. In the elderly aged 80 years and over, the rates for these patients were nearly the same (Figure 6).

2) Daily lives of the elderly

a) Oral prophylaxis (brushing) habit

The oral prophylaxis status in the elderly is different from that in the young and adults[42]. About 5% of the elderly do not brush their teeth at all or brush only occasionally, 35% brush once or twice a day, and 25% brush 3 times or more a day (Figure 7). The oral prophylaxis habit seems to change when the oral cavity environments is changed for example due to tooth loss and denture wearing. But the fact that the persons brushing their teeth at least once a day account for more than 90% even among the elderly indicates that oral prophylaxis has been established as a healthy daily habit among the Japanese people.

3) Risks in oral health of the elderly

a) Social oral health system

(1) Periodontal disease examination

All municipal governments perform periodontal disease check-ups at each established milestone age, and the target age range was expanded from fiscal 2005 to include the elderly aged 70 years (Table 2). According to the regional health promotion program report in 2012, those residents who received a periodontal disease check-up performed by each municipal government accounted for 266,606 (reception rate: 56.4%) and the elderly aged 70 years accounted for 76,652 (28.8%). Among the elderly aged 70 years who received a periodontal disease check-up, a "need for a detailed examination" was judged in 81.8% of the cases, a "need for instruction" was judged in 8.3% of the cases, and "no abnormality" was judged in only 9.4% of the cases.

[Discussion]

1. Oral tissue aging

1) Age-related changes in enamel

On discussing the age-related changes in enamel from the viewpoint of oral health, it is important to continuously supply fluoride to post-eruption teeth. This is because the fluoride content in enamel increases with aging but the fluoride in the surface enamel is lost due to tooth wear. In order to increase the fluoride content in the surface enamel, it is necessary to achieve a socioeconomic state in which the dentifrice containing fluoride can easily be used. In this respect, it was reported that Japan has the lowest cost in the world in terms of the number of work days needed for low-income families accounting for 10 % of all residents to obtain a one-year portion of dentifrice containing fluoride[46]. In other words, Japan is a country where people can receive benefits from a dentifrice containing fluoride most easily in the world, and the market share of the dentifrice containing fluoride has been improved up to 90% at present[47]. One of the key points in enamel-related measures in future oral health is how to cope with tooth wear such as acid erosion, occlusal wear and abrasion. This is an effective approach also in terms of oral functions such as mastication and pronunciation.

2) Age-related changes in dentin

In terms of oral health, a continuous supply of fluoride is also important for dentin. Experiments performed *in vitro* have revealed that the amount of fluoride incorporated into the root surface is apparently larger than that incorporated into the crown part enamel[48]. In addition, in the region where the fluoride concentration in the tap water was adjusted, the rate of persons with root decay was significantly lower[49]. Namely, the supply of fluoride is ranked as a significant measure for preventing root decay and improving the quality of dentin. This is also useful for preventing the onset of dentin hyperesthesia, although the morbidity of dentin hyperesthesia decreases with aging.

In regards to tooth wear, the abrasion represented by the "wedge-shaped defect" is considered to be a large problem in terms of dentin. In this respect, it is also important to select and use appropriate products for mouth cleaning hereafter[50], and it is also necessary to give a scientific rationale for the prevention of bruxism in order to maintain the masticatory function.

The age-related color tone change of teeth is considered to be a goal of aesthetic whitening, but Tsubaki[51] reported that whitening is difficult in the elderly for the following reasons: (i) when the dentin color is darkened by aging, external bleaching does not exert a sufficient effect, (ii) when the cervical part is exposed, whitening of only the crown part does not lead to white looking appearance of the entire tooth and (iii) when dentin is exposed, hyperesthesia might easily occur. If "white beautiful teeth" are one factor in a future healthy society, then further research will be needed to develop a means to achieve an aesthetic tooth color.

3) Age-related changes in cementum

The cement is exposed by gingival recession and this change is observed very frequently with aging. When exposed inside the oral cavity, the cement is lost or degenerated[52], and peeling or absorption of cement is caused by occlusion pressure. These changes are of course caused by pathological reactions but it is difficult to distinguish them completely from physiological age-related changes. It is therefore important to consider issues with gingiva and occlusion force from the viewpoint of oral health.

The cement is a relatively thin hard tissue covering the surface of the root dentin, and its objective is to clamp the tooth to the jaw bone. Therefore, when the cement is lost, peeled or degenerated, the tooth cannot be clamped in the correct position in the oral cavity. In order to prevent such a situation, gingival recession should be prevented by general methods to prevent periodontal disease, and abnormal occlusion pressured should be reduced by taking measures to avoiding bruxism.

4) Age-related changes in dental pulp

The protective function provided by pulp against microbial infection declines due to age-related changes in the pulp, and the regeneration ability of pulp is also significantly lowered by a marked decrease in blood flow. When their pulp undergoes such age-related changes resulting in damage, the recovery from the damage does not proceed in the same manner as in young people, even if

such damage does not require dental treatment. Therefore, tooth preservation should eventually be achieved by maintaining a favorable environment so that the pulp is free as far as possible from degenerative changes. Specifically, it is necessary to avoid the acid stimulation caused by the microorganisms in the dental caries and to correct bad habits causing occlusal wear and abrasion. But, the perceptual threshold value increases along with aging due to a decrease in myelinated nerves, and an increase of dentin thickness, and stenosis/closure of dentinal tubule. In other words, since various signs related to worsening oral health become less perceptible due to the degenerative changes caused by aging, it is important to periodically receive detailed dental checkups.

5) Age-related changes in periodontal tissues

One age-related change in periodontal tissues requiring attention in oral health is the complicated morphology caused by senescence-related gingival recession and absorption of alveolar bone. The bacterial flora of plaque might possibly change along with senescence[53], but as already mentioned, the rapid progression of gingivitis in the elderly[29] is considered greatly related to the fact that the area to which plaque firmly attaches is increased by the complicated morphology of periodontal tissues. It is therefore necessary to organize the key points after discussing what oral prophylaxis methods can be proposed by dental healthcare professionals to the elderly in whom the morphology of periodontal tissues has become complicated and furthermore whose motor ability has deteriorated.

6) Age-related changes in oral mucosa

Healing of wounds is delayed by aging[54], but it is unclear whether the risk of mucosal disease is higher in the elderly, since the relations with secondary factors such as systemic health status, presence/absence of denture, drugs used, and so on have not been investigated, and it is still unclear what measures can be taken for mucosa in the elderly from the viewpoint of oral health. Yet there is no doubt that decreased saliva secretion function is a local factor causing various effects on the health of mucosal tissues[55]. How to maintain the saliva secretion function in order to improve the state of oral mucosa should be considered as a countermeasure (this is also related to the next section).

7) Age-related changes in the salivary gland and saliva

There are many recent reports stating that there are no definite age-related changes in saliva secretion and saliva components, but clinically there are many elderly patients complaining of decreased saliva secretion and accompanying oral dryness. This fact suggests that a decrease in saliva secretion in the elderly occurs due to various pathological factors and it is not an age-related change. It is therefore necessary to carefully determine whether drugs having a side effect that decreases saliva secretion are being administered and whether the diseases, symptoms and treatments, and so on related to the decrease of saliva secretion or oral dryness such as Sjogren's syndrome, past radiation therapy, treatment with anticancer agent, gastroesophageal reflux disease, Parkinson's disease, mouth respiration, are present. The decrease in saliva inhibits important functions of the oral cavity such as mastication, and pronunciation, etc. It is essential to understand saliva and salivary gland in order to maintain a healthy oral cavity as well as its usual functions.

2. Oral diseases

As shown by the results of the dental disease actual status survey, the oral health status of the elderly is significantly changing in Japan. One of these changes is an increase in the number of remaining teeth. Here, the strategy is to increase the number of remaining teeth, or namely to use a strategy focusing on prevention of tooth loss which include various programs in a particular regions leading to various outcomes such as prevention of tooth decay, prevention of periodontal disease, a check-up system, an insurance system, a particular dental care level, healthy feeling of the residents, etc. The number of remaining teeth might be considered an index showing the health status of the elderly in each region or country. Increasing the number of remaining teeth will allow maintaining and improving oral functions such as mastication and pronunciation.

The mean number of DMFT (decay-missing-filled-index) per person increases along with aging. But, in our birth year cohort analysis of DMFT changes, it was found that age-related DMFT changes are markedly different depending on the particular generation. It is estimated that the number of decayed teeth (all of non-treated, treated and lost teeth) will hereafter decrease in the elderly. Currently however, the number of elderly patients with periodontal disease is tending to increase along with an increase in the number of remaining teeth. The need for maintaining oral functions required to eat well and to speak with smooth communication accompanied by aesthetic aspects should never be common among all generations but rather specific to the elderly. In other words, it is important to establish new diagnosis criteria and examination technologies for the elderly instead of handling the elderly by the same standards as used for young people.

3. Oral health behavior and daily habits

The dental consultation rate has tended to decrease in the

elderly thus far. But the dental consultation status is recently coming to resemble their medical consultation status. The reason for this is estimated as follows: the dental treatment of the elderly was mainly denture treatment of lost teeth in the past, but the elderly recently have many remaining teeth and so various dental needs have increased. However in the public medical/dental care system (health insurance, nursing insurance), the "granting of benefits for sickness" is the basic principle, and the diverse health needs of the elderly are not being met. How to evaluate the oral functions such as mastication and pronunciation and how to maintain and improve such functions will be critically important in the dental field of the future.

The essential points are therefore how to organize the risks to the health of the elderly and how to achieve a new understanding of the phenomenon of "aging" which is a phenomenon that cannot be avoided by human beings from the viewpoint of an "anti-aging" or "positive aging" approach needed in order to construct a model for the next generation. The following can be given as main risks to the health of the elderly: oral tissue senescence, systemic senescence, diseased state, life-style changes and the social system (Figure 8). We must secure evidence that will contribute to the progress of gerontology based on the above points as the means to achieve dental care that prolongs a healthy life-span[56,57].

[Conclusions]

The following can be given as people's complaints regarding age-related changes in the oral cavity,: the alveolar ridge getting thin, losing teeth, dentures wearing away, blood and pus coming from the alveolar ridge, alveolar ridge swelling, an increasing number of teeth fillings, teeth coverings, decreasing saliva, worsening of oral malodors, weakening taste sensations, difficulty in mastication, difficulty in swallowing, and difficulty in speaking.

These complaints can be roughly classified into morphological changes, functional changes and changes caused by a chronic disease. On taking measures against these "changes" according to the conventional disease-targeting strategy, each age-related change will be measured by a certain method and a tailor-made treatment program type will be prepared according to the threshold. But, many of the age-related changes are subjective ones. Taking the stance that considers "how to live daily life" by making the system more intimate with residents will prove more important, rather than taking the viewpoint of treating diseases or mental/physical troubles

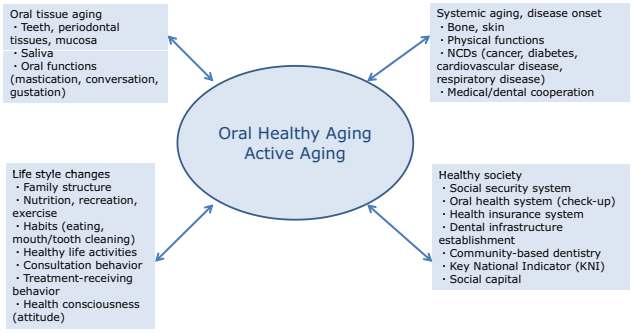


Figure 8: Risks to the oral health of the elderly

[Conflict of interest]

There are no items applicable to "conflict of interest" in this article.

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1. Oral health and aging

3) Mastication (including occlusion), swallowing (including oral dryness)

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[Abstract]

Among the senescence-related articles in the oral field those relating to mastication and swallowing and appearing in principle, in the past 5 years (from January 2009 to July 2014) were searched and 52 articles were utilized. The 52 articles were classified into 24 articles relating to "mastication/occlusion, eating/swallowing, life function", and 3 articles relating to "dementia and mastication/swallowing" and 15 articles relating to "oral functions such as lingual pressure, swallowing or nutrition, life prognosis", and the relationships among oral functions as well as their relations to systemic diseases, dementia, nutrition, life prognosis, and so on were investigated.

Among the search methods, the Internet search was performed using ICHUSHI and PubMed and articles among the hits were selected by manual search.

Results confirmed that all oral functions such as occlusion/mastication, saliva secretion, articulatory function and swallowing function decline while mutually affecting one another and it was also confirmed that oral functions are closely related to systemic diseases, dementia, motor functions and life functions.

[Introduction]

Along with the increasing elderly population, the decline in oral functions has been a big problem particularly in the elderly population aged 75 years and over. Dental care has so far achieved remarkable breakthroughs in the treatment of tooth decay, periodontal disease and tooth loss. On the other hand, in this super-aged society, the number of dependent elderly people (suffering from frailty) is increasing. Namely, the number of "patients who find it difficult to visit medical/dental institution" is increasing. Almost all dental institutions are clinics, and for those patients who find it difficult to visit a dental clinic, their only way to receive treatment is at home treatment. Since these treatment visits only happen based on the patient's request, such treatment is not performed unless the patient, their family or caretaker notices a change in the oral cavity. So a state without dental care might continue for a long period resulting in a state of "lowered oral functions" (oral frailty).

Administering oral hygiene care on those elderly persons having with inadequate oral hygiene, resulted not only in cleaning up the inside of the oral cavity but also considerably restored the original functions of the oral cavity. Furthermore, treatment in systemic diseases is enhanced, the patient's QOL is improved and family burden is reduced, so tremendous effects are obtained. In this respect, "improvement of oral functions" is a significant item ranked among "care prevention" items.

Performing oral hygiene care by oneself is generally regarded as a barometer of self-independence. In early childhood, oral hygiene instruction starts with a simple tooth brushing action and each parent then shows an example of the entire brushing action. Later in life, however, oral hygiene control by oneself is gradually ignored, and the oral cavity becomes soiled and this is coupled with a decline in oral functions. Taking care of the elderly like taking care of children in this regard is good but neither the caretaker nor the care receiver is proactive.

Oral functions include occlusion/mastication, taste perception, saliva secretion, articulation (pronunciation), communication, halitosis and other composite functions. All of these are essential for support of daily life and daily living. Many tissues and organs such as the teeth, tongue, gingiva, cheek, salivary gland, mucous membrane and perioral muscles are involved in complicated actions to achieve each oral function. In this study, a literature survey was performed centering on mastication and swallowing.

[Objective]

The objectives of this study were to perform a literature survey about what senescence-related changes occur in "mastication" and ""swallowing, that serve as the starting point for nutrition ingestion and to organize the information thus obtained.

[Methods]

An Internet survey was performed using ICHUSHI and PubMed and by targeting review articles and original articles. The key words used were "aging, chewing OR mastication, OR swallowing" as well as the Japanese words corresponding to those. The article selection criteria were interpretations, review articles and original articles excluding meeting notes, which were issued in the past 5 years (from January 2009 to July 2014) in principle. All the selected articles were subjected to a manual search and commercial journals were excluded. Those articles suitable to this study were then selected.

[Results]

All oral functions are closely correlated each other, and multiple functions were handled in each article. The selected articles could be roughly classified into the field of "occlusion and mastication" and the field of "oral environment such as saliva secretion and oral hygiene, functions and morphologies of the tongue and lip and articulation/communication". In this study, the latter field is expressed as the field of "oral functions". Each oral cavity-related item was to be combined with laryngeal pharynx dysfunction, dementia, systemic disease, life prognosis, etc.

As a result, the articles obtained by search could be classified into (1) "mastication/occlusion, eating/swallowing, life functions" (24 articles)[1-24], (2) "dementia and mastication/swallowing" (3 articles)[25-27], (3) "oral functions such as lingual pressure, swallowing or nutrition, life prognosis" (15 articles)[28-42], and (4) "saliva secretion and oral functions" (10 articles) [43-52]. Needless to say, multiple key words are included in each class in a complicated manner, showing mutual close relations.

1. "Mastication/occlusion, eating/swallowing, life function" (24 articles)

Among the 24 articles, 7 articles referred to the relation between occlusion/mastication and swallowing function (including suffocation)[1-7]. These articles were derived from cross-sectional studies targeting nursing facility residents or users and stated the relation between swallowing disorder and occlusion/mastication. It was already reported in the past that occlusion support loss would lead to a decline in mastication ability, but recently occlusion support loss has been discussed as a cause of swallowing disorder together with dementia and systemic weakness (= frailty). In regards to occlusion support, the number of remaining teeth was included in the investigative items of the main-stream studies, but occlusion in the molar region (Eichner classification) has been used in many cases recently. This fact is considered to emphasize the concept of an oral function. In other words, dental care as function restoration (rehabilitation) from dysfunction is shown as markedly influential on life functions of the elderly.

The data provided show that mastication is the function essential for nutrition ingestion. A decline in mastication ability brings about a state in which many functions decline (including malnutrition), and the items analyzed simultaneously include Barthal index and oral diadochokinesis showing the life function level and mutual relations have been reported[8-12].

In the study in which the relation between occlusion force and life function was investigated, it was reported that there were correlations among FIM cognition items, communication and social cognition[13]. Some studies have raised lingual pressure as a factor for estimating one's communication ability[14-15]. Some studies reported that the occlusion force and occlusion surface area are influential on mastication ability and saliva secretion[16-17], and other studies reported that the maximum occlusion force is markedly influential on mastication ability[18-19].

Many articles referred to the effects of occlusion force and mastication ability on life function including ADL and death rate[20-24], and the necessity for improving oral functions is described based on the correlations.

2. "Dementia and mastication/swallowing" (3 articles)

Dementia being a cognitive function disorder is classified into Alzheimer type, cerebrovascular type and Lewy body type, but all are central nervous system disorders. The eating motion starts from cognition, and the swallowing motion is centrally controlled by the nerves in the brain. It is therefore natural that there is a high correlation between dementia and mastication/swallowing. In 2 of the 3 articles, the swallowing disorder status was investigated by type of dementia[25,26], and it was shown that the swallowing disorder status was different among the dementia types, and this finding is considered clinically meaningful. In the one remaining article, those elderly having low cognitive functions were followed up on[27], and it was reported that independence in eating is a factor influential on the cognitive function which suggests the importance of oral functions.

3. "Oral functions such as lingual pressure, swallowing or nutrition, life prognosis" (15 articles)

Almost all oral functions are related to mastication but

some studies in which mastication was not raised as the investigation target were picked up on. It has now become possible to measure the lingual pressure quantitatively[28], and the involvement of lingual pressure as an oral function has been investigated in various cases[15,29-31]. Multiple articles reported that the decline in lingual pressure represents a decline in oral functions, and future developments are anticipated.

Some articles reported on the relation between the primitive reflex of oral cavity and eating function and discussed the correlations with nutrition status, the Barthal Index, denture environments, and the onset of pneumonia, etc.[32] In addition, since the lip pressure plays an important role in eating or swallowing, the relation between lip-closing function and items such as "food debris dropping while eating" was reported[33,34].

Many articles reported that the health of oral functions is essential for life functions, but in this study, only review articles were dealt with[35-37]. All of those stated the importance of oral function control and referred to the need for cooperating with healthcare professionals specializing in other fields.

There are also an increasing number of reports on evaluation of swallowing disorder and life prognosis recently[38-42]. The major conceivable factors are the progress in the rehabilitation field and the progress made in evaluation methods or in cooperation with healthcare professionals specializing in other fields.

4."Saliva secretion and oral functions" (10 articles)

Saliva is essential for oral functions. The original roles of saliva are demonstrated in the state of decreased saliva secretion. There are various methods to evaluate saliva[43], but actually the main one is measurement of the amount of saliva secreted. Clinically, it is said that not only the amount secreted but also the moisture (wetting degree) in the oral cavity is important[44-51]. In addition, saliva is also essential for swallowing and mastication[44,52]. Age-related changes in the salivary gland were reported[51], but whether the decrease in saliva secretion is an age-related change was not discussed. In addition, the relation between oral dryness and decreased mastication was also reported in detail[52].

[Discussion]

Age-related changes and senescence are recognized to be originally different but these two can be regarded as nearly the same in human life. Namely, in this study, the state that changes with aging is called senescence.

Occlusion, mastication, oral cavity wetting, swallowing, and so on are closely correlated to each other. It is therefore extremely difficult to classify the articles in terms of each individual item. So in this study, it was decided to handle occlusion/mastication as one item and express "oral environment such as saliva secretion and oral hygiene, articulation / communication ability, etc." as "oral functions" in one package. The articles handling the relations between age-related changes of those (or phenomena seen frequently in the elderly) and changes not related to the oral cavity were selected by manual search. Swallowing disorder was associated with the laryngeal pharynx dysfunction. It is well known that oral functions closely correlate with systemic problems, and articles referring in particular to the relations with "dementia", "nutrition", "suffocation and pneumonia" and "life prognosis" were frequently encountered.

In the coming super-aged society, the number of dependent elderly persons (frail elderly persons) will be increasing, and so the number of "patients with difficulty in visiting medical/dental institution" will also increase. Almost all dental institutions are clinics, and for those patients who have difficulty in visiting dental clinic, the only way to receive dental treatment is by way of home visits. Since the visiting treatment is based on the patient's request, no treatment is administered unless the patient, their family or caretaker notices a change in the oral cavity. Namely, a state where there is no dental care for a long time will result in "lowered oral functions" (oral frailty).

Performing oral hygiene care on the elderly having inadequate oral hygiene resulted not only in cleaning up the inside of the oral cavity but also considerably restored the original functions of the oral cavity. Furthermore, treatment in systemic diseases is enhanced, the patient's QOL is improved and the burden on the family is reduced, so it can be said to render a great effect. Performing oral hygiene care by oneself is regarded as a barometer of self-independence. In early childhood, oral hygiene instruction starts with a simple tooth brushing action and each parent then shows an example of the entire brushing action. Later in life however, oral hygiene control by oneself is gradually ignored, and the oral cavity becomes soiled and this is coupled with a decline in oral functions. Taking care of the elderly like taking care of children in this regard is good but neither the caretaker nor the care receiver is proactive.

Future dental care will require correctly monitoring oral functions. In order to accomplish this, it is essential to grasp the age-related changes in oral functions, and we would be happy if this article is utilized for that purpose.

Table 1: Age-related changes in mastication/swallowing function

Content	No.	Year	Author	Outline
Mastication/occlusion and eating/swallowing, life function	1	2004	Kasahara *et al*.	The nutrition conditions and degree of bedridden state of the elderly are related to the presence or absence of eating/swallowing disorder, denture suitability and food types.
	2	2011	Morisaki *et al*.	The eating/swallowing functions of the elderly needing nursing are related with basic ADL, especially meals (high in those capable of taking meals in a completely independent manner).
	3	2004	Miura *et al*.	In dependent frail elderly persons, a high rate of "difficulty in mastication of hard foods" and "fever" are seen (21.74% and 20.65%, respectively).
	4	2005	Ino *et al*.	In the elderly needing nursing, incomplete lip closure or mastication motion shows a significant relation with "food debris dropping while eating."
	5	2013	Tanaka *et al*.	The swallowing frequency per hour was 9.0±5.4 times in the elderly group (11.6±6.2 times in the semi-bedridden group, 7.7±4.6 time in the bedridden group) and 40.7±19.5 times in the normal adult group.
	6	2009	Teraoka *et al*.	In those elderly requiring nursing, there are relations between motivation and oral function indices including molar-region occlusion support and swallowing function.
	7	2012	Kikutani *et al*.	In the elderly, the risk of suffocation increases 3.1 times on losing the occlusion support.
	8	2007	Bordeur *et al*.	Inadequate dietary habits in middle-aged and older persons are not related to the tooth/denture status.
	9	2010	Okada *et al*.	In the elderly, mastication, tooth status, body weight and upper arm circumference are predictive factors for mastication ability, and age, grip strength and gender are the predictive factors of serum albumin concentration.
	10	2013	Kikutani *et al*.	In dependent frail elderly persons, occlusion loss is a risk factor of malnutrition.
	11	2012	Okada *et al*.	In independent elderly persons, the number of remaining teeth, occlusion support, presence or absence of denture wearing and self-evaluation of oral health/function are related to a favorable nutrition status.
	12	2011	Yoshida *et al*.	In the elderly who have lost molar occlusion contact, the amounts of vitamin and food fibers ingested are low (144.4←179.4 and 7.36←8.49, respectively).
	13	2012	Inatomi *et al*.	In the elderly aged 75 years or over who require nursing, occlusion force shows a significant positive correlation with four items (number of remaining teeth, FIM cognition item, communication and social cognition).
	14	2009	Kikutani *et al*.	In the elderly aged 80 years or over, the lingual pressure is low.

Table 1: (continued)

Content	No.	Year	Author	Outline
Mastication/occlusion and eating/swallowing, life function	15	2013	Okuno *et al*.	In those elderly capable of visiting a dental clinic, the number of food materials that cannot be ingested increases as the number of remaining teeth decreases, and the mastication efficiency decreases, however the lingual pressure does not change.
	16	2013	Ohara *et al*.	In the elderly, palpation of masseter muscle tension is a reliable method for evaluating mastication ability.
	17	2011	Yamamoto *et al*.	The amount of saliva secreted is significantly larger in the group where the number of remaining teeth is not less than 20 (1.58 g/min) than in the group in which the number of remaining teeth is not more than 19 (1.05 g/min).
	18	2010	Nokubi *et al*.	Irrespective of the number of lost teeth, it is possible to improve the masticatory function to the same level as persons with a toothed jaw by wearing bio-compatible dentures.
	19	2003	Nakashima *et al*.	The mastication ability in denture wearers is not more than 1/6th that of persons with a toothed jaw, and the presence of natural teeth seems to be important.
	20	2012	Iwasaki *et al*.	In those female elderly persons with high mastication ability, the open-eye one-leg stand time is significantly longer.
	21	2012	Toyoshita *et al*.	The candidates for special elderly persons showed low values for the following: mean number of remaining teeth per person, mastication score, lower-jaw denture floor shape suitability, upper-jaw denture suitability, denture satisfaction degree, and conversation smoothness.
	22	2012	Takata *et al*.	The elderly aged 80 years or over tend to live longer when the masticatory function is more favorable or when the number of remaining teeth is larger.
	23	2012	Iinuma *et al*.	In male super elderly persons, the maximum occlusion shows a significant relation with age, BMI and cognitive function. In the super elderly having low physical functions, the maximum occlusion force is low.
	24	2009	Takahashi *et al*.	In the elderly utilizing a visit nursing facility, the oral function showed a positive correlation with ADL and GOHAI.
Dementia and mastication, swallowing	25	2009	Suh *et al*.	The types of appearing swallowing disorder differ between Alzheimer's disease and vascular dementia.
	26	2010	Yamamoto *et al*.	Aspiration during swallowing contrast imaging is a risk factor for the onset of pneumonia in patients with Lewy body disease.
	27	2010	Morino *et al*.	In the elderly needing nursing, the degree of independence in taking meals (DFIM) is influential on the cognitive function (MMSE).
Oral functions such as lingual pressure and swallowing or nutrition, life prognosis	28	2012	Tsuga *et al*.	The lingual pressure is lower in dependent elderly persons (14 to 21 kPa) than in healthy elderly persons (31 to 33 kPa).

Table 1: (continued)

Content	No.	Year	Author	Outline
Oral functions such as lingual pressure and swallowing or nutrition, life prognosis	29	2006	Yoshida *et al*.	Lingual pressure is related to the lingual motor function and is low in persons with swallowing disorder (10.7 kPa, normal persons: 17.8 kPa)
	30	2010	Okayama *et al*.	In the elderly needing nursing, BMI and nursing period show a significant relation to the tongue thickness.
	31	2004	Kodama *et al*.	In the elderly needing nursing, oral functions (especially lingual functions) are related to nutrition conditions.
	32	2014	Hobo *et al*.	Appearance of the primitive reflex is related to the onset risk of malnutrition or aspiration pneumonitis.
	33	2009	Tamura *et al*.	The lip pressure was low in the persons who experienced food suffocation.
	34	2005	Fukui *et al*.	In the elderly, the lingual pressure decreases with aging, but lip functions are hardly influenced by aging.
	35	2010	Hamura	Interpretation and review about oral senile deterioration and countermeasures
	36	2007	Hebling *et al*.	Review of oral function-related QOL (OHRQoL)
	37	2012	Nasu	A review article stating that healthy life expectancy is long in the elderly with high mastication ability
	38	2007	Enomoto *et al*.	Life prognosis is shorter in the presence of cognition-phase disorder, swallowing dysfunction or BMI risk.
	39	2012	McMillan *et al*.	Interpretation of frailty
	40	2011	Nito *et al*.	Interpretation and review regarding the evaluation and prevention of senescence-related swallowing disorder
	41	2009	Hironaka	Interpretation and review regarding the evaluation of age-related changes and eating/swallowing function
	42	2009	Fujitani	Interpretation and review regarding age-related changes and eating/swallowing disorders
Saliva secretion and oral functions	43	2012	Morito *et al*.	Saliva secretion induced by stimulation decreases with aging.
	44	2012	Bing *et al*.	Review of oral dryness and systemic health status
	45	2013	Maeda	Among the elderly receiving home dental care, those taking nutrition parenterally show unfavorable systemic conditions and oral environments/functions.
	46	2013	Maeda *et al*.	In the elderly, intraoral dryness status cannot be correctly judged just by hearing the subjective symptoms of thirst and visually observing the moisture state.
	47	2012	Kawakami *et al*.	Among the elderly receiving home dental care, those complaining of oral dryness accounted for 38.6%, and 86.0% of those persons had actual objective oral dryness.
	48	2012	Matsuno *et al*.	Those persons with subjective symptoms of oral dryness were using hypotensive drugs most frequently, followed by gastrointestinal drugs, anti-anxiety drugs and hypnotic/sedative drugs in that order.
	49	2012	Kuraji *et al*.	The risk factors of oral dryness in the elderly are oxidation degree and antioxidative potential.
	50	2010	Funayama *et al*.	A sensation of oral dryness occurs significantly more often in persons having symptoms of neurosis or who regularly take a drug causing thirst.

Table 1: (continued)

Content	No.	Year	Author	Outline
Saliva secretion and oral functions	51	2009	Gueiros *et al*.	Interpretation regarding aging and oral dryness
	52	2009	Shinkawa *et al*.	The masticatory function is lower in persons with oral dryness (28.4) than in normal persons (29.1).

[Conclusions]

Among the many articles, all oral functions such as occlusion/mastication, saliva secretion, articulation, swallowing, and so on were confirmed to decline with aging while also mutually affecting one other. In addition, it was also confirmed that the decline in oral functions is also closely related with systemic diseases including dementia, motor functions, and life functions, etc.

[Conflict of interest]

There are no items applicable to "conflict of interest" in this article.

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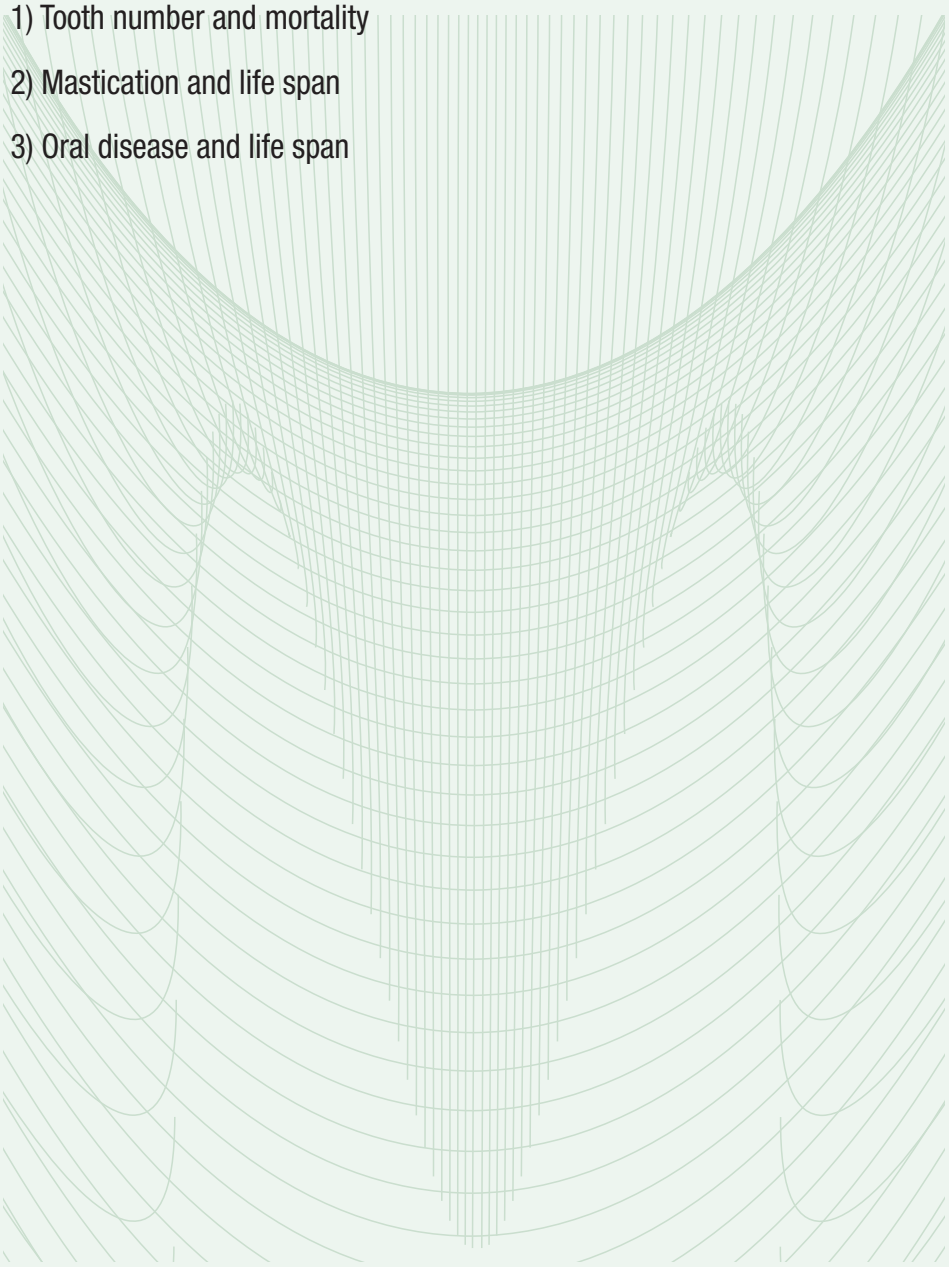
2. Oral health (tooth condition, mastication, oral diseases, etc.) and life span

1) Tooth number and mortality

2) Mastication and life span

3) Oral disease and life span



2. Oral health (tooth condition, mastication, oral diseases, etc.) and life span
1) Tooth number and mortality

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[Abstract]

The objective of this study was to review the existing body of evidence regarding the relationship between tooth number and life expectancy in humans. If such a relationship exists, it would indicate a clear link between maintenance of oral health and extension of healthy life expectancy. The PubMed database was used to collect the relevant literature from 1966 up through November 2014, while taking into consideration the strength of the evidence presented in each study. In this way, 36 articles were obtained and analyzed. The reviewed studies indicate that maintaining a larger number of teeth indeed results in an extension of life expectancy, with hazard ratios (HRs) of 1.1-2.7. With respect to improvement in vital prognosis due to denture use after tooth loss, an HR of about 1.3 was reported. In addition to a relationship between number of teeth and mortality in general, several reports showed a link between number of teeth and cardiovascular disease (CVD), a leading cause of death. There is thus clear evidence that tooth number is associated with life expectancy.

[Introduction]

Epidemiological data has shown a clear relationship between dental and oral health and general systemic health. Tooth number is a robust indicator of dental and oral health. The main causes of tooth loss include dental caries and periodontal disease, which are typical dental diseases, but also other systemic and oral risk factors such as smoking, diabetes mellitus, and chewing function. Moreover, tooth loss is directly linked to reduced oral function, including masticatory and speech functions.

Looking at populations as a whole, it is evident that oral health is improved by an increase in the mean number of teeth per person. A quarter of a century has passed since the 8020 campaign was initiated in Japan in 1989 with the goal of maintaining 20 or more teeth at the age of 80 years. During this time, tooth maintenance among Japanese people has improved significantly. According to a survey conducted in 2011, the percentage of people at the age of 80 years who retain 20 or more teeth had already reached 38%[1]. Dental care and oral health policies and campaigns help prevent dental diseases, and they also help control other factors that contribute to tooth loss.

On the other hand, average life expectancy is a strong indicator of systemic health status in a given country or region. In clarifying the relationship between oral health and systemic health, clear evidence can be provided by demonstrating a relationship between tooth number and vital prognosis.

Accordingly, in this review we have analyzed the existing body of research regarding tooth number and vital prognosis, mainly focusing on cross-sectional studies (cohort studies) in order to make claims regarding the extent to which an improvement in oral health can contribute to improved systemic health status. With regard to the underlying reason for the relationship between tooth number and life expectancy, the following two hypotheses can be considered: it may be due to the accumulated effect of dental disease such as periodontal disease, or it may be due to eating difficulty caused by reduced chewing and swallowing function. In the latter case, it is necessary to consider not only thedecreases in tooth number, but also the recovery of oral function that is possible with prosthetic treatment such as dentures. For this reason we also examine the relationship between dental prosthesis placement and vital prognosis. Furthermore, given that some studies have examined mortality by disease (i.e., cause of death) in addition to the relationship between tooth number and mortality in general, we will also discuss how particular causes of death are related to tooth number.

[Objective]

The objective of this review was to provide an overview of existing studies that have investigated the relationship between tooth number and vital prognosis, with the aim of providing epidemiological verification of the possible

contribution of tooth loss prevention to the extension of life expectancy.

[Methods]

This study was carried out by conducting a thorough search of the literature using PubMed (1966 to November 2014). I also performed a hand search for literature that could not be obtained through the PubMed search.

The keywords used for the PubMed search with regard to tooth number and life expectancy were as follows: (tooth OR teeth OR "tooth loss" OR "tooth number" OR "number of teeth" OR "dental disease" OR "dental status") AND (survival OR mortality OR death OR fatal OR lethal). With regard to dental prosthesis and life expectancy, the following keywords were used: ("replaced teeth" OR denture OR "dental prosthesis" OR "dental prostheses" OR RPD OR FPD) AND (survival OR mortality OR death OR fatal OR lethal). These were the same key words used in a previous systematic review and meta-analysis by Polzer *et al*. (2012)[2] Consequently, 5,766 articles regarding the number of teeth and life expectancy and 2,548 articles regarding dental prosthesis and life expectancy were obtained. Of these, Some articles[3-15] were eliminated, and 50 articles were selected based on title, content of the abstract, and/or the confounding factors examined[16-51]. Finally, we carefully examined the content of these articles, including additional studies located by hand searches, and arrived at a final list of 36 articles to be analyzed in this study.

[Results]

Table 1 summarizes the results of the 36 studies analyzed in this review. The studies were conducted in European countries (Italy, Sweden, Finland, Iceland, Denmark, Scotland, and Germany), the United States, and Asian countries (China and Japan).

1. Tooth loss and vital prognosis

In a 6-year cohort study of 1,929 Japanese institutionalized elderly people (mean age, 80 years) by Shimazaki *et al*. (2001), mortality was 1.8 times higher in participants with no teeth (and no dentures) than in those with 20 or more teeth (odds ratio (OR): 1.8, 95%; confidence interval (CI): 1.1-2.8)[17]. In a 15-year cohort study of 28,790 Chinese people in the age range of 40-69 years by Abnet *et al*. (2005), mortality was 1.1 times higher in participants with a tooth loss rate higher than the median for their age, relative to those below the median (hazard ratio (HR): 1.13, 95% CI: 1.09-1.18)[23]. In a 24-year cohort study by Cabrera *et al*. (2005) in Sweden consisting of 1,462 women between the ages of 38 and 60 years, mortality was 1.3 times higher in participants with 11 or more missing teeth compared to those with 10 or fewer missing teeth (HR: 1.27, 95% CI: 1.09-1.47)[24]. In a 10-year cohort study by Morita *et al*. (2006) on 118 Japanese participants 80 years and older, mortality was 2.7 times higher in men with less than 20 teeth compared to those with 20 or more teeth (HR: 2.71, 95% CI: 1.05-7.05)[27]. In a 15-year cohort study by Fukai *et al*. (2007) which consisted of 5,830 Japanese community-residing people between the ages of 40 and 89 years, mortality was 1.3 times higher in men with less than 10 teeth, relative to those with 10 or more functional teeth (HR: 1.33, 95% CI: 1.11-1.59)[30]. In a 15.5-year cohort study by Pdilha *et al*. (2008) in the United States consisting of 500 participants with a mean age of 57 years, mortality in the group with 1-19 teeth was 2.2 times higher than that of the group with 20 or more teeth (HR: 2.17, 95% CI: 1.50-3.13), and the group with 0 teeth had a mortality rate 1.8 times higher than the group with 20 or more teeth (HR: 1.76, 95% CI: 1.04-2.98)[34]. In a 21-year cohort study by Holm-Pedersen *et al*. (2008) in Denmark consisting of 573 participants between ages 70 and 90 years, mortality was 1.3 times higher in those with 0 teeth than in those with 20 or more teeth (HR: 1.26, 95% CI: 1.03-1.55)[35]. In a 12-year cohort study by Holmlund *et al*. (2010) in Sweden consisting of 7,674 participants between the ages of 20 and 89 years, mortality was 1.6 times higher (HR: 1.56, 95% CI: 1.15-2.13) in the group with 20-25 teeth compared to the group with 26 or more teeth; HRs for groups with 15-19 teeth, 10-14 teeth, and less than 10 teeth were 2.33 (95% CI: 1.66-3.27), 2.11 (95% CI: 1.44-3.10), and 2.75 (95% CI: 1.81-4.16), respectively[42]. In a 4-year cohort study by Hayasaka *et al*. (2013) consisting of 21,730 Japanese people 65 years of age or older, mortality in participants with 10-19 teeth (no dentures) was 1.3 times higher (HR: 1.34, 95% CI: 1.09-1.64) and mortality in participants with 0-9 teeth (no dentures) was 1.7 times higher (HR: 1.73, 95% CI: 1.47-2.04) than in those with 20 or more teeth[47]. In a study by Ando *et al*. (2014) on 7,779 men between ages 40 and 79 years, mortality among participants between ages 40 and 64 years was 1.9 times higher (HR: 1.94, 95% CI: 1.09-3.43) in those with 10-19 teeth and 2.8 times higher (HR: 2.75, 95% CI: 1.37-5.49) in the group with 0 teeth, relative to those with 20 or more teeth[51].

Table 1: Summaries of the results of studies on the relationship between tooth number and life expectancy.

Authors	Report year	Country	Subjects	Study design	Follow-up period	Classification of number of teeth	Confounding factors	Main results (mortality), HR, OR (95% CI)	Ref. no.
Appollonio *et al.*	1997	Italy	Aged 70-75 years, n=1,303 [followers: 1,201]	Cohort study	10 years	Dental status, denture wearers, naturally adequate dental staus, naturally inadequate dental status and subjects without dentures	Smoking, health service use, economic status	All-cause mortality Naturally adeequate dental status group VS. denture wearing group HR 1.34 (95%CI 1.06-1.70) Naturally inadequate dental status and subjects without dentures HR 1.51 (95%CI 1.11-2.05)	16
Shimazaki *et al.*	2001	Japan	Aged 79.7± 7.5 years n=1,929	Cohort study	6 years	Number of functional teeth (edentate with dentures, edentate without dentures, 1-19 teeth with dentures, 1-19 teeth without dentures, ≥ 20 teeth)	Age, gender, physical-mental heatlh status, type of institution, cerebrovascular disorder, cardiovascular disease, musculoskeletal disease	All-cause mortality ≥20 teeth group VS. edentate without denture wearing group OR 1.8 (95%CI 1.1-2.8)	17
Jansson *et al.*	2002	Sweden	Aged 18-66 years n=1,393	Cohort study (comparison 1970 year VS,1996 year)	26 years	Number of remaining teeth	Age, gender, smoking	All-cause mortality comparison the means for number of remaing teeth (aged 18-30, 31-40, 41-50, 51-60, 61-66 years) between survival and death during the 26 years, For all groups of age, median for number of remaing teeth, servival ＞death	18
Hämäläinen *et al.*	2003	Finland	Aged 80 years, n=226	Cohort sutdy	10 years	Number of missing teeth (0 teeth, 1-19 teeth, ≥20 teeth)	Gender, number of choronic diseases, self-rated health	All-cause mortality Number of missing teeth HR 1.026 (95%CI: 1.002-1.051)	19
Tuominen *et al.*	2003	Finland	Aged 30-39years, n=6,527	Cohort study	12 years	Number of teeth (≤10 teeth, 11-24 teeth, ≥25 teeth)	Age, education, hypertension, hypercholesterolemia, smoking, diabetes, number of caries, filled, retained roots, periodontal pockets, dental attendance	CHD mortality Group of ≥25 natural functional teeth VS. Male 11-24 teeth RR 0.8 (95%CI 0.5-1.3) 0-10 teeth RR 0.9 (95%CI 0.5-1.6) Female 11-24 teeth RR 0.5 (95%CI 0.2-1.8) 0-10 teeth RR 0.3 (95%CI 0.1-1.0)	20
Ragnarsson *et al.*	2004	Iceland	Aged 25-74 years, n=2,613	Cohort study	8-15 years	Number of teeth edentulous	Age, gender, cholesterol, systolic blood pressure, education, smoking	All-cause mortality number of teeth HR 0.987 (95%CI 0.975-0.999) edentate HR 1.30 (95%CI 1.05-1.64) CVD mortality number of teeth NS edentate HR 1.70 (95%CI 1.03-2.81)	21

Table 1: (continued)

Authors	Report year	Country	Subjects	Study design	Follow-up period	Classification of number of teeth	Confounding factors	Main results (mortality), HR, OR (95% CI)	Ref. no.
Hung *et al.*	2004	USA	Male Aged 40-75years n=41,407 Female Aged 30-55years n=58,974	Cohort study	Male 12 years Female 6 years	Self-reported number of teeth (0-10 teeth, 11-16 teeth, 17-24 teeth, 25-32 teeth)	Age, smoking,alcohol consumptiom, BMI, physical activity, family history of fMI, multuvutamin supplement use, vitamin E use, diabetes, history of hypertension, hypercholesterolemia, menopausal status, and hormonal use	CHD mortality Group of 25-32 functional teeth VS. Male 17-24 teeth HR 1.26 (95%CI 1.01-1.57) 11-16 teeth HR 1.19 (95%CI 0.79-1.80) 0-10 teeth HR 1.79 (95%CI 1.34-2.40) Female 17-24 teeth HR 1.02 (95%CI 0.66-1.55) 11-16 teeth HR 1.07 (95%CI 0.55-2.05) 0-10 teeth HR 1.6 (95%CI 1.11-2.46)	22
Abnet *et al.*	2005	China	Aged 40-69 years n=29,584 [followers: 28,790]	Cohort study	15 years	Number of age-specific missing teeth (median)	Age, gender, smoking, alcohol, height, weight, systolic blood pressure	Number of age-specific missing teeth (median) group VS Number of age-specific missing teeth (median) group All-cause mortality RR 1.13 (95%CI: 1.09-1.18) Upper GI cancer RR1.35 (95%CI: 1.14-1.59) Heart disease mortality RR 1.28 (95%CI 1.17-1.40) Stroke mortality RR 1.11 (95%CI 1.01-1.23)	23
Cabrera *et al.*	2005	Sweden	Aged 38-60 years n=1,462 female	Cohort study	24 years	Number of missing teeth (>10 teeth)	Age, waist-hip ratio, BMI, smoking, the husband's occupational category	All-cause mortality ≦10 missing teeth group VS. ≧11 missing teeth group HR 1.27 (95%CI: 1.09-1.47) CVD mortality HR 1.34 (95%CI 1.05-1.71) Cancer mortality NS	24
Hämäläinen *et al.*	2005	Finland	Aged 85 years n=94	Cohort study	5 years	Number of remaining teeth	Gender, chronic diseases, self-rated health, education, forced expiratory volume during first second, hand grip strength, urgent need of dental treatment, CPI	All-cause mortality Small number of remaining teeth group VS. high number of remaining teeth group HR 0.939 (95%CI 0.884-0.998)	25

Table 1: (continued)

Authors	Report year	Country	Subjects	Study design	Follow-up period	Classification of number of teeth	Confounding factors	Main results (mortality), HR, OR (95% CI)	Ref. no.
Yoshida *et al.*	2005	Japan	Aged ≥65 years n=1,030	Cohort study	8 years	Functionally adequate occlusal contacts, insuficient occlusal contacts with unilateral molar and/or anterior teeth remaining, no occlusal contacts with or without remaining teeth, wheter or not denture wearing	Age, gender	All-cause mortality No occlusal contact group VS. fanctionally adequate occlusal contact group HR 0.78(95%CI: 0.60-0.99) No occlusal contact with denture group VS. no occlusal contact with no denture group HR 1.52 (95%CI: 1.25-1.83)	26
Morita *et al.*	2006	Japan	Aged ≥80 years n=118	Cohort study	10 years	Number of teeth (≥20 teeth, <20 teeth)	Smoking, alcohol	All-cuase mortality ≥20 teeth group VS. <20 teeth group 78-month follow-up Male HR2.71 (95%CI: 1.05-7.05) Female NS	27
Ohrui *et al.*	2006	Japan	Aged 82.8± 7.7 years n=403	Cohort study	5 years	Functionally adequate dentition (natural teeth only or natural teeth with partial denture), edentate with dentures, edentate without dentures	Age, gender, cardiac disease, cerebrocascular disease, diabetes mellitus, cognitive function dementia, ADL	All-cause mortality Natural teeth only or natural teeth with partial denture group VS. edentate with or without dentures group 2-year follow-up HR 1.84 (95%CI 1.01-3.36) 5-year follow-up HR 1.30 (95%CI 0.90-1.88)	28
Semba *et al.*	2006	USA	Aged 70-79 years n=826 female	Cohort study	5 years	no denture, denture wearer (without difficulty chewing or swallowing), denture wearer (with difficulty chewing or swallowing)	Age, race, education, BMI	All-cause mortality no denture group VS. denture wearer group（with difficulty chewing or swallowing） HR 1.43 (95%CI 1.05-1.97)	29
Fukai *et al.*	2007	Japan	Aged 40-89 years n=5,830	Cohort study	15 years	Number of functional teeth （<10 teeth, ≥10 teeth）	Age, presence of systemic diseases, bedridden state	All-cause mortality ≥10 functional teeth group VS. <10 functional teeth group Male HR 1.33 (95%CI 1.11-1.59) Female NS CVD mortality Male p<0.05 Female NS Cancer mortality, pneumonia mortality, cerebrovascular mortality Male NS Female NS	30

Table 1: (continued)

Authors	Report year	Country	Subjects	Study design	Follow-up period	Classification of number of teeth	Confounding factors	Main results (mortality), HR, OR (95% CI)	Ref. no.
Osterberg *et al.*	2007	Denmark	Aged 75 years n=1,004	Cohort study	7 years	Self-reported number of teeth (0 teeth, 1-4 teeth, 5-9 teeth, 10-14 teeth, 15-19 teeth, ≥20 teeth)	Eduction, economic situation, smoking, alcohol consumption, self-assessed health, physical activity, social activity, ADL, comorbidity （CVD,respiratory disease, circulation disease, other chronic diseases） , BMI	All-cause mortality Female HR 0.87 (95%CI 0.78-0.97) Male NS	31
Tu *et al.*	2007	UK	Aged 16-30 years (median age 19 years) n=12,223	Cohort study	57 years	Number of missing teeth (0-4 teeth, 5-8 teeth, ≥9 teeth)	Age, gender, father's socioeconomic position, smoking, BMI, systolic blood pressure	All-cause mortality Number of missing teeth as either continuous HR1.01(95%CI: 1.00-1.02) CVD mortality Number of 0-4 missing teeth groupVS. number of ≧9 teeth group HR 1.35 (95%CI 1.03-1.77) Cancer mortality NS	32
Osterberg *et al.*	2008	Sweden	Aged 70 years 7-year fllow-up n=1803 18-year follow-up n=1,381	Cohort study	7 years and 18 years	Number of teeth (0 teeth, 1-19 teeth, 20-32 teeth)	BMI,history of ischemic heart disease, plasma glucouse, number of drugs, blood hemoglobin, serum triglycerides, self-rated health, smoking, socail activity, blood pressure	Edentulous（no teeth）group VS. All-cause mortality 7-year follow-up Female HR 0.97 (95%CI.: 0.95-0.99) Male HR 0.96 (95%CI 0.94-0.98) 18-year follow-up Female NS Male HR 0.97(95%CI: 0.97-0.99)	33
Pdiha *et al.*	2008	USA	Aged 57.46 ±17.37 years n=500	Cohort study	15-year 5-month(±90 months)	Number of teeth (0 teeth, 1-19 teeth, ≥20 teeth)	Age, white blood cell count, history of myocardinal infarction, history of diabetes	All-cause mortality ≧20 teeth group VS. 1-19 teeth group HR 2.17 (95%CI 1.50-3.13) 0 teeth HR 1.76 (95%CI 1.04-2.98)	34
Holm-Pedersen *et al.*	2008	Denmark	Aged 70, 75, 80, 85, 90 years n=573	Cohort study	21 years	Number of teeth (0 teeth, 1-19 teeth, 10-19 teeth, ≥20 teeth)	Education, income, smoking, tiredness, comorbidity, arteriostenosis	All-cause mortality ≥20 teeth group VS. 0 teeth（edentulous） HR 1.26(95%CI: 1.03-1.55)	35
Fukai *et al.*	2008	Japan	Aged 40—89 years n=5,688	Cohort study	15 years	<10 functional teeth with denture wearing, <10 functional teeth without deture wearing	Age, presence of systemic diseases, ADL	All-cause mortality ≤10 teeth without denture wearing group VS. ≤10 teeth with denture wearing group Male NS Female HR 0.72(95%CI: 0.58-0.91)	36

Table 1: (continued)

Authors	Report year	Country	Subjects	Study design	Follow-up period	Classification of number of teeth	Confounding factors	Main results (mortality), HR, OR (95% CI)	Ref. no.
Awano *et al.*	2008	Japan	Aged 80 years n=697	Cohort study	4 years	Number of teeth (1-9 teeth, 10-19 teeth, ≥20 teeth), periodontal pocket (≥4mm)	—	All-cause mortality Edentulous group VS. 1-9 teeth NS 10-19 teeth NS ≥20 teeth NS Pneumonia mortality 1-9 teeth, >10 teeth and no periodoontal pocket VS. 1-9 teeth (periodontal pocket) HR 3.9 (95%CI 1.1-13.9) >10 teeth (periodontal pocket) HR3.9(95%CI:1.1-13.9)	37
Thorstensson *et al.*	2009	Sweden	≥80 years (median 86 years) n=357	Cohort study	8 years	Number of teeth (0 teeth, 1-10 teeth, 11-20 teeth, ≥21 teeth) DFS% (Decayed, Filling Surface: <33, 33-66, >66)	—	Number of teeth : NS DFS : p=0.03 (Kaplan Meier)	38
Brown	2009	USA	≥18 years n=41,000	Cohort study	16 years	Edentate VS, dentate	Age, gender race, education, family income, living situation, health insurance, dental insurance, BMI, ADL, comorbidity (arthritis, diabetes, ischemic heart disease, cerebrovascular disease, cancer, athma, chronic bronchitis, emphysema, lung cancer)	All-cause mortality Aged 18-64 years RR 1.5 (95%CI 1.13-1.7) Aged ≥65 years RR 1.3(95%CI:1.2-1.4)	39
Fukai *et al.*	2010	Japan	Aged 65-74 years	Cross sectional	30 years every 6 years (in 1975, 1981, 1987, 1993, 1999, and 2005)	Number of remainimg teeth aged 65－74 years VS life expectancy	—	Male r 0.962 Female r 0.916	40

Table 1: (continued)

Authors	Report year	Country	Subjects	Study design	Follow-up period	Classification of number of teeth	Confounding factors	Main results (mortality), HR, OR (95% CI)	Ref. no.
Ansai *et al.*	2010	Japan	Aged 80 years n=1,282 [followers: 697]	Cohort study	4 〜5.5 years	Number of teeth	Gender, Smoking, serum total cholesterol, fasting serum glucose, serum albumin, place of residence, marital status, BMI	4-year follow-up Female OR 0.937 (95%CI 0.889-0.987) Male NS 5.5-year follow-up Female OR 0.946 (95%CI 0.907-0.987) Male NS	41
Holmlund *et al.*	2010	Sweden	Aged 20-89 years n=7,674	Cohort study	12 years (0.2-29 years)	Number of teeth (<10 teeth, 10-14 teeth, 15-19 teeth, 20-25 teeth, >25 teeth)	Age, gender, smoking	All-cause mortality ≥26 teeth group VS. 20-25 teeth HR 1.56(95%CI 1.15-2.13) 15-19 teeth HR 2.33(95%CI 1.66-3.27) 10-14 teeth HR 2.11(95%CI 1.44-3.10) <10 teeth HR 2.75(95%CI 1.81-4.16) CVD mortality 20-25 teethHR 1.94(95%CI 1.21-3.10) 15-19 teeth HR 3.13(95%CI 1.89-5.17) 10-14 teethHR 3.41(95%CI 1.98-5.86) >10 teeth HR 4.41(95%CI 2.47-7.85)	42
Fukai *et al.*	2011	Japan	Aged 40-89 years n=5,643	Cohort study	15 years	Number of critical functional teeth（gender and age specific, average number of dysphagia) Aged 40-49 years （male 20.0 teeth, female 19.0 teeth） Aged 50-59 years （male 17.5 teeth, female 14.7 teeth） Aged 60-69 years （male 14.0 teeth, female 12.7 teeth） Aged 70-79 years （male 10.1 teeth, female 4.0 teeth）	Age, ADL, presence of systemic diseases	All-cause mortaltiy ‹ gender and age specific, number of critical functional teeth group VS. ≥ number of critical teeth group Male HR 0.72 (95%CI 0.55-0.93) Female HR 0.71 (95%Ci 0.51-0.99)	43
Aida *et al.*	2011	Japan	Aged >65 years n=18,936	Cohort study	4.28 years (0.07-4.56 years)	Number of teeth, denture wearing, chewing ability（≥20 teeth, 19 or fewer & eat everything, 19 teeth or fewer & restricted eating	Gender, age, BMI, self-rated health, present illness, exercise, smoking, alcohol, education, income	≥20 teeth group VS ≤19 teeth & restricted eating group CVD mortality HR 1.83 (95%CI 1.12-2.98) Respiratory mortality HR 1.85 (95%CI 1.09-3.14) Cancer mortality NS	44

Table 1: (continued)

Authors	Report year	Country	Subjects	Study design	Follow-up period	Classification of number of teeth	Confounding factors	Main results (mortality), HR, OR (95% CI)	Ref. no.
Paganini-Hill *et al.*	2011	USA	Aged 52-105 yers n=5,611	Cohort study	17 years (median 9 years)	Numer of teeth （0 teeth, 1-15 teeth, 16-25 teeth, 26-32 teeth)	Age, smoking, alcohol, caffeine, activities, BMI, high blood pressure, angina, heart attack, stroke, diabetes, rheumatoid arthritis, and cancer	All-cause mortality 26-32 teeth group VS, 1-15 teeth group male HR 1.21 (95%CI 1.05-1.40), female HR1.17(95%CI 1.06-1.30) 0 teeth group male HR 1.18(95%CI 1.00-1.39), female HR 1.21(95%CI 1.07-1.37)	45
Watt *et al.*	2012	Scotland	Aged ≥35 (SD 48.7± 10.6) years n=12,871	Cohort study	8 years (SD3.3 years)	Chewing with only natural teeth, natural teeth + denture wearing, edentate)	Age, gender, socioeconomic group (occupation, marital status), BMI, alcohol	All-cause mortality Chewing with only natural teeth group VS. Edentate group HR 1.65 (95%CI :1.31-2.07) CVD mortality HR 1.76(95%CI: 1.19-2.59) Cancer mortality NS	46
Hayasaka *et al.*	2013	Japan	Aged >65 years n=21,730	Cohort sutdy	4 years	Number of remaining teeth (0-9 teeth, 10-19 teeth, ≥20 teeth) + denture wearing	Age, gender, education, smoking, alcohol, BMI, time spent walking daily, medical history, psychological distress, energy intake, protein intake	All-cause mortality ≥20 teeth group VS. 10-19 teeth（no denture） HR 1.34 (95%CI:1.09-1.64) 0-9 teeth （no denture） HR 1.73 (95%CI:1.47-2.04)	47
Ansai *et al.*	2013	Japan	Aged 80 years n=1,282 [followers: 697]	Cohort sutdy	12 years	Number of teeth （0 teeth, 1-9 teeth, 10-19 teeth, ≥20 teeth）	Gender, smoking, total cholesterol, serum albumin, fasting serum glucose, BMI, physical activity, place of residence	Total cancer mortality NS Orodigestive cancer HR 1.06 (95%CI: 1.01-1.13) CVD mortality NS Pneumonia mortality NS	48
Schwahn *et al.*	2013	Germany	Aged 64 years （median） n=1,803	Cohort study	9.9 years	Number of remaining teeth (0 teeth, 1-9 teeth, 10-19 teeth）, unreplaced teeth (0-8 teeth, ≥9 teeth）	Age, gender, education, marital status, regular dental check-ups, last oral visit because of pain	All-cause mortality 10-19 remaining teeth group 0-8 unreplaced teeth VS. ≥9 unreplaced teeth HR 2.19 (95%CI:1.19-4.01) CVD mortality 1-9 remaining teeth group 0-8 unreplaced teeth VS. ≥9 unreplaced teeth HR 4.11 (95%CI: 1.76-9.50)	49

Table 1: (continued)

Authors	Report year	Country	Subjects	Study design	Follow-up period	Classification of number of teeth	Confounding factors	Main results (mortality), HR, OR (95% CI)	Ref. no.
Janket *et al.*	2014	Finland	Aged 60 (median) years n=256 Coronary artery disease patients n=250 control	Cohort study	15 years	Number of teeth (0 teeth, 1-9 teeth, 10-19 teeth, ≥20 teeth)	Gender, age, smoking, hypertension, total HDL cholesterol, diabetes, edication, C-reactive protein, Fibrinogen	All-cause mortality NS CVD mortality Edentulous group VS. ≥21teeth HR 0.40 (95%CI:0.18-0.90)	50
Ando *et al.*	2014	Japan	Aged 40-79 years n=7,779 Male	Cohort sutdy	5.6 years	Number of teeth (0 teeth, 1-10 teeth, 11-20 teeth, ≥22 teeth)	Age, BMI, blood pressure, total HDL cholesterol, HbA1c, smoking, alcohol, education	Aged 40-79 years All-cause mortality NS Aged 40-64 years All-cause mortality ≥20 teeth group VS. edentulous group HR2.75 (95%CI: 1.37-5.49) 10-19 teeth group HR1.94 (95%CI: 1.09-3.43) Cancer mortality ≥20 teeth group VS. edentulous group HR4.06 (95%CI: 1.43-11.5) CVD mortality ≥20 teeth group VS. edentulous group HR9.40 (95%CI: 1.86-48.6) 1-9 teeth group HR5.34 (95%CI: 1.11-25.6) 10-19 teeth group HR4.35 (95%CI: 1.07-17.7)	51

2. Dental prosthesis and vital prognosis

In a 10-year cohort study in Italy by Appollonia *et al*. (1997) which consisted of 1,137 community residents between ages 70 and 75, mortality relative to participants who had maintained a sufficient number of teeth with no denture use was 1.3 times higher (HR: 1.34, 95% CI: 1.06-1.70) in those who used dentures and 1.5 times higher (HR: 1.51, 95% CI: 1.11-2.05) in those who had lost their teeth and did not use dentures[16]. As mentioned above, we found several studies that had classified participants into categories based on the current number of teeth or by the number of occlusal contact points, in addition to the presence or absence of dental prosthesis. One study that analyzed vital prognosis according to the presence or absence of dental prosthesis and also adjusted for tooth number was Fukai *et al*. (2008). This was a 15-year cohort study of 5,688 Japanese community residents between ages 40 and 89, and it provided follow-up results for participants with less than 10 functional teeth according to the presence or absence of dental prosthesis. Mortality was 0.7 times higher in women with dentures (HR: 0.72, 95% CI: 0.58-0.91) than in those with no dentures, revealing a clear effect[31].

3. Tooth loss and cause of death

Studies investigating the relationship of tooth loss and presence/absence of dentures with vital prognosis include those that performed the analysis with mortality in general as well as those that demonstrated a relationship between tooth loss and specific causes of death. There have been reports on mortality due to CVD, cancer, and respiratory disease. In particular, a number of studies have reported on the relationship between tooth loss and CVD mortality.

Regarding the relationship between CVD mortality and tooth number, Hung *et al*. (2004) reported the results of a cohort study in men between the ages of 40 and 75 (n=41,407, 12-year follow-up) and women between the ages of 30 and 55 (n=58,974, 6-year follow-up) in the United States. Relative to men with 25-32 teeth, the HR was 1.26 in those with 17-24 teeth (95% CI: 1.01-1.57), 1.19 in those with 11-16 teeth (95% CI: 0.79-1.80), and 1.79 in those with 0-10 teeth (95% CI: 1.34-2.40). In women, the HR was 1.02 in those with 17-24 teeth (95% CI: 0.66-1.55), 1.07 in those with 11-16 teeth (95% CI: 0.55-2.05), and 1.6 in those with 0-10 teeth (95% CI: 1.11-2.46)[22]. In a study by Cabrera *et al*. (2005) in Sweden (n=1,462, ages 38-60, females) the HR was 1.34 (95% CI: 1.05-1.71) for CVD mortality in the group with 11 or more missing teeth, relative to the group with 10 or fewer missing teeth[24]. Tu *et al*. (2007) conducted a 57-year cohort study in the United Kingdom consisting of 12,223 participants between ages 16 and 30, in which the HR for CVD mortality was 1.35 (95% CI: 1.03-1.77) in the group with 9 or more missing teeth, relative to the group with 0-4 missing teeth[32]. In a 12-year cohort study by Holmlund *et al*. (2010) on 7,674 participants in Sweden between the ages of 20 and 89, the HR for CVD mortality relative to those with 26 or more teeth was 1.94 in those with 20-25 teeth (95% CI: 1.21-3.10), 3.13 in those with 15-19 teeth (95% CI: 1.89-5.17), 3.41 in those with 10-14 teeth (95% CI: 1.98-5.86), and 4.41 in those with less than 10 teeth (95% CI: 2.47-7.85)[42]. Aida *et al*. (2011) conducted a 4.3-year study with 18,936 Japanese people 65 years or older, in which the HR for CVD mortality relative to the group with 20 or more teeth was 1.83 (95% CI: 1.12-2.98) in those with 19 or fewer teeth who had chewing difficulty[44]. In a study conducted by Ando *et al*. (2014), the HR for CVD mortality relative to the group with 20 or more teeth was 9.40 (95% CI: 1.86-48.6) in those with 0 teeth, 5.34 (95% CI: 1.11-25.6) in those with 1-9 teeth, and 4.35 (95% CI: 1.07-17.7) in those with 10-19 teeth (n=1,462, ages 40-79, males) [51].

Regarding the association between tooth loss and cancer mortality, while there have been a number of reports showing no significant relationship[24,30,32,44], a significant relationship was found by Abnet *et al*.[23] for upper digestive tract cancer (1.4 times higher), and by Ansai *et al*. (2013)[48] for orodigestive cancer (1.1 times higher). For all-cancer mortality, Ando *et al*. (2014) reported that compared to those with 20 or more teeth, the group with 0 teeth had a mortality rate 4.1 times higher[51]. For mortality due to respiratory disease, Aida *et al*. (2011)[44] reported a pneumonia mortality rate of 1.9 times higher and Awano *et al*. (2008)[37] reported a rate of 3.9 times higher in the group with periodontal pockets compared to the group with no periodontal pockets, regardless of whether participants had 9 or fewer teeth or 10 or more teeth.

[Discussion]

The results of the studies reviewed here indicate that maintaining a higher number of teeth improves vital prognosis by 1.1-2.7 fold. These results were from well-designed cohort studies in which adjustments for confounding factors were performed. Therefore, even from observational studies, it can be inferred that tooth loss can increase mortality over the long term. Based on these results, we examined the changes in the mean number of teeth per person (65-74 years old) and average life expectancy during a 30-year period spanning from 1975 through 2005 in Japan, as reported by Fukai *et al*.(2010), and found a strong correlation in both men and women (correlation coefficient,

≥0.9)[40]. These results undeniably show that an increase in the number of teeth maintained has contributed to the extension of average life expectancy among Japanese people. However, the method of placing participants into groups based on tooth number varied in the studies reviewed here. In addition, denture use was taken into consideration in many analyses, with various adjustments performed to account for confounding factors. Accordingly, as in Poltzer *et al*. (2012)[2], no meta-analysis was performed regarding the relationship between tooth number and life expectancy. At present, it is still difficult to estimate the contribution of a higher number of teeth to the extension of life expectancy in terms of a specific number of years. However, given that reports from Europe, the United States, and Asia consistently show a clear relationship between tooth number and life expectancy, a relationship between the two is strongly supported by the evidence regardless of race, medical environment, or other factors.

In the context of the relationship between dental prosthesis and vital prognosis, Poltzer *et al*. (2012)[2] performed a meta-analysis on selected reports including those of Yoshida *et al*.(2005)[26] and Fukai *et al*., (2008)[31] and reported a 1.31-fold effect of dental prosthesis on vital prognosis. These results indicate that it may be possible to assess the effect of dental care provision with life expectancy as the outcome.

Concerning the relationship between tooth number and specific causes of death, there have been reports suggesting a relationship between tooth number and CVD. CVD is one of the leading causes of death in industrialized countries, and it has been shown to play a role in the mechanism underlying the relationship between tooth number and life expectancy. Meanwhile, the relationship between tooth number and mortality from respiratory diseases such as pneumonia, which is another leading cause of death, has not yet been established. Compared with the increased risk of pneumonia due to oral hygiene difficulty, which is associated with higher numbers of teeth in the dependent elderly, tooth loss prevention has a more significant effect on the improvement of vital prognosis.

[Conclusions]

In this paper, we reviewed the literature in Japan and abroad regarding the relationship between tooth number and vital prognosis, taking into account the strength of the evidence presented in each study. The results clearly show that tooth loss prevention contributes to the extension of life expectancy, based on a large number of cohort studies from Europe, the United States, and Asia. Moreover, even with tooth loss, some improvement in vital prognosis can be expected with the use of prosthesis such as dentures. A relationship between CVD and tooth number was also found.

[Conflict of interest]

There are no items applicable to “conflict of interest” in this article.

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2. Oral health (tooth condition, mastication, oral diseases, etc.) and life span
2) Mastication and life-span

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[Abstract]

The masticatory function or chewing is a major task of the oral cavity. When considering the effects of the masticatory function on systemic health, the results from epidemiological survey studies using life-span as the outcome are helpful. Since there are no methods which are capable of evaluating the masticatory function on a real-time basis and also suitable for field work targeting the elderly people at the present point in time, it is common to adopt an indirect evaluation method in domestic and overseas epidemiological surveys such as evaluating the masticatory function and occlusion status using a questionnaire. In this article, literature are reviewed while focusing on the relationship between the total risk of death and masticatory function or occlusion status, and the effects of mastication and occlusion on systemic health are discussed.

[Introduction]

The oral cavity is known to fulfill many tasks such as saliva secretion and taste function in addition to the masticatory function, eating/swallowing function, articulatory/locutionary function and respiratory function. Among these, in the masticatory function, the concept of "Fletcherism" has long been known, and recently the Ministry of Health, Labour and Welfare has issued a Guideline entitled "Kaming Sanmaru" (Biting 30) to instruct people widely about this in parallel with dietary education. The mass media such as newspapers contains many popular articles referring for example to the link between quick eating and obesity and some articles report that mastication contributes to improved systemic health. In this paper we review the domestic and overseas literature referring to the relation between life-span and masticatory function and consider the mechanism by which mastication contributes to systemic health.

[Objective]

The objective of this study was to organize and discuss the relevant information obtained by literature survey using key words relating to mastication and life-span.

[Methods]

This study was performed by way of a literature survey. The literature inclusion criteria were as follows: (i) studies performed focusing on humans, (ii) literature written in English or Japanese, (iii) original articles or para-original articles, and (iv) literature published in or after 2000. PubMed and ICHUSHI were utilized in the Internet search, and a manual search was also performed for the literature not obtained by Internet search. In addition, the reported contents and titles/abstracts were also checked in detail and literature definitely different from the objective of this study, literature overlapping in contents and epidemiological survey studies not adjusted with confounding factors were excluded. The key words utilized were "Soshaku (mastication, chewing)," "Shika (dental)," "Shoku (eating)," "Gishi (denture)," "Kougou (occlusion)," "Shibou (death, mortality)," "Seizon (survival)" and "Tsuiseki kenkyu (follow-up study, cohort)."

[Results]

In the literature survey, a total of 15 texts were obtained which are outlined in Table 1.

1. Relationship between life-span and masticatory function

A study by Nakanishi et al.[1] on 1,405 community residents aged not less than 65 years (564 males, 841 females) for a period of 9 years reported that the higher the subjective masticatory function, the longer the life-span (hazard ratio [hereinafter abbreviated to HR]: 1.63, 95% confidence interval [hereinafter abbreviated into CI]: 1.30-2.03). A study by Yoshida et al.[2] followed up on 1,030 females aged not less than 65 years for 8 years. This study divided those subjects into the three categories of "molar region occlusion", "molar region occlusion + front tooth region occlusion" and the "absence of either occlusion" and analyzed the explanatory

Table 1: Literature showing relationship between life-span and masticatory function or occlusion status

Authors	Year	Country	Subjects	Methods	Follow-up time	Exposure	Risk factors considered	All-cause mortality	Ref.
Nakanishi *et al.*	2005	Japan	1,405 community residents aged 65 years or more Male: 564 Female: 841	Cohort study, Mortality rate, and questionnaire	9 years	Self-evaluation of masticatory function: "Can you eat anything?" (evaluated with points: 0 or 1)	None of the past medical history, regular medical and dental checkup, activities for promoting health, social participation, interpersonal relations, and lifestyle-related illnesses and the presence of having something to live for are included.	HR, 1.63 (1.30-2.03)	1
Yoshida *et al.*	2005	Japan	1,030 females aged 65 years or more	Cohort study, mortality rate, and type of occlusion: moral region occlusion (A) , moral region occlusion or front tooth region occlusion (B), and none of them ©	8 years	Presence of moral region occlusion	Age and gender only	A:HR, 0.78 (0.6-0.99) B: HR, 1.08 (0.85-1.36) C:HR, 1 [more detailed for C: using dentures vs. not using dentures: HR, 1.52 (1.25-1.83)]	2
Semba *et al.*	2006	Maryland	826 females aged 70-79 years	Cohort study	5 years	0: not using dentures, and 1: using dentures and feeling problems in mastication and/or swallowing (self-evaluation)	Age, race, academic history, smoking, BMI, and infirmity	HR, 1.43 (1.05-1.97)	3
Onder *et al.*	2007	11 Euro-pean countries	2,755 people (mean age: 82 years)	Cohort study, questionnaire	1 year	Whether having mastication problems: Yes or No	Age, gender, living alone or others, ADL, cognitive function, the presence of acute exacerbations of chronic diseases, the presence of a rapid weight loss, pain, obesity, cardiovascular diseases, diabetes mellitus, COPD, depression, cancer and intake of medicines	Risk of death was 1.45 to 1.62 times higher in subjects with mastication problems than those without mastication problems.	4
Lee *et al.*	2010	Taiwan	1,410 community residents aged 65 years or more Male:729, Female: 681	Cohort study, questionnaire, and metabolic syndrome examination	8 years	Self-evaluation of the masticatory function: "Whether there are food materials difficult to masticate?"(evaluated with points: 0 or 1), The presence of MS (metabolic syndrome) 3 or 5 parameters	Age, gender, self-evaluation of health status, appetites, and dietary balances. MS 3 parameters: waist circumference, fasting blood glucose level and neutral fat level, MS 5 parameters: above MS 3 parameters plus blood pressure and HDL	Decreased masticatory function with MS 5 parameters vs satisfactory masticatory function without MS 5 parameters: HR, 1.65 (1.11-2.46) For MS 3 parameters: HR, 2.58 (1.58-4.23)	5

Table 1: (continued)

Authors	Year	Country	Subjects	Methods	Follow-up time	Exposure	Risk factors considered	All-cause mortality	Ref.
Tsai and Chang	2011	Taiwan	2,766 males and females aged 65 years or more (National data of Taiwan)	Cohort study, questionnaire	4 years	Evaluation of nutrients intake, self-evaluation of the masticatory function, MNA, three categories for dentures status (removal dentures, fixed dentures, or none)	SES, life-style, and health-related factor	HR was significantly higher in the subjects using removal dentures than in those using fixed dentures [HR,1.31 (95% CI, 1.02-1.69)]	6
Ansai *et al.*	2007	Japan	824 community residents aged 80 years	Cohort study, questionnaire	4 years	Based on the Yamamoto's masticatory grade: A; 15 food materials, B; 10-14 food materials, C; 5-9 food materials, and D; 0-4 food materials	Gender, smoking, blood test, BMI, and blood pressure	D vs. A: HR, 2.4 (1.1-5.3) * HR was also analyzed by the cause of death.	7
Takata and Ansai	2012	Japan	824 community residents aged 80 years	Cohort study, questionnaire	12 years	Based on the Yamamoto's masticatory grade: A; 15 food materials, B; 10-14 food materials, C; 5-9 food materials, and D; 0-4 food materials	Gender, smoking, drinking, serum Alb, blood sugar, BMI, blood pressure, and the presence of hospital visit	D vs. A: HR, 2.1 (1.4-3.1); D vs. B: HR, 1.4; D vs. C: HR, 1.3 (all HR values showed significant differences)	8
Shimazaki *et al.*	2001	Japan	1,929 assisted-living residents (mean age: 79.7 years)	Cohort study, examination of the oral cavity	6 years	Number of teeth, and the condition of dentures	Age, gender, psychosomatic condition, and the type of facility, CVD, and musculo-skeletal disease	Edentulous jaw not using dentures: OD 1.8 (1.1-2.8) vs. ≥ 20 teeth	9
Watt *et al.*	2012	U.K	12,871 community residents (mean age: 53 years)	Cohort study, self-evaluation of the oral cavity status	8 years on average	Three classifications: natural teeth alone, natural teeth plus dentures, and dentures alone	Age, gender, SES, marital status, exercise habits, smoking, drinking, BMI, self-evaluation of health status, diabetes mellitus and hypertension	HR, 1.3 (1.12-1.50) for edentate * HR, 2.97 (1.46-6.05) for stroke mortality	10

Table 1: (continued)

Authors	Year	Country	Subjects	Methods	Follow-up time	Exposure	Risk factors considered	All-cause mortality	Ref.
Schwahn *et al.*	2013	Germany	1,803 community residents (Northeastern Germany) aged 49 years or more Male: 897 Female: 906	Cohort study, examination of the oral cavity	9.9 years (median)	Whether the number of teeth is less than 20 teeth, plus the number of unplaced teeth (9 or more, or 8 or less)	Model 1: age, gender, academic history, annual income, marital status, regular dental checkup, dental treatment for toothache Model 2: Model 1plus smoking, risky alcohol, exercise habits, obesity, hypertension, diabetes mellitus and dyslipidemia	Model 1: HR, 1.61 (1.16-2.23); RR, 1.57 (1.11-2.10) Model 2: HR, 1.47 (1.04-2.07); RR, 1.43 (1.05-1.96) * HR, 1.88 (1.10-3.21) for CVD mortality	11
Saarela *et al.*	2014	Finland	1,369 assisted-living residents aged 65 years or more	Cohort study, questionnaire, and MNA	3 years	Classified into three groups: group 1: subjects with edentulous jaw not using dentures, group 2: subjects with edentulous jaw using dentures, group 3: subjects with toothed jaw	Age, gender, comorbidity based on Charlson' s index, and MNA	HR, 1.19 (0.87-1.63) for group 1; HR, 1.15 (0.97-1.37) for group 2 vs. group 3	12
Janket *et al.*	2013	Finland	256 patients with CAD (mean age: 61 years) and 250 control subjects	Cohort study, examination of the oral cavity	15 years: CVD	Classified into four groups by the type of dentures: NT/NT (ref), NT/PD, PD/FD, and FD/FD	Age, gender, smoking, diabetes mellitus, hypertension, and academic history	HR for CVD was highest in PD/FD group at 2.27. HR for CVD of FD/FD group was 1.6 (NS).	13
Ansai *et al.*	2008	Japan	824 community residents aged 80 years	Cohort study, questionnaire	4 years: causes of death	Based on the Yamamoto's masticatory grade: A; 15 food materials, B; 10-14 food materials, C; 5-9 food materials, and D; 0-4 food materials	Gender, smoking, drinking, serum alb, blood sugar, BMI, blood pressure and the presence of hospital visit	D vs. A: HR, 4.6 (1.01-21.1) for CVD	14
Aida *et al.*	2011	Japan	4,425 community residents aged 65 years or more	Cohort study, questionnaire investigation	4 years: causes of death	Classified into five stages by the masticatory status	Gender, age, BMI, self-evaluation of health status, present illnesses, exercise habits, smoking, drinking, academic history, and annual income	Subjects with 19 teeth or less having problems with mastication: CVD mortality, HR, 1.83 (1.12-2.98)	15

variables in each category. Assuming the HR in the category of "absence of either occlusion" as 1, the HR was 0.78 (95% CI: 0.6-0.99) in the category of "molar region occlusion" and 1.08 (0.85-1.36) in the category of "molar region occlusion + front tooth region occlusion". In other words, it was found that those subjects with molar region occlusion lived significantly longer. Furthermore, in the category of "absence of either occlusion", the risk of death was higher in those subjects not using dentures (HR: 1.52 [95% CI: 1.25-1.83]). Next, a study by Semba *et al*.[3] followed up on 826 females aged 70 to 79 years for 5 years in the USA. Results of the study showed the risk of death was significantly higher in those subjects who answered that they were using dentures but were feeling problems in mastication or swallowing than in those subjects who answered that they were not using dentures (HR: 1.43 [95% CI: 1.05-1.97]). A study by Onder, *et al*.[4] followed up on 2,755 residents (mean age: 82 years) for one year in 11 European countries. Results of the study showed the risk of death was significantly higher in those subjects having mastication problems than in those subjects without problems (adjusted HR: 1.45 [95% CI: 1.05-1.99]). In a survey study conducted in Asia, there is a report[5] by Lee *et al*. that studied 1,410 community residents aged not less than 65 years (729 males, 681 females) for 8 years in Taiwan. This study analyzed results of self-evaluation of the masticatory function obtained by using a questionnaire (whether there are food materials difficult to masticate) together with 3 parameters in diagnosis of metabolic syndrome (waist circumference, fasting blood glucose level and neutral fat level) or 5 parameters (the above 3 parameters plus blood pressure and HDL). As a result, the HR was 2.58 (95% CI: 1.58-4.23) in the case of "decreased masticatory function plus 3 parameters" and 1.65 (95% CI: 1.11-2.46) in the case of "decreased masticatory function plus 5 parameters." Another survey conducted in Taiwan by Tsai *et al*.[6] followed up on 2,766 male and female subjects aged not less than 65 years for 4 years in relation to a government survey data. Results showed that the risk of death was higher in those subjects using removable dentures than in those subjects using fixed dentures (HR: 1.31 [95% CI: 1.02-1.69]). On the other hand, we performed a study on 824 community residents in Fukuoka prefecture (aged 80 years as a baseline) for 4 years. Analysis was performed by classifying the self-evaluated masticatory function into four categories (A: 15 food materials can be masticated without problem, B: 10 to 14 food materials can be masticated without problem, C: 5 to 9 food materials can be masticated without problem, D: 0 to 4 food materials can be masticated without problems). Results from analysis showed the risk of death was significantly higher in those subjects showing the lowest masticatory function than in those subjects showing the highest masticatory function (HR: 2.4, 95% CI: 1.1-5.3)[7]. Those subjects were further followed up continuously for a total of 12 years. The HR in those subjects showing the lowest masticatory function was 2.1 (95% CI: 1.4-3.1), being the comparable result 8. In addition, the difference between Category D and Category B and the difference between Category D and Category C, which had not been significant after a 4-year follow-up, became significant[8].

