Oral Health Care for Prevention and Control of Non-Communicable Diseases

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Healthy Longevity

Prevention and Control of Non-Communicable Disease

Oral Health Care

8020 Promotion Foundation
Preface .......................................................................................................................... 3
Chapter 1 Dental and Oral Health and Non-Communicable Diseases ........... 4
Chapter 2 Diabetes ........................................................................................................ 6
Chapter 3 Cancer .......................................................................................................... 8
Chapter 4 Cerebrovascular Disease (Stroke) ............................................................... 10
Chapter 5 Heart Disease ............................................................................................. 12
Chapter 6 Risk Factors .............................................................................................. 14
Chapter 7 Global Efforts and Japanese Efforts ............................................................ 18

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Everyone hopes to lead a long and healthy life. The second term of the National Health Promotion Movement for the 21st Century (Health Japan 21 (the second term)) began in 2013, with targets to be achieved by fiscal year 2022. This project, against the backdrop of an aging population with a falling birth rate and a transitioning disease structure, aims to improve the lifestyle and social environment of all citizens, from infants to the elderly, in such a way that everyone will have hope and a meaningful life in the context of mutual support. It aims to achieve a vibrant society in which people can live healthy and spiritually rich lives during each stage of life (i.e., infancy, childhood, adolescence, adulthood, old age, and so on), and it regards a sustainable social security system as necessary for achieving that aim.

The project lays out the basic policies for comprehensive implementation of national health promotion, including the following 5 targets:

1. Extension of healthy life expectancy and reduction of health disparities
2. Prevention of onset and progression of lifestyle-related diseases (non-communicable diseases)
3. Maintenance and improvement of the functions necessary for engaging in social life
4. Establishment of a social environment in which the health of individuals is protected and supported
5. Improvement of the social environment and lifestyle in the areas of nutrition and dietary habits, physical activity and exercise, rest, alcohol consumption, tobacco smoking, dental and oral health

Dental and oral health is considered an essential basic element of national health promotion in order to achieve targets 1 through 4 above. Thorough prevention and control of lifestyle-related diseases including cancer, cardiovascular disease, diabetes, and chronic obstructive pulmonary disease (COPD) is especially important. An effective way to prevent these diseases is to encourage all people to autonomously and continually reassess and try to improve their daily living habits throughout their lives. Personal efforts along with a social environment that supports such efforts are indispensable factors in maintaining healthy daily living habits. To avoid the misunderstanding that these diseases would be resolved if individuals were to take responsibility, the term “lifestyle-related diseases” is now usually replaced by “Non-Communicable Diseases (NCDs)”.

Dental and oral health is important to maintain eating and communication abilities, and greatly contributes to improvement of quality of life. Thus, the maintenance of healthy oral functions throughout life was set as a target of this promotion, and to achieve this goal, maintenance and improvement of oral functions is essential in light of their role in disease prevention as well as the prevention of periodontal disease, dental caries and tooth loss. The Japanese government is putting further emphasis on the promotion of public awareness regarding dental and oral health as well as continuing its “8020 Campaign”.

Health promotion requires change in people’s consciousness and actions. The aim of this book is to support active health promotion efforts by providing accurate information based on scientific evidence regarding the correlation between NCDs and dental and oral health. We hope that this book will be useful for many people and be utilized in many places to achieve healthy longevity for everyone.

Kenro Hori, President, 8020 Promotion Foundation
Dental and Oral Health is Important for Healthy Longevity

The current average life expectancy of Japanese people is over 83 years of age (men: 80.8 years; women: 87.1 years as of 2015), and a quarter of men and one half of women live to age 90. The number of centenarians exceeds 60,000, so the dream of living to be 100 is becoming attainable for a large swath of the population.

Healthy life expectancy (a term coined by the WHO in 2000) is defined as “the length of life that an individual lives without limitation in daily activities due to health problems” (Ministry of Health, Labour and Welfare). Unfortunately, the difference between actual life expectancy and healthy life expectancy is approximately 9 years in men and 12 years in women (Figure 1). Both as individuals and collectively as a society, we strive to reduce this gap so that we can live as much of our life as possible in good health.

