Tooth loss and decline in functional capacity: a prospective cohort study from the JAGES project

Yukihiro Sato, DDS,[1] Jun Aida, DDS, PhD, MPH,[1] Katsunori Kondo, MD, PhD, [2, 5] Toru Tsuboya, MD, PhD,[1] Richard G Watt, MSc, PhD, BDS,[3] Tatsuo Yamamoto, DDS, PhD,[4] Shihoko Koyama, DDS,[1] Yusuke Matsuyama, DDS,[1] Ken Osaka, MD, PhD, MPH[1]

[1]Department of International and Community Oral Health, Tohoku University Graduate School of Dentistry, [2]Center for Preventive Medical Science, Chiba University, [3]Department of Epidemiology and Public Health, University College London, [4]Departmentivision of Dental Sociology, Department of Oral Science, Graduate School of Dentistry, Kanagawa Dental University, [5]Department of Gerontology and Evaluation Study, Center for Gerontology and Social Science, National Center for Geriatrics and Gerontology

Corresponding Author

Yukihiro Sato, D.D.S.

Department of International and Community Oral Health, Tohoku University Graduate School of Dentistry

Address: 4-1, Seiryo-machi, Aoba-ku, Sendai, Miyagi 980-8575, Japan

Tel: +81-22-717-7639; Fax: +81-22-717-7644; E-mail: yukisatou-thk@umin.ac.jp

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ABBREVIATED TITLE (40/45 characters)

Tooth loss predicted functional decline.

STRUCTURED ABSTRACT

OBJECTIVES: To describe associations between tooth loss and changes in higher-level functional capacity.

DESIGN: Prospective cohort study.

SETTING: This study was conducted in 24 Japanese municipalities between 2010 and 2013.

PARTICIPANTS: Functionally independent community-dwelling persons aged 65 years or older (N=62,333).

MEASUREMENTS: Self-reported number of remaining teeth was used as an exposure variable. The outcome was changes in higher-level functional capacity measured by the Tokyo Metropolitan Institute of Gerontology Index of Competence (TMIG-IC). The TMIG–IC is composed of three domains: instrumental activities of daily living (IADL), intellectual activity and social roles. All the covariates were chosen from baseline demographic, socio-economic, health behavior, and health variables based upon evidence from previous studies.

RESULTS: The baseline response rate was 65.2%, and the follow-up rate was 70.1%. We used the inverse-probability weighting (IPW) with propensity score and multiple linear regression, estimating coefficients (β) and 95% confidence intervals (95%CI). The results showed a significant negative dose-response association between tooth loss and changes in

higher-level functional capacity in multiple linear regression models. In particular, being edentulous showed the highest β (-0.178, 95%CI: -0.221, -0.135) of the changes in higher-level functional capacity. In IPW models, the β of the treatment if edentulous participants had ≥20 teeth was 0.170 (95%CI: 0.114, 0.227).

CONCLUSION: The present findings suggest that tooth loss is associated with a future decline in higher-level functional capacity. IPW models suggested that the treatment for tooth loss attenuate the decline in higher-level functional capacity.

Key words:

Oral Health, Propensity Score, Independent Living, Tooth Loss

INTRODUCTION

In an aging society physical, cognitive and social ability are all important components for successful aging to improve healthy life-expectancy.[1] Higher-level functional capacity is a measurement not only for physical and cognitive functioning but also social ability such as skills for independent living within a community.[2] This measure is composed of three domains: instrumental activities of daily living (IADL), intellectual activity and social roles.[2] Higher-level functional disability is an important predictor for future onset of cognitive impairment,[3] and mortality.[2]

Oral diseases are an important public health problem due to their very high prevalence and significant burden in terms of disability-adjusted life years.[4] An increased number of studies have reported the effect of oral health on general health. Physical, cognitive, and social communicative abilities, which are components of higher-level functional capacity, have all been suggested to be affected by oral health.[5-10] However there are only cross-sectional studies examining the association between oral health or oral health behaviors and higher-level functional capacity.[11, 12] These studies did not use tooth loss as an exposure variable and only one study concluded that higher-level functional disability might lead to poorer oral health behavior.[12]

Propensity score technique is one of the best techniques to find out associations between exposure and outcome in observational studies.[13, 14] When examining the

association of tooth and higher-level functional capacity, the ideal research design would be an intervention study to increase the number of natural teeth amongst edentulous people. However, it is very difficult to estimate the treatment effects for tooth loss which is the effect of increment of natural teeth. Therefore, we performed inverse-probability weighting (IPW) with the propensity score and attempted to evaluate the treatment effects for tooth loss on higher-level functional capacity.[14]

We hypothesized that tooth loss at baseline would be predictive of future decline in higher-level functional capacity. Thus, the stated aim of this cohort study was to determine if there was an association between tooth loss and the decline in higher-level functional capacity.

METHODS

Data Sources and Participants

This study used the repeated measured data of the Japan Gerontological Evaluation Study (JAGES) project.[7, 10, 15] All of the participants were community-dwelling persons aged 65 years or older who were physically and cognitively independent, defined by not receiving a certification of needed long-term care. The baseline survey was conducted between August 2010 and January 2012, while the follow-up survey was conducted between January 2013 and December 2013. Self-administered questionnaires

were initially mailed to 24 municipalities in 9 prefectures in Japan. In 10 of the municipalities, we sampled the entire population, while in the remaining 14 municipalities, our samples were randomly based on the official residential registers obtained from the municipal governments. Self-administered questionnaires used for the follow-up survey were subsequently mailed to the same municipalities and participants.