2. Relationship between life-span and occlusion status

A study by Shimazaki *et al*.[9] followed up on 1,929 assisted-living residents in Kitakyushu city (mean age: 79.7 years) for 6 years. The study results showed the risk of death was significantly higher in those subjects with edentulous jaw not using dentures than in those subjects having at least 20 teeth (OR: 1.8 [95% CI: 1.1-2.8]). Further, a study by Watt, *et al*.[10] followed up on 12,871 community residents (mean age: 53 years) for 8 years in the UK. In this survey, the oral cavity status was not examined, and those subjects were classified by self-evaluation into the three categories of "natural teeth alone", "natural teeth + dentures" and "dentures alone", and analyses were performed among them. In results from this study, the risk of death was significantly higher in the category of "dentures alone" than in the category of "natural teeth alone" (HR: 1.3 [95% CI: 1.12-1.5]). A study in Germany by Schwahn *et al*.[11] followed up on 1,803 community residents aged not less than 49 years (897 males, 906 females) for 9.9 years (median value). This study focused on whether the number of teeth was less than 20 and whether the masticatory function was restored by appropriate prosthetic treatment. Those subjects were divided into two groups (a group having at least 9 teeth of inappropriate status and another group having 8 or fewer teeth of inappropriate status). Results from this study show the risk of death was significantly higher in those subjects having at least 9 teeth of inappropriate status (adjusted HR: 1.61 [95% CI: 1.16-2.23]). In a survey study related to edentulous jaw and denture, there is a report[12] by Saarela *et al*. who did a study on up 1,369 assisted-living residents (aged not less than 65 years) in Finland and performed an analysis by classifying those subjects into three groups based on answers to a questionnaire (Group A: subjects with edentulous jaw not using dentures, Group B: subjects with edentulous jaw using dentures, Group C: subjects with toothed jaw). In results from this study, the risk of death tended to be higher in Group A than in Group C (HR: 1.19 [95% CI, 0.87-1.63]) and tended to be higher in Group B

than in Group C (HR: 1.15 [95% CI, 0.97-1.37]), but no significant difference was found between the two groups.

As a supplement to the above, we refer to the risk of death due to cardiovascular disease rather than all causes of death. A study by Janket *et al*.[13] reported on the relation between maxillomandibular occlusion status and cardiovascular disease. They did a follow up study on 256 patients with coronary artery disease and 250 control subjects at Finnish hospitals for 15 years. The maxillomandibular occlusion status was classified into 4 types or namely natural teeth / natural teeth, natural teeth / partial dentures, partial dentures / complete dentures, and complete dentures / complete dentures. The risk of death due to cardiovascular disease was highest in the case of a combination of partial dentures / complete dentures (HR: 2.27 [95% CI: 1.06-4.87]). In case of a combination of complete dentures / complete dentures, there was no significant difference (HR: 1.6 [95% CI: 0.78-3.29, 1.06-4.87]). On the other hand, when we examined the risk of death due to cardiovascular disease in terms of number of food materials which could be masticated, the HR was 4.6 (95% CI: 1.01-21.1) in the group showing the lowest masticatory function (only 0 to 4 food materials could be masticated)[14]. Furthermore, in a report by Aida *et al*.[15], the risk of death due to cardiovascular disease was significantly higher in those subjects who had 19 teeth or less and had problems with mastication (HR: 1.83 [95% CI: 1.12-2.98]).

[Discussion]

1. Relationship between life-span and masticatory function

Previous reports suggested that the higher the masticatory function is, the longer the lifespan. In addition, it was also suggested that the probability of long life-span is high in the persons who can masticate in the molar region. But, in interpreting this, attention should be paid to the method to evaluate the masticatory function. As far as past reports are concerned, the masticatory function was subjectively evaluated by self-evaluation. In other words, it cannot be claimed that masticatory function was directly evaluated. Recent research, methods to directly measure the masticatory function include the gummy jelly method in which gummy jelly is masticated and the amount of dissolved glucose is measured as the mastication efficiency[16] and the chewing gum method using chewing gum that exhibits a color change when masticated[17]. At present, no large-scale follow-up studies have been performed using such methods. As mentioned previously, the questionnaire survey using simple questions such as "Can you masticate anything without problems?" or "Do you have a problem with mastication?" was performed in almost all cases; and the answering method was the two-value style of Yes/No in most cases. On the other hand in rare cases, step-wise answers such as "any materials are chewable", "chewable to some extent", "chewable materials are limited", "there are almost no chewable materials" and "only liquid foods can be eaten" were adopted[15], and as in Yamamoto's mastication efficiency judgment table, judgment was made by the number of food materials considered chewable among 15 food materials. Therefore, objective evaluation methods that are also simple to use need to be developed for future epidemiological surveys.

2. Relationship between life-span and occlusion status

It was found that maintaining a good occlusion status renders a rather large effect on improving systemic health. Maintaining the molar region occlusion is especially important in this regard. As Janket *et al*.[13] stated, when those subjects having both complete denture and partial dentures were compared with subjects having only complete dentures, the prognosis was worse for the former. The presence of partial dentures means that some natural teeth still remain and may to the contrary prevent sufficient oral care and induce gingival inflammation. In the study by Schwahn *et al*.[11] it was stated as essential to keep in mind that even when there are 10 to 20 remaining teeth, the risk of death is high if appropriate prosthesis is not performed for more than half of those remaining teeth. It seems to be a key point to reliably maintain a high level of mastication in the molar region.

3. Potential mechanisms

We would like to discuss the effects of the masticatory function on systemic health. At the present time point, the following five pathways are conceivable: (i) chronic inflammation pathway, (ii) nutrition ingestion pathway, (iii) sarcopenia pathway, (iv) brain activity stimulation pathway and (v) QOL improvement pathway. In this article, the evidence will center on the chronic inflammation pathway and nutrition ingestion pathway.

1) Chronic inflammation (especially periodontal disease) pathway

Many studies focusing on periodontal disease have been reported so far. The report which triggered this trend was published by Mattila, *et al*.[18] in 1989. They are the pioneers in worldwide research about the effects of periodontal disease on systemic health. Since the masticatory function is naturally related to the number of teeth, the positioning of periodontal disease as one of the

pathways is important. Infection by periodontal disease-causing microorganisms and chronic inflammation of the periodontal tissues are considered cumulative and inflammatory markers are transferred throughout the entire body through blood circulation resulting in plaque formation in blood vessels leading to the risks of arteriosclerosis and cerebrovascular diseases.

2) Nutrition ingestion pathway

Some overseas literature has reported that a decrease in masticatory function would affect the total energy ingestion[19]. The same effects were reported in the survey study targeting Japanese people and it was reported that the total energy ingestion was significantly low in the group with low masticatory function[20].

Also reported was that the masticatory function is influential on nutrition types and ingestion amounts. For example, it was reported that when persons with 20 or more teeth were compared with persons having less than 20 teeth, the ingestion amounts of vegetables and sea foods were larger in the former and furthermore the ingestion amounts of vitamin D, vitamin B1, niacin, vitamin B6 and pantothenic acid were larger in the former[21]. In terms of the nutrition ingestion status of Japanese people, it was reported in the analysis based on the National Health and Nutrition Examination Survey that not only the ingestion amounts of vitamins but also the ingestion amounts of minerals such as calcium, magnesium and zinc are small and the ingestion amount of cereal energy is large[22]. It was reported that the ingestion amounts of dietary fiber, proteins, calcium, iron, niacin, vitamin C, vitamin E, and so on were further smaller in elderly people with a lower masticatory function[19]. Furthermore, it was reported that the ingestion amounts of polyunsaturated fatty acids, dietary fiber and fruits was significantly lower in those persons who had lost at least 5 teeth in 8 years than in those persons who had not even lost one tooth (only male healthcare professionals were targeted)[23]. It was pointed out that vitamin C, vitamin E, carotenes, and so on function as antioxidant substances, and that balanced ingestion of vegetables (especially green and yellow vegetables) and fruits may be necessary for improved health.

In addition, there are some reports referring to effects depending on whether dentures are worn or not. In denture wearers, the ingestion amounts of vegetables and fibrous food materials were lower and vitamin C and βcarotene were not ingested sufficiently[24]. Also reported was that the ingestion amounts of vegetables and fruits were lower and the risk of malnutrition was higher in those persons not wearing dentures (in spite of the need for wearing them) and for partial denture wearers in comparison with bridge wearers[6].

Along with the recent increase in elderly people, the problem of sarcopenia has been pointed out. Sarcopenia is defined as the age-related decrease in the amount and strength of skeletal muscle. Research on the relationship between the masticatory function and sarcopenia has just begun and future developments are anticipated yet past research results suggest the possibility that the lowered masticatory function induces sarcopenia. For example, the relationship between occlusion support and frequency of falling[25], the relationship between occlusion support and motor ability[26], the relationship between masticatory function and motor ability[27] and the relationship between walking speed and oral function[28] were reported.

As mentioned above, maintaining and improving the masticatory function will likely lead to improved dietary habits and life functions in the elderly and also prove helpful in reducing the risk of falling into a negative health spiral.

[Conclusions]

In those persons with a high masticatory function or those persons with a stable occlusion status capable of masticating in the molar region, the systemic health status was also favorable and the risk of death was significantly lower.

[Conflict of interest]

There are no items applicable to “conflict of interest” in this article.

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2. Oral health (tooth condition, mastication, oral diseases, etc.) and life span
3) Oral disease and life span

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[Abstract]

Domestic and overseas research results up to the present point on the relation between oral health status and systemic health status were accumulated. The article from these research results were reviewed here utilizing dental caries (coronal, root), periodontal disease and oral health as key words and also utilizing death or survival as the outcome. These results revealed that there is almost no literature dealing with the relationship between dental caries and life span. However, since the American Heart Association (AHA) issued a review article on the relation between periodontal disease and life span in 2012, there has been a move towards reevaluating in particular the standardization of research design and study methodology in this field. In investigating the relationship between oral care habits and life span it was found that those persons that regularly brush their teeth and visit a dentist tended to live longer.

[Introduction]

The relationship between oral health status and systemic health status is widely known. Domestic and overseas researchers have been continuously making intensive research efforts to reveal the relation between periodontal disease and systemic health. The American Heart Association (AHA) published the outcomes of this research in the form of a statement in 2012 in an article on the relation between periodontal disease and cardiovascular diseases (atherosclerotic disease). This is a review article extending to 25 pages and describing the past history of this work [1]. Their conclusion was that though there are mutual correlations the causal relationships have not been clarified and there is still no evidence demonstrating that the treatment of periodontal disease is helpful in preventing cardiovascular disease. This review article seems to have accelerated a movement towards reconfirmation of these results by domestic and overseas researchers. Currently however there is almost no evidence supporting the relationship between oral diseases other than periodontal disease and systemic health or life span.

Therefore, in this article, we would like to discuss the relationship between life span and periodontal disease or tooth decay and furthermore the relation between life span and daily habits related to the oral cavity such as oral care, mouth cleaning, etc.

[Objective]

The objective of this study was to organize and discuss the relevant information obtained by a literature survey using key words related to oral diseases and life span.

[Methods]

This study was performed by way of a literature survey. The literature inclusion criteria were as follows: (i) studies performed focusing on humans, (ii) literature written in English or Japanese, (iii) original articles or para-original articles, and (iv) literature published on or after 2000. Here, PubMed and ICHUSHI were utilized in the Internet search, and manual search was also performed for literature not obtained by Internet search. In addition, the reported contents and titles/abstracts were also checked in detail, and literature definitely different from the objective of this study, literature with overlapping content and epidemiological survey studies not adjusted with confounding factors were excluded. The key words utilized were Ushoku (dental caries, root caries, dental decay), Kouku hoken (oral health), Shishubyou (periodontal disease), Shibou (mortality), Seizon (survival) and Tsuiseki kenkyu (cohort).

[Results]

In the literature survey, 8 texts were obtained which are outlined in Table 2.

1. Relationship between risk of death and tooth decay

Thorstensson and Johansson[2] made a study following up on 357 community residents aged 86 years (median value) for 8 years in Sweden and found that those with a high DF%

Table 1: Relationship between life span and dental caries, periodontal disease or oral care habit

Authors	Year	Country	Subjects	Methods	Follow-up time	Exposure	Risk factors considered	Mortality	Ref.
Thorstensson and Johansson	2009	Sweden	357 community residents aged 86 years (median value): Octagenarian twin study	Cohort study, examination of the oral cavity	8 years	Number of teeth, dental caries, restored teeth, and bone absorption due to periodontal disease	Based on the Kaplan-Meier method	Subjects with high DF% lived longer and those with severe periodontal disease lived shorter (only applicable to male subjects).	2
Kim *et al.*	2013	U.S.A	5,588 males and females aged 40 years or more, NHANES National Data	Cohort study, examination of the oral cavity	7 years	Number of teeth, tooth root decay, and periodontal disease evaluation by PD and CAL	Age, gender, academic history, race, heart disease, diabetes mellitus, stroke, cancer, obesity, and smoking	Tooth loss: OR, 1.34 (0.96-1.88); tooth root decay: OR, 1.29 (0.88-1.89); periodontal disease: OR, 1.30 (0.92-1.84)	3
Avlund *et al.*	2009	Denmark	1,914 people aged 70 years	Cohort study, CPI for all teeth	21 years	Whether the subject has at least three teeth with a PD of 6 mm or more, or 0 to two teeth with a PD of 6mm or more	Gender, annual income, tiredness (Mob-T scale), and smoking	Subjects with three or more teeth with inflammation: HR, 1.37 (0.97-1.92), and subjects with smoking habit: HR, 1.17 (1.06-1.30).	4
Holmlund *et al.*	2010	Sweden	7,674 patients with periodontal disease treated at university hospitals, aged 20 to 89 years, Male: 3,300, Female: 4,374	Cohort study, examination of the oral cavity, and dental photography	12 years	Number of teeth, PD, bone absorption, and periodontal severity index	Age, gender, and smoking	All-cause mortality, and mortality related to CVD and CHD had no relationships with periodontal disease. All-cause HR was 2.68 (1.96-3.67) for subjects with less than 10 teeth, which showed significant relation. Deaths related to CVD and CHD showed similar significant relation.	5
Xu and Lu	2011	U.S.A	10,849 males and females aged 30 years or more: NHANES III National data	Cohort study, probing	18 years	PD was classified into three groups: non, modest, and severe.	Age, gender, race, annual income, academic history, smoking, drinking, obesity, TC/HDL ratio, hypertension, and the history of heart disease	Female subjects showed no significant relation. Male subjects aged 65 years or more showed no significant relation. Male subjects aged 30 to 64 years showed significant relation: HR, 2.13 (1.37-3.31) for CVD; HR, 1.64 (1.25-2.15) for all-cause mortality.	6
Renvert *et al.*	2014	Sweden	870 community residents aged 60 to 96 years	Probing, and panoramic/tomographic photography	6 years	PD and bone absorption in panoramic/tomographic photography	Based on the Kaplan-Meier method and the Pearson's chi-square test	No significant relation between death and periodontal disease	7

Table 1: (Continued)

Authors	Year	Country	Subjects	Methods	Follow-up time	Exposure	Risk factors considered	Mortality	Ref.
Paganini-Hill *et al.*	2011	U.S.A	5,611 males and females aged 81 years (median value)	Cohort study, questionnaire	17 years	Number of teeth, dentures, habit of brushing teeth, usage of dental floss and/or mouthwash, habit of cleaning dentures, regular dental checkup	Age, smoking, drinking, caffeine consumption, exercise habits, BMI, blood pressure, heart attack, angina, stroke, diabetes mellitus, rheumatoid arthritis, and cancer	No habit of brushing teeth before going to bed: HR for male subjects; 1.34 (1.14-1.57), and HR for female subjects 1.19 (1.02-1.38), no usage of dental floss: HR for male subjects; 1.27 (1.11-1.46) and HR for female subjects 1.28 (1.16-1.42); no habit of brushing teeth every day: HR for male subjects; 1.37 (1.05-1.80), and HR for female subjects; 1.77 (1.38-2.28); no habit of cleaning dentures: HR for male subjects; 1.24 (1.03-1.48), no regular dental checkup: HR for male subjects; 1.23 (1.05-1.45), and HR for female subjects; 1.20 (1.07-1.35)	7
Hayasaka *et al.*	2013	Japan	21,730 community residents aged 65 years or more	Cohort study, questionnaire	4 years	Number of teeth (0-9, 10-19, and 20 or more), and oral care habits (brushing teeth at least twice a day, visiting a dentist at least once a year, and cleaning dentures)	Age, gender, academic history, smoking, drinking, BMI, walking, past medical history, stress, and nutrients and energy intake	Subjects having all three types of oral care habits (brushing teeth at least twice a day, visiting a dentist at least once a year, and cleaning dentures) : all-cause HR; 0.54 (0.45-0.64)	8

lived a long time and that those with severe periodontal disease lived a short time. But the relation between life span and periodontal disease was seen only in the male subjects. A study made by Kim *et al*.[3] mentioned root caries in this regard. In the survey related to US NHANES National Data, they followed up on 5,588 males and females aged not less than 40 years for 7 years and found that the probability of death tended to be higher in persons with root caries, but no significant relationship was found in the final model.

2. Relation between risk of death and periodontal disease

A study made by Avlund *et al*.[4] followed up on 1,914 persons aged 70 years for 21 years in Denmark and determined the CPI (Community Periodontal Index) for all teeth. The risk of death was higher in those persons having at least 3 teeth with PD of 6 mm or more than in those persons having 0 to 2 teeth with a PD of 6 mm or more (the HR (hazard ratio) adjusted with confounding factors: 1.37 (95% CI, 0.97-1.92)), but the difference was not statistically significant. On the other hand, Holmlund *et al*.[5] performed a study following up 7,674 patients with periodontal disease treated at university hospitals (aged 20 to 89 years, 3,300 males and 4,374 females) for 12 years, but the HR adjusted with confounding factors in all deaths showed no significant difference. The risk of death related to cardiovascular diseases also showed no relation. However, when using the number of teeth as an explanatory (independent) variable, the HR in all deaths was 2.68 (1.96-3,67) for persons having less than 10 teeth thus showing a significant relation. A similar significant relationship was seen also in cardiovascular disease-related deaths. In this area, Xu and Lu[6] made a study following up on 10,849 males and females aged 30 years or more for 18 years in the USA using NHANES III National Data. When limited to male patients with severe periodontal disease aged 30 to 64 years, a significant relation was seen in both deaths and cardiovascular disease-related deaths (HR was 2.13 [95%CI: 1.37-3.31] and 1.64 [1.25-2.15], respectively). No significant relationship was seen in males aged 65 years or more and in females of all ages. In the aforementioned report by Kim *et al*. no significant relationship was seen between periodontal disease and death (OR: 1.3 [95% CI, 0.92-1.84]). Also in the latest reports, similar results were obtained by Renvert *et al*.[7] who made a study following up on 870 community residents aged 60 to 96 years for 6 years in Sweden. However no significant relationship was seen between death and periodontal disease diagnosed with PD and bone absorption in panoramic/tomographic photography in the Kaplan-Meier method and in the Pearson's chi-square test.

3. Relationship between risk of death and oral care habits

In this respect, two reports were useful. One was a study by Paganini-Hill *et al*.[8] that followed up on 5,611 males and females aged 81 years (median value) for 17 years in the USA and found that the risk of death was significantly higher in persons having inadequate oral care habits. For example, the risk of death was significantly higher in those persons having no habit of brushing their teeth before going to bed (HR: 1.34 (95% CI, 1.14-1.57) in males and 1.19 (1.02-1.38) in females). Similarly, the risk of death was significantly higher, irrespective of gender in persons not using dental floss, persons not brushing their teeth every day, persons with dentures but not cleaning their dentures and the persons not periodically visiting a dentist at all for one year. In addition, Hayasaka *et al*.[9] did a study following up on 21,730 community residents aged 65 years or more for 4 years in Japan. The risk of death was significantly lower in those persons having adequate oral care habits (brushing teeth at least twice a day, visiting a dentist at least once a year, cleaning dentures) (HR in all deaths: 0.54 [95% CI, 0.45-0.64]).

[Discussion]

1. Relationship between life span and dental caries

There are almost no articles dealing with the relation between life span and dental caries, and only two articles were mentioned in this study. Thorstensson and Johansson[2] divided the DFS% of each subject into three levels and calculated an index called the LQ (Longevity Quotient). When the life span is equal to the standard life span defined from the age, gender and birth place, the LQ is 1, and when shorter than the standard life span, the LQ is lower than 1. In their article, the LQ was 0.7 (median value), being lowest in the group with a low DFS%. In other words, they stated that those persons with a high DFS% lived longer. They speculated that this was probably because many persons with a high DFS were at a higher level in terms of socioeconomic background and academic history. In addition, Kim *et al*.[3] performed a similar analysis for the 3 items of tooth loss, periodontal disease and tooth root decay using the NHANES National Data, but when adjusted with covariates such as socioeconomic background, academic history, and healthy activity no significant relationship was seen. These discussions suggest that environmental factors such as oral care habits render significant effect in comparison with the effects of organic changes alone (number of teeth, periodontal disease, etc.) as mentioned later.

2. Relationship between life span and periodontal disease

Since the AHA published the review article [1] in 2012 there has been a movement towards standardization of study design and methodology [10]. The AHA also referred in the review article, to standardization of periodontal disease evaluations (i.e., definition of PD depth or area), the cohort period, and selection of appropriate confounding factors or effect modifiers. A study by Polzer *et al*.[11] made the following proposals about study design: 1) subjects aged less than 65 years should be excluded, 2) changes in exposure factors during the follow-up period should be evaluated and a model suitable to such changes should be used, 3) the exposure factors (e.g., periodontal disease and number of unreplaced teeth) should be clearly defined according to the hypothesis, 4) appropriate confounding factors should be incorporated into the model, and 5) if the nutrition pathway is discussed, then subjects with a history of cancer should be excluded (because it is likely that food materials and dietary habits will change). Hereafter, the research study design will have to modify to include these factors.

3. Relationship between life span and oral care habits

It is reasonable to conclude that persons with adequate oral care habits live longer lives. The interesting point in the study by Paganini-Hill *et al*.[8] is that there were no sexual differences. However, the risk of death was significantly higher in males not cleaning their dentures at all but showed no relation in corresponding females. In addition, the risk of death was significantly higher in persons not using dental floss at all irrespective of gender, but such a relation was not seen in use of mouth-washing fluid or toothpicks.

[Conclusions]

The relationship between life span and oral disease (dental caries or periodontal disease) was examined, but sufficient evidence was not obtained to conclude a clear relation. On the other hand, it was found that persons with regular oral care habits lived a long time.

[Conflict of interest]

There are no items applicable to “conflict of interest” in this article.

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3. Oral health and lifestyle-related diseases, non-communicable diseases (NCDs)

1) Diabetes
   – Impact of diabetes mellitus on oral cavity and effects of dental care in patients with diabetes mellitus –
2) Respiratory diseases including pneumonia
   – Oral care and prevention of aspiration pneumonia and ventilator associated pneumonia –
3) Cancer
   – Role of oral care in cancer treatment –
4) Cardiovascular diseases (heart and blood vessel diseases and cerebral vascular diseases)
   – Oral health and cardiovascular diseases –
5) Metabolic syndrome (obesity, dyslipidemia, hypertension, diabetes mellitus)
6) Risk factors for NCDs (smoking, excessive alcohol consumption, lack of exercise, and eating habits) and oral health

3. Oral health and lifestyle-related diseases, non-communicable diseases (NCDs)

1) Diabetes

– Impact of diabetes mellitus on oral cavity and effects of dental care in patients with diabetes mellitus –

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[Abstract]

A number of studies have reported on the association between oral diseases including periodontal diseases and diabetes. This review provides an overview of these relationships, as well as the effects of dental treatment.

We searched articles published in 2000 and thereafter regarding the associations between diabetes and dental caries, periodontal disease, and implants, using electronic search databases, and conducted a hand search. A total of 16 articles were found to be relevant with the association between dental caries and diabetes, suggesting a possible correlation with type 1 diabetes. There were 7 reports on the association with implant treatment outcoms. As for the association between diabetes and periodontal disease, three systematic reviews were found, as well as one original research article published after the end of the search period covered by those review articles, all of which demonstrating the association between the two diseases. Five meta-analyses and three intervention studies conducted after the search period of those above-mentioned meta-analyses reported on the improved glycemic control following periodontal treatment, suggesting that periodontal treatment is effective in improving diabetes. One study (two reports) addressed the screening of diabetes patients in dental setting, indicating the possible contribution of dental care to prevent exacerbation of diabetes.

Taken together, diabetes affects diseases of the oral cavity, and in particular, it is closely associated with periodontal diseases. Dentists could contribute to the improvement and control of diabetes by working in cooperation with physicians.

[Introduction]

Diabetes is a metabolic disease caused by abnormalities such as disorders of glucose metabolism and exhibits chronic hyperglycemia. In Japan, more than 20 million people are affected by diabetes, including those with borderline diabetes. People who are affected by diabetes or those at the pre-diabetic stage develop insulin resistance, with an increased likelihood of developing complications such as macrovascular and microvascular diseases (e.g., nephropathy, retinopathy, peripheral neuropathy). Thus, diabetes is regarded as a major disease that directly leads to QOL decrease and currently accounts for 15% of national health care expenditures. For these reasons, measures against diabetes represent an issue to be addressed in the entire medical field.

The characteristics of oral cavity in diabetic patients tend to show the high occurrence and progression of periodontal disease and dental caries, due to the increased susceptibility to infection and proneness and decreased saliva secretion. In addition, healing after dental treatment is known to be poor. Evidence that suggests a bi-directional link between diabetes and oral diseases (especially periodontal disease) has been accumulating in recent years, then the collaborative care by dental and medical professions has attracted increasing attention.

[Objective]

This review aims to 1) examine the associations between diabetes and dental diseases such as dental caries and periodontal disease, as well as implant treatment, and 2) examine the effects of dental care on the prevention of diabetes and exacerbation of diabetes, with a focus on periodontal treatment for which evidence has already been gradually accumulating.

[Methods]

We used PubMed as an electronic search database to conduct our searches (last search date: July 10, 2014). The literature search strategy is as follows: with regard to periodontal diseases ("periodontal diseases"[mh]

OR periodontium[mh] OR periodontics[mh]), dental caries ("dental caries"[mh]), and dental implant ("dental implant" OR "osseointegration"[mh]), we referred to a review by Teeuw *et al.*[1] and performed searches with relevant terms ("diabetes mellitus"[mh] OR "diabetes insipidus"[mh] OR diabet*[tiab] OR "dm 1"[tiab] OR "dm i"[tiab] OR "dm 2"[tiab] OR "dm ii"[tiab] OR "hemoglobin a, glycosylated"[mh] OR a1c[tiab] OR "hb a1c"[tiab] OR hba1c[tiab] OR "blood glucose"[mh] OR "blood sugar"[tiab] OR ((glucose[ti] OR sugar[ti]) AND (level[ti] OR control[ti])) OR hyperglycemia[mh] OR hypoglycemia[mh] OR glycemi*[tiab] OR glycaemi*[tiab] OR hyperglyc*[tiab] OR hypoglyc*[tiab]), using "Humans" and "English" as filters.

The search period was set as May 2012 and thereafter, given that a number of systematic reviews and meta-analyses have been conducted for the same purpose regarding periodontal disease covering the period up to this date. With regard to dental caries, the search period was set as January 2000 and thereafter.

We conducted a hand search of retrieved literature to select the literature in accordance with the purpose of this review.

[Results]

1) We found 185 reports on the association between dental caries and diabetes. Of these, original articles that matched the purpose of this review included 12 articles which targeted patients with type 1 diabetes (Table 1), three articles which targeted patients with type 2 diabetes (Table 2), and one article concerning insulin resistance due to obesity (Table 3).

With respect to the association between periodontal disease and diabetes, three meta-analyses and systematic reviews had been reported (Table 4), and among the 135 reports extracted within the present search period, only one observational study was not included in these reports (Table 5). In addition, there were 61 reports regarding the association between implant treatment and diabetes, of which seven were reports on the success rates of

Table 1: Literature regarding the association between dental caries and type 1 diabetes

Authors	Report year	Place of survey	Study design	Main results	Ref. no.
Moore *et al.*	2001	U.S.A	Retrospective	406 persons in the long-term diabetes group showed a significantly higher incidence of root surface caries than that in 202 persons in the non-diabetes group.	2
Twetman *et al.*	2002	Sweden	Prospective (2 years)	In 64 diabetic persons (8-15 years old), high value of HbA1c was associated with incidence of caries.	3
Syrjälä *et al.*	2003	Finland	Cross-sectional	In 149 diabetic persons no association was observed between HbA1c and DMFT.	4
Lalla *et al.*	2006	U.S.A	Case control	No significant difference was observed in incidence of caries between the group of 182 diabetic persons and the group of 160 non-diabetic persons (8-18 years old).	5
Bakhshandeh *et al.*	2008	Iran	Cross-sectional	In 299 diabetic persons high value of HbA1c was associated with DMFT.	6
Siudikiene *et al.*	2008	Lithuania	Prospective (2 years)	No significant difference was observed in the number of caries experienced between the diabetic group of 63 persons and the non-diabetic group of 63 persons (10-15 years old).	7
Saes Busato *et al.*	2010	Brazil	Cross-sectional	The diabetic group of 51 persons showed a significantly higher DMFT than that in the non-diabetic group of 51 persons.	8
Miko *et al.*	2010	Hungary	Cross-sectional	The diabetic group of 259 persons showed a significantly higher DMFT than that in the non-diabetic group of 259 persons	9
Tagelsir *et al.*	2010	Belgium	Cross-sectional	No significant difference was observed in the number of caries experienced between the diabetic group of 52 persons and the non-diabetic group of 50 persons (3-16 years old).	10
Rai *et al.*	2011	India	Cross-sectional	The diabetic group of 100 persons showed a significantly higher incidence of caries experienced than that in the non-diabetic group of 100 persons.	11
Akpata *et al.*	2012	Kuwait	Cross-sectional	The diabetic group of 53 persons showed a significantly higher incidence of caries experienced than that in the non-diabetic group of 53 persons (12-15 years old).	12
El-Tekeya *et al.*	2012	Egypt	Cross-sectional	No significant difference was observed in the number of caries experienced between the diabetic group of 50 persons and the non-diabetic group of 50 persons (6-9 years old).	13

Table 2: Literature regarding the association between dental caries and type 2 diabetes

Authors	Report year	Place of survey	Study design	Main results	Ref. no.
Sandberg *et al.*	2000	Sweden	Cross-sectional	102 persons in the diabetic group shoed a significantly higher incidence of caries than that in 102 persons in the non-diabetic group.	14
Hintao *et al.*	2007	Thailand	Cross-sectional	105 persons in the diabetic group shoed a significantly higher incidence of root surface caries than that in 103 persons in the non-diabetic group.	15, 16
Jawed *et al.*	2011	Pakistan	Cross-sectional	398 persons in the diabetic group showed a significantly higher DMFT than that in 395 persons in the non-diabetic group.	17

Table 3: Literature regarding the association between dental caries and insulin resistance

Authors	Report year	Place of survey	Study design	Main results	Ref. no.
Loyola-Rodriguez *et al.*	2011	Mexico	Cross-sectional	The DMFT of 4.78 for the group of onset of insulin resistance due to obesity was significantly higher than DMFT of 3.02 for the group of healthy individuals.	18

Table 4: Literature regarding the association between periodontal disease and diabetes (meta-analyses, systematic reviews)

Authors	Report year	Study design	Main results	Ref. no.
Khader *et al.*	2006	18 meta-analyses (Search period: 1970-October 2003)	Compared to the control group, the diabetic group showed attachment loss of 0.612mm (95% confidence interval: 0.462, 0.761).	19
Chávarry *et al.*	2009	27 meta-analyses (Search period: January 1980-June 2007)	Compared to the control group, the diabetic group showed attachment loss of 1.00mm (95% confidence interval: 0.15, 1.84).	20
Borgnakke *et al.*	2013	17 systematic reviews (Search as of January 2013)	Type 2 diabetic patients was associated with periodontal disease[22-24], and incidence of diabetes complication increased along with advance of periodontal disease[25,26]. Diabetic prevalence increased in patients with severe periodontitis [27-29].	21

Table 5: Literature regarding the association between periodontal disease and diabetes after the analyses shown in Table 4

Authors	Report year	Place of survey	Study design	Main results	Ref. no.
Arora *et al.*	2014	U.S.A.	Cross-sectional	Of 1,165 non-diabetic subjects, those with severe periodontal disease showed a higher probability of being in the pre-diabetes stage. Odds ratio: 2.05 times (95% confidence interval: 1.24, 3.39)	30

Table 6: Literature on the association between implant treatment and diabetes

Authors	Report year	Place of survey	Study design	Main results	Ref. no.
Morris *et al.*	2000	New Zealand	Prospective (3 years)	No significant difference was observed in failure rates between implantation to diabetic patients (20/255 teeth, 7.8%) and that to non-diabetic patients (180/2,632 teeth, 6.8%).	31
Olson *et al.*	2000	U.S.A.	Prospective (5 years)	The failure rate of implantation to type 2 diabetic patients was 9.0% (16/178 teeth) and the factor affecting the failure rate was "duration of diabetes."	32
Tawil *et al.*	2008	Lebanon	Prospective (Average: 42 months)	Failure rate of implantation was significantly higher in the diabetes group (6/255 teeth, 2.4%) than that in the non-diabetes group (2/244 teeth, 0.8%). The higher HbA1c is, the more bone resorption caused by peri-implantitis becomes.	33
Oates *et al.*	2009	U.S.A.	Prospective (3 years)	(Type 2) diabetes group with HbA1c of 8.1% or higher: Average 12 weeks to achieve initial fixation of 12 teeth The non-diabetic group & the diabetic group with HbA1c of 8.0% or less: Average 4 weeks to achieve initial fixation of 30 teeth	34
Anner *et al.*	2010	Israel	Retrospective (31±28 months)	Diabetic group: failure rate was 2.8% (5/177 teeth), non-diabetic group: failure rate was 4.8% (72/1480 teeth). Thus, diabetes has no association with success rate of implant treatment.	35
Ferreira *et al.*	2006	Brazil	Cross-sectional	Adjusted odds ratio of onset of peri-implantitis was 1.9 times (1.0-2.2) higher for the diabetic group, where peri-implantitis developed in 7/29 teeth (24.1%) for the diabetic group and 11/183 teeth (6.5%) for the non-diabetic group.	36
Renvert *et al.*	2014	Sweden	Retrospective	Onset of peri-implantitis was significantly associated with diabetes history, where 10 of 172 persons who developed peri-implantitis had diabetes history while 1 of 98 persons who developed peri-implant mucositis or had healthy mucous had diabetes history (Odds ratio: 6.1).	37

Table 7: Literature on improved blood glucose level associated with periodontal treatment (meta-analysis)

Authors	Report year	Study design	Main results	Ref. no.
Janket *et al.*	2005	10 studies/9 meta-analyses[39-47] (Search period: 1980-January 2005)	HbA1c decreased by 0.38% after periodontal treatment (95% confidence interval: 0.7, 1.5)	38
Teeuw *et al.*	2010	5 meta-analyses[45, 48-51] (Search period: 1960-March 2009)	HbA1c decreased by 0.40% after periodontal treatment (95% confidence interval: 0.04, 0.77)	1
Simpson *et al.*	2010	3 meta-analyses[48, 49, 53] (Search as of March 2010)	HbA1c decreased by 0.40% 3 weeks after periodontal treatment (95% confidence interval: 0.01, 0.78)	52
Engbretson *et al.*	2013	11studies/9 meta-analyses[48-50, 53, 55-59] (Search period: October 2009-July 2012)	HbA1c decreased by 0.36% 3 months after periodontal treatment (95% confidence interval: 0.54, 0.19)	54
Sgolastra *et al.*	2013	6 studies/5 meta-analyses[48, 55, 58, 59, 61] (Search as of May 2012)	HbA1c decreased by 0.65% 3 months after periodontal treatment (95% confidence interval: 0.43, 0.88)	60

Table 8: Literature published after the analyses shown in Table 7 regarding the effects of periodontal treatment on glycemic control

Authors	Report year	Place of survey	Study design	Main results	Ref. no.
Santos *et al.*	2013	Brazil	RCT	With 38 patients with chronic periodontal disease, 2 groups were compared, i.e. with and without application of chlorhexidine gel to full-mouth scaling or mouthrinsing within 24 hours. As a result, neither group showed any significant improvement in HbA1c.	62
Munenaga *et al.*	2013	Japan	RCT	Of the subgroups with high-sensitive CRP, the group that received periodontal treatment together with antibacterial agent (42 persons) significantly improved in HbA1c in 3 months, compared with the non-treatment group (62 persons).	63
Engebretson *et al.*	2013	U.S.A.	RCT	From comparison in 6 months between the periodontal treatment group (257 persons) and non-treatment group (257 persons), no significant improvement was observed in HbA1c.	64

Table 9: Literature on the prediction of diabetes by dental examination

Authors	Report year	Place of survey	Study design	Main results	Ref. no.
Lalla *et al.*	2011	U.S.A.	Prospective	Subjects are 506 new patients of dental clinics who have never been diagnosed as having diabetes. The screening conditions and results obtained are as follows: (1) Persons with periodontal pockets of 5mm or more accounted for 26% or more, (2) Probability that persons with 4 or more lost teeth are diagnosed as having diabetes is 73%, and (3) When the additional condition of HbA1c of 5.7% or more is added to the above, the probability reaches 92%.	65
Lalla *et al.*	2013	U.S.A.	Prospective	When the number of subjects in the above article 65 is increased to 1,097 persons, the screening sensitivity in combination with HbA1c is 90%.	66

implantation (including peri-implantitis) (Table 6).

2) With regard to the prevention of exacerbation of diabetes associated with dental treatment, there had been five meta-analyses particularly concerning periodontal treatment (Table 7), and three intervention studies that were conducted during the period not covered by those analyses (Table 8).

In addition, in terms of the prevention of diabetes associated with dental care, we found two relevant reports suggesting the possibility that dental examination might help screen patients with diabetes, as well as those at the pre-diabetic stage (Table 9).

[Discussion]

Based on the results of the present searches, dental caries, periodontal disease, and implant treatment have been shown as the impacts of diabetes on the oral cavity.

The 13 reports regarding the association between dental caries and type 1 diabetes targeted children and young patients, and seven found associations in some way or other. In terms of the mechanisms of association, it has been observed that high viscosity and sugar concentrations in the saliva of patients with diabetes have impacts on the increase in active dental caries in these patients[7]. Lifestyles that likely induce dental caries are possibly interrelated with the deterioration of glycemic control. In fact, a 3-year retrospective cohort study of patients with type 1 diabetes (8-16 years old) reported that the group with high risk-assessment scores for dental caries, which were obtained based on dental caries preventive behaviors and saliva properties (26 patients), showed a significantly worsened glycemic control (odds ratio (OR), 7.3-fold: 95% confidence interval (CI), 2.0-26.5) compared to the group with low scores (38 patients)[67].

The studies that targeted type 2 diabetes suggested an association with root surface caries. The attachment loss of periodontal tissue in patients with diabetes is large, which could increase exposure of the root surface, and hence, increase root surface caries. There was no difference in the prevalence of coronal caries, but in a study that reported a ≥2-fold incidence of root surface caries[15], the amount of saliva was lower in the group of patients with diabetes compared to the group of healthy individuals, while the buffer capacity of saliva was about the same. Moreover, the condition of plaque formation was observed to be slightly worse in the group of patients with diabetes. Similarly, the progression of periodontal disease and high incidence of root surface caries in patients with type 2 diabetes have been observed in another report as well[14]. In a bacteriological analysis, while there was no difference in the number of periodontal pathogens, significantly more *Streptococcus mutans* and lactic acid bacteria associated with dental caries were detected, suggesting that their oral environment is likely to develop dental caries[16].

Periodontal disease has long been associated with diabetes, and is indeed expressed as "the sixth complication"[68]. Several systematic reviews and meta-analyses have already been performed in this point. Recent analyses targeting large-scale studies have focused on associations between type 2 diabetes and periodontal disease. Although patients with type 1 diabetes reportedly have a higher incidence of periodontal disease compared to healthy individuals[69], the most recent systematic review found no appropriate evidence supporting this[21]. Moreover, Morita *et al*. have reported that patients with type 2 diabetes have an increased risk of alveolar bone resorption compared to healthy individuals[24]. Another cohort study conducted in Japan[70] found no significant difference except in female subjects with moderate periodontitis, and thus, future investigation is necessary for reliable evidence.

Among topics receiving the most attention today is the improvement of glycemic control with dental treatment. So far, a number studies have been conducted, including recent clinical studies with high-level evidence; there have also been several analyses on those studies. Among the studies that targeted patients with type 1 diabetes, several reported no significant difference in the improvement of glycemic control[44], and no consensus has been obtained in the effect

of periodontal treatment on glycemic improvements. Recent analyses demonstrated the effectiveness of periodontal treatment intervention on type 2 diabetes , including several meta-analyses[1,52,54,60], and according to the relevant literature, it is expected that a 0.4-0.6% decrease in HbA1c can be achieved as a 3-month post-treatment assessment after non-surgical periodontal procedures such as scaling and root planing. The largest randomized controlled study to date recently reported that non-surgical periodontal treatment (scaling and root planing) had almost no effect on glycemic control[64]. However, in this report, the periodontal parameters after periodontal therapy also did not improved adequately. The control of periodontal tissue inflammation, it is crucial point, was not performed as reflected by residual periodontal pockets and gingival bleeding on probing (BOP) in 40% postoperatively. Considering the mechanisms of glycemic improvements associated with periodontal treatment, it was likely to be difficult to detect any effects. This report has received a number of comments, including one that pointed out the lack of thoroughness in periodontal infection control[71]. Future clinical studies that employ multi-center and large-scale designs are necessary to obtain higher-level evidence.

With regard to the impact of diabetes on implant treatment, several basic experiments have demonstrated that under hyperglycemic condition, the calcification ability of osteoblasts is decreased[72], raising concerns about the impact on osseointegration. In this review, a significant decrease in success rates of implant treatment was found in a number of reports, but this did not lead us to conclude that sufficient evidence has been gathered. Moreover, increased occurrence of peri-implantitis, as well as the influence of hyperglycemia on periodontitis, has been concerns. A recent retrospective risk factor analysis showed that patients with diabetes whose glycemic control has not been achieved clearly had a higher risk of developing peri-implantitis[37]. Since only a few large-scale data exist with regard to peri-implantitis itself, in terms of the effects of diabetes as well, future investigation with a sufficient sample size and control studies are required.

Increased tooth loss is known to be an oral characteristic of patients with diabetes[73]. In a large-scale epidemiological study, patients aged 50 years and older who were affected with diabetes had a 2.25-fold OR for becoming edentulous[74]. Given such characteristic and progression of periodontal disease, an attempt has been made to screen diabetes based on oral findings. According to the results of a clinical study conducted at Columbia University, among undiagnosed diabetes patients, 73% of those who had lost four or more teeth and had periodontal pockets of which 26% or more were 5 mm or deeper could be diagnosed with diabetes. Furthermore, checking the HbA1c could increase the accuracy of screening. Adding the HbA1c >5.7% increased the correct identification up to 92%[65]. The reliability of this model has already been confirmed by increasing the number of sawples[66].

[Conclusions]

Diabetes affects diseases in the oral cavity, and in particular, periodontal disease has a close association with diabetes. In this context, dentists have a potential role in contributing to the improvement of glycemic control. Moreover, there is a possibility that performing oral health care may lead to early detection of diabetes or provide an opportunity to edify patients in the pre-diabetic stage, underscoring the need to further promote medical-dental cooperation in the future.

[Conflict of interest]

There are no items applicable to conflict of interest in this article.

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3. Oral health and lifestyle-related diseases, non-communicable diseases (NCDs)

2) Respiratory diseases including pneumonia – Oral care and prevention of aspiration pneumonia and ventilator associated pneumonia –

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[Abstract]

It has widely recognized that oral care can prevent aspiration pneumonia in the elderly. Moreover, it has been demonstrated the relationship between oral care practice and prevalence of ventilator-associated pneumonia in the Western countries. The role of oral care in the prevention of respiratory diseases has been emphasized, however the dentists cannot play an important role in this field. We have to develop a new strategy for our future.

[Introduction]

After we reported the possibility of oral care to prevent aspiration pneumonia in Lancet in 1999,[1] the activities of oral care has been progressing. And now oral care is one of medical term and nursing routine practice for the prevention of aspiration pneumonia[2].

Moreover, oral care has also been reported to be effective against ventilator-associated pneumonia (VAP), which is a major problem in Intensive Care Unit (ICU) management. Some oral care kits for ICU care are available commercially in Western countries today.

Oral care has significantly decreased pharyngeal bacteria[3], indicating that dentistry can play a major role for the prevention of respiratory infection. Therefore, the dentist should play more active roles for the prevention of aspiration pneumonia. In this study, we address what we should do for the future medical-dental cooperation.

[Objective]

The aim of this study is to clarify the scientific evidence from recent review articles and address what to do next to establish the task of dentist for prevention of respiratory diseases.

[Methods]

We used PubMed to search recent review articles published from January 2010 to January 2014 regarding oral care, aspiration pneumonia, and VAP, because old review articles do not provide recent information. In addition, we performed an individual search for the latest papers.

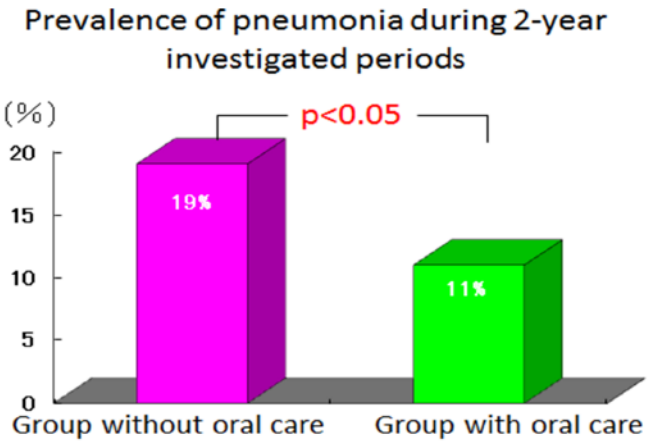

Figure 1: Prevalence of pneumonia duaring 2-year Investigated periods

From references 1 and 10

Yoneyama T, Yoshida M, Matsui T, Sasaki, H. Oral care and pneumonia. Lancet 1999; 354(9177): 515.

Yoneyama T, Yoshida M, Mukaiyama H, Okamoto H, Hoshiba K, Ihara S, Yanagisawa S, Ariumi S, Morita T, Mizuno Y, Ohsawa T, Akagawa Y, Hashimoto K, Sasaki H. Oral care reduces pneumonia of elderly patients in nursing homes. J Am Geriatr Soc 2002; 50(3): 430-433.

(Bar graph created by authors based on original data)

[Results]

Six review articles were found with regard to oral care and prevention of aspiration pneumonia[4-9]. These studies addressed that the highest level of evidence was published by our group[1,10]. This study was a randomized controlled trial (RCT), in which residents of nursing care homes for the elderly were randomly assigned into two groups: one received professional oral cleaning by a visiting dentist or dental hygienist once a week (oral care group), and the other (control group) received conventional care. During the 2-year intervention period, the incidence of pneumonia was decreased about 40% (Figure 1, Table 1). However, another RCT studies are not available up to date, no meta-analysis has been performed to provide more reliable evidence.

There were seven review articles with regard to oral care

Table 1: Comparisons Between Oral Care and No Oral Care Groups

Group	Number of Patients	Age, Years, mean ± SD	F/M	ADLs at Baseline, mean ± SD	MMSE at Baseline, mean ± SD	Number of Patients with Fever (%)	Number of Patients with Pneumonia (%)	Number of Patients Dying (%)
Oral care	184	82.0 ± 7.8	148/36	16.3 ± 6.5	13.6 ± 6.9	27** (15)	21* (11)	14** (7)
No oral care	182	82.1 ± 7.5	145/37	16.2 ± 6.7	13.9 ± 6.9	54 (29)	34 (19)	30 (16)

*$P < .05$ and **$P < .01$ show significant differences between groups with oral care and no oral care.
SD = standard deviation; F/M = female/ male; ADLs = activities of daily living; MMSE = Mini-Mental State Examination.

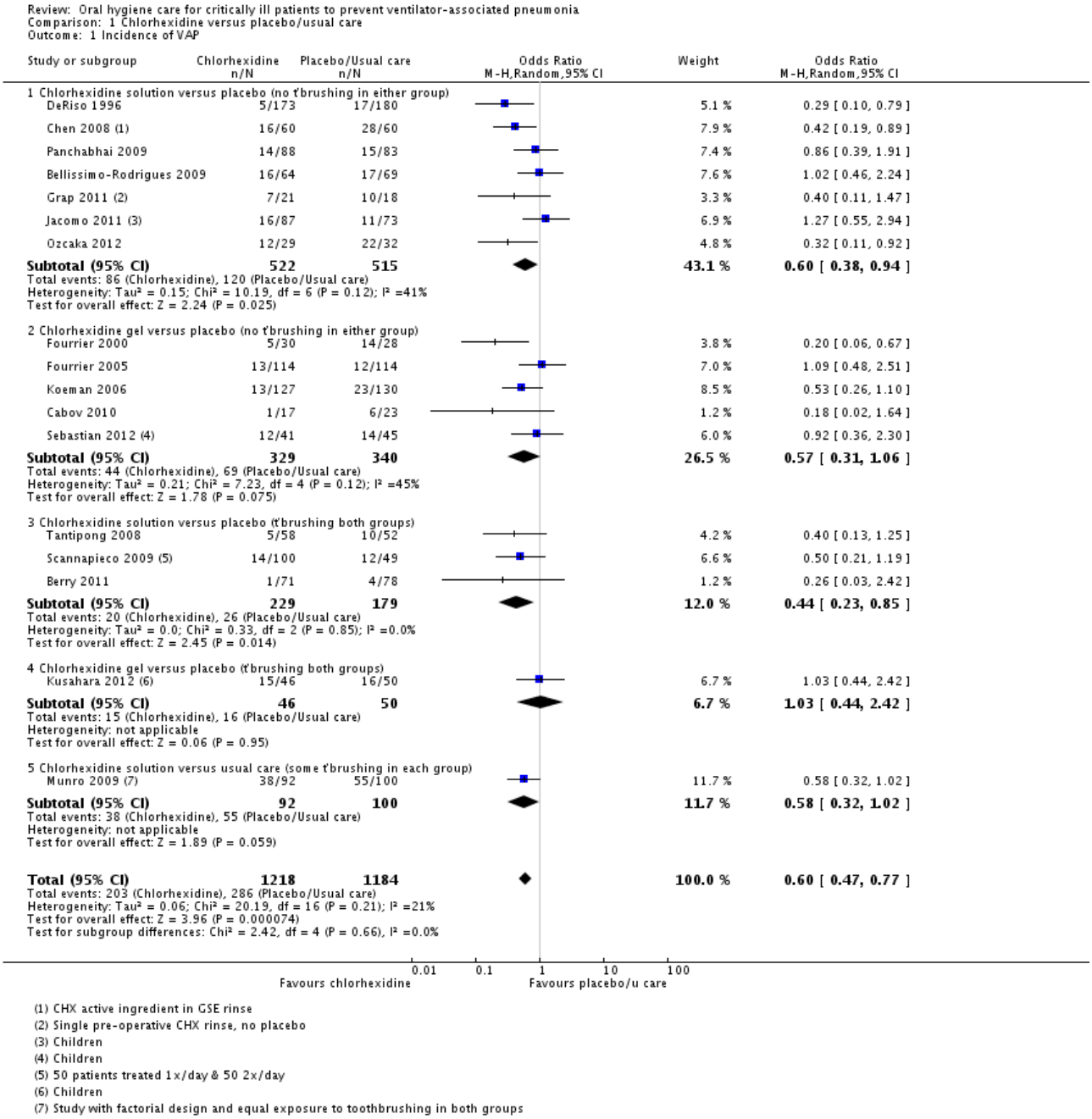

Figure 2: The effects of chlorhexidine mouth cleaning on VAP prevention

and VAP prevention[11-17], and meta-analyses have already been performed. The Cochrane Library study conducted meta-analysis with 17 RCTs and demonstrated that the occurrence of VAP was 0.60 times (95% confidence interval (CI), 0.47-0.77) decreased with chlorhexidine oral cleaning. Also, Labeau *et al*. reported similar conclusion in Lancet that VAP occurrence was 0.72 (95% CI, 0.55-0.94) times decreased according to 12 RCTs (Figure 2)[16]. On the other hand, it was not fully demonstrated that oral care with povidone-iodine or toothbrush can prevent VAP occurrence.

[Discussion]

The preventive effect of oral care on aspiration pneumonia has been widely recognized in the world, although in terms of evidence, only one RCT serves as a cornerstone. Thus, well-designed RCTs are necessary to establish more robust results in the future. Furthermore, standard guidelines and/or manuals are needed to establish both assistant and professional oral care procedure.

With regard to the effects of oral care on VAP prevention, meta-analyses were already conducted and sufficient evidence has been accumulated. They recommended the use of 0.12-0.2% chlorhexidine for mouth cleaning, however in Japan, the use of chlorhexidine at these concentrations in the oral cavity has not been approved yet. We urgently have to conduct clinical trials to establish its safety applying such concentration chlorhexidine. Moreover, we have to demonstrate whether oral care using a toothbrush can prevent VAP for addressing the importance role of dental profession.

Swallowing dysfunction is also the causes of aspiration pneumonia and VAP[18-21], and the dentists can play an important role for dysphagia rehabilitation with dental prostheses[22]. Our mission for prevention of respiratory diseases with oral care and dental works has to be established with well-designed RCTs.

[Conclusions]

Although it has already worldwide supported that oral care leads to the prevention of aspiration pneumonia in the elderly, more planned RCTs are necessary establishing the guidelines and/or manuals of oral care program. Regarding the link between oral care and prevention of VAP, the use of scientific evidence-based concentrations of chlorhexidine has not been approved in Japan. We have to start high-quality clinical trials fixing this issue. With the effort of these approaches, we can address the role and importance of dental profession in the prevention of respiratory disease.

[Conflict of interest]

There are no items applicable to “conflict of interest” in this article.

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3. Oral health and lifestyle-related diseases, non-communicable diseases (NCDs)

3) Cancer
– Role of oral care in cancer treatment –

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[Abstract]

During cancer treatment, various adverse events attributable to the oral cavity occur at high frequency, which not only increase patient suffering but also cause negative effects on cancer treatment itself. Oral health status of patients with cancer is associated with the incidence rate and the degree of severity of oral complications. Effective oral hygiene management before initiating cancer treatment will contribute to the reduction of oral complication risks, and provide important support to facilitate smooth cancer treatment.

[Introduction]

Cancer has been the number one cause of death among Japanese people since 1981. However, due to the advancement in treatment and development of new drugs, cancer cure has become a feasible expectation with early detection and treatment, and even without a cure, it is now possible to live with the disease for a long time. Cancer treatments in recent years are performed intensely and thoroughly, and problems related to associated side effects and complications have also grown to be serious issues. As such, side effect measures in cancer treatment comprise an essential component requisite for the success of treatment. Alleviation and suppression of treatment side effects and complications have been reported to not only decrease pain and increase patient quality of life during cancer treatment and recuperation, but also have favorable effects on the prognosis of cancer treatment. Thus, "supportive care," which includes nutritional management, infection control, and pain relief during cancer treatment, to support smooth treatment has gained recognition in the field of cancer care.

During cancer treatment, patients also develop side effects associated with the oral cavity[1]. The frequency is high; in some form or other, oral troubles have been reported to occur in about 40% of patients undergoing anti-cancer therapy, 80% of patients undergoing hematopoietic stem cell transplantation, and almost all patients undergoing radiotherapy in the oral region[2,3]. Oral side effects are directly linked to ingestion problems, and may even serve as a source of various infections such as aspiration pneumonia, thereby exacerbating systemic conditions, and sometimes preventing the completion of cancer treatment with negative effects on treatment prognoses.

Oral bacteria have been suggested to have considerable effects on the occurrence frequency and severity of oral complications that arise in association with cancer treatment[4], and "oral function management (oral care)," which aims to provide support and management of the oral cavity for the maintenance of good oral hygiene status and healthy oral function, plays a role as supportive cancer therapy[5-7].

In this paper, we review the relationship between cancer treatment and the oral cavity, particularly with regard to oral complications that arise in association with treatment, and the significance of oral function management to address the issues.

[Objective]

The objective was to conduct a literature search and organize information obtained from the search with regard to the content and frequency of oral complications that arise as the side effects of cancer treatment, their negative effects on cancer treatment, and implementation of oral function management by dentists to address those issues.

[Methods]

We ranged extensively over the literature using the Internet (PubMed) search. The period of literature search was set to span January 2014 through March 2014. We also conducted a hand search to collect the literature that could not be retrieved from the Internet search. No restriction was set for the year of publication of the literature. Among the information obtained, the literature with high levels of evidence, such as guidelines, meta-analyses, systematic reviews, and RCTs, were mainly selected to organize the

content.

[Results]

1. The frequency and risk of developing oral complications due to cancer treatment

1) Odontogenic infections during the period of myelosuppression

Most of anti-cancer drug regimens, although to a varying extent, lead to adverse events due to myelosuppression, and patients experience a period of immunocompromised, infection-prone condition during cancer treatment. The presence of dental caries, untreated odontogenic infection foci, and periodontal disease are potential infection risks, and these chronic odontogenic infections could develop into acute infections during the period of myelosuppression, which, in particular, could have a serious impact on the treatment prognosis including death if spread to cause systemic infections[8,9].

- Examination of the oral cavity in 48 candidates of hematopoietic stem cell transplantation revealed that 29% and 60% had periodontitis and gingivitis, respectively. During treatment, in the period of neutropenia, 96% of patients had fever, and 29% of these patients had bacteria detected in their blood. CNS was detected the most. Oral mucositis affected 89.6% of patients, and patients with gingivitis or periodontitis had a high frequency of mucositis[10].
- Examination of 78 febrile seizures that had occurred in 46 patients with hematological cancer revealed that 92% were due to acute infection; a definitive diagnosis could not be reached in the remaining 8%. Acute oral infection was observed in 78% of the patients with fever, and the oral cavity was considered the source of fever in 14%, while it was considered the possible source of fever in 26%[11].
- A review of 38 patients with non-lymphocytic leukemia who had developed systemic infections during treatment revealed that the focal of infection, which was likely the source of infection, was found in the oral cavity of 12 patients (38%); no source of fever other than the oral cavity could be determined in seven of the 12 (58%) patients (36%, periodontal tissue; 18%, oral mucosa; ≤5%, teeth; 18%, lungs; 9%, skin; ≤5%, pharynx, ear, unknown). Infectious foci in the oral cavity (especially periodontitis) are thus likely to be involved in systemic complications in patients with leukemia[12].
- A survey of 56 patients with malignant lymphoma who had undergone chemotherapy revealed that during chemotherapy (continuous period of 5.2 months was inferred), 26 patients (46%) experienced 38 febrile seizures. No source of infection other than the oral cavity could be detected in 42% of the patients. Severe odontogenic infections were observed in many of the patients with febrile seizures (P=0.02). Moderate to severe gingivitis was observed in 58% of the patients[13].
- Seventy-eight febrile seizures that had occurred in 46 immunocompromised patients with hematological cancer were examined. Among patients who had developed sepsis, the oral cavity was considered the source of fever in 10.5%, and 31.6% had lesions in the oral cavity that were considered the possible source of fever. These results suggested that preventive management of odontogenic infections could contribute to decreased systemic infections and mortality[14].

A review article has also been reported[15], which identified the causative bacteria of systemic infections during the period of myelosuppression, and demonstrated that the likelihood of those bacteria actually being oral bacteria was high[15].

- When dental screening was performed before initiation of treatment in 181 patients who were scheduled to undergo bone marrow transplantation (BMT), 53 patients (29%) were found to have dental chronic infection foci that required treatment, and 10 patients (6%) postponed BMT due to odontogenic infections. Sepsis during the period of neutropenia was observed in 59 patients, of whom 24 (41%) had oral microorganisms that were identified as the causative agents[16].
- A survey of 61 patients who had undergone myeloablative allogeneic hematopoietic stem cell transplantation (HSCT) revealed that 31 patients developed bacteremia during the period of neutropenia, and 19 (61%) of the 31 patients had Viridans streptococci, an indigenous organism of the oral cavity, identified as the causative agent[17].

Moreover, with regard to infections originating from the oral cavity, it has been reported that the risk of specific infections with Candida (fungus) and herpes (virus), in addition to common bacteria, also increases.

- The prevalence of oral fungal infections with clinical symptoms in all cancer treatment was 7.5% before treatment, 39.1% during treatment, and 32.6% after treatment completion; the oral fungi-carrying rate was 48.2% before treatment, 72.2% during treatment, and 70.1% after treatment. Radiotherapy and chemotherapy in the head and neck region were each and independently associated with a significant increase in the risk of oral fungal infections, and the risk of clinically significant oral fungal infections was shown to increase during cancer

treatment[18].

- Examination of the prevalence of oral candidiasis in patients undergoing chemotherapy and/or radiotherapy revealed that the prevalence of Candida infection was 9.6% (95% confidence interval [CI], 8.4%-11.0%) in all patients, and 22.0% in patients undergoing chemoradiotherapy[19].
- In patients undergoing anti-cancer drug therapy for hematological malignancies, the detection rate of herpes virus from oral ulcers during the period of neutropenia was 33.8%. Patients with neutropenia who had undergone treatment for hematologic malignancies are likely to have an increased risk of virus infection[20].
- When the incidence of HSV-1 in patients undergoing radiotherapy for head and neck cancer was examined, HSV-1 was isolated from 29.1% of the patients[21].

2) Oral mucositis

Among non-hematological toxicities due to cancer medications, oral mucositis occurs at high frequency, and while its frequency and severity vary by type of cancer and content of anti-cancer drugs, use of almost all anti-cancer drugs leads to the onset of mucositis[22-25]. Moreover, in radiotherapy, oral mucositis is inevitable when the oral cavity is included in the field of irradiation, and the extent of infection tends to be more severe and prolonged compared to mucositis caused by medications. Oral mucositis does not only distress patients due to pain, but also prevent oral ingestion as the condition becomes severe, causing malnutrition and dehydration. It also serves as a serious risk factor for the development of systemic infections such as sepsis due to secondary infection at the ulcer site[26]. Therefore, the issue does not remain local, as it will negatively affect cancer treatment itself, determining life prognosis and laying significant medical and economical burdens[27-29].

- A survey of 429 transplant patients revealed that oral mucositis occurred in 425 (99%) patients, of whom 289 (67.4%) had severe (grade 3 or 4) oral mucositis. In the multivariate analysis, the only independent risk factor for oral mucositis was differences in pretreatment regimens ($P<0.00005$)[30].
- A retrospective study of 281 patients with hematological cancer revealed that 76% of patients experienced grade ≥2 mucositis. Grade of oral mucositis was associated with the number of TPN days, the amount of analgesic, the number of days with fever, the incidence of serious infection, and the length of hospital stay[31].
- A retrospective study of 115 patients with multiple myeloma, who had undergone pre-transplant treatment with high-dose melphalan, revealed that 48% of the patients experienced grade ≥2 mucositis, and that grade of mucositis was significantly associated with the number of TPN days, the amount of analgesics, and the length of hospital stay ($P<0.05$)[32].
- The severity of oral mucositis was correlated with fever ($P<.01$), serious infections ($P <.01$), the number of TPN days ($P <.0001$), use of opioids ($P <.0001$), length of hospital stay ($P <.01$), cost of hospitalization ($P <.01$), and mortality ($P<.0001$)[27].
- Radiotherapy in the head and neck region led to oral mucositis in 91% patients, of which 66% were grade 3-4. The presence or absence of oral mucositis was significantly associated with pain (54% vs. 6%: $p<0.001$) and ≥5% weight loss (60% vs. 17%: $p<0.001$), and an additional cost of $1,700 - 6,000 was required with increasing severity of mucositis[33].
- The mean incidence of oral mucositis due to radiotherapy in the neck and head region was 80%, hospitalization due to oral mucositis was 16%; 11% of patients discontinued treatment because of mucositis[34].
- The occurrence of severe oral mucositis (grade ≥3) was noted in 29-66% of patients undergoing radiotherapy for head and neck cancer[35].

3) Medication-associated osteonecrosis of the jaws

Due to the long-term use of bone-modifying agents such as bisphosphonates and anti-RANKL antibody used for fracture prevention and symptom relief in patients with bone metastases, or molecular targeted agents with angiogenesis inhibitory effects, the occurrence of osteonecrosis of the jaws (ONJ) has been reported. With regard to osteonecrosis caused by bisphosphonates, the risk of occurrence increases with the cumulative amount of medication used, and thus, while the risk remains low with administration of a single or a few doses (e.g., administration in treatment of hypercalcemia), the frequency of occurrence gradually increases if the use is continued beyond six months, ultimately reaching the rate of about 1-2%. The frequency of occurrence due to anti-RANKL antibody is about the same as or slightly higher than that of bisphosphonates. If osteonecrosis progresses, patient QOL markedly decreases, such as pain, and in addition, the management often becomes difficult with the development of resistance to treatment, posing a major clinical issue.

- A prospective study targeting 80 patients with a history of bisphosphonate use showed that 22 (28%) patients developed ONJ. The sites of development were the mandible in most cases (13 patients, 59%), the maxilla in six patients (27%), and both jaws in three patients

(14%). The onset of osteonecrosis was triggered after tooth extraction in most patients (17 patients, 77%; p<0.001); in five patients, however, ONJ occurred with no identifiable trigger event (23%)[36].

- The prevalence of bisphosphonate-associated osteonecrosis in cancer patients is likely to be high (13.3%)[37].
- A systematic review regarding the occurrence frequency of bisphosphonate-associated osteonecrosis reported that the occurrence frequency was 6.1% in all studies, 13.3% in studies reporting follow-up, 0.7% in studies reporting no follow-up, and 1.2% in epidemiological studies[38].
- The occurrence frequency of osteonecrosis due to denosumab (anti-RANKL antibody) was almost the same as that of bisphosphonates-associated osteonecrosis (denosumab: 2.0%, zoledronic acid: 1.4%; p=.39)[39].
- Investigation of 300 multiple myeloma patients who had received zoledronic acid treatment revealed that 14 patients (4.7%) developed ONJ[40].

2. Late effects after head and neck cancer radiotherapy

1) Radiation-induced osteonecrosis of the jaws

The jawbones, when included in the field of irradiation, become susceptible to osteonecrosis, which could be caused by surgical invasion such as tooth extraction, infections of dental origin, or mucosal damage due to ill-fitting dentures. The mandibular molar region represents the common site of infection. The reason is said to be that damaged blood vessels in the jawbones due to irradiation decrease the blood flow, and reduced tissue oxygenation causes the delay in repair or healing. In particular, the onset of osteonecrosis is often triggered by inadvertent tooth extraction, and when the condition becomes serious, fistula formation and pathologic fractures might occur, sometimes requiring surgical resection[41].

- A systematic review regarding the prevalence of osteoradionecrosis (ORN) in patients with head and neck cancer reported that the weighted prevalence of ORN was 7.4% in conventional radiotherapy, 5.1% in intensity-modulated radiotherapy (IMRT), 6.8% in chemoradiotherapy, and 5.3% in implant radiation therapy[42].
- The total incidence of ORN in the field of irradiation following tooth extraction was 7%, and the highest risk was observed in patients who had undergone mandibular molar extraction in the field of irradiation with a radiation dose exceeding 60 Gy[43].
- In a retrospective study targeting 830 patients who had undergone head and neck radiotherapy, the incidence of ONJ was 8.2%, was higher in men, and was commonly observed in the mandibular molar region. The onset was triggered by tooth extraction in 50% of cases. In 40% of ORN cases, surgery and treatment with antibiotics led to a complete cure[44].
- Investigation of 80 patients with radiation-induced ONJ revealed that the onset was triggered by tooth extraction in more than half the patients. However, in one-third of the patients, the condition had developed out of the blue. The onset was noted within three years after radiotherapy in 74% of cases (however, ONJ due to tooth extraction had no time relation). Most of first-occurrence cases were asymptomatic[45].
- Investigation of 104 patients who had developed radiation-induced ONJ revealed that the common site of occurrence was the mandible (99 patients, 95.2%); the maxilla was involved in five patients (4.8%). The triggering event was tooth extraction in 93 cases (89.4%), whereas 11 cases were of spontaneous occurrence. Conservative treatment led to a complete cure in 34 cases (32.6%), while symptoms stabilized and became chronic in 44 cases (42.3%). In 26 cases (25.1%), the condition did not stop progressing and developed into a severe disease[46].

2) Radiation caries

After radiotherapy, the oral cavity suffers the impact of treatment, such as decreased saliva secretion and qualitative changes in the oral flora, with an increased cariogenicity and high risk of tooth loss[47].

- With regard to the rate of tooth loss through radiotherapy, 97% was caused by dental caries[48].
- In a retrospective study regarding oral conditions from before the initiation of radiotherapy until its completion, 57.9% of patients had dental problems before initiating radiotherapy (periodontal disease, 41.0%; apical lesion, 21.2%; dental caries, 12.0%; candidiasis, 7.2%; unerupted teeth, 5.8%; dry mouth, 9.1%), and 50.2% of patients required tooth extraction prior to treatment initiation. During radiotherapy, oral mucositis in 61.7%, Candida infection in 45.8%, and dry mouth in 62.6% were observed. After radiotherapy, prolonged oral mucositis in 19.2% and candidiasis in 21.1% were observed. Radiation caries occurred in 11.0% of patients, and ORN in 5.5%[49].
- Oral prevention efforts in 935 patients who had undergone radiotherapy in the head and neck region resulted in radiation caries in 4%, and osteonecrosis in 1%[50].

3. The significance of oral function management as a strategy to address oral complications associated with cancer treatment

The presence of oral bacteria has no small effect on the occurrence frequency and degree of oral complications that arise in association with cancer treatment[51]. Therefore, as a strategy, it is effective to support and manage the oral cavity for the purpose of maintaining good oral hygiene status and preserving healthy oral function[52,53].

Oral management for dental infections should be provided with consideration of the extent and duration of expected myelosuppression: before initiating cancer treatment, it is recommended to examine the presence of infection foci inside the oral cavity, and perform treatment to the extent permitted by the situation; during the period of myelosuppression, it is recommended to control the risk of infection through oral cleaning, mainly with brushing. In particular, periodontal infections sometimes cause infections during cancer treatment, and thus, pre-treatment assessment and management must be implemented. The effectiveness of these oral management efforts on the prevention of systemic complications during cancer treatment has been suggested[54-56].

In terms of oral management for oral mucositis, no prevention or therapeutic methods to completely suppress the development of mucositis have been identified[57]. Thus, management will be centered around the alleviation of symptoms such as pain and the reduction of secondary infection risk to facilitate healing[58-65]. During cancer treatment, impaired saliva secretion causes dryness in the oral cavity, and due to nausea and fatigue, conditions overlap in such a way that proper oral management cannot be performed easily, making it difficult to maintain good oral hygiene status. However, with proper oral hygiene instruction tailored to each situation and efforts to maintain clean and moisturized oral status, the alleviation of mucositis symptoms, suppression of exacerbation, and shortening of disease duration can be expected[66-69].

- Investigation of 30 patients with hematological cancer undergoing chemotherapy revealed that 21.9% of patients developed oral mucositis, of which 4.1% were grades 3 and 4. Severe (grade 4) neutropenia was a risk factor for oral mucositis ($P<0.001$). The possibility was suggested that enforcement of basic oral care could delay oral mucositis[70].
- Investigation of 97 patients who had undergone hematopoietic stem cell transplantation suggested the possibility that oral health factors (hygiene status, chronic dental foci) before initiating treatment were predictors of the occurrence and severity of oral mucositis[71].
- Oral care intervention during chemotherapy largely decreased bleeding gums and values of the plaque index in almost all patients. The incidence of oral mucositis was 66% in the control group, but was 20% in the intervention group. There is a possibility that oral care may reduce the incidence of oral mucositis due to chemotherapy[72].
- In a prospective comparative study performed to the end of clarifying the effectiveness of a preventive oral care protocol for oral mucositis in pediatric cancer patients undergoing chemotherapy, the incidence of mucositis with ulcers decreased by 38% with the oral care protocol. The severity of oral mucositis ($P = 0.000002$) and related pain ($p = 0.0001$) also greatly decreased due to intervention[73].
- After oral care guidance, the occurrence of oral mucositis in hematopoietic stem cell transplant patients clearly decreased. Multiple logistic analysis revealed that content of pre-treatment regimen and oral care were independent risk factors for the occurrence of oral mucositis[74].
- Oral mucositis occurred in 87% of hematopoietic stem cell transplant patients. Grade of mucositis was affected by the number of lost teeth ($p<0.016$) and the DMFS index ($p<0.038$). The possibility that oral conditions before treatment initiation could affect the severity of mucositis was suggested[75].

  A before-after study that had compared incidence of mucositis with or without oral care intervention showed that the incidence of oral mucositis with ulcers was significantly decreased in the oral care intervention group. The results suggested the possibility that the care geared toward maintaining the clean and moisturized oral environment could reduce oral mucositis in hematopoietic stem cell transplant patients[76].
- The results of an RCT targeting 26 breast cancer patients scheduled to undergo chemotherapy, who were divided into two groups (the oral self-care group and the professional preventive oral care group), showed that the intervention group with professional preventive oral care had a significantly lower OAG score (score of oral adverse events), compared to the self-care group. The results suggested the possibility that intervention with professional preventive oral care for patients with breast cancer undergoing chemotherapy could decrease the risk of oral mucositis[77].

4. Measures against osteoradionacrosis and radiation caries

As the risk of osteonecrosis following irradiation does

not change even after many years have passed, prophylactic measures are of importance. Teeth with poor prognosis within the field of irradiation need to be appropriately treated, such as by tooth extraction, at least two weeks before initiating treatment. Moreover, even after the completion of treatment, easy surgical treatment at a general dental clinic should be avoided, and when receiving dental treatment, patients should be instructed not to undergo tooth extraction without permission of a radiotherapist. Extraction of a tooth within the field of irradiation is a strong risk factor for radiation-induced ONJ. As the oral cavity after radiotherapy remains highly cariogenic, it is important to implement continuous dental oral management in order to avoid tooth extraction to the extent possible[78-81].

- In a retrospective study regarding tooth loss risks in patients after head and neck cancer radiotherapy, a decrease in the risk of tooth loss from 19.2% in 1993 to 7.8% in 2005 was observed, as a result of enhanced preventive measures with fluorides[82].
- A retrospective study searched risk factors for radiation-induced ONJ, and found that oral health status after radiotherapy was associated with ORN onset[83].

5. Oral care reduces the risk of medication-related osteonecrosis of the jaws (MRONJ)

Although the pathogenesis of osteonecrosis caused by medications such as bone-modifying agents has not yet been clarified, poor oral hygiene status, presence of dental infectious foci, use of ill-fitted dentures, and tooth extraction during bone-modifying agent use have been reported to be strong risk factors for the onset. It has been reported that risk factors associated with the occurrence of ONJ could be reduced by prophylactic measures, which include reducing oral risk factors before initiating treatment to the extent possible, and continuously managing good oral conditions during treatment[84-86]. The clinical practice guidelines for cancer in Japan as well as other countries recommend that patients visit a dental department before initiating the use of medications, and undergo oral screening as well as perform appropriate oral management[87,88].

- A retrospective longitudinal cohort study, which examined risk factors for ONJ in 1,621 patients with long-term use of bisphosphonates, reported that the incidence rate of ONJ was 0.94-18.6%. The independent predictors associated with the development of ONJ, based on multivariate analysis, were tooth extraction experience and use of dentures. Periodontitis treatment and root canal treatment did not increase the risk of ONJ[89].
- After implementing dental prophylactic measures prior to initiation of treatment with bisphosphonates, the risk of developing ONJ was investigated. ONJ was observed in 2.9%. The prophylactic program decreased the incidence of osteonecrosis from 3.2% to 1.3%. When subjects were restricted to patients who had used zoledronic acid, the prophylactic dental intervention significantly contributed to a decrease in the risk of developing ONJ (7.8% to 1.7%; P=0.016)[90].
- One study investigated the risk of developing ONJ in 128 patients with multiple myeloma who had undergone treatment with zoledronic acid, and who were divided into two groups according to whether they had received oral care intervention or not. Although 16 patients (12.5%) developed ONJ, a significant decrease in the risk of development was achieved with oral care intervention, such that ONJ was noted in eight patients (26.3%) in the non-intervention group, as opposed to two patients (6.7%) in the oral care intervention group (P=0.002). Moreover, no patients in the oral care intervention group developed stage 3 ONJ[91].

Osteonecrosis is not an incurable condition, but rather, the achievement of cure, symptom relief, and suppression of progression are considered feasible with conservative treatment, if provided early. The "stage 0" conditions, i.e., prodromal symptoms of ONJ with exposed sequestra due to mucolasis, have been proposed[92], and treatment initiated at this stage could yield favorable outcomes. Therefore, regular dental screening is important to allow for early detection.