To extend healthy life expectancy, it is necessary to: 1) prevent diseases that lead to death or to the need for nursing care, and 2) maintain a body and mind that are not susceptible to illness, and slow the progression of dementia. NCDs such as cancer, heart disease, cerebrovascular disease, and diabetes account for approximately 60% of deaths and also 30% of cases requiring care. It is well known that paying attention to good diet, physical exercise, rest, moderate alcohol intake, and not-smoking can contribute to maintaining a body that is less prone to illness. In addition to these, improvement of lifestyle and a social environment that promotes dental and oral health are also considered to be fundamental elements to achieve the goals of Health Japan 21 (the second term).

Evidence

There have been remarkable improvements in the dental and oral health of the Japanese people over the past three decades. In order to continue eating whatever you want to throughout your life, it is important not to lose teeth due to dental caries or periodontal disease. The 8020 Campaign was initiated in 1989 in Japan as a national movement, with the objective of helping
individuals keep 20 or more teeth until 80 years of age. At present, 40% of Japanese people have achieved the 8020 Campaign's goal, which is 6 times higher than the baseline figure.

The survival rate of people who maintain more teeth is 1.1-2.7 times higher than that of people who lose many teeth. It can not be denied that improvement of dental and oral health is one of the factors contributing to extended life expectancy in Japan. In addition, the number of teeth is correlated with the need for nursing care. In a follow-up study of residents aged 65 years or older, it was reported that individuals with 19 or fewer teeth had a 1.2 times higher risk of needing nursing care compared with those with 20 or more teeth. In a follow-up study of adults, it was shown that people with advanced periodontal disease had a 1.6 times higher risk of developing metabolic syndrome conditions such as obesity, hypertension, or dyslipidemia.

More and more studies are demonstrating a relationship between dental and oral health and general health (Figure 2). The evidence shows that maintaining dental and oral health and not losing too many teeth is an important factor contributing to the extension of healthy life expectancy. Therefore, further evidence-based efforts are needed to prevent NCDs and promote dental and oral health.

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Periodontal Disease is Closely Related to Diabetes

Complications of diabetes are terrifying
Diabetes is a systemic disease that causes chronic hyperglycaemia. In Japan, more than 20 million people are believed to be affected by diabetes, including those with prediabetes. Diabetes is a health condition where a hormone called insulin, which is necessary to absorb nutrition into the body, becomes dysfunctional so that blood glucose is used ineffectively, resulting in an elevated blood glucose level. In advanced cases, injuries develop in the capillaries of the retina, the kidney, nerves of the feet, or the aorta. Such “diabetes complications” largely affect the quality of everyday life. Recently, it has been revealed that diabetes is associated with oral health and prognosis of dental treatment.

Harmful relationship between diabetes and periodontal disease
It is known that there is a relationship between diabetes and periodontal disease. The primary cause of periodontal disease is “plaque” that is stuck to the surface of unbrushed teeth. Plaque basically consists of bacteria including periodontopathic bacteria. The bacteria grow in gaps (or “periodontal pockets”) between the teeth and gums and cause inflammation of the gums, leading to the destruction of tooth-supporting periodontal tissues. Physiologically active substances associated with inflammation are released from periodontal pockets and then delivered to all parts of the body, where they increase insulin resistance. These substances also increase susceptibility to the development or progression of diabetes. By reverse correlation, the hyperglycaemic state weakens the immune function which protects the body from bacterial infection, leading to easy development and progression of periodontal disease. Recently, it has become known that diabetes affects negatively the success rate of implant treatment performed after tooth loss as well as long-term stability.

Figure 1. Interactive relationship between periodontal disease and diabetes
Plaque control is an essential step

The essential step for periodontal disease treatment is plaque control, namely removal of dental plaque, the cause of periodontal disease. There are two types of plaque control: self-care by the patient after receiving guidance for correct tooth brushing from dentists or dental hygienists, in addition to the professional care performed at dental clinics. When dental plaque is firmly stuck to the teeth, it calcifies and forms dental calculus. To remove it, special tools such as dental ultrasonic or hand scalers are necessary; this procedure is called scaling and root planing.

![Scaling and root planing](image)

**Figure 2. Treatment of periodontal disease improves glycaemic control**

Treatment of periodontal disease is effective for the treatment of diabetes

It has become clear that glycaemic control can be improved by providing scaling and root planing of all periodontal pockets. Clinical trials of diabetic patients with periodontal disease have been performed globally, including Japan, to observe the influence of tooth brushing training as well as scaling and root planing. Among these, many studies for type 2 diabetes patients showed a decrease in hemoglobin A1c (HbA1c), the marker of glycaemic control. It was also reported in several papers that markers of insulin resistance were also lowered. A statistical analysis combining these study results showed that HbA1c was reduced by 0.66%, 0.46%, and 0.40%, respectively after treatment of periodontal disease.

The data indicate that although diabetes and periodontal disease have an interactive relationship, appropriate treatment of periodontal disease can improve glycaemic control. Thus, cooperation between internists and dentists can contribute to successful prevention and improvement of diabetes.

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Oral Care Is an Essential Factor for Smooth Cancer Treatment

Oral care has lately been spotlighted as a way of achieving safer and better cancer treatment with less pain, and supporting a better quality of life for patients with cancer. By maintaining good oral hygiene, patients can eat properly and maintain their physical strength, thus decreasing the risk of infections caused by oral bacteria, and subsequently reducing the risk of oral complications associated with cancer treatment.

Oral complications during cancer treatment

During cancer treatment, oral side effects and complications frequently occur, causing much suffering to patients. Oral complications are directly linked to problems with food intake, thus neglecting measures for oral complications will not only cause deterioration of patients' quality of life during cancer treatment and turn the treatment itself into a torment, but become a huge obstacle to smooth cancer treatment, sometimes with negative effects on treatment responses.

Effects of oral bacteria

It is known that the incidence rate and the degree of severity of oral complications are significantly associated with the effects of oral bacteria. Oral care (maintaining good oral hygiene and supporting/managing healthy oral function) helps to prevent oral complications from becoming severe, improve the quality of life during treatment while alleviating symptoms, and facilitate smooth cancer treatment.

Figure 1. Typical cancer treatments and oral complications
Prevent oral complications through oral care
To decrease the risk of oral complications during cancer treatment, patients are recommended to visit a dentist for oral cleaning and check-up before starting cancer treatment and keep the mouth clean to prevent oral complications such as infections. During cancer treatment, patients are also recommended to maintain good oral hygiene by self-care treatment of tooth brushing.

Evidence

Surgical cancer treatment
Perioperative oral care can reduce the risks of postoperative pneumonia, problems related to tracheal intubation (dental fractures, dislodgement, etc.), and postoperative complications after oropharyngeal/oesophagus surgical procedures.

- In a study including 3,319 patients who were admitted to a hospital surgical ward, a postoperative pneumonia-prevention program (respiratory rehabilitation and oral care) performed before surgery reduced the incidence rate of pneumonia to one fourth.

- In an intervention study on postoperative complications in patients with advanced head and neck cancers comparing a preoperative oral care group (56 patients) with a non-oral care group (35 patients), oral care intervention reduced the risk of developing oral complications to one seventh.

Medical cancer treatment
Pretreatment oral care taking the risk of anticipated oral complications into consideration can help reduce patients’ suffering during cancer treatment by managing infections, supporting oral food intake, and relieving pain, which all contribute to the successful completion of cancer treatment and thus the patient’s prognosis.

- In a randomized comparative study including 26 breast cancer patients scheduled for chemotherapy, oral adverse events (especially the risk of oral mucositis) were significantly decreased in the group that received prophylactic professional oral health care.

- In a prospective study including 128 patients with multiple myeloma treated with zoledronic acid, the incidence rate of osteonecrosis of the jaw was significantly reduced from 26.3% to 6.7% by oral care intervention (P=0.002), and also contributed to prevent the disease from becoming more severe.

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Sequela of cerebrovascular disease may lead to fatal results

In 2011, a change was noted in the top 3 leading causes of death among Japanese people. Cerebrovascular disease, which had firmly been in 3rd place, was replaced with pneumonia (Figure 1). However, cerebrovascular disease still represents the main cause of conditions requiring long-term care (Figure 2). Although cerebrovascular disease is no longer a direct cause of death, it causes movement disorders that not only affect the extremities but also the orofacial area, and even causes deterioration of oral hygiene status. Furthermore, if an individual suffers from a swallowing disorder due to sequelae of cerebrovascular disease, it may lead to the onset of secondary pneumonia and the possibility of death (Figure 3).