- A survey of ONJ incidence and risk factors revealed that 89 (1.6%) of 5,723 patients had developed osteonecrosis; 61.8% of osteonecrosis development was related to tooth extraction. More than 95% of the patients underwent conservative treatment for osteonecrosis, and 36% achieved a cure (cure rate: zoledronic acid, 29.7%; denosumab, 40.4%)[93].
- A retrospective study of 4,019 patients with bisphosphonate use revealed that 16 (1.2%) of 1,338 patients with breast cancer and 13 (2.4%) of 548 patients with multiple myeloma had developed ONJ. A search of risk factors for ONJ in breast cancer patients (multivariate analysis with Cox proportional hazards regression models) identified zoledronic acid (HR=15.01, 95% CI: 2.41-93.48; p = 0.0037) and tooth extraction (HR=53.19, 95% CI: 18.20-155.46; p < 0.0001). A search of risk factors for ONJ in multiple myeloma patients identified tooth extraction (HR=9.78, 95% CI: 3.07-31.14; p = 0.0001) and osteoporosis (HR=6.11, 95% CI: 1.56-23.98; p = 0.0095). Oral health conditions and history

Table 1: Outline of the reviws 1

Authors	Report year	Study design	Outline	Ref. no.
Brennan, Elting, Spijkervet	2010	Systematic review	Systematic review with regard to frequency of, and measures against, oral complications associated with cancer treatment, and its effects on cancer treatment.	1
Campos , Campos, Aarestrup, Aarestrup	2014	Systematic review	Causes of, and therapeutic strategy taken by dentists against, oral mucositis associated with cancer treatment.	2
Peterson	2006	Review	Therapeutic strategy based on currently available evidence regarding oral mucositis.	3
Peterson	1990	Review	Risk of odontogenic infections during the period of myelosuppression while in chemotherapy.	4
Raber-Durlacher, Barasch, Peterson, Lalla, Schubert, Fibbe	2004	Review	Risk of oral complications during chemotherapy and relevant countermeasures.	5
Sonis, Woods, White	1990	Review	Dental check prior to treatment is essential as measures against the risk of oral complications during chemotherapy.	6
Epstein, Stevenson-Moore	2001	Systematic review	Acute development of periodontal diseases often hinders cancer treatment during chemotherapy or head and neck radiotherapy . Dental check prior to treatment is essential.	7
Raber-Durlacher, Epstein, Raber, van Dissel, van Winkelhoff, Guiot, van der Velden	2002	Review	Periodontitis becomes the source of fever causing systemic infections for cancer patients during the period of neutropenia. Assessment of periodontal conditions in patients prior to treatment is essential for diagnosis and management of potential risk of infections.	9
Lalla, Latortue, Hong, Ariyawardana, D'Amato-Palumbo, Fischer, Martof, Nicolatou-Galitis, Patton, Elting, Spijkervet, Brennan, Fungal Infections Section, Oral Care Study Group, Multinational Association of Supportive Care in Cancer (MASCC)/International Society of Oral Oncology (ISOO).	2010	Systematic review	The risk of clinically significant oral fungal infections increases during cancer treatment. The prevalence of oral fungal infections during overall cancer treatment was 7.5% before treatment, 39.1% during treatment, and 32.6% after treatment completion; the oral fungi-carrying rate was 48.2% before treatment, 72.2% during treatment, and 70.1% after treatment. Head and neck radiotherapy and chemotherapy were each and independently associated with a significant increase in the risk of oral fungal infections.	18
Elad, Zadik, Hewson, Hovan, Correa, Logan, Elting, Spijkervet, Brennan,Viral Infections Section, Oral Care Study Group, Multinational Association of Supportive Care in Cancer (MASCC)/International Society of Oral Oncology (ISOO).	2010	Systematic review	The incidence of oral herpes simplex (HSV) infection during the period of neutropenia was at a high frequency of 49.8% in patients undergoing head and neck radiotherapy. HSV infection rate further increased when oral ulcers existed.	20
Rosenthal	2007	Review	Most patients who underwent head and neck radiotherapy developed mucositis and severe mucositis required interruption, or change in schedule, of treatment, affecting the prognosis of treatment.	22
Rubenstein, Peterson, Schubert, Keefe, McGuire, Epstein, Elting, Fox, Cooksley, Sonis, Mucositis Study Section of the Multinational Association for Supportive Care in Cancer; International Society for Oral Oncology.	2004	Guideline	Oral mucositis is the adverse events that occur at a high frequency during cancer treatment. The article provides the clinical practice guideline based on medical evidences regarding prevention, evaluation, and treatment of oral mucositis.	23
Eilers, Million	2011	Review	Although the frequency and severity vary, oral mucositis developed in almost all cancer patients This report summarizes evidences related to nursing care plan critical to the management of mucositis.	25
Murphy	2007	Review	Oral mucositis associated with cancer treatment hampers efficacy of cancer treatment, leading to decreased quality of life. Measures to lower incidence, and prevent increased severity, of mucositis is necessary from the health economic aspect as well.	28

Table 1: (continued)

Authors	Report year	Study design	Outline	Ref. no.
Trotti, Bellm, Epstein, Frame, Fuchs, Gwede, Komaroff, Nalysnyk, Zilberberg	2003	Systematic review	The incidence of oral mucositis due to head and neck radiotherapy was 80%, of which 34% was "severe" (Grade 3-4). Treatment had to be interrupted for 11% of patients due to mucositis.	34
Elting, Keefe, Sonis, Garden, Spijkervet, Barasch, Tishler, Canty, Kudrimoti, Vera-Llonch	2008	Systematic review	The incidence of oral mucositis due to head and neck radiotherapy was 80%, of which 34% was "severe" (Grade 3-4). Treatment had to be interrupted for 11% of patients due to mucositis.	35
Nalliah	2012	Review	The prevalence of bisphosphonate-associated osteonecrosis in cancer patients was 13.3%.	37
Migliorati, Woo, Hewson, Barasch, Elting, Spijkervet, Brennan. Bisphosphonate Osteonecrosis Section, Oral Care Study Group, Multinational Association of Supportive Care in Cancer (MASCC)/International Society of Oral Oncology (ISOO).	2010	Systematic review	The overall mean frequency of developing bisphosphonate-associated osteonecrosis was 6.1% (mean); 13.3% in studies with follow-up, 0.7% in studies with no follow-up, and 1.2% in epidemiological studies.	38
Peterson, Doerr, Hovan, Pinto, Saunders, Elting, Spijkervet, Brennan	2010	Systematic review	The frequency of developing osteoradionecrosis was 7.4% in conventional RT, 5.2% in IMRT, 6.8% in RT and CT, and 5.3% in brachytherapy.	42
Nabil, Samman	2011	Systematic review	The incidence of osteoradionecrosis caused by tooth extraction after radiotherapy was 7%. In the case of tooth extraction provided with use of prophylactic antibiotics, the onset frequency of osteonecrosis was 6%. In the case of tooth extraction using prophylactic hyperbaric oxygen therapy in combination, the incidence was 4%. The highest risk was observed in patients who had undergone mandibular molar extraction in the field of irradiation with a radiation dose exceeding 60 Gy.	43
Nabil, Samman	2012	Systematic review	The risk of developing osteonecrosis of the jaw after radiotherapy was 2%. The risk of developing osteonecrosis is decreasing in recent years.	96
Koga, Salvajoli, Alves	2008	Review	In order to manage radiation-induced osteonecrosis of the jaw, it is necessary to receive oral check and to have teeth with poor prognosis extracted prior to radiotherapy. Full attention is required when tooth extraction becomes indispensable after irradiation.	41
Epstein, van der Meij, Lunn, Stevenson-Moore	1996	Review	With regard to the rate of tooth loss through head and neck radiotherapy, 97% was caused by dental caries.	48
Kielbassa, Hinkelbein, Hellwig, Meyer-Lückel	2006	Review	Radiation-induced dental caries is a persistent risk and can trigger osteonecrosis of the jaw. Preventive dental care is important.	47
Epstein, Schubert	1999	Review	Good oral hygiene prevents oral mucositis from advancing in severity, mitigating the risk of bacteremia. Oral care currently recommended is to maintain good oral hygiene by frequently rinsing out the mouth with normal saline solution or bicarbonate, and use local anesthetic drug or analgesic drug for pain. Cryosurgery can serve as a potential ancillary approach in some cases.	51
Larson, Miaskowski, MacPhail, Dodd, Greenspan, Dibble, Paul, Ignoffo	1998	Review	The PRO-SELF oral care program to provide self-care guidance for mucositis management that is practiced at home without direct supervision of medical staff can reduce incidence of oral mucositis induced by chemotherapy.	52

Table 1: (continued)

Authors	Report year	Study design	Outline	Ref. no.
Gürgan, Özcan, Karakuş Ö, Zincircioğlu, Arat, Soydan, Topcuoglu, Gürman, Bostancı	2013	Review	By providing initial periodontal treatment before pre-transplant, severity of periodontitis was significantly mitigated (P<0.001). Of all the subjects, 14 persons (48.3%) did not develop GVHD and 17 persons (58.6%) did not develop oral mucositis. Scope of BOP(+) were correlated to the development of oral mucositis (r=-0.518、P<0.05). As a result of periodontal hygiene management, as well as improvement in periodontitis, decrease in incidence and severity of oral mucositis was observed.	53
Gabriel, Shea, Olajida, Serody, Comeau	2003	Review	Reducing severity and disease duration of oral mucositis for patients with bone marrow transplantation (BMT) has a major impact on reduction in mortality and medical expenditure.	54
Shih, Miaskowski, Dodd, StottsA, MacPhail	2002	Systematic review	Oral mucositis is one of the most common oral complications in patients with head and neck cancer undergoing radiotherapy. Although some strategies and products have been investigated, a fully satisfactory medical treatment has not yet been established. Provision of dental care and the initiation of standardized oral hygiene protocol prior to cancer treatment are most effective approach against the oral mucositis problem. The most effective means to treat mucositis was frequent gargle with non-irritating mouthwash (e.g. saline solution or sodium bicarbonate).	55
Epstein, Klasser	2006	Systematic review	Oral mucositis increases the risk of local and systemic infection especially in patients during the period of myelosuppression. Severe oral mucositis can have an effect on treatment of primary disease. Mucositis care is basically performed for the palliation purpose, which includes maintenance of appropriate oral hygiene, use of non-irritating food/oral care products, mouth rinsing, and use of local anesthesia and systemic opioids painkiller, etc. Keratinocyte growth factor was approved by FDA (Palifermin, Amgen) in 2004, providing a new approach to prevent oral mucositis in patients undergoing hematopoietic stem cell transplantation.	56
Stokman, Spijkervet, Boezen, Schouten, Roodenburg, de Vries	2006	Systematic review	Oral mucositis increases the risk of local and systemic infection especially in patients during the period of myelosuppression. Severe oral mucositis can have an effect on treatment of primary disease. Mucositis care is basically performed for the palliation purpose, which includes maintenance of appropriate oral hygiene, use of non-irritating food/oral care products, mouthrinsing, and use of local anesthesia and systemic opioids painkiller, etc. Keratinocyte growth factor was approved by FDA (Palifermin, Amgen) in 2004, providing a new approach to prevent oral mucositis in patients undergoing hematopoietic stem cell transplantation.	57
McGuire, Fulton, Park, Brown, Correa, Eilers, Elad, Gibson, Oberle-Edwards, Bowen, Lalla; Mucositis Study Group of the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO).	2013	Guideline	An evidence-based practice guideline for prevention and treatment of oral mucositis induced by chemotherapy or head and neck radiotherapy.	58
McGuire, Correa, Johnson, Wienandts	2006	Guideline	An evidence-based practice guideline for prevention and treatment of oral mucositis induced by chemotherapy or head and neck radiotherapy.	59

Table 1: (continued)

Authors	Report year	Study design	Outline	Ref. no.
Bensinger, Schubert, Ang, Brizel, Brown, Eilers, Elting, Mittal, Schattner, Spielberger, Treister, Trotti AM 3rd.	2008	Guideline	Therapeutic strategy for oral mucositis by NCCN.	60
Keefe, Schubert, Elting, Sonis, Epstein, Raber-Durlacher, Migliorati, McGuire, Hutchins, Peterson , Mucositis Study Section of the Multinational Association of Supportive Care in Cancer and the International Society for Oral Oncology.	2007	Guideline	Guideline for oral mucositis published by the American Cancer Society in 2007.	61
Elad, Bowen, Zadik, Lalla, Mucositis Study Group of the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO).	2013	Guideline	Guideline for oral mucositis by MASCC/ISOO.	62
Worthington Clarkson, Bryan, Furness, Glenny, Littlewood, McCabe, Meyer, Khalid	2011	Systematic review	Systematic review on oral mucositis based on Cochrane Database.	63
Jensen, Peterson	2014	Review	Review of scientific evidence-based therapeutic guideline for prevention and treatment of oral mucositis.	64
Alvariño-Martín, Sarrión-Pérez	2014	Systematic review	Literature review on prevention and treatment of oral mucositis related to chemotherapy.	65
McGuire, Rubenstein, Peterson	2004	Guideline	Evidence-based therapeutic guideline for clinical nurses to manage oral mucositis.	67
Scully, Epstein, Sonis	2004	Review	Mucositis care is basically performed for the palliation purpose, which includes maintenance of appropriate oral hygiene, use of local anesthesia and systemic opioids painkiller, etc.	68
Harris, Eilers, Harriman, Cashavelly, Maxwell	2008	Review	Review of empirical evidence about mucositis management.	69
Chung, Sung	2006	Review	Review on importance and details of dental management in chemotherapy and head and neck radiotherapy.	78
Wahl	2006	Review	Regular oral care is important for prevention of radiation-induced osteonecrosis of the jaw. Concurrent use of hyperbaric oxygen therapy or antibacterial drug is recommended in tooth extraction after radiotherapy.	79
McCaul	2012	Review	Provision of consistent oral care in collaboration with dental care teams is recommended in head and neck radiotherapy.	80
Moore, Burke, Fenlon, Banerjee	2012	Review	General dental clinics serve an important role in oral management in head and neck radiotherapy.	81
Otto, Hafner, Grötz	2009	Review	In the medication-induced osteonecrosis of the jaw, dysesthesia in the paresthesia of the chin including the lower lip (Vincent's symptom) is often observed as the initial symptom prior to bone exposure.	97
Yarom, Fedele, Lazarovici, Elad	2010	Review	In the medication-induced osteonecrosis of the jaw, initial symptoms such as pain, fistula formation, pus discharge, and dysesthesia in the paresthesia of the chin were observed in 45% of patients prior to bone exposure.	98
Khosla, Burr, Cauley, Dempster, Ebeling, Felsenberg, Gagel, Gilsanz, Guise, Koka, McCauley, McGowan, McKee, Mohla, Pendrys, Raisz, Ruggiero, Shafer, Shum, Silverman, Van Poznak, Watts, Woo, Shane E;American Society for Bone and Mineral Research.	2007	Guideline	Report of investigation results and recommendations by the taskforce regarding osteonecrosis of the jaw.	84
Fehm, Felsenberg, Krimmel, Solomayer, Wallwiener, Hadjii	2009	Review	Summary of recommended preventive measures for osteonecrosis of the jaw for patients with breast cancer on medication of bisphosphonates.	86

Table 1: (continued)

Authors	Report year	Study design	Outline	Ref. no.
Grewal, Fayans	2008	Review	Pharmacological properties and pathological mechanism of bisphosphonates; recommendations through clinical picture of oral lesions by FDA on oral management of patients treated with bisphosphonates	87
Van Poznak, Temin, Yee, Janjan, Barlow, Biermann, Bosserman, Geoghegan, Hillner, Theriault, Zuckerman, Von Roenn, American Society of Clinical Oncology.	2011	Guideline	Guidelines provided by ASCO (bone metastatis from breast cancer) All the patients scheduled to be administered bone-modifying agents are strongly recommended to receive prophylactic dental check and treatment and consistently maintain good oral hygiene.	88

Table 2: Outline of the reviws 2

Authors	Report year	Subjects	Study design	Outline	Ref. no.
Peterson, Minah, Overholser, Suzuki, DePaola, Stansbury, Williams, Schimpff	1987	24 patients who underwent chemotherapy that induces myelosuppression	Prospective cohort	From examination of causative bacteria of patients who developed fever due to neutropenia during chemotherapy, it was found highly possible that oral disease, especially periodontal diseases, could be the source of fever for acute infection.	8
Fernandes, Torres, Garnica, de Souza Gonçalves, Junior, de Vasconcellos, Cavalcanti, Maiolino, de Barros Torres	2014	48 candidates of hematopoietic stem cell transplantation	Prospective cohort	Of the candidate patients, 96% developed fever due to neutropenia. Oral mucositis was observed in 89.6% of patients.	10
Bergmann	1989	46 patients who developed fever due to neutropenia during chemotherapy	Prospective cohort	Acute development of odontogenic infections was observed in 78% of patients who developed fever due to neutropenia. The possibility was suggested that 14-26% of those patients developed fever caused by odontogenic infection.	11
Peterson, Overholser	1981	38 patients with acute non-lymphocytic leukemia	Prospective cohort	Of these patients, 22 developed infection during treatment and 12 of them had infection source in the oral cavity. Periodontal disease was the greatest infection source.	12
Laine, Lindqvist, Pyrhönen, Strand-Pettinen, Teerenhovi, Meurman	1992	56 patients with malignant lymphoma	Prospective cohort	During chemotherapy, 26 patients (46%) experienced fever 38 times. Severe odontogenic infection was frequently observed during fever (P=0.02). Moderate to severe gingivitis was observed in 22 patients (58%). No source of infection other than the oral cavity could be detected in 42% of the patients.	13
Bergmann	1988	46 immunocompromised patients with hematological cancer	Prospective cohort	A total of 78 times of fever was observed in 46 patients, of which 19 patients developed sepsis. From a bacteriological examination, 10.5% of sepsis was diagnosed as having the source of fever in the oral cavity and 31.6% was diagnosed as possibly having the source of fever in the oral cavity.	14
Kennedy, Morrison, Kaufmann, Jackson MS, Bagg, Gibson, Gemmell, Michie	2000	A 15-year old patients who developed multibacillary bacteremia repeatedly after bone marrow transplantation	Case report	Oral mucosa and central vein lines should be taken into consideration as a source of infection for bacteremia by coagulase-negative staphylococci in immunocompromised patients.	15
Heimdahl, Mattsson, Dahllö f, Lönnquist, Ringdén	1989	181 candidates of bone marrow transplantation	Prospective cohort	Chronic dental focus that needs to be treated prior to bone marrow transplantation was observed in 53 patients (29%). Start of marrow transplantation was postponed for 10 patients (6%) because of dental infection. Sepsis was developed in 59 patients during the period of neutropenia, of which 24 (41%) had oral microorganisms (alpha chain coccus) as causative bacteria.	16
Graber, de Almeida, Atkinson, Javaheri, Fukuda, Gill, Barrett, Bennett	2001	61 patients who underwent bone marrow transplantation	Cohort	Of 31 patients who developed bacteremia during the period of neutropenia after transplantation, 19 (61%) had *Viridans Streptococcus,* an indigenous organism of the oral cavity, as the causative bacteria. In 7 of the 19 patients, multiple number of *Viridans Streptococci* were detected in the same blood culture.	17
Gligorov, Bastit, Gervais, Henni, Kahila, Lepille, Luporsi, Sasso, Varette, Azria; Candidoscope Study Group.	2011	2,042 patients who underwent chemotherapy (± radiotherapy)	Retrospective	The incidence of oral candidiasis was 9.6% (95%CI, 8.4%-11.0%). High rates were observed in the regimen where chemoradiotherapy was concurrently used (22.0%) and where more than two kinds of cytocidal anticancer drugs were concurrently used (16.9%).	19

Table 2: (continued)

Authors	Report year	Subjects	Study design	Outline	Ref. no.
Nicolatou-Galitis, Athanassiadou, Kouloulias, Sotiropoulou-Lontou, Dardoufas, Polychronopoulou, Gonidi, Kyprianou, Kolitsi, Skarleas, Pissakas, Papanikolaou, Kouvaris	2006	60 patients subject to radiotherapy for head and neck cancer	Prospective	Ulcerative mucositis developed in 48 patients and the swab was collected from 29 of them. HSV-1 was isolated from 14 from the 29 cases	21
				The incidence of HSV-1 infection during the period of radiotherapy was 29.1%.	
Elting, Cooksley, Chambers, Cantor, Manzullo, Rubenstein	2003	599 patients who underwent chemotherapy that induces myelosuppression	Retrospective	37% developed mucositis during 1,236 cycles of chemotherapy. A significant association was observed between mucositis and bleeding (P=0.04). A significant association was also observed between mucositis and infection symptoms (P<0.0001). Management of mucositis is important both clinically and economically.	26
Wardley, Jayson, Swindell, Morgenstern, Chang, Bloor, Fraser, Scarffe	2000	420 patients who underwent hematopoietic stem cell transplantation	Prospective cohort	Oral mucositis occurred in 425 patients (99%), of whom 289 (67.4%) had severe (Grade II-IV) oral mucositis. According to multivariate analysis, the only independent risk factor for mucositis was the content of pretreatment regimens (P<0.00005).	30
Vera-Llonch, Oster, Ford, Lu, Sonis	2007	420 patients who underwent hematopoietic stem cell transplantation	Prospective cohort	Oral mucositis occurred in 425 patients (99%), of whom 289 (67.4%) had severe (Grade II-IV) oral mucositis. According to multivariate analysis, the only independent risk factor for mucositis was the content of pretreatment regimens (P<0.00005).	31
Vera-Llonch, Oster, Ford, Lu, Sonis	2007	115 patients who were treated with high-dose melphalan before hematopoietic stem cell transplantation	Retrospective	Oral mucositis of grade ≥2 occurred in 55 patients (48%). Grade of mucositis was significantly associated with the number of TPN days and the length of hospital stay (P<0.05).	32
Sonis, Oster, Fuchs, Bellm, Bradford, Edelsberg, Hayden, Eilers, Epstein, LeVeque, Miller, Peterson, Schubert, Spijkervet, Horowitz	2001	92 candidates of hematopoietic stem cell transplantation	Prospective multicenter	Grade of oral mucositis was significantly associated with fever (>38.0 ℃), the incidence of serious infection, the number of TPN (total parenteral nutrition) days, the length of hospital stay, and total cost of hospitalization, etc. (P<0.05). Mucositis is also problematic from the health economic aspect.	27
Elting, Cooksley, Chambers, Garden	2007	204 patients who underwent head and neck radiotherapy	Retrospective cohort	Oral mucositis of grade 3-4 occurred in 91%, of which 66% was severe (Grade 3-4). Medical cost increased in proportion to the grade.	33
Vera-Llonch, Oster, Hagiwara, Sonis	2006	450 patients who underwent head and neck radiotherapy	Retrospective cohort	Oral mucositis was a risk factor for interruption of radiotherapy and unforeseen urgent hospitalization.	29
Boonyapakorn, Schirmer, Reichart, Sturm, Massenkeil	2008	80 patients who were receiving medication of bisphosphonates	Prospective cohort	Osteonecrosis of the jaws occurred in 22 patients (28%). By region, the mandible accounted for the greatest percentage (13 patients: 59%) while the maxilla accounted for 27% (6 patients) and the both jaws 14% (3 patients). Five patients (23%) developed osteonecrosis with no identifiable trigger event, while, in 17 patients (77%), a surgical treatment such as tooth extraction served as the trigger (P<0.001).	36

Table 2: (continued)

Authors	Report year	Subjects	Study design	Outline	Ref. no.
Stopeck, Lipton, Body, Steger, Tonkin, de Boer, Lichinitser, Fujiwara, Yardley, Viniegra, Fan, Jiang, Dansey, Jun, Braun	2010	1,026 patients who were randomly allocated to administration of zometa, denosumab, or placebo	RCT	The incidence of osteonecrosis of the jaws was observed in administering both of these two drugs (denosumab: 2.0%, zoledronic acid 1.4%, P=0.39).	39
Berenson, Yellin, Crowley, Makary, Gravenor, Yang, Upadhyaya, Flinn, Staszewski, Tiffany, Sanani, Farber, Morganstein, Bolejack, Nassir, Hilger, Sefaradi, Shamouelian, Swift	2011	300 patients with multiple myeloma who were administered with zoledronic acid	Retrospective	Osteonecrosis of the jaws occurred in 14 patients (4.7%).	40
Reuther, Schuster, Mende, K übler	2003	830 patients who underwent head and neck radiotherapy	Retrospective	The incidence of radiation-induced osteonecrosis of the jaws was 8.2%, which was higher in men and more frequently observed in the mandibular molar region. It was triggered by tooth extraction in 50% of the cases. In 40% of osteoradionecrosis, surgery and treatment with antibiotics led to a complete cure.	44
Thorn, Hansen, Specht, Bastholt	2000	80 patients who developed radiation-induced osteonecrosis of the jaws	Retrospective	The onset was triggered by tooth extraction in more than half of the patients. However, in one-third of the patients, osteonecrosis developed out of the blue. The onset was noted within 3 years after radiotherapy in 74% of cases. (However, osteonecrosis due to injury caused by tooth extraction had no association with time.) Almost all cases developed within the field of irradiation and most of first-occurrence cases were asymptomatic.	45
Curi, Dib	1997	104 patients who developed radiation-induced osteonecrosis of the jaws	Retrospective	The common sites of occurrence were the maxilla (5 cases, 4.8%) and the mandible (99 cases, 95.2%). The triggering event was tooth extraction in 93 cases (89.4%), whereas 11 cases (10.6%) were of spontaneous occurrence with no identifiable triggering event. Conservative treatment led to a complete cure in 44 cases (42.3%), while symptoms stabilized and became chronic in 34 cases (32.6%). In 26 cases (25.1%), the condition did not stop progressing and became acute.	46
Jham, Reis, Miranda, Lopes, Carvalho, Scheper, Freire	2008	207 patients who underwent head and neck radiotherapy	Retrospective	During RT, oral mucositis in 80 patients (61.7%), candida infection in 60 patients (45.8%), and dry mouth in 82 patients (62.6%) were observed. After RT, oral mucositis in 21 patients (19.2%), candidiasis in 23 patients (21.1%), and dry mouth in 58 patients (53.2%) were reported. Radiation caries were observed in 12 patients (11.0%) and osteonecrosis of the jaws in 6 patients (5.5%).	49
Horiot, Schraub, Bone, Bain, Ramadier, Chaplain, Nabid, Thevenot, Bransfield	1983	935 patients who underwent head and neck radiotherapy	RCT	Dental prophylactic measures mainly with fluorides was provided on a regular basis after radiotherapy. Rampant caries occurred in 4% patients and osteonecrosis in 1% patients. Fluoride application was found most effective in preventing dental caries that can occur after completion of radiotherapy.	50

Table 2: (continued)

Authors	Report year	Subjects	Study design	Outline	Ref. no.
Martinez, Pereira, Chacim, Mesquita, Sousa, Martins, Azevedo, Mariz	2014	30 patients with hematological cancer who are subject to high dose chemotherapy	Prospective survey	Oral mucositis was observed in 21.9% (n=16), of which 4.1% was severe (Grade 3-4). Neutropenia increased the risk of mucositis ($p<0.001$). Patients who had not undergone oral prophylactic measures had a higher risk of mucositis ($p<0.05$).	70
Coracin, Santos, Gallottini, Saboya, Musqueira, Barban, Chamone Dde, Dulley, Nunes	2013	97 patients who are subject to hematopoietic stem cell transplantation	Prospective survey	It was suggested that oral environment (accumulation of dental plaque and severity of periodontal disease) can be a predictor of mucositis grade.	71
Lugliè, Mura, Mura, Angius, Soru, Farris	2002	30 patients who are subject to chemotherapy	Prospective cohort	Intervention of oral care led to a substantial improvement in bleeding and plaque index score in almost all patients. The incidence of oral mucositis was 66% in the control group, but it was 20% in the oral care intervention group. Specialized oral hygiene management and use of chlorhexidine can contribute to reduction of the incidence of oral mucositis induced by chemotherapy.	72
Cheng, Molassiotis, Chang, Wai, Cheung	2001	42 pediatric cancer patients aged 6-17 years	Prospective controlled	Intervention was provided based on the oral care protocol consisting of brushing and mouthwash using 0.2% chlorhexidine and 0.9% normal saline solution. The incidence of ulcerative mucositis decreased by 38% and severity ($P=0.000002$) as well as pain ($p=0.0001$) of oral mucositis also decreased.	73
Ohbayashi, Imataki, Ohnishi, Iwasaki, Ogawa, Inagaki, Shigeta, Ohue, Tasaka, Kitanaka, Kubota, Tanaka, Ishida, Miyake	2008	96 patients for hematopoietic stem cell transplantation	Before-after	After oral care intervention, the occurrence of oral mucositis decreased clearly. Multiple logistic analysis revealed that pre-treatment and oral care were independent risk factors for the occurrence of oral mucositis. Cryotherapy did not show sufficient effect on preventing oral mucositis.	74
Hernández-Fernández, Oñ ate-Sánchez, Cabrerizo-Merino, de Arriba-de la-Fuente, Heras-Fernando, Vicente-García	2012	72 patients for hematopoietic stem cell transplantation	Prospective survey	Oral mucositis was observed in 87% of patients. Grade of mucositis was affected by the number of lost teeth ($p<0.016$) and DMFS index (analysis of variance $p<0.038$).	75
Soga, Sugiura, Takahashi, Nishimoto, Maeda, Tanimoto, Takashiba	2010	53 patients for hematopoietic stem cell transplantation	Before-after	With regard to incidence of oral mucositis, comparison was made between the group that did not perform regular oral care (2003-2004) and the group that performed regular oral care (2005-2006). The incidence of oral mucositis with ulcers was significantly decreased by intervention of oral care.	76
Wuketich, Hienz, Marosi	2012	298 cancer patients subject to chemotherapy	Before-after	Oral mucositis was observed in 18 patients (6%). Severe mucositis of Grade 3-4 accounted for 1%. The incidence rates were significantly higher in patients who smoked ($p<0.05$) and patients who had not undergone dental check for 12 months or more ($P<0.01$). Indexes to show conditions of dental plaque and periodontitis were significantly higher in the group of oral mucositis ($p<0.01$).	66
Sennhenn-Kirchner, Freund, Grundmann, Martin, Borg-von Zepelin, Christiansen, Wolff, Jacobs	2009	73 patients who underwent radiotherapy for head and neck cancer	Before-after	In patients with head and neck cancer before/after radiotherapy, comparison was made between the 1984-1993 oral management group and the 1998-2005 oral management group. Dental check before radiotherapy (65% → 97.2%), use of fluorides (0% → 100%), and the number of decayed teeth (19.2%→7.8%).	82

Table 2: (continued)

Authors	Report year	Subjects	Study design	Outline	Ref. no.
Katsura, Sasai, Sato, Saito, Hoshina, Hayashi	2008	39 patients who underwent radiotherapy for head and neck cancer	Retrospective	Osteonecrosis of the jaws occurred in 6 patients. Oral health status after radiotherapy (grade of periodontal pocket, plaque, and alveolar bone resorption) was associated with osteonecrosis of the jaws.	83
Vahtsevanos, Kyrgidis, Verrou, Katodritou, Triaridis, Andreadis, Boukovinas, Koloutsos, Teleioudis, Kitikidou, Paraskevopoulos, Zervas, Antoniades	2009	1,621 patients with long-term use of bisphosphonates	Retrospective cohort	The approximate incidence rates of osteonecrosis of the jaws caused by drugs were 8.5% (multiple myeloma), 3.1% (breast cancer), and 4.9% (prostate cancer). The independent predictors associated with the development of osteonecrosis of the jaws, based on multivariate analysis (logistic regression analysis), were tooth extraction and use of dentures. Periodontitis treatment and root canal treatment did not increase the risk of osteonecrosis.	89
Ripamonti, Maniezzo, Campa, Fagnoni, Brunelli, Saibene, Bareggi, Ascani, Cislaghi	2009	966 patients who used bisphosphonates	Retrospective cohort	Osteonecrosis of the jaws caused by drugs was observed in 28 patients (2.9%). Intervention of dental/oral management prior to start of treatment reduced incidence of osteonecrosis of the jaws from 3.2% to 1.3%. Especially in patients who were administered with zoledronic acid, the risk of osteonecrosis of the jaws was significantly reduced by oral care intervention. (7.8% → 1.7%; P=0.016), IR:0.30 (95% confidence interval 0.03-1.26).	90
Dimopoulos, Kastritis, Bamia, Melakopoulos, Gika, Roussou, Migkou, Eleftherakis-Papaiakovou, Christoulas, Terpos, Bamias	2009	128 patients with multiple myeloma who were administered with zoledronic acid	Prospective, multicenter intervention	Incidence of osteonecrosis of the jaws: Oral care intervention group: 6.7%, non-oral care intervention group: 26.3% (P=0.002). Osteonecrosis in stage 3 was not observed in the intervention group. Osteonecrosis caused by drugs was reduced by prior implementation of dental prophylactic measures.	91
Saad, Brown, Van Poznak, Ibrahim, Stemmer, Stopeck, Diel, Takahashi, Shore, Henry, Barrios, Facon, Senecal, Fizazi, Zhou, Daniels, Carrière, Dansey	2012	5,723 cancer patients subject to administration of bone-modifying agents	RCT (3 Phase III studies)	Patients were randomly allocated to be administered with either denosumab (120mg) or i.v. zoledronic acid (4mg) in every 4 weeks. The onset of osteonecrosis of the jaws was observed in 37 patients (1.3%) with zoledronic acid and in 52 patients (1.8%) with denosumab, and no significant difference was observed between the two groups (P=0.13). Of the patients who developed osteonecrosis, more than 95% underwent conservative treatment and 36.0% (29.7% of zoledronic acid patients and 40.4% of denosumab patients) achieved a cure.	93
Hoff, Toth, Altundag, Johnson, Warneke, Hu, Nooka, Sayegh, Guarneri, Desrouleaux, Cui, Adamus, Gagel, Hortobagyi	2008	4,019 patients who received intravenous administration of bisphosphonates	Retrospective	Osteonecrosis of the jaws occurred in 16 patients (1.2%) of 1,338 breast cancer patients and in 13 patients (2.4%) of 548 multiple myeloma patients. Therapeutic experience and duration of treatment with pamidronic acid or zoledronic acid were much longer in the osteonecrosis (p<0.0001) patients. Based on a multivariate analysis with Cox proportional hazards regression model, tooth extraction was a significant risk factor for osteonecrosis (breast cancer patients: HR, 53.19; 95% CI:18.20-155.46; p<0.0001, Multiple myeloma patients: HR, 9.78;95% CI:3.07-31.14; p=0.0001). Conservative treatment has led 23% of osteonecrosis to a cure.	94
Badros, Terpos, Katodritou, Goloubeva, Kastritis, Verrou, Zervas, Baer, Meiller, Dimopoulos	2008	97 patients who developed bisphosphonate-induced osteonecrosis of the jaws	Prospective observational	60 patients (62%) of osteonecrosis of the jaws achieved a cure. Osteonecrosis relapsed in 12 patients (12%) after cure and 25 patients (26%) could not achieve a cure.	95
Mawardi, Treister, Richardson, Anderson, Munshi, Faiella, Woo	2009	5 patients who developed bisphosphonate-induced osteonecrosis of the jaws	Case report	Although there is no obvious bone exposure, fistula formation was locally observed and clinical condition of so-called "stage 0," which would eventually result in bone exposure, existed.	92

Table 2: (continued)

Authors	Report year	Subjects	Study design	Outline	Ref. no.
Walter, Al-Nawas, du Bois, Buch, Harter, Grötz	2009	117 breast cancer patients who were administered with bisphosphonates	Retrospective	Osteonecrosis of the jaws occurred in 4 patients (5.3%), and tooth extraction was the inducing factor in 2 of these cases. Appropriate dental care before bisphosphonate treatment can reduce osteonecrosis	85
Zenda, Matsuura, Tachibana, Homma, Kirita, Monden, Iwae, Ota, Akimoto, Otsuru, Tahara, Kato, Asai	2011	101 patients who are subject to chemoradiotherapy for head and neck cancer mainly using cisplatin	Prospective multicenter	Treatment completion rate was improved through introduction of supportive therapy (oral care, active use of opioid, PEG, etc.) (Retrospective pilot study: CRT completion rate 85%→this study: completion rate 99%)	99
Hirokazu Saito & Yutaka Watanabe & Kazumichi Sato & Hiroaki Ikawa & Yoshifumi Yoshida & Akira Katakura & Shin Takayama & Michio Sato.	2014	26 breast cancer patients scheduled to undergo chemotherapy	RCT	Oral prophylactic measures reduced oral adverse events (oral mucositis) induced by chemotherapy.	77

of tooth extraction were significant risk factors for ONJ. Conservative treatment led to a cure in 23% of patients with ONJ[94].

- A follow-up study of 97 patients with bisphosphonate-associated osteonecrosis found that 60 patients (62%) achieved a cure. On the other hand, 12 people (12%) noticed recurrence of osteonecrosis after cure, and 25 patients (26%) achieved no cure[95].

[Discussion]

It is not necessarily the case that oral complications due to cancer treatment can be prevented completely by the implementation of oral care. However, given that oral health status of cancer patients is associated with the incidence and severity of oral complications, effective oral hygiene management could be promising in terms of its contribution to risk reduction for oral complications. In particular, with respect to infections arising from dental foci, the risk of onset could be reduced by dental check prior to initiation of cancer treatment, emergency procedures, and care centering around brushing during treatment, which are useful for infection control during treatment that likely leads to myelosuppression. Oral mucositis during the period of myelosuppression especially serves as a strong risk factor for systemic infection, and thus, infection management through oral care is important[26].

The occurrence frequency of ONJ, the most serious oral late effect of radiotherapy in the head and neck region, has been suppressed relative to that previously reported due to prophylactic dental intervention (e.g., preventive tooth extraction prior to treatment initiation, regular dental management after treatment completion)[96]. However, it still occurs at a certain frequency, threatening patients' quality of life. As the biggest triggering event leading to onset is tooth extraction within the field of irradiation, how well the oral cavity can be maintained and tooth extraction be avoided is the cornerstone of prevention. In this context, oral management assumes a heavy responsibility.

It is desirable to deal with medication-induced ONJ early on, before bone exposure appears (stage 0). Initial symptoms of stage 0 ONJ reportedly include pain in the oral cavity, fistula formation, prolonged infection symptoms such as pus discharge, and paresthesia of the chin including the lower lip (Vincent's symptom)[97,98], and we think it is important to not miss these findings in a dental setting, and to perform regular oral screening as well as care intervention.

The purpose of oral management during cancer treatment is not to attain 'zero' oral complications; rather, it aims to provide support by reducing their frequency and severity to the extent possible, so that cancer treatment proceeds safely and smoothly as planned.

"Supportive care" for cancer, which aims to help make the patient's life under treatment less painful by managing infection risks during cancer treatment, supporting oral ingestion to assist nutritional management, and relieving pain, could improve the completion rate of cancer treatment and contribute to treatment prognosis[99]. Although the evidence of oral care in such cancer treatment is not yet sufficient in many aspects, even based on that fact, the importance of oral hygiene and maintenance of oral function should not be denied. However, as specific contents and frequency regarding dental intervention vary from report to report, unified measures as well as consent acquisition will be necessary in the future.

[Conclusions]

Oral adverse events that occur in association with cancer treatment interfere with smooth cancer treatment, and sometimes affect patient life prognosis. Appropriate oral hygiene management prior to initiation of cancer treatment is useful in reducing the risk of occurrence and severity of oral adverse events.

[Conflict of interest]

There are no items applicable to "conflict of interest" in this article.

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3. Oral health and lifestyle-related diseases, non-communicable diseases (NCDs)

4) Cardiovascular diseases (heart and blood vessel diseases and cerebral vascular diseases) – Oral health and cardiovascular diseases –

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[Abstract]

Cardiovascular diseases, including cardiac and cerebrovascular diseases, account for 27.9% of deaths among Japanese people. In particular, cardiac disease, which tends to go higher up in the list of causes of death with increasing age group, represents a disease that cannot be ignored when discussing the public health of the Japanese people. There have been various discussions with regard to associations between oral health conditions and cardiovascular disease. Accordingly, we summarized evidence focusing on seven review articles published to date. The results confirmed that there has been a consensus to a certain degree, with regard to the fact that periodontal disease is associated with cardiovascular disease, according to studies reported up to the present. Moreover, there have been new findings, such as that relative risks (RR) of cardiovascular disease among people with periodontal disease increase when subjects are limited to those aged 65 years or younger, that the association of periodontal disease with acute myocardial infarction is stronger than that with chronic coronary heart disease, and that those affected with periodontal disease with accompanying systemic bacterial infections have a higher risk of coronary heart disease. However, a few studies have reported on reduction in the risk of developing cardiovascular disease or decrease in serum antibody titers associated with the treatment of periodontal disease, and the causality of these relationships have not been clarified. Future research is desired, with more follow-up and intervention studies.

[Introduction]

Cardiovascular diseases, including cardiac and cerebrovascular diseases, account for 27.9% of deaths among Japanese people. This percentage is close to that of malignant neoplasm (28.7%), the number one cause of death among the Japanese people. Moreover, cardiac disease and cerebrovascular disease account for 15.8% and 9.7% of causes of death, respectively, and these diseases have long been ranked as the second and third causes of death among the Japanese people. In particular, there is a tendency that the higher the age group, the higher the ranking of cardiac disease in the list of causes of death (ranked third in the age group of 35-49 years, second in 50-89 years, and first in 90-99 years). As such, cardiac disease cannot be ignored when discussing public health of Japanese people. Various discussions have been carried out with regard to oral health conditions and cardiac disease, with no settlement of dispute to date. Therefore, this review assessed studies conducted to date in terms of what parameters have been used to evaluate oral health conditions in order to demonstrate an association with cardiac disease.

[Objective]

Since Mattila *et al*. reported that oral health was associated with acute myocardial infarction in 1989, associations between the two have attracted much attention. However, there have also been many negative reports since then, developing this topic into a big controversy. In 2009, a consensus was reached by the journal editorial board of the American Heart Association and the American Academy of Periodontology, that "no causal relationship has been established between periodontal disease and heart disease," putting a certain end to the dispute. Meanwhile, it is also true that prospective studies have not been performed to a sufficient degree, and there is a possibility that new evidence might emerge in the future. The relationship between oral health conditions and cardiovascular disease, if proven, will be so significant, given the high mortality rate of cardiovascular disease. Accordingly, this review aimed to organize evidence demonstrated to date.

[Methods]

Using PubMed, we conducted a search of the literature under "cardiovascular," "CVD," and "CHD." In addition, search terms such as "oral health" and "periodontitis" were used. From the retrieved articles as well as articles cited in the literature, we summarized the relationship between oral health conditions and cardiovascular disease. The articles were mainly cited from meta-analysis papers published from April 2003 through April 2014.

[Results]

Seven review articles regarding the relationship between oral health conditions and cardiovascular disease were retrieved; these articles cited a total of 59 papers, which reported 17 cross-sectional studies, 19 case-control studies, and 23 cohort studies (one was a retrospective cohort study).

Below are points of view provided by each review article, listed in chronological order (see Tables 1 and 2).

Janket *et al*.[1] performed a meta-analysis, in which they cited nine cohort studies. The results showed that the RR of cardiovascular disease in individuals with periodontal disease was 1.19 (95% confidence interval (CI), 1.08-1.32); when analysis was limited to individuals at the age of 65 years or younger, the RR was 1.44 (95% CI, 1.20-1.73), showing an increase.

Khader *et al*.[2] performed a meta-analysis citing seven cohort studies and four cross-sectional studies. As a result, the RR of coronary heart disease was calculated to be 1.15 (95% CI, 1.06-1.25) in subjects with periodontitis.

Bahekar *et al*.[3] performed a meta-analysis citing five cohort studies, five case-control studies, and five cross-sectional studies. The RRs of developing cardiovascular disease in individuals with periodontitis were calculated to be 1.14 (RR; 95% CI, 1.074-1.213) in cohort studies, 2.22 (odds ratio (OR); 95% CI, 1.594-3.117) in case-control studies, and 1.59 (OR; 95% CI, 1.329-1.907) in cross-sectional studies. Furthermore, in an analysis of the relationship between number of teeth and incidence of coronary heart disease, the RR of developing coronary heart disease in individuals with less than 10 teeth was calculated to be 1.24 (95% CI, 1.14-1.36).

Mustapha *et al*.[4] performed a meta-analysis with the results of 11 studies. Coronary heart disease and carotid intima-media thickening (CIMT) were used as measures of early atherosclerosis, and systemic bacterial exposure was measured with bacterial count, periodontal disease-specific serology, and C-reactive protein (CRP). The results of seven of these studies revealed that subjects with periodontal disease with elevated markers of systemic bacterial exposure showed a very strong association with coronary heart disease, and the OR was calculated to be 1.75 (95% CI, 1.32-2.74). Moreover, although these groups were not associated with stroke or cardiovascular disease events, the mean CIMT was increased by 0.03 mm compared to the group with no periodontal disease. Furthermore, this meta-analysis assessed systemic inflammation compared to previous studies that employed clinical assessments of periodontal disease alone (Janket *et al*., 2003; Khader *et al*., 2004), and thus, the authors state that the association between periodontal disease accompanying systemic bacterial infections and coronary heart disease events or early atherogenesis was more strongly demonstrated.

Humphrey *et al*.[5] performed a meta-analysis citing seven cohort studies. The association between cardiovascular disease and each item was assessed by outcome, with an RR of 1.24 (95% CI, 1.01-1.51) for periodontal disease, RR of 1.34 (95% CI, 1.10-1.63) for number of teeth (0-10 teeth), and RR of 1.35 (95% CI, 0.79-2.30) for gingivitis. Moreover, RRs were calculated by dividing the cases into two groups according to outcomes (onset of cardiovascular disease or death by cardiovascular disease), sex and follow-up period (less than 15 years or 15 years or more), assessment methods of periodontal disease (dental examination or subjective examination), and quality of research (good or fair); however, the values were almost the same. Based on these results, the authors concluded that periodontal disease

Table 1: Summary of review articles related to periodontal disease and cardiovascular disease

Review articles	Janket *et al.*, 2003[1]	Khader *et al.*, 2004[2]	Bahekar *et al.*, 2007[3]	Mustapha *et al.*, 2007[4]	Humphrey *et al.*, 2008[5]	Blaizot *et al.*, 2009[6]	Dietrich *et al.*, 2013[7]
Outcome measure	CVD	CHD	CHD	CVD	CHD	CVD	CVD
RR by meta-analysis	1.19	1.15	1.14	1.75	1.24	1.34	No value (Review)
95% CI	1.08-1.32	1.06-1.25	1.07-1.21	1.32-2.34	1.01-1.51	1.27-1.42	-
Main results	RR increases to 1.44 (1.2-1.7) in individuals aged ≤65 years	Fatal CHD or number of teeth and CHD are not associated	RR is 1.21 (1.14-1.36) in individuals with less than 10 remaining teeth	Periodontal disease accompanying systemic bacterial infection and CHD are associated	Periodontal disease is an independent risk factor or risk marker	Periodontal disease is more strongly associated with chronic coronary heart disease than with acute myocardial infarction	The association between periodontitis and incidence of secondary cardiovascular disease has not been confirmed

∗ Abbreviations CHD; coronary heart disease CVD; cardiovascular disease

Table 2: List of bibliographic citations from each review article

Author	Year of publication	Type of study	Janket *et al.*, 2003[1]	Khader *et al.*, 2004[2]	Bahekar *et al.*, 2007[3]	Mustapha *et al.*, 2007[4]	Humphrey *et al.*, 2008[5]	Blaizot *et al.*, 2009[6]	Dietrich *et al.*, 2013[7]	RR	Parameters of oral health conditions
Abnet	2005	Cohort						○		3.77(1.46-9.74)	Percentage of CAL ≥3 mm
Ajwani	2003	Cohort				○	○		○	-	Community Periodontal Index of Treatment Needs (CPITN), CRP
Andriankaja	2006	case-control						○		2.24(1.6-3.13)	PPD, CAL
Andriankaja	2007	case-control							○	-	Mean CAL ≥3 mm, PPD
Arbes	1999	cross sectional		○	○			○		1.38(0.75-2.54)	CAL ≥3 mm
Beck	1996	Cohort	○	○			○			1.49(1.07-2.15)	PPD, alveolar bone defects
Beck	2005	cross sectional				○				Smokers 1.3(1.00-1.80), Non-smokers 1.2(0.80-1.80)	Pg IgG
Beck	2005	cross sectional				○CIMT				Smokers 1.5(1.20-2.10), Non-smokers 1.4(1.00-1.90)	Pg IgG
Brarilli	2006	case-control						○		61(17.26-214.86)	PPD ≥6 mm
Briggs	2006	case-control			○			○		3.06(1.02-9.17)	PPD, BOP
Buhlin	2002	cross sectional		○	○			○		1.60(1.19-2.15)	Self-reported gingival bleeding, tooth mobility, periodontal pockets
Buhlin	2003	cross sectional			○			○		1.70(1.08-2.69)	Questionnaire survey on disease frequency and treatment
Buhlin	2005	case-control			○			○		3.8 (1.68-8.74)	Number of remaining teeth, PPD, denture use
Cabrera	2005	Cohort						○		1.46(1.15-1.85)	Missing teeth ≥10
Coelho	2005	case-control						○		4.03(0.42-32.43)	PPD, CAL

Table 2: (continued)

Author	Year of publication	Type of study	Janket *et al.*, 2003[1]	Khader *et al.*, 2004[2]	Bahekar *et al.*, 2007[3]	Mustapha *et al.*, 2007[4]	Humphrey *et al.*, 2008[5]	Blaizot *et al.*, 2009[6]	Dietrich *et al.*, 2013[7]	RR	Parameters of oral health conditions
Cueto	2005	case-control						○	○	3.31(1.42-7.71)	Percentage of CAL ≥3 mm
DeStefano	1993	Cohort	○	○	○		○	○		1.25(1.06-1.48)	G, P (mild, moderate, advanced)
Desvarieux	2005	cross sectional				○CIMT				-	*Pg/Aa*
Dietrich	2008	Cohort							○	-	PPD, alveolar bone defects
Dorn	2010	Cohort							○	Smokers 1.0(0.9-1.2), Non-smokers 1.4(1.1-1.9)	Mean CAL ≥3 mm, PPD
Elter	2004	cross sectional			○			○		1.5(1.11-2.02)	PPD, CEJ measurements
Frisk	2003	cross sectional						○		2.70(1.49-4.87)	Missing teeth ≥16
Geerts	2004	case-control			○			○		6.5(1.82-23.24)	PPD, BOP, PI, furcation involvement, tooth mobility
Geismar	2006	case-control						○		2.0(0.77-5.08)	Alveolar bone defects ≥4 mm
Genco	1997	Cohort	○							2.68(1.30-5.50)	Tooth loss, alveolar bone defects
Grau	2004	case-control							○	-	PPD, CAL
Gotsman	2007	cross sectional						○		1.03(1.01-1.04)	CAL ≥5 mm
Holmlund	2006	cross sectional						○		2.69(1.12-6.46)	PDSI
Howell	2001	Cohort	○	○	○		○			1.01(0.86-1.15)	Self-reported history of periodontal disease
Hujoel	2000	Cohort	○	○						1.14(0.96-1.36)	Healthy, G, P
Hung	2004	Cohort					○	○		♂1.36(1.11-1.67), ♀1.64(1.31-2.05)	Self-reported tooth loss
Jansson	2002	Cohort						○		1.5(1.04-2.14)	Number of missing teeth, alveolar bone defects, dental caries, plaque

Table 2: (continued)

Author	Year of publication	Type of study	Janket *et al.*, 2003[1]	Khader *et al.*, 2004[2]	Bahekar *et al.*, 2007[3]	Mustapha *et al.*, 2007[4]	Humphrey *et al.*, 2008[5]	Blaizot *et al.*, 2009[6]	Dietrich *et al.*, 2013[7]	RR	Parameters of oral health conditions
Joshipura	1996	Cohort	○	○	○					1.04(0.86-1.25)	Questionnaire-based subjective evaluation, number of remaining teeth
Jimenez	2009	Cohort							○	-	Periapical X-ray score
Katz	2001	cross sectional						○		5.14(1.37-19.28)	PPD
Latronico	2007	case-control						○		5.85(1.03-33.12)	Mean CAL ≥3.5 mm
Loesche	1998	cross sectional		○	○			○		4.6(1.32-16.0)	Number of remaining teeth, BOP
Lopez	2002	case-control							○	3.17(1.31-7.65)	PPD, CAL
Malthaner	2002	cross sectional			○			○		1.64(0.47-5.75)	Mean CAL ≥3.5 mm
Mattila	1995	Cohort	○		○					1.21(1.08-1.36)	TDI, PGI
Mendez	1998	Cohort							○	2.3(1.3-3.9)	Periapical X-ray score
Montebugnoli	2004	case-control						○		4.61(1.00-23.20)	CPSS
Morrison	1999	retrospective Cohort	○	○			○	○		2.15(1.25-3.72)	Healthy, moderate periodontal disease, advanced periodontal disease
Nicolosi	2003	cross sectional						○		2.04(1.23-3.38)	Number of sections with PPD ≥3 mm
Nonnemacher	2007	case-control						○		3.2(1.2-9.0)	CAL ≥3 mm
Pussinen	2003	cross sectional				○				1.50(0.95-2.50)	*Pg/A* Complex IgG
Pussinen	2004	Cohort				○				-	Pg IgA, *Pg* IgG
Pussinen	2005	Cohort				○				-	Pg IgA, *Pg* IgG
Pussinen	2005	cross sectional				○CIMT				2.43(1.73-3.10)	*Pg/Aa* Complex IgG

Table 2: (continued)

Author	Year of publication	Type of study	Janket *et al.*, 2003[1]	Khader *et al.*, 2004[2]	Bahekar *et al.*, 2007[3]	Mustapha *et al.*, 2007[4]	Humphrey *et al.*, 2008[5]	Blaizot *et al.*, 2009[6]	Dietrich *et al.*, 2013[7]	RR	Parameters of oral health conditions
Rech	2007	case-control						○		4.5(1.30-15.60)	PPD
Renvert	2004	case-control						○		7.67(1.13-51.92)	PPD
Rutger	2003	case-control						○		14.1(5.8-34.4)	Alveolar bone defects ≥40%
Sim	2008	case-control							○	-	Number of teeth with CAL ≥6 mm
Spahr	2006	case-control			○					1.67(108-2.58)	Total periodontopathic bacteria, supragingival biofilm, need for periodontal treatment
Taniguchi	2003	cross sectional				○CIMT				-	Pg IgG
Tuominen	2003	Cohort					○	○	○	-	Dental caries, PI, number of remaining teeth, denture use
Wu	1999	Cohort	○							1.17(1.04-1.31)	Healthy, G, P, edentulous
Wu	2000	Cohort		○	○					1.66(1.15-2.39)	Healthy, G, P, edentulous
Xu	2011	Cohort							○	-	PPD, CAL

∗ Abbreviations

Aa; Actinobacillus actinomycetemcomitans
CAL; clinical attachment loss
CEJ; cement enamel junction
CHD; coronary heart disease
CIMT; carotid intima-media thickness
CPSS; clinical periodontal sum score
CRP; C-reactive protein
CVD; cardiovascular disease
G; gingivitis
OPGI; orthopantomography index
P; periodontitis
PDSI; periodontal severity index
Pg; Porphynomonas gingivalis
PI; plaque index
PPD; probing pocket depth
RR; relative risk
TDI; total dental index

is a risk factor or risk marker for coronary heart disease, independent of traditional coronary heart disease risk factors.

Blaizot *et al*.[6] cited 29 studies and calculated OR and RR of developing cardiovascular disease in individuals with periodontal disease. The OR calculated from 12 case-control studies and 10 cross-sectional studies was 2.35 (95% CI, 1.87-2.96), and the RR calculated from seven cohort studies was 1.34 (95% CI, 1.27-1.42). These results show that in Scandinavia and the United States, compared to southern Europe, the association between periodontal disease and coronary heart disease is weaker, and that acute myocardial infarction, compared to chronic coronary heart disease, has a stronger association with periodontal disease. In addition, the authors discussed the need of further studies with regard to reduction in the risk of developing cardiovascular disease associated with the treatment of periodontitis.

Dietrich *et al*.[7] conducted a systematic review to discuss the relationship between periodontal disease and incidence of atherosclerotic cardiovascular disease. This review cited 12 studies, of which 11 found associations; however, these associations were stronger in younger adults, and no association was found between periodontal disease and incidence of coronary heart disease in individuals aged 65 years or older. Moreover, the authors concluded that, since only a few studies exist that reported on the association between periodontal disease and incidence of secondary cardiovascular events in patients who had already developed cardiovascular disease, further epidemiological studies are necessary.

[Discussion]

We searched the literature published in 2000 and thereafter regarding oral health conditions and cardiovascular disease. Developing a plan for a study excluding all confounding factors that appear to affect these two is probably extremely difficult. However, based on the results reported so far, there seems to be a consensus with regard to the association between periodontal and cardiovascular diseases. Yet, only a few reports exist regarding the reduction of risk of cardiovascular events and decrease in serum antibody titers associated with treatment for periodontal disease, and thus, the causal relationship between these two remains to be clarified. Moreover, only a few studies have examined the association between periodontal disease and incidence of secondary cardiovascular events in patients who have already developed cardiovascular disease, and in this context, the impact of periodontal disease on the recurrence of cardiovascular disease has not yet been clarified to the full extent. Furthermore, although some study findings indicate a link between cardiovascular disease and number of lost teeth or that of remaining teeth, a very few studies have adopted use of dental prosthesis and number of functional teeth as indicators of oral health conditions; therefore, it might be necessary to accurately grasp the conditions of the oral cavity. There have been new findings, such as that RRs of cardiovascular disease in individuals with periodontal disease increase when subjects are limited to those aged 65 years or younger, that a stronger association was found between periodontal disease and acute myocardial infarction compared to chronic coronary heart diseases, and that periodontal disease accompanying systemic bacterial infections increases the risk of coronary heart disease. Future studies should first address these issues, and carry out well-planned follow-up and/or intervention studies.

[Conclusions]

This review examined studies up to the present regarding the association between oral health conditions and cardiovascular disease. The results showed that although many reports acknowledge the association between periodontal disease and cardiovascular disease, currently the causal relationship is still unclear. In the future, new studies are required to assess associations between oral health conditions and cardiovascular disease using indices other than periodontitis, and to investigate prevention of cardiovascular disease or its recurrence through treatment of periodontal disease.

[Conflict of interest]

There are no items applicable to "conflict of interest" in this article.

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3. Oral health and lifestyle-related diseases, non-communicable diseases (NCDs)

5) Metabolic syndrome (obesity, dyslipidemia, hypertension, diabetes mellitus)

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[Abstract]

An increase in lifestyle-related diseases in adults has become a major health issue, and metabolic syndrome is known to increase the risk of lifestyle-related diseases such as diabetes mellitus and arteriosclerotic diseases.

In recent years, the association between metabolic syndrome and oral health, including periodontal disease, has been reported. Therefore, in this review, we searched articles that had demonstrated the association between metabolic syndrome and oral health, and examined their correlations.

With regard to research on the association between metabolic syndrome and oral health, numerous studies have been reported from various countries, with a relatively high volume of Japanese studies. The results of those studies, although many were cross-sectional studies, suggested that individuals with metabolic syndrome have a high risk of periodontal disease, and that many patients with periodontal disease have metabolic syndrome.

Since many aspects of metabolic syndrome and oral health, such as the direction and underlying mechanisms of the association, remain unclear, accumulation of further studies is necessary in order to clarify their relationship.

[Introduction]

Obesity plays an important role in lifestyle-related diseases in adults, and Japan is no exception to the trend of increase in the number of obese men. In particular, along with insulin resistance, visceral fat obesity has been strongly associated with hyperglycemia, hypertension, and dyslipidemia, and metabolic syndrome, which combines them, affects many people.

Obesity, hyperglycemia, hypertension, and dyslipidemia each increases the risk of arteriosclerotic diseases such as stroke and myocardial infarction, but when the condition is such that these abnormalities manifest concurrently, the risk is said to increase even higher. For this reason, the condition in which obesity and insulin resistance are combined with hyperglycemia, hypertension, and dyslipidemia has been referred to as syndrome X, deadly quartet, insulin resistance syndrome, visceral fat syndrome, or multiple-risk factor syndrome. As for the criteria for the diagnosis of metabolic syndrome, World Health Organization (WHO) indicated diagnostic criteria in 1998, and then, the U.S. National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) and the International Diabetes Federation (IDF) each developed criteria in 2001 and 2005, respectively. In addition, in 2005, eight academic societies in Japan jointly announced the diagnostic criteria for metabolic syndrome in Japan.

Periodontal disease is a multifactorial disease that is affected by various factors, and its association with obesity, which has the central presence in metabolic syndrome, has been reported by many studies up to present[1]. Moreover, periodontal disease is referred to as the sixth complication of diabetes mellitus[2], and today, it is said that periodontal disease and diabetes mellitus are bi-directionally associated[3,4]. Similarly, hypertension and dyslipidemia have been shown to be associated with periodontal disease[5,6]. Against this backdrop, numerous study results have been reported with regard to the association between metabolic syndrome and periodontal disease.

Therefore, in this review, we searched articles demonstrating the association between metabolic syndrome and oral health, with a main focus on periodontal disease, to examine findings that have been clarified to date.

[Objective]

The objective of this review is to examine the association between metabolic syndrome and oral health by searching articles with regard to the association between metabolic syndrome, which is deeply associated with lifestyle-related diseases, and oral health such as periodontal disease.

[Methods]

In this review, we conducted searches of articles using PubMed, and cited articles that were available for verification as of July 2014. During the searches, combinations of keywords were used, and in principle, articles on human subjects and those written in English were retrieved. With regard to the association between metabolic syndrome and periodontal disease, 102 articles were extracted by a literature search with keywords "metabolic syndrome" and "periodontal disease." In addition, 29 review articles and nine systematic review articles were extracted by a search with the type of articles limited to reviews or systematic reviews only. With regard to the association between metabolic syndrome and tooth loss, 15 articles were extracted by a search with terms "metabolic syndrome" and "tooth loss." Content of each article was checked, and articles demonstrating the association between metabolic syndrome and oral health were selected and subjected to our review.

[Results]

The results of the searches regarding the association between metabolic syndrome and oral health are shown in Table 1.

Of the 26 articles, there were 22 cross-sectional studies, two case-control studies, and two cohort studies. With respect to the location where these studies were conducted, Japan was most frequently noted (nine articles), followed by the United States (six articles), Korea (four articles), Taiwan (two articles), and Sweden, Jordan, China, Finland, and France (one article each). As for the criteria used for metabolic syndrome diagnosis, although criteria for obesity differed from study to study, the criteria based on the NCEP-ATP III criteria were most frequently used (14 articles), whereas three articles used the Japanese diagnostic criteria, three used the criteria according to the American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement (AHA/NHLBI), one used the IDF criteria, one used the European Group for the Study of Insulin Resistance (EGIR) criteria, and four used integrated diagnostic criteria. As for the indicators of oral health, a variety of criteria were used for the assessment of periodontal status: some assessed the presence of periodontal pocket depth (PD) of ≥4 mm based on the Community Periodontal Index (CPI), while others assessed PD and clinical attachment loss (CAL) individually, or in combination. Also used were self-reported presence or absence of periodontal disease, degree of alveolar bone resorption, bleeding on probing (BOP), the plaque index, and serum antibody titers. There were also studies that had examined the association between metabolic syndrome and tooth loss and frequency of tooth brushing.

In one of our studies, Japanese women with a higher number of positive items regarding metabolic syndrome according to the NCEP-ATP III diagnostic criteria had a higher risk of periodontal disease[7]. Other studies also showed that many of the individuals with a high number of positive items regarding metabolic syndrome had periodontal disease[8-13]. Moreover, it has been shown that, compared to individuals without metabolic syndrome, those with metabolic syndrome had a higher risk of periodontal disease[14-17], or had a higher serum antibody titer for *Porphyromonas gingivalis*, which is profoundly involved in periodontal disease[18].

On the other hand, individuals with a poor periodontal status have been shown to have a high risk of metabolic syndrome[19-25]. Case-control studies based on the presence/absence of metabolic syndrome showed that individuals with periodontal disease have a high risk of metabolic syndrome[26,27]. Moreover, one study showed that, although no association was found between metabolic syndrome and periodontal status, individuals with a high HOMA index, i.e., an indicator of insulin resistance, have a high risk of periodontitis[28], and another study showed results indicating that individuals with metabolic syndrome have a high plaque index[29]. Furthermore, individuals with metabolic syndrome has been shown to have a fewer number of teeth[30].

Studies that demonstrate a longitudinal association between metabolic syndrome and oral health are limited. A Japanese cohort study targeting working adults showed that, among those with no positive items of metabolic syndrome at baseline, those with a high PD had a higher risk of acquiring positive items of metabolic syndrome four years later[31]. Moreover, a longitudinal study that had examined the association between number of tooth brushing and metabolic syndrome showed that individuals with more frequent tooth brushing had a low risk of developing metabolic syndrome[32].

Several reviews have been reported with regard to the association between metabolic syndrome and periodontal disease[33-45]. Results of a meta-analysis using data from 18 studies showed that the odds ratio for periodontitis in patients with metabolic disease was 1.71 (95% confidence interval: 1.42-2.03), suggesting that the association between the two is significant[42].

[Discussion]

Obesity plays a central role in metabolic syndrome,

Table 1: Study reports that demonstrate the association between metabolic syndrome (MetS) and oral health

Author	Report year	Study area Study subjects	Subjects, number of subjects, age	Study design	MetS diagnostic criteria	Adjustment factors	Main results	Ref. No.
Shimazaki *et al.*	2007	Japan Hisayama-cho study	584 women, 40-79 years old	Cross-sectional	NCEP-ATP III	Age, smoking, lipid-lowering drugs, total cholesterol	Positive MetS items ≥3 → odds ratio for mean PD ≥2 mm, 4.7 (2.4-9.7) odds ratio for mean CAL ≥3 mm, 3.3 (1.2-8.8)	7
Holmlund *et al.*	2007	Sweden	1,016 men and women, 70 years old	Cross-sectional	NCEP-ATP III	Smoking, education, height, white blood cell count	Individuals with MetS → lower number of teeth	30
D'Aiuto *et al.*	2008	USA NHANES III	13,994 men and women, ≥17 years old	Cross-sectional	NCEP-ATP III	Age, gender, years of education, poverty rate, ethnicity, general condition	Non-smokers aged ≥45 years: severe periodontitis → odds ratio for MetS, 2.31 (1.13-4.73)	19
Khader *et al.*	2008	Jordan	MetS: 78 subjects, ≥25 years old Healthy: 78 subjects, ≥25 years old	Cross-sectional	NCEP-ATP III	Age, gender, education, income, smoking, toothbrushing frequency, plaque index	Individuals with positive MetS items → periodontitis severity, extensiveness ↑	8
Li *et al.*	2009	China	MS: 152 subjects, 37-78 years old Healthy: 183 subjects, 37-78 years old	Case-control	IDF Waist circumference: Men ≥90 cm Women ≥80 cm	Age, gender, smoking	CAL↑, PD↑, plaque index ↑ → odds ratio for MetS ↑	26
Morita *et al.*	2009	Japan Workplace medical check-up	2,478 men and women, 24-60 years old	Cross-sectional	Japanese standards Obesity: BMI ≥25	Age, gender, smoking	Positive MetS items ≥3 → odds ratio for PD ≥4 mm, 2.4 (1.7-2.7)	14
Kushiyama *et al.*	2009	Japan Periodontal disease screening	1,070 men and women, 40, 50, 60, and 70 years old	Cross-sectional	NCEP-ATP III Obesity: BMI ≥25	Age, gender, smoking	3 positive MetS items → odds ratio for PD ≥4 mm, 2.13 (1.22-3.70) ≥4 positive MetS items → odds ratio for PD ≥4 mm, 2.34 (1.08-5.08)	9
Morita *et al.*	2010	Japan Workplace medical check-up	1,023 men and women 20-56 years old	Cohort 4 years	Japanese standards Obesity: BMI ≥25	Age, gender, smoking, exercise, snacking, healthy weight	PD ≥4 mm → odds ratio for an increase of ≥1 positive MetS items, 1.6 (1.1-2.2)	31
Han *et al.*	2010	Korea Shiwha-Banwol Environmental Health Study	1,046 men and women, 18-84 years old	Cross-sectional	Integrated classification Waist circumference: Men ≥90 cm Women ≥85 cm	Age, gender, income, smoking, drinking, toothbrushing frequency, physical activity	3 positive MetS items → odds ratio for PD ≥4 mm, 1.53 (1.05-2.23) ≥4 positive MetS items → odds ratio for PD ≥4 mm, 2.20 (1.28-3.78)	10
Nesbitt *et al.*	2010	USA BLSA	112 men (mean age, 56.7 years), 78 women (mean age, 60.0 years)	Cross-sectional	NCEP-ATP III positive items ≥2	Age, gender, ethnicity, smoking	Moderate or severe alveolar bone resorption → odds ratio for MetS, 2.61 (1.1-6.1)	20

Table 1 : (continued)

Author	Report year	Study area Study subjects	Subjects, number of subjects, age	Study design	MetS diagnostic criteria	Adjustment factors	Main results	Ref. No.
Timonen *et al*.	2010	Finland Randomly selected specimen	2,050 men and women, 30-64 years old	Cross-sectional	EGIR	Age, gender, education, plaque index, toothbrushing frequency, dental visits, drinking	Individuals with MetS → odds ratio for PD ≥4 mm, 1.19 (1.01-1.42)	15
Andriankaja *et al*.	2010	USA NHANES III	7,431 men and women, ≥20 years old	Cross-sectional	NCEP-ATP III	Age, ethnicity, years of education, family history of heart disease, smoking	Women (no significant association in men): 2 positive MetS items → odds ratio for mean PD ≥2.5 mm, 5.6 (2.2-14.4) ≥3 positive MetS items → odds ratios for mean PD ≥2.5 mm, 4.7 (2.0-11.2)	11
Benguigui *et al*.	2010	France MONA LISA survey	255 men and women, 35-74 years old	Cross-sectional	NCEP-ATP III HOMA index	Age, gender, years of education, smoking, drinking, CRP, plaque index	No significant association between MetS and periodontitis HOMA index ↑ → severe periodontitis ↑	28
Bensley *et al*.	2011	USA WAHS	672 men and women, ≥25 years old	Cross-sectional	AHA/NHLBI	Age, gender, income, smoking, psychosocial stress	Self-reported severe periodontitis → relative risk for MetS, 1.5 (1.2-2.1)	21
Chen *et al*.	2011	Taiwan Hemodialysis patients	253 men and women >18 years old	Cross-sectional	NCEP-ATP III Waist circumference: Men ≥90 cm Women ≥80 cm	Age, gender, high sensitivity CRP, serum albumin, smoking, education	Moderate or severe periodontitis → odds ratio for MetS, 2.736 (1.293-5.790)	22
Kwon *et al*.	2011	Korea KNHANES	7,178 men and women, ≥19 years old	Cross-sectional	NCEP-ATP III Waist circumference: Men ≥90 cm Women ≥85 cm	Age, gender, income, education, childhood background, dental floss use, interdental brush use, drinking, smoking, untreated dental caries, DMFT, current number of teeth	PD ≥4 mm → odds ratio for MetS 1.55 (1.32-1.83)	23
Han *et al*.	2012	Korea Shiwha-Banwol Environmental Health Study	MetS: 167 subjects, Healthy: 166 subjects, 20-60 years old	Case-control	Integrated classification Waist circumference: Men ≥90 cm Women ≥85 cm	(Matching: age, gender), income, smoking, drinking, physical activity, diabetes mellitus	PD ≥4 mm → odds ratio for MetS 1.76 (1.06-2.93)	27

Table 1 : (continued)

Author	Report year	Study area Study subjects	Subjects, number of subjects, age	Study design	MetS diagnostic criteria	Adjustment factors	Main results	Ref. No.
Kobayashi *et al*.	2012	Japan Sendai wholesaler study	Men and women, Cross-sectional: 925 subjects Longitudinal: 685 subjects	Cross-sectional Cohort 3 years	AHA/NHLBI Waist circumference: Men ≥90 cm Women ≥80 cm	Age, gender, smoking, drinking, breakfast intake, education, occupation, depressive symptoms, physical activity, calorie intake	Relative to toothbrushing frequency of once daily Toothbrushing frequency of twice daily → odds ratio for MetS, 0.8 (0.49-1.31) Toothbrushing frequency of three times or more daily → odds ratio for MetS, 0.43 (1.19-0.97)	32
Fukui *et al*.	2012	Japan Workplace medical check-up	6,421 men and women 34-77 years old	Cross-sectional	NCEP-ATP III Obesity: BMI ≥25	Age, gender, smoking, drinking, toothbrushing frequency, CRP, current number of teeth	Both PD and CAL are 4-5 mm → odds ratio for MetS, 1.25 (1.03-1.52) Both PD and CAL are ≥6 mm → odds ratio for MetS, 1.35 (1.03-1.77)	24
Sora *et al*.	2013	USA Patients with type 2 diabetes mellitus	283 men and women, 26-87 years old	Cross-sectional	NCEP-ATP III	Age, gender, smoking, BMI, current number of teeth, HbA1c, CRP	Individuals with MetS → ratio of percentage for the number of sites with CAL ≥6 mm, 2.77 (1.11-6.93)	16
Furuta *et al*.	2013	USA Hisayama-cho study	2,370 men and women, 40-70 years old	Cross-sectional	Integrated classification Waist circumference: Men ≥90 cm Women ≥80 cm	Age, smoking, drinking, toothbrushing frequency, current number of teeth	Positive MetS items ≥3 → Men: odds ratio for mean PD ≥2.0 mm, 1.64 (1.02-2.64) odds ratio for mean PD ≥2.5 mm 1.86 (1.17-2.97) Women: odds ratio for mean PD ≥3.0 mm 3.06 (1.42-6.59) odds ratio for mean PD ≥3.5 mm 3.60 (1.03-12.61)	12
Tu *et al*.	2013	Taiwan Participants of medical examination	33,740 men and women	Cross-sectional	NCEP-ATP III Waist circumference: Men ≥90 cm Women ≥85 cm BMI: ≥27	Age, occupation, smoking,	Women: gingivitis, periodontitis → odds ratio for MetS, 1.42 (1.30-1.56), 1.52 (1.41-1.63) Men: no significant association between MetS and gingivitis or periodontitis	25
Lee *et al*.	2014	Korea Local residents	399 men and women, ≥60 years old	Cross-sectional	BMI: ≥25, SBP/DBP: >140/>90 mmHg, FPG: >126 mg/dl, cholesterol: >240 mg/dl	Age	1 positive MetS item → odds ratio for PD ≥4 mm 3.82 (1.87-7.79) ≥2 positive MetS items → odds ratio for PD ≥4 mm, 10.54 (4.98-22.29)	13
Minagawa *et al*.	2014	Japan Niigata study of the elderly	234 men and women, 80 years old	Cross-sectional	Japanese standards HbA1c: ≥6.0%	Gender, income, education, smoking, dental visits, toothbrushing frequency, exercise habits, energy intake, food consumed	Individuals with MetS → odds ratio for periodontitis (three stages), 2.10 (1.03-4.28)	17

Table 1 : (continued)

Author	Report year	Study area Study subjects	Subjects, number of subjects, age	Study design	MetS diagnostic criteria	Adjustment factors	Main results	Ref. No.
LaMonte *et al*.	2014	USA OsteoPerio Study	657 postmenopausal women, 50-79 years old	Cross-sectional	AHA/NHLBI	Age, smoking, hormone therapy, history of heart disease, toothbrushing frequency, regular dental visits, physical activity, fat intake	No significant association between MetS and alveolar bone resorption, severe periodontitis, or bleeding gums MetS-positive individuals → odds ratio for plaque index ≥50%, 1.47 (1.00-2.16)	29
Iwasaki *et al*.	2014	Japan Niigata study of the elderly	216 men and women,79 year old	Cross-sectional	NCEP-ATP III Waist circumference: Men ≥90 cm Women ≥80 cm	Gender, income, education, smoking, dental visits, toothbrushing frequency	Individuals with MetS → odds ratio for high Pg serum antibody titer, 2.91 (1.24-6.85)	18

NCEP ATP III: National Cholesterol Education Program Adult Treatment Panel III, PD: pocket depth, CAL: clinical attachment loss, IDF: International Diabetes Federation, BMI: body mass index, EGIR: European Group for the Study of Insulin Resistance, HOMA: homeostasis model assessment, AHA/NHLBI: American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement, CRP: C-reactive protein

and is an important risk factor for diabetes mellitus and arteriosclerotic diseases. Many studies have reported that obesity is also associated with periodontal disease[1,46-50], and in particular, a strong association between visceral fat obesity and periodontitis has been demonstrated[46,51]. Moreover, longitudinal studies reporting an increased risk of periodontal disease progression among obese people[47,49,50] suggest the possibility that obesity affects periodontal status. However, systematic reviews and reports of meta-analyses regarding the association between obesity and periodontal disease point out the fact that, while many studies have shown the association between obesity and periodontal disease, there still lacks sufficient evidence to address the mechanisms and causal relationship[1]. Hence, accumulation of further studies is necessary in order to elucidate further the association between the two.

Adipose tissue secretes various adipocytokines, including adiponectin, leptin, and human tumor necrosis factor-α (TNF-α), as physiologically active substances, and the abnormal production of adipocytokines associated with obesity and metabolic syndrome leads to insulin resistance and arterial stiffening[52]. An increase in TNF-α in blood due to obesity triggers periodontal disease via promotion of inflammation in periodontal tissue, and TNF-α produced due to periodontal tissue inflammation induces insulin resistance, which works negatively in the context of blood glucose metabolic regulation[53]. It has been shown that the serum leptin concentration is higher in obese individuals than in thin individuals[54], and in individuals with periodontal disease, the level of leptin is low in gingival crevicular fluid and high in serum[55]. Moreover, the serum leptin concentration in individuals with periodontitis has been shown to correlate with interleukin-6 (IL-6) and C-reactive protein (CRP), and treatment of periodontitis decreased serum leptin, IL-6, and CRP[56], suggesting that the association between metabolic syndrome and periodontal disease involves adipocytokines playing a role as a mediator.

It has been suggested that diabetes mellitus and periodontal disease have a bi-directional relationship[3,4]. The diagnostic criteria for metabolic syndrome include hyperglycemia, and in patients with type 2 diabetes mellitus, those who apply to two of the four items of the NCEP-ATP III diagnostic criteria other than hyperglycemia have been shown to have a high periodontitis risk[16]. Moreover, individuals with more extensive periodontitis showed a greater increase in HbA1c over a five year period, and this tendency was particularly prominent in those with a high CRP value[57]. These results suggest that chronic inflammation caused by periodontal disease may induce abnormal glucose metabolism, consequently leading to diabetes mellitus. With regard to the mechanisms underlying the association between metabolic syndrome and periodontal disease, the formation of oxygen free radicals, oxidative stress, lipid peroxidation products, and advanced glycation end products have been indicated to play an important role[35,36]. In fact, one study using a mouse model of diabetes mellitus showed that alveolar bone resorption, which occurs as a complication of diabetes mellitus, is possibly caused by local periodontal oxidative stress[58]. On the other hand, periodontal treatment for periodontitis patients with type 2 diabetes mellitus was effective in improving metabolic regulation, such as a decrease in blood glucose levels or HbA1c[59]. Adiponectin decreases blood glucose by improving insulin resistance, which is one of the characteristics of type 2 diabetes mellitus, and is also said to improve lipid metabolism abnormalities. Periodontal treatment in patients with type 2 diabetes mellitus, therefore, not only improves their periodontal status but also leads to decreased HbA1c and increased serum adiponectin[60-62]. In these contexts, it might be possible to decrease the risk of diabetes mellitus by performing anti-inflammatory periodontal treatment in individuals with abnormal glucose metabolism or metabolic syndrome.

People with high triglycerides and low HDL cholesterol have a high periodontitis risk[63], and a case-control study has shown that those with periodontitis have low HDL cholesterol and high LDL cholesterol[64]. Increased triglyceride levels in patients with periodontal disease have been suggested to be due to the effect of endotoxin from periodontal pathogens (lipopolysaccharide or LPS)[65]. In an animal study in which periodontitis was induced by LPS from periodontal pathogens in obese rats, administration of statins, which decrease blood cholesterol, inhibited alveolar bone resorption and suppressed LPS-induced leukocyte infiltration and osteoclast formation in periodontal tissue[66]. In addition, a study has confirmed that by performing periodontal treatment in patients with both metabolic syndrome and periodontal disease, decreases in serum CRP values and white blood cell counts, a decrease in triglyceride levels, and an increase in HDL cholesterol were achieved[67]. Thus, performing periodontal treatment in addition to dyslipidemia treatment likely helps improve metabolic syndrome, as well as maintains periodontal health status.

With regard to the association between hypertension and periodontal disease, individuals with periodontitis have been shown to have an increased risk of hypertension[68,69]. A study that examined the bacterial distribution in the subgingival plaque region showed that individuals with

more periodontopathic bacteria had a higher blood pressure and a higher risk of hypertension[70]. Meanwhile, periodontal treatment in refractory hypertension patients with periodontitis not only decreased blood pressure but also decreased CRP and IL-6, which are associated with inflammation and hypertension, as well as fibrinogen, left ventricular hypertrophy, and values indicating the hardening of the arterial wall[71], suggesting that periodontal treatment can be expected to decrease the cardiovascular risk in patients with hypertension.

With regard to the association between metabolic syndrome and periodontal disease, several studies have reported results indicating a stronger association in women[7,11,12,25], while other report has suggested a stronger association in men than in women[14]. In a study that targeted post-menopausal women, no significant association was observed between metabolic syndrome and indices of periodontal status[29]. While some results demonstrated the association between obesity and periodontal disease being stronger in women[47,72], others suggested that obesity in men increases the risk of periodontal disease progression[50]. Differences by sex are not necessarily consistently demonstrated in the context of association between obesity or metabolic syndrome and periodontal disease. The possible causes include differences in the diagnostic criteria for obesity or metabolic syndrome and evaluation indices of oral health, and differences in age, attributes, and race of the target populations. Therefore, in order to clarify why the associations differ by sex, even more studies are necessary. In any case, when examining the association between obesity or metabolic syndrome and oral health, it might be desirable to perform separate examinations by sex.

As periodontal disease is affected by common risk factors of systemic diseases such as diabetes mellitus, heart disease, and cancer, when providing health guidance at a dental care facility, it is recommended to provide health guidance aimed at promoting both oral and systemic health management, by including guidance on quitting smoking, restriction on sugar intake, and weight management[73]. Similarly, it is believed that there are also lifestyle habits and risk factors common to both periodontal disease and metabolic syndrome. Studies have shown that people who brush their teeth frequently had a significantly lower risk of developing metabolic syndrome[32], and those with poor mouth cleaning habits had a high risk of developing heart disease[74]. These results might suggest that oral hygiene habits may serve as a barometer that reflects a high level of awareness regarding health.

Since 2008, implementation of the Specific Medical Examination and Specific Health Guidance to detect metabolic syndrome has become a requirement for all medical insurers for the purpose of discovering early on the signs of lifestyle-related diseases to prevent their onset, exacerbation, and complication. However, items related to dentistry are not included in those of the Specific Medical Examination. Although a dental examination for adults is available, such as a periodontal disease examination targeting people at their specified age, but the rate of participation is extremely low. The epidemiological association between metabolic syndrome and periodontal disease has been demonstrated by a number of studies, and treatment of periodontal disease has been suggested to potentially improve the health status of individuals with metabolic abnormalities. Therefore, in addition to the Specific Medical Examination, providing an adult population with an opportunity to check their own oral status and perform preventive and/or early measures against oral diseases might prove effective in controlling lifestyle-related diseases as well.

[Conclusions]

As demonstrated by many study results shown in this review, there is no doubt that metabolic syndrome and oral health, mainly periodontal disease, are associated with each other in some way or other. However, sufficient evidence is still lacking with regard to the direction or causality of their association. Therefore, in order to elucidate the association between metabolic syndrome and oral health, it is necessary to continue to accumulate many studies. Furthermore, not only observational epidemiological studies involving human subjects, but also basic and clinical intervention to reveal the relevant mechanism should be performed, as this will further clarify the association between the two.

[Conflict of interest]

There are no items applicable to "conflict of interest" in this article.

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3. Oral health and lifestyle-related diseases, non-communicable diseases (NCDs)

6) Risk factors for NCDs (smoking, excessive alcohol consumption, lack of exercise, and eating habits) and oral health

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[Abstract]

Lifestyle habits such as smoking, excessive alcohol consumption, lack of exercise, and unhealthy diet are deeply associated with lifestyle-related diseases.

Meanwhile, associations between those lifestyle habits and oral health are also profound, and various studies have been performed. In this paper, we searched articles regarding associations between risk factors for lifestyle-related diseases and oral health in an attempt to examine the impact of lifestyle habits on oral health.

Smoking, drinking, exercise, and eating habits were each associated with oral health conditions, including periodontal disease. In particular, the effects of smoking on periodontal health status were clearly demonstrated. Although intake of alcohol in large amounts has been suggested to affect periodontal status, some studies showed variable trends. Individuals with exercise habits, and those who consume food and nutrients that are said to have health benefits, tended to have good periodontal health status.