Oral environment prone to cerebrovascular disease

As described above, it is expected that cerebrovascular disease causes deterioration of the oral environment, but putting it the other way around, which oral conditions are prone to cerebrovascular disease? Several studies have been conducted to answer this question, and the conclusion is that the 3 conditions noted in patients with periodontal disease, namely, losing many teeth, male gender, and relatively younger (65 years or younger) seem to be factors. Even though some other study results do not meet these conditions, attention should be paid to “female gender, elderly people, and people who retain most of their teeth.” It is difficult to assure that treatment of periodontal disease will prevent cerebrovascular disease, but proper oral care should be applied to reduce the possibility.
Severe periodontal disease is a risk factor for stroke

A study showed that in the male population, those with fewer than 24 teeth had a 1.57 times higher risk of developing ischemic stroke (so-called cerebral infarction), compared with those with 25 or more teeth.\(^1\)

Next, according to a study that compared the results of periodontal disease checkups among 3 groups (inpatients with stroke, inpatients with other causes than stroke, and healthy subjects), the depth of periodontal pockets was deepest in the group of inpatients with stroke, and had severer periodontal disease. By adding the factors of male gender and younger than 60 years, severe periodontal disease will be a risk factor for stroke.\(^2\)

Another study also suggested that not only periodontal pockets but also the degree of loss of tooth-supporting bone was associated with the onset of stroke. The study also pointed out that the correlation was higher in male individuals younger than 65 years.\(^3\)

Seemingly, other study results regarding stroke and periodontal disease showed a correlation, not with cerebral haemorrhage, but with cerebral infarction. The underlying mechanism affecting the correlation is yet to be clarified, but efforts to avoid periodontal disease before entering old age and to keep as many as teeth as possible may lead to the prevention of death from stroke.

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Heart diseases affected by oral bacteria are grouped into 2 types: one is called infective endocarditis induced by bacteria released into the bloodstream, and the other is called coronary artery disease which is lifestyle-related heart diseases. Most lifestyle-related heart diseases are acquired diseases of the coronary arteries that provide blood to the heart muscles. They are also called ischaemic heart diseases, because blood supply to heart muscles is interrupted when stenosis or infarction occurs in the coronary arteries. Triggers of coronary artery disease are found in daily living habits such as nutrition intake, physical activity and exercise, rest, alcohol drinking, tobacco smoking, and deterioration of oral health caused by improper tooth brushing. Now, let us think about why oral health caused by improper tooth brushing is associated with heart disease.

**Infective endocarditis**
Oral bacteria that are released from lesions of periodontal disease and dental caries enter the bloodstream, and sometimes cause the focus of infection in the endocardium and the heart valves. This is called infective endocarditis and is categorized as infection. In a rat model study of heart diseases, many strains of oral streptococci cause the focus of infection in the endocardium and the heart valves (Table 1\(^5\)) almost 100% of the time. Thus, the prevention of heart disease requires prophylaxis of periodontal disease or dental caries.

**Lifestyle-related heart disease**
As to lifestyle-related heart disease, experimental studies were conducted at 2 universities in Germany and the United States, aiming to monitor subjects’ health after refraining from tooth brushing three weeks. Interruption of tooth brushing caused inflammation of the gums, and bacteria in accumulated dental plaque on the surface of teeth entered the bloodstream from the periodontal tissues, and caused endotoxemia due to endotoxin.\(^2\) The entering of endotoxin in the bloodstream caused elevation of blood markers indicating arterial sclerosis.\(^3\) After starting tooth brushing again, endotoxemia resolved, and blood markers indicating arterial sclerosis returned to normal.

This experimental study clearly shows that tooth brushing influences the health level of systemic
vessels. Chronic inflammation due to endotoxin develops in coronary arteries, and this is a trigger for subsequent stenosis or infarction, which will lead to heart disease.

A study group at Harvard University conducted a cross-sectional analysis of the results of 11 studies, and reported that it was noted from 7 of those studies that patients who suffered from periodontal disease and had elevated markers of systemic bacterial infection also had a strong correlation with coronary artery disease markers.4) Here is the evidence that shows a relationship between oral conditions and heart disease.

**Evidence**

A study group of Helsinki University conducted a study to evaluate clinical history data between 102 patients with myocardial infarction and 100 healthy subjects at a university hospital. The results indicated that the oral conditions of patients with myocardial infarction were significantly poor compared with those of healthy subjects. Investigative items included the presence of dental caries, periodontal disease, lesions in the apical area surrounding the root end of the teeth, and pericoronitis. Correlation between oral conditions and the onset of myocardial infarction was reported based on these results.4)

In Japan, a research group of the University of Tokyo carried out a questionnaire survey of 31,894 employees of a financial and insurance firm in Japan. The questionnaire covered such items as myocardial infarction or angina pectoris at present, age, sex, body mass index (BMI), smoking, drinking, hypertension, diabetes, periodontal disease at present, and frequency of tooth brushing. The reported results indicated that there was an association between periodontal disease and coronary artery disease with an odds ratio of 1.51.5)

A systematic review conducted by the American Heart Association also pointed out that because periodontal disease and ischaemic heart diseases share several common risk factors including aging, smoking, alcohol intake, race or ethnicity, sex, education, income, diabetes, and obesity, it is difficult to perform analysis showing a significant causative association.6) The review, however, also reports improvement of systemic inflammation markers or vascular functions by applying periodontal therapy.