Improvements in lifestyle habits are likely to have good effects on not only systemic but also oral health, but evidence needs to be accumulated further in order to start incorporating lifestyle habits other than smoking into oral health guidance.

[Introduction]

According to World Health Organization (WHO), diseases of which the development and progression are associated with common lifestyle habits such as smoking, unhealthy diet, lack of exercise, and excessive drinking, and which can be prevented by improving those lifestyle habits, are collectively referred to as non-communicable diseases (NCDs).

In recent years, there have been changes in disease structure, with an increase in lifestyle-related diseases. Against this backdrop, in 2000, the Ministry of Health, Labour and Welfare advocated the "Second-phase Measures for National Health Promotion for the 21st Century (Healthy Japan 21)," and since April 2013, the Ministry has been promoting the Healthy Japan 21 (second phase) as a basic policy aimed at achieving the overall promotion of improvement in the people's health. The extension of healthy life expectancy and reduction in health disparities are among its central goals. Dental and oral health is featured as a target of improvements in lifestyle habits and social environment, along with nutrition, eating habits, physical activities and exercise, rest, drinking, and smoking, in the basic direction of the Healthy Japan 21 (second phase).

The definition of NCDs does not necessarily apply to all oral diseases, as some conditions such as dental caries and periodontal diseases involve specific oral bacteria. Yet, risk factors for NCDs, including smoking, alcohol consumption, exercise, and eating habits, are also deeply associated with oral diseases. In particular, as in the case of many lifestyle-related diseases, periodontal disease increases after adult years, and given the high prevalence, it is said to be a multifactorial disease that is also associated with risk factors for NCDs.

Accordingly, this paper examines the associations between oral health with a main focus on periodontal disease and risk factors for NCDs, mainly, smoking, drinking, exercise, and eating habits, through searches of the literature reported to date.

[Objective]

The purpose of this paper was to search articles reporting on the associations between oral health and smoking, drinking, exercise, and eating habits, i.e., risk factors for lifestyle-related diseases, in order to examine the associations between these risk factors and oral health.

[Methods]

In this paper, searches of articles were conducted using PubMed, and articles confirmed as of July 2014 were cited.

The searches were conducted using a combination of key words, targeting, in principle, articles on human subjects and those written in English.

With respect to the association between smoking and oral health, articles regarding periodontal disease were searched using key words "smoking" and "periodontal disease," and 2,699 articles were extracted. Since the number was too many for us to go through all of the articles, as for cross-sectional studies, some articles were picked selectively. As there have been many longitudinal as well as clinical studies conducted previously, the key word "longitudinal" was added to the search, and 255 articles were extracted. Then, the type of articles was restricted to "clinical trial," and 29 articles were extracted. The content of these articles was checked, and articles that had demonstrated a longitudinal association between smoking and periodontal disease, or the effects of smoking or smoking cessation on periodontal treatment, were further examined. In addition, with regard to the association between smoking and tooth loss, a search with key words "smoking" and "tooth loss" was conducted, from which 646 articles were extracted; these were narrowed down to 114 articles by adding "longitudinal."

With respect to the association between drinking and oral health, 222 articles were extracted through a search using key words "drinking" and "periodontal disease," and with respect to tooth loss, 81 articles were extracted with "drinking" and "tooth loss." The content of articles was checked, and those demonstrating the association between drinking and oral health were further examined. In the present paper, we did not examine the association between drinking and dental caries.

With respect to articles on the association between exercise (physical activity) and periodontal disease, 67 articles were extracted through a search with key words "exercise" and "periodontal disease," and 108 articles with "physical activity" and "periodontal disease." Among those, articles demonstrating the association between exercise (physical activity) and periodontal disease were further examined. The present paper does not address the association between exercise (physical activity) and tooth loss, as there is a separate section (2-(5)) regarding the effects of tooth loss on motor function.

With respect to the association between eating habits and oral health, there were a number of food items or nutrients that have been reported to have an association with oral health. Therefore, those were classified as vitamins, calcium, dairy products, and other, and their associations with tooth loss and dental caries, with a main focus on periodontal disease, were examined accordingly. A total of 159 articles were retrieved with "periodontal disease" and "vitamin C" used as the key words, 158 articles with "vitamin D,"1,320 articles with "calcium," and 33 articles with "dairy product." With regard to other food items and nutrients, an arbitrarily search was conducted. Among the extracted articles, those reporting relatively new studies and longitudinal studies were mainly selected for further examination, in terms of the association between oral health and dietary intake of each food or nutrient.

[Results]

1. Smoking

1) Smoking and periodontal disease

To date, numerous study results have been reported with regard to the epidemiological relationship between smoking and periodontal disease, demonstrating that, compared to non-smokers, smokers tend to have a poorer dental status[1, 2], and are more prone to alveolar bone resorption[3-6]. In Japan, a number of studies have been conducted with regard to the association between smoking and periodontal disease. In a cross-sectional study targeting working adults, the risk of periodontitis was significantly higher in individuals having a higher pack-year, which represents smoking experience from the past[7]. In addition, studies that had followed populations of working adults and male adults found a higher risk of periodontal disease progression with an increasing amount of smoking[8,9]. Even in a follow-up study of elderly individuals, those with smoking habits showed a significantly higher risk of periodontitis progression[10]. On the other hand, when participants of a workplace medical check-up were divided into non-smokers, passive (second-hand) smokers, and active (first-hand) smokers based on salivary cotinine levels, and compared in terms of the risk of periodontitis exacerbation, the results showed that the risk of periodontitis progression was significantly higher among second-hand smokers, with no difference from that of first-hand smokers[11].

Among studies that examined the influence of smoking on periodontal treatment, one study compared the effects of non-surgical periodontal treatment in reducing periodontal pockets and improving attachment levels between male smokers and non-smokers. The assessment was performed by multi-level analysis, which simultaneously analyzed associations at each level of individual after periodontal treatment, tooth position, and tooth condition. The results showed that reduced dental pocket was associated with non-smoker at the individual level, anterior teeth at the level of tooth position, and not having plaques at baseline at the level of tooth condition[12]. On the other hand, smoking

status did not seem to have any effect on attachment level improvement.

During the period of supportive periodontal therapy (SPT) for patients who completed periodontal treatment, smokers who smoked 20 cigarettes or more a day had a significantly higher risk of periodontal disease progression compared to non-smokers, although smoking status did not have a significant effect on tooth loss during the period of SPT[13]. On the other hand, in a three-year follow-up study, smokers and non-smokers who underwent maintenance therapy after periodontal treatment at intervals of three to four months were compared, no difference was observed in the plaque index or bleeding on probing (BOP) at the beginning of and throughout the follow-up period. Moreover, no difference was observed in changes in periodontal pockets and clinical attachment loss (CAL) between the two groups[14].

Regarding the effect of smoking cessation on periodontal treatment, a study was conducted on patients with periodontal disease who wished to quite smoking. After initiation of periodontal treatment, changes in periodontal status were examined, revealing that while many of the participants could not quit smoking, those who succeeded in quitting smoking showed a significant reduction in periodontal pockets[15]. Another study examined the effects of smoking cessation on periodontal treatment and showed that, while many were unable to quit smoking, the group of patients who successfully quit smoking showed changes in CAL that suggested the formation of a new periodontal tissue attachment was achieved[16], compared to the group of patients who continued smoking. However, no difference in BOP or periodontal pockets was observed between the groups.

2) Smoking and tooth loss

Regarding the association between smoking and tooth loss or becoming edentulous, a number of studies have been performed in Sweden, demonstrating that smokers have a fewer number of teeth, and many with edentulous jaws[17-20]. There have also been many investigations in the U.S.[2,3,21-24]. In Japan, a longitudinal study targeting male adults has shown that smokers are at an increased risk of tooth loss, although this effect was limited to individuals younger than the age 50 years[9]. In addition, studies from various countries have shown that the risk of becoming edentulous is higher among smokers[25-27]. A review on smoking and tooth loss has suggested a causal relationship between the two[28].

According to a study that had examined the association of tooth loss and periodontitis progression with socio-economic status and systemic inflammatory conditions, a higher C-reactive protein (CRP), which is a marker for systemic inflammation, was associated with tooth loss and periodontitis progression[29]. When subjects were classified according to high/low CRP, the high-CRP group showed stronger effects of smoking and socio-economic status on tooth loss, compared to the low-CRP group.

2. Drinking and oral health

1) Drinking and periodontal disease

The results of the article search regarding drinking and periodontal disease are shown in Table 1.

Of the 17 articles, 11 were cross-sectional studies[30-40], and six were longitudinal studies[9,10,41-44]. A relatively high volume of studies (seven reports) was performed in Japan. As for the method of assessment, nine reports examined the amount of alcohol consumption, and eight examined drinking habits and frequency. Eleven reports[30,32-34,36,37,39-41,43,44] suggested that drinking negatively affected periodontal tissue in some way or other, whereas five reports[9,10,31,35,42] found no association. One report[38] showed that drinking was good for periodontal status.

2) Drinking and tooth loss (edentulous jaw)

Six articles[9,25,42,45-47] were extracted as a result of a search with regard to the association between drinking and tooth loss (edentulous jaw); of these, two were investigations conducted in Japan (Table 2).

Among the six reports, there were three cross-sectional studies and three longitudinal studies. As for the method of evaluation for drinking, two reports examined the amount of alcohol consumption, two examined drinking frequency, and two used the presence or absence of drinking habits. Unlike the association with periodontal disease, only two reports showed that drinking was a risk for tooth loss[9,45], one report found no association[42], and three reports showed that the number of teeth was higher among drinkers[25,46,47].

3. Exercise (physical activity) and periodontal disease

A study targeting a Japanese adult population showed that individuals with a low maximum oxygen uptake ($\dot{V}O_{2max}$), a physical fitness index representing endurance, have a higher risk of periodontal disease[48]. The authors also analyzed the relationship between obesity (BMI) and physical fitness ($\dot{V}O_{2max}$) and periodontitis, and found that skinny individuals and physically fit individuals had a significantly lower risk of severe periodontitis. Furthermore, individuals who satisfied both of those conditions had an extremely low risk of severe periodontitis[49].

Among American male health professionals, those with no self-reported periodontitis at baseline were followed

Table 1: Relationship between drinking and periodontal disease

Author	Report year	Study area Study subjects	Subjects, number of subjects, age	Study design	Adjustment factors	Main results	Ref. No.
Sakki *et al.*	1995	Finland Local residents	527 men and women ≥55 years old	Cross-sectional	Eating habits, smoking, toothbrushing frequency	Drinking frequency ↑ → periodontal disease ↑	30
Shizukuishi *et al.*	1998	Japan Workplace medical check-up	310 men and women Mean age, 38.7 years old	Cross-sectional	Age, gender, smoking, toothbrushing frequency, cleaning of the cervical area, interdental cleaning tools	Drinking habits → periodontal disease (no association)	31
Tezal *et al.*	2001	USA Erie County Study	1,371 men and women 25-74 years old	Cross-sectional	Age, gender, education, diabetes mellitus, allergies, smoking, plaque index, subgingival bacterial species	Drinking frequency ↑ → gingival bleeding ↑, CAL ↑	32
Ogawa *et al.*	2002	Japan Niigata study on the elderly	394 men and women 70 years old	Cohort 2 years		Drinking habits → ≥3 mm increase in CAL in one place or more (no association)	10
Pitiphat *et al.*	2003	USA Medical professionals	39,461 men 40-75 years old	Cohort 4 years	Age, smoking, diabetes mellitus, BMI, physical activity, total calories	Amount of alcohol ↑ → periodontal disease (self-reported) ↑	41
Nishida *et al.*	2004	Japan Workplace medical check-up	372 men and women 20-59 years old	Cross-sectional	Age, gender, BMI, smoking, toothbrushing frequency	$ALDH_2$ *1/*2 Alcohol ≥33 g/d → periodontal disease ↑	33
Tezal *et al.*	2004	USA NHANES III	13,198 men and women ≥20 years old	Cross-sectional	Age, gender, race, education, income, smoking, diabetes mellitus, current number of teeth, gingival bleeding	Drinking frequency ↑ → CAL ↑	34
Torrungruang *et al.*	2005	Thailand	2,005 men and women 50-63 years old	Cross-sectional	Age, gender, education, plaque index, smoking, diabetes mellitus	Drinking habits → periodontal disease (no association)	35
Shimazaki *et al.*	2005	Japan Hisayama study	961 men and women 40-79 years old	Cross-sectional	Age, gender, smoking, glucose tolerance, current number of teeth, plaque index	Alcohol ≥15 g/d → extensive PD ≥4 mm ↑	36
Bouchard *et al.*	2006	France NPASES I	2,132 men and women 35-64 years old	Cross-sectional	Age, gender, BMI, white blood cell count	Non-drinkers, daily drinkers (compared to occasional drinkers) → CAL ≥5 mm ↑ *No significance with oral variables	37
Okamoto *et al.*	2006	Japan Participants of medical check-ups	1,332 men 30-59 years old	Cohort 4 years	Age, smoking	Baseline: subjects with a CPI code ≤2 Alcohol consumption ↑ → periodontal disease (CPI code ≥3) (no association)	9
Jansson	2008	Sweden	477 men and women Mean age, 54.9 ± 12 years old	Cohort 20 years	Age, gender, smoking, education, dental visits, toothbrushing frequency, interdental cleaning tools, diabetes mellitus, heart disease, rheumatoid arthritis	Alcohol consumption ↑ → alveolar bone resorption NS	42
Kongstad *et al.*	2008	Denmark CCHS	1,521 men and women 20-95 years old	Cross-sectional	Age, smoking, education, income, BMI, physical activity, diabetes mellitus, current number of teeth, plaque index	Drinking frequency ↑ → (Men) CAL ↓ *especially with wine (Women) CAL (no association)	38
Yoshihara *et al.*	2009	Japan Niigata study on the elderly	261 men and women 70 years old	Cohort 6 years	Gender, BMI, education, number of family members, current number of teeth, food consumed	Alcohol consumption ↑ → CAL progression ↑	43

Table 1: (continued)

Author	Report year	Study area Study subjects	Subjects, number of subjects, age	Study design	Adjustment factors	Main results	Ref. No.
Nishida *et al*.	2010	Japan Workplace medical check-up	183 men and women ≥18 years old	Cohort 4 years	Age, gender, smoking	$ALDH_2$ *1/*2 Alcohol ≥33 g/d → 2 or more teeth with PD ≥2 mm increase ↑	44
Lages *et al*.	2012	Brazil Examinee of medical institutions	542 men and women 22-55 years old	Cross-sectional	Age, gender, income, education, diabetes mellitus	Drinking frequency ↑ → periodontal disease ↑ Strength of the association: smokers > former smokers > non-smokers	39
Park *et al*.	2014	Korea KNHANES	8,645 men 11,584 women	Cross-sectional	Age, smoking, BMI, physical activity, education, income, white blood cell count, diabetes mellitus, hypertension, toothbrushing frequency, metabolic syndrome	Men: alcohol consumption ↑ → CPI code ≥3 ↑ Women: alcohol consumption ↑ → CPI code ≥3 (no association)	40

CAL: clinical attachment loss, BMI: body mass index, $ALDH_2$: aldehyde dehydrogenase-2, NHANES: Third National Health and Nutrition Examination Survey, PD: pocket depth, NPASES: First National Periodontal and Systemic Examination Survey, CPI: Community Periodontal Index, CCHS: Copenhagen City Heart Study, KNHANES: Korea National Health and Nutrition Examination Survey

Table 2: Relationship between drinking and tooth loss (edentulous jaw)

Author	Report Year	Study area Study subjects	Subjects, number of subjects, age	Study design	Adjustment factors	Main results	Ref. No.
Copeland *et al.*	2004	USA Group 1: BLSA Group 2: VADLS	Group 1: 94 men and women 30-69 years old Group 2: 481 men 25-75 years old	Cohort ≥10 years	Group 1: gender, current number of teeth, treated tooth rate, average PD Group 2: age, smoking, current number of teeth, treated tooth rate, average PD	Drinking ≥2 times a day → Group 1: Tooth loss ↓ Group 2: tooth loss ↑	45
Okamoto *et al.*	2006	Japan Participants of medical examination	1,332 men 30-59 years old	Cohort 4 years	Age, smoking	Heavy drinkers in their 30s → tooth loss ↑	9
Hanioka *et al.*	2007	Japan National Health and Nutrition Examination Survey	2,200 individuals, ≥60 years old	Cross-sectional	Age, smoking, vitamin C intake, vitamin E intake, BMI, blood glucose level	Drinkers → (Women) edentulous ↓ (Men) edentulous (no association)	25
Jansson	2008	Sweden	477 men and women Mean age, 54.9 ± 12 years old	Cohort 20 years	Age, gender, smoking, education, dental visits, toothbrushing frequency, interdental cleaning tools, diabetes mellitus, heart disease, rheumatoid arthritis	Alcohol consumption ↑ → tooth loss (no association)	42
Heegaard *et al.*	2011	Denmark CCHS	783 men and women 65-95 years old	Cross-sectional	Age, education, income, marital status, smoking, physical activity, saliva secretion, dental visits, health self-assessment, social participation, diversity of social relationships, physical dysfunction, medication	Drinking frequency ↑ → (Women) 19 teeth or less ↓ * Particularly with wine and spirits (Men) 19 teeth or less ↓ *With beer	46
Morse *et al.*	2014	Denmark CAMB	1,517 men and women 50-61 years old	Cross-sectional	Age, gender, smoking, social class, cognitive abilities, history of periodontal treatment, BMI	With drinking habits, drinking frequency ↑ → missing teeth ≥6 ↓	47

BLSA: Baltimore Longitudinal Study of Aging, VADLS: VA Dental Longitudinal Study, PD: pocket depth, BMI: body mass index, CCHS: Copenhagen City Heart Study, CAMB: Copenhagen Aging and Midlife Biobank

and compared in terms of the risk of being subsequently diagnosed with periodontitis according to physical activity. The risk of periodontitis was decreased by 3% for every 10-MET increase in average physical activity, which was calculated from questionnaire responses[50]. Moreover, in a study based on the National Health and Nutrition Examination Survey Ⅲ (NHANES Ⅲ) in the U.S., participants who engaged in moderate physical activity at least five times a week or vigorous physical activity at least three times a week had a significantly lower periodontitis risk[51]. However, this association was only observed in non-smokers or former smokers. Moreover, when the levels of physical activity were classified into three levels (low, intermediate, high) based on the international standard physical activity questionnaire, those at the low physical activity level had a significantly higher periodontitis risk compared to those at the high physical activity level[52].

4. Eating habits and oral health

1) Vitamins, calcium

Although smokers with a low dietary vitamin C intake had a high risk of periodontal disease, no association was found in non-smokers[53]. In another study that targeted the same subjects, individuals with a low dietary calcium intake were shown to have a high risk of periodontal disease[54]. However, the association was significant only in women and men aged 20-39 years, and men aged 40-59 years, and no association was found in elderly individuals. In a follow-up study targeting elderly individuals, the risk of periodontal disease progression was lower in those with a high dietary intake of antioxidants (i.e., vitamin C, vitamin E, and *β*-carotene)[55].

A cross-sectional study of elderly men showed that those with a high dietary vitamin D intake had a low periodontitis risk[56]. Also, among postmenopausal women, those with a high concentration of serum 2,5-hydroxyvitamin D (25OHD), which reflects the total amount of dietary vitamin D intake and vitamin D produced in the skin, had low values for indicators associated with periodontal tissue inflammation such as BOP and periodontal pockets, but no correlation was found with indicators associated with alveolar bone resorption and tooth loss[57].

On the other hand, in a follow-up study of an adult population, a high level of 25OHD had a suppressive effect on tooth loss[58]. Moreover, a long-term follow-up study also showed a lower risk of tooth loss in individuals with a higher serum 25OHD, and this tendency was more pronounced in those aged less than 65 years, relative to those aged 65 years and older[59]. However, the effect of vitamin D on tooth loss was greater when considering the amount of exposure to ultraviolet light than that from the diet. With regard to the development of periodontitis, the association was not as clear as the one observed with tooth loss[59]. Also, in the follow-up study targeting postmenopausal women, no association was observed between 25OHD levels at baseline and changes in periodontal status[60].

2) Dairy products

It has been reported that a high calcium intake from dairy products markedly decreases the risk of tooth loss in both men and women[61]. In addition, calcium intake has been shown to negatively correlate with periodontal disease[54], and individuals who consume a large amount of dairy products rich in calcium tend to show a low prevalence of periodontal disease[62]. In a study conducted by the authors, only dairy products that showed a significant association with periodontal disease were food containing lactic acid bacteria, such as yogurt and lactic acid bacteria beverage, and consumption of other dairy products, such as milk and cheese, showed no association with periodontal disease[63]. A study on Dutch elderly subjects showed that the periodontitis risk was lower in those with high calcium intake amounts, which were calculated based on consumption of dairy products as a whole, milk, and lactic acid bacteria. Moreover, the amounts of consumption of dairy products as a whole, milk, and lactic acid bacteria food themselves were negatively associated with periodontitis[64].

3) Other

A longitudinal survey of American male medical professionals showed that the risk of developing periodontitis was low in individuals with a high intake of whole grain[65]. On the other hand, no significant association was found with regard to refined grain. Another follow-up study of male adult subjects demonstrated that individuals aged 65 years and older with a high dietary intake of fiber from high-quality food and fruits had a low risk of periodontitis progression and tooth loss[66]. However, no association was found between total dietary fiber and periodontitis progression, and furthermore, no association with periodontal disease, regardless of the type of dietary fiber, was found in individuals aged less than 65 years. In a study of Japanese female college students, the risk of periodontal disease was lower in those who consumed a large amount of soy products or tofu[67].

Individuals with a high intake of docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), which are among polyunsaturated fatty acids called omega-3 fatty acids, had a low CRP, and those with a high intake of DHA had a low periodontitis risk[68]. On the other hand, a follow-up study

of elderly individuals showed that non-smokers with a high intake of saturated fatty acids had a significantly higher risk of periodontal disease progression[69].

[Discussion]

1. Smoking

Smoking is a well-known lifestyle habit associated with periodontal disease. As shown in this paper, based on the observational studies and clinical studies that had examined the treatment effects, there is no doubt that smoking affects periodontal status.

With regard to the mechanisms underlying the effects of smoking on periodontal tissue, there are various possibilities. Smokers, compared to non-smokers, have high serum cadmium and lead levels, and smokers with extensive periodontitis have even higher serum cadmium and lead levels. Therefore, it is possible that increased levels of heavy metals due to smoking might affect the condition of periodontal tissue inflammation[70]. Gingival blood flow is decreased in patients with periodontitis compared to individuals with healthy gums regardless of smoking status, and smoking has been shown to decrease gingival blood flow[71]. Furthermore, given that smoking cessation increases gingival blood flow in smokers who do not have periodontitis[72], a decrease in gingival blood flow due to smoking is likely to affect periodontal status.

An article regarding a meta-analysis performed on the basis of the two studies[15,16] mentioned in this paper, which had examined the effects of smoking cessation on periodontal treatment, demonstrates that smoking cessation was effective in reducing periodontal pockets[73]. The microbial composition of subgingival plaques in individuals who could not quit smoking during periodontal treatment resembled that observed at baseline, whereas clear changes were observed in the microbial composition of those who succeeded in quitting smoking[74]. These findings suggest that differences in the treatment effects associated with successful or unsuccessful smoking cessation might be influenced by variable changes in the microbial composition. However, given that no significant difference was observed in attachment levels or BOP associated with successful or unsuccessful smoking cessation, it has been concluded that the effect of smoking on periodontal treatment is limited[73]. Moreover, since both studies left the success of smoking cessation to the autonomy of the patient, it is also possible that differences in characteristics of patients themselves, in terms of whether they were able to quit smoking or not, could have affected the differences in treatment effects.

In maintenance therapy following periodontal dynamic therapy, BOP is used as a risk indicator for periodontal disease progression[75]. On the other hand, as smoking affects peripheral blood flow in periodontal tissue, BOP is low in smokers, including those who had smoked in the past[76], hence, caution is required when assessing BOP in individuals with smoking experience. The follow-up study on maintenance therapy in smokers and non-smokers showed that even in smokers, maintenance of periodontal status to the degree almost equivalent to that achieved in non-smokers can be expected if they undergo regular maintenance therapy[14]. However, as for individuals undergoing long-term SPT, it is ideal to recommend smoking cessation to the extent possible when performing periodontal treatment for smokers, since smokers have a higher risk of tooth loss compared to non-smokers[77].

Since smoking increases the risk of periodontal disease and tooth loss as well as various lifestyle-related diseases, it goes without saying that guidance on smoking cessation as primary prevention should be promoted, and it is also important to encourage patients who are undergoing periodontal treatment to quit smoking by explaining that smoking exacerbates periodontal disease and affects treatment prognoses. Moreover, given the fact that second-hand smoking also increases the risk of periodontitis[11], consideration of others around smokers, l*et al*one smokers themselves, will be necessary.

2. Drinking and oral health

Drinking is a lifestyle habit that is strongly associated with liver disease and circulatory disease. However, not much is known about the association between drinking and periodontal disease, and it is rare that drinking is addressed as one of lifestyle habits that affect periodontal disease.

Reports on the association between drinking and periodontal disease are scarce compared to those concerning the association with smoking, and results do not necessarily show consistent trends. The inconsistency in results could be explained by the different methods used to assess drinking and periodontal disease, or by the effect of ethnic differences in target populations.

In the body, consumed alcohol is broken down, generating acetaldehyde in blood. Thus, whether an individual can handle his or her liquor is determined by differences in the ability to decompose acetaldehyde, which depends on the chromosomal genotype of acetaldehyde dehydrogenase (ALDH). Nishida *et al*. showed the association between alcohol consumption and periodontitis according to the type of ALDH2 in working adult men[33, 44]. The risk of periodontitis was high among individuals

with the $ALDH_2$*1/*2 genotype, the type predominant in Japanese people, who can drink alcohol but cannot hold much due to their low acetaldehyde decomposition ability. This result suggests that the effects of drinking on periodontal health status may be influenced by individual constitution. Since many Westerners have the $ALDH_2$*1/*1 genotype, i.e., they can hold their alcohol, it is likely that the association between drinking and periodontal disease differ between Japanese and Western people. One of the reasons that many of the reports regarding the association between drinking and periodontal disease are from Japanese studies may be related to the fact that a high proportion of Japanese people cannot hold their alcohol.

In the study that examined periodontitis by severity, drinking did not have any effect on mild to moderate periodontitis, but the amount of alcohol consumption was associated with an increased risk of severe periodontitis[36], suggesting that drinking may serve as an exacerbating factor for advanced (to a certain degree) periodontitis. An animal experiment with rats confirmed the effects of ethanol intake on alveolar bone resorption, only when ethanol was ingested under the condition where periodontal tissue was artificially loaded[78]. On the other hand, even if teeth were ligated, no difference relative to the control group was observed in alveolar bone resorption when 10% ethanol was ingested. Since a small amount of drinking is associated with a low risk of hypertension and heart disease[79,80], the effects of drinking on periodontal diseases might not necessarily follow a dose-response relationship.

The results regarding the association between drinking and tooth loss were not necessarily consistent either. The articles mentioned in this paper point to the possibility that there may be some ethnic differences that influence the effects of drinking on tooth loss. In addition, the effects of drinking on periodontal disease might not be necessarily linked to tooth loss. However, at present, sufficient information has not been obtained.

Evidence needs to be accumulated to clarify the effects of drinking on oral health in order to incorporate guidance on drinking in oral health directions.

3. Exercise (physical activities) and periodontal disease

Physical activities, including exercise, play an important role in the prevention of various lifestyle-related diseases, such as obesity and diabetes. Although a number of studies have reported on the association between obesity and periodontal disease[81-84], not many address the association between physical activities and periodontal disease. The reports introduced in this paper have assessed exercise and physical activities based on physical fitness indicators and questionnaire surveys, demonstrating that physically fit individuals and those who engage in many physical activities have good periodontal status.

The effects of diabetes mellitus on periodontal disease have long been recognized[85], and given that changes in exercise habits in individuals with high blood glucose levels are more effective than anti-diabetic drugs in preventing the development of diabetes mellitus[86], a continued exercise habit may be effective in maintaining healthy dental status as well.

Periodontal disease is a local inflammatory condition of the periodontium, and has been shown to be associated with inflammatory cytokines such as interleukin-1 (IL-1) and tumor necrosis factor (TNF), as well as a systemic inflammation marker CRP[87,88]. Meanwhile, the effect of exercise training to increase $\dot{V}O_{2max}$ or to decrease serum TNF-α in patients with heart disease has been confirmed[89]. In addition, individuals who engage in many physical activities had significantly low IL-1β and CRP in gingival crevicular fluid, and those with periodontitis had a significantly higher CRP compared to those without periodontitis[90]. One study examined the interaction between physical activity and periodontitis in terms of CRP and found that, among individuals with low physical activity, there was a large difference in CRP between those with periodontitis and those without. On the other hand, with increasing physical activity, differences in CRP with or without periodontitis decreased[90]. These results suggest the possibility that physical activity may suppress inflammatory responses caused by periodontitis.

4. Eating habits and oral health

1) Vitamins, calcium

Vitamins and calcium represent nutrients associated with periodontal disease. Collagen fibers are an important component of periodontal tissue, and vitamin C is involved in the synthesis of collagen fibers. Vitamin C deficiency impairs collagen synthesis, which is said to cause the inhibition of wound healing and the rupture of capillaries. Since the impact of vitamin C deficiency on periodontal disease is more pronounced in smokers[53], vitamin C deficiency is likely to enhance the effects of smoking on periodontal tissue. Grapefruit consumption increases blood vitamin C concentration in individuals with periodontal disease in both non-smokers and smokers[91], and thus, preventive effects on periodontal disease may be expected even in smokers with active consumption of vitamin C.

Vitamin D plays a role in maintaining calcium

concentrations, and thus, vitamin D deficiency disrupts calcium deposition in bones, thereby increasing the likelihood of the development of bone-related diseases. Therefore, vitamin D deficiency also affects the alveolar bone that supports teeth, and may thus lead to the progression of periodontal disease and tooth loss. However, the results obtained so far have not been necessarily consistent in terms of the relationship between vitamin D and periodontal disease and tooth loss, due to differences in the method of vitamin D assessment as well as study design.

Vitamin D is abundantly contained in fish and mushrooms. According to the Dietary Reference Intakes for Japanese (2010 version), the recommended intake amount of vitamin D in adults is 5.5 μg per day (50 μg daily upper limit). The results of the National Health and Nutrition Survey showed that the average intake amount of vitamin D was about 8 μg in both men and women, which exceeded the recommended amount; however, given that the amount of intake required for the treatment of osteoporosis ranges from 10 to 20 μg, it will be ideal to aim for an even higher intake. In the case where postmenopausal women had insufficient vitamin D, supplementation of vitamin D (i.e., taking vitamin D supplement) was shown to be effective[92]. On the other hand, in addition to dietary intake, vitamin D is also synthesized in the skin by exposure to moderate sunlight (ultraviolet rays), and therefore, exposure to ultraviolet rays in daily life is also important. In this context, when considering the impact of vitamin D on periodontal disease and tooth loss, not only dietary intake but also other factors need to be taken into account. In any case, keeping vitamin D levels above certain levels is likely beneficial for the maintenance of oral health.

2) Dairy products

Among dairy products, consumption of cheese and other dairies, or the amount of calcium contained, have not been shown to have any association with periodontal disease[63,64]. In addition, no association has been observed between periodontal disease and intake amount of calcium from sources other than dairies[64]. Therefore, the effect of calcium in the context of association between dairy intake and periodontal disease might not be so significant.

In contrast, consumption of food containing lactic acid bacteria has been shown to have preventive effects on periodontal disease[63,64]. Yogurt, which contains several lactic acid bacteria with probiotic action, prevents the growth of periodontal pathogens, although no effects have been observed on the growth of *Streptococcus sanguinis*[93]. Moreover, in an intervention study, when subjects who drunk a commercial lactic acid bacteria beverage (test group) and those who did not drink anything (control group) were given restricted oral cleaning, the results showed that BOP and gingival crevicular fluid volume were significantly lower in the test group compared to the control group[94]. From these reports, lactic acid bacteria contained in lactic acid bacteria food are likely to exert preventive effects on periodontal disease as probiotics in the oral cavity.

3) Other

In the context of the association between consumption of cereals and periodontal disease, since whole grain showed an association, whereas refined grain did not[65], it has been suggested that periodontal disease might be suppressed by increasing consumption of whole grain without changing the nutritional intake. As for intake of dietary fiber and periodontal disease, no consistent trend has been observed; some found no association[65], while others only found an association in individuals aged 65 years and older[66]. Although the reasons are unclear, intake of dietary fiber might not have a major effect on periodontal tissue early in life.

Intake of unsaturated fatty acids has been shown to suppress arterial stiffening[95], and good results have been obtained for periodontal tissue as well[68]. On the other hand, intake of saturated fatty acids, which affects arterial stiffening and hypertension[95], increased the risk of periodontal disease in non-smokers[69]. As for the reason why intake of saturated fatty acids did not have any effect on periodontal disease in smokers, the effect of smoking on periodontal disease might have strongly influenced the results.

Meals are indispensable in our daily life and are deeply involved in a variety of health issues. As we have shown in this paper, while there are many reports regarding food and nutrients associated with oral health, none has shown remarkable effects on oral health or suggested serious risks, which leads us to think that many of food products and nutrients that appear to have associations with oral health might also be commonly associated with health other than that of the oral cavity. Individuals with healthy eating habits not only benefit from the effects of dietary intake, but they also have high interest in health, and are likely to possess favorable lifestyle habits other than eating habits.

One study investigated the association between periodontitis and three health-promoting behaviors (maintenance of ideal body weight, performance of exercise at recommended levels, high-quality diet), and showed that the prevalence of periodontitis significantly decreased with an increasing number of three health-promoting behaviors[96]. Another study investigated the association between physical

activity and healthy diet and periodontal disease, and showed that individuals with low physical activity and unhealthy eating habits had a higher risk of periodontal disease[52]. The association between obesity and periodontitis has been reported by many studies, suggesting that paying attention to moderate exercise and healthy eating habits, in addition to the maintenance of normal body weight, will not only prevent lifestyle-related diseases but also contribute to the maintenance of healthy periodontal status.

[Conclusions]

This paper examined lifestyle habits such as smoking, drinking, exercise, and eating habits associated with NCDs in an attempt to determine the association between these risk factors and oral health. Many interesting studies have been reported with regard to each factor. However, except for smoking, it is not necessarily the case that enough evidence has been established to actively incorporate those factors into clinical and health guidance. Apart from smoking, improved lifestyle habits such as drinking, exercise, and eating habits are expected to promote oral health maintenance. Such knowledge should be widely spread out, as this could lead to an increased awareness among people with regard to oral health. To that end, it will be necessary to further accumulate evidence concerning the association between daily lifestyle habits and oral health.

[Conflict of interest]

There are no items applicable to "conflict of interest" in this article.

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4. Association between oral health and main illnesses underlying conditions that necessitate long-term care

1) Cerebrovascular disease
   – Oral health and cerebrovascular disease –

2) Dementia

3) Falls and fractures

4) Articular diseases
   – Periodontal disease and rheumatoid arthritis –

5) Other diseases
   – Oral health and conditions that necessitate long-term care –

4. Association between oral health and main illnesses underlying conditions that necessitate long-term care

1) Cerebrovascular disease – Oral health and cerebrovascular diseases –

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[Abstract]

Cerebrovascular disease is the number one cause of conditions that necessitate long-term care among Japanese people. Cerebrovascular disease causes movement disorders that affect not only the extremities but also the orofacial area, and even causes deterioration of oral hygiene status. In this context, investigation of the association between oral health conditions and cerebrovascular disease, which represent the main cause of conditions requiring long-term care, is a very important issue. In this paper, we focused on five review articles published previously with regard to oral health conditions and cerebrovascular disease and organized the evidence. The results showed that, regarding the association between periodontal disease and stroke, the risk of stroke had been reported to increase in young people and those with many missing teeth, as well as in cases where clinical attachment loss (CAL) and probing pocket depth (PPD) are high. Moreover, studies have shown that the association between periodontal disease and non-hemorrhagic (ischemic) stroke, compared to hemorrhagic stroke, was stronger. However, due to the lack of sufficient reports with regard to decreased risk of developing cerebrovascular disease associated with treatment of periodontal disease, the causality of the relationship is still unclear. Therefore, future studies will be necessary to explore these issues, such as by conducting follow-up studies and intervention studies.

[Introduction]

Cerebrovascular disease is the number one cause of conditions that necessitate long-term care among Japanese people. The Comprehensive Survey of Living Conditions, which has been conducted each year up to present, suggests that the rate has been on a declining trend; however, the latest one from 2010 reported that it accounted for 21.5% of the total. Cerebrovascular disease causes movement disorders that affect not only the extremities but also the orofacial area, and even causes deterioration of oral hygiene status. Moreover, lifestyle habits that are likely to lead to the development of cerebrovascular disease could simultaneously cause the deterioration of oral health status, and in this context, there may be common risk factors that affect both cerebrovascular disease and oral health conditions. As such, it has been suggested that oral health conditions and cerebrovascular disease are closely related to each other, and many studies have been reported. Accordingly, in this study, we decided to summarize the research up to date with regard to the association between oral health conditions and cerebrovascular disease.

[Objective]

In 2011, some changes were noted in ranking of the top three causes of death among Japanese people; pneumonia has overtaken cerebrovascular disease, which had long and firmly held its number-three position. Although cerebrovascular disease is no longer a direct cause of death, patients could develop secondary pneumonia from dysphagia due to sequelae, with a high enough possibility of death. Moreover, in the age group of 60-79 years, cerebrovascular disease is still ranked third as the cause of death, and thus, experience of cerebrovascular disease from before reaching old age toward later life stages could have a significant effect in the aspect of long-term care. Accordingly, investigation of the association between oral health conditions and cerebrovascular disease, *i.e.,* the major cause of conditions that necessitate long-term care, is a very important issue. This study aimed to organize evidence demonstrated to date regarding oral health conditions and cerebrovascular disease.

[Methods]

Using PubMed, we conducted a literature search using search terms such as "oral health," "tooth loss," and "periodontitis," in addition to "cerebrovascular disease," "CVD," and "stroke." We then summarized the association between oral health conditions and cerebrovascular disease based on the retrieved articles and articles cited in these articles. We targeted review articles published from April 2003 to April 2014, as well as their cited literature.

[Results]

Five review articles had reported on the association between oral health conditions and stroke, and articles cited in these reviews included a total of 17 studies, comprising two cross-sectional studies, three case-control studies, and 12 cohort studies (one of which was a retrospective cohort study).

The viewpoints of each review article are shown below chronologically (see Tables 1 and 2).

Janket *et al.*[1] calculated the relative risk (RR) of 2.85 (95% confidence interval (CI), 1.78-4.56) for stroke due to periodontal disease based on two studies (Beck *et al.,* 1996; Wu *et al.,* 2000), concluding that there was an association between the two.

Khader *et al.*[2] calculated the RR based on four studies (Grau *et al.,* 1997; Morrison *et al*., 1999; Howell *et al.,* 2001; Buhlin *et al.,* 2002), in addition to the ones cited by Janket in the previous year. Grau *et al.* targeted a group of 166 patients with acute cerebrovascular ischemia and a group of age- and sex-matched healthy controls, and examined whether dental infections serve as a risk factor for stroke. The authors assessed the total dental index (TDI), which is based on examinations of dental caries, periapical radiograph, periodontitis, and other dental radiographs, as well as the orthopantomography index (OPGI), and found that the patient group tended to have a poorer dental status (TDI: p=0.070; OPGI: p=0.062). Moreover, there were significantly more individuals with severe periodontitis (p=0.047) and periapical radiograph (p=0.027). Based on age-adjusted logistic regression analysis, the authors reported that poor dental status was an independent risk factor for cerebrovascular ischemia (OR=2.6; 95% CI, 1.18-5.7). The study by Buhlin *et al.* was performed in Sweden and examined the associations between history of stroke and questionnaire-based subjectively evaluated bleeding gums, unstable teeth, deep periodontal pockets, and use of dentures. The odds ratios (OR) were 1.83 (95% CI, 0.78–4.31, p=0.17), 1.83 (95% CI, 0.66-5.12, p=0.25), 0.68 (95% CI, 0.22-2.05, p=0.49), and 1.81 (95% CI, 0.74-4.42, p=0.20), respectively, showing that there was no significant difference in any of the items evaluated subjectively. The RRs were ≥1.00 in all six studies including the above-mentioned cross-sectional studies, although only half of these studies (Beck *et al.,* Grau *et al*., and Wu *et al*.) detected a significant difference. Relative to healthy individuals, overall RRs for cerebrovascular disease in patients with gingivitis and periodontitis were calculated to be 1.37 (95% CI, 1.10-1.73, p=0.006) and 1.13 (95% CI, 1.01-1.27, p=0.032), respectively, but when the analysis was restricted to the four prospective cohort studies, the RR was 1.11 (95% CI, 0.98-1.25, p=0.106), showing no significant difference. Moreover, the RR for cerebrovascular disease in edentulous individuals, relative to healthy individuals, was 1.46 (95% CI, 0.80-2.66, p=0.222), which also showed no significant difference.

Mustapha *et al.*[3] cited two studies (Pussinen *et al.,* 2004; Johansson *et al.,* 2005) that had used serum antibody titers. Pussinen *et al.* compared *Pg* IgA and *Pg* IgG values in four groups of patients classified according to history of CVD at baseline and incidence of stroke (first or recurrent) during follow-up, but found no significant differences. Johansson *et al.* compared sex-specific *Aa* LNA values, with stroke as an outcome, and calculated ORs of 0.28 (95% CI, 0.13–0.59) in women and 0.88 (95% CI, 0.52–1.51) in men. The results of these reports suggested no overall statistical significance. At present, the number of studies itself remains low with regard to studies that had evaluated serum antibody tiers for periodontopathic bacteria, and this paper is the only report that summarized the association with stroke as an outcome.

Yoshida *et al.*[4] showed the association between tooth loss and stroke, citing four cohort studies. Joshipura *et al.* (2003)

Table 1: Summary of review articles regarding periodontal disease and stroke

Review articles	Janket *et al.* , 2003[1]	Khader *et al.* , 2004[2]	Mustapha *et al.* , 2007[3]	Yoshida and Akagawa, 2011[4]	Dietrich *et al.* , 2013[5]
Main results	RR=2.85 95% CI; 1.78-4.56	RR=1.13 95% CI; 1.01-1.27	There was no association between stroke and serum antibody titers	There was an association between tooth loss and stroke, but the mechanism is unknown	The association was stronger in men than in women

Table 2: List of bibliographical citations from each review article

Author	Year of publication	Study type	Janket *et al.*, 2003[1]	Khader *et al.*, 2004[2]	Mustapha *et al.*, 2007[3]	Yoshida and Akagawa, 2011[4]	Dietrich *et al.*, 2013[5]	
Beck	1996	Cohort	○	○				Overall risk (OR) of individuals with periodontal disease having a stroke is 2.8
Grau	1997	cross sectional		○				Periodontal disease is an independent risk factor for stroke
Morrison	1999	retrospective Cohort	○	○				No significant difference
Wu	1999	Cohort	○					There is a stronger association between periodontal disease and stroke in young people between ages of 25-54 years
Wu	2000	Cohort		○				Periodontal disease is particularly associated with non-hemorrhagic stroke
Howell	2001	Cohort	○	○				There is no association between CVD and self-reported periodontal disease in middle age men
Buhlin	2002	cross sectional		○				No significant difference
Joshipura	2003	Cohort				○		Relative risk (RR) for ischemic stroke is 1.57 in men with less than 24 teeth
Grau	2004	case-control					○	Severe periodontal disease is a risk factor for stroke in men aged 60 years or younger
Pussinen	2004	case-control	Cohort		○			No significant difference
Abnet	2005	Cohort				○		For all strokes, the RR is 1.11 based on the median of missing teeth
Johansson	2005	Cohort			○			No significant difference
Sim	2008	case-control					○	OR for stroke is 4.0 in individuals with CAL ≥6 mm
Heitmann	2008	Cohort				○		For all strokes, the RR is 3.25 in individuals with periodontal disease
Choe	2009	Cohort				○		For all strokes, the RR is 1.3 in men and 1.2 in women among those with periodontal disease
Jimenez	2009	Cohort					○	There is a strong association between stroke and history of periodontal disease in men aged 65 years and younger
Pradeep	2010	case-control					○	OR for stroke is 8.5 in individuals with PPD ≥4.5 mm

CAL; clinical attachment loss

CVD; cerebrovascular disease

OR; odds ratio

PPD; probing pocket depth

RR; relative risk

calculated an RR of 1.57 (95% CI, 1.24–1.98) for ischemic stroke in men when subjects are divided into two group (≥25 or <25 remaining teeth). Abnet *et al.* (2005) divided subjects into two groups by median number of lost teeth and obtained an RR of 1.11 (95% CI, 1.01–1.23) for all strokes. Heitmann and Gamborg (2008) compared two groups (≥28 teeth vs. edentulous) and calculated an RR of 3.25 (95% CI, 1.48–7.14) for all strokes. Choe *et al.* (2009) divided subjects into two groups based on the number of lost teeth at follow-up after three years (≥7 or <7 teeth), and calculated RRs of 1.3 (95% CI, 1.2-1.4) in men and 1.2 (95% CI, 1.0-1.3) in women. The authors concluded that, although tooth loss is associated with both ischemic and hemorrhagic strokes, it is difficult to exclude the various common confounding factors, and that the determination of the underlying mechanisms is a challenge.

Dietrich *et al.*[5] cited five relatively new studies which had not been cited previously (Grau *et al.,* 2004; Sim *et al.,* 2008; Jimenez *et al.,* 2009; Pradeep *et al.,* 2010; Xu and Lu, 2011). Grau *et al.* divided patients into three groups as follows; a group of 303 hospitalized patients who had acute ischemic stroke or transient ischemic attack within seven days; a group of 300 healthy individuals; and a group of 168 hospital controls who had non-vascular disease, and examined dental status for all patients in terms of clinical attachment loss (CAL) and radiographic findings. Individual mean CAL was calculated as the mean of CAL in all teeth measured on a 4-point scale and used as the indicator of periodontitis. CAL was higher in the group of hospitalized patients compared to groups of healthy individuals and hospital controls, and when adjusted for other factors, the risk of cerebral ischemia further increased with the condition of severe periodontitis. The OR for stroke onset was 4.3 (95% CI, 1.85–10.2) in patients with severe periodontitis, *i.e.,* a mean CAL ≥6 mm, relative to those with mild periodontitis (CAL ≤3 mm) or without periodontitis. Moreover, the authors stated that severe periodontitis serves as a risk factor for stroke in men or in younger (≤60 years) subjects. On the other hand, gingivitis and severe radiological bone loss were independent risk factors for cerebral ischemia but were not correlated with dental caries. The study by Sim *et al.* was conducted in Korea, targeting a group of 265 chronic stroke patients and a group of 214 healthy controls. In the patient group, stroke was diagnosed by medical specialists by using MRI or CT, and CAL was measured by a dentist. In patients with teeth with a CAL ≥6 mm, the risk of stroke was calculated to be OR=4.0 (95% CI, 2.3-7.0) even after adjusting for all potential confounding factors, and in cases where CAL was ≤5 mm, the risk of stroke increased with a dose-response effect. Moreover, the association between periodontitis and stroke was stronger in adults younger than age 60 and normotensives. This study was the first to investigate the relationship between periodontal disease and stroke in a non-Western country, and the association was reported to be much stronger than those reported by studies from Western countries (RR = 2.8). Furthermore, according to Jimenez *et al.,* while no association was found between periodontal pocket depth (disease condition of periodontitis) and stroke onset, there was an association between alveolar bone loss (history of periodontitis) and stroke (HR=3.52; 95% CI, 1.59-7.81), and this association was stronger especially in individuals aged 65 years or younger (HR=5.81; 95% CI, 1.63-20.7). On the contrary, the case-control study conducted by Pradeep *et al.* reported that when the plaque index, gingival index, probing pocket depth (PPD), and CAL were compared between a group of 100 controls and a group of 100 patients who had ischemic attack within five days, PPD ≥4.45 mm was the most powerful risk factor, with a calculated OR of 8.5 (95% CI, 1.1-68.2). The authors reported these findings, and summarized that while the association between periodontal disease and coronary heart disease has been reported to show no difference by sex, or to be stronger in women than in men, the association between periodontal disease and cerebrovascular disease has been reported to be stronger in men than in women according to three reports.

[Discussion]

A systematic search of articles published since 1996 was conducted with regard to the association between oral conditions and stroke. As it stands, studies on the association between oral conditions and stroke are mostly reported as part of studies that examined the association between oral health conditions and cardiovascular disease, and the number of such reports comprise less than 30% of all reports concerning cardiovascular disease. To summarize the main articles cited in the five review articles, with regard to the association between periodontal disease and stroke, the risk of stroke seems to increase in populations of young adults and those with more tooth loss, and in cases where CAL and PPD are high. Moreover, it was mentioned that the association of periodontal diseases was stronger with non-hemorrhagic (ischemic) stroke than with hemorrhagic stroke. However, similar to the results obtained for cardiovascular disease, the causal relationship is still unclear due to the lack of sufficient reports regarding decreased risk of developing stroke associated with treatment of periodontal disease. However, while some reports showed

that the association between periodontal disease and coronary heart disease did not differ by sex, or was stronger in women than in men, the association between periodontal disease and cerebrovascular disease is viewed as being stronger in men than in women. As such, it is true that the associations of oral health conditions with cardiovascular disease and stroke have both similarities and differences. Furthermore, since only a few studies have been performed on serum antibody titers for periodontopathic bacteria, it is not necessarily the case that the effects on stroke have been fully discussed. Although it is difficult to develop a study plan excluding all confounding factors that are likely to affect both oral health conditions and stroke, future research is necessary and should include well-planned follow-up studies and interventions studies, which will allow for investigation of these issues as well.

[Conclusions]

This paper examined studies to date regarding the association between oral health conditions and cerebrovascular disease. The results showed that the association between periodontal disease and cerebrovascular disease is stronger in groups of younger adults and those with increased tooth loss, as well as in cases where CAL and PPD are high. However, the direct causal relationship between the two has not been clarified, and future research is needed, including more follow-up studies and intervention studies.

[Conflict of interest]

There are no items applicable to “conflict of interest” in this article.

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4. Association between oral health and main illnesses underlying conditions that necessitate long-term care
2) Dementia

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[Abstract]

While aging populations steadily increase in the world, dementia, a cause of conditions that necessitate long-term care, has become a major issue. A number of cross-sectional studies have pointed out that individuals with dementia have poor oral health status. In these cross-sectional studies, poor oral health status was generally considered the results of dementia. However, recent studies have begun to show that oral health affects future onset of dementia or cognitive decline. This review examined original papers of longitudinal or intervention studies from Japan and abroad to determine whether oral health is associated with future onset of dementia and cognitive decline. The results found that, in most of the studies, significant associations were reported. In addition, oral hygiene, periodontal disease, number of teeth, occlusion, mastication, whether or not having a regular dentist, and dental visit were reported as oral health likely associated with the onset of dementia and cognitive decline.

[Introduction]

Dementia is a condition in which normal social life can no longer be carried out due to brain and physical disorders that cause impairment of memory, judgment, and other functions. According to the results of the 2010 Comprehensive Survey of Living Conditions conducted by the Ministry of Health, Labour and Welfare of Japan, dementia accounted for 15.3% of causes for conditions that necessitate long-term care, the second highest after stroke (21.5%)[1].

As the aging of society progresses in many countries across the world, an increase in the number of patients with dementia has become a major issue. It is estimated that by 2040, roughly 81 million people worldwide will be affected with dementia[2]. According to the estimates of the Ministry of Health, Labour and Welfare of Japan, there are roughly 2.8 million elders (9.5% of the population of people aged 65 years and older) with dementia (the degree of independence in ADL assessment criteria for elders with dementia II or higher) as of 2010, and by 2025, the number is expected to reach 4.7 million (12.8% of the population of people aged 65 years and older)[3].

A number of cross-sectional studies have shown that patients with dementia have poor oral health status. In other words, compared to healthy individuals, patients with dementia have more dental caries[4-6], more lost teeth[4,5,7-13], a higher prevalence of periodontal disease[5,6,10,12,14], unstable dentures[15], and poor dental and denture hygiene[6,15]. However, it is not possible to show any causal relationship from the results of these cross-sectional studies. It is generally conceivable that poor oral health status is attributed to dementia[16], and in fact, to this date, this has been the understanding regarding their association.

On the other hand, more reports now suggest the association between oral health and future onset of dementia or cognitive decline. However, there are only a few review articles that summarize these reports[17].

[Objective]

In this review, we organized reports from Japan and abroad on the association between oral health and dementia or cognitive decline. In particular, we examined original research papers of longitudinal or intervention studies to determine whether or not poor oral health are associated with future onset of dementia and cognitive decline. Furthermore, we summarized findings up to date to identify details of the oral health that are associated with dementia onset and cognitive decline.

[Methods]

From April to May 2014, we conducted searches of the literature that had examined associations between oral health and future onset of dementia or cognitive decline. Inclusion criteria for the literature were longitudinal or

intervention studies with human subjects, and original papers written in English or Japanese.

A search of the literature was conducted using ICHUSHI-Web[18] with "Ninchisho (dementia)," "Kuchi (oral)," and "Ha (teeth)" as search terms, and a literature list of 251 articles excluding conference proceedings was obtained. Then, a search of the literature using PubMed[19] was performed with "dementia" and "dental health" as search terms, and a list of 484 literature articles was retrieved. First, literature articles that clearly differed from the point of this review were excluded based on their titles and abstracts. Furthermore, among the literature cited in the main text of the collected literature, those in accordance with the point of the present review were obtained.

[Results]

1. Oral hygiene

Two cohort studies have reported on the association between oral hygiene and future onset of dementia. One study[20] followed 4,425 Japanese people aged 65 years or older for four years and found, that the hazard ratio was 1.76 (0.96-3.20) in individuals who responded that they did not pay attention to oral hygiene (tooth brushing, mouthwash, denture care), relative to those who responded that they did pay attention, although there was no significance (p=0.07) after adjusting for age, income, body mass index (BMI), presence of disease under treatment, drinking habit, exercise habit, and presence of self-perceived forgetfulness. The other study[21] followed 5,468 Americans (median age, 81 years) for 18 years and found that, in women, those who did not brush their teeth daily had a significantly higher hazard ratio of 1.65 (1.05-2.62), relative to those who brushed their teeth three times a day, even after adjusting for factors such as age, smoking status, drinking habit, exercise habit, BMI, present illness such as hypertension, educational attainment, presence of head trauma, and family history of dementia.

With respect to oral hygiene, an intervention study (randomized controlled study)[22] has been reported, wherein a nurse or caregiver cleaned the teeth of the subject with a toothbrush for about 5 minutes after each meal, and if necessary, a dentist or dental hygienist performed the removal of dental plaque and dental calculus once a week. This intervention was performed in 90 patients with dementia who were residents of 10 facilities (intervention group), and when a comparison was made with 99 residents who did not receive this intervention (control group) based on assessments by Mini-Mental State Examination (MMSE), cognitive decline was suppressed in the intervention group six and 12 months later.

2. Periodontal disease

Five cohort studies have examined the association between the periodontal status and future onset of dementia or cognitive decline; some reported a significant association, while others reported no significant association.

There were three studies that had set dementia diagnosis as an outcome, and of these, one found a significant association, whereas the other two found no significant association. In a cohort study of 158 participants in the US[23], serum antibody levels to *Fusobacterium nucleatum* and *Prevotella intermedia* were significantly increased in participants who developed Alzheimer's disease (mean follow-up period: 10.8 years) compared to those who remained cognitively intact (mean follow-up period: 12.5 years), even after adjusting for age, MMSE, and apolipoprotein ε4 genotype. Meanwhile, in a study that followed 405 French individuals aged 66-88 years for 15 years[24], no significant relationship was found between assessments of periodontal tissue according to the Community Periodontal Index (CPI) and dementia onset. Moreover, a study that followed 11,140 individuals with type 2 diabetes mellitus for five years[25] found no significant relationship between dementia onset and periodontal status, as assessed by self-reported number of days of spontaneous gingival bleeding, gingival bleeding during brushing, or gingival bleeding during meals.

Three reports have examined cognitive decline as an outcome, of which two showed a significant difference, whereas the other one did not show any significant relationship. In a U.S. cohort study[26], 597 men (28-70 years) were followed for 32 years; a significant cognitive decline (assessed by MMSE or spatial copying task [SCT]) was observed in individuals who showed a greater increase in alveolar bone resorption and pocket depth over a 10-year period, especially when subjects were restricted to older individuals aged ≥45.5 years (n=300), even after adjusting for factors such as age, educational attainment, drinking habit, and diseases such as ischemic heart disease. Moreover, in a cohort study that followed cognitive function of 947 Americans (70-79 years) for 2 years[27], a significant decrease in cognitive function (assessed by MMSE) was observed in individuals with a higher mean gingival index, even after adjusting for factors such as age, sex, educational attainment, race, and risk of ischemic heart disease. On the other hand, in the above-mentioned study[25] that followed 11,140 individuals with type 2 diabetes mellitus for five years, no significant relationship was found between cognitive decline (assessed by MMSE) and periodontal status, as assessed by number of days of self-reported spontaneous gingival

bleeding, gingival bleeding during brushing, or gingival bleeding during meals.

3. Number of teeth

Eight original articles of longitudinal studies that had examined the influence of number of teeth on future dementia onset or cognitive decline were available. Of these, six showed that tooth loss was a risk factor for future onset of dementia or cognitive decline. Of the remaining two, one found no significant relationship, and the other showed an opposite trend that the higher the number of teeth lost, the lower the risk.

Among the six papers that examined dementia onset as an outcome, two were case-control studies, and the remaining four were cohort studies; except for one cohort study, all showed tooth loss to be a risk factor for future dementia onset. In Japan, a case-control study compared 60 patients (43-89 years) with Alzheimer's disease and 120 healthy individuals matched for sex and age[28], and showed that experience of losing more than half of the teeth and use of complete denture were risk factors for Alzheimer's disease. Moreover, in Sweden, a case-control study targeting 310 patients (≥65 years) with Alzheimer's disease and 3,063 healthy individuals[29] showed that an experience of tooth loss before the age of 35 years served as a risk factor for Alzheimer's disease, even after adjusting for factors such as age, sex, history of cerebrovascular disease, educational attainment, and exercise habit.

The oldest cohort study that examined Alzheimer's disease as an outcome is an American study that followed 144 nuns (75-98 years) for 12 years[30]; this study showed that the fewer the number of teeth, the higher the risk of developing Alzheimer's disease. In the other words, after adjusting for factors such as age, educational attainment, and apolipoprotein E genotype, individuals with 0-9 teeth had a hazard ratio of 2.20 (1.1-4.5) relative to those with 10-28 teeth. In the above-mentioned cohort study[20], wherein 4,425 Japanese individuals aged 65 years or older were followed for four years, the hazard ratio for dementia onset was 1.85 (1.04-3.31) in individuals with almost no teeth and without denture use, relative to individuals with 20 or more teeth, even after adjusting for age, income, BMI, presence of illness under treatment, drinking habit, exercise habit, and presence of self-perceived forgetfulness. Also, in the above-mentioned study[25] that followed 11,140 type 2 diabetes patients for five years, the hazard ratios for dementia onset adjusted for risk factors such as age, sex, socio-economic status, and cardiovascular disease were 1.24 (1.05-1.46) in individuals with 1-21 teeth, and 1.48 (1.24-1.78) in edentulous individuals, both of which were significantly higher relative to those with 22 or more teeth. On the other hand, a cohort study conducted in France followed 405 individuals (66-80 years) for 15 years[24] and found that, after adjusting for factors such as sex, BMI, diabetes mellitus, depression, hypertension, and history of ischemic heart disease and stroke, there was no significant association between number of teeth and dementia onset in highly educated individuals (n=312). Among those with low educational attainment (n=93), the hazard ratio was 0.30 (0.11-0.79) in individuals who had lost 11 or more teeth, which was significantly lower relative to those who had lost less than 11 teeth, contrarily to other studies[20,25,28-30].

As for studies that had used cognitive decline as an outcome, three articles were available; two showed a significant relationship, while the other one showed no significant relationship. In the above-mentioned U.S. cohort study[26] that followed 597 men (28-70 years) for 32 years, cognitive function (assessed by MMSE or SCT) was significantly declined in individuals with a higher number of lost teeth over 10 years, even after adjusting for factors such as age, educational attainment, drinking habit, and ischemic heart disease. Also, the above-mentioned study[25] that followed 11,140 patients with type 2 diabetes mellitus for five years showed significantly higher hazard ratios for cognitive decline (assessed by MMSE) in individuals with 1-21 teeth (1.23, 1.10-1.38) and edentulous individuals (1.39, 1.21-1.59) relative to those with 22 or more teeth, after adjusting for risk factors such as age, sex, socio-economic status, and cardiovascular disease. On the other hand, in a cohort study[31] that followed 517 residents (59-107 years) of a Japanese institution for six years, the association between number of teeth and cognitive decline (assessed relative to baseline in terms of good, no change, and poor) disappeared after adjusting for age and history of cerebrovascular disease.

4. Occlusion

With respect to occlusion, two cohort studies have examined the association between denture use (with or without) and dementia onset, and both studies reported a significant relationship. The above-mentioned cohort study[20] that followed 4,425 Japanese people aged 65 years and older for four years, the hazard ratio for dementia onset was 1.85 (1.04-3.31) in individuals with almost no teeth and without use of dentures, relative to individuals with 20 or more teeth, even after adjusting for age, income, BMI, presence of illness under treatment, drinking habit, exercise habit, and presence of self-perceived forgetfulness, whereas the hazard ratio in individuals with almost no teeth but with

denture use was 1.16 (0.78-1.74), which was not significantly different compared to that in individuals with 20 or more teeth. In the above-mentioned study[21] that followed 5,468 Americans (median age, 81 years) for 18 years, in men, relative to individuals with 10 or more upper teeth and six or more lower teeth, the hazard ratio adjusted for factors such as age, smoking status, drinking habit, exercise habit, BMI, presence of illness such as hypertension, educational attainment, presence of head trauma, and family history of dementia was significantly higher in individuals with less than 10 upper teeth and less than six lower teeth, who did not use dentures 1.91, (1.13-3.21).

There was one cohort study that examined whether using or not using dentures was associated with cognitive decline. This cohort study[31], which was mentioned above, followed 517 Japanese facility residents (59-107 years) for six years and found that the association between use or non-use of dentures and cognitive decline (good, no change, or poor relative to baseline) disappeared after adjusting for age and history of cerebrovascular disease.

5. Mastication

There was one cohort study that examined the association between chewing ability and dementia onset. The above-mentioned cohort study[20], which followed 4,425 Japanese people aged 65 years and older for four years, showed that the hazard ratio for dementia onset was 1.47 (0.95-2.25) in individuals who responded that they could not hardly chew, relative to those who responded that they could chew anything well, even after adjusting for age, income, BMI, presence of illness under treatment, drinking habit, exercise habit, and presence of self-perceived forgetfulness; however, there was no statistical significance.

6. Other

The above-mentioned cohort study[20], which followed 4,425 Japanese people aged 65 years and older for four years, reported that the hazard ratio for dementia onset was 1.44 (1.04-2.01) in individuals who did not have a regular dentist, relative to those who did, even after adjusting for age, income, BMI, presence of illness under treatment, drinking habit, exercise habit, and presence of self-perceived forgetfulness. In addition, another study has confirmed that having a regular dentist reflected regular dental visit among the residents of the area targeted in this study[32]. Moreover, the above-mentioned study[21] that followed 5,468 Americans (median age, 81 years) for 18 years found that in women, those who had not visited a dentist in the past year had a significantly higher hazard ratio of 1.89 (1.21-2.95) relative to those who had visited a dentist more than twice in the past year, when adjusted for factors such as age, smoking status, drinking habit, exercise habit, BMI, present illness such as hypertension, educational attainment, presence of head trauma, and family history of dementia.

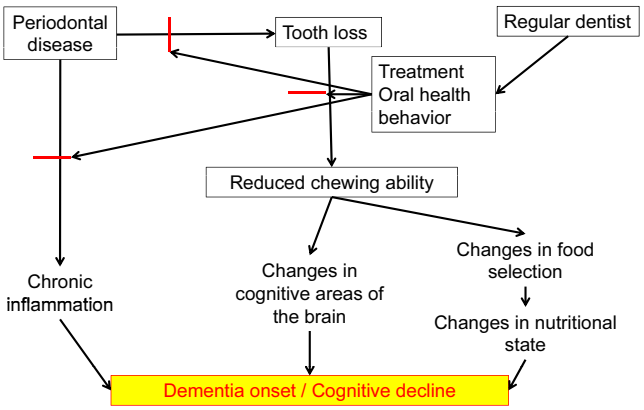

Figure 1: Predicted path leading to the onset of dementia and cognitive decline from oral health

[Discussion]

We examined whether or not oral health is associated with future onset of dementia or cognitive decline based on the original articles of longitudinal and intervention studies performed in Japan and abroad, and found that the majority of these studies had reported significant associations. Moreover, oral hygiene, periodontal disease, number of teeth, occlusion, mastication, presence or absence of a regular dentist, and dental visit were among the oral health likely associated with dementia onset and cognitive decline.

The predicted path leading to the onset of dementia and cognitive decline from oral health is shown in Figure 1. Periodontal disease, a long-term chronic inflammation, is a known cause of tooth loss[33], but could also affect systemic organs due to various inflammatory materials liberated from periodontal tissue via blood, as indicated by some research[34]. On the other hand, blood inflammatory markers have attracted much attention as a cause of or exacerbating factor for dementia[35]. Therefore, it is plausible to consider that these periodontal diseases underlie the path leading to the onset of dementia and cognitive decline.

Also, since loss of teeth decreases chewing ability, it is possible that degenerative changes in the cognitive domains of the brain occur due to decreased mastication-induced stimuli to the brain[36]. Furthermore, as chewing ability decreases, intake of food such as raw vegetables decreases, and this is expected to cause nutritional deficiency (e.g., vitamins)[37]. Insufficient nutrients such as vitamins constitute a risk factor for dementia onset, and thus, the

route involving these nutrients is also a possibility[38].

Having a regular dentist leads to making regular dental visits, and prevention of periodontal disease or tooth loss can be expected through dental health education and preventive treatment provided during regular visits. Therefore, as shown in Figure 1, the route involving a regular dentist is another possibility.

Clinicians should understand how oral health affects future onset of dementia and cognitive decline and engage in their practice. When they provide health education to patients, it is necessary to emphasize the importance of tooth loss prevention, and for those who have had the misfortune to lose their teeth, to inform the significance of treatment with prostheses such as dentures.

Researchers need to conduct studies regarding the effects of dental intervention on the development of dementia and cognitive decline. In addition, the mechanisms of how periodontal disease and tooth loss may lead to cognitive decline need to be elucidated by experiment using animals, etc.

Policy makers should understand how important oral health is in preventing dementia and cognitive decline, and promote participation of dental health care workers in long-term care prevention programs for the elders, and clarify the position of dentistry in the prefectural medical care plan concerning mental illness.

[Conclusions]

This review examined whether oral health is associated with future onset of dementia and cognitive decline based on the original articles of longitudinal and intervention studies from Japan and abroad. As a result, a significant association was found, as reported by the majority of the studies. In addition, oral hygiene, periodontal disease, number of teeth, occlusion, mastication, presence or absence of a regular dentist, and dental visit were reported as oral health that are likely associated with the onset of dementia and cognitive decline.

[Conflict of interest]

There are no items applicable to “conflict of interest” in this article.

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4. Association between oral health and main illnesses underlying conditions that necessitate long-term care

3) Falls and fractures

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[Abstract]

Falls and fractures, especially hip fractures, account for 10% of all causes leading to a state in which elders become in need of care. Little had been known about associations between oral health and falls and fractures. However, in recent years, it has been pointed out that loss of occlusion reduces balance function, and that periodontal disease and osteoporosis are associated with each other. Because the association between balance function and falls and hip fractures and that between osteoporosis and hip fractures have been known, it is possible that oral health may be related to future falls and hip fractures.

Accordingly, we organized the literature from Japan and abroad regarding the association between oral health and falls or hip fractures, while taking into account the levels of evidence. In particular, we examined whether poor oral health lead to an increased risk of future incidence of falls and fractures. Moreover, we summarized the oral health status that are associated with falls and fractures.

As a result, although the number of original articles was low, we were able to obtain some cohort study reports. Many of those studies had demonstrated that loss of occlusal support and not using dentures after tooth loss were risk factors for future falls. Moreover, it was also revealed that having periodontal disease or low number of teeth increased the risk of future hip fractures.

[Introduction]

Falls and fractures (especially hip fractures) cause conditions that necessitate long-term care in many elders, and have become medical and economical issues along with Quality Of Life (QOL) decrease among the elders. According to the 2010 Comprehensive Survey of Living Conditions by the Japanese Ministry of Health, Labour and Welfare, falls and fractures accounted for 10.2% of all causes for conditions that necessitate long-term care[1]. Moreover, according to the literature from Japan and abroad, about one in three elders reportedly experience a fall, and of these, roughly 6% have fractures, and roughly 24% have severe injuries[2,3]. Furthermore, the possibility has been pointed out that, after a fall incident, people become sequestered in their house for fear of recurrent falls, and consequently become frail and in need of long-term care. In Japan, about 730 billion yen is spent annually as medical and long-term care expenses after falls; this cost is estimated to be equivalent to roughly 5% of medical and long-term care expenses used annually for the people in Japan[4].

Risk factors for falls have been reported, including older age, past fall experience, diseases such as rheumatoid arthritis and cerebrovascular disease, depression, and decreased muscle strength and balance function[5]. Among these risk factors, fall prevention programs aimed at improving balance function have been shown to have certain promising effects[6]. However, integrated fall prevention programs, which take into account other risk factors as well, have shown almost no effect[7]. Therefore, there is a need to further identify risk factors that might allow for intervention to prevent falls.

Recent studies have indicated the possibility that poor oral health might be a risk factor for falls. A longitudinal study has revealed that loss of occlusion subsequently leads to decreased leg strength and balance function[8]. Sine decreased balance function is a risk factor for falls[5], loss of occlusion might serve as a risk factor for falls.

Osteoporosis is also a well-known risk factor for hip fractures[9]. In recent years, the systemic effects of periodontal disease, especially, the effects on diabetes mellitus, ischemic heart disease, cerebrovascular disease, and low birth weight delivery, have been pointed out[10], and the association between osteoporosis and periodontal disease has been indicated as well[11]. Thus, the likelihood of having a hip fracture might be increased due to the increased

osteoporosis risk associated with periodontal disease.

However, recent research results have not been organized to say the least, in terms of whether or not poor oral health leads to future falls and fractures.

[Objective]

In this review, we organized the literature from Japan and abroad regarding the association between oral health and falls or fractures (especially, hip fracture that leads to conditions requiring long-term care), while taking into consideration the levels of evidence. In particular, we examined whether poor oral health lead to an increased risk of incidence of falls and fractures in the future. We also summarized previous findings in order to identify oral health status that are associated with falls and fractures.

[Methods]

From April to May 2014, we searched the literature with regard to whether poor oral health increase the future risk of incidence of falls and hip fractures. Inclusion criteria for the literature were as follows: studies performed with human subjects, and original or review articles (including systematic reviews) written either in English or Japanese.

We conducted a search using ICHUSHI-Web[12] with search terms "Tentou (falls)," "Kuchi (oral)," and "Ha (teeth)," and obtained 419 titles and abstracts of the literature excluding conference proceedings. We also performed a search using terms "Daitaikotsu keibu kossetsu (hip fracture)," "Kuchi (oral)," and "Ha (teeth)," and obtained 26 titles and abstracts of the literature excluding conference proceedings.

Then, using PubMed[13], we obtained 173 literature titles and abstracts with search terms "falls," "elderly," and "dental health," and 332 literature titles and abstracts using search terms "falls" and "tooth." In addition, we obtained 204 literature titles and abstracts with terms "hip fracture" and "dental health," and 15 literature titles and abstracts with terms "hip fracture" and "tooth loss."

First, we excluded literature articles that clearly differed from the purpose of this review based on their titles and abstracts. Furthermore, among the literature cited in the main text of the literature articles of which full text was obtained, we obtained full text if the literature matched the purpose of this review.

Based on the obtained literature, we examined whether poor oral health become the future risk of incidence of falls and fractures. In addition, we summarized the results obtained from the literature in terms of what kind of oral health status are associated with falls and fractures.

[Results]

1. Relationship between oral health and falls

Two cohort studies have indicated the possibility that the lack of occlusal support contributes to an increased risk of future falls[14-16]. Yoshida *et al*.[14,15] prospectively studied the presence or absence of experience of two or more falls over a 1-year period following an examination of occlusion in 146 ambulatory patients (42 men, 104 women; mean age, 82.2 years old) who, after hospitalization, continued to visit a specialized hospital for patients with severe dementia exhibiting abnormal behavior. The results showed that those whose occlusion was not maintained by either natural or prosthetic teeth had a 3.65-fold (95% confidence interval [CI], 1.42-9.33) higher risk of fall relative to those whose occlusion is maintained by natural dentition, and a 3.73-fold (1.99-6.98) higher risk of fall relative to those whose occlusion is maintained by denture(s), even though their teeth are partially or completely missing.

Yamamoto *et al*.[16] examined the associations of self-reported number of teeth by a questionnaire, denture use, and chewing ability with falls three years later (two or more falls during the previous year) in 1,763 community-dwelling individuals aged 65 years and older, who were completely independent in carrying out activities of daily living, and who responded at baseline that they had no experience of falls in the previous year. The results showed that participants who responded to have 19 or fewer teeth with no use of dentures had a 2.50-fold (1.21-5.17) higher risk of fall relative to those who responded to have 20 or more teeth, even after adjusting for all of the factors including sex, age, presence of care-need certificate during the follow-up period, depression, self-rated health, and educational attainment. Moreover, those who responded that they were not able to chew very well had a 1.47-fold (0.64-3.37) higher risk of fall relative to those who responded that they were able to chew anything, even after adjusting for the aforementioned factors such as sex and age; however, the relationship was not significant.

There was one cross-sectional study that examined the relationship between occlusal state and experience of fall accident, although this study found no significant relationship between the two[17]. In this study, 253 patients (105 men, 148 women; age, 30-94 years) who visited seven medical institutions were asked to answer a question, "Can you chew well with your own teeth?," on a self-administered questionnaire. The rate of experience of fall accident tended to be higher (29.7%) among the patients who answered "yes" compared to those who answered "no" (21.4%); however, the relationship was not significant.

2. Relationship between oral health and hip fractures

1) Relationship between periodontal disease and hip fractures

A 3-year cohort study conducted in Sweden targeting 788 residents (375 men, 413 women; ages, 62-96 years) examined the relationship between periodontal disease and hip and hand fractures[18]. The results showed that participants with periodontitis (periodontitis was defined as when sites with ≥5 mm distance from the cemento-enamel junction to the alveolar bone level in the interdental space, as measured on the panoramic radiograph, was ≥30% of the entire jaw) had a 2.1-fold (95% CI, 1.1-4.0) higher risk of hip and hand fractures, even after adjusting for age. The study also found that having both periodontitis and osteoporosis increased the hip or hand fracture risk by 12.2-fold (3.5-42.3).

2) Relationship between number of teeth and hip fractures

Wakai *et al*.[19] followed 9,992 male dentists aged 50 years and older (mean, 61.1 years; standard deviation, 9.6 years) for a mean period of 6.0 years, and obtained the self-reported number of teeth at baseline and subsequent hip fractures from the medical care fee claim bills to determine the relationship between the two using the data. The results showed that participants who had lost 15-27 teeth and those who had lost 28 teeth (edentulous) had 4.1-fold (95% CI, 1.2-14.2) and 4.5-fold (1.1-18.0) higher risks of fracture, respectively, relative to those who had lost 0-14 teeth (excluding third molars), even after adjusting for all of the factors including age, drinking habit, smoking status, history of diabetes mellitus, mental distress, use of sleeping pills, total dietary intakes of energy and calcium, height, body weight, and vigorous physical activity. Similarly, even after adjusting for all of the factors including age, the risk of fracture increased by 1.06 (1.01-1.12) for every tooth loss.

[Discussion]

1. Relationship between oral health and falls

Although the number of original articles was low, the cohort studies clearly demonstrated the possibility that loss of occlusal support leads to an increase in the risk of future falls. While the mechanisms are unknown, the following possibility could be considered.

In humans, the center of gravity of the body lies in the upper body, because the head is heavy. The balance of the head is maintained by afferent fibers from the masticatory muscles and periodontal ligaments[20]. In this context, loss of occlusal support could reduce afferent signals from masticatory muscles and periodontal ligaments, destabilizing the head. As a result, the center of gravity becomes unstable, and the risk of fall increases. In a study that examined the effects of the presence or absence of dentures in edentulous individuals on the sway of the center of gravity of the body[21], it was revealed that when those individuals were wearing dentures, the center of gravity sway was less, and the upright posture was stabilized, as compared to when they were not wearing dentures; thus, these results supported these hypotheses.

2. Relationship between oral health and hip fractures

Although only a few original articles exist regarding this theme, the possibility has been suggested that having periodontal disease or tooth loss may increase the risk of future hip fractures. The mechanisms underlying this too have not been clarified in detail, but tooth loss, as described above (loss of occlusion), could increase the risk of fall, consequently increasing the risk of hip fractures. Another likely route is that, as a result of long-term chronic inflammation caused by periodontal disease, the risk of osteoporosis may increase, and this could then increase the risk of hip fractures. However, due to insufficient evidence, the direct impact of periodontal disease on osteoporosis is in the midst of discussions[22], and thus, further research is anticipated.

It is desired that clinicians have a good understanding of findings with regard to the relationship between oral health and falls, or hip fractures, and utilize them in clinical practice. In particular, the importance of occlusion in the elders needs to be understood, and the information should be provided to patients and residents. Ideally, for elders with no occlusal support in the molar region, prosthetic treatment should be actively performed.

Given a few original research articles available with respect to the relationship between oral health and falls, or hip fractures, researchers should conduct more studies, and verify reproducibility of the results. Intervention studies should also be performed to further examine the causal relationship.

Based on these study results, policy makers should consider promoting long-term care prevention collaboration for the purpose of improving motor and oral function under the public long-term insurance system. For example, it may be even possible to reduce the fall risk by incorporating a visit by dental professionals to perform an occlusion check in a fall prevention class that highlights balance function improvement.

[Conclusions]

We organized the literature from Japan and abroad regarding the association between oral health and falls, or hip fractures, while taking into consideration the levels

of evidence. In particular, we examined whether poor oral health lead to the future risk of incidence of falls and fractures. We also summarized the oral health status that are associated with falls and fractures.

As a result, although the number of original research articles was low, some cohort studies were available, and many of them had demonstrated that loss of occlusal support and not using dentures after tooth loss were risk factors for future falls. Moreover, it was revealed that having periodontal disease and a low number of teeth increase the risk of future hip fractures.

[Conflict of interest]

There are no items applicable to "conflict of interest" in this article.

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4. Association between oral health and main illnesses underlying conditions that necessitate long-term care

4) Articular diseases – Periodontal disease and rheumatoid arthritis –

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[Abstract]

Much progress has been made in research on the association between periodontal disease and rheumatoid arthritis. In this review, we selected five articles on intervention studies from the literature published to date. In addition, three articles on case-control studies, and four articles on cross-sectional studies were selected.

The results of those studies showed that periodontal disease is associated with rheumatoid arthritis, and that the prevention and periodontal treatment can improve symptoms and surrogate markers of rheumatoid arthritis. However, as the effects have only been observed in some symptoms and surrogate markers, further examination will be necessary.

The mechanisms underlying the association have been clarified by basic studies. Some periodontal disease-associated bacteria (*Porphyromonas gingivalis*) have an enzyme (peptidylarginine deiminase (PAD)) that converts arginine to citrulline in peptides, and carries out post-translational modifications of proteins and peptides in vivo. PAD contained in *P. gingivalis* is called PPAD. Modified proteins and peptides (non-self proteins and peptides) citrullinated by *P. gingivalis* or PPAD, or within periodontal tissue, enter the bloodstream from the site of inflammation in periodontal tissue; from there, they are carried throughout the body. This causes autoimmune disease in various parts of the body. Exacerbation of rheumatoid arthritis is likely to occur as a result of autoimmune reactions in the joints, which are caused when the bacteria, enzyme, or modified proteins or peptides enter the joint synovial fluid.

[Introduction]

Rheumatoid arthritis (RA), an autoimmune disease, results in the destruction of joint tissue due to inflammation that occurs in the synovial membrane of the joint. Information on the morbidity and prevalence of RA in Japan has not been fully grasped, but in general, the number of patients is estimated to be roughly 700,000 to 800,000 (source: the report of the Rheumatism and Allergy Control Committee, Health Sciences Council in August 2011). The national share of medical costs for bone and joint diseases in Japan, as determined by patient surveys, the report of national medical expenditures, and the Survey of Medical Care Activities in Public Health Insurance, has been compared internationally. According to this report, RA accounts for 102.9 billion yen or 336,000 yen per patient in Japan (Epidemiology of rheumatoid arthritis: A study on care receiving dynamics among patients: Grant for Health Sciences, FY2004 comprehensive research report). Considering that joint diseases as a whole cost is 485,000 yen per patient, the cost for rheumatoid arthritis takes up the majority of this expense.

This review selected articles from the previously published literature, with a focus on intervention studies. From the PubMed database, 262 articles were extracted, and five articles[1-5] that had examined improvements in RA due to periodontal disease intervention were selected. In addition, three articles[6-8] on case-control studies, and four articles[9-12] on cross-sectional studies were selected.

Patients with RA produce autoantibodies specific to RA, and all autoantibodies are produced upon recognition of proteins and peptides that are citrullinated by peptidylarginine deiminase (PAD) as non-self (autoantigens)[13].

PAD is an enzyme that converts arginine residues in proteins and peptides to citrulline residues, and PAD1-PAD4, as well as PAD6 enzymes are distributed in the body. Among these, PAD4 is able to migrate into the nucleus, where it is involved in histone citrullination and demethylation[7,8].

PADs in the body play their individual roles, maintaining their own homeostasis. On the other hand, *P. gingivalis,* a

periodontal pathogen, secretes an enzyme (PPAD) that has the same function as the PADs in the living body[14]. Due to PPAD, proteins and peptides become citrullinated and changed into non-self proteins and peptides. In addition, since PPAD itself becomes citrullinated, anti-PPAD antibodies are produced as living organisms recognize citrullinated PPAD as an antigen[15]. Patients with periodontal disease develop bacteremia on a daily basis, and thus, not only periodontal pathogens (*P. gingivalis*) and PPAD, but also citrullinated proteins and peptides enter their joint synovial fluid. For this reason, autoimmune disease is likely to develop in the synovial membrane of the joint.

As described above, the molecular mechanisms underlying the causal relationship between periodontal disease and RA has been inferred, and in the future, the clinical and epidemiological evidence is anticipated. In this review, we mainly selected clinical studies from the literature in the PubMed database and organized epidemiological evidence currently available with regard to the association between periodontal disease and RA.

[Objective]

The objective of this review is to provide the overview of the literature regarding periodontal disease and RA, and to epidemiologically confirm that RA can be improved by preventing and/or treating periodontal diseases.

[Methods]

We searched the literature using PubMed to extract only original research articles published up to June 1, 2014.

In the PubMed search, the literature was searched and extracted using "arthritis, rheumatoid"[MeSH Terms] AND "periodontitis" [MeSH Terms] OR "periodontal diseases"[MeSH Terms], with "Clinical Trial" and "Humans" as filters.

As a result, 262 articles were extracted from the PubMed database. Among these, articles that overlapped and those that clearly differed from the gist of this review were excluded by carefully reading the reports, titles and abstracts. Of the remaining 14 articles, five articles reporting intervention studies (English only) were selected (Table 1). In addition, four articles that had examined correlations mainly focusing on case-control studies were selected (Table 2).

[Results]

1. Intervention studies

A study from Federal University of Rio de Janeiro (Ribeiro J)[1], reported in 2005, examined the effects of periodontal treatment in patients with RA. The methods of intervention included oral hygiene instruction, professional mechanical tooth cleaning (PMTC), and full-mouth scaling and root planing (SRP). Subjects were 42 patients with RA, the mean age was 51.6 years, and 88.5% were women. G1 (control group) included 16 patients, and G2 (treatment group) included 26 patients. Both G1 and G2 groups showed improvements in the periodontal disease parameters. While no significant differences in rheumatoid factor (RF) and

Table 1: Periodontal disease and rheumatoid arthritis intervention studies

Author's name (reference No.)	Years of publication	Research design	Subjects	The methods of intervention	clinical end-point	Inspection item	Results	Conclusion
Ribeiro *et al.* (1)	2005	intervention	42 patients with RA, the mean age was 51.6 years, and 88.5% were women. G1 (control group) included 16 patients, and G2 (treatment group) included 26 patients.	oral hygiene instruction, professional mechanical tooth cleaning (PMTC), and full-mouth scaling and root planing (SRP).	HAQ、PI、GI、PPD、CAL	RF、ESR	Both G1 and G2 groups showed improvements in the periodontal disease parameters. While no significant differences in rheumatoid factor (RF) and erythrocyte sedimentation rate (ESR) were observed in G1 patients, who were submitted to oral hygiene instruction and PMTC only, a significant improvement in ESR was observed in G2 patients who received full-mouth SRP in addition to oral hygiene instruction and PMTC. However, no significant difference was observed in RF.	a significant improvement in ESR was observed in G2 patients who received full-mouth SRP in addition to oral hygiene instruction and PMTC.
Al-Katma *et al.* (2)	2007	intervention	38 RA patients at a mean age of 55 years (treatment group, 19 patients; control group, 19 patients) (88% women).	oral hygiene instruction along with scaling/rootplaning	DAS28、VAS、PI、GI、PPD、,CAL	ESR	DAS28(76.4%)、VAS(58.8%) and ESR are improved in the treatment group. Statiscally significant differences are found in DAS28 and ESR values between the treatment and control groups. This intervention led to a significant improvement in all periodontal clinical parameters.	The results showed that symptoms of RA (DAS28, VAS, and ESR) improved with treatment of periodontal disease.
Pinho *et al.* (3)	2009	intervention	75 RA and non-RA patients (mean age, 50 years; 60% women) by dividing them into five groups.	non-surgical periodontal treatment (NSPT)	HAQ、DAS28、PPD、GI、PI	α-1 acid glycoprotein (AAG)、RF、ESR、CRP	In patients with RA and periodontal disease, periodontal treatment significantly improved RA symptoms (DAS28) in a 3-month period.	The relationship between RA and PD disease activities is not clear, but the importance of periodontal treatment in the control of inflammation to avoid tooth extraction is evident.
Ortiz *et al.* (4)	2009	intervention	A total of 40 RA patients. The four groups were: A (periodontal treatment only) with a mean age of 69 years (80% women); B (no anti-TNF-α drug, no periodontal treatment) with a mean age of 49 years (100% women); C (received both anti-TNF-α drug and periodontal treatments) with a mean age of 54 years (80% women); and D (received anti-TNF-α drug treatment only; no periodontal treatment) with a mean age of 63 years (90% women).	non-surgical periodontal treatment (NSPT)	DAS28、VAS、CAL、PPD、BOP	ESR、TNF-α	The results showed that, with or without anti-TNF-α drug treatment, periodontal treatment improved RA symptoms (DAS28, VAS)	non-surgical periodontal treatment (NSPT) reduces the symptoms of RA.
Okada *et al.* (5)	2013	intervention	55 RA patients (mean age, 62.7 years; 82.8% women).	tooth brushing instruction and PMTC or SRP	DAS28、VAS、GI、PPD、CAL	CRP, anti-CCP and serum antibody (IgG) to P. gingivalis、TNF-α	The intervention including tooth brushing instruction and PMTC or SRP improved RA symptoms (DAS28-CRP). Moreover, anti-CCP and serum antibody (IgG) to P. gingivalis were decreased. At the same time, improvements were observed in periodontal pocket depth and clinical attachment level (CAL).	The intervention including tooth brushing instruction and PMTC or SRP improved RA symptoms (DAS28-CRP).

Table 2: Periodontal disease and rheumatoid arthritis case-control studies

Author's name (reference No.)	Years of publication	Research design	Subjects	Clinical end-point	Inspection item	Odds ratio (OR)	Conclusion
Mercado *et al.* (6)	2001	case-control studies	65 patients with RA and matched healthy individuals. The mean age was 56.4 years old, and 74.6% were women.	PD,BOP、OPG、VAS、HAQ	ESR、CRP	The results showed that patients with RA had a 1.64-fold higher risk of bleeding gums, 2.27-fold higher risk of alveolar bone resorption, and 2.47-fold deeper periodontal pockets.	The association between RA and periodontal disease was demonstrated by this study.
Pischon *et al.* (7)	2008	case-control studies	57 patients with RA and 52 healthy individuals.	plaque index (PI), gingival index (GI), probing depth (PD), clinical attachment loss (CAL). smoking, education, alcohol consumption, and body mass index (BMI),	N/A	The results revealed an 8.05-fold higher risk of periodontal disease in patients with RA. The risk remained significantly high even after various adjustments (6.21-, 6.39-, and 6.09-fold higher).	There is an association between periodontal disease and rheumatoid arthritis
Chen *et al.* (8)	2013	case-control studies	13,779 newly diagnosed patients with RA (age ≥16 years) as the study group and 137 790 non-patients with RA matched for age, sex, and initial diagnosis date (index date) as controls.average age 52.6、77.4% are woman	RA: ICD9-CM codes714.0、periodontitis: ICD9-CM codes523.3-5	N/A	An association was found between a history of periodontitis and newly diagnosed RA. The strength of this association remained statistically significant after adjustment for potential confounders (OR=1.16; 95% CI 1.12 to 1.20).	An association was found between a history of periodontitis and newly diagnosed RA.

Table 3: Periodontal disease and rheumatoid arthritis cross-sectional studies

Author's name (reference No.)	Years of publication	Research design	Subjects	clinical end-point	inspection item	Results	Conclusion
Ogrendik *et al.*(9)	2005	cross-sectional	Thirty patients (5 men, 25 women) who fulfilled the American College of Rheumatology criteria for RA and 20 (5 men, 15 women) healthy donors.	DAS28	Pathogen-specific immunoglobulin (Ig)G、ESR、serum CRP、RF	The IgG levels of *P gingivalis, P. intermedia, P. melaninogenica,* and *B. forsythus* were found to be significantly higher in RA patients when compared with those of the controls. A positive correlation between serum IgG antibody levels against *P gingivalis* and serum CRP was clearly detected in patients with RA.There was significant correlation between serum IgG antibody levels against *P. intermedia* and ESR	The antibodies formed against *P gingivalis, P intermedia, P melaninogenica*, and *B forsythus* could be important to the etiopathogenesis of RA.
de Pablo *et al.*(10)	2008	cross-sectional (NHANESIII)	The sample consisted of 4,461 participants, of whom 103 were classified as having RA.	attachment loss and probing depth	–	Participants with RA had more missing teeth (20 vs 16 teeth; p < 0.001), but less decay (2% vs 4%; p < 0.001) than participants without RA. After adjusting for age, sex, race/ethnicity, and smoking, subjects with RA were more likely to be edentulous [odds ratio (OR) 2.27, 95% confidence interval (CI) 1.56 3.31] and have periodontitis (OR 1.82, 95% CI 1.04 3.20) compared with non-RA subjects. In participants with seropositive RA there was a stronger association with dental health status, in particular with edentulism (OR 4.5, 95% CI 1.2 17).	RA may be associated with tooth loss and periodontitis.
Dissick *et al.*(11)	2010	cross-sectional	Sixty-nine patients with RA (57 males and 12 females) and 35 patients with OA (30 males and five females)	Attachment loss and probing depth, dental panoramic radiographs,	RF, anti-CCP	Moderate to severe periodontitis was more prevalent in patients with RA (51%) than controls (26%) (P = 0.03). Patients with RA who were seropositive for rheumatoid factor (RF) were more likely to have moderate to severe periodontitis (59%) than patients who were RF negative (15%) (P = 0.02). Likewise, patients with RA who were positive for the anti-cyclic citrullinated peptide (CCP) antibodies were more likely to have moderate to severe periodontitis (56%) than patients who were anti-CCP negative (22%) (P = 0.01).	Periodontitis was more common and severe in patients with RA compared to patients with OA.
Mikuls *et al.*(12)	2012	cross-sectional	Autoantibody positive (n = 113)、Autoantibody-negative individuals (n = 171) . None of the284 study subjects satisfied the criteria for RA. Of the 113 categorized as autoantibody positive, 38 were further categorized as high-risk based on the presence of a positive ACPA or positivity to two or more RF assays.	–	RF, anti-citrullinated protein antibody (ACPA) , Antibody to Pg, Pi, and Fn	Immunity to Pg, but not Pi or Fn, is significantly associated with the presence of RA-related autoantibodies in individuals at risk for RA.	These results support the hypothesis that infection with Pg may play a central role in the early loss of tolerance to self-antigens in RA pathogenesis.

erythrocyte sedimentation rate (ESR) were observed in G1 patients, who were submitted to oral hygiene instruction and PMTC only, a significant improvement in ESR was observed in G2 patients who received full-mouth SRP in addition to oral hygiene instruction and PMTC. However, no significant difference was observed in RF[1].

A study from Cleveland University Hospital[2] examined the effects of periodontal treatment in 38 RA patients at a mean age of 55 years (treatment group, 19 patients; control group, 19 patients) (88% women). The results showed that symptoms of RA (DAS28, VAS, and ESR) improved with periodontal treatment[2].

A study from the University of São Paulo[3] examined 75 RA and non-RA patients (mean age, 50 years; 60% women) by dividing them into five groups. In patients with RA and periodontal disease, periodontal treatment significantly improved RA symptoms (DAS28) in a 3-month period; however, the significance disappeared in a 6-month period, showing that the relationship was ambiguous. Yet, periodontal treatment suppressed inflammation at least temporarily, demonstrating that periodontal treatment for RA patients could be beneficial[3].

A study in Cleveland University Hospital[4] collected a total of 40 RA patients, 20 each based on the difference in terms of whether patients were taking an anti-TNF-α drug or not. The group of 20 patients who were taking an anti-TNF-α drug was randomly divided into two groups (treatment group and non-treatment group). Meanwhile, the group of 20 patients who were not taking an anti-TNF-α drug was similarly divided into two groups (treatment and non-treatment group). The four groups were: A (periodontal treatment only) with a mean age of 69 years (80% women); B (no anti-TNF-α drug, no periodontal treatment) with a mean age of 49 years (100% women); C (received both anti-TNF-α drug and periodontal treatments) with a mean age of 54 years (80% women); and D (received anti-TNF-α drug treatment only; no periodontal treatment) with a mean age of 63 years (90% women).

The results showed that, with or without anti-TNF-α drug treatment, periodontal treatment improved RA symptoms (DAS28, VAS)[4].

A study from Niigata University[5] targeted 55 RA patients (mean age, 62.7 years; 82.8% women). The intervention including tooth brushing instruction and PMTC or SRP improved RA symptoms (DAS28-CRP). Moreover, anti-CCP and serum antibody (IgG) to *P. gingivalis* were decreased. At the same time, improvements were observed in periodontal pocket depth and clinical attachment level (CAL). Therefore, tooth brushing instruction and PMTC (or SRP) likely improve oral and systemic symptoms in patients with RA.

2. Case-control study

Case-control studies on the relationship between periodontal disease and RA are shown in Table 2.

A case-control study published in 2001 (Mercado *et al.*)[6] examined 65 patients with RA and matched healthy individuals. The mean age was 56.4 years old, and 74.6% were women. The results showed that patients with RA had a 1.64-fold higher risk of bleeding gums, 2.27-fold higher risk of alveolar bone resorption, and 2.47-fold deeper periodontal pockets. The association between RA and periodontal disease was thus demonstrated by this study.

A case-control study published in 2008 (Pischon *et al.*)[7] compared 57 patients with RA and 52 healthy individuals.

The results revealed an 8.05-fold higher risk of periodontal disease in patients with RA. The risk remained significantly high even after various adjustments (6.21-, 6.39-, and 6.09-fold higher).

A case-control study published in 2013 (Chen *et al.*)[8] examined 13,779 patients with RA and 137,790 patients with no RA. The mean age was 52.6 years, and 77.4% were women. The results showed that patients with RA had a 1.64-fold higher risk of bleeding gums, 2.27-fold higher risk of alveolar bone resorption, and 2.47-fold deeper periodontal pockets.

3. Cross-sectional study

A cross-sectional study published in 2005 (Ogrendik *et al.*)[9], which surveyed 30 patients with RA and 20 healthy individuals, reported that serum antibody titers to *P. gingivalis, P. intermedia, P. melaninogenica,* and *B. forsythus* were significantly higher in patients with RA, and that significant positive correlations were observed between the antibody titer to *P. gingivalis* and CRP, and between the antibody titer to *P. intermedia* and ESR.

Another cross-sectional study (de Pablo *et al.*) published in 2008[10] used aggregated data from a large-scale health survey in the United States (NHANESIII). That study analyzed 103 patients with RA (57% women) and found that the risk of edentulous jaw was 2.27-fold higher in RA patients than in non-RA patients (95% confidence interval (CI), 1.56 to 3.31). It was revealed that patients with RA have a 1.82-fold higher risk of periodontal disease compared to non-RA patients (95% CI, 1.04 to 3.20).

In a report from a U.S. Veterans Hospital in 2010[11], 69 patients with RA and 35 patients with osteoarthritis (OA) were examined. The results showed that, when American veterans suffering from RA were compared to controls (i.e., osteoarthritis patients), more patients with RA whose RF and anti-CCP were high had severe periodontal disease, relative to patients with osteoarthritis.

A report in 2012 (Mikuls *et al.*)[12] examined 284 individuals who were determined not to have RA. Subjects included 171 autoimmune antibody-negative individuals and 113 autoimmune antibody-positive individuals. Of 113 individuals, 38 were considered high risk based on the results of anti-citrullinated peptide antibodies (ACPA) and RF tests. In high-risk individuals, antibody titers to *P. g* were significantly higher among antibody-positive individuals, compared to antibody-negative individuals. No differences were found in antibody titers to *P. i.* and *F. n.*

4. Ongoing investigation

In addition to those describe above, there is also ongoing research. Monsarrat P *et al.*[16] has announced a plan to survey two university hospitals in southwest France.

[Discussion]

Of the five intervention studies, four have found the effects of intervention in the periodontal treatment for

patients with RA. As for the remaining one study, the effect of intervention of periodontal treatment was positively evaluated. While previous studies performed tooth-brushing instruction and PMTC or SRP as methods of intervention, consideration of the technical aspect remains to be clarified. In the future, clearer results will be obtained by improving the technologies for the prevention and periodontal treatment.

Moreover, three case-control studies, as well as a cross-sectional study with data from NHANESIII, all showed associations between periodontal disease and RA (Table 2). These data are important in reinforcing the results of the intervention studies.

Patients with RA produce RA-specific autoantibodies, which are all generated when the body recognizes proteins and peptides citrullinated by PAD as non-self (autoantigen)[13].

PADs are enzymes that convert arginine residues in proteins and peptides to citrulline residues, and these enzymes, including PAD1-PAD4, as well as PAD6, are distributed in the body. Of these, PAD4 is capable of migrating into the nucleus, where it is involved in the citrullination and demethylation of histones[17,18].

Each PAD in the body plays a role while maintaining its own homeostasis. On the other hand, *P. gingivalis,* a periodontal disease-associated bacterium that resides in the oral cavity, secretes an enzyme (PPAD) that has the same function as the PADs in our body[14]. Because of this PPAD, not only self-proteins and peptides are citrullinated and changed into non-self proteins and peptides, but PPAD itself is also citrullinated, which is recognized as an antigen against which anti-PPAD antibodies are generated[15]. Patients with periodontal disease develop bacteremia on a daily basis, and thus, not only periodontal pathogens (i.e., *P. gingivalis*) but citrullinated PPAD also enter the synovial fluid of the joint. For this reason, it is likely that autoimmune disease develops in the synovial membrane of the joint.

[Conclusions]

The results of the intervention studies, case-control studies, cross-sectional studies, and basic studies showed that periodontal disease is associated with RA, and the prevention and periodontal treatment can improve some of the symptoms of RA. However, these improvements were part of the evaluation items, and the improving effects were ambiguous in some articles; therefore, further investigative research is necessary.

[Conflict of interest]

There are no items applicable to "conflict of interest" in this article.

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4. Association between oral health and main illnesses underlying conditions that necessitate long-term care

5) Other diseases – Oral health and conditions that necessitate long-term care –

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[Abstract]

For an aging society, extension of healthy life expectancy without being in need of care is an important issue. In recent years, it has been pointed out that poor oral health condition could increase the risk of stroke, a major cause leading to conditions that necessitate long-term care. Moreover, oral health affects nutrient intake, as well as conversation and smile involved in social interaction, and is correlated with the maintenance of health status of older individuals. Therefore, this review examined whether oral health in older individuals is associated with the incidence of conditions that necessitate long-term care, by narrowing down our search to cohort and intervention studies. Seven reports were included in this review and our results suggested a possibility that good oral health may be associated with the prevention of future occurrence of conditions that necessitate long-term care. Moreover, those with a primary care dentist might be less prone to develop a condition requiring long-term care. Furthermore, specialized services aimed at maintaining oral health might play a role in preventing an increase in the level of care need. Favorable oral health conditions, including use of dentures, were also associated with a lower future occurrence of conditions that necessitate long-term care. There is a possibility that the incidence of conditions requiring long-term care could be decreased by further spreading health care interventions aimed at maintaining oral health of the older individuals.

[Introduction]

An increase in the number of older people who develop conditions that necessitate long-term care increases burdens on their families and costs associated with long-term care facilities[1]. Moreover, the condition that necessitates care itself raises the mortality rate[2]. In terms of extension of healthy life expectancy and reduction of social burdens, it is extremely important to prevent the occurrence of conditions that necessitate long-term care.

The predictive factors for the occurrence of conditions that necessitate long-term care include old age, cognitive dysfunction, visual impairment, low subjective health[3], decreased or increased body mass index (BMI), decreased function of the extremities, decreased exercise or social interaction, and smoking[4]. In recent years, the possibility that oral health might be related with some of the risk factors associated with these care-requiring conditions has been gradually pointed out. A decrease in the number of remaining teeth and reduction in oral function cause unbalanced food intake and nutrition[5,6]. It is also possible that a decrease or increase in BMI is caused by decreased oral function[7]. It is likely that decreased nutritional status is linked to the development of frail and care-requiring conditions among the older people[8]. Moreover, chronic inflammation associated with periodontal disease may be a risk factor for cerebrovascular disease, and periodontal disease could increase the risk of stroke according to a meta-analysis[9]. Stroke can cause paralysis of the extremities, leading to a condition requiring long-term care; this is a major factor that decreases the disability-adjusted life year[10]. Moreover, poor oral condition had been suggested as a possible reason for falls[11], and falls contribute to fractures and subsequent development of conditions that necessitate long-term care among the older people. Furthermore, a link between oral function and cognitive decline has been indicated[12], and this too could lead to the development of care-requiring conditions. Oral health is also likely to affect social activities, such as exchange with friends and going out for that purpose[13], through conversation[14], facial appearance[15], smile[16], and dietary function[5, 6]. Since social participation has been reported to prevent the development of care-requiring conditions among the older individuals[17], oral health conditions might play an important role from the social aspect as well.

[Objective]

Due to various factors, a decrease in oral health could serve as a risk factor for the occurrence of conditions that necessitate long-term care among the older individuals. As for oral health, intervention is often possible; therefore, clarifying the association between oral health and occurrence of conditions that necessitate long-term care could contribute to the prevention of developing such conditions. Therefore, in this section, we aimed to review prospective cohort studies as well as intervention studies with regard to oral health and conditions that necessitate long-term care.

[Methods]

To examine cohort studies, the following search expressions were used to conduct a PubMed search: #1 "Long-Term Care"[majr] OR "Intellectual Disability"[majr] OR "Disabled Persons"[majr] OR Disability[tiab] OR impaired[tiab] OR "dependent elderly"[tiab] OR "dependent older persons"[tiab] OR "activities of daily living" [tiab]; #2 Periodontitis OR "periodontal disease" OR "tooth disease" OR caries OR denture OR teeth OR dental OR "oral care" OR "Oral health"[MeSH Terms] OR dentistry[MeSH Terms]; and #3 "cohort" OR "longitudinal" OR "randomized controlled trial"[PT]. As for the terms to be excluded, we used #4, "child"[MeSH Terms] OR "child"[All Fields], and #5, "adolescent"[MeSH Terms] OR "adolescent"[All Fields]) NOT Charcot-Marie-Tooth. The PubMed search was conducted with (#1 AND #2 AND #3 NOT #4 NOT #5). From 324 articles retrieved, we narrowed down to three articles based on titles and abstracts.

In addition, we obtained 49 articles through a search of ICHUSHI using the following search expressions: #1: You kaigo ('care need') /AL and (Ha ('teeth')/TH or Ha/AL), #2: (Kuchi ('mouth')/TH or Kouku ('oral cavity')/AL), #3: (Kohoto ('cohort')/AL or Kainyu ('intervention')/AL), narrowing down to original research articles only (#1 AND #2 AND #3). From these, we selected two articles based on titles and abstracts. We also performed a hand search and selected one article (report).

[Results]

As a result of the searches, five prospective cohort studies and one intervention study were included[18-23]. In addition, as an intervention study, one article from one report was included[24]. An overview of each article is shown in Table 1.

The incidence of conditions that necessitate long-term care during the follow-up period was significantly higher in cases where there were problems with teeth[18], where there was no primary care dentist[19, 20], or where the number of remaining teeth was 19 or less[21], compared to cases where there was no problem, where there was a primary care dentist, and where the number of remaining teeth was 20 or more, respectively. Moreover, in older individuals with 19 teeth or less and no denture use, the incidence of physical dysfunction was significantly higher compared to those with 20 teeth or more[22]. In a randomized controlled trial that examined the effects of multimodal intervention including nutrition, exercise, and oral cavity in the institutionalized older individuals, the intervention group showed significantly higher body weight, BMI, and protein intake compared to the non-intervention group[23]. Moreover, while the non-intervention group showed a decrease in social and physical function, no decrease was observed in the intervention group. In a report examining the effects of long-term care prevention services, odds ratios were significantly higher for maintenance and improvement of care-need levels when specialized services by dental hygienists were provided, as compared to when no such services were provided[24].

[Discussion]

Although there were only a few cohort studies and intervention studies with regard to oral health and incidence of conditions requiring long-term care, this review suggested the following association; that is, there is a possible association between good oral health and prevention of future occurrence of conditions that necessitate long-term care. Moreover, it was suggested that people with a primary care dentist may be more unlikely to develop a condition that necessitates long-term care. Furthermore, it might be possible to prevent an increase in care-need levels by providing specialized services aimed toward the maintenance of oral health.

We found that the lower the number of remaining teeth, the higher the incidence of conditions that necessitate long-term care[21]. Malnutrition due to a decreased number of remaining teeth can make the older people weak and lead to the onset of a condition that necessitates long-term care[8]. In the Japanese older individuals, it has been shown that Japanese food can reduce the risk of developing conditions that necessitate long-term care[25], suggesting that studies on meal patterns, as well as nutritional state, in relation to number of remaining teeth should be further promoted in the future. Furthermore, while stroke is known as a disease that causes care-requiring conditions, the possibility that tooth loss may be a risk factor for stroke has been suggested[9]. Periodontal diseases, along with dental caries, account for more than 40% of tooth loss in Japanese

Table 1: Prospective cohort studies and an intervention study regarding oral health and incidence of conditions that necessitate long-term care

Reference No.	Author	Study period	Study design	Age	Subjects	Sample size	Main predictor	Outcomes	Covariates	Content
18	Kohase, Watanabe	2006-2010	Prospective cohort	65 or more	Community dwelling elderly	3,952	Presence of dental troubles	Occurrence of conditions that necessitate long-term care	Age	This 4-year follow-up study clarified factors leading to new certification of long-term care need in community-dwelling elderly people. The results of age-adjusted logistic regression analysis revealed that items associated with certification of long-term care need after 4 years were: having a history of one or more diseases and/or eye troubles in men, and having a history of two or more diseases and/or eye or tooth troubles in women (odds ratio for cases in women with tooth troubles, 1.90; 95% confidence interval [CI] = 1.20-3.02). Differences existed between men and women in factors that were significantly associated with certification of long-term care need. Disease, health management, ability to move, and physical activities in daily life were considered to have major impacts on certification of long-term care need even after 4 years.
19	Komiyama, Ohi, Miyoshi, Tsuboi, Hattori, Tomata, Kakizaki, Tsuji, Watanabe	2003-2011	Prospective cohort	70 or more	Community dwelling elderly	834	Presence of a primary care dentist	Occurrence of conditions that necessitate long-term care	Age, sex, history of illnesses, smoking, drinking, highest education level, nutritional state, depressive tendency, cognitive function, social support, current number of teeth	This prospective cohort study examined whether the presence of a primary care dentist was associated with certification of long-term care need in community-dwelling elderly people. Examinations including oral examination and follow-up were performed in 834 community-dwelling elderly people aged ≥70 years. At baseline, 86% of the total (778 subjects) had a primary care dentist. After a mean follow-up period of 6.2 years, 37% (304 subjects) had certification of long-term care need. The Cox proportional hazards analysis revealed that not having a primary care dentist was independently associated with certification of long-term care need (hazard ratio: 1.4, 95% CI = 1.0-1.9). On the other hand, reasons for visit and timing of the last visit did not show a significant association.
20	Inoue	2001-2004	Prospective cohort	65 or more	Community dwelling elderly	13,066	Presence of a primary care dentist	Occurrence of conditions that necessitate long-term care	Basic activities of daily living (BADL), instrumental activities of daily living (IADL), number of illnesses under treatment, subjective sense of health, health relative to the previous year, feeling of satisfaction about life, frequency of going out, hobbies and activities, annual income	The factors contributing to the prevention of conditions that necessitate long-term care over a 3-year period in community-dwelling elderly people included: subjective sense of health, higher activity of daily living (BADL, IADL), and being engaged in hobbies/activities. High annual income and having a primary care dentist showed a significant association only in women. The results of multivariate logistic regression analysis revealed a 1.250-fold higher independent odds ratio (95% CI = 1.012-1.544) for having a primary care dentist. Improving these factors may contribute to the prevention of conditions that necessitate long-term care.

Table 1 : (continued)

Reference No.	Author	Study period	Study design	Age	Subjects	Sample size	Main predictor	Outcomes	Covariates	Content
21	Aida J, Kondo K, Hirai H, Nakade M, Yamamoto T, Hanibuchi T, Osaka K, Sheiham A, Tsakos G, Watt RG.	2003-2007	Prospective cohort	65 or more	Community dwelling elderly	4,425	Number of remaining teeth, chewing ability	Occurrence of conditions that necessitate long-term care	Age, sex, BMI, subjective sense of health, history of illnesses, smoking, drinking, exercise, equivalent income	A mail survey was conducted targeting healthy people aged 65years or older in Aichi Prefecture in 2003.The 4-year follow-up study was conducted to determine whether oral health would contribute to the occurrence of conditions that necessitate long-term care in community-dwelling elderly people. During the follow-up period, 519 subjects (11.7%) developed conditions requiring long-term care. More subjects with 19 teeth or less (14.0%) and those with reduced chewing ability (21.5%) tended to develop conditions that necessitate long-term care. Multivariate Cox proportional hazards analysis revealed that the risk of occurrence of conditions that necessitate long-term care was significantly increased (21%) in subjects with 19 or less teeth, compared to those with 20 or more teeth (hazard ratio; 1.21, 95% CI; 1.06-1.40). The relationship between chewing ability and occurrence of conditions that necessitate long-term care could be explained by systemic health conditions as well as other factors, showing no significance (HR = 1.17 for subjects who could not chew well, relative to those who could eat anything 95% CI = 0.88-1.56). Oral health conditions were associated with the future occurrence of conditions that necessitate long-term care.
22	Shimazaki Y, Soh I, Saito T, Yamashita Y, Koga T, Miyazaki H, Takehara T.	1988&89-1994&95	Prospective cohort	59 or more	Elderly facility residents	Physical function: N=483, Cognitive function: N=517, Death: N=1,762	Teeth and denture use	Physical function disorder, cognitive function, death	Age, facility type, health indicators	This 6-year prospective cohort study was conducted to clarify whether dental conditions would affect physical function, cognitive function, and mortality in elderly residents of 29 elderly facilities. Univariate logistic regression analysis revealed that individuals with poor oral conditions had significantly more physical function disorders, cognitive function disorders, and deaths. Even in multivariate analysis, significantly more physical function disorders (N=483, OR=6.0, 95% CI=1.9-19.3) and deaths (N=1,769, OR=1.8, 95% CI=1.1-2.8) were observed in individuals with less than 19 teeth who did not use dentures. With respect to cognitive function, no significant difference was found in multivariate analysis.

Table 1 : (continued)

Reference No.	Author	Study period	Study design	Age	Subjects	Sample size	Main predictor	Outcomes	Covariates	Content
23	Beck AM, Damkjaer K, Sorbye LW.	2006	Randomized controlled trial	65 or more	Elderly facility residents	121	Nutrition, exercise, and oral care complex intervention	Body weight, BMI, energy and protein intake, ADL	–	This 11-week randomized controlled study examined whether complex intervention of nutrition, exercise, and oral cavity would affect functional state of elderly nursing home residents. Nutritional (chocolate, homemade oral supplement), group exercise (moderate to high intensity), and oral care intervention were performed in 121 residents (≥65 years) of 7 facilities, and body weight, BMI, energy and protein intake, and ADL were measured. Body weight, BMI, and protein intake were significantly higher in the intervention group compared to the non-intervention group (percent changes [%] in body weight in the intervention and non-intervention groups, 1.3 vs. -0.6%, p=0.005; percent changes [%] in BMI, 0.4 vs. -0.2%, p=0.003; in energy intake, 0.7 vs. -0.3 MJ/day, p=0.084; in protein intake, 5 vs. -2 g/day, p=0.012). Moreover, social function and physical function decreased in the non-intervention group, but not in the intervention group. Following the 11-week intervention, measurements at 27th week post-intervention showed no changes in cognitive function, while body weight and physical function decreased in both intervention and non-intervention groups. Complex intervention might be effective for the maintenance of social and physical function in elderly people.
24	Tsuji, Ohbushi, Sugiyama, Ueda, Ohhara, Yasumura, Honma, Ohno, Suzuki, Okubo, Tango	2007-2008	Non-randomized intervention study	40 or more	Users of long-term care prevention services at a local comprehensive support center	9,105	Oral function improvement services	Maintenance and improvement of conditions that necessitate long-term care	Sex, age, each parameter of oral function improvement services	The effects of long-term care prevention services were examined using data from a local comprehensive support center. In cases where professional services by dental hygienists were provided, the odds ratio for sustained or improved level of care need was 3.81-fold higher (95% CI=1.16-12.59) relative to cases where no such services were provided.

people[26], but periodontal diseases, which cause the loss of teeth, may simultaneously increase the risk of stroke due to resulting chronic inflammation. In a short term, treatment for periodontal disease decreases chronic inflammation and endothelial dysfunction[27]. However, evidence is lacking as to whether periodontal treatment has any effect on the prevention of stroke onset itself[27], and future verification is needed.

The incidence of conditions that necessitate long-term care was lower in cases when there was a primary care dentist[19,20]. One reason for this might be that those with a primary care dentist have good oral health conditions. Denture use and oral care could prevent lowering of nutritional state in older individuals[28,29], and it has been suggested that oral care and denture use (for those with fewer teeth) could decrease the risk of developing a care-requiring condition[22-24]. The presence of a primary care dentist, in the aspect of oral health improvement, might be effective. Moreover, poor oral conditions could lower social activities[13] through conversation[14], facial appearance[15], smile[16], and dietary function[5,6]. Social participation has been reported to prevent development of care-requiring conditions among the older individuals[17], and the presence of a primary care dentist might reflect the fact that the older person does go out and participates in the society; this in turn might lead to the prevention of the development of conditions that require long-term care. Figure 1 shows the predicted mechanism between oral health and occurrence of conditions that necessitate long-term care.

In the intervention study, the possible role of specialized services by dental hygienists in preventing the occurrence of conditions that necessitate long-term care was indicated[24]. However, this study was ambiguous in terms of the details of care content, and given that it was not a randomized controlled study, further studies are necessary in the future. Randomized controlled studies on oral care associated with the health of the older people conducted to date have demonstrated that frequent oral healthcare intervention by a dentist can prevent decreases in BMI, serum albumin, and HDL cholesterol[29]. Dental intervention aimed at preventing decreased nutritional state might lead to a decreased future occurrence of conditions that necessitate long-term care. Furthermore, in a randomized controlled study, mixed intervention, including nutrition, exercise, and oral care, showed effectiveness in the maintenance of functional status in the older individuals[23], although it did not solely target the oral cavity. For these reasons, there is a sufficient possibility that oral intervention could prevent the occurrence of conditions that necessitate long-term care.

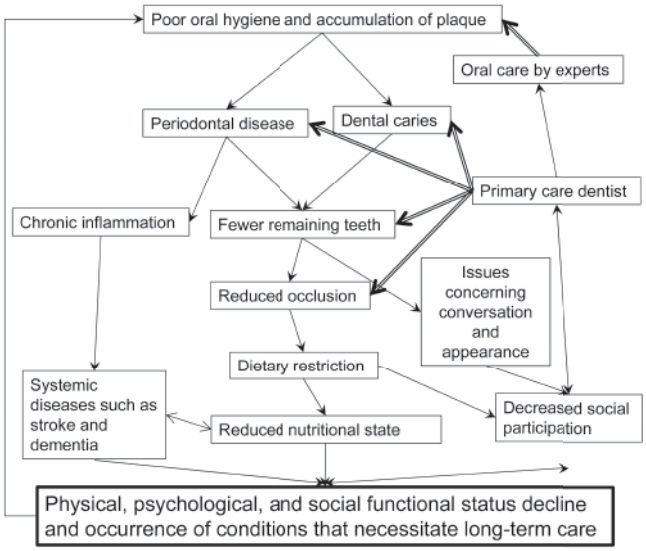

Figure 1: Main predicted mechanism between oral health and occurrence of conditions that necessitate long-term care

Future research is anticipated.

[Conclusions]

Good oral health conditions including denture use were associated with a lower incidence of conditions that necessitate long-term care in the future. Further promotion of healthcare intervention to maintain oral health among the older people might lead to a decreased incidence of conditions that necessitate long-term care.

[Conflict of interest]

There are no items applicable to "conflict of interest" in this article.

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5. Exercise (including ADL)
– Oral health, physical fitness and ADL among the elderly –

5. Exercise (including ADL)
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[Abstract]

A decrease in functional fitness has an effect on carrying out activities of daily living (ADL) for the elderly. Although recent reports have indicated an association between oral health status and functional fitness or ADL, their evidence levels vary considerably. Therefore, this review provides a review of the previously published literature and organizes the results based on evidence level. Document searches were made using PubMed and ICHUSHI, a total of 904 papers were extracted, publications were examined focusing primarily on epidemiological research incorporating adjustment of confounding factors, and ultimately 14 papers relating to the oral health and physical fitness and four papers relating to the oral health and ADL were selected.

According to those results, balance function, lower extremity muscle strength and upper extremity muscle strength were indicated to be related to occlusion and masticatory performance, and deterioration in occlusal condition was indicated to have a detrimental effect on balance function and lower extremity muscle strength over time. However, it was considered that intervention by dental treatment and sample bias should be taken into consideration for interpreting the results.

In addition, since the association between oral health status and ADL is thought to be indirect as a result of being mediated by nutritional status and physical fitness, maintenance of oral health status and rehabilitation of oral function were considered to ultimately lead to prevention of decreases in ADL through these mediators.

[Introduction]

Decreases in physical fitness have a considerable effect on performing activities of daily living (ADL) for the elderly. This is because elements of physical fitness including muscle strength and balance function are closely involved in basic movements during the course of activities performed by an individual both indoors and outdoors, such as daily activities or climbing stairs. These elements of physical fitness are referred to as functional fitness.

Meanwhile, decreases in physical fitness among the elderly are also known to be a significant factor attributable to falling. In a meta-analysis investigating factors involved in falling, decrease in muscle strength, decrease in walking ability and decrease in balance function were all found to be risk factors higher than the effects of aging and decrease in cognitive capacity[1]. The transition to bedridden for the elderly, which is triggered by remaining indoors or falling due to decreased ADL, causes a dramatic decrease in quality of life (QOL). Thus, maintaining physical fitness or preventing decreases in physical fitness in advanced age contributes to more than simply extending biological life, but rather can be an important element for prolonging so-called healthy life expectancy with the emphasis on QOL.

Intervention studies investigating the effects of experimental occlusal interference on the vestibular system and body sway, which govern the body's muscle activity and balance function, were actively conducted through the 1990s by primarily prosthetic researchers in Japan. Kobayashi *et al*.[2] stated in a review summarizing these intervention researches that problems with occlusion have an effect on the sound conduction system of the middle ear, balance perception, auditory brainstem response, autonomic nervous system function, emotions and sleep, and concluded that occlusal function is closely related to motor function. Thus, occlusion unquestionably is related to physical fitness.

When focusing on the elderly, decreases in physical fitness with aging, loss of teeth and accompanying changes in occlusal status or deterioration of masticatory function gradually progress in units of years or tens of years while being affected by various background factors. Thus, since an apparent association would appear quite readily as a result of simply investigating the correlation between oral health status and physical fitness or ADL, it is necessary to adjust for confounding factors. Therefore, in this review, publications were selected focusing primarily on epidemiological research that incorporated adjustment of confounding factors based on a multivariate analysis, and scientific evidence was then organized with respect to the

currently known association between the oral health and physical fitness or ADL.

[Objective]

This review was conducted for the purpose of reviewing the literature regarding the association between oral health status and functional fitness or ADL in the elderly, and organizing those results based on their evidence level.

[Methods]

Document searches were made using PubMed and ICHUSHI, and only original papers written in English or Japanese that were published from January 1, 1995 to April 1, 2014 were extracted.

Papers were extracted from PubMed using MeSH terms relating to dentistry consisting of "dentistry", "oral health", "mouth edentulous", "mastication", "tooth loss" or "dental occlusion"; terms relating to exercise or ADL consisting of "physical fitness", "activities of daily living", "hand strength", "motor activity", "exercise", "postural balance" or "muscle strength"; and terms relating to research on the elderly consisting of "aged", "aged 80 and older" or "middle aged".

Papers were extracted from ICHUSHI using terms relating to dentistry consisting of "Shikagaku (dentistry)", "Kougou (occlusion)", "Soshaku (mastication)", "Shisuu (number of teeth)" or "Mushigaku (edentulousness)"; terms relating to exercise or ADL consisting of "Seikatsu tairyoku (functional fitness)", "Tairyoku (physical strength)", "Shintai kinou (physical fitness)", "Undou nouryoku (motor performance)", "Shisei baransu (postural balance)", "Heikou kinou (balance function)", "Undou ginou (motor skill)", "Binshousei (agility)", "Kinryoku (muscle strength)", "Nichijou seikatsu katsudou (activities of daily living)", "Nichijou seikatsu dousa (movements of daily living)" or "ADL"; and combinations of the terms "Koureisha (elderly)" and "Seijin (adult)". Each of these searches was carried out according to the search formulations indicated below.

PubMed: ("Dentistry"[MH] OR "Oral Health"[MH] OR "Mouth, Edentulous"[MH] OR "Mastication"[MH] OR "Tooth loss"[MH] OR "Dental occlusion"[MH]) AND ("Physical Fitness"[MH] OR "Activities of Daily Living"[MH] OR "Hand strength"[MH] OR "Motor Activity"[MH] OR "Exercise"[MH] OR "Postural Balance"[MH] OR "Muscle Strength"[MH]) AND ("Aged"[MH] OR "Aged, 80 and over"[MH] OR "Middle Aged"[MH]) AND (eng[LA] OR Jpn[LA]) NOT ("Meta-Analysis"[PT] OR "Review"[PT]) AND 1995 : 2014/4/1 [DP]

ICHUSHI: ((Koureisha/TH OR Koureisha/AL OR Seijin/TH)) AND ((Shikagaku/TH OR Shikagaku/AL) OR (Kougou/TH OR Kougou/AL) OR (Soshaku/TH OR Soshaku/AL) OR Shisuu/AL OR (Mushigaku/TH OR Mushigaku/AL)) AND (Seikatsu tairyoku/AL OR (Tairyoku/TH OR Tairyoku/AL) OR Shintai kinou/AL OR (Undou nouryoku)/TH OR Undou nouryoku/AL) OR (Shisei baransu/TH OR Heikou kinou/AL) OR (Undou kinou/TH OR Binshousei/AL) OR (Kinryoku/TH OR Kinryoku/AL) OR (Nichijou seikatsu katsudou/TH OR Nichijou seikatsu dousa/AL) OR (Nichijou seikatsu katsudou/TH OR ADL/AL)) AND (PT=Gencho ronbun) AND (DT=1995:2014). As a result of the aforementioned searches, 514 papers were extracted from PubMed AND 390 papers were extracted from ICHUSHI for a total of 904 papers.

Those papers that overlapped in terms of content or were found to have an objective that was clearly different from that of this review as determined by carefully reading the report, title or abstract were excluded. In addition, in the case of epidemiological studies, those papers that did not at least adjust confounding factors such as age and gender by stratified analysis or multivariate analysis were also excluded. As for intervention studies, those studies that made comparisons between use and no use of dentures only, and not based on aggressive intervention in the manner of occlusal interference were selected. Ultimately, 14 papers on the association between the oral health and physical fitness (four in Japanese and 10 in English) and four papers on the association between the oral health and ADL (English only) were selected.

[Results]

1. Relationship between oral health status and physical fitness

Physical fitness measurements consists several elements such as upper extremity muscle strength, lower extremity muscle strength, balance function, etc., and are performed both independently and integrally. An overview of the results for the association between oral indicators and physical fitness indicators for each of the selected papers is shown in Table 1.

1) Relationship with upper extremity muscle strength

Hand grip strength is often used as an indicator of upper extremity muscle strength. Hand grip strength was evaluated in nine of the papers and a significant association was observed in five of those papers.

First, in a cross-sectional study analyzing the association with self-assessed masticatory performance while dividing the subjects into age groups consisting of an early elderly group (65 to 74 years old) and a late elderly group (75 to 84 years old), there was a

Table 1: Association between oral health and physical fitness

Author	Year	Study design	Subjects	Age (Yr)	Sample size	Oral indicators	Physical fitness indicators	Analysis methods	Adjustment factors	Results	#Ref.
Ishijima *et al.*	1998	Interven-tion	Edentulous patients	62.2±7.7	10	Wearing or not wearing denture	Reaction time/in-air time/jumping ability when jumping	Paired t-test	None	Reaction time (ms) decreased with denture wear (382.8±32.6 vs 400.2±37.8, P<0.01).	12
Okubo *et al.*	2010	Interven-tion	Edentulous volunteers	75.6±6.1	34	Wearing or not wearing denture	Standing ability (locus of center of mass), gait stability (gait velocity, stride and gait cycle)	Paired t-test	None	The locus of center mass significantly shortened with denture wear (P=0.004, while walking speed (P=0.049) and harmonic ratio of vertical angular velocity (P=0.048) significantly increased.	15
Yoshida *et al.*	2009	Case control	Community -dwelling elderly	75.6±4.3 75.9±3.9	35+35	Users/non-users of (those not requiring) complete denture	Hand grip strength, leg extensor strength, one-leg standing time with eyes open, functional reach, body sway area, and body sway	Mann Whitney's U-test, Wilcoxon's signed rank test	Age, gender, body fat and muscle composition were matched in sampling.	Significant differences were observed in one-leg standing time with eyes open and functional reach (P=0.013 and P=0.037, respectively), body sway area and body sway (P=0.035 and P=0.048, respectively).	8
Yamaga *et al.*	2002	Cross-section	Community -dwelling elderly	70, 80	591+158	EI	Hand grip strength, leg extensor strength, leg extensor power, stepping rate, one-leg standing time with eyes open	Multiple regression analysis	Age, gender, body height, weight, past medical history, blood pressure, serum albumin, low back pain, smoking, with/ without spouse, and education	Associated with leg extensor power (R^2=0.627, P<0.05), stepping rate (R^2=0.159, P<0.05), and one-leg standing time with eyes open (R^2= 0.179, P<0.05).	9
Takata *et al.*	2004	Cross-section	Community -dwelling elderly	80	697	Number of teeth, masticatory performance (number of foods able to be chewed)	Hand grip strength, leg extensor strength, leg extensor power, stepping rate and one-leg standing time with eyes open	Multiple regression analysis, Logistic regression analysis	Gender, body height, weight, blood pressure, fasting blood sugar, serum albumin, smoking, alcohol drinking, with/without spouse, sports habit, medical administration, and low back pain	Associations were observed in multiple regression analysis with regard to leg extensor strength (masticatory performance, R^2=0.478, P=0.0366) and one-leg standing time with eyes open (number of foods able to be chewed, R^2=0.121, P=0.0248); and in logistic regression analysis, with regard to leg extensor power (masticatory performance, OR=4.89, 95% CI= 1.39-17.16) and one-leg standing time with eyes open (masticatory performance, OR=2.60, 95% CI=1.11-6.08).	11
Morikawa *et al.*	2007	Cross-section	Community -dwelling elderly	71.8±5.6	281	EI	Gravity center sway	Multiple regression analysis	Age, gender	Associated with gravity center sway area when eyes are closed (R^2=0.038, P=0.016) and when leaning backward (R^2=0.035, P=0.010).	14
Murata *et al.*	2007	Cross-section	Community -dwelling elderly	65-74, 75-84	180+135	Masticatory performance (self evaluation)	Hand grip strength and one-leg standing time with eyes open	Stepwise regression analysis	Age, living, social activities, and educational background	Women in the early elderly group (65-74 years old) alone showed association in hand grip strength (R^2=0.110, P=0.027).	3

#Ref.: Reference number, EI: Eichner index, TUG: Timed Up and Go Test, MMSE: Mini Mental State Examination, R^2: Coefficient of determination, OR: Odds ratio, CI: Confidence interval

Table 1: (Continued)

Author	Year	Study design	Subjects	Age (Yr)	Sample size	Oral indicators	Physical fitness indicators	Analysis methods	Adjustment factors	Results	#Ref.
Moriya *et al.*	2009	Cross-section	Community-dwelling elderly	65-74, 75-84	484+337	Masticatory performance (self-rating), EI	Hand grip strength and one-leg standing time with eyes open	Stepwise regression analysis	Age, gender, work, social interaction, education, systemic disease, serum albumin, and BMI	In the group of 65-74 years old, masticatory performance was used as a significant variable against grip strength (R^2=0.69, P<0.01), and EI and masticatory performance against one-leg standing time with eyes open (R^2=0.15, P<0.05 and P<0.01, respectively).	4
Moriya *et al.*	2011	Cross-section	Community-dwelling elderly	67-74	381	Masticatory performance (number of foods able to be chewed)	Hand grip strength, skeletal muscle mass (SMM)	Order regression analysis	Gender, education and occlusal support pattern (*masticatory performance used as a dependent variable)	Significantly associated with hand grip strength (β=0.10, 95% CI=0.04-0.16).	6
IwasakI *et al.*	2012	Cross-section	Community-dwelling elderly women	65-74	138	Masticatory performance (chewing gum)	One-leg standing time with eyes open	Logistic regression analysis	Number of present teeth, age, and decline in motility function	Significantly associated with one-leg standing time with eyes open (OR=3.61, 95% CI=1.14-11.4).	13
Iinuma *et al.*	2012	Cross-section	Community-dwelling elderly	85 +	489	Maximum occlusal force	TUG, chair-stand test, one-leg standing time with eyes open, and hand grip strength	Logistic regression analysis	Age, education, smoking, MMSE, BMI, ischemic cardiac disease, coronary heart disease, diabetes, high blood pressure, serum albumin, CRP, and number of remaining teeth	Associated with TUG in both man and women (men: OR=2.34, 95% CI=1.02-5.38; women: OR=2.44, 95% CI=1.12-5.33). In men only, associations were observed with chair-stand test (OR=2.39, 95% CI=1.10-5.21), one-leg standing time with eyes open (OR=2.35, 95% CI=1.01-5.45) and grip hand strength (OR=2.31, 95% CI=1.04-5.14).	5
Tanimoto *et al.*	2013	Cross-section	Community-dwelling elderly	65 +	1,074	Masticatory ability (can chew/cannot chew), diversity of diet	Sarcopenia (determined from skeletal muscle mass, hand grip strength, and normal walking speed)	Logistic regression analysis	Household status, chronic disease hospitalization history in past 1 year, lifestyle habit (alcohol drinking, smoking, exercise), and mental state (health degree, depression)	Associated with diversity of diet in men (OR=3.03, 95% CI=1.17-7.86) and masticatory ability in women (OR=3.22, 95% CI1.65-6.29).	16
Okuyama *et al.*	2011	Cohort (8 years)	Community-dwelling elderly	71 (Baseline)	348	EI at baseline	Deterioration of hand grip strength, leg extensor strength, leg extensor power, stepping rate, or one-leg standing time with eyes open	Logistic regression analysis	Age, gender, body height, weight, past medical history, blood pressure, serum albumin, low back pain, smoking, with/without spouse, and education	Among the upper 50%, significant association was observed with deterioration of leg extensor power (OR=4.61, 95% CI=1.44-14.75) and of one-leg standing time with eyes open (OR= 4.27, 95% CI=1.14-15.98).	10

#Ref.: Reference number, EI: Eichner index, TUG: Timed Up and Go Test, MMSE: Mini Mental State Examination, R^2: Coefficient of determination, OR: Odds ratio, CI: Confidence interval

Table 1: (continued)

Author	Year	Study design	Subjects	Age (Yr)	Sample size	Oral indicators	Physical fitness indicators	Analysis methods	Adjustment factors	Results	#Ref.
Moriya *et al.*	2012	Cohort (1 year)	Community-dwelling elderly	65 +	154	Occlusal support pattern at baseline, improvement of masticatory performance after 1 year	Improvement of hand grip strength or one-leg standing time with eyes open	Logistic regression analysis	Gender and age	In 121 persons who had undergone dental treatment, hand grip strength was significantly associated with occlusal support pattern at baseline (complete loss vs no loss, OR=5.02, 95% CI=1.15-21.90), and one-leg standing time with eyes open was associated with improvement of masticatory performance (deterioration/no change vs improvement, OR= 4.05, 95% CI=1.25-13.16).	7

#Ref.: Reference number, EI: Eichner index, TUG: Timed Up and Go Test, MMSE: Mini Mental State Examination, R^2: Coefficient of determination, OR: Odds ratio, CI: Confidence interval

significant association only among women in the early elderly group (coefficient of determination (R^2)=0.110, P=0.027)[3]. In a similar cross-sectional study, a significant association was observed with self-assessed masticatory performance only among the early elderly group (R^2=0.69, P<0.01)[4]. In addition, in a study conducted on community residents aged 85 and older, an association was observed with maximum occlusal force among men only (odds ratio (OR)=2.31, 95% confidence interval (CI)=1.04-5.14)[5]. Conversely, in a study consisting of a factor analysis of masticatory performance evaluated based on the number of foods considered chewable for community residents aged 67 to 74 were able to chew, hand grip strength was found to be a significant variable (partial regression coefficient (β)=0.10, 95% CI=0.04-0.16)[6]. In addition, in a cohort study investigating the effect on the presence or absence of improvement of hand grip strength among community residents aged 65 and older who had undergone dental treatment, those subjects having occlusal support by natural teeth at the baseline demonstrated improved hand grip strength (OR=5.02, 95% CI=1.15-21.90), although there was no significant association with improvement of masticatory performance after one year[7].

Meanwhile, there were no significant associations with hand grip strength observed in a case control study comprising subjects using complete dentures and those not using complete dentures[8], in a cross-sectional study investigating the association with Eichner index (EI) in community residents aged 70 and 80[9], in a cohort study in which the same subjects (70 year old subjects only) were monitored for eight years[10], and in another cross-sectional study investigating the association with number of teeth or masticatory performance targeted at 80-year-old community residents[11].

2) Relationship with lower extremity muscle strength

Methods used to evaluate lower extremity muscle strength consisted of instrument-measured leg extensor strength and leg extensor power as well as the timed up and go (TUG) test and chair-stand test that do not require specialized instruments. Six papers were selected and associations were observed in four of the papers.

First, in a cross-sectional study, a significant association was observed between EI and leg extensor power among elderly community residents aged 70 and 80 (R^2=0.627, P<0.05)[9]. Similarly, significant associations were observed between leg extensor strength, leg extensor power and masticatory performance among 80-year-old elderly community residents (leg extensor strength: R^2=0.478, P=0.0366, leg extensor power: OR=4.89, 95% CI=1.39-17.16)[11]. In addition, in a study targeted at elderly subjects aged 85 and older investigating the associations among maximum occlusal force, TUG test or the chair-stand test, a significant association with TUG test was observed among both men and women (men: OR=2.34, 95% CI=1.02-5.38; women: OR=2.44, 95% CI=1.12-5.33) and a significant association with the chair-stand test was observed among men (OR=2.39, 95% CI=1.10-5.21)[5].

In addition, in an 8-year follow-up cohort study as well, baseline EI was observed to have a significant effect on deterioration of leg extensor power (OR=4.61, 95% CI=1.44-14.75)[10].

However, in an intervention study in which comparisons were made in reaction time, in-air time and jumping ability when subjects were made to jump on a force plate while wearing or not wearing complete dentures, there were no significant differences in jumping ability, although reaction time was significantly shorter in the subjects wearing complete dentures[12]. In a case control study making comparisons between use and no use of complete dentures, there were no statistically significant differences observed, although leg extensor power tended to be somewhat higher in the test group[8].

3) Relationship with balance function

In epidemiological studies, measuring one-leg standing time with eyes open was frequently used to evaluate balance function and functional reach was also often employed. In addition, center of gravity sway (body sway, trunk movement) was also examined in instrument analyses of intervention studies and case control studies. This was used most frequently as a parameter for measuring physical fitness, and was observed in 11 papers. In terms of individual parameters, one-leg standing time with eyes open was observed in nine papers, functional reach was observed in one paper, and body sway examination was observed in three papers (with some overlapping), with some form of association with oral indicators being observed in 10 of the 11 papers.

First, in a cross-sectional study, an association with EI was observed in community-dwelling elderly aged 70 and 80 years old (R^2=0.179, P<0.05)[9], while in a stratified analysis dividing the subjects into an early elderly group and late elderly group, an association was observed with EI and masticatory performance only in the early elderly group (R^2=0.15, values for EI and masticatory performance: P<0.05, P<0.01, respectively)[4]. In addition, an association with masticatory performance was

observed among 80-year-old elderly community residents (OR=2.60, 95% CI=1.11-6.08)[11], while an association with masticatory performance as evaluated using gum was observed among community-dwelling elderly women (OR=3.61, 95% CI=1.14-11.4)[13]. In a study investigating the association with maximum occlusal force among subjects aged 85 and older, an association with maximum occlusal force was observed only among men (OR=2.35, 95% CI=1.01-5.45)[5]. However, there were no significant associations in a cross-sectional study investigating the association with masticatory performance[3].

In a cohort study, baseline EI was found to have an effect on decreased one-leg standing time with eyes open eight years later (OR=4.27, 95% CI=1.14-15.98)[10], while improvement of masticatory performance due to dental treatment was found to have an effect on improvement of one-leg standing time with eyes open one year later (OR=4.05, 95% CI=1.25-13.16)[7].

In a cross-sectional study investigating the association with body sway, EI was found to have an association with body sway area when eyes are closed (R^2=0.038, P=0.016) and when leaning backward (R^2=0.035, P=0.010)[14]. Moreover, in an intervention study examining differences in standing and walking stability when wearing and not wearing complete dentures, the locus of center of mass was significantly shortened as a result of wearing dentures (P=0.004)[15].

In a case control study comparing between use and no use of complete dentures, one-leg standing time with eyes open in a test group (P=0.013) significantly exceeded that of a control group along with functional reach (P=0.037), body sway area (P=0.037) and body sway (P=0.048)[8].

4) Other

In a cross-sectional study targeted at community residents aged 65 and older, factors relating to sarcopenia were investigated. As a result, an association with diversity of diet was observed in men (OR=3.03, 95% CI=1.17-7.86) while an association with masticatory ability was observed in women (OR=3.22, 95% CI=1.65-6.29)[16].

2. Relationship between oral health and ADL

Studies investigating the association between oral health and ADL that included a multifaceted analysis incorporating adjustment of confounding factors were unexpectedly few in number, and only four papers were selected for use in this review. An overview of the results is shown in Table 2.

First, in a study investigating the association between masticatory performance (number of foods able to be chewed) and independent/dependent among 80-year-old community residents, the risk for dependence increased the lower the level of masticatory performance; namely, the fewer the number of foods able to be chewed, although there was no significant association with number of teeth[17].

Furthermore, Yu *et al.*[18] investigated the relationship between dentition status or periodontal status and degree of functional dependence among 3,856 subjects of the National Health and Nutrition Examination Survey (NHANES) conducted in the U.S. Degree of functional dependence was evaluated using a questionnaire covering five domains consisting of ADL (eating, dressing, walking between rooms on the same floor, etc.), instrumental activities of daily living (IADL) (doing household chores, preparing meals, etc.), leisure and social activities (LSA), lower extremity mobility (LEM) and general physical activities (GPA) (standing up from an armless chair, lifting or carrying 10 pounds, etc.). As a result, although edentulism demonstrated a significant association with functional decreases in IADL, LSA, LEM and GPA, while severe periodontitis demonstrated a significant association with functional decreases in IADL, LSA and LEM, neither had an association with ADL.

In a case control study matching the institutionalized elderly based on gender, age and level of independence, changes in the Functional Independence Measure (FIM) were investigated six weeks after intervention by dental treatment. As a result, significant improvement was only observed for the expression score[19].

Furuta *et al.*[20] examined the direct and indirect relationships among number of teeth, denture use, swallowing function, nutritional status, cognitive ability and ADL as evaluated according to the Barthel Index using a path analysis targeted at homebound elderly aged 60 and older receiving home care services due to physical disabilities. As a result, there was a tendency for subjects having few teeth and not using dentures to have swallowing disorders and for subjects having swallowing disorders to have poor nutrition, and ADL tended to become low in the presence of malnutrition and cognitive disorders.

[Discussion]

1. Relationship between oral health and physical fitness

In summarizing the results of the literature review by parameter, associations were observed for upper extremity muscle strength in five of nine papers, for lower extremity muscle strength in four of six papers, for balance function in 10 of 11 papers, and an association was indicated with sarcopenia in one paper.

Those parameters used as oral indicators, in descending order, consisted of masticatory performance (10 papers),

Table 2. Associations between Oral Health and ADL

Author	Year	Study design	Subjects	Age (Yr)	Sample size	Oral indicators	Physical fitness indicators	Analysis methods	Adjustment factors	Results	#Ref.
Takata *et al.*	2004	Cross-section	Community-dwelling elderly	80	823	N. of teeth, masticatory ability (N. of chewable foods)	Independent/dependent	Logistic regression analysis	Gender, smoking, dental/medical routine checkup and oral selfcare	As for OR for dependence in ADL, compared to persons who could chew all 15 food items, those who could chew 4 items or less showed 7.5 (95% CI=2.98-19.1) and those who could chew 5-9 items showed 3.3 (95% CI=1.47-7.56). No significant association with number of teeth was observed.	17
Yu *et al.*	2011	Cross-section	Participants in NHANES aged 60 years and older	71.2±7.7	3,856	Edentulism, periodontal disease severity	Self-reported functional dependence in five domains	Logistic regression analysis	Age, gender, race, education, BMI, BOP, number of remaining teeth, CRP, chronic disease and smoking	Although no association with ADL was observed, significant associations were observed between lower extremity movement and severe periodontal disease (OR=1.63, 95% CI=1.13-2.34)/edentulism (OR=1.31, 95% CI= 1.04-1.66), and between general physical activity and edentulous jaw (OR=1.45, 95% CI=1.17-1.79).	18
Naito *et al.*	2010	Case control	Institution-alized elderly	80±9	11+14	Intervention by dental treatment	FIM (Change in 6 weeks after intervention)	ANCOVA	Age, gender, frequency of private training, frequency of group training, frequency of recreation activities, independence level at baseline and facilities	Significant improvement was observed only for the expression score (P=0.03).	19
Furuta *et al.*	2013	Cross-section	Homebound elderly aged 60 and older	84.5±7.9	286	N. of teeth, denture use/nonuse, swallowing function	Barthel Index	Path analysis	Age, gender, comorbid condition, nutritional status and cognitive ability	Swallowing disorders tended to occur in those with a small number of teeth and not using denture, and relationship was observed between swallowing disorders and malnutrition. Furthermore, ADL tended to decrease due to malnutrition or cognitive disorder.	20

#Ref.: Reference number, NHANES: National Health and Nutrition Examination Survey, BOP: Bleeding on probing, OR: Odds ratio, CI: Confidence interval, FIM: Functional Independence Measure, ANCOVA: Analysis of Covariance

EI (five papers), use of dentures (four papers), number of teeth (three papers), and occlusal force, diversity of diet, periodontal disease, intervention of dental treatment and swallowing function in one paper each (overlapping included). Although a direct discussion is not possible since oral indicators and physical fitness indicators have not been standardized, as far as can be determined from these results, there appears to be strong associations between deterioration of occlusion and masticatory performance and balance function, lower extremity muscle strength and upper extremity muscle strength in that order.

In studies investigating the relationship between physical fitness and oral health in the elderly, since cross-sectional studies are numerous with respect to epidemiological studies, the cause-and-effect relationship between the two was unclear. The results of an eight-year cohort study targeted at 70-year-old community-dwelling elderly subjects reported in 2011[10] suggested that oral health status has an effect on maintaining or decreased physical fitness. A catalog of abstracts along with the results of a cross-sectional study[9] serving as the basis of this finding are shown separately. In this study, oral indicators were determined by measuring EI, and physical fitness was determined by measuring hand grip strength, leg extensor strength, leg extensor power, stepping rate and one-leg standing time with eyes open. In a cross-sectional study targeted at subjects aged 70 and 80, leg extensor power, stepping rate and one-leg standing time with eyes open demonstrated a significant association with EI. Moreover, in a cohort study, there was a significant association between baseline EI and deterioration of leg extensor power and one-leg standing time with eyes open eight years later. In other words, occlusal state in the elderly clearly has a detrimental effect on balance function and lower extremity muscle strength after several years have elapsed.

However, in the aforementioned cohort study, the small coefficient of determination (R^2) in the logistic regression analysis and the large width of the 95% CI (leg extensor power: R^2=0.221, 95% CI=1.44-14.75, one-leg standing time with eyes open: R^2=0.135, 95% CI=1.14-15.98) do not necessarily indicate a well-defined cause-and-effect relationship. Two possible reasons for this are indicated below.

The first reason involves the intervention of dental treatment. In the case of losing teeth, normally a prosthetic appliance is set up in developed countries like Japan where there is easy access to dental care. What is more, in this study, physical fitness was measured for those subjects wearing dentures or without. Thus, it is possible that occlusion restored by the prosthesis and compensation for masticatory performance contributed to inhibition of decreases in physical fitness. This is supported by the results of intervention studies[12,15] and a case control study[8] that made comparisons between those subjects with dentures and those without and results indicating that one-leg standing time with eyes open improved when masticatory function was improved as a result of dental treatment[4].

The second reason relates to the difficulty accompanying measuring physical fitness in the elderly. The participation rate in measurements of physical fitness by survey participants eight years later was comparatively high for hand grip strength at 86.5%, but the participation rates for leg extensor strength, leg extensor power and one-leg standing time with eyes open were 68.4%, 64.9% and 76.4%, respectively, with none of these reaching 80% of the total number of participants[10]. This is the result of subjects who were excluded from measurements at the discretion of their physician in consideration of their general condition due to their advanced age, and subjects who themselves decided to withdraw from the study in fear of the burden placed on them by the tests, which may constitute the limitations of cohort studies on elderly subjects. When also considering that the follow-up rate of the entire survey in the case of excluding 69 subjects who died was 71.9%, there is a possibility that the samples were biased towards so-called persons having confidence in their physical fitness. It has been pointed out that in actuality when conducting a longitudinal survey by measuring physical fitness, the baseline physical fitness level and the status of engaging in exercise may influence their participation in subsequent measurement of physical fitness[21]. Although it is critical to accumulate high quality results of cohort studies in order to enhance the evidence level about the association between physical fitness and oral health status in the elderly, in addition to interpreting the results while taking into consideration the potential for the sample in such cases being a population that has better physical fitness than the parent population, considerations must also be given to reducing the number of dropouts, and more specifically, it is necessary to urge the subjects to continue their participation, provide assistance when measuring physical fitness, and employ a testing method that minimizes the burden on the subjects.

The pathological state in which the skeletal muscle mass decreases due to aging is referred to as sarcopenia. This concept was first advocated by Rosenberg[22] in 1989 and has been clearly determined to be related to functional fitness based on cross-sectional studies[23,24] and be related to

decreases in ADL on the basis of a cohort study[25]. Although there are hardly any reports regarding the association between sarcopenia and oral health due in part to the lack of standardization of evaluation standards, Tanimoto *et al*.[16] assessed sarcopenia based on the muscle mass, hand grip strength and normal walking speed of 1,074 independent elderly residents aged 65 and older and investigated their factors, and suggested that less diversity of diet in men, as determined by a report obtained from self-administered questionnaires, and poor masticatory ability in women are factors that are associated with sarcopenia. It is hoped that the cause-and-effect relationship with more objective indicators of oral health will be determined accompanying standardization of evaluation criteria in the future.

2. Relationship between oral health and ADL

Activities of daily living (ADL) are divided into activities directly related to maintaining life, including basic defecation, movement, food consumption and dressing, referred to as basic ADL, and activities related to social life such as shopping, preparing meals or managing money referred to as instrumental ADL (IADL). The Barthel Index (BI) and Functional Independence Measure (FIM) are used to evaluate basic ADL, while the Tokyo Metropolitan Institute of Gerontology (TMIG) index is widely used in Japan to evaluate IADL. In this report, ADL refers to basic ADL.

In the papers selected for use in this review, while it was suggested in a cross-sectional study focusing on 80-year-old community residents that a lower level of masticatory performance leads to increased risk for dependence[17], Yu *et al*.[18] did not recognize an association between oral health and ADL in a cross-sectional study, although an association between oral health and IADL or exercise was indicated. In addition, in a case control study[19] investigating improvement of FIM six weeks after intervention of dental treatment in the institutionalized elderly, there were no significant improvements other than those parameters relating to communication and expression.

Although decreased physical fitness has a considerable effect on decreased ADL, questions remain as to whether or not there is a direct association between ADL and oral health status based on the above results. In view of these circumstances, Furuta *et al*.[20] demonstrated interesting findings from a cross-sectional survey targeted at homebound elderly receiving home care services due to physical disabilities. In this study, direct and indirect relationships were examined in terms of number of teeth, denture use, swallowing function, nutritional status, cognitive ability and BI using a path analysis, it was determined that swallowing disorders tend to occur in cases of a large number of missing teeth and not using dentures, a relationship with malnutrition is observed when swallowing disorders are present, and ADL decreases when both malnutrition and cognitive disorders are present. Thus, since the association between oral health and ADL is indirect association mediated by multiple factors, maintaining oral health status and restoring function through dental treatment up to old age are believed to prevent decreases in ADL through various mediators including physical fitness.

[Conclusions]

As for the relationship between oral health status and physical fitness in the elderly, balance function, lower extremity muscle strength and upper extremity muscle strength are associated with deterioration of occlusion and masticatory performance, and loss of occlusion affects balance function and lowering extremity muscle strength over time. However, it is necessary to interpret results in consideration of intervention by dental treatment in the manner of prosthetics as well as sample bias.

In addition, the association between oral health status and ADL is indirect due to the interposition of mediators such as nutritional status and physical fitness, and maintaining oral health status and restoring function are thought to ultimately lead to prevention of decreases in ADL through these mediators.

[Conflict of interest]

There are no items applicable to “conflict of interest” in this article.

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6. Nutrition
– Dental/oral health and nutrition –

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[Abstract]

We have conducted a review of the English papers published between August 2001 and April 2014 on associations between dental/oral health (tooth loss, dental prosthesis status, dental prosthesis treatment, orofacial pain) and nutrition. Finally, 36 papers were chosen for review.

On the basis of a number of observational studies, it was clarified that tooth loss was associated with dietary intake of predominantly vegetables and fruit and a decrease in nutrient intake of mainly vitamins with the antioxidative effect. An association between tooth loss and an increased risk of noncommunicable diseases (NCDs) was also indicated. Particularly in the elderly, it was clarified that tooth loss was associated with malnutrition. Furthermore, it was shown that self-rated oral pain was associated with malnutrition. One intervention study indicated that hardly any improvement of nutrient intake status was gained after dental prosthesis treatment alone and that nutrition counseling is necessary for healthy dietary intake and nutritional status improvement accompanied by behavioral changes.

This review, in which the association between dental/oral health and nutrition was investigated, suggests that prevention of tooth loss contributes to extension of healthy life expectancy. However, to identify other factors behind the association between the two, studies with a higher evidence level should be performed including cohort studies.

[Introduction and objective]

Nutrition and diet are indispensable parts for sustaining life and leading a healthy life, both of which play important roles in the prevention of NCDs and extension of healthy life expectancy[1].

A scenario consisting of "tooth loss → deterioration of chewing ability → adverse effect on nutrient intake → adverse effect on general health" has long been advocated[2,3], where teeth have been considered as one of the main pathways that connect oral health to general health. A number of studies have been conducted on the associations between these two. Ritchie *et al*.[4] reviewed papers published between 1966 and July 2001 and reported that (1) tooth loss affects food selection and dietary intake of individuals, which as a result causes changes in nutrient intake that are expected to adversely affect health leading to systemic diseases, and (2) dental prosthesis provides only a minimal improvement in dental health and nutrient intake status. Since then, a number of studies have been carried out up to the present and new findings of large-scale epidemiological surveys on the association between tooth loss or dental prosthesis status and nutrition, intervention studies on that between dental prosthesis treatments such as implant-supported overdenture (IOD) and nutrition, observational studies on that between tooth/oral pain and nutrition, and other studies. In this review, we examined papers on associations between dental/oral health (tooth loss, dental prosthesis status, dental prosthesis treatment, orofacial pain) and nutrition that were published between August 2001 and 2014 and organized the evidence reported in these papers.

[Methods]

English papers (excluding Meta-Analyses and Reviews) published between August 2001 and April 2014 were searched using PubMed as the database.

The selected search terms on oral health were "dentistry", "oral health", "tooth loss", "mouth", "edentulous", and "dental prosthesis". Those on nutrition were "nutrition status", "dietary intake", and "nutrient intake". Furthermore, on orofacial pain, All-Fields search was adopted using the words "oral pain" and "mouth pain" for identifying associations with nutrition. The search expression was as follows:

Search (dentistry[MeSH Terms] OR oral health[MeSH Terms] OR tooth loss[MeSH Terms] OR mouth, edentulous[MeSH Terms] OR dental prosthesis[MeSH Terms]) AND (nutrition status[MeSH Terms] OR dietary intake[MeSH Terms] OR nutrient intake[MeSH Terms]) AND english[Language] NOT ("Meta-Analysis"[PT] OR "Review"[PT]) AND 2001/08/01: 2014/04/01 [DP],

and

Search ([oral pain] OR [mouth pain]) AND (nutrition status[MeSH Terms] OR dietary intake[MeSH Terms] OR nutrient intake[MeSH Terms]) AND English[Language] AND (NOT ("Meta-Analysis"[PT] OR "Review"[PT]) AND 2001/08/01: 2014/04/01 [DP].

[Results]

The number of papers searched from the database was 149. Next, these 149 papers were screened on the basis of the following exclusion criteria:

- The study did not use any objective index for dental/oral health.
- The subjects were frail elderly, inpatients, institutionalized residents, patients in home dental treatment, dementia patients, children, or animals.

After a close examination of the 149 papers, 33 were extracted. In addition, one paper on an intervention study of dental prosthesis treatment and nutrition that focused on nutritional guidance was chosen as a related literature. With regard to "orofacial pain", partly because studies that used an objective index could not been identified, two papers, namely, a cross-sectional study of community residents and another cross-sectional study of institutionalized residents and inpatients both with self-rating oral pain as the index were chosen. In total, 36 articles (24 observational studies and 12 intervention studies) were chosen for the review.

Furthermore, the validity of the literature search and that of the papers were separately examined by two of the authors (M.I. and A.Y.), whose findings were checked by the other two authors (Y.A. and H.M.).

1. Tooth loss, dental prosthesis status, and nutrition (observational study) (Table 1)

In and after 2001, findings of epidemiological studies on tooth loss and nutrition[5-11] have been reported. All of them show strong associations between the two.

The largest scale study of community residents was conducted by Nowjack-Raymer *et al*.[6], which surveyed 6,985 participants in the National Health and Nutrition Examination Survey (NHANS) in the U.S. who were 25 years and older with one or more teeth present and who did not use a denture. The participants were divided into four groups on the basis of the number of teeth present (1-10, 11-20, 21-27, and 28 and more). Then, associations between the number of teeth and food group/nutrient intake determined by the 24-hour dietary recall and questionnaire methods were evaluated. In addition, the association between the number of teeth and nutrient index determined by blood biochemical examination was evaluated. As a result, in comparison with the group with 28 teeth and more, the other three groups with 27 teeth or less showed lower intakes of carrot, dressed salad, dietary fiber, serum β-carotene, folic acid, and vitamin C. A similar finding has been reported in a survey of 753 individuals aged 65 years and older in the U.K. Marcenes *et al*.[5] divided the participants into dentate and edentulous participants, and compared their nutrient intake determined by the 4-day dietary records method and their nutrition index determined by blood biochemical examination. As a result, compared with dentate participants, the edentulous participants showed significantly lower intakes of nonstarch polysaccharides, protein, calcium, iron, niacin, and vitamin C. Moreover, the edentulous participants had significantly lower intake of serum vitamin C and vitamin A. The dentate participants were further divided into subgroups with 1-10, 11-20, and 21-32 teeth and their body mass index (BMI) was determined. As a result, the edentulous participants compared with the groups with 11 teeth or more showed a significantly higher prevalence of underweight (BMI<20). On the other hand, the odds ratio of obesity in the groups with 20 teeth or less (1-10, 11-20) was significantly higher (BMI>30) than that in the group with 21 teeth and more. The authors concluded that tooth loss tends to limit the variety of food, cause nutrient imbalance, and is associated with obesity or being underweight while being influenced by age, sex, race, and other factors. On the basis of data collected from 20,366 dentists, Wakai *et al*.[10] reported on the association between tooth loss and nutrient imbalance as follows. Individuals with 25 teeth or more showed higher intakes of carotene, vitamin C, and vitamin A (by 14.3%, 8.6%, and 6.1%, respectively) and a lower intake of carbohydrates than edentulous individuals. Moreover, Individuals with 25 teeth or more showed higher intakes of dairy products, brightly colored vegetables, and all other vegetables (by 26.3%, 11.9%, and 5.6%, respectively), whereas their dietary intakes of rice and confectionery were lower (by 9.5% and 29.6%, respectively) than those of edentulous individuals. These findings revealed that edentulous individuals tend to consume low-nutrition, high-calorie foods. Yoshihara *et al*.[11], on the basis of their survey of 57 elderly Japanese aged 74 years using a highly reliable weighing method, reported that the groups with 19 teeth or less showed a significantly lower intake of nutrients including protein, sodium, vitamin D, vitamin B1, vitamin B6, niacin, and pantothenic acid, and also a significantly lower dietary intake of vegetables and sea food than those with 20 teeth or more.

There are also a number of studies[12-21] that assessed

Table 1: Observational studies referred in this literature related to teeth, oral health, and nutrition.

Author	Year	Number of subjects	Age (Yr)	Study country	Study design	Exposure	Outcome	Key findings	#Ref.
Cousson *et al.*	2012	50（fully dentates） 47（CD wearers）	70±6 (fully dentates) 70±8 (CD wearers)	France	Cross-section	Fully dentates/ CD wearers	MNA score	MNA scores showed that more individuals in the CD group risked malnutrition than those in the dentate group (21.3% vs. 0%).	24
Ervin *et al.*	2012	4,462	60 +	U.S.A.	Cross-section	Four category variables defined by the presence of natural and replaced teeth (bridge pontics and removable dental restorations) ・Complete natural dentition (21-28 natural teeth only, without replaced teeth) ・Incomplete natural dentition (1-20 natural teeth, without replaced teeth) ・Complete mixed dentition (21-28 natural teeth and replaced teeth) ・Incomplete mixed dentition (1-20 natural teeth and replaced teeth)	Nutrient intake	Men with complete natural dentition had a significantly higher energy intake than those of other groups. Women with a complete natural dentition had a higher beta-carotene intake than those of other groups. Men with an incomplete mixed dentition had a significantly lower vitamin C intake than those with a complete natural dentition. Significant difference for nutrient intake was not seen between the complete natural dentition group	14
Perera *et al.*	2012	437	60 +	Sri Lanka	Cross-section	Number of teeth present With or without prosthesis treatment with dentures	Underweight (BMI<18.5)	With a unit decrease in missing teeth, the odds of being underweight increased by a factor of 1.08 (95% CI = 1.03-1.12). The odds of being underweight in non-denture wearers compared with denture wearers was 5.62 (95% CI = 1.96-16.14)	18
De Marchi *et al.*	2012	471	60-89	Brazil	Cross-section	Four category variables defined by number of teeth present and dental status. ・Number of teeth present, 9 + ・Number of teeth present, 1-8 ・Edentulous using denture on either the mandibular or maxillary jaw ・Edentulous using dentures on both jaws (reference)	Central obesity (Waist/ hip ratio; women ≥ 0.85, men ≥1.00, waist circumference; women ≥ 0.80m, men ≥0.94m)	Those individuals with at least 9 teeth were less likely to have central obesity, as measured by the waist/ hip ratio [odds = 0.49 (95% CI = 0.32-0.87)], while those individuals with only 1-8 natural teeth were more likely to have central obesity when assessed by waist circumference [odds = 3.28 (95% CI = 1.43-7.52].	23
Yoshida *et al.*	2011	182	65-85	Japan	Cross-section	Molar occlusion with natural teeth (retained contact group)/ with removable partial dentures (lost contact group)	BMI Food and nutrient intake	The lost contact group consumed fewer vegetables and more confectionaries than the retained contact group. The lost contact group also consumed significantly less vitamin C and dietary fiber.	22
de Andrade *et al.*	2011	887	N/A	Brazil	Cross-section	Three category variables defined by the number of POP ・POP = 5-8 ・POP = 1-4 ・POP = 0	Nutrient intake	Odds for insufficient intake of vitamin C, calcium, riboflavin, and zinc was significantly higher in those individuals with no POP compared with those individuals with a POP of 5 or more.	12
Samnieng *et al.*	2011	612	69±6	Thailand	Cross-section	Nutritional status based on MNA (3 categories: normal, at risk of malnourishment, and malnutrition)	Number of teeth present FTU	Those individuals with malnutrition assessed by MNA score had a lower number of teeth and FTUs than those with normal nutrition.	7

#Ref. = reference number, BMI = body mass index, CD = complete denture, HEI = healthy eating index, IOD = implant (-supported) overdenture, MNA = mini nutritional assessment, POP = posterior occluding pairs of teeth.