Nobuhiro Hanada, Professor, Department of Translational Research, Tsurumi University School of Dental Medicine

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Risk Factors for Lifestyle-related Diseases (Smoking, Snacking, Obesity, Hypertension)

Lifestyle-related diseases are diseases caused by daily living habits such as dietary, exercise, rest, smoking or drinking habits. They used to be called adult diseases and are now also called non-communicable diseases (NCDs). More than half of the deaths are due to lifestyle-related diseases such as cancer, cardiovascular diseases, etc. in Japan.

Lifestyle-related diseases may be prevented by improvement of the daily living habits. Daily living habits that serve as risk factors for lifestyle-related diseases are also risk factors for oral diseases including dental caries and periodontal disease, so the improvement of daily living habits is considered to be good for oral health. Here is evidence that explains the relationship between risk factors such as smoking or snacking (which are associated with lifestyle-related diseases), and obesity or hypertension (which increases the risk of lifestyle-related diseases) and oral health.

Evidence

Smoking

Smoking is a risk factor for many lifestyle-related diseases and is closely related to oral health. The effects of smoking on periodontal disease are correlated with cigarette consumption and smoking duration. It is reported that individuals who consumed many cigarettes presented an approximately 3 times higher risk of aggravation of periodontal disease within 4 years compared with non-smokers or

![Figure 1. Relationship between Cigarette Consumption and Deterioration of Periodontal Disease](image1)

![Figure 2. Relationship between Smoking Conditions and Deterioration of Periodontal Disease](image2)
individuals who have quitted smoking (Figure 1). The term “involuntary smoking” means non-smokers’ exposure to secondhand tobacco smoke. In a comparison of changes of the gums between smoking environments, not only voluntary smokers but involuntary smokers presented with deterioration of periodontal disease (Figure 2). This indicates that exposure to tobacco smoke may aggravate periodontal disease.

Smoking is related to systemic cancer as well as perioral cancer. Individuals who consume both tobacco and alcohol have an approximately threefold increased risk of oral and pharyngeal cancer compared with those who don’t have either of these habits (Figure 3).

**Snacking**

In 2015, the World Health Organization (WHO) released a new guideline that recommended reducing the daily intake of fats, carbohydrates, and sugars for the prevention of obesity and lifestyle-related diseases. The target for sugar reduction is below 25 grams per day (equivalent in refined sugar).

It is well known that sugar contained in snacks is a cause of dental caries. Carbonated beverage contains approximately 10 grams of sugar per 100 mL. A large study conducted in the United States revealed that a high prevalence of dental caries was noted among individuals who consumed carbonated beverages in all age groups (Figure 4).

As dental caries increased in individuals who frequently consumed sugar-containing beverages such as coffee and black tea (Figure 5), caution is necessary, not only for sugar contained in food, but also in beverages taken when having a snack.
**Obesity**

Obesity is closely associated with lifestyle-related diseases such as diabetes and cardiovascular disease, and especially, visceral fat-type obesity is an underlying cause of metabolic syndrome, which increases the risk of developing disease. Body mass index (BMI) is frequently used as an indicator of obesity. It is calculated by dividing weight (kg) by height (m) squared. If BMI is between 25 and 29.9, the person is considered as overweight, and if BMI is over 30, the person is considered as obese.

A study in the Japanese population revealed that overweight or obese people had a higher risk of developing periodontal disease compared with underweight people (BMI less than 20). In a follow-up study of a population of Japanese adults, participants with a BMI indicating overweight or obese were more likely to experience deterioration of periodontal disease within 5 years and the trend was significant in women compared with men (Figure 6). Physical exercise plays an important role in obesity and lifestyle-related diseases. A study that investigated the relationship between obesity and physical fitness and severe periodontal disease revealed that thin, physically strong individuals were less likely to develop periodontal disease (Figure 7). Thus, the prevention of obesity by exercise may also prevent periodontal and lifestyle-related diseases.