Table 1: (continued)

Author	Year	Number of subjects	Age (Yr)	Study country	Study design	Exposure	Outcome	Key findings	#Ref.
Savoca *et al.*	2011	635	60 +	U.S.A.	Cross-section	Number of teeth present Number of occlusal contacts Frequency of denture use during meals (3 categories: always, sometimes, never)	HEI Number of foods avoided	Those individuals with fewer than 11 teeth present without dentures, and those individuals with CDs on one or both jaws had a lower HEI score and avoided more foods than all other groups. Those who removed their dentures before eating had a lower HEI score and avoided more foods than those who ate with dentures. Among those who always eat with dentures, there was no relationship between the numbers of occlusal contacts and the foods that were avoided.	20
Savoca *et al.*	2010	635	60 +	U.S.A.	Cross-section	Number of teeth present, fewer than 11/ at least 11	HEI	Those individuals with fewer than 11 teeth present had a lower HEI score than those individuals with at least 11 teeth.	8
Wakai *et al.*	2010	20,366	52±12	Japan	Cross-section	Five category variables defined by the number of teeth present ・0 ・1-9 ・10-19 ・20-24 ・25-28	Food and nutrient intake	Intake of carotene, vitamin C, and vitamin A in those individuals with at least 25 teeth present was higher than those in the respective edentulous subject groups of 14.3%, 8.6%, and 6.1%, and intake of carbohydrate was 6.1% lower Intake of dairy products and green-yellow vegetables and total vegetables in those individuals with at least 25 teeth present was higher than the intake by edentulous individuals by 26.3%, 11.9%, 5.6% respectively, and consumption of rice and confectioneries was lower by 9.5% and 29.6%.	10
de Andrade *et al.*	2009	816	60-96	Brazil	Cross-section	Three category variables defined by the number of POP ・POP = 5-8 ・POP = 1-4 ・POP = 0	Nutrient intake	Intake of energy, carbohydrate, protein, calcium, iron, and phosphorus was significantly lower in those individuals with no POP compared with the individuals with 5 or more POP.	21
De Marchi *et al.*	2008	471	60 +	Brazil	Cross-section	Four category variables defined by number of teeth present and dental status ・Number of teeth present, 9 + ・Number of teeth present, 1-8 ・Edentulous using denture on either the mandibular or maxillary jaw ・Edentulous using dentures on both jaws (reference)	MNA score	Odds of malnutrition assessed by MNA score in the group of edentulous individuals using denture on either the upper or lower jaw was 3.26 (95% CI = 1.39-7.67), whereas the odds of malnutrition in the group of the individuals with 1-8 teeth was 0.53 (95% CI = 0.29-0.98).	13
Muller *et al.*	2008	53	53 (Mean)	Canada	Cross-section	IOD group: 29 (fabrication of IODs 1 year previously) CD group: 24 (fabrication of CDs 1 year previously)	Self-evaluation of masticatory function Nutrient intake Blood levels of nutrition biochemical indicators	The individuals in the CD group had more food items regarded as difficult to chew but no significant difference was found for nutrient intake and nutritional indicators.	17

#Ref. = reference number, BMI = body mass index, CD = complete denture, HEI = healthy eating index, IOD = implant (-supported) overdenture, MNA = mini nutritional assessment, POP = posterior occluding pairs of teeth.

Table 1: (continued)

Author	Year	Number of subjects	Age (Yr)	Study country	Study design	Exposure	Outcome	Key findings	#Ref.
Nowjack-Raymer *et al.*	2007	6,985	25 + (Dentate and no dental prostheses)	U.S.A.	Cross-section	Five category variables defined by the number of teeth present ・1-10 ・11-20 ・21-27 ・28 +	Food and nutrient intake Blood levels of nutrition biochemical indicators	Those individuals with fewer than 28 teeth had a significantly lower intake of carrots, tossed salads dietary fiber and lower serum levels for beta-carotene, folate, and vitamin C than those individuals with at least 28 teeth.	6
Liedberg *et al.*	2007	481		Sweden	Cross-section	Nutrient status defined by nutrient intake Adequate/ inadequate	Number of teeth present Number of occlusal contacts Denture status	No significant differences between those with adequate or inadequate nutrition were found with regard to the number of teeth present, occlusal contacts, and denture wearing status.	16
Yoshihara *et al.*	2005	57	74	Japan	Cross-section	Number of teeth present, fewer than 20/ at least 20	Food and nutrient intake	Nutrient intake of protein, sodium, vitamin D, vitamin B1, vitamin B6, niacin, and pantothenic acid and food intake of vegetables and fish were significantly lower in those individuals with fewer than 20 teeth present compared with those individuals having at least 20 teeth.	11
Liedberg *et al.*	2004	44 (with fixed prosthesis) 40 (with removable prosthesis)	67-68 (Males)	Sweden	Cross-section	Fixed prosthesis group: individuals treated with fixed dentures in more than 2 teeth, without treating using removable dentures Partial prosthesisgroup: individuals treated with dentures in fewer than 8 teeth. Individuals with CDs were excluded.	Energy and nutrient intake	Intake of energy and nutrients did not differ significantly between the groups.	15
Sahyoun *et al.*	2003	4,820	50 +	U.S.A.	Cross-section	Three category variables defined by the number of teeth present and prosthetic condition. ・Number of teeth present, 18 + ・Group with self-perceived good-fitting dentures. ・Group with self-perceived ill-fitting dentures.	HEI Nutrient intake Blood levels of nutrition biochemical indicators	The group with self-perceived ill-fitting dentures had a significantly lower HEI total score, vegetables, varieties, and vitamin C and carotene intake compared with the group with at least 18 teeth present. The group with self-perceived good-fitting dentures did not differ significantly from the group having at least 18 teeth. The groups wearing dentures had significantly lower serum levels of vitamin C, vitamin E, beta-carotene, folate, lutein, and lycopene compared with the group having at least 18 teeth.	26

#Ref. = reference number, BMI = body mass index, CD = complete denture, HEI = healthy eating index, IOD = implant (-supported) overdenture, MNA = mini nutritional assessment, POP = posterior occluding pairs of teeth.

Table 1: (continued)

Author	Year	Number of subjects	Age (Yr)	Study country	Study design	Exposure	Outcome	Key findings	#Ref.
Marcenes *et al.*	2003	753	65 +	U.K.	Cross-section	Dentate (subgroup: number of teeth present 1-10, 11-20, 21-32)/ Edentate	Foods with masticatory difficulties Nutrient intake Blood levels of nutrition biochemical indicators BMI	Intake of non-starch polysaccharides, protein, calcium, iron, niacin, and vitamin C was significantly lower in the edentulous individuals compared with the dentate individuals. The edentulous individuals had significantly lower serum levels of vitamin C and vitamin A compared with the dentate individuals. The number of underweight (BMI < 20) individuals was significantly larger among the edentulous individuals compared with the individuals with more than 10 teeth. The odds of being obese (BMI > 30) was significantly higher in those individuals with fewer than 21 (1-10, 11-20) teeth compared to those individuals with at least 21 teeth.	5
Nowjack-Raymer *et al.*	2003	3,794	25 +	U.S.A.	Cross-section	Fully dentate (having at least 28 teeth)/ Edentulous jaw using CDs on both jaws	Food and nutrient intake Blood levels of nutrition biochemical indicators	Denture-wearers had significantly lower intake of carrots, tossed salads, dietary fiber and lower serum levels for beta-carotene, folate, and vitamin C than the fully dentate individuals.	25
Sahyoun *et al.*	2003	5,958	50 +	U.S.A.	Cross-section	Four category variables defined by the number of POP and dental status ・POP = 5-8 ・POP = 1-4 ・CD ・POP = 0 (without dentures)	HEI Nutrient intake Blood levels of nutrition biochemical indicators	HEI score, fruits intake, serum levels of vitamin C and beta-carotene in the group with 1-4 POP, CDs, and no POP were significantly lower than those in the group with 5-8 POP.	19
Srisilapanan *et al.*	2002	623	60-74	Thailand	Cross-section	Number of teeth present, fewer than 20/ at least 20	Underweight (BMI<20)	Odds of being underweight was 2.27 (95% CI = 1.25-4.13) for those individuals with fewer than 20 teeth present compared with those individuals with at least 20 teeth present in the older age group (68-74 years).	9

#Ref. = reference number, BMI = body mass index, CD = complete denture, HEI = healthy eating index, IOD = implant (-supported) overdenture, MNA = mini nutritional assessment, POP = posterior occluding pairs of teeth.

dental/oral health and its association with nutrient intake in terms of not only tooth loss but also dental prosthesis treatment. There are various methods of assessing dental prosthesis. In a study by Sahyoun *et al*.[19] posterior occluding pairs of teeth (POP), which include fixed prosthesis such as a bridge pontic considered as posterior occlusion, and use of dentures were used as the evaluation index of dental/oral health. In this study, 5,958 subjects aged 50 years and older participated in the National Health and Nutrition Examination Survey (NHANES). They were divided into groups of POP=5-8, POP=1-4, complete denture (CD), and edentulousness without a denture, and were compared in terms of Healthy Eating Index (HEI) score, nutrient intake, and nutrition indexes determined on the basis of blood biochemical examination. As a result, compared with the POP=5-8 group, the POP=1-4, CD and edentulous groups showed significantly lower HEI score, lower fruit, serum vitamin C and *ß*-carotene intakes.

Many of the persons with many teeth lost and with denture prosthesis showed a poor nutrient balance and do not have the appropriate body shape and weight. Yoshida *et al*.[22] investigated 182 local Japanese residents aged 65-85 years and reported that the group wearing a removable partial molar denture showed a lower intake of vegetables, a higher intake of confectionary, and significantly lower intakes of vitamin C and dietary fiber than the group whose occlusion was maintained with natural teeth. De Marchi *et al*.[23] surveyed 471 adults aged 60-89 years in Brazil and evaluated the association of dental/oral health with centripetal obesity by dividing the subjects into four groups (with nine or more teeth, with 1-8 teeth; with denture in one jaw; and with dentures in both jaws, which was used as the reference group) on the basis of the number of teeth present and the prosthesis status. As a result, the odds ratio for centripetal obesity, which was defined as the abdominal circumference/buttocks ratio, was 0.49 (95% confidence interval (CI): 0.32-0.87) in the group with nine or more teeth. On the other hand, in the group with 1-8 teeth, the odds ratio for centripetal obesity was 3.28 (95% CI: 1.43-7.52).

Although it has been reported[24, 25] that nutrient intake is low and the malnutrition rate is high even among the elderly wearing dentures, there is an interesting study taking the fitness of dentures into consideration. Sahyoun *et al*.[26] surveyed 4,820 adults aged 50 years and older who participated in NHANES. They divided them into three groups on the basis of the number of teeth present and the prosthesis status (the group with 18 teeth or more, the group with self-perceived good-fitting dentures, and the group with self-perceived ill-fitting dentures). They compared their HEI score, nutrient intake, and nutrition indexes on the basis of blood biochemical examination. As a result, the group with self-perceived ill-fitting dentures showed significantly lower HEI score, vegetable intake, food diversity, vitamin C intake and carotene intake than the group with 18 or more teeth. On the other hand, there were no significant differences between the group with 18 teeth or more and the group with self-perceived good-fitting dentures. The authors concluded the importance of regular dental maintenance and retention of fitness/function of dentures.

2. Dental prosthesis treatment and nutrition (Intervention study) (Table 2)

Since 2001, randomized controlled trials have been conducted, in which IOD and CD were compared in terms of their contribution to the improvement of the nutrition status. One of the randomized controlled trials[27] showed in the follow-up assessment (after six months) significant improvements in percent body fat and skin-fold thickness at the biceps, subscapularis, and abdomen, significant decreases in waist circumference and waist-hip ratio, and significant increases in serum albumin, hemoglobin and vitamin B12 levels only in the IOD group. However, in other studies, although significant improvement was observed in chewing ability, no significant contribution of IOD to the improvement of nutrition status was observed when compared with lower jaw CD[28-30]. Hamdan *et al*.[29] conducted a randomized controlled trial targeting 255 edentulous patients aged 65 years and older. In the follow-up assessment (after 12 months), calorie and nutrient intakes were compared between the intervention group (127 patients; mean age, 71 years) with IOD and the control group (128 patients; mean age, 70 years) with CD. As a result, they found no significant difference between these two groups.

Among all the intervention studies that evaluated the effects of general dental prosthetics such as CD and partial denture, only one[31] showed improvement of nutritional status[32-35]. Furthermore, Wöstmann *et al*.[35] assessed the effects of adjustment, repair or fabrication of dentures of 47 patients aged 60 years and older who required dental prosthesis treatment on their chewing ability and nutritional status after six months. As a result, although improvement was observed in chewing ability, no improvement in their nutritional status was observed.

3. Orofacial pain and nutrition (Observational study) (Table 3)

Previous studies have shown significant associations between orofacial pain and nutritional status/nutrient

Table 2: Intervention studies referred in this literature related to teeth, oral health, and nutrition.

Author	Year	Subjects	*n*	Age (Yr)	Study country	Interventional methods	Outcome	#Ref.
Müller *et al.*	2013	Edentulous adults	34	85 & 84 (Mean by group)	Switzer-land	Group 1 (intervention, *n* =16) Mandibular IOD prosthesis retention Group 2 (control, *n* =18) Conventional reline of lower denture	In the follow-up evaluation (12 months), BMI decreased in both groups, but the decline tended to be smaller in the intervention group; blood markers and the MNA did not confirm this tendency.	30
Hamdan *et al.*	2013	Edentulous adults	255	65 +	Canada	Group 1 (intervention, *n* =127) with mandibular IOD Group 2 (control, *n* =128) with mandibular CD	There were no differences between the intervention and the control groups in the amount of intake of energy and nutrients in the follow-up evaluation (12 months).	29
Moynihan *et al.*	2012	Edentulous adults	54	73 & 66 (Mean by group)	U.K.	Dietary counseling	The IOD group had a significantly lower % energy intake from saturated fat and higher intake of non-starch polysaccharide compared with the CD group in the follow-up evaluation (3 months). Both groups showed improvements in serum antioxidant status however, the IOD group had significantly higher plasma antioxidant capacity post intervention compared with the CD group in the follow-up evaluation (3 months and 6 months).	48
Prakash *et al.*	2012	Edentulous adults	94	50-80	India	Wearing CD Nutritional counseling	MNA score after treatments had significantly improved in the follow-up evaluation (6 months and 9 months) compared with the baseline study.	49
McKenna *et al.*	2012	Persons with missing teeth	44	65 +	Ireland	Group 1 with prosthesis by removable partial dentures Group 2 with only a shortened dental arch without intervention by dentures	MNA score significantly improved in the both groups in the follow-up evaluation (1 month). However, there were no differences in the biochemical examination of blood between the groups.	34
Shigli *et al.*	2012	Edentulous adults	35	68	India	Wearing CD	Intake of vegetables, fruits and dairy products significantly improved in the follow-up evaluation (1 month) compared with the baseline study.	31
Awad *et al.*	2012	Edentulous adults	255	71 & 70 (Mean by group)	U.A.E.	IOD group (intervention; mandibular IOD and maxillary CD) CD group (control; mandibular and maxillary CD)	There were no differences in blood levels of nutrition biochemical indicators in the follow-up evaluation (6 months and 12 months). The IOD group had a greater nutrient intake from fruits and vegetables.	28
Gunji *et al.*	2009	Edentulous adults	30	74 (Males) 73 (Females)	Japan	Wearing newly fabricated dentures	The masticatory performance significantly improved in the follow-up evaluation (2 months after the last adjustment for newly fabricated dentures). However, participants did not have a significant improvement in the intake of energy and nutrients in the follow-up evaluation.	33
Wöstmann *et al.*	2008	Persons with need for prosthesis treatment	47	60 +	Germany	Adjustment, repairs, or new fabrications of dentures	At six months from adjustments, repairs, or new fabrications of dentures, the masticatory performance improved. However, the nutritional status was not improved.	35
Bradbury *et al.*	2006	Edentulous adults	58	65 & 67 (Mean by group)	U.K.	Group 1 with normal dental treatment, and nutritional counselingby dietician Group 2 with normal dental treatment, only	Self-assessment for the masticatory performance showed significant improvement in the both groups in the follow-up evaluation (6 weeks). Intake of fruits and vegetables significantly increased only in the group 1.	47
Allen *et al.*	2005	Edentulous adults	35	52-77	U.S.A.	Wearing newly fabricated dentures	There were no differences in food selections and MNA score in the follow-up evaluation (2 months after wearing newly fabricated dentures).	32
Morais *et al.*	2003	Edentulous adults	60	65-75 (70: mean in both group)	U.S.A.	IOD group (intervention; mandibular IOD and maxillary CD) CD group (control; mandibular and maxillary CD)	Improvements in the percent body fat, skin-fold thickness, decreases in waist circumference and waist / hip ratio, and increases of concentrations of serum albumin, hemoglobin, and vitamin B12 were detected in the IOD group in the follow-up evaluation (6 months). These improvements were not detected in the CD group. No significant between-group differences were found.	27

#Ref. = reference number, BMI = body mass index, CD = conventional (complete) denture, IOD = implant (-supported) overdenture, MNA = mini nutritional assessment.

Table 3: Observational studies referred in this literature related to orofacial pain and nutrition.

Author	Year	Subjects	Number of subjects	Age (Yr)	Study countr	Study design	Exposure	Outcome	Key findings	#Ref.
Soini *et al.*	2006	Residents in nursing homes Hospital patients	2,036 1,052	83 (Mean) 81 (Mean)	Finland	Cross-section	Oral pain by self-assessment	Nutritional status based on MNA (MNA = 17-23.5: at risk of malnutrition, MNA<17: malnourished)	The ratio of malnourished subjects assessed by MNA score was higher in those subjects with oral pain.	37
Bailey *et al.*	2004	Individuals without CSP Individuals with CSP continuing for 1 year	125 22	73 (Mean) 74 (Mean)	U.S.A.	Cross-section	CSP	HEI Nutrient intake	The CSP (+) group showed lower HEI score and intakes of vitamin A indicating a higher percentage of persons with insufficient intakes of vitamin A and B6, compared to the CSP (-) group.	36

#Ref. = reference number, CSP = chewing, swallowing, and mouth pain, HEI = healthy eating index, MNA = mini nutritional assessment.

intake[36, 37]. Bailey *et al.*[36] compared the HEI score and nutrient intake between 125 persons without chewing, swallowing, and mouth pain (CSP) (mean age, 73 years) and 22 persons with CSP throughout a year (mean age, 74 years). As a result, the CSP (+) group showed lower HEI score and intakes of vitamin A indicating a higher percentage of persons with insufficient intakes of vitamin A and B6, compared to the CSP (-) group.

[Discussion]

This review reconfirmed that tooth loss negatively affects nutritional status and nutrient intake.

Tooth loss decreases chewing ability. It has been reported that low chewing ability limits the variety of food that can be easily eaten. In particular, because many vegetables and fruit are regarded to be difficult to chew[38], persons with many teeth lost tend to show lower intake because they avoid eating such foods. Vegetables and fruit are sources of vitamins and dietary fiber, which contain less calories and fat but rich in components that help maintain good health and prevent diseases. The Japanese Food Guide Pyramid[39] defines that vegetables should be eaten in every meal and recommends that fruit be taken once daily. According to Healthy Japan 21[40], the adequate intake per day for an adult is 350 g of vegetables including 120 g or more of brightly colored ones. From the Japanese Food Guide Pyramid, it is desirable to eat 200 g of fruit daily. When the intakes of vegetables and fruit were low, decreased levels of vitamin C, vitamin E, and carotene in serum were observed persons with many teeth lost. It is recognized that these are important nutrients with the antioxidative effect[41], whose adequate intake is considered helpful in the prevention of many NCDs such as cardiovascular disease[42,43].

Furthermore, many persons who lost many teeth showed abnormal weight (underweight or overweight). Abnormal weight in some of these persons may be due to an inverse causal association, for example, tooth loss caused by obesity and diabetes through periodontal disease. However, it is highly presumable that the decrease in chewing ability due to tooth loss may lead to the increase in the intake of high-calorie foods but with low nutritional value such as confectionery leading to obesity, or it may lead to the decrease in total calorie intake leading to being underweight. There are many reports about the association of tooth loss with poor nutrition especially in the elderly. It is said that mental and physical deterioration occurs markedly in the elderly, resulting in a higher risk of malnutrition caused by decreased sense of taste and smell, use of medicines, physical/mental complaints, and social isolation among others[44]. In the elderly, malnutrition and being underweight are the independent risk factors for nursing care requirement and all-cause mortality[45]. Furthermore, a study of the association between chewing ability and activities of daily living (ADL)[46] suggests that eating is not just a means of nutrient intake but also has the psychological effect of evoking behavioral motivation, which contributes to maintenance of physical functions.

Although deterioration in nutrition status was observed among persons who lost many teeth, no decrease in the intake of foods such as vegetables and fruit or of nutrients such as vitamins has been observed among persons who lost many teeth but with well-fitted and well-maintained dentures.

From the above, it is suggested that regular dental maintenance can prevent tooth loss, and well-fitting dentures contribute to the reduction of the risk of NCDs, prevention of malnutrition and decrease in ADL in the elderly, and eventually extend healthy life expectancy.

This review of the findings of previous intervention studies indicated that IOD and other dental prosthesis treatments hardly improved nutrient intake status. Although significant improvement in chewing ability has been shown in all studies, few of them showed significant improvement in nutrition index. This review clarified that improvement in chewing ability alone cannot induce a behavioral change that leads to a healthy dietary habit. With regard to the above, we would like to introduce an interesting survey on the associations between dental prosthesis treatment and nutrient intake status. In a randomized controlled trial[47] conducted in the U.K., 58 edentulous patients had dentures fabricated, of which 30 patients were given, in addition to normal dental treatment, a nutritional counseling by a dietician (intervention group), whereas 28 patients were given normal dental treatment only (control group). The 6-week follow-up assessment showed that although there was improvement in self-rated chewing ability in both groups, a significant increase in the intake of vegetables and fruit was observed only in the intervention group. In the same study group[48], nutritional counseling was also provided to 28 edentulous patients with IOD (IOD group) and 26 edentulous patients with CD (CD group). After three months, the nutrient intake levels and serum antioxidant capacity in both groups were assessed. As a result, the IOD group showed a lower calorie intake from saturated fatty acid and a significantly higher intake of nonstarch polysaccharides than the CD group. Furthermore, although the serum antioxidant capacity improved significantly in both groups, the IOD group showed higher antioxidant

capacity. A favorable effect of nutritional counseling has also been observed in an intervention study conducted in India[49]. These findings suggest the need of introducing nutritional counseling in dental treatment in order to effect behavioral changes that will lead to improvement of patients' nutritional status and general health condition. This review has clarified the importance of interdisciplinary cooperation.

As there has hardly been any survey of community residents that assess orofacial pain and nutritional status, further research will be required in this field in the future. In this review, we selected only the community-resident- based observational studies that focused on health promotion among community residents. However, it is presumed that the frequency of complaints is high among people with some diseases or reduced mental/physical functions such as inpatients and institutionalized residents.

[Conclusions]

The following are the findings of this review:

- Tooth loss is associated with decreases in dietary intake mainly vegetables and fruit and decreases in the intake of nutrients mainly vitamins with the antioxidative effect.
- Tooth loss is associated with obesity or being underweight. This association is influenced by age, sex, and race among others. Particularly in the elderly, this is associated with a decrease in the total calorie intake and malnutrition.
- Compared with dentate persons, edentulous persons with CD show a poor nutrient intake status. However, in the case of persons with well-fitted dentures, such an association is not observed.
- Self-rated orofacial pain is associated with malnutrition.
- Dental prosthesis treatment alone can hardly bring about any improvement in nutrient intake status. Nutritional counseling is essential for a behavioral change that will lead to improvements in dietary intake and thus nutritional status.

Regarding the methodological challenges in future studies, observational studies on associations between dental/oral health and nutrition have been designed by focusing on cross-sectional studies, which makes the assessment of causal relationships difficult. We consider it an important future task to accumulate evidence by cohort and other highly reliable studies to further disclose the associations between the two. With regard to intervention studies, it is desirable to further develop studies of assessing the effects of nutritional improvement through collaboration with other occupational groups such as dieticians.

[Conflict of interest]

There are no items applicable to "conflict of interest" in this article.

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7. Rest/communication and QOL

7. Rest/communication and QOL

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[Abstract]

Oral diseases not only cause pain and functional impairment but also have adverse psychological and social effects. It is considered in an aging society that associations between oral health and quality of life (QOL) will become increasingly important. In this regard, with the aim of clarifying the associations of oral health with health-related QOL, we reviewed articles. Furthermore, we summarized findings regarding associations of QOL-related rest and communication with oral health.

We conducted a literature search using PubMed and the Igaku Chuo Zasshi website database (ICHUSHI) to identify the study results reported in English and Japanese, respectively. The major concepts were "QOL," "communication," and "rest." In the search for the word "rest," also included the concepts " stress reduction" and "sleep disorder (excluding sleep apnea)." In total, 14 original articles on "QOL" and eight on "rest/communication" were extracted from the search for review.

As a result of the review, a significant association was identified between oral health and health-related QOL, and a possible contribution of maintenance/improvement of good oral health to the enhancement of QOL was suggested. Furthermore, it was also indicated that stress and sleep, which are related to communication and rest, are associated with oral conditions.

With regard to this subject, continued accumulation of evidence is required along with further discussion.

[Introduction]

In general, the outcome indicators most often used in medical studies are morbidity and mortality. In addition to these typical objective indicators, since the 1980s, subjective self-evaluation by patients or persons to be studied has become increasingly adopted in those studies to obtain outcome indicators. Along with development of such studies, the indicators obtained from the subjective self-evaluation by patients have become widely recognized as patient-based outcomes [1].

QOL is the abbreviation of "quality of life," which is often translated literally as "*seikatsu no shitu*" in Japanese. As the expression implies different meanings depending on the field it is used, its definition is difficult. For example, QOL can also include improvement of parks and sewerage and pleasantness of housing. In recent years, the term "health-related QOL" has become widely used to indicate QOL particularly related to human health.

Health-related QOL is one of the typical patient-based outcomes. Health-related QOL generally consists of "physical functioning," "mental health," and "social functioning" as the basic elements. The representative and comprehensive evaluation scales of health-related QOL include *MOS-Short Form 36 (SF-36)*[2], *Sickness Impact Profile*[3], *Nottingham Health Profile*[4], and *WHOQOL*[5].

As oral diseases not only cause pain and functional impairment but can also have adverse psychological and social effects, their association with health-related QOL is considered to be more significant in an aging society. The number of epidemiological studies using QOL as an evaluation indicator has been gradually increasing since the 2000s, on the basis of which accumulation of evidence is expected.

With these as a background, we conducted a literature review with the aim of clarifying the associations between oral health and QOL. Furthermore, we focused on the associations of rest and communication that affect QOL with oral health. The related lines of evidence were also collected separately.

[Objective]

The objective of this review was to summarize findings that have been reported in papers regarding the two research questions: "does maintenance/improvement of good oral health contribute to the enhancement of QOL?" and "is oral health associated with rest and communication?"

[Methods]

We conducted a literature search in PubMed and the website database of ICHUSHI to identify the study results that were reported in English and Japanese. The search was conducted on May 18, 2014.

The major concepts were "QOL," "communication," and "rest." In the search for the word "rest," we also included the concepts "stress reduction," "sleep disorder," and "relaxation."

"QOL" was defined as health-related QOL and the articles only dealing with oral health-related QOL were excluded after their abstracts were examined.

In the PubMed search, "oral health" [MeSH Terms], "dentistry" [MeSH Terms], "epidemiologic studies" [MeSH Terms], "humans" [MeSH Terms], and "adult" [MeSH Terms] were added to the keywords pertaining to the concepts. As for the search in ICHUSHI, "Shikagaku (dentistry)/TH OR Shika (dentistry)/AL" and "Ekigakuteki kenkyu (epidemiologic studies)/TH OR Ekigaku kenkyu (epidemiologic studies)/AL" were added to each search expression. Targets were limited to original articles.

A total of 622 articles on QOL, 419 articles on communication, and 451 rest-related articles were extracted from both databases. These articles were narrowed down by examining their titles and abstracts.

The QOL studies targeting the general population or patients with lifestyle-related diseases were adopted as the review targets for "QOL." Among the articles that were searched for "QOL," those that were considered to be more concerned with "communication" or "rest" were moved to the corresponding category in the phase of narrowing. As for "rest," articles on sleep apnea syndrome were excluded. Some of the articles were excluded after their full texts were checked and identified as not fitting the purpose of this review.

Finally, 14 original articles on "QOL," three on "communication," and six on "rest" were chosen as sources for the article review (Table 1).

[Results]

1. Associations of oral health with health-related QOL

We have extracted 14 articles on the associations between oral health and health-related QOL. The QOL evaluation scales used included SF-36 or SF-8 in five articles, WHOQOL in two articles, and others in the remaining seven articles.

Mariño *et al*.[6] conducted a cross-sectional study of the associations between self-rated oral condition and QOL in 4,766 men and women aged 60 years and older in Chile. The QOL was scored in five grades. Among persons with a high QOL score, the number of persons with an edentulous jaw was smaller than that with a low QOL score [odds ratio (OR), 1.5; 95% confidence interval (CI), 1.10-2.00]. Compared with those with a high QOL score, persons with a low QOL score tended to have problem in masticatory function (OR, 2.33; 95%CI, 1.65-3.29). Persons whose QOL was "very poor" showed an even higher OR (OR, 4.69; 95%CI, 2.44-9.03) and a higher risk of having problem in masticatory function.

Hugo *et al*.[7] and Fontanive *et al*.[8] reported the results of their cross-sectional studies conducted on randomly sampled residents in southern Brazil using WHOQOL-BREF. The former group targeted 872 men and women aged 60 years and older in their study, which showed significant associations between the reduced number of teeth/dissatisfaction with chewing force and worsened QOL. In particular, dissatisfaction with chewing force indicated association with all the subscales, such as functional, mental, environmental, and social QOL. The latter group conducted a study on 720 men and women aged 50-74 years. They found that the use of a denture on the upper jaw significantly contributed to the reduction in the subscales of functional QOL, DMFT to the reduction in the social QOL, and the use of a denture on the lower jaw to the reduction in the environmental QOL.

Lee *et al*.[9] and Wang *et al*.[10] reported the results of their studies conducted in Taiwan. The former group targeted 1,600 men and women aged 65 years and older, whereas the latter 15,501 men and women aged 18-64 years. In both studies, SF-36 was used as the measurement scale. In the study conducted by the former group, the oral-related QOL scores determined using Oral Health Impct Profile (OHIP) showed significant association with both physical and mental component summary scores on SF-36. In the case of the study conducted by the latter group, the oral health-related items (e.g., oral hygiene condition and dental attendance frequency) showed a significant association with SF-36 scores.

Appollonio *et al*.[11] conducted a cohort study targeting 1,124 men and women aged 70-75 years living in northern Italy and subjected the baseline data to cross-sectional analysis for QOL evaluation. Beck's Depression Inventory, IADL, and Linn's SELF scale were used as the QOL evaluation scales. Persons who needed dentures but did not use them indicated a lower QOL score than those who did not need dentures and those who were using dentures appropriately.

There were studies conducted by Japanese. Naito *et al*.[12] conducted a cross-sectional study on patients visiting dental clinics across Japan. The study was conducted using SF-8 on 3,238 men and women aged 40-92 years. The patients whose oral-related QOL score determined using Geriatric / General Oral Assessment Index (GOHAI) was higher than the national norm showed a significantly higher QOL score measured using SF-8 (OR, 1.76; 95%CI, 1.52-2.04). Shimada *et al*.[13] targeted new patients at the dental department of a university hospital. In the study, 177 men and women aged

Table 1: Summary of characteristics and main findings of included studies for systematic reviews

Authors	Report year	Place of survey	Subjects	No. of subjects	Methods (study design)	Measures used	Major results	Reference number
Mariño *et al.*	2013	Chile	Local residents aged 60 or older	4,766	Cross-sectional	Questionnaire of the authors' own designing	Persons with low QOL tended to have problems with chewing more than those with high QOL (OR 2.33, 95%CI 1.65-3.29).	6
Hugo *et al.*	2009	Brazil	Local residents aged 60 or older	872	Cross-sectional	WHOQOL-BREF	Decrease in the number of teeth and dissatisfaction with chewing abilities were significantly associated with decline in QOL.	7
Fontanive *et al.*	2013	Brazil	Local residents aged 50-74	720	Cross-sectional	WHOQOL-BREF	The use of a denture on the upper jaw was significantly associated with subscale functions, DMFT with sociability, and the use of a denture on the lower jaw with decline in environmental QOL.	8
Lee *et al.*	2007	Taiwan	Local residents aged 65 or older	1,600	Cross-sectional	SF-36, OHIP	The oral QOL scores based on OHIP were significantly associated with the results of SF-36 in terms of both physical and mental aspects.	9
Wang *et al.*	2013	Taiwan	Local residents aged 18-64	15,501	Cross-sectional	SF-36	All oral health-related items (e.g., oral hygiene condition and dental attendance frequency) were significantly associated with the SF-36 scores.	10
Appollonio *et al.*	1997	Italy	Local residents aged 70-75	1,124	Cross-sectional	Beck's Depression Inventory, IADL, Linn's SELF scale	The QOL of persons who needed dentures but did not use them was lower than that of those who did not need dentures and those who were using dentures appropriately.	11
Naito *et al.*	2010	Japan	Persons aged 40-92 who visit a dental clinic	3,238	Cross-sectional	SF-8, GOHAI	Persons whose GOHAI-based oral QOL scores were higher than the national norm had significantly higher QOL as evaluated using SF-8 (OR 1.76, 95%CI 1.52-2.04).	12
Shimada *et al.*	2005	Japan	Patients who visit the dental department of a university hospital for the first time (aged 16-79)	177	Cross-sectional	SF-36	The perception of oral health as related to functions and pain was significantly associated with SF-36 subscales.	13

Table 1: (continued)

Authors	Report year	Place of survey	Subjects	No. of subjects	Methods (study design)	Measures used	Major results	Reference number
Brennan *et al.*	2008	Australia	Local residents aged 45-54	879	Cross-sectional	EQ-VAS, OHIP, Satisfaction with Life Scale	The QOL score increased as the chewing force evaluated using functional units/chewing score increased (P<0.01).	14
Huang *et al.*	2013	USA	Diabetics aged 65 or older	70,363	Cross-sectional	Healthy Days Core Module	Tooth loss due to tooth decay or periodontal disease was significantly associated with decrease in the General Health status score as the QOL indicator (OR 1.25, 95%CI 1.13-1.37).	15
Sandberg *et al.*	2003	Sweden	Persons living in the same area who visit a dentist (as chosen by matching diabetics, gender, and age)	204	Case-control	SF-36	Among the diabetic patients, those with edentulous jaw or with 1-9 teeth showed lower bodily function and physical role function scores than those with 20 teeth and more, but no significant difference was observed in the control group.	16
Zhou *et al.*	2011	China	Patients with chronic obstructive pulmonary disease	306	Cross-sectional	SGRQ	The larger the number of missing teeth and the higher the plaque index was, the lower QOL score was (P<0.05).	17
Ingram *et al.*	2005	USA	Male cancer patients who declare that they have difficulties in eating due to problems of teeth or mouth	150	Cross-sectional	EORTC QLQ-30	Persons who declared that they had difficulties in eating due to problems of teeth or mouth had lower QOL than those who declared otherwise in terms of all EORTC QLQ-30 subscales (P<0.05).	18

Table 1: (continued)

Authors	Report year	Place of survey	Subjects	No. of subjects	Methods (study design)	Measures used	Major results	Reference number
Duke *et al.*	2005	USA	Head and neck carcinoma patients who have survived for five years	86	Cross-sectional	UWQOL, FACT, Performance Status Scale for Head and Neck	Persons who became edentulous during the period from start of cancer treatment to immediately after its completion, those with a high DMF score, those with a decreased degree of opening their mouth, or those with an edentulous jaw not using dentures showed a decrease in QOL score ($P<0.05$).	19
Naito *et al.*	2010	Japan	Elderly persons who live in nursing facilities	30	Controlled	FIM, GOHAI	From the comparison between the baseline and change in the score after the intervention, a significant increase in the score of the expression was observed in the intervention group compared with the control group.	20
Yiengprugsawan *et al.*	2011	Thailand	Local residents aged 15-87	87,134	Cross-sectional	GOHAI	With regard to "speaking," which is one of the components of oral-related QOL, persons with 20 teeth and more had less difficulty in speaking than those with less than 20 teeth (OR 6.43, $P<0.001$).	21
Bekiroglu *et al.*	2012	Turkey	Denture wearers aged 55 or older	105	Cross-sectional	Questionnaire of the authors' own designing	Sixty percent of the subjects aged 75 years and older responded that they had sleeplessness/stress/unpleasantness caused by communication problems and pain caused by the dentures worn	22
Ikebe *et al.*	2002	Japan	Persons aged 60 or older who participate in a college for the aged	3,967	Cross-sectional	Questionnaire of the authors' own designing	For those with complete denture, the oral function with the lowest satisfaction score was "speech."	23
Jones *et al.*	2003	USA	Local elderly men	721	Cross-sectional	OHIP, GOHAI, OHQOL, DELTA	The percentage of those who had trouble in relaxing due to teeth/mouth problem was higher among those with an edentulous jaw than among those with 1-24 teeth or 25 teeth and more.	24
Tadatsu *et al.*	2006	Japan	Company workers	459	Cross-sectional	Questionnaire of the authors' own designing	The age groups 20-49 years and 50 years and older with overstress both showed significantly lower oral health promotion scores (which mean higher risks of having oral health problems) than the group without overstress.	25

Table 1: (continued)

Authors	Report year	Place of survey	Subjects	No. of subjects	Methods (study design)	Measures used	Major results	Reference number
Locker *et al.*	2000	Canada	Local residents aged 50 or older (at baseline)	334	Cohort	Perceived Life Stress Questionnaire, Index of Morale, Life Satisfaction Scale, GHQ	Persons with high self-rating scores showed lower subjective stress scores four years later ($P<0.05$).	26
Emami *et al.*	2012	Canada	Edentulous persons aged 65 or older	173	Cross-sectional	Pittsburgh Sleep Quality, Epworth Sleepiness Scale, OHIP, SF-36	Persons having frequent problems with their dentures tended to show more daytime sleepiness than those not having such problems ($P=0.034$). The OHIP-based oral-related QOL was identified to be one of predictive factors for sleep quality ($P=0.001$).	27
Fukai *et al.*	2009	Japan	Local residents aged 40 or older	5,584	Cross-sectional	Questionnaire of the authors' own designing	There was a tendency that the percentage of persons having physical complaints increases proportionally to the decrease in the number of teeth without functional problems ($P<0.001$).	28

16-79 years were evaluated using SF-36. Oral conditions determined in terms of function and pain were significantly associated with the scores of SF-36 subscales.

Brennan *et al*.[14] studied the associations between tooth loss, chewing force, and QOL, targeting 879 men and women aged 45-54 years living in southern Australia. QOL was assessed using the visual analogue scale of EuroQol (EQ-VAS) and Satisfaction with Life Scale. It was found that the QOL score increased as the chewing force evaluated using functional units/chewing score increased (P<0.01).

Six articles were extracted as reports on patients with lifestyle-related diseases. Studies on diabetes included those by Huang *et al*.[15] and Sandberg *et al*.[16]. The former study was conducted on 70,363 diabetic patients aged 65 years and above in the U.S. using the Healthy Days Core Module. Tooth loss due to tooth decay or periodontal disease was significantly associated with decrease in the General Health status score as the QOL indicator (OR, 1.25; 95%CI, 1.13-1.37).

The latter study was a case-control study conducted, on a group of 102 diabetic patients and a sex- and age-matched control group of 102 residents in the same area in Sweden. QOL was evaluated using SF-36. Among the diabetic patients, those with edentulous jaw or with 1-9 teeth showed lower physical functioning and role-physical scores than those with 20 teeth and more, but no significant difference was observed in the control group. In the combined analysis of both groups, dissatisfaction with the teeth and mouth and complaints of mouth dryness showed significant associations with the scores of all the subscales.

Regarding chronic obstructive pulmonary diseases, Zhou *et al*.[17] conducted a cross-sectional study targeting 306 patients aged 30 years and older using the St George's Respiratory Questionnaire (SGRQ). The number of missing teeth and the plaque index showed a significant association with the SGRQ scores, and a decrease in QOL score was observed (P<0.05).

Ingram *et al*.[18] and Duke *et al*.[19] conducted studies on cancer patients in the U.S. The former group examined 150 male cancer patients (median age: 67 years) in a cross-sectional study using EORTC QLQ-30. Persons who declared themselves "having difficulty in eating due to problems of teeth or mouth" showed lower scores of all the subscales of EORTC QLQ-30 than those without such difficulty (P<0.05).

The latter group conducted a cross-sectional study using University of Washington Quality of Life Questionnaire (UWQOL) and Functional Assessment of Cancer Therapy (FACT) on 86 patients with head and neck carcinoma (average age: 64 years) surviving for more than five years following completion of cancer treatment. Persons who became edentulous during the period from start of cancer treatment to immediately after its completion, those with a high DMF score, those with a decreased degree of opening their mouth, or those with an edentulous jaw not using dentures showed a decrease in QOL score (P<0.05).

2. Associations between oral health and rest/communication

In total, nine articles were extracted with regard to rest (including the concepts of stress reduction, relaxation, and sleep) and communication.

Studies in Japan, Thailand, and Turkey showed the associations between oral health and communication. Naito *et al*.[20] conducted a study on dental treatment as an intervention targeting 30 Japanese elderly persons living in a nursing facility. The score of the Expression of the Functional Independence Measure (FIM) was used as the evaluation index for communication. From the comparison between the baseline and change in the score after the intervention, a significant increase in the score of the measure was observed in the intervention group compared with the control group.

Yiengprugsawan *et al*.[21] conducted a cross-sectional study on the oral-related QOL, targeting 87,134 Thai men and women aged 15-87 years. With regard to "speaking" which is one of the components of oral health-related QOL, persons with less than 20 teeth had more difficulty in speaking than those with 20 teeth and more (OR 6.43, P<0.001).

Bekiroglu *et al*.[22] conducted a cross-sectional study on complaints regarding oral problems, targeting 105 Turkish persons aged 55 years and older who wore dentures. Approximately 60% of the subjects aged 75 years and older responded that they had sleeplessness/stress/unpleasantness caused by communication problems and pain caused by the dentures worn.

Among similar studies on the use of dentures, that by Ikebe *et al*.[23] on 3,967 local Japanese elderly persons (average age: 67 years) showed that for those with complete denture, the oral function with the lowest satisfaction score was "speech."

Furthermore, there were studies in the U.S., Japan and Canada on rest including the concepts of stress reduction and sleep. In a study [24] targeting 721 local elderly men living in the U.S., the percentage of those who had trouble relaxing due to teeth/mouth problems was higher among those with an edentulous jaw than among those with 1-24 teeth or 25 teeth and more.

Tadatsu *et al*.[25] conducted a cross-sectional study

targeting 459 Japanese company workers. The age groups 20-49 years and 50 years and older with overstress both showed significantly lower oral health promotion scores (which mean higher risks of having oral health problems) than the group without overstress.

In a cohort study[26] targeting local residents aged 50 years and older in Canada, the impact of self-rated oral status in the third year of the study on the mental health conditions in the seventh year was examined. As a result, persons with high self-rating scores showed lower subjective stress scores four years later ($P<0.05$).

There was also a study in Canada, in which Emami *et al*.[27] analyzed the associations between sleep quality/daytime sleepiness and oral health, targeting 173 persons with an edentulous jaw aged 65 years and older. Persons having frequent problems with their dentures tended to show more daytime sleepiness than those not having such problems ($P=0.034$). Furthermore, the oral health-related QOL was identified to be one of predictive factors for sleep quality ($P=0.001$).

Using the baseline data of a cohort study, Fukai *et al*.[28] analyzed in a cross-sectional way the association between physical complains due to an unidentifiable cause (including sleep disorder) and oral conditions, targeting 5,584 local residents in Japan aged 40 years and older. There was a tendency that the percentage of persons having physical complaints increases proportionally to the decrease in the number of teeth ($P<0.001$).

[Discussion]

1. Associations between oral health and health-related QOL

It was recognized in all the reports that significant associations were observed between oral health and health-related QOL. On the basis of this observation, it is suggested that the maintenance/promotion of oral health can contribute to improvement of QOL.

In general, oral health conditions indicated a wide range of associations, not limited to specific factors (e.g., physical functioning) that affect health-related QOL. Although most of the articles we reviewed were about cross-sectional studies based on which the causal associations could not be identified, it is interesting that these studies suggest the possibility of association of oral health conditions with physical, mental, and social aspects of health-related QOL. Further clarification of these associations by cohort studies and intervention studies is awaited.

Furthermore, six out of 14 articles were about large-scale epidemiological research with at least 1,000 research subjects. Most of these research studies used the profile-type scales that measure health multidimensionally and whose reliability and adequacy had been psychometrically validated.

On the other hand, various "oral health" indicators were used in these research studies, including the number of teeth, use of dentures, oral health-related QOL scores, and oral hygiene status. Also, for the assessment of health-related QOL, there were some studies in which multiple scales were used in one analysis; in total, 14 different scales were used.

Considering that studies using QOL scores as the evaluation indicators vary widely in topic and subject, analyzing obtained findings comprehensively is not easy. It is also considered necessary to further accumulate evidence.

All of 14 articles reviewed here were published in and after 1997. Considering that four of them were published within the last two years, increase in the number of reports and further research development are expected.

2. Association between oral health and rest/communication

There are only a small number of original articles under this topic, and future studies are awaited. The number of articles available is small maybe because the topic is on QOL-related matters and is, therefore, likely discussed as part of QOL and not independently.

Associations between a reduced number of teeth or denture use and communication were shown in three research reports. An intervention study also suggested that betterment of oral conditions can contribute to improvement in communication functions (expression). Further, the six articles on stress or a relaxed psychosomatic state and a sleep state related to resting showed their association with oral conditions and denture use.

It is presumed that rest and communication are associated with survival time, ADL, social participation, and QOL among others; eventually, rest and communication affect the extension of healthy-life expectancy. Although the associations of stress[29] and the number of sleeping hours[30] with mortality risk have already been reported, it is considered worthwhile in view of public health to clarify the associations of these factors with oral health. We believe that it is important to further accumulated evidence.

[Conclusions]

With the objective to clarify the associations of oral health with rest, communication, and QOL, we conducted a review of relevant articles that have been published inside and outside Japan. As a result, a significant association was

observed between oral health and health-related QOL, and the possible contribution of maintenance/improvement of good oral health to the enhancement of QOL was suggested. Further, stress and sleep states, which are related to communication and rest, were also associated with oral conditions. As the number of reports available on this topic is small, further accumulation of evidence is considered important.

[Conflict of interest]

There are no items applicable to "conflict of interest" in this article.

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8. Oral health and social determinants
– Oral health inequality and social determinants of oral health –

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[Abstract]

Health inequality and social determinants of health, which are the greatest causes of such inequality, are attracting public attention. The first item of the Basic Matters Related to the Promotion of Dental and Oral Health stipulated under the Act concerning the Promotion of Dental and Oral Health in Japan is "the reduction of health inequality to maintain and promote oral health." The social determinants of health are "the causes of causes" that determines the health and behavior of people. We provide an overview of systematic reviews and meta-analyses of studies related to oral health inequalities and their social determinants. We furthermore examine evidence of such inequality in Japan. Results confirmed that there is indeed health inequality, with persons with higher incomes and school educational levels having better oral health and observing better oral-health-related behaviors. Studies in Japan, where dental treatment is covered under the government's universal health insurance system, also found similar health inequality. Health inequality greatly depends on not only inequality in the treatment of diseases but also inequality in the incidence of diseases. For this reason, it is found that there is health inequality even when treatment fee is covered by health insurance. In order to reduce health inequality, efforts to reduce inequality in the incidence of dental diseases and their treatment would be necessary. It is difficult to take preventive measures for patients who do not change their behavior readily even when education is provided many times or for those who do not visit clinics for dental examinations in the first place. In order to promote the health of society as a whole, including these patients, it is necessary to consider the social determinants of health that underlie the behavior of these patients when taking preventive measures for them. Clarifying the social determinants that affect health and creating an environment that enables health promotion are needed to reduce health inequality.

[Introduction]

One problem faced by dentists when they provide dental treatment is how to deal with patients who do not change their behavior even when education is provided many times and those who do not visit clinics for dental examinations in the first place. Previously, traditional psychology and studies of health education directed attention to the importance of guidance to motivate patients to observe better oral-health-related practices. However, such education does not reach patients who do not come to clinics for guidance in the first place. There are also patients who do not mend or improve their behavior although they receive education repeatedly and have sufficient knowledge, just as some doctors and dentists cannot stop people from smoking or make people decrease excess weight. However, many of these people, who do not come to clinics for guidance or cannot mend their behavior, rush to dental clinics once they are affected by dental diseases, which is quite a familiar situation. These problems are actually often encountered in the field of health care and are also called the "inverse care law[1]" and "inverse prevention law[2]." The notion that studies of public health and social epidemiology have recently clarified these problems as they developed is called the "social determinants of health," which affect the health and behavior of people.

In recent years, the social determinants of health have attracted public attention. This notion has been introduced into government policies, as well as the subject of research and studies, in various countries of the world, including Japan. The social determinants of health encompass diverse physical and social environments, including medical insurance systems, which affect people as they are born and raised, live, work, and become old[3,4]. These represent the greatest causes of health inequality found in a country and between countries, and these can be avoided if dealt with appropriately[3,4]. The social determinants of health, considered as "the causes of causes" of diseases, affect the behavior of people and raise the risk of diseases[4]. Figure 1 shows the notion applied to dental diseases. The background factors that affect the direct causes of dental

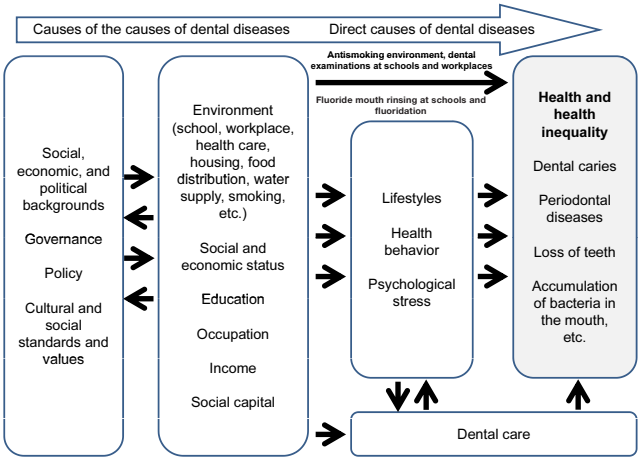

Figure 1: Social determinants affecting dental diseases and health-related behaviors

diseases are defined as the social determinants of dental health. The International Association of Dental Research (IADR) positions health inequality as one of its important research subjects[5] and started accumulating evidence to reduce health inequality organizationwide[6]. Health inequality is also regarded as a major problem in Japan. The government's health policy known as "Healthy Japan 21" (second phase covering the period from fiscal 2013 to 2022) states that the first priority is "the extension of healthy life expectancy and reduction of health inequality," emphasizing the necessity of reducing such inequality and positioning it as one of its important policies[7]. The first item of the Basic Matters Related to the Promotion of Dental and Oral Health stipulated under the Act concerning the Promotion of Dental and Oral Health is "the reduction of health inequality to maintain and promote oral health," and emphasis is also placed on reducing health inequality in Japan. Importantly, health inequality considered as problematic in this context actually means "social gradients." The term "health inequality" immediately evokes an image of "polarization with some impoverished people in a poor state of health." However, the social determinants affect the health of all people and their health-related behavior. For this reason, even in a group of people who earn relatively high incomes, several levels of differences in health arise with those who have higher incomes being healthier than others with lower incomes in the group[8-10]. Health inequality represents social gradients that affect all people rather than a polarization of people[11,12]. Therefore, all people in a society have a risk of health deterioration. Therefore, not only a high-risk approach that focuses on some people with high-risk factors, but also a population-health approach that focuses on society as a whole, plays an important role in eliminating health inequality.

Underlying the focus on the social determinants of health as described above are deep insights into the real nature of human beings. This means that people tend to assume that they decide by their own will alone as to how to act. However, in reality, their decisions are affected by various factors. It is known, for example, that if people around you stop smoking you are likely to stop smoking or if those around you are overweight, you likely become overweight[13,14]. It has been reported that the physical environment and condition of the locality where one stays affects one's habit of exercise[15]. Living in an environment where people trust one another can help them maintain their health[16-18]. It is also known that the income of a household and the situation of a society affect the health of the members of the household and society and their lifestyles[19,20]. The knowledge accumulated from public health and social epidemiological studies has clarified that it is important to pay attention to various social determinants of health in addition to individuals' biological factors and lifestyles, to which attention was previously directed. Indeed, this is also drawing public attention in fields other than health care. In 2002, Daniel Kahneman, who is also a psychologist, won a Nobel Prize in economics. Economics had been theretofore conducted on the basis of "rational individuals" who make choices so that they profit even if the profit is only one yen. Kahneman raised doubts about this assumption and established behavioral economics, which clarifies economic activities in a real society taking into consideration biases in the actions of people and their choices. In the field of health and health care, as well, taking into account the health in an actual society and its social determinants will contribute greatly to health promotion.

Therefore, in this review, we provide an overview of the social determinants of general health and oral health.

[Objective]

The purpose of this review is to provide an overview of systematic reviews and meta-analyses of studies related to oral health, the social determinants of health, and health inequality worldwide including Japan.

[Methods]

As search terms, #1:"Social Determinants of Health" OR income OR education OR "social network" OR "social support" OR "social capital" OR "social cohesion" OR "social isolation" OR race OR ethnic OR socioeconomic OR job OR occupation OR "social class"; #2: "Periodontitis" OR "periodontal disease" OR "tooth disease" OR caries OR denture OR "oral prosthesis" OR teeth OR dental OR "oral care" OR "Oral health" OR "dentistry"; and #3: "meta-

analysis" OR "systematic review" were used. Using PubMed database, we conducted searches with [#1 AND #2 (titles and abstracts only) AND #3]. The last search was conducted on July 1, 2014. Furthermore, in order to retrieve Japanese articles, we also conducted searches with [#1 AND #2 (titles and abstracts only) AND #4 using #4]: "Japan OR Japanese." Moreover, a search was conducted manually to retrieve other articles that could not be obtained from the above searches.

[Results]

1. Systematic reviews or meta-analyses of studies regarding social determinants of oral health and oral health inequality

In total, twelve articles were found. When they were classified according to the outcomes of observational studies of social determinants and oral conditions, five of them were on dental caries[21-25], two on periodontal diseases[26,27], one on the oral quality of life (OHQoL)[28], and one on health-related behavior[29]. Three articles were on interventional studies to reduce health inequality[30-32]. Table 1 shows a summary of these articles. In many observational studies, the associations between the social determinants of oral health and dental diseases or dental health-related behavior were examined. These studies showed that people with lower school educational levels and incomes showed a higher risk of contracting dental diseases and observed poorer health-related practices. These people tended to be reluctant to seek dental treatment.

There were also reviews of intervention studies that took into consideration of reducing health inequality (Table 2). A review by Fox cited studies mainly of inequality in secondary prevention such as dental care and health examinations[30]. The measures that contributed to reducing inequality in dental treatment caused by socioeconomic conditions included providing dental treatment to students by visiting schools, offering dental care through dental access centers publicly established in communities with many people who were in poor oral health but did not undergo periodic oral examinations, and having nurses visiting homes to provide dental health education and distribute vouchers for dental treatment. Dental health examinations at schools were cited as a measure to reduce inequality in dental examinations. There were also studies of health promotion campaigns at shopping centers. A review of interventional studies of a high-risk group of natives of Alaska, many of whom had carious teeth, showed that educational interventions for families and communities, administration of fluoride, xylitol, chlorhexidine, and similar substances to pregnant women for maintaining dental health, and training of dental care providers helped reduce dental caries in this group[31]. A review study of water fluoridation showed that such fluoridation contributed to reducing health inequality in terms of dental caries by generally reducing the number of carious teeth of people in whole society especially in socioeconomically disadvantaged people[32].

2. Studies of social determinants of oral health and health inequality in Japan

As there has been no systematic-review or meta-analysis on the studies of oral health inequality in Japan, this section reviews individual studies in Japan. A review of studies of the social determinants of oral health and health inequality in Japan found articles on the number of elderly people's remaining teeth[33,34], health inequality among users of dentures[35, 36], health inequality among those with carious teeth[33,37-39], health inequality among those with periodontal diseases[9], income gap in health care including dental care[40], local environments related to dental treatment[41], social capital and oral health[42-45], and oral health of foreigners residing in Japan[46]. Table 3 shows a summary of these studies. These studies indicated that people with higher educational levels and incomes had more remaining teeth[33,34] and used more dentures,[35,36] whereas those with lower school education levels and incomes showed the opposite trend, indicating inequality. It was also found that there was inequality in terms of dental caries or the number of lost teeth[38] and periodontal diseases[9] owing to occupation. Furthermore, it was found that elderly people living in communities with a larger income inequality had fewer remaining teeth.[34] Moreover, three-year-old children living in communities with higher incomes had fewer carious teeth[45]. Another study showed that three-year-old children living in communities with highly educated people and a smaller number of siblings (those with a lower total fertility rate) or communities in municipalities with more topical fluoride application projects showed fewer carious teeth[37]. Other studies indicated that elderly people living in communities with a larger social capital showed more remaining teeth[43,44] and that three-year-old children living in such communities had fewer carious teeth[45]. Social capital was also related to young people's subjective ideas on oral health although they varied in the course of action they take[42]. People with higher incomes received dental treatment more frequently[40], and elderly women with more dental clinics in their neighborhood had their regular dentist[41]. A larger number of Brazilian children residing in Japan experienced dental caries more frequently when their mother had lower educational levels or when they had not

Table 1: Systematic reviews or meta-analyses of studies related to social determinants of oral health and oral health inequality

Authors	Survey year	Study design	Age	Subjects	No. of articles	Main predictors	Outcomes	Covariates	Details	Ref. no.
Hooley, Skouteris, Boganin, Satur, Kilpatrick	Articles since December 2005 (2006 - 2011)	Systematic review	Children aged 0-6	Infants	55	Parents' educational history, ethnicity, income	Dental caries in childhood	Parents' feeding practices, behaviors, and oral conditions, etc.	Although up to the present, many studies have been performed on individual factors that affect early childhood caries (ECC), the focus has shifted to studies regarding broader socioeconomic factors in recent years. The objective was to conduct a systematic review regarding parental influences, which are likely associated with the intermediary mechanism between these factors and dental caries, on the development of caries in children aged 0 - 6 years. Fifty-five articles from 2006 - 2011 reporting the association between ECC and parent attributes (socioeconomic status, oral health conditions, feeding practices, and knowledge) were collected. Many studies have examined parents' social factors, feeding practices, and diet, and only a few studies have explored parents' attributes, attitudes, and beliefs, with none focusing on the mechanisms.	21
Costa, Martins, Bonfim Mde, Zina, Paiva, Pordeus, Abreu	Articles up to August 2012, with no restrictions placed on the year of publication	Systematic review	Adults aged 19-60	Adults	41	Socioeconomic status	Dental caries	Gender, age, oral health indicators, etc.	An increasing number of studies are performed on the association between socioeconomic factors and dental caries. This study conducted a systematic review regarding the association between dental caries in adults and socioeconomic factors. Forty-one articles were extracted from seven databases and were evaluated using the Newcastle-Ottawa scale. The socioeconomic indicators used included educational level, income, occupation, socioeconomic status, and the community index. Education, income, occupation, and the Gini coefficient were associated with the development of dental caries (the association was such that the worse the condition, the more dental caries). Future studies will require standardization of socioeconomic indicators. Socioeconomic factors are associated with dental caries.	22
Harris, Nicoll, Adair, Pine	Studies from 1995 to 2000	Systematic review	6 years old or younger	Children	77	Oral hygiene status, eating habits, bacterial flora of the mouth, enamel hypoplasia	Dental caries	Gender, age, other socioeconomic factors, etc.	This study examined risk factors for dental caries in deciduous teeth of children aged 6 years or younger through a systematic review. Seventy-seven articles were found applicable, of which 43 were cross-sectional studies, 19 were cohort studies, 8 were case-control studies, and 7 were intervention studies. For dental caries, 106 risk factors were confirmed. It was suggested that children infected with Streptococcus Mutans at an early age are most likely to develop caries, although other factors could partially explain the incidence. Low socioeconomic status was associated with a high caries experience. Yet, there was a shortage of studies with an excellent design.	23

Table 1 : (continued)

Authors	Survey year	Study design	Age	Subjects	No. of articles	Main predictors	Outcomes	Covariates	Details	Ref. no.
Reisine, Psoter	Articles in English published since 1975 with regard to behaviors, and those published since 1990 up to 2000 with regard to socioeconomic status	Systematic review	≤6 months after birth - 65 years	General population	272	1. Socioeconomic status (SES), 2. Tooth-brushing, 3. use of the baby bottle	Incidence and prevalence of dental caries	Water fluoridation situation, weaning, snacking, etc.	This study investigated whether the incidence and prevalence of dental caries are associated with 1) socioeconomic status (SES), 2) tooth-brushing, and 3) the use of a baby bottle. Articles in English published since 1975 were used (272 articles). There was strong evidence that low SES increased the risk for caries among children aged <12 years old. This evidence tended to be stronger in children, and weaker in adults. There was weak evidence suggesting that tooth-brushing prevented dental caries. However, the effect of tooth-brushing alone was uncertain, as it included fluoride-containing dentifrices, or mechanical plaque removal. No correlation was found between the use of a baby bottle and dental caries risk. These results show that SES is a risk for dental caries, and tooth-brushing needs to be recommend along with fluoride-containing dentifrices. It should also be recommended that the use of a baby bottle be refrained after 12 months have passed since the birth.	24
Castilho, Mialhe, Barbosa Tde, Puppin-Rontani	Studies from 1980 to June 2012	Systematic review	3-15 years	General population	13	Parents' oral health-related behaviors	Dental caries in children	Sugar consumption, parents' occupation, mother's age, etc.	This study examined parents' oral health-related behaviors and their children's dental caries. Through a search of studies from 1980 up to December 2012 targeting children, 13 studies that had conducted a dental health examination were included in analysis. Parents' dental health habits affect children's oral health. Socioeconomic status, such as parents' occupation, affected oral health of their children. Oral health education programs aimed at encouraging preventive actions are necessary not only to promote good oral health in children but also achieve higher quality of life. Attention should be directed toward the entire family, concerning lifestyle as well as oral health habits.	25
Boillot, El Halabi, Batty, Range, Czernichow, Bouchard	Studies until November 2010	Meta-analysis	35 years old or older	General population	18	Educational attainment	Periodontal diseases	Gender, age, other socioeconomic factors, etc.	The impact of socioeconomic inequalities on health is large, and periodontal disease is associated with cardiovascular diseases and other conditions. Previously, there existed no meta-analysis of health inequalities related to periodontal disease. Through a search of studies up to November 2010, targeting the general population aged 35 years or older, 18 studies were included in analysis. Compared to individuals with high educational attainment, those with low educational attainment showed a higher risk for periodontal disease (OR: 1.86[95%CI:1.66-2.10]; p,0.00001).This relationship could be partially explained by covariates. Criteria for periodontal disease and educational attainment varied among the studies. No significant publication bias was observed. The studies found health inequalities in periodontitis. Early life intervention is likely necessary.	26

Table 1 : (continued)

Authors	Survey year	Study design	Age	Subjects	No. of articles	Main predictors	Outcomes	Covariates	Details	Ref. no.
Klinge, Norlund	Studies from 1965 to 2004	Systematic review	17 years old or older	General population	47	Educational attainment, income, occupation	Periodontal diseases	Smoking, health behaviors, gender, age, race, etc.	Previous studies have reported variable associations between socioeconomic status and periodontal diseases. Accordingly, a systematic review was conducted to clarify the association between socioeconomic status and periodontal disease. As a result, 29 of 36 cross-sectional studies and 5 of 11 longitudinal studies supported the association between socioeconomic status and periodontal diseases. There were 17 cross-sectional studies that had taken smoking into consideration, and the association between socioeconomic status and periodontal diseases was supported by 11 of those. From this review, although socioeconomic status is associated with periodontal diseases, its importance is likely not as great as that of smoking.	27
Kumar, Kroon, Lalloo	Studies until August 2013	Systematic review	Less than 18 years old	General population	36	Socioeconomic status, home environment, family structure, number of siblings, household crowding, parents' age, and parents' oral health literacy	Oral QOL	Various covariates (analysis results before and after adjustment for covariates are shown)	Socioeconomic status and home environment have various impacts on children, and also affect their oral health-related quality of life. Accordingly, a systematic review was conducted regarding the effects of socioeconomic status and home environment on oral health-related QOL in children. Studies on the effects of socioeconomic status, home environment, family structure, number of siblings, household crowding, parents' age, and parents' oral health literacy on oral health-related QOL in children were searched, and 36 studies were included in the review. Common findings from the majority of the studies suggested that children from families with good income, educational attainment, and economical status had better oral health-related QOL. Moreover, mothers of lower age, family structure with a single parent, more crowded household, and higher number of siblings were significantly associated with poorer oral health-related QOL in children. However, a definitive conclusion could not be derived due to large differences in methods, etc., among the studies.	28
Smith, MacEntee, Beattie, Brondani, Bryant, Graf, Hornby, Kobayashi, Wong	Articles in English published between January 1, 1950 and June 25, 2010	Meta-synthesis	Elderly people	Elderly Chinese immigrants	40	The influence of culture	Oral health-related behavior and oral care	Socioeconomic status, educational attainment, etc.	It is predicted that the cultural background of immigrants affects their oral health behaviors. In particular, Chinese immigrants are expected to have worsened oral conditions due to a distrust of Western medicine. In this study, 40 English articles published between January 1, 1950 and June 25, 2010 were used to perform a meta-synthesis. Few studies have investigated temporal changes in Chinese immigrants to accept Western oral healthcare from the perspective of traditional values. Furthermore, the effects of socioeconomic status, education, and cultural background on dental clinic visit have not been adequately studied. Sufficient medical services need to be provided for immigrants with various cultural backgrounds.	29

Table 2: Studies of oral health inequality and social determinants of oral health in Japan

Authors	Survey year	Study design	Age	Subjects	No. of articles	Main predictors	Outcomes	Covariates	Details	Ref. no.
Fox	Studies from 1950 to September 2009	Review	0 year -adult	Families from deprived areas	6	Dental access center, dental health examination at schools, mobile dental unit at school premises, dental health promotion education at shopping centers	Increased dental attendance	-	Socioeconomic factors are important determinants of oral health inequalities. While people in lower socioeconomic groups or those living in areas of low socioeconomic status have higher risks of diseases, they have difficulty visiting a dentist. This study searched studies that had targeted families from deprived areas up to September 2009, and examined 6 studies that had evaluated the effectiveness of various approaches aimed at increasing dental attendance in deprived areas. Two approaches were confirmed to be the most effective in increasing dental attendance by families from deprived areas: the mobile dental unit at school premises and the dental access center (DAC). It is necessary to determine the best ways to address the treatment needs of families and children of lower socioeconomic status and conduct higher quality research.	30
Chi	Until October 5, 2012	Systematic review	Less than 18	Alaska Native children	9	1) Education intervention for families and communities, 2) dental chemotherapeutics for pregnant women (use of fluoride, xylitol, chlorhexidine, etc.), 3) training of mid-level dental care providers	Dental caries in children	-	Dental caries show the highest prevalence among pediatric diseases, and the spread of pediatric dental caries is a serious issue in Alaska Native communities. When untreated, dental caries cause pain, infection, systemic health problems, hospitalization, and sometimes even death. Apart from these health issues, dental caries also lead to absence from and poor grades at school, and low quality of life (QOL). However, the extent of the effect of population-based oral health interventions on dental caries among Alaska Native pediatric populations is unknown. Accordingly, the present study was conducted with the following two aims targeting Alaska Native children below the age 18: 1) to conduct a systematic review of oral health interventions, and 2) to present a multi-level intervention model (individual, family, community, state, and other various levels) and case study aimed at reducing sugar-sweetened beverage (SSB) intake. Searches using "Alaska Native," "children," and "oral health" resulted in identification of 85 studies in Medline, Embase and Web of Science databases, and 66 studies in GoogleScholar. Of these, 9 publications were qualitative review articles. These publications described the following three interventions aimed at reducing pediatric dental caries: 1) education interventions for families and communities, 2) use of fluoride, xylitol, and chlorhexidine to promote dental health in pregnant women, and 3) training of mid-level dental care providers. These interventions are likely to reduce dental caries in Alaska Native children, but on the other hand, it appeared necessary that some aspects be resolved in terms of intervention acceptability, comprehensiveness, and sustainability. Further research is needed to reduce health inequalities.	31

Table 2 : (continued)

Authors	Survey year	Study design	Age	Subjects	No. of articles	Main predictors	Outcomes	Covariates	Details	Ref. no.
Parnell, Whelton, O'Mullane	From January 1, 2000 to October 17, 2008	Review of systematic reviews	—	Subjects were not narrowed down at the stage of search	3 systematic reviews and 3 guidelines. Discussion is mainly based on the 3 systematic reviews.	Water fluoridation	Dental caries and safety	—	The purpose of this study was to conduct a systematic review (SR) of the effectiveness and safety of water fluoridation. Although the quality of included SRs was high, the studies included in the SRs were of moderate to low quality. All of the three SRs showed that water fluoridation was effective in reducing pediatric dental caries. With the exception of dental fluorosis, no adverse effects were observed. Fluoridation reduces dental caries for all social classes. There is evidence that it even reduces the oral health gap between social classes. Water fluoridation is technically feasible, and if the region is culturally open to the idea, it still offers a reasonable option as a population-level dental caries prevention measure.	32

Table 3: Systematic review of intervention studies to reduce oral health inequality

Authors	Survey year	Study design	Age	Subjects	No. of subjects	Main predictors	Outcomes	Covariates	Details	Ref. no.
Morita, Nakagaki, Yoshii, Tsuboi, Hayashizaki, Igo, Mizuno, Sheiham	April 2005-March 2006	Cross-sectional	20-69 years	Japanese male workers	15,803 men	Seven groups classified by occupation	CPI	Age, diabetes mellitus, smoking history	This study aimed to examine whether disparities by occupation existed concerning periodontal diseases in a Japanese working population. Study participants were 15,803 Japanese male workers aged 20-69 years, and differences among seven groups classified by occupation were examined. The community periodontal index (CPI) was used as an indicator of periodontal diseases. The percentage of professionals with a CPI score of 3 or 4 was significantly lower, in comparison with those in other job classes. There were also clear disparities in those with a CPI score of 4. After adjusting for age, diabetes mellitus, and smoking history, the risk of scoring the CPI of 3 or 4 was higher by 2.0 fold in drivers, 1.5 fold in those in service sector, 1.4 fold in salespersons, and 1.4 fold in business managers, compared to professionals. After adjusting for age, diabetes mellitus, and smoking history, the risk of scoring the CPI of 4 was higher by 2.1 fold in drivers, 1.5 fold in those in service sector, 1.5 fold in salespersons, and 1.2 fold in business managers, compared to professionals.	9
Ueno, Ohara, Inoue, Tsugane, Kawaguchi	May 2005	Cross-sectional	55－75 years	Community dwellers	10,236	Education level	20 or more/less than 20 teeth, number of remaining teeth, number of filled teeth, number of functional teeth	Gender, age, household size and diet, dental health behaviors, smoking, oral hygiene status	In Japan, where dental care is included in the universal health insurance coverage, whether health inequalities exist by education level was examined. In the general population (age range, 55-75 years), the proportion of subjects with 20 or more teeth, number of remaining teeth, number of filled teeth, and number of functional teeth were lower in those of a lower education level.	33
Aida, Kondo, Kondo, Watt, Sheiham, Tsakos	2003	Cross-sectional	65 years old or older	Community dwellers	3,451	Income inequality, social capital	20 or more/less than 20 teeth, self-rated health	Gender, age, education, marital status, individual- and community-level equivalent income, and smoking	In 2003, a postal survey of healthy individuals aged 65 or older was conducted to investigate what kind of people had poor self-rated health and a low number of remaining teeth (19 or less). Data from 3,451 participants were used. The results showed that residents of areas with large income disparities reported lower self-rated health and a fewer number of remaining teeth. In particular, the trend was stronger with respect to the number of remaining teeth. Community-level social capital attenuated the relationship between income inequality and self-rated health, only by 16%.	34

Table 3 : (continued)

Authors	Survey year	Study design	Age	Subjects	No. of subjects	Main predictors	Outcomes	Covariates	Details	Ref. no.
Yamamoto, Kondo, Aida, Suzuki, Misawa, Nakade, Fuchida, Hirata	July 2010-January 2012	Cross-sectional	65 years old or older	Community-dwelling elderly	54,388	Age, marital status, equivalent income, education, number of remaining teeth, present illness, social participation, social support, social networks, community social capital	Denture or bridge use	—	The use of dental prosthesis has been suggested to prevent disorders in the elderly. This study examined factors - mainly social determinants that promote prosthesis use - in Japanese community-dwelling elderly. The results showed that prosthesis use was significantly higher in individuals with high equivalent income, a fewer number of remaining teeth, or present illness, as well as those living in densely populated areas. The result of stratified analysis by gender revealed that men with high education attainment, and women with high social participation, used dental prosthesis significantly more. No significant association was found between social capital and prosthesis use.	35
Matsuyama, Aida, Takeuchi, Tsakos, Watt, Kondo, Osaka	2010	Cross-sectional	65 years old or older	Community-dwelling elderly	4,001	Income (household income)	Denture or bridge use	Gender, age, education, and size of household	Health inequalities exist in many countries. In Japan, where the universal health insurance system has been implemented, a survey targeting community-dwelling elderly individuals aged 65 or older revealed the following facts: 1) 31.2% of individuals who do not have a sufficient number of teeth use no dental prosthesis (denture or bridge); 2) the rate of prosthesis use differed by income, and low-income respondents tended to not use dental prosthesis; and 3) compared to the lowest-income respondents, those in the next (higher) income bracket showed a higher rate of prosthesis use. With regard to 1), partially, and 2), it is possible that the financial burden of making prosthesis may be associated with reduced dental visits. With regard to 3), possible explanations include the impact of the medical expense assistance system for welfare-payment recipients, and encouragement by administrative staff etc., for low-income people to visit a dentist at the time of utilization of various social security systems. Prosthesis use is important for the maintenance of masticatory and conversational functions, and measures to facilitate prosthesis use will be necessary.	36

Table 3 : (continued)

Authors	Survey year	Study design	Age	Subjects	No. of subjects	Main predictors	Outcomes	Covariates	Details	Ref. no.
Aida, Ando, Aoyama, Tango, Morita	2000	Ecological	3 years	All Japanese 3-year-old children	3,251 municipalities	Sociodemographic factors (the proportion of residents with high educational background, total fertility rate, the proportion of workers in the manufacturing industry, unemployment rate) and dental health indicators (density distribution of dental clinics in the area, presence of dentists and dental hygienists at a healthcare center, administrative fluoride application and health guidance, attendance rate of dental check-up)	Caries prevalence in 3-year-old children	Health and hygiene budget, size of household, percentage of children attending a nursery school	This study examined the extent to which social factors and public dental health services contribute to caries prevalence in 3-year-old children in each municipality. The disease map indicated regional disparities in caries prevalence in 3-year-old children. Education and total fertility rate were the variables that contributed the most to regional disparities in caries among 3-year-old children (accounting for 26% and 8%, respectively). Regions with a high proportion of residents with high education levels had a lower prevalence of caries, and regions with a high total fertility rate (i.e., a greater number of siblings) had a significantly higher caries prevalence. (The income indicator was not put in, as the correlation with the education indicator was too high.) Among the indicators of dental health care, the frequency of fluoride application was the only indicator significantly associated with dental caries (a decreasing trend), but this association was weaker compared to social factors.	37

Table 3 : (continued)

Authors	Survey year	Study design	Age	Subjects	No. of subjects	Main predictors	Outcomes	Covariates	Details	Ref. no.
Morita, Nakagaki, Yoshii, Tsuboi, Hayashizaki, Mizuno, Sheiham	April 2005-March 2006	Cross-sectional	20-69 years	Japanese male workers	16,261 men	Seven groups classified by occupation	DMFT, number of missing teeth	Age, number of natural teeth, number of healthy teeth	This study aimed to examine whether there are disparities in oral status by job classification in Japanese workers. Differences among seven job groups were examined through a survey of 16,261 Japanese male workers aged 20-69 years. The number of decayed, missing, or filled teeth (DMFT) and the number of remaining teeth were used to assess oral status. Professionals, managers, and office workers had better oral status than those in service sector or drivers. Professionals had significantly more natural and healthy teeth compared to workers of other job types. The DMFT of professionals was significantly lower than those of workers of other job types. Professionals had a significantly higher number of restored teeth compared to workers of other job types. The number of restored teeth was significantly higher in office workers compared to that of managers, engineers, salespersons, those in service sector, or drivers. Drivers and those in service sector had more caries compared to professionals (1.8 fold and 1.3 fold, respectively). Engineers, salespersons, those in service sector, and drivers had more lost teeth (1.3 fold, 1.3 fold, 1.4 fold, and 2.1 fold, respectively). The number of people with 20 or more teeth was lower in engineers, those in service sector, and drivers compared to professionals aged 50-69 years (1.7 fold, 1.7 fold, and 3.1 fold, respectively).	38
Tanaka, Miyake, Sasaki, Hirota	2001-2003	Cohort	41-50 months old	Japanese infants	315	Maternal or paternal education, income, occupation	Caries experience	Maternal age, smoking, children's gender, breast-feeding period, dietary habit, teeth eruption time, tooth-brushing, fluoride application, and dental check-up	In a cohort of 315 infants, the relationship between caries experience and socioeconomic status was investigated. Children of parents with ≥15 year of education had less caries experience compared to children of parents with ≤ 13 years of education. (Odds ratio = 0.34, 95% confidence interval = 0.14; 0.70.) No significant association with income or occupation was observed. A higher level of parental education, especially among mothers, is likely associated with a low risk of caries in children.	39

Table 3 : (continued)

Authors	Survey year	Study design	Age	Subjects	No. of subjects	Main predictors	Outcomes	Covariates	Details	Ref. no.
Watanabe, Hashimoto	1986-2004	Time-series cross-sectional	20 years or older	Subjects of the national tax survey	45,586 people and 16,177 households	Household income	Access to healthcare, subjective health status, healthcare need	Marital status, number of doctors per thousand people in residential areas, etc.	The aim of universal health insurance is to ensure access to appropriate medical care at an affordable cost. However, it might not be an effective measure for impoverished families. Accordingly, we investigated the relationship between household income and access to health care including dental visit, subjective health, and healthcare need. Time-series cross-sectional data concerning 45,586 individuals from 16,177 households between 1986 and 2004 were used to perform this analysis. The results showed that the higher household income, the better access to healthcare. In particular, it was suggested that inequalities in healthcare access had increased since the 2000s. High equality was achieved among those aged 65 or older. However, among people aged 20-64, differences by household income were observed. Changes in household income and copayment policy were suggested to be the major causes of inequalities in healthcare use and differences in subjective health status. It was also suggested that the achievement of fairness in medical care through universal coverage needs to be recognized as an ongoing project.	40
Hanibuchi, Aida, Nakade, Hirai, Kondo	2003	Cross-sectional	65 years old or older	General elderly population	2,192	Six types of accessibility to a dental clinic (distance to a dental clinic, number of dental clinics, number of dentists)	Presence of a primary care dental clinic	Age, marital status, equivalent income, GDS, IADL, frequency of going out, number of remaining teeth	Accessibility to dental treatment is a serious issue. To date, no study has investigated the opportunity to receive dental treatment in Japan. In 2003, a survey of elderly individuals aged 65 or older was conducted to investigate the presence of a primary care dental clinic and geographical accessibility to a dental clinic. An association between having a primary care dental clinic and geographical accessibility was only found in women. Among individuals with a primary care dental clinic, the distance to the closest dental clinic was shortest (OR: 0.62 [0.43-0.90]). In addition, the number of dental clinics at the school district level was higher (OR: 1.14 [1.03-1.26]), the number of dental clinics at the municipality level was higher (OR: 1.02 [1.00-1.05]), and the density distribution of dental clinics was higher (OR: 1.56 [1.11-2.19]). These relationships could be partially explained by covariates; the significance disappeared for the distance to and the number of dental clinics, while only the density distribution of dental clinics showed a significant relationship. There are large gender differences concerning accessibility to a dental clinic, and in elderly women, those with a nearby dental clinic visited a dental clinic more.	41

Table 3 : (continued)

Authors	Survey year	Study design	Age	Subjects	No. of subjects	Main predictors	Outcomes	Covariates	Details	Ref. no.
Furuta, Ekuni, Takao, Suzuki, Morita, Kawachi	2010	Cross-sectional	18-19 years	University students	967	Social capital	Self-rated oral health	Gender, self-perceived household income, oral health behaviors, fear of dental treatment, etc.	This study investigated the impact of social capital on self-rated oral health among Japanese university students. A cross-sectional survey was conducted in 2010, targeting 967 first-year university students aged 18-19 years. Of these, 22% responded poor self-oral health. After adjusting for covariates, a significant association was found between a lower level of neighborhood trust and poorer self-rated oral health (OR: 2.22, 95% CI: 1.40-3.54). In addition, a lower level of vertical trust in school was associated with poorer self-rated oral health (OR: 1.71, 95% CI: 1.05-2.80). However, an association was found between low informal social control and better self-rated oral health (OR: 0.54, 95% CI: 0.34-0.85). High trust in community will promote better self-rated oral health.	42
Aida, Kuriyama, Ohmori-Matsuda, Hozawa, Osaka, Tsuji	2006	Cross-sectional	65 years old or older	Community-dwelling elderly	21,736	Social capital	20 or more/less than 20 teeth	Age, gender, education, frequency of tooth-brushing, duration of tooth-brushing, use of a dental floss and interdental brush, dental visits for purposes other than treatment, intake frequency of confectionery, history of diabetes mellitus, self-rated health, social networks and support	Social capital refers to social resources arising from the trust and network among people. It has been reported that richer social capital promotes better health. There is a possibility that with richer social capital, information regarding health could spread faster, and good heath behaviors could take root more easily (e.g., by mimicking neighbors). Moreover, residents may become more involved in efforts to promote active community healthcare services. However, even with consideration given to various lifestyle habits and individual connections (social networks), or the presence of any individual who could help (social support), whether there is an association between neighborhood social capital and dental health is still unknown. In this context, this study investigated what kind of association exists between social capital and the number of remaining teeth. The results of multilevel logistic regression analysis showed that residents of areas with rich social capital based on friend networks had a 1.17-fold higher odds ratio for having 20 or more teeth (95% CI = 1.04-1.30).	43

Table 3 : (continued)

Authors	Survey year	Study design	Age	Subjects	No. of subjects	Main predictors	Outcomes	Covariates	Details	Ref. no.
Aida, Hanibuchi, Nakade, Hirai, Osaka, Kondo	2003	Cross-sectional	65 years old or older	Community-dwelling elderly	5,560	Horizontal and vertical type social capital	20 or more/less than 20 teeth	Age, gender, education, income, dental health behaviors, primary care dentist, smoking, depressive state, frequency of going out	There exists no study that examined individual- and community-level social capital and dental health among elderly individuals. Moreover, only a few studies have examined the association of social capital, classified as horizontal or vertical, with health. For these reasons, this study was conducted with data concerning elderly Japanese. The results of multilevel logistic regression analysis revealed that, compared to individuals who participated in horizontal groups (i.e., groups of equals), those who did not participate had a 1.45-fold higher risk of having 19 or less teeth (95% CI = 1.21-1.73). On the other hand, individuals who participated in vertical groups (i.e., groups that encouraged hierarchical relations) showed no statistical difference compared to those who did not. Furthermore, even in cases where individual group participation was considered statistically similar, residents of areas with fewer horizontal groups, compared to residents of areas with more horizontal groups, had a 1.25-fold higher risk of having 19 or less teeth (95% CI = 1.03-1.52). On the other hand, no statistical differences were found between residence areas with more and less vertical groups.	44
Aida, Ando, Oosaka, Niimi, Morita	May 2005-February 2006	Cross-sectional	3 years	3-year-old children randomly extracted from municipalities	3,086	Community-related social background (social cohesion related to social capital, average income, etc.)	Number of deciduous teeth with dental caries (dmft)	Gender, birth order, living with grandparents, parental smoking, parental occupation, age at which tooth-brushing was started, frequency of tooth-brushing, use of fluoride dentifrices, weaning age, intake frequency of sweets and drinks	In addition to individual behaviors, community-related factors have also been reported to affect individual health. However, there have been no studies regarding dental caries experience in people living various regions. Accordingly, this study was conducted, targeting 3-year-old children in Japan. The results showed that 90.8% of variance in caries occurred at the individual level, and 9.2% at the municipal level. However, individual factors such as dietary habits only explained 6.6% of the individual-level variance in caries. On the other hand, community-level variables, such as social cohesion and income, explained 47.2% of the community-level variance in caries. At the community level, higher social cohesion and income were associated with fewer dental caries, whereas a higher number of food and drink retailers per person and higher expenses for public health services were associated with more dental caries. The social environment in community was associated with dental caries in 3-year-old children.	45

Table 3 : (continued)

Authors	Survey year	Study design	Age	Subjects	No. of subjects	Main predictors	Outcomes	Covariates	Details	Ref. no.
Hashizume, Shinada, Kawaguchi	—	Cross-sectional	6-14 years	Brazilians living in Japan	378	Maternal educational level, with/without paternal health insurance, frequency of sugary snack intake, use of dental treatment in Brazil	With or without caries experience	Gender, age	Among the Japanese population, the third largest ethnic group consists of immigrants from Brazil. So far, no reports exist regarding factors associated with the prevalence of caries in Brazilian children living in Japan. A survey of Brazilian children aged 6-14 living in five areas in Japan, where large numbers of Brazilian immigrants had settled, was conducted. Data from 378 children were included for this analysis. Of these, 61.9% of children were caries-free, with a mean DMFT of 1.28±2.22 (mean± SD). Children of mothers with low educational attainment had more caries experiences compared to children of mothers with high educational attainment (OR: 3.48 [95%CI:1.3-8.9];p = 0.001). Moreover, children who had not made any dental visit in Brazil, compared to those who had, had more caries experiences (OR: 2.69 [95%CI:1.0-6.7]; p = 0.034).	46

received dental treatment in Brazil[46].

[Discussion]

These systematic reviews and meta-analyses confirmed that there was indeed health inequality, with people with higher incomes and educational levels being in better oral health and observing better oral-health-related behaviors. A similar health inequality was confirmed by studies in Japan, where dental treatment is covered by the government's universal health insurance system. Health inequality is greatly affected by not only inequality in the treatment of diseases but also that in the incidence of diseases. From these findings, it is determined that health inequality exists even when treatment fee is covered by health insurance. Efforts to reduce inequality in both the incidence of dental diseases and their treatment would be necessary.

Health inequality represents social gradients that affect all people rather than a polarization of people with only some of them affected by ill health[11,12]. A high- risk approach does not involve interventions in people who have a certain degree of risk but not considered to be high. Since there is a prevention paradox[47] that the incidence of diseases is higher in a large number of low-risk people than in a small number of high-risk people, it is necessary to carry out preventive measures in a large number of low-risk people. In addition, it is difficult to obtain effects when undertaking preventive measures that depend on self-responsibility mainly because some of the high-risk people are poor or otherwise disadvantaged and are therefore reluctant to seek treatment even when they are recommended to do so. On the other hand, a population-health approach aims to change the environment of the entire group, and is effective in diminishing health inequality by achieving large effects among a small number of high-risk people and small effects among a large number of low-risk people[48]. Examples of projects effectively using population-health approaches, by which the living environment is changed for better health, include dental examinations and treatment at schools to reduce inequality in treatment opportunities[30], group mouth rinsing at schools using fluoride to reduce inequality in the occurrence of dental caries[49,50], and water fluoridation[32,51]. The World Health Organization (WHO) reviews measures to abolish health inequality on a disease-by-disease basis, and the review includes measures to cope with dental diseases as described above[52].

It was also suggested that various social determinants affected oral health as exemplified by the effects of the distance to clinics on whether people were willing to seek dental treatment and the influence of the cooperative human relationships that brought about a greater social capital on the health of people. It is necessary to clarify the social determinants that improve health and create an environment conducive to health promotion.

[Conclusions]

There exist health inequality in terms of oral health, dental diseases, and health-related behavior. Clarifying the social determinants that affect oral health and creating an environment conducive to health promotion are needed.

[Conflict of interest]

There are no items applicable to "conflict of interest" in this article.

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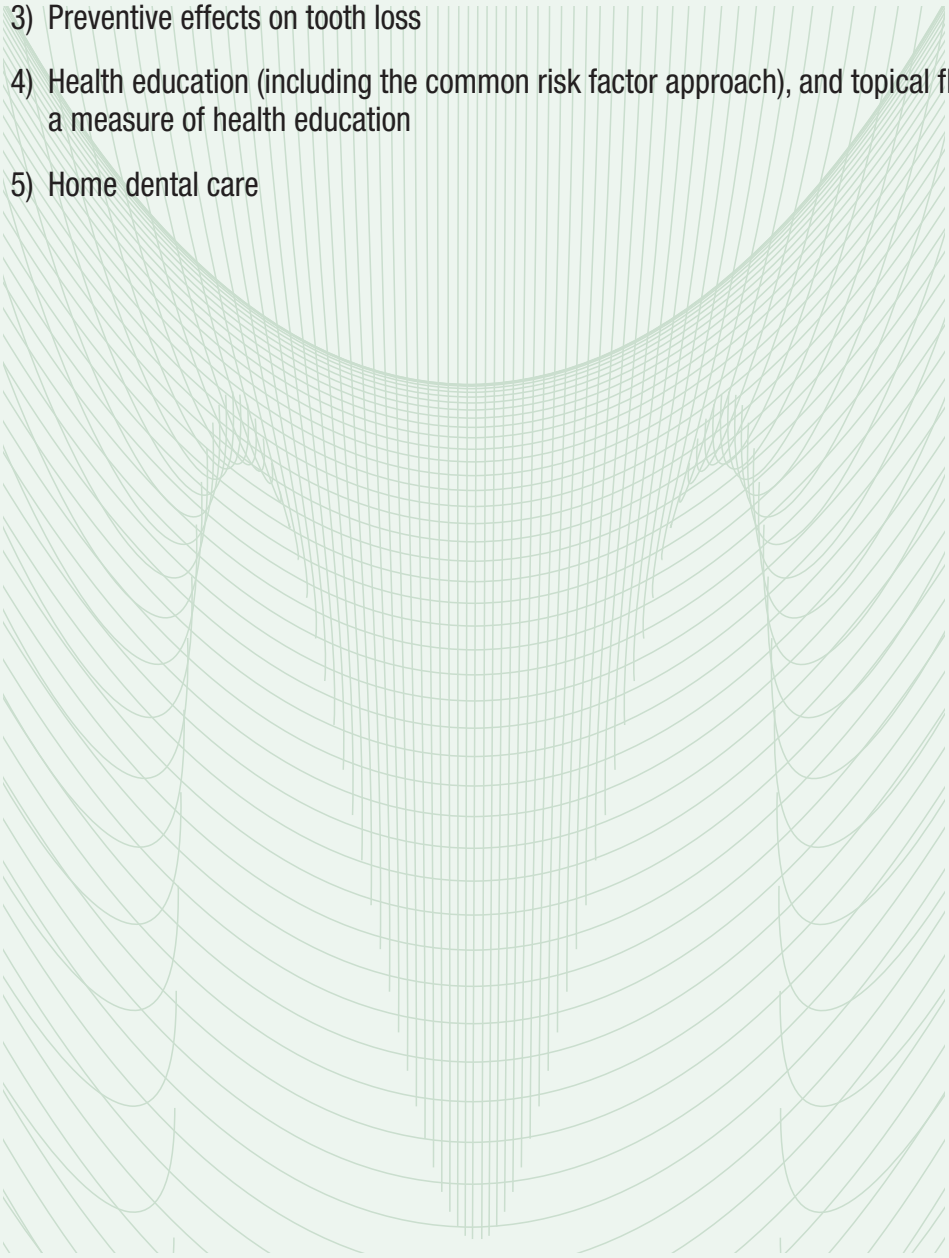
Ⅱ Issue-specific reviews of the evidence

9. Effects of dental care

1) Effects of oral care on postoperative recovery period and state (including multidisciplinary cooperation)
   – Role of oral care in perioperative complications in surgery –
2) Oral function deterioration prevention and recovery
3) Preventive effects on tooth loss
4) Health education (including the common risk factor approach), and topical fluoride application as a measure of health education
5) Home dental care



9. Effects of dental care

1) Effects of oral care on postoperative recovery period and state (including multidisciplinary cooperation)

– Role of oral care in perioperative complications in surgery –

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[Abstract]

Inhibiting perioperative complications in surgery has significance not only in terms of improving prognosis but in medical economic terms as well. Since some postoperative complications occur in relation to the environment in the oral cavity (including sanitary conditions and dental diseases), proper perioperative oral management can be expected to decrease the risk of pneumonia and other infectious complications, support resumption of oral ingestion following surgery, and contribute to postoperative recovery.

[Introduction]

Surgery is a form of treatment that subjects the body to a high degree of invasion. In order to provide high quality health care, it is necessary to reduce postoperative complications as much as possible with the aim of achieving a rapid recovery. In order to accomplish this, it is necessary for all members of the medical staff as a team, as well as the surgeon functioning as the primary physician, to provide support for the patient and prepare for surgery. Within that approach, the significance of perioperative dental support therapy and oral care performed by dentists, dental hygienists and other persons engaged in the providing of dental treatment is currently attracting attention as a means of reducing the risk of postoperative complications and enabling early discharge from the hospital[1].

Sanitary conditions within the oral cavity can easily be exacerbated around the time of surgery, infections within the oral cavity can easily be induced accompanying a decrease in general condition, dental caries and periodontal disease that were asymptomatic prior to surgery easily become acute, alveolar gingiva may become emaciated during the fasting period after surgery, or periodontal disease may be exacerbated causing teeth to become loose, resulting in problems such as no longer being able to wear dentures[2]. These conditions not only impair resumption of oral ingestion, but may even have an effect on restoration of general condition following surgery. In order to prevent such problems, it is recommended to undergo a dental examination prior to surgery and have first-aid dental procedures performed, including improvement of sanitary conditions in the oral cavity, correction of improperly fitting dentures and temporarily filling cavities whenever possible.

In addition, evidence is also being established which indicates that proper perioperative oral management makes it possible to reduce the risk of infectious complications caused by oral bacteria.

This review provides an overview of the relationship between the perioperative period in surgery and the oral cavity along with the potential for oral functional management to have a favorable effect on postoperative progress.

[Objective]

The purpose of this review is to conduct a search of the literature on the relationship between the perioperative period in surgery and the oral cavity, the potential for oral functional management to have a favorable effect on postoperative progress, and the significance of oral functional management performed by dentists during the perioperative period in surgery, followed by organizing the data obtained from this search.

[Methods]

An extensive search of the literature was made using the Internet (PubMed). The search covered the period from January 2014 to March 2014. A manual search was also performed in order to collect publications unable to be obtained from the Internet search. There were no restrictions placed on the year of publication of the literature. The contents of the search were organized from the resulting data.

[Results]

1. Oral Health Status of Patients Scheduled for Surgery

The majority of patients scheduled for surgical procedures have a latent potential for dental infectious lesions in the oral cavity in the manner of dental caries or periodontal disease. In addition, the environment in the oral cavity of patients in a hospital environment has been reported to exacerbate easily.

Terezakis E. *et al*. reported that oral health status (including accumulation of plaque, inflammation of gums and mucosal membrane status) tends to exacerbate during hospitalization and exacerbation of the environment in the oral cavity is related to risk of nosocomial infections to lower the quality of patient convalescence, and stated that this tendency is particularly prominent in patients that have undergone intubation[3]. In addition, Sjögren P. *et al*. reviewed five publications and reported that significant increases in caries, plaque accumulation, inflammation of the gums and oral mucositis are observed in the oral cavity during hospitalization[4]. In a survey of bacterial actually present in the oral cavity, Robert R. *et al*. reported that the number of plaque colonies increased proportional to the number of days spent in the ICU[5].

2. Risk of Damage to Teeth Accompanying Intubation for General Anesthesia

Highly invasive surgery is performed under general anesthesia by securing an airway by intubation. Tooth deciduation, subluxation, deciduation of metal crowns, fracture of alveolar bone, damage to oral mucosa and other damage to teeth that occurs as a problem associated with intubation constitute one of the most common types of perioperative complications[6].

Although there are considerable differences in the incidence of these problems depending on the particular institution, Warner, M. E. *et al*.[7] reported that they occur in one of 4,537 cases of general anesthesia, while Newland *et al*.[8] reported that they occur in one of 2073 cases, and although these numbers do not constitute an extremely high incidence, these problems not only increase the risk of accidental swallowing or accidental ingestion during surgery, but also can cause sharp edges of teeth to break through the cuff or impair resumption of oral ingestion following surgery. Once damage to teeth has occurred, a complete recovery becomes difficult, resulting in mastication disorders and decreased aesthetic properties, while also increasing the economic burden of dental treatment. Actually, the majority of the medical ligation brought against anesthesiologists is attributable to damage to teeth, and it is certainly one of serious complications[9].

According to a search for risk factors for teeth damage, the proficiency of the intubation procedure does not constitute a significant risk[10], while the factor that relates most closely with teeth damage is the poor condition of teeth, and is said to occur more easily during emergency intubation than during scheduled intubation[11]. Newland *et al*.[8] reported that teeth in poor condition during intubation have 20 times greater risk of damage than healthy teeth, while Werner, ME *et al*. reported the risk to be 50 times greater. Teeth damage occurs most frequently in anterior maxillary teeth, and according to a report by Givol *et al*.,[11] 86% of teeth damage was observed in anterior maxillary teeth, while Vogel *et al*. reported that incidence to be 75% or more.

The most effective means of risk management against teeth damage during intubation consist of endeavoring to employ a protective procedure during intraoral manipulation such as intubation, detubation or attaching a bite block, preliminarily ascertaining the presence of loose teeth, isolated teeth or teeth for which the eruption site is likely to obstruct the intubation procedure (poor teeth alignment, and particularly when anterior maxillary teeth are protruding forward) by having the patient undergo a dental examination and an examination of the oral cavity prior to surgery, and undergoing first-aid procedures as necessary (immobilization of loose teeth or preliminary extraction)[12]. The production of a mouthpiece for protecting the teeth is recommended as being effective unless it obstructs intubation.

3. Oral care related to cardiovascular surgery

Patients who have undergone cardiovascular surgery are known to be at greater risk of infections such as infective endocarditis, focal infections or pneumonia. Dental caries, untreated dental focal infections or periodontal disease constitutes a latent risk for infection, and the occurrence of such infections immediately following cardiovascular surgery has the potential for having a serious effect on prognosis and may even be fatal. Therefore, it is recommended to carefully examine for and treat focal infections in the oral cavity prior to surgery to as far as the situation allows[13-15]. In addition, since dental treatment performed on patients following cardiovascular surgery is accompanied by a risk of infective endocarditis[16], it is recommended to have dental procedures performed prior to surgery for this reason as well. Based on findings from the literature, specialized oral care starting prior to surgery was suggested to have the potential to reduce infections following cardiovascular surgery (infective endocarditis and

pneumonia). According to a report by DeRiso *et al*., oral care using 0.12% chlorhexidine gluconate (CHX) was found to be effective in preventing hospital-acquired pneumonia according to an RCT survey targeted at 352 patients undergoing cardiac bypass surgery (decrease in incidence of nosocomial infection: 65%, 24/180 versus 8/173, $p<0.01$)[17]. In addition, Bergan *et al*. stated that the incidence of postoperative pneumonia decreased significantly as a result of implementing an oral care protocol prior to surgery in patients undergoing cardiac surgery[18]. Current CDC guidelines for pneumonia describe that oral care using chlorhexidine gluconate (0.12%) solution during the perioperative period is recommended for adult patients undergoing cardiac surgery[19].

4. Oral care related to organ transplant surgery

Patients who have undergone heart, liver, kidney or other organ transplant surgery are at high risk to the occurrence of various infections since immunosuppressants are used for the purpose of suppressing acute rejection. The most serious problem following kidney transplant surgery is complications caused by infections, and the most common cause of death soon after surgery is reported to be septicemia[20,21]. Screening for infection risk factors in the oral cavity prior to surgery and significance of proper oral care have been reported in order to reduce the risk of these infections[22].

Zweich R. *et al*.[23] has reported that the health status of the oral cavity is correlated with the risk of occurrence of complications at an early stage after transplant in the form of acute rejection and infection among patients who have undergone renal allograft.

In addition, Somacarrera ML *et al*.[24] conducted a survey of 530 heart, liver and kidney transplant patients, and concluded that perioperative dental intervention is effective in reducing the risk of complication.

Perioperative dental management and guidance and education for maintaining sanitary conditions in the oral cavity are important in contributing to effective infection management in patients susceptible to infections following organ transplant[25-27].

5. Postoperative pneumonia and oral care

Following surgery under general anesthesia, in addition to a temporary decrease in respiratory function and increased susceptibility to the occurrence of dependent (load-side) lung disease or atelectasis due to immobilization of the patient, bacterial count in the oral cavity increases as a result of patient preoperative fasting or the placement of a foreign object such as an intubation tube, nasogastric tube or bite block in the oral cavity, which results in a state where it becomes easier for bacteria to access to the respiratory tract. Consequently, there is increased risk of the occurrence of postoperative complications such as pneumonia[28,29]. In order to reduce the risk of postoperative pneumonia, significance of providing oral care prior to surgery is reported.

Bagyi *et al*.[28] investigated the relationship between post-neurosurgical pneumonia and periodontal disease or oral bacteria, and reported that pneumonia occurred significantly in a severe periodontal disease group (number of sites of periodontal disease: $p=0.031$, severity of periodontal disease: $p=0.002$), and that a group having high periodontal disease scores demonstrated an incidence of pneumonia that was 3.5 times higher than that of a group having low scores ($p<0.0001$).

In addition, Weren *et al*.[29] implemented a postoperative pneumonia prevention program (consisting of oral care, respiratory rehabilitation, walking and lifting the head) targeted at 3,319 general surgery patients, and as a result, the incidence of pneumonia in the general surgery ward decreased significantly from 0.78% to 0.18% ($p<0.006$), indicating the usefulness of introducing preoperative oral care for the prevention of postoperative pneumonia.

In particular, since surgery for esophageal cancer involves surgery at a location surrounded by vital organs such as the trachea, heart, lungs, aorta, internal carotid artery, jugular vein and recurrent laryngeal nerve, it is a highly invasive and extremely high risk procedure among cancer surgery. It offers the potential for the occurrence of perioperative complications, and is associated with numerous complications involving respiratory organs and particularly postoperative pneumonia (such as aspiration pneumonia) and atelectasis. Oral care has been reported to be useful in diminishing the risk of these perioperative respiratory complications associated with surgery for esophageal cancer.

Akutsu *et al*. conducted a survey of oral bacteria and causative agents during the occurrence of postoperative pneumonia in 39 patients who underwent esophagectomy for thoracic esophageal cancer, and reported that oral bacteria (bacteria present in plaque) constitute a high proportion of the causative agents of postoperative pneumonia associated with esophageal cancer[30]. After further conducting a survey of the significance of oral care intervention among 86 thoracic esophageal cancer patients, it was found that postoperative pneumonia decreased remarkably from 32% to 9% ($p=0.013$) as a result of oral care intervention, and the frequency of postoperative

pneumonia requiring tracheotomy in particular decreased from 12% to 0% due to intervention[31], indicating the potential for intervention of oral care consisting primarily of brushing to serve as a simple means for preventing postoperative pneumonia in esophageal cancer patients.

6. Oral care related to surgery for cancer of the head and neck region

In the case of surgery for cancer of the head and neck region, an unsanitary site like the oral cavity is included in the site where surgery, which requires an exhaustive sterilization procedure, is to be performed. This kind of surgery is recognized to have a high risk of postoperative infection. Hirakawa *et al*.[32] conducted a retrospective study of 227 head and neck region cancer patients and found that infections at the surgical site occurred at an incidence of 32.1% and that the incidence was significantly high following reconstructive surgery. Meanwhile, Girod Da *et al*.[33] conducted a survey of 159 patients who underwent a surgical procedure involving the head and neck region and reported that the incidence of complications was 63%, with infections at the wound site accounting for 22%, other infections accounting for 22%, non-infectious complications accounting for 51% and overall intraoperative mortality rate being 1.2% (two patients), and that reconstructive surgery is a significant risk factor ($p<=0.05$). In a report by Karakida *et al*.[34], the incidence of wound infections following oral cancer surgery consisting of reconstruction of the vascular pedicle free flap was 40.6%, while Lee DH *et al*.[35] reported the incidence to be 18.4% and Lotofi CJ *et al*.[36] reported the incidence to be 38.8% (reconstructive surgery was a significant affector in all cases). Thus, the incidence of local complications such as bacterial infections at the surgical wound during reconstructive surgery is reported to be extremely high in comparison with surgeries at other sites. In addition, impairment of food ingestion and swallowing function following surgery not only causes a prominent decrease in patient QOL, but can also cause aspiration pneumonia, potentially resulting in the risk of death. In this way, oral bacteria are intimately involved in postoperative complications following surgery of the head and neck region, and oral management starting prior to surgery is useful for reducing that risk.

In an intervention comparative study of a group of 56 advanced head and neck cancer patients who performed oral care prior to surgery and a group of 35 such patients who did not perform oral care prior to surgery, Ohta[37] reported that a significant difference was observed in the incidence of postoperative complications between the oral care group (16.1%, 9/56 cases) and the non-oral care group (63.6%, 21/33 cases), and also reported that a significant difference was similarly observed in the number of days until resumption of oral ingestion between the oral care group at an average of 10.6 days and median of nine days and the non-oral care group at an average of 40.2 days and median of 16 days. In multivariate analysis as well, intervention of oral care was an independent affector that lowered the risk of the incidence of postoperative complications to 1/7. Since a reduction in complications through oral care intervention are directly connected to improvement of patient postoperative QOL and reduction in the number of days of hospitalization, this was expected to be beneficial in health care economic terms as well. In addition, Satoh *et al*.[38] conducted a survey of 66 oral squamous cell carcinoma patients who underwent surgery in order to determine the effectiveness of oral care intervention, and reported that postoperative wound infections were observed in three patients (9%) of an oral care group and in 11 patients (33%) of a control group ($p<0.025$). This difference is the result of wound infections being an independent risk factor as determined by multivariate logistic regression analysis ($p=0.04$, odds ratio: 6.0), indicating that perioperative oral management has the potential to reduce the risk of postoperative wound infections following surgery in oral cancer patients.

[Discussion]

In conventional health care, the oral health status of patients around the time of surgery was generally not recognized to be a major area of concern with respect to surgery itself, and the need for such concern was only recognized to be necessary in certain surgeries such as cardiovascular surgery, organ transplant surgery or oral surgery. More recently however, accompanying the increasing level of sophistication of surgical procedures, surgeries have become increasingly invasive and require longer periods of time, and there are a growing number of cases in which patients are at high risk for surgery, such as elderly patients or patients with pre-existing diseases. Perioperative oral management is considered to be highly significant as a means for promoting reduction of the risk of postoperative infection (and particularly infectious complications such as aspiration pneumonia) and accelerating postoperative recovery for such high-risk patients. In addition, in surgeries involving the head and neck region, which are at high risk to postoperative infectious complications, preoperative oral care intervention was thought to be an important method for reducing the risk of perioperative infection.

Table 1: Outline of the reviews

Author	Report year	Type	Outline	Ref. no.
Yasny, Herlich	2012	Review	Treatment of acute dental infection prior to surgery is effective for controlling infection during the perioperative period.	1
Yasny, Silvay	2010	Review	Review to indicate, in view of oral characteristics of the elderly, importance of oral infection to be treated before surgery	2
Terezakis, Needleman, Kumar, Moles, Agudo	2011	Systematic review of 5 articles	Hospitalization deteriorates oral conditions, increases risks of nosocomial infection, and lowers QOL. The tendency is especially prominent among patients who have undergone endotracheal intubation.	3
Sjögren	2011	Systematic review of 5 articles	Hospital environment is correlated with deterioration of oral conditions.	4
Robert, Doré, Grollier	1999	Review	The number of plaque colonies increased proportional to the number of days spent in the ICU.	5
Chidyllo, Zukaitis	1990	Review	Dental management before undergoing general anesthesia is important. Especially, use of a mouthpiece for protecting the teeth is effective.	9
Yasny, White	2009	Review	An odontogenic infection focus that is untreated has been found to have harmful effects at the time of cardiac surgery. If time and resources allow, patients are recommended to receive a dental exam before surgery. Prior management like this can contribute to substantial improvement in operation results.	13
Yasny	2010	Review	An odontogenic infection focus that is untreated has been found to have harmful effects at the time of cardiac surgery. If time and resources allow, patients are recommended to receive a dental exam before surgery. Prior management like this can contribute to substantial improvement in operation results.	14
Wilson, Taubert, Gewitz, Lockhart, Baddour, Levison, Bolger, Cabell, Takahashi, Baltimore, Newburger, Strom, Tani, Gerber, Bonow, Pallasch, Shulman, Rowley, Burns, Ferrieri, Gardner, Goff, Durack, American Heart Association	2008	Systematic review	Report collection recommended by the American Heart Association (AHA) for prevention of infective endocarditis	16
Ofelia Larry Richard, Carolyn Rana	2003	Guideline	CDC guidelines for pneumonia prevention	19
Guggenheimer, Eghtesad, Stock	2003	Review	Guidelines and basis for recommendation of dental exam & care for treatment of transplant patients	21
Sakurai, Drinkwater, Sutherland, Fleischmann, Hage, Yonemura	1995	Review	Organ transplant surgery has risen dramatically in number, which, however, is a treatment that greatly disturbs the quality of life. It is important to understand precautions for dental treatment of patients before/after organ transplant surgery.	22
Shetty, Gilbert	2008	Review	Cardiac transplant patients require special dental care. Effectiveness of oral care for cardiac transplant patients is reviewed.	25
Glassman, Wong, Gish	1993	Review	Review on importance of oral care for liver-graft patients.	26
Wakefield, Throndson, Brock	1995	Review	Review on importance of oral care for liver-graft patients.	27

Table 2: Outline of the reviews 2

Author	Report year	Subjects	Methods	Outline	Ref. no.
Gaudio, Barbieri, Feltracco, Tiano, Galligioni, Uberti, Ori, Avato	2011	235 legal cases pertaining to dental damage during general anesthesia	Retrospective study	As a result of the retrospective study of litigation files, dental intervention to patients who undergo general anesthesia prior to surgery can reduce insurance premium and court costs.	6
Warner, Benenfeld, Warner, Schroeder, Maxson	1999	598,904 persons undergoing general anesthesia	Retrospective survey	132 cases of teeth damage occurred during intubation. The largest number of teeth damage occurred in anterior maxillary teeth, and risk factors included poor condition of teeth and cases of technical difficulties of intubation.	7
Newland, Ellis, Peters, Simonson, Durham, Ullrich, Tinker	2007	161,687 persons undergoing general anesthesia	Case-control study	78 cases of teeth damage occurred during intubation. Risk factors for teeth damage included poor condition of teeth and cases of technical difficulties of intubation.	8
Givol, Gershtansky, Halamish-Shani, Taicher, Perel, Segal	2004	Survey slips of medical insurance for 40 hospitals issued during 1992-1999	Retrospective study	203 cases of teeth damage occurred during general anesthesia. 86% of damaged teeth were anterior maxillary teeth.	11
Fukuda, Sugimoto, Yamashita, Toyooka, Tanaka	2011	32 anesthesiologists and 32 medical students	Controlled study	Difference in risks of teeth damage between beginners and experts during intubation was surveyed by using mannequins. Stress on teeth was especially high for emergency intubation among beginners. However, it was not so high as to cause teeth damage. Condition of patients' teeth is considered to be a major risk factor for teeth damage than operators' skill.	10
Vogel, Stübinger, Kaufmann, Krastl, Filippi	2009	115,151 persons undergoing general anesthesia	Retrospective study	Teeth damage occurred with 130 patients during intubation. Anterior maxillary teeth damage was largest in number. Mousepiece did not seem very effective and dental checkup prior to surgery seemed important.	12
Hayes, Fasules	2001	209 child patients undergoing cardiovascular surgery	Prospective cohort study	Dental diseases were observed in 175 child patients out of 209 (84%). 71 patients (34%) received invasive dental treatment, and the cardiac surgeries for 24 patients (12%) were postponed.	15
DeRiso, Ladowski, Dillon, Justice, Peterson	1996	353 patients undergoing coronary artery bypass surgery	RCT	Patients were randomized into the oral care group treated with 0.12% chlorhexidine gluconate (CHX) oral rinse and the control group. The nosocomial infection rate decreased by 65% among the oral care group. (24/180 vs, 8/173, $p<0.01$). Oral care intervention using CHX oral rinse has reduced the respiratory infection rate and the usage rate of systemic administration of antibiotic for patients undergoing cardiac surgery.	17
Bergan, Tura, Lamas	2014	226 patients undergoing cardiovascular surgery	Prospective intervention study	Oral care intervention using chlorhexidine gluconate before surgery has significantly reduced incidence of postoperative pneumonia.	18
Barbero, Garzino Demo, Milanesio, Ottobrelli	1996	80 liver transplant recipients	Cohort study	Risk of infection by immunosuppressants used following transplant surgery is a serious problem. Dental checkup prior to surgery found out that 45% of patients had chronic gingivitis, 20% had periapical pathosis, and 67% had caries teeth. Poor dental health was observed in 85% of patients. Dental checkup prior to liver transplant surgery is necessary for prevention of complications and improvement in patients' QOL.	20
Zwiech, Bruzda-Zwiech	2013	91 kidney transplant recipients	Cohort study	Oral health index (OHI-S) and Community Periodontal Index of Treatment Needs (CPITN) were found to be correlated with complications after transplant. Poor oral health condition can increase risk of acute rejection and hospitalization among renal allograft recipients.	23
Somacarrera, Lucas, Cuervas-Mons, Hernández	1996	Patients scheduled for heart transplant and liver transplant (46 patients each)	Cohort survey	Oral health training and motivation program were found to be effective for improvement of oral health. Dental preventive treatment was found to be effective in reducing risk of postoperative complications. It was considered that all transplant patients should be monitored by dentists.	24
Bágyi, Haczku, Márton, Szabó, Gáspár, Andrási, Varga, Tóth, Klekner	2009	23 patients undergoing brain surgery	Prospective cohort study	Oral checkup before surgery and time-dependent bacteria culture were conducted. Severity of periodontal diseases was significantly associated with incidence of postoperative pneumonia ($p=0.002$).	28
Wren, Martin, Yoon, Bech	2010	Subjects: 3,319 general surgery patients	Prospective cohort study	The postoperative pneumonia prevention program (respiratory rehabilitation plus oral care) performed prior to surgery has reduced incidence of postoperative pneumonia to 25%.	29
Akutsu, Matsubara, Okazumi, Shimada, Shuto, Shiratori, Ochiai	2008	39 thoracic esophageal cancer patients scheduled for surgery	Prospective cohort study	Dental checkup and oral bacteria culture were performed before surgery. Postoperative pneumonia was observed in 14 patients (35.9%). Bacteria present in plaque was a risk factor for postoperative pneumonia for thoracic esophageal cancer patients.	30
Akutsu, Matsubara, Shuto, Shiratori, Uesato, Miyazawa, Hoshino, Murakami, Usui, Kano, Miyauchi	2010	Subjects: 39 thoracic esophageal cancer patients scheduled for surgery	Prospective cohort study	Dental checkup and oral bacteria culture were performed before surgery. Postoperative pneumonia was observed in 14 patients (35.9%). Bacteria present in plaque was a risk factor for postoperative pneumonia for thoracic esophageal cancer patients.	31

Table 2: (continued)

Author	Report year	Subjects	Methods	Outline	Ref. no.
Hirakawa, Hasegawa, Hanai, Ozawa, Hyodo, Suzuki	2013	277 head and neck cancer patients undergoing surgery at the National Cancer Center	Retrospective survey	Infections at the surgical sites were observed in 92 cases (32.1%). Based on multivariate logistic regression analysis, the independent risk factors for infections at the surgical sites included reconstructive surgery (p=0.04; odds ratio 1.77) and chemoradiotherapy (p=0.01; odds ratio 1.93). No difference in 5-year survival rate was observed for patients of infection at the surgical site.	32
Girod, McCulloch, Tsue, Weymuller	1995	159 head and neck cancer patients undergoing surgery at University of Washington	Retrospective survey	Postoperative complications were observed in 63%. The total intraoperative mortality rate was 1.2% (2 patients). Preoperative radiation therapy was correlated with an increase in wound infection rate (p=0.05).	33
Karakida, Aoki, Ota, Yamazaki, Otsuru, Takahashi, Sakamoto, Miyasaka	2010	276 head and neck cancer patients undergoing surgery at Tokai University	Retrospective survey	Incidence of postoperative wound infection was 40.6% (112/276). Occurrence of SSI is significantly correlated with oral cancer surgery and with the rating of ASA (anesthesiologist index).	34
Lee, Kim, Nam, Choi, Choi, Roh	2011	697 head and neck cancer patients undergoing surgery	Retrospective survey	Postoperative wound infection was observed in 128 patients (18.4%). Based on multivariate analysis, the independent risk factors for postoperative would infection included oral cancer surgery and with presence/absence of preoperative radiation therapy and/or tracheotomy.	35
Lotfi, Cavalcanti Rde, Costa e Silva, Latorre Mdo, Ribeiro Kde, Carvalho, Kowalski	2008	258 head and neck cancer patients scheduled for surgery	Retrospective survey	Incidence of postoperative would infection was 38.8%. In final models based on logistic regression analysis, the independent risk factors for SSI included smoking (odds ratio [OR]=2.96), metastatic involved lymph node (OR=2.05), flap reconstruction (OR=2.20) and administration of prophylactic antimicrobial agent over 48 hours (OR=1.89).	36
Ota	2004	91 head and neck cancer patients scheduled for reconstructive surgery	Prospective cohort study	Postoperative wound infection was significantly low in the oral care intervention group. Based on multivariate logistic regression analysis, oral care intervention (odds ratio:6.93, 95% CI 2.38-20.20) and pre-existing diabetes (odds ratio: 7.25, 95% CI 1.38-38.13) were the independent factors for postoperative wound infection. It was suggested that oral care intervention prior to surgery reduces postoperative complications.	37
Sato, Goto, Harahashi, Murata, Hata, Yamazaki, Satoh, Notani, Kitagawa	2011	66 head and neck cancer patients scheduled for surgery	Prospective cohort study	Postoperative wound infection was significantly low in the oral care intervention group. (p<0.025). Based on multivariate logistic regression analysis, tissue transplant (p=0.01; odds ratio, 24.5) and lack of oral health management (p=0.04; odds ratio, 6.0) were the independent risk factors for postoperative wound infection.	38

Although damage to teeth accompanying intubation during general anesthesia is unable to be avoided by the anesthesiologist alone in many cases, preoperative dental management, including temporary immobilization of loose teeth, performing dental procedures such as tooth extraction, or producing a protector for protecting the teeth prior to surgery, are useful in avoiding such damage.

Examples of problems pertaining to perioperative oral care intervention at the time of surgery include: 1) restrictions on time and personnel when attempting to implement perioperative oral care, and smooth and effective oral care may be difficult to implement depending on various circumstances unique to each health care institution, and 2) evidence-based oral care has yet to be established and the procedures and contents of that care are not standardized. In the future, it will be necessary to collect further evidence relating to the usefulness of perioperative oral care and develop a specific standardized protocol (while securing consensus) for perioperative oral management so that a constant level of oral care based on evidence will be implemented at all health care institutions.

[Conclusions]

The implementation of perioperative oral care during surgery can be expected to yield the following effects: 1) reduced risk of postoperative pneumonia, 2) reduced risk during intubation (teeth damage or deciduation), 3) reduced risk of infection during cardiovascular surgery, 4) reduced risk of infection during organ transplant surgery, and 5) reduced risk of postoperative complications (including respiratory organ complications and wound infections) during oral, pharyngeal and esophageal surgery.

[Conflict of interest]

There are no items applicable to “conflict of interest” in this article.

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9. Effects of dental care
2) Oral function deterioration prevention and recovery

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[Abstract]

In order to examine ways to prevent deterioration of oral function and achieve recovery through dental care, we conducted a search of the literature over the past five years (between January 2009 and July 2014) as a general rule, as a result of which 28 papers were extracted. These papers were classified into "maintenance/recovery of swallowing function and improvement of mastication and nutritional status through oral function training and the like" (6 papers), "recovery of occlusion/mastication and nursing care prevention through the use of dentures " (8 papers), and "maintenance/recovery of oral function for the frail elderly" (14 papers), after which we assessed the degree of contribution of dental care to oral function deterioration prevention and maintenance/recovery, and its effects on general health problems and vital prognosis.

Searches were conducted using the Internet while focusing on ICHUSHI and PubMed. Target papers were further narrowed down by manual searches of literature extracted from the Internet.

As a result, recovery of mastication and enhancement of masticatory performance through dental prosthetic treatment for missing teeth were confirmed to greatly contribute to general physical condition, and the provision of specialized care for patients in whom oral function has decreased to the point they were unable to chew was confirmed to result in improvement of oral function.

[Introduction]

Dental care and dental medicine have heretofore invested considerable efforts in the development of various treatment methods, pharmaceutical agents, materials and instruments targeted at a small number of diseases. Although the objective of these efforts is unquestionably the elimination and the prevention of recurrence of disease, it is also a fact that efforts have been made with the aim of maintaining and restoring the various functions of the oral region. On the other hand, emphasis has also been placed on only "treating the disease" based on the purport of health insurance, while the numerous aspects of dental care in the form of "maintenance and improvement of function" has been somewhat avoided since it overlaps with the concepts of "preventive measures" and "rehabilitation." In recent years, it has become necessary for dentistry to become involved in the treatment of eating and swallowing disorders. Also, oral hygiene management of the homebound elderly and hospitalized patients is currently unthinkable without the field of dentistry. Therefore, "maintenance and improvement of oral function" has become an important issue.

Oral function can be said to deteriorate with aging in the same manner as other organs. When considering that inadequate development of oral function during the developmental stage is the focus of examination and diagnosis, it is thought that some form of measures should be devised with respect to "oral function in the declining stage."

With an eye to preventing the deterioration of oral function and contributing to oral function maintenance and improvement, we introduce herein reports that we believe would serve as a reference for future clinical applications, which were chosen from among numerous reports published in the past.

[Objective]

The objective of this review is to examine whether oral function deterioration could be prevented or oral function could be maintained and restored through dental care intervention, what types of materials and techniques were used to achieve the goal of intervention, and the extent to which their effects were obtained.

[Methods]

We conducted a search of ways to prevent the deterioration of oral function AND achieve recovery through dental care. Literature searches in Japanese were targeted at ICHUSHI. Key words consisted of (Hotetsu (prosthetic) OR Gishi (denture) OR Burijji (bridge)) AND (Soshaku (mastication) OR Sesshoku (eating) OR Enge (swallowing) OR Shinbi (esthetic) OR Kinou (function)) AND (Koujou (improvement) OR Iji (maintenance)) AND

(Shika (dental) OR Shigaku (dentistry)). Conditions for narrowing down the search results consisted of focusing on commentaries, reviews AND original papers excluding proceedings, AND searches were limited to the past five years (between January 2009 AND July 2014) as a general rule. English language searches were made targeted at PubMed. Key words consisted of (prosthetic OR denture OR bridge) AND (mastication OR chewing OR eating OR swallowing OR esthetic) AND (increase OR retain) AND (dental OR dentistry). The results were narrowed down with the terms: review, 10 years, human AND English. As a result, 483 papers were extracted. A manual search was then made targeted at these papers AND 29 papers were selected after excluding commercial publications.

[Results]

1. Maintenance/recovery of swallowing function and improvement of mastication and nutritional status through oral function training and the like (6 papers)

Improvement of oral function is essential for maintaining and restoring swallowing function. In the field of medical rehabilitation, considerable effects are demonstrated through intervention by professions, such as speech and language therapists, together with dentists and dental hygienists. Recovery of swallowing function through chewing training[1], improvement of nutritional status through oral function training[2], and improvement of mastication performance and swallowing function through motor function training of the tongue and so forth[3-6] have been reported.

2. Recovery of occlusion/mastication and nursing care prevention through the use of dentures (8 papers)

Improvement of masticatory function through the use of dentures[7-11] represents one of the standard themes of dental prosthetics, and research has been conducted from various perspectives. Reviews were mainly discussed in this review. First, experimental data is indicated with respect to the significance of "chewing," and then, effects are discussed relating to numerous parameters of vital prognosis, including physical and mental development, brain activation and relaxation, reduction of carcinogenicity, elimination of active oxygen, inhibition of obesity, control of blood sugar level, improvement of motor function, and suppression of aging.

The effects of therapeutic interventions, such as health improvement by occlusal force enhancement[12], motor function improvement through an oral function improvement program[13], and tongue motor function training[14], are also discussed.

3. Maintenance/recovery of oral function for the frail elderly (14 papers)

As for cases in which oral function deteriorated due to dry mouth and the like, numerous improvements by use of moisturizing agents or salivary gland massage have been reported[15-18]. Moreover, treatment was performed in anticipation of the effects of moisture retention agents and ameliorative effects have also been reported[19-23]. There are many cases in which management of the oral function of patients recovering at home and hospitalized patients is carried out primarily not only by dentists, but also by dental hygienists. In addition, there are also not a few cases in which this role is fulfilled by nurses. Many results of specialized oral care are also reported[24-28].

[Discussion]

Mastication becomes difficult when teeth are lost. Occlusion can be restored by inserting a denture at the location of a missing tooth. Once occlusion has been restored, masticatory function will be restored.

Once masticatory function has been restored, one of the conditions for the oral nutrition intake will be met. However, the effects of mastication are not limited to just this. Recovery of masticatory function has been determined to lead to recovery of general motor function, improvement of mental status, and promotion of recovery from systemic disease. In other words, dental care can be said to play an important role not only in terms of daily activities, but also in the form of care to maintain and improve health[8-10].

In elderly persons whose oral function has deteriorated significantly to a state where mastication is not possible, it is first necessary to begin with hygiene management of the oral cavity[15-28]. Since this state is accompanied by dryness of the mouth and /or atrophy or functional deterioration of muscles within or surrounding the oral cavity, efforts are made to improve oral function with rehabilitation in mind[1-7,11-14,25-28]. At this stage, dental care may overlap with nursing care, resulting in the need for ensuring a mutual understanding among caring, nursing and rehabilitation personnel. As dentistry has developed only at dental clinics, dentists may be taken aback by the expansion of dental care services. Nevertheless, dentists have a huge responsibility as experts of the oral cavity. It is hoped that this review will be as beneficial as possible for dental care of the future.

[Conclusions]

Many discussions have surfaced regarding expectations on the positive effects of dental treatment on oral function deterioration. However, we have not reached the stage

Table 1: Oral function deterioration prevention and recovery

Details	No.	Year	Author	Outline
Maintenance/ recovery of swallowing function and improvement of mastication and nutritional status through oral function training and the like	1	2006	Otsuka	By offering mastication training to inpatients with severe dementia, swallowing function was improved in the "modified water swallow test," along with improved ADL.
	2	2003	Kikutani *et al.*	In the elderly requiring nursing care, their diet became softer and ADL deteriorated; in the case of severe dementia, BMI also decreased.
	3	2009	Kikutani *et al.*	In the elderly, the tongue performs compensatory action when the teeth are lost.
	4	2011	Izumi	Explanation on rehabilitation of eating/swallowing functions for aging of oral cavity and laryngopharynx
	5	2011	Mukai	Explanation on oral cavity and dietary education for aging of oral cavity and laryngopharynx.
Recovery of occlusion/ mastication and nursing care prevention through the use of dentures	6	2010	Kanenaka *et al.*	When elderly inpatients requiring nursing care showed improved oral function through oral care, eating/swallowing training, and use of dentures, improvements were observed, including shift to oral nutrition, increase in intake amount, lowered risk of malnutrition, and enhanced ADL/CRP levels.
	7	2009	Teraoka *et al.*	Vitality index in the elderly requiring nursing care is associated with occlusion state of molar region and swallowing function as the index of oral function.
	8	2012	Akagawa	Explanation on the impact of prosthodontic care on healthy life expectancy
	9	2012	Ikebe	Review of occlusion/mastication and healthy life expectancy
	10	2011	Kobayashi	Explanation on occlusion/mastication and healthy life expectancy
	11	2008	Shiina *et al.*	Patients having low evaluation of the old dentures tended to have high evaluation of new dentures.
	12	2012	Nakamura *et al.*	Through full-body exercise and occlusion exercise, gripping force/occlusion force tended to increase in the elderly.
	13	2011	Watanabe *et al.*	Improved motor function and nutrition in the elderly requiring nursing care enhanced occlusal pressure, tongue motion, RSST result, and oral-related QOL, and nursing care level is lowered.
	14	2009	Kikutani *et al.*	Tongue coat is increased as tongue pressure and tongue motor function are decreased.
Maintenance/ recovery of oral function for the frail elderly	15	2012	Ooka *et al.*	In the elderly requiring nursing care, oral care using dentifrice containing moisturizing agents improved saliva humidity and oral mucosa humidity.
	16	2013	Nozawa	Oral humidity was improved in long-term tube-fed elderly by massaging orbicularis oris muscles/buccinators muscle.
	17	2008	Kakinoki *et al.*	Explanation on guidelines for diagnosis of dry mouth
	18	2008	Tokunaga *et al.*	Oral humidity was improved by providing salivary gland massage and point acupressure to the elderly with dry mouth.
	19	2012	Yoshiyama *et al.*	Saliva wetness was improved in the elderly by using hyaluronic acid spray (2.2mm to 3.6mm)
	20	2012	Mochizuki	Salivary secretion was increased by dosing patients with abnormal oropharyngeal sensation with dry-mouth-improving drug.
	21	2011	Tsugayasu *et al.*	By applying oral care gel in the elderly requiring nursing care, improvements were observed in dental plaque accumulation, inflammation, tongue coat status, halitosis, dry mouth, and candida count.
	22	2010	Hayashi *et al.*	By using oil spray for parenteral alimentation patients, dry mouth was improved.
	23	2009	Yokobayashi *et al.*	By providing oral care using moisturizing gel to the elderly with dry mouth, dryness was improved.
	24	2012	Kurokawa *et al.*	By providing professional oral care to patients with eating/swallowing disorders, comprehensive oral assessment improved together with reduction in the number of days with fever, and improvement in mean body temperature and oral ingestion rate.
	25	2011	Mori *et al.*	By providing dental prosthetic treatment and oral hygiene instructions to dry mouth patients requiring occlusion treatment, mouth dryness and cleanliness were improved.
	26	2010	Ooka *et al.*	By providing oral care to hospitalized patients, oral cavity related problems (lips, oral mucosa, dry mouth, sputum retention, tongue coat, dental plaque, bleeding) were improved. However, the improvement varied widely depending on the type of causative disease.
	27	2008	Suzuki *et al.*	By providing oral care using a combination of diluted oxydol solution and mouthwash containing hyaluronic acid to parenteral alimentation patients, dry mouth and tongue coat were improved.

Table 1: (continued)

Details	No.	Year	Author	Outline
Maintenance/ recovery of oral function for the frail elderly	28	2004	Takei *et al.*	By performing mouth cleaning in nursing home residents, saliva wetness and halitosis were improved. However, in patients with bleeding, halitosis deteriorated.

where we can confirm the validity of the method to test oral function and the cutoff value for the extent of deterioration, both of which are major themes for future research. Because of this, we have to await future research to understand how much oral function can be improved by dental treatment or what extent of deterioration dental treatment is effective for.

[Conflict of interest]

There are no items applicable to "conflict of interest" in this article.

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9. Effects of dental care
3) Preventive effects on tooth loss

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[Abstract]

Prevention of tooth loss not only leads to the maintenance of oral function and aesthetics but also promotes the maintenance of systemic health. In this review, we provide an overview of findings obtained to date, placing emphasis on the preventive effects of dental care on tooth loss, in particular, on the prevention of tooth loss through maintenance.

We conducted a literature search on articles that had examined the association between the presence or absence of maintenance visit and tooth loss using an electronic search database, and found 16 relevant articles. Of these, 13 reports showed a fewer number of lost teeth in the group of subjects who underwent maintenance regularly, as compared to the group of subjects who did not make regular maintenance visits.

In conclusion, receiving proper dental care and continuing subsequent maintenance likely leads to the prevention of tooth loss.

[Introduction]

Purposes of dental care include the removal of discomfort such as pain, recovery of dental and oral function, and improvement of aesthetics. Furthermore, in recent years, the improvement of quality of life through happiness of eating has been added to the goals. Taken together, extending the life span of teeth by implementing early disease detection and early treatment will ultimately lead to the promotion of not only oral but also systemic health maintenance.

In 1989, the Ministry of Health and Welfare and the Japan Dental Association at the time proposed the "8020 campaign," which aimed to urge people to try to have at least 20 remaining teeth at the age of 80 years. "Healthy Japan 21" also set specific target values, and as the campaign spread widely among the public, it has greatly contributed to the promotion of oral health. According to the latest Survey of Dental Diseases[1], the mean number of permanent teeth teeth lost per person in each age bracket is decreasing every year (Figure 1).

In a broad sense, it is believed that this improvement was achieved as a result of dental care, including educational activities, which effectively led to the prevention of tooth loss. In other words, a set of goals aimed at maintaining healthy teeth in a wide range of life stages and leading a fun and satisfying dietary life has gained acceptance of the people, which in turn led to the promotion of the 8020 campaign.

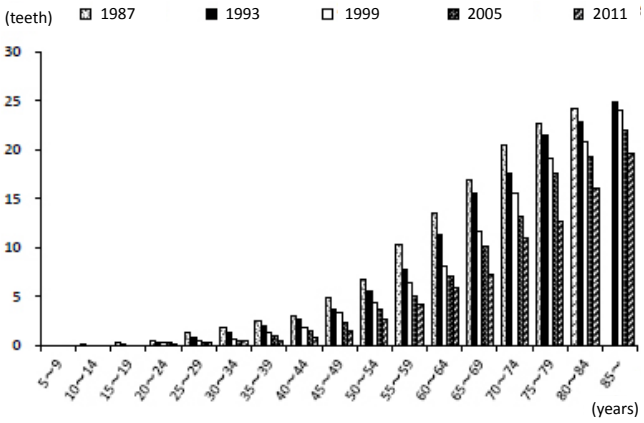

Figure. 1: Annual change in the mean number of permanent teeth lost per person

[Objective]

The purpose of this review was to examine the preventive effects of dental care on tooth loss through a comprehensive review of evidence obtained to date. In particular, we collected data with a focus on the prevention of tooth loss through maintenance following periodontal treatment.

[Methods]

Searches of the literature were conducted using PubMed as an electronic database (last search date: July 7, 2014).

First, a search under "Maintenance AND Tooth loss AND Randomized Controlled Trial [ptyp] AND Humans [MeSH Terms]" was conducted, yielding 35 hits. However, all of these articles differed in content from that targeted in this review, i.e., assessment of the effects of dental care on tooth loss prevention. Conducting a randomized control trial (RCT) of patients requiring dental treatment, where patients are divided into treatment and non-treatment groups, will certainly be perceived as ethically unacceptable. In this sense,

it is presumable that no RCT data that directly support the effects of dental care, including maintenance, on tooth loss prevention could be found. Therefore, we decided to consider available evidence to extrapolate our conclusion in a way that goes along with the theme of this review.

Next, a search was conducted under

#1 Maintenance (12,765 hits)

#2 Tooth loss (218,011 hits)

#3 Periodontal disease (76,100 hits)

#4 #1 AND #2 AND #3 (458 hits)

#5 #4 AND Humans [MeSH Terms] (437 hits)

#6 #5 AND English [lang] (405 hits),

yielding 405 relevant articles.

Among the selected articles, articles that analyzed the association between maintenance and tooth loss were selected through a review of titles and abstracts, and furthermore, a search of original research articles featured in reviews included in the 405 articles was conducted with the aim of selecting those with content in accordance with the theme of this review; 16 relevant articles [2-17] were thus identified.

[Results]

The 16 articles that matched the theme of this review are as follows (Table 1).

Many reports concluded that the group of subjects who underwent maintenance had lost fewer teeth compared to the group of subjects who did not make regular maintenance visits.

[Discussion]

Among practices of dental care that are linked to the prevention of tooth loss, one for which the most literature has been accumulated is the maintenance following periodontal treatment. A position paper from the American Academy of Periodontology (AAP) provides a summary of periodontal treatment and subsequent maintenance [18].

Maintenance refers to regular health management to

Table 1: List of articles that compared tooth loss between those who made regular visits for maintenance and those who made visits only on an irregular basis

(Maintenance group: a group of subjects who made regular visits for maintenance, non-maintenance group: a group of subjects who did not make regular visits for maintenance, including those who were uncooperative with maintenance)

Author	Report year	Study area	Study subjects	Number of subjects	Study design	Observation period	Main results	Reference number
Reports that the maintenance group had less tooth loss								
Wilson *et al.*	1987	USA	Maintenance patients after periodontal treatment	162	Case-control	≥5 years	The mean number of lost teeth per person per year was 0 in the maintenance group and 0.06 in the non-maintenance group.	2
Bostanci *et al.*	1991	Turkey	Subjects with moderate to severe periodontitis who underwent periodontal surgery	43	Case-control	10 years	The mean number of lost teeth per person per year was 0.069 in the maintenance group and 0.363 in the non-maintenance group.	3
Checchi *et al.*	2002	Italy	Maintenance patients after periodontal treatment	92	Case-control	Average of 7 years	The overall mean number of lost teeth per year was 0.07; the number of lost teeth in the non-maintenance group was 5.6-fold higher compared that in the maintenance group.	4
Cortellini *et al.*	2004	UK, Italy	Individuals who underwent surgical periodontal treatment by the GTR method	175	Case-control	Average of 8 years	The proportion of individuals who had lost teeth was significantly higher in the non-maintenance group	5
Al-Shammari *et al.*	2005	Kuwait	Individuals who had tooth extraction during the period of investigation, who were aged 18 years or older	1,775	Cross-sectional	-	The number of lost teeth in the non-maintenance group was 1.48-fold higher compared to that in the maintenance group.	6
Pretzl *et al.*	2008	Germany	Maintenance patients after periodontal treatment	100	Case-control	10 years	The mean number of lost teeth per person per year was 0.055 in the maintenance group and 0.268 in the non-maintenance group.	7
Tsami *et al.*	2009	Greece	Patients with severe periodontitis who received periodontal treatment and were under maintenance	280	Case-control	Average of 11 years	The overall mean number of lost teeth per year was 0.3; the number of lost teeth in the non-maintenance group was 1.52-fold higher compared that in the maintenance group.	8
Miyamoto *et al.*	2010	Japan	Maintenance patients after periodontal treatment	295	Case-control	≥15 years	Under certain conditions, the maintenance group showed a significantly lower rate of tooth loss compared to the non-maintenance group	9
Ng *et al.*	2011	Singapore	Maintenance patients after periodontal treatment	312	Case-control	Average of 10-11 years	The mean number of lost teeth per person per year was 0.04 in the maintenance group and 0.22 in the non-maintenance group.	10
Baumer *et al.*	2011	Germany	Patients with invasive periodontitis who have undergone periodontal treatment and were under maintenance	84	Case-control	Average of 11 years	The mean number of lost teeth per person per year was 0.075 in the maintenance group and 0.150 in the non-maintenance group.	11
Ravald *et al.*	2012	Sweden	Maintenance patients after periodontal treatment	64	Case-control	Average of 13 years	The overall mean number of lost teeth was 0.23; the rate of tooth loss was significantly lower in the maintenance group than in the non-maintenance group.	12
Costa *et al.*	2012	Brazil	Maintenance patients after periodontal treatment	164	Cohort	3 years	The mean number of lost teeth per person per year was 0.22 in the maintenance group and 0.26 in the non-maintenance group.	13
Kim *et al.*	2014	Korea	Maintenance patients after periodontal treatment	134	Case-control	Average of 11 years	The mean number of lost teeth per person per year was 0.14 in the maintenance group and 0.21 in the non-maintenance group.	14
Reports that there was no significant difference in tooth loss between the maintenance and non-maintenance groups								
Konig *et al.*	2001	Germany	Maintenance patients after periodontal treatment	188	Case-control	≥10 years	No significant difference was found in the rate of remaining teeth between the maintenance and non-maintenance groups	15
Seirafi *et al.*	2014	Iran	Maintenance patients after periodontal treatment	72	Case-control	10 years	The mean number of lost teeth per person per year was 0.15 in the maintenance group and 0.14 in the non-maintenance group, with no significant difference.	16
Reports that the maintenance group had more tooth loss								
Miyamoto *et al.*	2006	Japan	Maintenance patients after periodontal treatment	505	Case-control	≥10 years	Compared to the non-maintenance group, the proportion of individuals who had lost teeth was significantly higher in the maintenance group.	17

maintain the tissue healed by a series of dental treatments over a prolonged period. It is a term similar to recall and supportive periodontal therapy (SPT), and these terms are rarely distinguished in summing up previous publications. However, today, the various terms have converged to 'maintenance' across the world.

According to the above-mentioned position paper, patients receiving maintenance on a regular basis have decreased tooth and attachment loss compared to patients who receive irregular or no maintenance at all, as confirmed by many of the literature. Moreover, other reviews[19,20]reported that proper maintenance leads to the prevention of tooth loss.

Bostanci and Arpak reported a study that directly investigated the effectiveness of maintenance on the prevention of tooth loss[5]. Periodontal treatments, including surgical periodontal treatment, were performed on 43 patients with moderate to advanced periodontitis. Following treatment, patients were followed-up for the period up to 10 years, and the rate of tooth loss was measured in 16 patients who underwent regular maintenance at intervals of 3 to 6 months, and 27 patients who only made irregular visits when problem arose. The results showed that the rate of tooth loss over the 10-year period was 3.6±1.8% in the maintenance patient group, and in comparison, that of the irregular-visit patient group was higher, at 14.1±3.5%. Moreover, while the mean number of lost teeth due to periodontal disease over the 10-year period following treatment was 0.69 teeth per person in the maintenance patient group, the number was 3.63 in the irregular-visit patient group. These findings suggest that the preventive effects of maintenance visit on tooth loss are more pronounced in patients with advanced periodontal disease – advanced to the extent that periodontal surgery was necessary. On the other hand, this report requires some caution in interpretation, in terms of the fact that the number of subjects was relatively low. It should also be understood that, like many other reports, this study was a retrospective case-control study.

A report by Wilson *et al*.[2] also infers the effects of maintenance in preventing tooth loss. The authors assessed the relationship between patient compliance with maintenance schedules and subsequent tooth loss, given that not all people make visits for maintenance. Among 162 individuals with data of at least 5 years up to 8 years, none of the 58 individuals who had complied with maintenance schedules extracted a tooth during the maintenance period. On the other hand, in 104 individuals who made irregular visits, the total number of extracted teeth during the maintenance period was 60 teeth, which could be converted to 0.06 teeth per person annually. Moreover, the reason for extraction was periodontal disease in 34 teeth (57%), which was considerably high. It should be noted, however, that 34% of all patients comprised those who had never made visits for maintenance, and data on those patients, due to the lack of visit, were not included in the study results. The authors concluded that people who make regular maintenance visits have a lower number of lost teeth compared to those who do not.

A caution should be exercised when interpreting this paper with regard to the fact that the follow-up rate was low; at the beginning, the study aimed to collect data from 961 subjects, but the number of subjects the study could actually analyze was reported to be 162 subjects. Although it is understandably difficult to follow up all subjects, given that some had never showed up for maintenance, descriptions regarding reasons for drop-out were somewhat insufficient. Furthermore, while it is also true for other reports, the decision to perform tooth extraction is naturally left to the discretion of the dentist. In this article, the number of extracted teeth was zero in the maintenance patient group, which differed slightly from the values reported elsewhere.

While many were retrospective case-control studies, there was one report of a prospective cohort study that evaluated the effects of maintenance in preventing tooth loss[7]. In this report, the usefulness of a previously proposed risk assessment model for periodontal diseases was examined, while at the same time investigating subsequent tooth loss between those who made regular maintenance visits and those whose visits were irregular. Subjects were 75 patients who regularly visited for maintenance, and 89 patients who visited on an irregular basis. After periodontal treatment, maintenance was performed at a mean interval of 3.3 months for three years. The results showed that among those who visited for maintenance on a regular basis, periodontitis recurrence and loss of teeth were significantly lower. During the maintenance period of three years, the mean number of lost teeth was 0.65±1.4 per person among regular visitors, as compared to 0.78±2.1 teeth among irregular visitors. The likelihood of losing teeth was 2.35-fold higher (95% confidence interval (CI), 1.02-5.23, p=0.015) in irregular visitors than in regular visitors. Moreover, the study also demonstrated the usefulness of the periodontal disease risk assessment model, and showed that bleeding on probing, tooth and bone loss, diabetes, and smoking were associated with the subsequent risk of exacerbation.

Among studies with a relatively large sample size is a report by Ng *et al*.[10]. The authors investigated patient compliance with maintenance schedules and tooth loss in

312 subjects who had been followed-up for at least 7 years after periodontal treatment. While subjects who visited for maintenance had only lost 0.04 teeth per person per year, subjects who did not comply with regular maintenance had lost an average of 0.22 teeth per person per year. A significant difference was found between the two groups, suggesting, in this report as well, the usefulness of maintenance in tooth preservation.

A number of other reports can be found, all of which confirming the preventive effects of maintenance on tooth loss[4-9,11,12,14]. On the other hand, however, there exist some studies that reported no significant difference in the number of lost teeth between patients who visited for maintenance and those who did not[15,16]. Moreover, one study reported that, contrarily, patients who visited for maintenance had a higher number of lost teeth[17]. Since intervals between maintenance visits and contents of actual medical practice differ from study to study, some aspects remain unsolved and will depend on future study outcomes in terms of what specific interventions might prove effective.

The effectiveness of maintenance has been recognized, to a certain degree, for decades. Axelsson and Lindhe carried out an observational study to assess the effectiveness of maintenance in periodontal treatment, although the study did not directly address the effects of maintenance on tooth preservation[21]. Periodontal treatment was performed in 90 patients with advanced periodontitis, and patients were divided into two groups of those who received subsequent maintenance through a thorough program at a university hospital, and of those who received maintenance at a local general dental clinic; patients were then observed over the course of six years. The results showed that in the group that underwent university hospital maintenance, the mean number of remaining teeth after six years was 19.4, which was not so different from 19.6 at baseline. On the other hand, in the group that underwent maintenance at a local dental clinic, the number decreased from 18.0 at baseline to 17.3 after six years, although there was no significant difference between the two groups. With respect to the periodontal tissue attachment condition, the better outcomes were obtained in patients who received maintenance at a university hospital. From these results, proper maintenance is suggested to be effective, but considering the endpoint of tooth preservation, the observation period of six years might have been too short.

The same research group has published outcomes of a group of patients who underwent 30 years of maintenance[22]. Maintenance was initiated in 1972, and patients were followed-up for 30 years until 2002. The numbers of remaining teeth were compared between the group of subjects who were aged between 51 and 65 years at the time of registration in 1972, and those who were aged between 20 and 35 years in 1972, and who reached the ages of 51 to 65 years in 2002 after 30 years of maintenance (Figure 2).

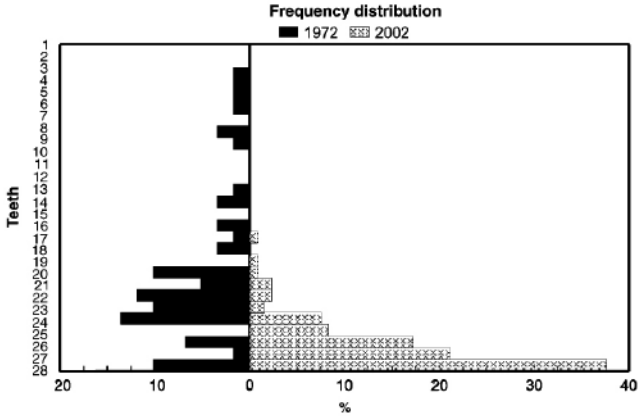

Figure. 2: The number of remaining teeth in patients aged between 51 and 65 years in 1972 and 2002
(The left-hand side is a plot showing the numbers of remaining teeth in 85 subjects who were aged between 51 and 65 years, as measured in 1972. The right-hand side is a plot showing the number of remaining teeth in each of 133 subjects who underwent 30 years of maintenance from 1972, and who were aged between 51 and 65 years in 2002.)

Although differences in subject background, including the age difference, should be taken into consideration, the number of remaining teeth in almost all subjects who underwent 30 years of maintenance was 24 teeth or more. Moreover, many of them had 28 remaining teeth. On the other hand, the number of remaining teeth in many of the subjects who were aged between 51 and 65 years old in 1972 was 20 to 24. From these results, it is presumed that continued maintenance over a long period is effective for tooth preservation.

1. Loss of teeth as an endpoint of clinical research

In clinical research on periodontal diseases, one report investigated the characteristics of endpoints[23]. This report analyzed 92 studies reported from 1988 to 1992, including 82 RCTs, in terms of the number of items set as the endpoints, as well as items frequently adopted as an endpoint. The results showed that the most frequently observed number of endpoints in one study was six. The following three items were particularly frequently set as an endpoint: mean probing depth (78%), mean probing attachment level (66%), and plaque index (37%). There was no study that had set tooth loss as a true endpoint. Therefore, it is evident that clinical studies conducted to determine the effects of dental care on tooth loss in RCT settings are lacking, at least in the relevant period. Given that the duration of time leading to tooth loss is generally long, clinical research could be hard to

establish.

2. Systemic infection by oral bacteria

Following a report[24] in 1989 that patients with acute myocardial infarction have increased dental caries and periodontal disease, the association between poor oral hygiene and acute myocardial infarction has been pointed out. To date, many studies have reported on periodontal disease in association with systemic infection, including the circulatory system.

With regard to systemic infections caused by oral bacteria, an infection with *Arcanobacterium haemolyticum*, an organism belonging to the oropharyngeal flora, reportedly caused brain abscess[25]. Moreover, Lemierre's syndrome, which is a type of sepsis and a condition that is rarely observed but leads to serious prognoses, is caused by bacteria in the unhygienic oral cavity. In general, *Fusobacterium necrophorum* is detected in patients with this syndrome, and suppurative thrombophlebitis of the internal jugular vein, or formation of metastatic abscess in the lungs and brain, are observed[26]. Furthermore, some reported that the DNA of *Streptococcus mutans* was detected in the oral cavity as well as atheroma of patients with carotid artery stenosis or aortic aneurysm, even though the patients were edentulous[27].

From these reports, it is clear that there is a possibility that oral bacteria can affect systemic infections. It is thus important to keep the oral cavity clean, in the context of preventing systemic diseases that originate from oral bacteria. Recent years have seen an increase in the number of remaining teeth. This means that the area to which oral bacteria could attach has increased; therefore, oral hygiene should be practiced with higher awareness.

3. Preventive effects of other dental treatment on tooth loss

Some reported that placing a complete veneer crown on the tooth subjected to root canal treatment decreases the rate of tooth loss, compared to the one without a crown[28]. This study was conducted for the purpose of investigating whether dental operculum following root canal treatment could improve the number of remaining teeth. The results revealed a 6-fold higher hazard ratio for tooth extraction after adjusting for tooth type and the presence or absence of dental caries in cases with no complete veneer crowns, compared to those with crowns (95% CI: 3.2-11.3).

The results of this study provide another ground for argument that this treatment intervention, i.e., placement of complete veneer crown, could lead to the prevention of tooth loss.

[Conclusions]

Continuation of proper maintenance with the aim of preventing deterioration of dental diseases, such as dental caries and periodontal disease, will almost certainly lead to the prevention of tooth loss, as many studies have reported. While all of these reports demonstrated performance of necessary dental treatments leading up to maintenance, early detection of diseases during the maintenance period, as well as early treatment, should also be implemented. Therefore, it is considered that performing appropriate dental treatment and further continuing maintenance will lead to long-term tooth preservation. Similarly, doing dental treatment alone and not continuing on with maintenance could lead to tooth loss.

[Conflict of interest]

There are no items applicable to “conflict of interest” in this article.

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9. Effects of dental care

4) Health education (including the common risk factor approach), and topical fluoride application as a measure of health education

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[Abstract]

The purpose of health guidance is to help patients modify their own health behaviors through knowledge and techniques acquired from experts. A large volume of literature exists with regard to dental health education including dental health guidance, and textbooks also cover this topic. However, recent research results have not necessarily been organized academically.

The purpose of this review is to organize the literature in Japan and abroad with regard to the effectiveness of dental health education in improving oral health. In particular, we examined how effective dental health education can be in terms of behavior modification and oral health status improvement in participants. Moreover, we focused on the associations between dental diseases and common risk factors associated with systemic chronic diseases, and aimed to contribute to the common risk factor approach from the perspective of dental health education, as well as to explore its potentiality based on the literature. Furthermore, we summarized present findings regarding the effectiveness of topical fluoride application, a measure of the health education to prevent dental caries.

The results revealed that dental health education is effective in promoting knowledge acquisition and attitude change in participants, and is somewhat effective in preventing and/or improving dental caries, plaque deposition, and periodontal disease. However, while we were able to confirm the effects of dental health education based on the literature, many of them were short-term, and long-term effects still remain unclear. Among the common risk factors (nutrition, hygiene, smoking, alcohol, stress, injuries), smoking was one in which dental support has been shown to be effective according to Cochrane Database of Systematic Review. In relation to dental health education, topical fluoride application methods including fluoride-containing dentifrices and fluoride mouthrinsing have been shown to be effective in preventing dental caries in primary teeth as well as permanent teeth in young people.

[Introduction]

The goal of dental health guidance is to help participants (e.g., patients and residents) modify their own health behaviors in daily life by providing appropriate knowledge and techniques regarding oral health from an expert perspective. In particular, dental caries and periodontal disease, which represent two of the major dental diseases, have both aspects of infectious disease and lifestyle-related disease. Therefore, in the clinical setting, it is believed that improved lifestyle habits will lead to a reduced risk of dental caries and periodontal dintal health guidance performed in conjunction with treatment, which has been shown to greatly affect prognoses, occupies an important place in dental care.

Health guidance belongs to the category of health education. Health education is defined as an educational activity that is performed to achieve goals related to health[1]. The target of health education is not only individuals but also groups. There are various methods of health education, including one-on-one guidance provided in places such as a doctor's office, group work, e-learning, lectures, group discussion, role playing, and the mass media. There are also a wide range of instruments available for health education, such as black/white boards, leaflets, posters, videos, and computer programs. Furthermore, health education can be provided at various places, from a clinic to hospital, and even at school, workplace, community, and facilities for elders.

Dental health guidance is specified as a duty of dentists and dental hygienists according to the Dental Practitioners Act and the Dental Hygienists Act in Japan. Moreover, there is a whole chapter dedicated to dental health guidance in a dentistry textbook. There even exist some textbooks that have compiled only the information related to dental health guidance. As such, dental health guidance has been

recognized as something that should not be neglected in clinical and public health activity settings, regardless of its effect. However, it is not necessarily true that recent research results have been organized academically with regard to dental health guidance.

[Objectives]

Accordingly, the present review aimed to organize domestic and international reports regarding the effects of dental health guidance on oral health improvement. The scope of our search was broadened to cover dental health education, especially for English articles. In particular, a search of the literature was conducted to examine how effective dental health education can be in changing participants' oral health behaviors and improving their oral health status. Moreover, in the context of the approach to "common risk factors" associated with dental diseases as well as systemic chronic diseases, findings concerning dental health education up to present were summarized, with the aim of contributing to the common risk factor approach from the perspective of dental health education, and exploring its potentiality. Furthermore, we summarized findings up to date regarding the preventive effects of topical fluoride application, one of measures to prevent dental caries in dental health education.

[Methods]

From April to May 2014, a search of the literature regarding the effects of dental health education on changes in oral heath behaviors and improvements in oral health status was conducted. The inclusion criteria for the literature were as follows: reports of studies on human subjects, written in Japanese or English, and original research articles or reviews. A search on "ICHUSHI-Web"[2] using "Shika (dental)" and "Hoken shidou (health guidance)" as search terms retrieved 82 articles excluding conference proceedings. Also, a search on PubMed[3] using "effect (title)" and "dental health education (title)" as search terms retrieved 13 articles. Another search using "effect (title)" and "oral health education (title)" as search terms retrieved eight articles. Furthermore, a search on Cochrane Summaries[4] using "dental health education (title)" as the search term retrieved 149 articles. First, literature articles that clearly differed from the purpose of the present review according to the title and abstract were excluded. Furthermore, among the literature articles cited in the main text of the collected literature, those that were in accordance with the purpose of the present review were obtained. Since there were many original research articles on the topics of this paper, the searches were performed with a focus on reviews (including systematic reviews), and the literature was collected accordingly.

In addition, during the same period (April - May 2014), a PubMed search was conducted for articles related to "common risk factor approach (title)," which retrieved relatively old (in publication year) articles[5,6] that had likely served as an original source of this particular term. In reference to the retrieved literature, literature searches were conducted using ICHUSHI-Web[2], PubMed[3], and Cochrane Summaries[4] with regard to each common risk factor (diet, hygiene, smoking, alcohol, stress, injuries) associated with both dental and systemic chronic diseases. Search terms included "Shokuji (diet)," "Seiketsu (hygiene)," "Kitsuen (smoking)," "Inshu (alcohol)," "Sutoresu (stress)," and "Gaishou (injuries)," each of which was used in combination with "Shika hoken shidou (dental health education, oral health education)." First, based on the title and abstract, literature articles that clearly differed from the purpose of this review were excluded. Furthermore, among the literature articles cited in the main text of the collected literature, those that were in accordance with the purpose of the present review were obtained.

Furthermore, from May to June 2014, literature articles with a title containing "fluoride," "dental caries," and "prevention" were searched on PubMed, retrieving 140 articles. Also, on Cochrane Summaries[4], 149 articles with "Health topics" classified under "Dentistry & oral health" were retrieved. First, based on the title and abstract, literature articles that clearly differed from the purpose of this review were excluded. Furthermore, among the literature articles cited in the main text of the collected literature, those that were in accordance with the purpose of the present review were obtained. In addition, materials were obtained by inquiring an expert, who was well versed in the preventive effects of topical fluoride application on dental caries. In the present review, topical fluoride application methods were limited to fluoride-containing dentifrices and fluoride mouthrinsing used in dental health education.

[Results]

1. Effects of dental health education on oral health behaviors and oral health status

1) Oral hygiene knowledge and attitudes

Two systematic reviews[7,8] reported that dental health education increases knowledge of participants and positively affects their attitudes. Kay and Locker[7] collected 14 articles published between 1982 and 1994, and reported that in all of those studies, the effectiveness of dental health education in

improving knowledge and attitudes was demonstrated. The education methods employed in each article varied, ranging from leaflets, expert guidance and programs at school, to movies. Moreover, it was mentioned that some articles did not clearly describe the methods such as statistical methods of evaluation, that the cost-effectiveness was not so great as more effective methods tended to cost more, and that the effects were short-term, although no specific period was indicated. Nakre and Harikiran[8] collected articles published in 1990 and thereafter, and reported that significant effects of dental health education were observed in all of the collected articles including 13 articles regarding knowledge and four articles regarding attitudes.

2) Dental caries

A systematic review[7] that summarized the literature from 1982-1994 found no effect of dental health education on the prevention of dental caries in all four articles. Moreover, a systematic review[8] that summarized the literature published in 1990 and thereafter reported that, although the preventive effects of dental health education on dental caries were observed in five of nine articles, the remaining four articles found no significant preventive effects. In this systematic review, the subjects of the collected articles included school-age children, young people, teachers, and mothers. The follow-up period ranged from 12 months to six years, and the location included school (seven articles), home (one article), and health center (one article).

Cochrane Database of Systematic Review examined the effects of elementary school dental health education on the prevention of dental caries through behavior modification[9]. Regarding this theme, 1,518 related articles were examined, and four of these articles were included in this review. Among these, only one article noted the suppression of dental caries in children who had received health education during the study period. This review concluded that further studies were necessary to verify the results (i.e., the effects of dental health education on caries prevention).

3) Plaque and periodontal disease

Two systematic reviews[7,8] and one review[10] reported that dental health education contributes to decreased plaque deposition and improved periodontal tissue status. Kay and Locker[7] reviewed 15 articles published between 1982 and 1994, and reported that eight of those articles found some effects, whereas seven concluded that there was no effect. Nakre and Harikiran[8] collected articles published in 1990 and thereafter, and reported that the effectiveness was demonstrated in nine of 10 articles with regard to plaque, and all of seven articles with regard to periodontal status. Furthermore, with regard to bleeding on probing, all of seven articles demonstrated the effectiveness. Watt and Marinho[10] reviewed six systematic reviews published in the 1990s and 13 articles published from 1995 to 2003. The results showed that, in the majority of the studies, dental health education led to a decrease in plaque and improvement in gingival bleeding. It should be noted, however, that those changes were often observed over a short period (up to six months), and whether they are of clinical or public health significance is unclear; therefore, it is mentioned that further studies would be necessary to confirm whether these short-term changes would continue afterwards or not.

2. Potentiality of contributing to the common risk factor approach from the dental standpoint

In the past, health education in dentistry had often been performed in the dental area alone, disconnected from the other part of the body. Meanwhile, a number of oral diseases share common risk factors that are associated with systemic chronic diseases. Guidance in health education solely focused on the dental area frequently overlapped with that of other areas, and was inefficient in this regard.

Given that oral diseases share common risk factors associated with systemic chronic diseases, there arose the concept of common risk factor approach, which aims to address common risk factors in order to promote more efficient prevention (Figure 1)[5,6].

The common risk factors include nutrition, hygiene, smoking, alcohol, stress, and injuries. According to the literature currently available, non-smoking support in the dental clinical setting and nutritional guidance at school are among the examples of contribution from the dental area to common risk factors[6].

In particular, with regard to non-smoking support provided by dental professionals at dental care facilities, 14 studies including more than 10,500 participants have reported on its effectiveness according to the Cochrane Database of Systematic Review[11].

3. Effects of dental disease prevention measures on oral health status

We obtained review articles (including systematic reviews) on the preventive effects of fluoride-containing dentifrices and fluoride mouthrinsing, one of preventive measures for dental diseases in dental health education, on dental caries.

1) Fluoride-containing dentifrices

In a review article on the methods of topical fluoride application, Ripa[12] pointed out that the effect of fluoride-

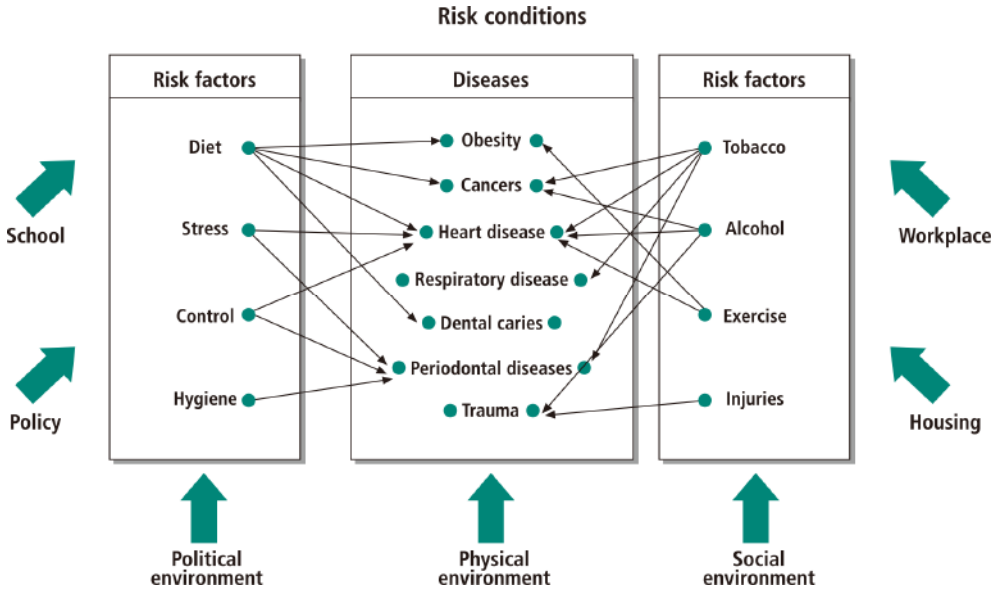

Figure 1: Common risk factor approach
Reproduced, with the permission of the publisher, from the Watt RG. Strategies and approaches in oral disease prevention and health promotion. Bull World Health Organ 2005; 83: 711-718. (Fig. 2, Page 715 http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2626336/pdf/16211164.pdf, accessed 01 July 2014)

containing dentifrices is incontrovertible based on studies in the past 35 or more years, and that the widespread use of fluoride-containing dentifrices has greatly contributed to the recent reduction in caries. Among the systematic review articles regarding fluoride-containing dentifrices, those published in the 2000s have mainly examined their preventive effects on caries in permanent teeth[13-15]. As for the more recent systematic reviews, most of them have examined the association between the preventive effects on caries in primary teeth and dental fluorosis in permanent teeth[16-18].