**Hypertension**

Hypertensive disease is the most prevalent disease in Japan. Elevated blood pressure increases the risk of stroke or myocardial infarction. It is also known that many adults have periodontal disease, and reports suggest that people who suffered from advanced periodontal disease have a higher risk of refractory hypertension (hypertension that responds poorly to antihypertensives). In a study, no differences were found regarding the risk that a university student with normal blood pressure (systolic blood pressure (SBP) of less than 120 mmHg and diastolic blood pressure (DBP) of less than 80 mmHg) at university entrance will develop prehypertension (SBP 120-139 mmHg or DBP 80-89 mmHg) at the time of graduation with the presence of periodontal disease. However, if a student with prehypertension at entrance had periodontal disease, the risk of hypertension at graduation increased to 2.7 times (Figure 8). Thus, periodontal disease seems
to influence an increase in blood pressure of people with elevated blood pressure.

Considering that there is a study reporting periodontal treatment applied to refractory hypertensive patients reduced the blood pressure at 6 months after the treatment (Figure 9), periodontal treatment is also effective for blood pressure control in patients with hypertension.

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Smoking

Snacking

Obesity

Hypertension
Non-Communicable Diseases (NCDs) are Global challenges

There are 3.9 billion people globally who suffer oral diseases including dental caries and periodontal disease, and it is needless to say that oral diseases are regarded as international problems both in developed and developing countries. Many studies have reported that oral health is closely associated with systemic disease, and daily living habits particularly have a significant impact.

Global Efforts and Japanese Efforts

Global efforts
Oral disease was recognized as one of NCDs at the UN High Level Meeting held in 2011, and the necessity of controlling risk factors associated with NCDs such as smoking, an unhealthy diet, and excessive drinking was acknowledged at the same time. The UN declaration which required international cooperation was adopted, and the World Health Organization (WHO) has set the 9 global targets for NCDs including a 30% relative global reduction in the tobacco use, at least 10% relative reduction in the excessive intake of alcohol, etc. at the time by 2025, and encouraged reconsideration of daily living habits (Figure 1).

Oral disease can have negative effects on the quality of life (QOL) in all generations from children to elderly people, therefore appropriate measures are necessary to maintain good mental and physical health.

Japanese efforts
In Japan, a project to promote the national health called “Health Japan 21” has started in 2000, and many efforts are implemented to improve people’s daily living habits for the prevention of NCDs. Targets were set in 9 areas (nutrition and dietary habits; physical activity and exercise; rest and mental health; tobacco smoking; alcohol drinking; oral health; diabetes; cardiovascular disease; and cancer) (Figure 2), based on the 3 pillars of the project, namely, increasing self-care ability, providing support and regular management by specialists, and promoting public awareness activities.

Discussions on sugar intake have also been advancing, since NCD-inducing factors such as weight gain and the prevalence of obesity have become huge social issues. The WHO published a new guideline to recommend a reduction in the daily free sugar intake by adults to below 5-10% of the total energy intake (Figure 3). This is equivalent to 25 grams (5-6 teaspoons) of sugar, and seems to be very strict. To meet this target, reconsideration of daily living habits as well as establishing a social environment with less influential risk factors are equally important. A sugar tax to be paid on sugar-sweetened soda has been under consideration in Western countries such as the U.K.
From Knowledge to Practice

In the future, it will become even more necessary to promote public awareness by accumulating evidence that shows that maintenance of oral health prevents NCDs. Accordingly, we have to give greater consideration on how we put learned knowledge into practice in our daily lives.

<table>
<thead>
<tr>
<th>WHO recommendation on sugar intake</th>
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<tbody>
<tr>
<td>WHO recommends a reduced intake of free sugars throughout the life course (Strong recommendation)</td>
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<tr>
<td>In both adults and children, WHO recommends reducing the intake of free sugars to less than 10% of the total energy intake (Strong recommendation)</td>
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<tr>
<td>WHO suggests a further reduction of the intake of free sugars to below 5% of the total energy intake (Conditional recommendation)</td>
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Figure 3. WHO guideline Sugar Intake for Adults and Children

Hiroshi Ogawa, Dental Officer, Department of Global Oral Health Programme, World Health Organization

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3) WHO. Sugars intake for adults and children Guideline. World Health Organization, Geneva;