Twetman *et al*.[13] collected 54 pieces of literature from 1966 to 2003 regarding the effect of fluoride-containing dentifrices in preventing caries in subjects of various ages, and performed an analysis particularly focusing on differences in the fluoride concentration, as well as whether or not brushing was performed under supervision by school teachers, etc. The results showed that fluoride-containing dentifrices were significantly more effective in preventing caries in permanent teeth of young people compared to placebo dentifrices, with a caries prevention rate of 24.9% according to evaluation per tooth surface. Moreover, the fluoride concentration of 1,500 ppm showed a 9.7% higher caries prevention rate compared to 1,000 ppm, and brushing under supervision showed a 23.3% higher caries prevention rate compared to no supervision. Cochrane Database of Systematic Review[14,15] summarized studies targeting individuals aged 5-16 years old, with a follow-up period of at least one year (literature no. 14: 74 articles from 1966 to 2000; literature no. 15: 75 articles from 1966 to 2009). The conclusions were as follows: Fluoride-containing dentifrices have preventive effects on caries in permanent teeth (the caries prevention rate was 24% according to evaluation per tooth surface in literature no. 14, and 23% in literature no. 15); the effects are observed regardless of whether the subjects reside in fluoridated regions or not; it is more effective to use fluoride-containing dentifrices at least twice a day than once a day or less; and no effect could be expected at a fluoride concentration below 1,000 ppm.

At present, the following results are predominant with regard to the relationship between the effect of fluoride-containing dentifrices on the prevention of caries in primary teeth and dental fluorosis in permanent teeth: No preventive effects on caries in primary teeth could be expected at a fluoride concentration less than 600 ppm, but at 1,000 ppm or higher, the effects could be expected (the caries prevention rate was 31% according to evaluation per tooth surface, compared to placebo dentifrices, as reported by literature no. 18)[16-18]. Moreover, when dentifrices containing fluoride at a concentration of 600 ppm were compared to those containing fluoride at a concentration of 1,000 - 1,500 ppm, the risk of developing dental fluorosis was almost the same[16].

2) Fluoride mouthrinsing

Cochrane Database of Systematic Review summarized 36 articles published between 1966 and 2000, which targeted individuals aged up to 16 years old with a follow-up period of at least one year, and reported that those studies had

demonstrated a significant effect of fluoride mouthrinsing on the prevention of caries in permanent teeth (the caries prevention rate of 26% according to evaluation per tooth surface)[19]. It was also shown that this effect was not associated with the severity of dental caries or fluoride application (i.e., whether or not the area of residence was fluoridated, whether or not a fluoride-containing dentifrice was used) in subjects at baseline. Twetman *et al*.[20] reviewed 25 pieces of literature published from 1966 to 2003 reporting randomized controlled studies with at least two years of follow-up period, and concluded that fluoride mouthrinsing was effective in preventing caries in permanent teeth during school age and young adulthood. However, the clear effect was observed only under the limited condition of fluoride application (the caries prevention rate of the fluoride mouthrinsing agent was 31% according to evaluation per tooth surface, compared to the placebo mouthrinsing agent), leading to a conclusion that the additional effect of fluoride mouthrinsing under the condition where fluoride dentifrices are used was unclear. According to a report[21] by the American Dental Association Council on Scientific Affairs Expert Panel on Topical Fluoride Caries Preventive Agents, a summary of 71 articles up to 2012 led to a conclusion that mouthrinsing with a mouthwash containing 0.09% fluoride (at least once a week, or once a day in adults with root surface caries) should be recommended for individuals aged six years or older who are at risk of caries progression.

[Discussion]

1. Effects of dental health education on oral health behaviors and oral health status

Dental health education encourages participants to acquire knowledge and change their attitudes. While it is effective to some extent in preventing and/or improving plaque and periodontal disease, many of the confirmed effects are short-term (up to six months), and its long-term effects remain unclear. In the future, some ethical issues will arise in conducting long-term intervention studies on dental health education, of which the effects over a short-term period have been confirmed. That is, the control group will likely suffer a long-term disadvantage, and it will be difficult to conduct an intervention study for the purpose of verifying long-term effects.

Clinicians should understand that dental health education is effective in the short run, up to six months, and provide dental health guidance accordingly. Based on the fact that dental caries and periodontal disease, i.e., two major dental diseases, possess characteristics of lifestyle-related diseases, and that health education has short-term effects, it is important to encourage patients to make a regular visit at least every six months. At each visit, dental health guidance should be provided, and this effort should be continued.

Researchers need to consider the cost-effectiveness of various types of dental health education in order to efficiently perform dental health education in clinical and public health settings. While dental health education has been performed in the settings of clinical practice and public health, different views of dental professionals, in some situations, confuse patients and residents regarding dental health information. We think that clinicians and researchers should always gather the latest research results, and that efforts should be made to build unity of purpose with regard to dental health information among dental professionals. In the United Kingdom, an attempt has already been made to reach unified decisions regarding diet, toothbrushing, dental visit, and fluoridation[1].

Policy makers, based on the fact that dental health education has short-term effects of up to six months, should make a system that allows all the people at every life stage to make regular dental visits and receive regular dental checkups. In Japan, legal foundation has already been established in the areas of maternal and child dental health and school dental health, and regular dental checkups are being performed. However, workplace or community dental checkups and dental health education have been left to the efforts of each company and local government. Development of legal infrastructure is also required in the workplace and community. Moreover, in the clinical setting, regular dental visit should be introduced and established as part of the public insurance system, and in terms of compulsory education, there is a need to nurture a culture in which regular dental visit is considered a common practice.

2. Possible contribution from the dental area to the common risk factor approach

The common risk factors associated with both oral and systemic chronic diseases include nutrition, hygiene, smoking, alcohol, stress, and injuries. Sheiham and Watt, the advocates of the common risk factor approach, recommended that measures for chronic diseases including oral diseases should be taken effectively and efficiently by an approach that targets these common risk factors[5]. There is strong evidence of the effects of dental support in smoking, one of the common risk factors

Clinicians should understand that smoking cessation counseling in the dental setting is effective. Policy makers should develop the legal infrastructure to facilitate the provision of smoking cessation counseling in the dental

setting based on this evidence. In particular, there is a need for cooperation and collaboration with smoking cessation intervention in the medical setting, which has been introduced to the public healthcare insurance system.

Researchers need to advance research that will form the basis for the common risk factor approach. In particular, epidemiological and basic research regarding the associations between oral diseases and nutrition, hygiene, alcohol, stress, and injuries, and furthermore, intervention studies on common risk factors should be performed, and their results be examined.

3. Effects of dental disease prevention measures on oral health status

We collected review articles regarding preventive effects of fluoride-containing dentifrices and fluoride mouthrinsing, one of topical fluoride application methods related to dental health education, on dental caries. The content examined suggested that both methods were effective in preventing caries in primary as well as permanent teeth in young people.

Clinicians, based on the evidence, should obtain patient information regarding the methods of topical fluoride application at the time of dental health guidance and give appropriate instructions.

Researchers should further engage in the collection of information regarding the preventive effect of topical fluoride application on caries in adults, and on root surface caries in the elders.

Policy makers should make legislative preparations in order to promote further spread of fluoride dentifrice use. In Japan, where fluoridation of water is not performed, the people's caries prevention will likely be greatly linked with the popularization of the methods of topical fluoride application. The most recent survey reported that the rate of fluoride-containing dentifrice use in school-age children was approximately 90%[22]. In this report, it was suggested that parents who have their children use a non-fluoride-containing dentifrice likely purchase dentifrices aimed at preventing periodontal disease and share them with their children[23]. The companies that manufacture dentifrices should be urged to make sure their products contain fluoride, or, the position of fluoride as an essential component of dentifrices should be legally established. Moreover, under the circumstance where the spread of fluoride dentifrices is sluggish, spread of fluoride mouthrinsing is also urgently needed. We think that political interventions might be necessary to promote the widespread use of fluoride mouthrinsing in school and at home.

[Conclusions]

We collected domestic and international literature regarding dental health education and examined how effective dental health education can be in modifying participants' oral health behaviors and improving their oral health status. In addition, in the context of the approach to common risk factors associated with both oral diseases and systemic chronic diseases, we explored the potential contribution from the perspective of dental health guidance. Furthermore, we summarized the literature in Japan and abroad regarding caries prevention effects of topical fluoride application that is used in dental health education.

The results revealed that dental health education has positive impacts on the knowledge and attitudes of participants, and is effective to some extent in preventing and improving caries, plaque deposition, and periodontal diseases. However, most of the effects that could be confirmed were short-term, i.e., over periods spanning up to six months, and long-term effects remain unclear.

The common risk factors include nutrition, hygiene, smoking, alcohol, stress, and injuries. Among these, smoking is one in terms of which support from the dental area has been demonstrated to be effective, according to Cochrane Database of Systematic Review.

As for the methods of topical fluoride application in relation to dental health education, which include fluoride-containing dentifrices and fluoride mouthrinsing. Both have been shown to be effective in preventing caries in primary as well as permanent teeth in young people.

[Conflict of interest]

There are no items applicable to "conflict of interest" in this article.

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9. Effects of dental care
5) Home dental care

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[Abstract]

In Japan, which is currently witnessing an increase in the size of the high older population, it is of the utmost urgency to deploy measures for accommodating older persons requiring nursing care, the number of which is expected to rapidly increase in the future. Although there is a system in Japan that allows home dental care to be performed within the framework of the public health insurance system, the number of cases of home dental care is not keeping pace with the rapidly growing number of elders requiring nursing care despite demonstrating an increasing trend. Amidst the importance of home dental care being widely recognized, this study summarized research conducted both in Japan and overseas on the effects of dental care when dental care is provided to the elders residing at home or in a facility by visitation. As a result, in addition to reducing bacterial counts, dental care was demonstrated to contribute to improvement of the incidence of fevers and pneumonia, and cognitive function during the time specialized oral care was provided by dental professionals on a regular basis at nursing homes and other facilities. Since the underlying diseases and oral health status of the elders requiring nursing care at home or in a facility vary considerably, systematic research on the effects of home dental care per se was unable to be acquired.

[Introduction]

In Japan, a system of public health insurance for the whole nation was established in 1961 in the form of public health insurance, a system is available that enables accommodation of home medical/dental care for patients convalescing at home or in a facility for whom it is difficult to commute to a hospital. As the size of the older population grows and amidst the increasing number of persons requiring nursing care, the importance of home dental care has come to be widely recognized. However, various problems still exist.

According to the results of the Comprehensive Research on Aging and Health Project of the Ministry of Health, Labour and Welfare[1], despite having judged that roughly 90% of persons requiring nursing care require some form of dental care, only 27% of those persons have actually undergone a dental treatment. As is indicated from this result as well, a survey conducted in Niigata Prefecture found considerable imbalance between the supply and demand for dental care among persons requiring nursing care. As evidence of this according to nationwide data, Fukai[2] simulated the imbalanced status of a system for providing dental care required by persons including the elders requiring nursing care within a grand design (2005) for promoting home dental care. According to this report, as of 2005, 18.2% of dental clinics among all dental clinics nationwide performed an average of 12.6 home dental care per month (total for patient homes and non-patient homes), resulting in a sufficiency rate of 3.6% in the case of assuming that all persons requiring nursing care receive dental care once a month. In addition, according to a similar simulation conducted in 2011[3], 20.3% of dental clinics performed home dental care, and were estimated to have performed an average of 22.1 home dental care (total for homebound and institutionalized) per month, resulting in a dental care sufficiency rate for persons requiring nursing care of 5.8%. In other words, those health care institutions providing home dental care account for roughly 20% of the total, and the number of home dental care performed by dental clinics can be seen to demonstrate a rapidly increasing trend. Since dental care had previously been provided primarily through out-patient services, the number of dental clinics attempting to accommodate this situation is not increasing despite rapidly growing needs. Thus, in consideration of the current situation in which dental care for all persons requiring nursing care cannot be said to be adequate, measures are required for eliminating the imbalance between supply and demand with respect to dental care provided to the elders requiring nursing care.

"Home dental care support clinics" were newly established as a part of the medical service payment system in 2008 for the purpose of promoting home dental care, and following the revision of the medical service payment system in 2012, additional allocations were newly established when dental hygienists of home dental care support clinics assist in providing home dental care . In addition, "Training

Seminars for Dentists in Promotion of Dental and Oral Health" as the project for budget allocations of the Ministry of Health, Labour and Welfare, have been conducted since 2008 in order to train dentists and dental hygienists specializing in home dental care or oral care. In this manner, numerous policies have been established for home dental care. In addition, since a large amount of evidence data[4] has been disclosed in recent years indicating that dental and oral health contribute to general health, it is thought that the importance of home dental care will continue to grow in the future.

[Objective]

With this in mind, the purpose of this review was to organize reports from Japan and overseas regarding effects when implementing some form of dental care for convalescing patients at home or in nursing care facilities.

[Methods]

A search of the literature was made for topics relating to the therapeutic effects of home dental care for the period of April to June of 2014. Furthermore, papers were also gathered that related to specialized oral care provided at nursing care facilities and the like. The inclusion criteria for the literature consisted of studies conducted on human subjects that were written in English or Japanese and were submitted by the original author or in the form of reviews. A search was made of ICHUSHI using the search terms "Zaitaku shika iryou (home dental care)" and "Shika houmon shinryou (another words for 'home dental care' in Japanese)", and five papers in Japanese were obtained that coincided with the purpose of this review. A search was also made of PubMed using the phase "home dental care", and 6 papers in English were obtained that coincided with the purpose of this review.

[Results]

1. Effects of specialized oral care

1) Relationship between specialized oral care and incidences of pneumonia and fever

Yoneyama *et al*.[5,6] conducted a survey targeted at residents of special nursing homes for elders located at 11 locations throughout the country, randomly divided the subjects of each facility into two groups consisting of a group that received routine oral cleaning by a care provider while also receiving specialized oral care by a dentist or dental hygienist once or twice a week, and a group that received routine oral cleaning only by a care provider, and compared the incidence of fevers and pneumonia, the number of deaths

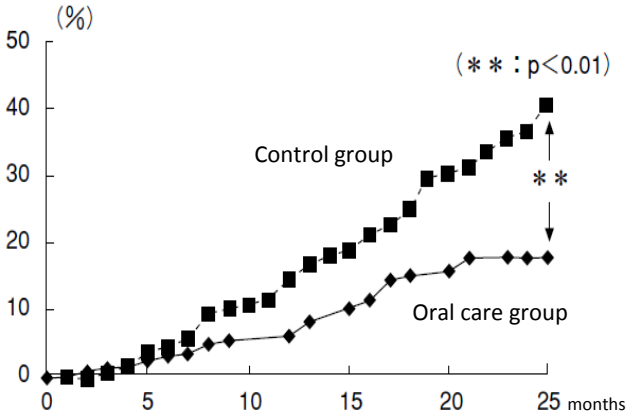

Figure 1: Incidence of fever during survey period

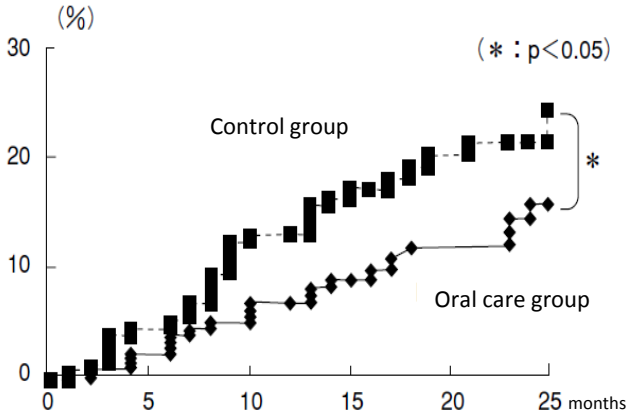

Figure 2: Incidence of pneumonia during survey period

for pneumonia and cognitive function. As a result, the findings shown in Figures 1 and 2 (reprinted) were obtained.

Following the start of the survey, the number of subjects in the oral care group that ran a fever two years later was 54 (29%) and the number in the control group was 27 (15%), indicating a significantly lower number in the oral care group ($p<0.01$), while those subjects in the oral care group that exhibited pneumonia was 21 (11%) and the number in the control group was 34 (19%), again indicating a significantly lower number in the oral care group ($p<0.05$). Moreover, although there were 14 deaths (7%) attributable to pneumonia in the oral care group, there were 30 (16%) in the control group, representing a significantly larger number ($p<0.01$). Although there were no differences observed between the groups with respect to Activities of Daily Living (ADL) that was observed once every six months during the survey period, MMS was significantly lower two years later in the control group in comparison with the oral care group ($p<0.05$).

2) Relationship between specialized oral care and oral bacterial count

Ishikawa *et al*.[7] conducted a comparison of oral health status after five months between a group that received

specialized oral care and a group that only gargled with Isodine. As a result, it was reported that bacterial counts were observed to have decreased significantly in the group that received specialized oral care by a dental hygienist as compared with the group that gargled after meals. In addition, Kokubu *et al*.[8] conducted a study in which the subjects were randomly divided into two groups, and oral bacterial counts were observed to decrease significantly in a group that received specialized oral care, including mucosal membrane care, from a dental hygienist twice a month in comparison with a group that did not receive such care. Moreover, Nishiyama *et al*.[9] demonstrated the effect of adding musical membrane care to specialized oral cleaning. In a randomized control trial (RCT), bacterial counts were observed to decrease significantly in a group in which mucosal membrane care was not conducted in conjunction with specialized oral cleaning as compared with a group in which mucosal membrane care was performed.

2. Effects of home dental care

1) Correlation between home dental care and ADL

Suzuki *et al*.[10] conducted a survey consisting of providing dental care for 70 disabled elders requiring dental care followed by investigating the effect on ADL before and after treatment. As a result, improvement was reported to be observed for numerous parameters, including total Functional Independence Measure (FIM) scores, six weeks following completion of treatment. In addition, Sugihara *et al*.[11] also performed home dental care on 100 residents of a nursing care facility for elders to conduct an intervention survey on whether or not there is improvement of ADL. As a result, FIM scores following treatment were reported to have decreased significantly in comparison with prior to treatment. Moreover, retaining at least one tooth prior to treatment and having a high degree of motivation with respect to daily life prior to treatment were indicated as factors having an influence on improvement of ADL.

2) Correlation between home dental care and condition of requiring nursing care

Nishiyama *et al*.[12] examined the effects of home dental care in 53 elders subjects requiring nursing care. As a result, ADL and the degree of the need for nursing care were reported to significantly worsen when the subjects were reevaluated following home dental care. On the other hand, as a result of performing home dental care by a dental professional, significant improvement was reported to be observed with respect to oral cleanliness, gingival inflammation and halitosis. Moreover, eleven of the subjects were confirmed to have died within six months after reevaluation, and in the group of subjects that died, there was reported to be a significantly large number of subjects who exhibited swallowing disorders.

3. Other

1) Correlation between functional oral care and lingual function

Kikutani *et al*.[13] conducted an evaluation of oral function by continuously providing functional oral care through group training for a period of six months targeted at 98 residents of a long-term elders nursing care facility. As a result, the average value of maximum tongue pressure in an oral care group was observed to increase significantly in comparison with the values at baseline.

2) Preventive dental hygiene program and oral health status

Budtz et al.[14] examined the effects of a preventive dental hygiene program that included tooth brushing instruction provided by dental hygienists. In a group that participated in the dental hygiene program, Candida counts on oral mucosa and dentures were reported to decrease significantly in comparison with a group that did not participate in the program, and oral hygiene status was reported to have improved.

In addition, Nicol et al.[15] reported that, as a result of implementing an oral hygiene educational program by dental hygienists targeted at facility staff members, significant improvements were reported to be observed in denture cleaning and denture sores in comparison with a group that did not participate in the program.

[Discussion]

1. Effects of specialized oral care

Results were able to be confirmed in previous reports in which significant improvement was observed not only with respect to decreased oral bacterial counts, but also in terms of the incidence of fevers and pneumonia, and MMS throughout the study period as a result of providing regular specialized oral care by dentists and dental hygienists. Since the frequency at which specialized oral care was provided as well as the protocol, instruments used and other factors are not standardized, it is thought to be necessary in the future to conduct research oriented towards the establishment of standardized procedures, instruments and frequency. Moreover, a certain degree of effectiveness was also observed with respect to gargling and mucosal membrane care.

2. Effects of home dental care

Due to the small number of original papers, although there were reports indicating that ADL improved as a result of home dental care, there were also those that

reported it conversely decreased. This is thought to be the result of differences in the degree to which nursing care is required, underlying disease and oral health status among elders requiring nursing care that received invention. Since the status of patients varies considerably in comparison with patients examined as out-patients, there is the problem of difficulty in compiling a study design. However, accompanying the continuing growth of the older population in the future, the opportunities for home dental care is predicted to increase, and it was therefore thought to be important to gather cases at numerous health care institutions.

3. Other

Although few in number, the effects of group oral function training targeted at elders persons requiring nursing care are beginning to be reported with respect to improvement of oral function. In addition to accommodation of caries and periodontal disease that were the targets of the majority of dental care provided in the past, it is thought to be imperative to establish dental care systems that also focus on tongue exercises, masticatory function and swallowing function, including masticatory disorders caused by missing teeth. In addition, dental hygiene programs consisting mainly of those implemented overseas were reported to be effective in improving oral hygiene status. Although the range of insurance coverage of dental care available to the elders differs between Japan and other countries, it is presumed that such educational programs will also be implemented in Japan as part of the nursing care insurance system. It is hoped that large-scale demonstration research will be conducted in the future.

On the basis of the above, results were obtained from studies targeted at facilities and groups that indicated that dental care is beneficial to elders requiring nursing care. However, it was also clearly determined that there is the problem of difficulty in conducting large-scale surveys and standardization of methodology with respect to dental care provided at home. As the size of the older population increases, the providing of home dental care to persons requiring nursing care is thought to be a pressing issue. It is also thought that it will be necessary for clinicians and researchers to establish guidelines for instruments and methodology relating to home dental care. In addition, government policymakers will be required to establish a system that enables persons recovering from any disease to receive the necessary dental care regardless of their location.

[Conclusions]

This review has provided a summary of previous reports regarding the effects of specialized oral care, home dental care, and oral function training provided by dentists and dental hygienists.

According to those results, periodical specialized oral care provided by dental professionals was determined to not only reduce bacterial counts, but also contribute to improvement of the incidence of fevers and pneumonia, and cognitive function during the time such care is provided. In addition, reports indicating that home dental care both improve and decrease ADL were observed. Improvement of lingual function was observed with respect to group oral function training.

[Conflict of interest]

There are no items applicable to “conflict of interest” in this article.

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III Conclusion

Conclusion

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The realization of a "society of longevity" is a result of human advancement. On the other hand, the decline of vital functions and health with age is something we cannot avoid biologically. To address this seemingly paradoxical issue, we urgently need to develop a social structure and health care system that will allow elderly individuals to lead their lives with purpose and dignity. To this end, specific measures have been taken to reduce health inequalities among generations and regions, thereby extending healthy life expectancy in each and every individual.

Since the implementation of a universal health insurance system in 1961, the health status of the people of Japan has improved considerably and the country has achieved a level of longevity greater than anywhere else in the world. As the nation standing at the forefront of the society of longevity, Japan has a responsibility to report its experiences to the world, particularly concerning its healthcare policies and campaigns as well as our attempts to reform its healthcare system.

As the evidence and analyses presented in this publication confirm, basic dental and oral functionality is associated with self-expression and socialization -which are fundamental human rights- through diet and communication. In the long run, dental and oral health is also associated with vital prognosis in humans. In fact, an accumulation of evidence suggests that dental care and oral health can and do contribute to the realization of healthy longevity.

Against this backdrop, and based on the analyses in this book, I make the following recommendations regarding healthy longevity, dental care, and oral health.

1. Health and medical care systems should be developed in such a way that even in old age, anyone can receive the dental care and oral health services they need, no matter where they live.
2. Dental health care personnel should make continuous efforts to communicate the current evidence regarding dental care, oral health, and healthy longevity to citizens and health policymakers.
3. The development of health and medical technology should be promoted, in addition to training human resources that provide evidence-based health and medical services.
4. A strong body of evidence shows that the prevention of tooth loss contributes to healthy longevity. Through bidirectional efforts involving medical and community health services, greater efforts should be made to prevent dental diseases (e.g., dental caries and periodontal disease) and the tooth loss that results from these diseases.
5. Dental health care personnel and relevant organizations should work together to enact measures that target the risk factors which are common to both oral diseases and non-communicable diseases (NCDs), and they should also work to develop health systems based on a continuous life-course approach covering the period from adulthood to old age.
6. Efforts should be made, from the standpoint of dental health care provision, to accumulate evidence regarding the effects of maintaining and recovering masticatory function and occlusal support, as well as the effect of prevention and control of dental diseases on systemic health.
7. High-quality research should be conducted to accumulate evidence which further clarifies the causal relationship linking dental and oral health to healthy longevity.
8. Efforts should be made to estimate the medical economic effects of dental and oral health policy implementation as well as evidence accumulation.
9. Evidence-based health policies which reflect the association between current dental and oral health and the extension of healthy life expectancy should be implemented, and studies verifying the effectiveness of these policies should be undertaken.

IV Appendix

1. 8020 Campaign

2. Medical insurance system in Japan (universal health insurance system)

IV Appendix

1. 8020 Campaign

1. 8020 Campaign

The 8020 Campaign for oral health promotion in Japan Its History, Effects, and Future Visions

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1: 8020 Promotion Foundation 2: Tokyo Dental College, Social Security for Dentistry

[Abstract]

The 8020 Campaign for oral health promotion, which aimed to encourage people to keep 20 of their own teeth even until the age of 80, is a long-term oral health campaign that Japan launched in 1989 ahead of the rest of the world as it saw its population aging rapidly in the second half of the 1980s.

As part of the efforts to lay the foundation for the spread of the Campaign, the 8020 Promotion Foundation was established in 2000. Over the years, the Foundation has continued to promote research on the association between oral health and general health, as well as the dissemination of the concept of oral health and the education of the people on this concept.

Later, the Japanese people showed remarkable improvement in terms of the number of teeth they kept. The Survey of Dental Diseases conducted by the Ministry of Health, Labour and Welfare in 2011 indicated that the number of missing teeth had decreased. Moreover, 40% of those surveyed had achieved the 8020 Campaign's goal of having 20 teeth when they are 80 years old. In terms of oral health as well, continuous improvement was confirmed, as exemplified by the decrease in the number of carious teeth among children as well as the increases in the number of children who underwent dental health examinations of periodontal diseaseand the percentage of those who used fluoride-containing tooth paste. On the basis of the population's growing interest in health promotion including dental health care services and the accumulation of research data showing the association between oral health and general health, the Act concerning the Promotion of Dental and Oral Health was established in 2011, setting new oral health goals.

In 2014, as part of its dental health system for adults and the elderly, the Japanese government established a new scheme. Through this scheme, dental health examinations for the elderly aged 75 or older are subsidized. In the future, to contribute to health promotion as the dental health of people improves, it is essential to further push the 8020 Campaign forward while advancing related research projects and consider ways to contribute to "the best mix of oral health/general health service and dental care provision" so that new phases of the Campaign will be developed.

1. Introduction

The 8020 Campaign for oral health promotion, whose goal is to encourage people to keep 20 of their own teeth until they become 80, is a national oral health campaign that has been carried out for the past quarter century under the leadership of the Japanese government and the Japan Dental Association (JDA).

At first, as the population was rapidly aging, the Campaign was implemented in order to improve and spread dental health services for adults and the elderly for whom such services had not been provided in earnest. It was originally positioned as one of Japan's important issues to be addressed when taking measures to promote dental health.

Twenty-five years has passed since this campaign was launched in 1989. Initially, in 1987, the percentage of those who had 20 teeth at the age of 80 was less than 10% of the population. During this interval, however, the dental and oral health of people in Japan improved substantially, and the Survey of Dental Diseases conducted in 2011 showed that 40.2% of those aged 75 to 84 owned 20 of their teeth.

Moreover, research reports emphasizing that the promotion of the 8020 Campaign contributed to general health improvement have been accumulated.

In the beginning of the 8020 Campaign, the Ministry of Health, Labour and Welfare established a new scheme. Through this scheme, the Campaign was subsidized to promote it as it started to implement measures to improve dental health and thus promote the dental health of adults and the elderly.

In 2000, more than ten years after the launch of the Campaign, the 8020 Promotion Foundation was set up through the efforts of persons concerned with dental care to further promote the Campaign, the dissemination of the concept of oral health, education of the people on this

concept, and related research.

In the same year, a new special project to promote the 8020 Campaign was also organized in all prefectures of the country, marking the establishment of a basis for pushing the campaign forward on a nationwide scale.

Later, in December 2008, an official ceremony and symposium to commemorate the 20th anniversary of the Campaign's launch was held under the sponsorship of JDA, the Japanese Association of School Dentists, the 8020 Promotion Foundation, and the Yomiuri Shimbun with the support of related organizations such as the Ministry of Health, Labour and Welfare and the Ministry of Education, Culture, Sports, Science and Technology.

August 2011 saw the enactment of the Act concerning the Promotion of Dental and Oral Health.

From the start of the Campaign to the present, the number of carious teeth has declined, and an increasing number of elderly people have achieved the 8020 Campaign's goal. Thus, the dental health condition of people in the country has improved as the number of teeth they kept continued to increase.

In 2013, to further promote the 8020 Campaign, the 8020 Promotion Foundation proposed policies toward the "best mix of oral health/general health service and dental care provision"In this article, we discuss the 8020 Campaign's past initiatives and results and its future plans and touch on its visions for the future as the Foundation aims to further enrich and develop the 8020 Campaign.

2. What is the 8020 Campaign?

In July 1987, some of the dental administrators and those involved with local dental associations held a workshop under the concept that if people had lost only around ten of their teeth, they would practically have no problem chewing food. During the workshop, they proposed that they should promote the new idea of "8010 (keeping the number of teeth lost before becoming 80 at ten or less)" as the ultimate goal of the dental health measures for adults.

Subsequently in December 1989, in its interim report, the then Ministry of Health and Welfare's "meeting to consider adult dental health measures" proposed the "8020 Campaign to keep 20 or more of their own teeth even until the age of 80" by developing the idea of "8010" into a more proactive one. This led to the launch of Japan's national oral health campaign known as the 8020 Campaign.

The 8020 Campaign has been carried out by the Japanese government through the Ministry of Health, Labour and Welfare, JDA, the 8020 Promotion Foundation, and other organizations as a national campaign to promote dental health over a relatively long period of time. Even today, it is being implemented actively. It is also introduced by the World Health Organization(WHO) to the rest of the world[1]. Indeed, with an oral health goal that we can confidently recommend to other countries, the 8020 Campaign can promote the dissemination of the concept of dental and oral health and the education of people on this concept on a continuous basis.

The Surveys of Dental Diseases, which have been conducted every six years since 1957, have shown that with each survey after the launch of the 8020 Campaign, the number of those who achieved the Campaign's goal increased, indicating that the number of teeth kept by people increased.

Table 1: History of the 8020 Movement and its recent developments

1989	The Ministry of Health and Welfare's "group to consider adult dental health measures" published its interim report (in which the 8020 Movement was proposed).
1991	The "promotion of the 8020 Movement" was held up as one of the priority goals for the Dental Health Week.
1992	The Ministry of Health and Welfare started "a project to take measures to promote the 8020 Movement" as one of its new budget subsidy projects.
1992	WHO's panel of experts on "the recent progress in oral health" included a description of the 8020 Movement in its report.
1993	The Japan Dental Association (JDA) set up a "meeting to consider the promotion of the 8020 Movement."
1994	JDA's "meeting to consider the promotion of the 8020 Movement" compiled a report.
1995	Examinations for periodontal diseases were added to the list of general health examination items.
1996	JDA's Public Health Committee drew up a report on the "promotion of the 8020 Movement."
1997	Special projects to promote the 8020 Movement were launched by municipal governments and Tokyo's 23 ward governments.
1998	JDA established a "committee for considering the organization of the 8020 promotion foundation (tentative name)."
1999	JDA's "committee for considering the organization of the 8020 promotion foundation (tentative name)" put together a report.
2000	The Healthy Japan 21 project (first phase) was launched. "Special projects to promote the 8020 Movement" were launched by prefectural governments as one of the Ministry of Health and Welfare's new budget subsidy projects. The 8020 Promotion Foundation was established.
2002	The Health Promotion Act was established.
2004	People aged 60 and 70 were added to the list of people who should undergo examinations for periodontal diseases as part of the health projects for the elderly.
2007	"Examinations for periodontal diseases" were included in the examination items as stipulated by the Health Promotion Act (transferred from the health projects for the elderly).
2008	The latter-stage elderly healthcare system began. Dental clinics to support home medical care were institutionalized. An official ceremony and symposiums to commemorate the 20th anniversary of the 8020 Movement's foundation were held.
2011	The Act concerning the Promotion of Dental and Oral Health was established.
2012	Basic Matters Related to the Promotion of Dental and Oral Health were stipulated. The Healthy Japan 21 project (second phase) was launched.
2013	The Ministry of Health, Labour and Welfare started its oral health promotion projects.
2014	The Ministry of Health, Labour and Welfare launched a project to subsidize insurers when providing dental examinations for people aged 75 or older.

3. History of the 8020 Campaign

Table 1 shows the history of the 8020 Campaign. At first, when the Campaign was proposed[2], the then Ministry of Health and Welfare proposed the 8020 Campaign as the priority goal of the Dental Health Week and took actions such as subsidizing prefectural governments' model projects and other new projects.

In 1993, JDA set up a "meeting to consider the promotion of the 8020 Campaign" and conducted various discussions about the Campaign, and in 1994, it put together its first report on the initiative.

Later, there was a growing interest in establishing the 8020 Promotion Foundation, and in 1998, JDA established a "committee for considering the organization of the 8020 promotion foundation." In the following year in 1999, JDA compiled a report on the subject, and in 2000, the 8020 Promotion Foundation was duly established, which promoted dissemination and educational projects, and subsidized research projects to be implemented more actively than before[3].

The projects that have been carried out since the establishment of the 8020 Promotion Foundation involved the (1) promotion of the Campaign as a national campaign, (2) gathering of information and provision of information for the nation, and (3) advancement of research and studies. To date, emphasis has been placed on promoting the Campaign as a national campaign, but in the future, it is necessary to shift project implementation to research and studies that enable us to make policy recommendations. For this reason, the focus of activities is beginning to shift not only to the examination of individual dental diseases but also to research and studies of noncommunicable diseases (NCDs) and other dental health issues related to the lifestyles of people. In this backdrop, in 2013, the 8020 Promotion Foundation published its recommendations for the policies of the best mix of oral health/general health service and dental care provision and for high-priority future research subjects (Tables 2, 3, and 4).

In August 2011, the Act concerning the Promotion of Dental and Oral Health was established. It took a long time for this to be realized, although since the 1950s there had been several waves of growing interest in enacting it. Moreover, dental and health care professionals had hoped for such legislation. In 2012, following the enactment of the law, the Basic Matters Related to the Promotion of Dental and Oral Health was laid down. At the same time, the Healthy Japan 21 (second phase) was launched, setting the goal of increasing the percentage of people with 20 teeth at the age of 80 to 50% in fiscal 2022 (Table 5).

These initiatives resulted in the formulation of dental health and dental care programs for the future from a new perspective, including the appropriate positioning of goals related to oral functions in these programs.

The Ministry of Health, Labour and Welfare's initiatives that followed the establishment of the Act included subsidizing new projects related to cooperation between medicine and dentistry. Oral health promotional projects aimed at developing oral health centers, which targeted all prefectures, core cities, and cities allowed to establish health centers, were also subsidized.

In fiscal 2014, the Ministry started to subsidize insurers when they provided dental examinations for those aged 75 or older. It was the first subsidy of its kind since fiscal 2004 when those aged 60 and 70 were newly required to undergo examinations for periodontal diseases under the then Health and Medical Services Act for the Aged.

4. Effects of the 8020 Campaign and changes in the dental health status

Although its effects cannot be grasped directly, the 8020 Campaign has played a part in promoting dental health measures in Japan even before the formulation of the Act concerning the Promotion of Dental and Oral Health. The measures included initiatives to prevent dental diseases in the daily lives of people as envisaged in the basic idea of the Act., the early detection and treatment of dental diseases throughout the life, and the promotion of appropriate and effective dental and oral health from infancy to old age.

Furthermore, it is believed that the Campaign has made substantial contributions to dental health promotion as the Foundation accumulated many research and study materials related to dental health (designated research projects, research projects collected from the public, and dental health activity support projects). In the following section, on the basis of the status affected by dental diseases and dental health as discovered by the Surveys of Dental Diseases as well as the results of verification obtained from Healthy Japan 21 (2000 to 2012), we will discuss the effects related to the long-standing 8020 Campaign from the viewpoint of changes in dental health[4].

1) Changes in the percentage of people with 20 teeth or more and that of edentulous people (Table 5)

Data on people with 20 teeth or more obtained from Surveys of Dental Diseases from 1975 to 1987 (i.e., prior to the launch of the 8020 Campaign) were compared with those after its launch. The comparison showed that the percentage of people with 20 teeth increased in each age group. In particular, the percentage of people aged 55-

Table 2: Proposals through this designated research

Proposals

This designated research makes proposals for oral health and dental care policy to realize a healthy society of longevity from the viewpoint of establishing a more effective and efficient oral health and dental health care provision system and working out effective measures to prevent the loss of teeth, a specific measure to achieve the goal, as follows:
Proposal 1: Measures to prevent the loss of teeth contribute to realization of a healthy society of longevity.
Proposal 2: A new system that combines oral health and dental care in the optimal way is necessary to effectively prevent the loss of teeth.
(1) Best mix of oral health and dental care to prevent the loss of teeth
(2) Best mix of health promotion (health) and dental care
Proposal 3: A shift to a system of medical treatment fees that favorably evaluates efforts to prevent the occurrence of dental diseases and prevent the loss of teeth is necessary.
Proposal 4: Initiatives to address high-priority research subjects in order to prevent dental diseases more effectively and provide medical service to achieve the goal are necessary.
Proposal 5: Establish a national center dedicated to dental health and medical research (or reestablish the existing one)

Table 3: Specific measures through this designated research

Specific measures

Measure 1: Cooperation (best mix) between public health and health care
- Improve the examinations for periodontal diseases based on the Health Promotion Act and take appropriate actions after the examinations
- Provide health guidance and education in local community centers and clinics in an integrated manner (Create and effectively use a risk evaluation chart shared by dental examiners and dental care providers)
- Cooperation among schools and local communities to prevent dental caries, and dental care systems

Measure 2: Establish common evaluation indicators to ensure cooperation among physicians, dentists, and nutritionists in the prevention of lifestyle-related diseases (NCDs)
Measure 3: Evaluation of efforts to maintain the present teeth under the medical insurance system
(1) Best mix of oral health and dental care to prevent the loss of teeth
i) Optimal combination of population strategy and high-risk strategy
Present-teeth maintenance and management method (1) (addition): Draft plans for taking actions to improve the local disease structure
ii) Evaluation of patients' oral health behavior
Present-teeth maintenance and management method (2) (addition): Draft plans for taking actions to encourage patients' oral health behavior
iii)Draft plans for evaluating patients' efforts to maintain the present teeth according to the condition of their mouth
(2) Best mix of health promotion (health) and dental care
i) Efficient response to common risks involved in NCDs and dental diseases
ii) Make dental care responsible for some of the roles to prevent medical diseases from occurring and becoming serious (in terms of treatment, preventive actions, health guidance)
Measure 4: Establish a national center dedicated to dental health and medical research (or reestablish the existing one)
Its necessity and functions:
(1) Monitoring of dental diseases and examination of risk factors
(2) Establishment of the best mix of oral health and dental care based on Act concerning the Promotion of Dental and Oral Health, Healthy Japan 21, etc. and its dynamic verification using the PDCA cycle
(3) Monitoring of dentist demand and supply from the viewpoint of medical economics and proposals
(4) Encouraging the national center to display its functions in terms of the use of fluoride

Table 4: Effects expected of this designated research

Effects expected of research in the best mix of dental health and health care and measures taken to achieve it
(1) Working out more effective measures to prevent the loss of teeth
- Development of technology to diagnose dental diseases and improvement of dental examination systems
- Ensuring sharing of NCD risk information between physicians and dentists (Example: Improvement of the quality of health guidance by dentists and dental hygienists through greater effects in health guidance (EBM) such as information on diabetes)
- Acceleration of people's voluntary efforts for dental and oral health such as receiving dental examinations over the years (for example, giving incentives to people by reflecting their efforts, such as partly decreasing copayment for the dental examinations)

(2) Establishment of a more effective health and health care provision system
- Response to common risk factors for NCDs taking into consideration limited financial and human resources in medicine and dentistry
- Systems to prevent the loss of teeth can also be used for approaches to prevent lifestyle-related and other diseases from occurring and becoming serious. Furthermore, economic effects such as reductions in health and health care expenses through prevention and control of NCDs can be expected.

(3) Effective realization of a healthy society
- The health inequality arising from lack of cooperation between health promotion and health care (not only dental diseases but also NCDs related to medical/dental common risks) will be abolished, and as a result, the (healthy) life expectancy will be extended.

Table 5: Dental Health Goals Set in Relation to the 8020 Movement in the Past

Healthy Japan 21 First Phase, (2000)		
Goal for the period up to 2010	When the project started (2000)	Goal (2010)
Increase the percentage of people who keep 20 of their own teeth or more until they become 80	11.5%	20%
Healthy Japan 21 Second Phase, (2012) and Basic Matters Related to the Promotion of Dental and Oral Health		
Goal for the period up to 2022	When the project started (2012)	Goal (2022-23)
Increase the percentage of people who keep 20 of their own teeth or more until they become 80	25%	50%

64, 65-74, and 75 or older with 20 teeth or more increased after the launch of the Campaign. In 2011, the percentage of those aged 65-74 with 20 teeth was 60%, three times as many compared with the period prior to the launch of the Campaign.

2) Percentage of those who had carious teeth and those who had teeth left untreated (Table 7)

Between 1975 and 1987, there was no major change in the percentage of those who had dental caries. However, since 1987, when the 8020 Campaign began, there has been a conspicuous tendency to have less carious teeth in the young age groups. In addition, certain percentages of people with teeth left untreated came to be found in young age groups and those aged 5 or older.

3) Application of fluoride (Figure 1)

A comparison with past surveys indicates that an increasing percentage of people have used fluoride for their teeth.

During this period, fluoride-containing tooth paste has increased its market share rapidly. Moreover, the use a mouth rinse with fluoride has spread at elementary and junior high schools. These indicate that the local application of fluoride in children has become remarkably popular.

4) Final assessment of Healthy Japan 21 (October 2011)

In 2000, Healthy Japan 21 set its targets for 2010. This national campaign established 13 dental health indicators. The targets were achieved for five of them, and improvements were made for seven whose targets were not attained. Overall, results indicated that the degree of improvement for all dental health indicators was high.

Tables 8 and 9 show the goals established for dental diseases, dental health, and dental prophylaxis; the circumstances of the period when the goals were established; and the results of the final assessment of the national campaign after the completion of final goals in 2010.

In terms of dental diseases, the indicators for the number of teeth present, dental caries, and periodontal diseases generally showed improvements[5].

In terms of dental health, which decreases the incidence of dental diseases, many indicators improved as exemplified by the increase in the number of those who underwent periodic dental examinations, the percentage of users of interdental cleaning tools, and percentage of those who had fluoride applied to the surface of their teeth and users of fluoride-containing dentifrices.

This final assessment indicated that promoting the 8020 Campaign was the most important among all principal measures taken to achieve the goals for individual indicators.

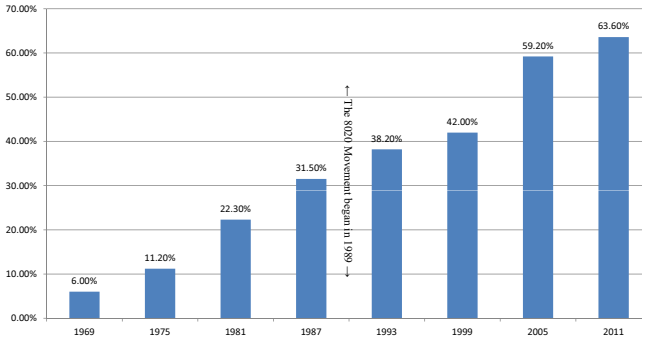
5) Final assessments of the Surveys of Dental Diseases and Healthy Japan 21

The results of these surveys and final assessments indicate that in Japan, through the 8020 Campaign, the number

Table 6: Changes in the percentage of people with 20 teeth or more

	Age groups				
	Aged 45-54	55-64	65-74	Aged 75 or older	Aged 80 or older
1975	66.4	37.4	17.7	6.3	5.8
1981	72.0	40.9	19.1	6.9	5.0
1987	76.8	48.1	21.7	8.5	7.0
1993	82.9	58.7	28.9	9.5	8.9
1999	87.2	70.2	42.5	15.5	9.9
2005	91.7	76.1	50.1	22.9	17.3
2011	94.9	81.3	60.4	36.5	25.1

1) The 8020 Movement was launched in 1989.
2) This table has been created using the Ministry of Health, Labour and Welfare's "Results of the Surveys of Dental Diseases."



Source: Surveys of Dental Diseases carried out by the Ministry of Health, Labour and Welfare

Figure1: Percentage of people who have used fluoride for their teeth

Table 7: Changes in the percentage of people who had carious teeth and those who have teeth left untreated

	Percentage of people with carious teeth			Percentage of people who have teeth left untreated		
	Primary teeth (Aged 1-14)	Primary + permanent teeth (Aged 5-14)	Permanent teeth (Aged 5 or older)	Primary teeth (Aged 1-14)	Primary + permanent teeth (Aged 5-14)	Permanent teeth (Aged 5 or older)
1975	62.0	96.9	85.1	58.4	83.3	62.9
1981	57.8	96.3	86.0	49.8	76.3	59.1
1987	58.8	93.6	84.8	45.1	66.7	54.4
1993	56.9	90.4	85.6	26.5	58.8	49.1
1999	45.2	78.3	85.9	26.4	45.5	41.8
2005	41.6	68.1	85.0	23.9	36.9	35.8
2011	35.3	53.4	85.7	20.4	22.1	34.3

1) The 8020 Movement was launched in 1989.
2) This table has been created using the Ministry of Health, Labour and Welfare's "Results of the Surveys of Dental Diseases."

of missing teeth lost is generally continuing to decrease, and that the dental health of people is also improving continuously.

In 2011, Moriya *et al*.[6] studied changes in the oral health of Japanese on the basis of the National Surveys of Dental Diseases and tooth extraction surveys conducted during the period until 2005 and the progress of Healthy Japan 21. As a result, they suggested that the dental health of the people had improved primarily owing to the government's health policy and the 8020 Campaign. The 2011 survey and details of the results of Healthy Japan 21 showed a similar tendency.

These results give a glimpse of the effects of the implementation of the 8020 Campaign aimed at promoting the dental health of the nation.

5. Effects of the 8020 Campaign on health

There have been many studies investigating the association between oral health and general health, and, actually, these are too numerous to mention in this limited space. Additionally, these are still being accumulated on a daily basis.

In the case of diabetes, for example, many intervention studies have suggested that periodontal diseases aggravate blood sugar levels, and therefore, treatment of periodontitis results in improved blood glucose control[7,8].

The study conducted by Yoneyama *et al*[9]. on the institutionalized elderly indicated that the number of the subjects who developed fever or pneumonia, or died from pneumonia actually reduced by intensive oral care. They also found that oral care was effective for preventing aspiration pneumonia.

Furthermore, the results of a 15-year cohort study carried out in Miyakojima Island of Okinawa Prefecture showed that elderly people who preserved their teeth tended to maintain their life prognosis well. It also showed that people with fewer functional teeth were more likely to complain about their physical conditions such as pain in their lower back, shoulders, and upper and lower limbs[10].

Other studies showed that dental care tended to prevent the subjects from suffering declined physical functions who require nursing care due to the reduced activities of daily living (ADL)[11].

To achieve "society where the healthy life of people is extended," a vision published in August 2013 by the Ministry of Health, Labour and Welfare, aims to push forward with initiatives for prophylaxis and health care. The Ministry aims to make the public realize these by providing oral care in combination with preventive care for aspiration pneumonia in the elderly and by preventing the progression of diabetes through health examinations and health guidance including treatment of periodontal diseases. It is hoped that many researches ascertaining favorable effects of 8020 Campaign

Table 8: Goals for Healthy Japan 21 (first phase) and the condition of dental diseases at the time of goal setting and final assessmen

		When the goal was initially set (partly interim assessments) (At the time of baseline survey)		Final assessment (Partly the results of the survey conducted close to the year of goal setting)	
Dental health goals set for Healthy Japan 21 (first phase) (2000)					
(1) Present teeth					
		1993		2011 (Results of a survey conducted close to the year of goal setting)	
Percentage of people who have 20 of their own teeth or more at the age of 80	Aged 75 - 84: 20% or more	11.5%	Survey of Dental Diseases	40.2%	Survey of Dental Diseases
Percentage of people who have 24 of their own teeth or more at the age of 60	Aged 55 - 64: 50% or more	44.1%	Survey of Dental Diseases	65.3%	Survey of Dental Diseases
(2) Carious teeth					
		FY1998		FY2009	
Increase in the number of 3-year-old children who have no caries teeth	80% or more	59.5%	Dental health exams for 3-year-old children	77.1%	Dental health exams for 3-year-old children
		1999		2010 (Results of a survey conducted close to the year of goal setting)	
Decrease in DMFT for 12-year-old children	1 or less	2.9	Report on school health statistics	1.3	Report on school health statistics
(3) Periodontal diseases					
		2004 (Interim assessment)		2009	
Decrease in the number of people with a progressive periodontal disease (with periodontal pocket depth of CPI ≥4mm)	Aged 40: 22% or less	23.8%	National Health and Nutrition Survey	18.3%	National Health and Nutrition Survey
	Aged 50: 33% or less	36.8%	National Health and Nutrition Survey	27.6%	National Health and Nutrition Survey

Table 9: Goals for Healthy Japan 21 (first phase) and the condition of dental health at the time of goal setting and final assessment

		When the goal was initially set (partly interim assessments) (At the time of baseline survey)		Final assessment (Partly the results of the survey conducted close to the year of goal setting)	
Dental health goals set for Healthy Japan 21 (first phase) (2000)					
(1) Prevention of tooth loss					
		1993		2009	
Increase in the number of people who have undergone periodic dental examinations during the past year	Aged 60 (55-64): 30% or more	16.4%	Survey of trends in health and welfare	36.8%	National Health and Nutrition Survey
		2004 (Interim report)		2009	
Increase in the number of people who have undergone periodic scaling and cleaning of the tooth surface during the past year	Aged 60 (55-64): 30% or more	43.2%	National Health and Nutrition Survey	43.2%	National Health and Nutrition Survey
(2) Prevention of periodontal diseases during the adulthood					
		1993		2009	
Increase in the use of interdental cleaning tools	Aged 40 (35-44): 50% or more	19.3%	Survey of trends in health and welfare	44.6%	National Health and Nutrition Survey
	Aged 50 (35-44): 50% or more	17.8%		45.7%	National Health and Nutrition Survey
		1998		2008	
Dissemination of full knowledge of the effects of smoking on health (periodontal diseases) (Percentage of people who know these effects)	100% or more	27.3%	Survey of attitudes toward smoking and health problems	40.4%	National Health and Nutrition Survey
		2001		2008	
Percentage of municipalities that provide smoking cessation support programs	100% or more	32.9%	Report on local health and elderly health projects	38.9%	Report on local health and elderly health projects
(3) Prevention of dental caries during the babyhood and the school age					
		1993		2011 (Results of a survey conducted close to the year of goal setting)	
Percentage of people who have used fluoride for their teeth	50% or more	39.6%	Survey of Dental Diseases	63.6%	Survey of Dental Diseases
		2004 Interim report		2009	
Percentage of people who have a habit of eating and drinking sweet foods and beverages between meals three times a day or more	15% or less	22.0%	National Health and Nutrition Survey	19.5%	National Health and Nutrition Survey
		2004 Interim report		2009	
Increase in the use of fluoride-containing dentifrices during the school age	90% or more	56.5%	National Health and Nutrition Survey	86.3%	National Health and Nutrition Survey
		2004 Interim report		2009	
Increase in the percentage of school children who have received individual guidance in oral prophylaxis during the past year 30% or more	30% or more	16.5%	National Health and Nutrition Survey	20%	National Health and Nutrition Survey

on general health will be further conducted by various groups in the future.

6. Future development of the 8020 Campaign

In the Basic Matters Related to the Promotion of Dental and Oral Health, compiled after the Act concerning the Promotion of Dental and Oral Health was established in 2011 by the Ministry of Health, Labour and Welfare, emphasis is placed on the need to implement dental health plans. These plans include the prevention of periodontal diseases and the dissemination of methods to prevent worsening of such diseases (such as teeth and mouth cleaning and periodontal disease examinations), in order to achieve the goal of increasing the percentage of people with 20 or more of their teeth at the age of 80 to 50% by fiscal 2022.

In addition, increasing the number of people who could chew well has been included in the new goals recently set for the "maintenance and improvement of oral functions to raise the quality of life." The 8020 Campaign is expected to develop new initiatives to achieve this goal. In the future, it is necessary to ensure that the Campaign is implemented not only as part of the local health programs but also as part of the daily dental care and position the Campaign as one of the efforts to promote health in cooperation with other various health professionals.

In terms of research, as shown in Table 10, the Ministry stated in the "basic matters" stipulated in July 2012 that research on the associations between oral conditions and general health, between dental diseases and lifestyles, and

Table 10: Basic Matters Related to the Promotion of Dental and Oral Health (July 23, 2012) (Excerpts)

2.Promotion of research

In order to contribute to effectively improving the dental and oral health of people, the national and local governments shall promote research in the subjects listed below, reflect the results of such research on their policy, and provide people and other parties concerned with full and appropriate information.

- Relationships between the oral condition and general health
- Relationships between dental diseases and lifestyles
- Relationships between dental/oral health and medical expenses
- More effective prevention, treatment, and methods for dental diseases

between dental/oral health and medical expenses, as well as on methods to prevent and treat dental diseases more effectively, should be promoted actively. The results of such research should be reflected on policies made. Moreover, sufficient and appropriate information on dental and oral health should be provided to all parties concerned, including general consumers.

It takes some time to accumulate evidence-based, reliable research data, but such data available should be reflected on the government's dental health and dental care policy. The 8020 Promotion Foundation needs to continue necessary research and study projects in the future, including the research subsidies it has granted since 2001. It is important to continue research associated with the Foundation's 2013 designated research project entitled "policy recommendations toward the best mix of oral health/general health service and dental care provision based on the Act concerning the Promotion of Dental and Oral Health and pursuing high-priority research subjects in the future[12]."

7. Conclusions

In this article, we discussed the development of the 8020 Campaign, including its history and future plans. It is necessary to aim for a society where more than 50% of the people have achieved the 8020 goal and further improve dental care and oral health to realize such a society. In addition to the previous indicator of increasing the number of remaining teeth, it is also necessary to establish new evaluation indicators and new goals from the perspective of enhancing oral functions while considering the need to evaluate such functions. It is highly likely that the promotion of the 8020 Campaign at the sites of medical services will become necessary in the years to come. Moreover, the Act concerning the Promotion of Dental and Oral Health stipulates that necessary measures should be taken for persons with disabilities and others who have difficulties in receiving dental care. It is essential that dental organizations, including the 8020 Promotion Foundation, should further develop the projects they have implemented up to now and recommend policies for improving dental and oral health. To further promote the 8020 Campaign in the field of dental and oral health while monitoring the progress made by the government in promoting dental and oral health, it is also essential to consider ways to offer the best mix of oral health/general health service and dental care provision[12] while taking into consideration the relationship between the Campaign and medical services.

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2. Medical insurance system in Japan (universal health insurance system)

2. Medical insurance system in Japan (universal health insurance system)

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Year and Month of Revision		Medicine	Dentistry
1961	4	Establishment of the public health insurance for the whole nation system	
	7	12.5% increase in total medical fees. Hospitalization costs, additional nursing fees, and fees for a doctor's visit are increased.	Special increase in dental prosthesis costs.
	12	2.3% increase in total medical fees.	
1965	1	9.5% increase in total medical fees.	
		The first-visit fee and hospitalization-related costs are increased.	The charge related to fillings, inlays, and dental prostheses are increased.
1967	12	Medicine: 7.68% increase	Dentistry: 12.65% increase
		Fees for hospitalization costs and operations are increased.	Technical fees are separated from material costs.
1970	2	Medicine : 8.77% increase	Dentistry: 9.73% increase
		The first follow-up consultation fees and hospitalization fees are increased.	Dental operation costs increase by about 80%. New dental fee items are established for crown restoration and dental prostheses.
1972	2	Medicine: 13.7% increase	Dentistry: 13.7% increase
		The first-visit fees and the technical fees for procedures/physical therapy/specific treatments for psychiatric diseases/operations/anesthesia, etc. are increased. Integration of Tables A and B is initiated to help ensure appropriate medical fees. ◯ The instruction fee for chronic diseases is first added to Table B. ◯ The average drug price system for calculating medication cost is abolished. ◯ A special class for standard nursing is first established. ◯ Hospitalization costs are broken out into the room charge, nursing care fee and other fees, and the variation of NHI points based on hospitalization duration is abolished. ◯ The medical care fees during hospitalization are categorized for hospitals and clinics and are increased. The hospitalization period is also categorized in Table A.	New categories are established for diagnosis for prosthesis and crown formation, and the categories for crown restoration and lost-tooth prosthesis are modified.
1974	2	Medicine: 19.0% increase	Dentistry: 19.9% increase
		◯ The general follow-up consultation fee and the follow-up consultation fee for internal medicine in Table B are increased; the after-hours fee, the late-night fee, and the holiday fee are first established as additional premiums. ◯ Hospitalization-related medical fee items including the nursing fee and room charge are increased; medical management fees during hospitalization are a particular focus for adjustment. ◯ Rehabilitation-related medical fee items including occupational therapy for disabled persons, psychiatric day care, etc. are first established. ◯ Actions are taken to update the items in Table A and B which had not previously been integrated, such as medical procedures and injections, etc.	◯ The first-visit fee is increased. The additional fee for mentally and/or physically disabled individuals is first established. The dentistry-specific technical fees are increased. New dental fee items are established for the taking of bite impressions and evaluation of temporary bases. ◯ Dental fee items are revised in accordance with the revisions in Medicine.
	10	Medicine: 16.0% increase	Dentistry: 16.2% increase
		◯ The fees for follow-up consultations, examinations, and operations, etc. are increased. The increases are substantial, particularly in the case of operations or examinations which require advanced techniques, doctor's visits and prescriptions, etc. ◯ Hospitalization fees, including the nursing fee, medical care fee, food service charge, etc., are generally increased. In addition, the Special Category II Nursing is first established.	◯ The first-visit fee, the charge for procedures and operations, the charge for crown restoration and prosthesis, and the charge for physical therapy, etc. are increased. Inhalation sedation is added as a new medical fee item. ◯ Dental fees are revised in accordance with the revisions in Medicine.
1976	4	Medicine: 9.0% increase	

Year and Month of Revision		Medicine	Dentistry
	8	○ The first-visit fee, the after-hours premium fee, the X-ray diagnosis fee, and the charge for injections, etc. are increased and new medical fee items are established for examinations, procedures, and operations. ○ The overall hospitalization cost, including the room charge, the nursing care fee, the food service fee, etc., is increased, and the hospital gown charge is added as a new medical fee item.	Dentistry: 9.6% increase
1978	2	Medicine: 11.5% increase	Dentistry: 12.7% increase
		○ The consultation fee, examination fee, and charges for X-ray diagnosis, physical therapy, specific treatment for psychiatric diseases, procedures and operations, and anesthesia, etc. are increased. New technologies such as computed tomography (CT) and kidney transplantation are introduced. Artificial dialysis re-evaluation is done. ○ The medical fees for items related to hospitalization costs are largely increased in order to resolve copayment issues. The additional fees for medical diet, specified intensive care unit management, and the Class II Special Additional Fee are first established.	The charge for endodontic treatments such as root canal therapy, crown restoration, dental prosthesis, etc. are increased, and the additional fee for consultations regarding infants aged less than 4 years is first established. The differential fee system for materials is partially implemented and types of care that have not been covered by conventional insurance are to be covered. Dental fees are revised in accordance with the revisions in Medicine.
1981	6	Medicine: 8.4% increase	Dentistry: 5.9% increase
		In order to prioritize technical fees and medical care fees during hospitalization, the accepted hospitalization cost (including the first-visit fee) is increased, along with a 40% increase in operation fees. Newly developed technologies such as cell-free and concentrated ascites reinfusion therapy (CART) are introduced. Meanwhile, the medical fees for artificial kidneys are specified separately for materials or implants and techniques. The fees for items related to rehabilitation are substantially increased, resulting in an approximately 80% increase in the charge for physical therapy. The instruction fee for chronic diseases, the charge for cooperative instruction by research hospitals, and other management charges are significantly increased to enrich the primary care experience. A comprehensive re-evaluation of items related to the examination fee is conducted and fees for self-injection of insulin preparations and human growth hormone preparations are introduced. An additional room charge and a premium nursing care fee for seriously injured individuals are established in order to reduce copayment, thereby dealing with the amenity bed issue and the issue of private nursing care.	The technical fees specific to dentistry are increased, primarily for prostheses and similar procedures and items. The additional medical fee for mentally and physically disabled persons for whom dental care would be very difficult is established in order to secure dental care for these individuals. The age of infants subject to an additional medical fee is raised from less than 4 years old to less than 6 years old. Examinations are to be handled based on Table A and examinations specific to dentistry are now included in this table. Dental fees are revised in accordance with the revisions in Medicine.
1984	3	Medicine: 3.0% increase	Dentistry: 1.1% increase
		○ An evaluation focusing on emergency medical care (including emergency medical care centers) is conducted. The medical management fee during hospitalization and hospitalization costs are increased. The basic technical fee is increased to enrich primary care. An evaluation is conducted on diseases subject to the instruction fee for chronic diseases for which consultations and instructions are considered to be effective for treatment. The additional fee for an emergency doctor's visit is first established. ○ CAPD is introduced for home medical care,. The scope of additional fees for operations using a laser knife is expanded. New medical technologies such as digital angiography (computed angiography system) are introduced. ○ Home medical care is promoted and the amount allocated for long-term hospitalization is corrected.	The technical fee for crown restoration and dental prostheses is increased and the fees for techniques for glazing and hardening material for resin surfaces are first established.
1985	3	Medicine: 3.5% increase	Dentistry: 2.5% increase
		New medical technologies such as NMR (magnetic resonance CT), percutaneous transluminal coronary angioplasty (PTCA), and ultrasonic knives are introduced into the health insurance system. The cost of operations is increased by an average of 14%, placing an emphasis on the technical fee. The period of artificial dialysis is set on a four-hour basis, and the points for 4 to 5 hours are increased, while the points for 5 hours or more are decreased. Instead, a premium for the introduction period is first established.. The fees for prescriptions and issuance of prescriptions are made comprehensive.	To help streamline medical fees, the follow-up consultation fee, endodontic treatment, and crown restoration fees are rationalized and emphasis is placed on technical fees. The charge for instruction on/management of pyorrhea and the charge for instruction on oral hygiene for infants, schoolchildren, adolescents, and pregnant patients are first established.

Year and Month of Revision		Medicine	Dentistry
		In Table B, the prescription fee is included in the medical care fees during hospitalization. The fees for multiple-item examinations which can be performed automatically are decreased. The fees for endoscopy and pathological examinations are increased. Emphasis is placed on the evaluation of fees for inpatient care at hospitals and outpatient care at clinics. The fee for provision of patient medical information is introduced and the term is changed from "the fee for introducing hospitalized/ discharged patients" in order to develop a community healthcare plan to form functional partnerships between hospitals (for hospitalization) and clinics (for non-hospitalization care).	
1986	4	Medicine: 2.5% increase	Dentistry: 1.5% increase
		Medical care fees are specified to help rationalize and stabilize medical practices in order to: (1) Evaluate fees for each function of hospitals and clinics; (2) Promote home medical care; (3) Remedy long-term hospitalization and excessively long hospitalization issues; (4) Emphasize technical fees; (5) Apply the medical insurance system to highly advanced medical care; (6) Revise medical fees for older patients, making them more appropriate and effective to 1) promote home medical care, 2) ensure proper medical care during hospitalization, and 3) specify medical care fees appropriate for elders' hospitals.	(1) Establishment of Dental fees with an emphasis on technical fees; (2) Provision of health benefits for veneer cast crowns; (3) Ensuring dental care for individuals with severe physical and/or mental disabilities etc.; (4) Measures to ensure proper use of dental materials including revision of standard dental material prices; (5) Modification to ensure appropriate fees for elders' dental care.
1988	4	Medicine: 3.8% increase	Dentistry: 1.0% increase
		Several changes are made to ensure efficient, high-quality medical care: (1) Evaluation of the primary care function of clinics and the advanced-level function of hospitals, along with the creation of a system to introduce patients to highly specialized hospitals; (2) Appropriate reduction of long-term hospitalization; (3) Establishment of a category for home medical care and the subsequent promotion of home medical care; (4) Re-organization of overall specimen examination practices; (5) Establishment of the basic nursing care fee; and (6) Re-evaluation of the use of highly advanced medical technology.	
1989	4	Consumption tax increase	
1990	4	Medicine: 3.8% increase	Dentistry: 1.4% increase
		To help prioritize the technical fee, several efforts are conducted, including:Determining the medical fee in an effort to streamline this fee; Evaluating the function and characteristics of medical institutions; Ensuring proper hospitalization; Promoting home medical care;Ensuring proper examination; and Reviewing the medical care for the elders. A medical management fee for hospitalization in designated geriatric-care hospitals is established as a part of the medical fee for the elders.	
1992	4	Medicine: 5.4% increase	Dentistry: 2.7% increase
		Guidelines for the evaluation of hospitals and clinics are clearly specified. Medical institutions are evaluated based on their functions and characteristics. Efforts including the appropriate evaluation of basic nursing are made to ensure stable and effective provision of nursing services. These efforts reduce the differences between Table A and Table B. ◯ The drug price calculation method is changed from the bulk-line method to the weighted average method. ◯ Interferon is added as a therapeutic agent for hepatitis. ◯ Intraocular lenses for cataract patients are approved for health insurance coverage.	
1994	4	Medicine: 3.5% increase	Dentistry: 2.1% increase
		As a result of the direction of a discussion in the report by the Central Social Insurance Medical Council subcommittee for medical fee basic issues, the conventional medical fee system established in 1958 is reformed.	

Year and Month of Revision		Medicine	Dentistry
		Evaluations are conducted based on the functions/characteristics of medical institutions; emphasis is placed on techniques; technology is prioritized; home medical care is promoted,; medical care appropriate for the specific mental and physical needs of older patients is promoted; and drug use/examination are evaluated and adjusted to streamline medical fees and better respond to a variety of patients' needs. ◯ Points in Tables A and B are integrated and a new medical fee points table is established. ◯ A two-stage revision takes place in April and October; the October revision follows the Health Insurance Act, etc. ◯ Community-level differences are introduced, including the addition of the hospitalization environmental fee.	
1994	10	Medicine: 1.7% increase	Dentistry: 0.2% increase
		As part of revising the medical insurance and elders' welfare systems, efforts are made to provide appropriate, high-quality medical services based on the principles of "resolution of economic concern about disease risks," "improvement of quality of services and response to a variety of patients' needs," "implementation of fair copayment practices," and "prioritization of insurance benefits" by implementing the following: (1) Establishment of the new nursing care system and abolishment of private nursing care; (2) Evaluation and promotion of home medical care; (3) Re-examination of standard food services and evaluation of the improvement of diet quality; ◯ Promotion of the establishment of a system providing one nursing staffer for every 2 patients; ◯ Target expansion of a home-visit nursing care project to include patients with intractable diseases, seriously handicapped individuals, the mentally disabled, etc. ◯ Integration of standard food services into the fee for meals during hospitalization as part of an effort to improve the diet quality for hospitalized patients; for example, provision of a variety of menus, eating in a dining room, guidance on nutrition and diet during hospitalization, etc.	
1996	4	Medicine 3.6% increase	Dentistry 2.2% increase
		Institutional cooperation and practical growth and development in medical institutions is promoted, with particular attention paid to constructing convalescent wards, appropriately evaluating acute-phase medical care and long-term care, and promoting functional divisions in hospitals and clinics. In addition, efforts are made to rationalize medical fees and drug costs by promoting proper use of drugs and appropriate separation of dispensaries from medical practices; the method for determining drug prices is reviewed. Medical fees for the areas with the highest needs, including acute-phase medical care, pediatric care, psychiatric care, and treatment for periodontal diseases, etc. are evaluated with a focus on technical fees to provide high-quality medical services while still rationalizing medication costs. Further, in order to respond to patients' medical care needs, information provision to patients is promoted and the Special Healthcare Expenditure is promoted to help patients take advantage of their choices. ◯ Conversion from general wards to convalescent wards is promoted; functional division of medical institutions through adequate evaluation and consultation is promoted. ◯ Outpatient consultation for children younger than 3 years is integrated into one comprehensive category. ◯ Inclusion of outpatient medical care for elders with chronic diseases into one comprehensive category.	
1997	4	Consumption tax increase	
		Consumption tax increase for medicine: 0.32% Medical fee increase for medicine: 0.32%	Consumption tax increase for Dentistry: 0.43% Medical fee increase for medicine: 0.32%

Year and Month of Revision		Medicine	Dentistry
		As a temporary and exceptional measure due to the consumption tax increase, medical fees are revised as needed to address the tax burden of insurance-approved medical institutions, etc., and rationalization of medical fees is promoted along with reforms to the medical insurance system. Because patients in Japan stay in hospital longer than those in foreign countries, efforts are made to reduce long-term hospitalization and to enrich services for acute-phase short-term hospitalization. In addition, medical technologies are evaluated to make medical services more efficient and a trial implementation of the fixed medical fee payment system for hospitalization is initiated in national hospitals in an attempt to review and modify the medical fee system. ◯ The medical management fee during hospitalization in an insurance-approved medical institution is systematized according to the average number of hospital days. ◯ Medical technologies etc. are evaluated to make medical services more efficient. ◯ A trial implementation of the fixed medical fee payment system for hospitalization is initiated in national hospitals. ◯ The points table is simplified.	
1998	4	Medicine: 1.5% increase	Dentistry: 1.5% increase
		The Medical fees increase by 1.5% to address the increase in manpower and material costs borne by medical institutions. Long-term hospitalization practices are evaluated and examinations and imaging diagnoses are rationalized to save financial resources, evaluate acute-phase medical services, and promote provision of medical information to patients.	
2000	4	Medicine: 2.0% increase	Dentistry: 2.0% increase
		The following are primary revision topics: (1) Promotion of a system of comprehensive medical fees, including establishing a basic hospitalization fee, and reviewing and modifying the degressive medical fee system; (2) Establishment of more comprehensive medical fee evaluations based on the functions of each medical institution, including, the provision of additional fees for designated acute hospitals and those for continuous follow-up; and (3) Systematic review and revision of operation fees, evaluation of appropriateness of fees for "objects" and "techniques," including an increase of in the prescription fee, and the development of more appropriate evaluations to help implement the nursing insurance system..	
2002	4	Medicine: 1.3% decrease	Dentistry: 1.3% decrease
		The following are primary revision topics: (1) Efficient evaluation of the medical care provision system; (2) Evaluation of medical care depending on patient characteristics; (3) Appropriate evaluation of medical technologies; (4) Rationalization of drug use and review of the drug-related technical fee; and (5) Review of the Special Healthcare Expenditure.	
2004	4	Medicine: no increase	Dentistry: no increase
		1. Various practices are evaluated and reviewed, including: (1) Evaluation based on the degree of difficulty, time required, technical performance, etc.; (2) Appropriate evaluation and re-evaluation of medical techniques; (4) Evaluation of dispensing techniques. 2. Adjustments are made to evaluate and appropriately reflect the costs borne by medical institutions, including: (1) Evaluation depending on characteristics of diseases, etc.; evaluation of medical care for acute-phase hospitalization, etc.; evaluation of pediatric care, psychiatric care, and home medical care; (2) Evaluation of medical institutions depending on their functions, etc. (e.g., the first-visit fee difference between hospitals and clinics is corrected and the scope of the outpatient visit fee is expanded, taking into consideration quality improvements, consolidation of clinical training programs, and the clarification of functions of medical institutions for outpatient practice.) 3. Patients' viewpoints are emphasized: (1) Promotion of information provision; (2) Promotion of patients' choice. 4. The ideal medical fee system is outlined. A review of some medical fee items, including addition, subtraction,	(3) Evaluation of techniques specific to Dentistry;

Year and Month of Revision		Medicine	Dentistry
		degression, and limited calculation, is conducted as a first step toward simplifying and rationalizing the system. Paperwork is also simplified and rationalized. 5. Other rationalizations are made for specific areas of interest, including establishing the special provisions on oxygen price and the additional fee for hospitalization on remote islands.	For some dental practices, the general and elders' medical care fees are integrated as a first step toward reviewing the medical fee system in consideration of the specific needs of older patients.
2006	4	Medicine: 1.5% decrease	Dentistry: 1.5% decrease
		1. Viewpoints that are transparent for patients can help implement effective medical care and enhance patients' quality of life (QOL): (1) Simplification of the medical fee system; (2) Issuance of a receipt that itemizes the medical care fee; (3) Emphasis on patients' viewpoints; (4) Evaluation of preventative care, keeping lifestyle-related diseases etc. from progressing to severe conditions; and (5) Evaluation of surgery scope and practices. 2. Viewpoints that promote differentiation of functions in medical institutions and emphasize cooperation can help encourage efficient, high-quality medical care: (1) Evaluation of home medical care; (2) Evaluation of first follow-up consultation; (3) Evaluation of DPC; (4) Evaluation of rehabilitation; and (5) Evaluation of psychiatric care. 3. Viewpoints for exploring ideal methods of evaluation in specific medical areas that warrant a stronger focus in the future in Japan: (1) Evaluation of pediatric care and pediatric emergency care; (2) Evaluation of obstetric care; (3) Evaluation of anesthesia; (4) Evaluation of pathological examinations; (5) Evaluation of acute-phase medical care during hospitalization; (6) Evaluation of the introduction of information technology for medical care; (7) Evaluation of medical care safety measures; and (8) Evaluation of medical techniques. 4. Viewpoints for exploring ideal evaluation methods in fields for which the allocated medical cost can be streamlined: (1) Evaluation of chronic-phase medical care during hospitalization; (2) Evaluation of meals provided during hospitalization; (3) Evaluation of medical services related to contact lenses; (4) Evaluation of examinations;	(5)Dental medical fee changes: ◯ Abolishment of the first/follow-up visit fee for home dentists ◯ Evaluation of clinical training for dentists ◯ Emphasis on patients' viewpoints (information provision to patients for instruction/management, etc.) ◯ Review of the instruction/ management system for dental diseases (establishment of general instruction fee for dental diseases, etc.) ◯ Review of evaluation of periodontal diseases (establishment of a fee for mechanical tooth surface cleaning, review of basic periodontal treatments and periodontal surgeries, etc.)
		(6) Dispensing fee changes: ◯ Review of the basic dispensing fee ◯ Review of the overall dispensing fee ◯ Review of the instruction and management fee as part of dispensing fee. ◯ Review of the pharmaceutical quality information fee (7) Other reviews and updates: ◯ In order to develop an environment that promotes the use of generics, the prescription form is changed. ◯ The existing system, in which the basic hospitalization fee is reduced when the number of allocated doctors and nurses for medical treatment is below the predetermined rate is reorganized. ◯ The currently-specified number of nursing staffs that should be allocated to general beds in a combined ward is below the standard specified by the Medical Service Act after March 2006; therefore, this standard is abolished as of September 30, 2006.	

Year and Month of Revision		Medicine	Dentistry
		○ Medical services related to dialysis are evaluated for appropriateness; this includes a reduction of the outpatient medical care fee for chronic maintenance dialysis patients (2006), reduction of the additional fee for night and holiday medical services related to artificial kidneys, and comprehensive evaluation of erythropoietin preparations for artificial kidneys. ○ The fee related to long-term administration is increased and the prescription charge is decreased. ○ The publicly announced oxygen price is appropriately modified in order to make it consistent with the pricing system for drugs and materials.	
2008	4	Medicine: 0.42% increase	Dentistry: 0.42% increase
		Reducing the burden on hospital doctors working in obstetrics and pediatrics departments becomes urgent: (1) Evaluation places emphasis on obstetrics and pediatrics; (2) Division of roles in clinics and hospitals is emphasized; (3) Reduction of paperwork for hospital doctors is prioritized; and (4) Measures for emergency medical care are implemented. 1. Viewpoints that are transparent for patients can help promote effective medical care and enhance patients' quality of life (QOL): (1) Provision of information on details of medical fees; (2) A transparent medical care fee system; (3) Medical services placing emphasis on quality of daily life; and (4) Strengthening the functionality of designated insurance pharmacies. 2. Viewpoints for promoting division/cooperation of medical care functions to help provide efficient, high-quality medical care: (1) Promotion of efficient, high-quality medical care during hospitalization; (2) Exploring a method for evaluating medical service quality ; (3) Evaluation based on medical care needs; (4) Promotion of home medical care; (5) Support of home healthcare for mentally disabled individuals; (7) Review of the dispensing fee. 3. Viewpoints for exploring ideal methods of evaluation of specific medical areas that warrant increased focus in the future in Japan: (1) Promotion of cancer care; (2) Preventive measures against stroke; (3) Preventive measures against suicide and emphasis on children's mental healthcare; (4) Promotion of medical safety and evaluation of new techniques, etc.; and (5) Promotion of the online system and information technology. 4. Viewpoints for exploring ideal methods for evaluation in fields for which the allocated medical cost can be streamlined: (1) Updating practices with the use of new techniques; (2) Promotion of the use of generics, etc.; and (3) Other items that should be made more effective or appropriate. 5. Medical fee adjustments for late-life older patients: (1) Medical care during hospitalization; (2) Home medical care; (3) Outpatient medical care; and (4) Terminal medical care.	(6) Enrichment of dental care;
2010	4	Medicine: 1.74% increase	Dentistry: 2.09% increase
		Measures for addressing high-priority issues: (1) Evaluation of emergency medical care centers and secondary emergency medical institutions; (2) Evaluation and enhancement of care for high-risk pregnant and parturient women and evaluation of intensive care for high-risk newborns. (3) Increase in operation fees including operation fees for children. (4) Better evaluation of the additional fee for the paperwork system and evaluation of team medical care provided by various professionals. Four viewpoints (e.g., evaluation of the fields that need to be enriched, realization of medical care that is transparent for patients): Promotion of cancer care/dementia care/anti-infection measures/anti-hepatitis measures, freely provided bills, etc. Medical fees for the extremely elders. Abolishment of the medical fee system with a particular focus on those 75 and older. 1. Better evaluation of emergency medical care: (1) Enrichment of emergency medical care during hospitalization; and (2) Evaluation of emergency care in cooperation with the community. Evaluation of outpatients:	

Year and Month of Revision		Medicine	Dentistry
		2. Better evaluation of obstetric/pediatric care: (1) Better management of high-risk pregnant and parturient women; (2) Evaluation of intensive care for newborns; and (3) Enrichment of pediatric care during hospitalization. 3. Reduction of burden on hospital doctors: (1) Reduction of burden on hospital doctors; (2) Evaluation of medical care during hospitalization under a careful nursing system with a sufficient number of staff members; and (3) Evaluation of team medical care provided by various professionals. 4. Appropriate evaluation of operation fees: (1) Increase in operation fees utilizing the draft proposal of "Gaihoren" (Association of Surgical Specialties Social Insurance Committees); (2) Increase in the fees for pediatric operations; and (3) Introduction of novel medical techniques into the health insurance system. 5. Promotion of bill issuance: (1) Promotion of bill issuance; and (2) Support with medical fees related to bill issuance.	
2012	4	Medicine: 1.55% increase	Dentistry: 1.7% increase
		High-priority issues: 1. Reduction of burden on heavily burdened medical workers: (1) Promotion of emergency/perinatal stage medical care; (2) Measures to improve the working environment for hospital workers; (3) Division of functions of emergency outpatient units and outpatient units; and (4) Promotion of team medical care involving hospital pharmacists and dentists. 2. Division of functions of medical care and nursing care and cooperation between these functions; enrichment of home care: (1) Promotion of division of functions of medical institutions responsible for home care and cooperation among them; (2) Enrichment of overall medical care including terminal care; (3) Enrichment of home dentistry and home medication management; and (4) Enrichment of home-visit nursing care and smooth cooperation between medical care functions and nursing care functions. 3. Promotion of effective new technologies for treating diseases such as cancer and dementia and introduction of such technologies: (1) Appropriate evaluation of medical techniques, enrichment of cancer care and measures against lifestyle-related diseases, measures for psychiatric diseases/dementia, enrichment of rehabilitation, and enhancement of dental care in consideration of QOL; (2) Enrichment of medical safety measures and measures to support patient counseling; (3) Appropriate evaluation of inpatient medical care and inpatient chronic-phase medical care depending on hospital functions, consideration for communities with poor resources, and evaluation depending on functions of clinics; and (4) Promotion of the use of generics, adequate reduction of long-term hospitalization, and appropriate evaluation of drugs based on actual market prices.	(4) Promotion of team medical care involving hospital pharmacists and dentists. (3) Enrichment of home dentistry and home medication management; (1) Appropriate evaluation of medical techniques, enrichment of cancer care and measures against lifestyle-related diseases, measures for psychiatric diseases/dementia, enrichment of rehabilitation, and enhancement of dental care in consideration of QOL;

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