Study Design

The present study design was a prospective cohort study.

Exposure Variable: tooth loss at baseline

The self-reported number of remaining teeth at baseline was used as an exposure variable. To obtain the information, the survey questionnaire asked, *"What is the status of your dental health?"* with the possible answers for the respondents including, *"I have 20 or more natural teeth"*, *"I have 10 to 19 natural teeth"*, *"I have 1 to 9 natural teeth"*, and *"I have no natural teeth"*. These four answers were defined as "having ≥20 teeth", "having 10-19 teeth", "having 1-9 teeth", and "being edentulous", respectively.

Outcome Variable: changes in higher-level functional capacity

Higher-level functional capacity measured by the Tokyo Metropolitan Institute of Gerontology Index of Competence (TMIG-IC) was used as an outcome variable.[2] The TMIG-IC has been widely used in Japan, and has been validated.[2, 3, 16-18] TMIG-IC is based upon responses to 13 questions. Supplemental Table 1 shows the thirteen questions in the

TMIG-IC. The responses to each question included *"yes"* (able to do, scored "1") or *"no"* (unable, scored "0"). The TMIG-IC score ranged from 0 (lowest function, unable to independently live in the community) to 13 (highest function, able to independently live in the community). The outcome was based on the changes in higher-level functional capacity measured by TMIG-IC, which was calculated by the total TMIG-IC score at the follow-up minus the total TMIG-IC score at the baseline.

Covariates

Health and health behavior variables which possibly related to TMIG-IC and oral health were included into the model: Sex (female or male), age (65-69, 70-74, 75-79, 80-84, ≥85), medical history (heart disease, stroke, diabetes, respiratory disease), depression as calculated by the geriatric depression scale 15 (GDS-15)[19] (0-4: no depression, 5-9: depressive tendency, 10-15: depression),[18] number of falls over the past year (none, once, more than once),[15] smoking status (never a smoker, former smoker, current smoker), drinking alcohol status (current drinker, former drinker, never a drinker), body mass index (BMI, m2/kg) (≥25, 18.5-24.99, <18.5),[17] and the baseline TMIG-IC. In addition, it was known that as a broader range of social determinants affected individual's behavior and oral health,[20] equalized household income (≥ JPY 4 million, JPY 2-3.99 million, <JPY 2 million. JPY = Japanese Yen, 100 JPY was approximately equal to $1 US at the time of the analysis. The poverty line in Japan in 2009 was 1.25 million yen[21]), years of education (≥13

years, 10-12 years, 6-9 years, <6 years), marital status (married, widowed, divorced, never married),[6] family members (live alone, only with spouse, with spouse and child(ren), with only child(ren), other),[10] and residential areas (24 municipalities) were also included into the model. We used the baseline TMIG-IC score as a continuous covariate, because the baseline TMIG-IC score indicated health status, and because it was possible that the high and low score participants might exhibit different trends associated with changes in their TMIG-IC scores. To avoid the effect of the different socio-environmental background and variation in the follow-up periods in each municipality, dummy variables of the 24 municipalities were included in our models.

Statistical Analysis

Prior to using the regression analysis models and IPW models, we performed multiple imputation (MI) by chained equations (MICE) to determine estimates for the missing values and created 10 imputed data sets.[22] The supplemental Table 2 lists the variables used in the MI. Because of the TMIG-IC has no cut-off point[2] and the changes in higher-level functional capacity had a normal distribution, multiple linear regression models were used. After completion of the MI, we used multiple linear regression models and IPW models, estimating non-standardized coefficients (β) and 95% confidence intervals (95%CI) to analyze the association between tooth loss and the changes in higher-level functional capacity as continuous outcomes. The IPW models show

quasi-experimental results of the treatment effects.[13] Therefore, we used IPW models that can estimate average treatment effect (ATE) and average treatment effect on the treated (ATET) by multivariate independent variable.[14] The ATE is the average effect of the treatment in the total population. When estimating ATE, we assumed all participants of this study were edentulous. If all of them got natural teeth, the higher-level functional capacity would be improved. The difference of the higher-level functional capacity between the former and later situation was the ATE. The ATET is the average treatment effect among the exposed population. The ATET of this study shows the treatment effects if the edentulous participants had natural tooth. After calculating the propensity score, we checked the balance in each of the imputed data sets. To judge the success of the balancing of the IPW, we used standardized differences and variance ratios. Generally, increasing number of standardized difference close to zero (within ±0.1) and variance ratios close to one indicate the appropriateness of the balancing of IPW.[14] The variables selected in the analysis were chosen from previously listed potential confounders. Analyses were performed using Stata version 14.0 (Stata Corp., College Station, TX).

Ethical Approval

The JAGES project protocol was reviewed and approved by the ethics committee involving Human Participants, Nihon Fukushi University (10-05, 13-14) and the Ethics Committee of the Tohoku University Graduate School of Medicine (24-29).

RESULTS

After mailing the baseline survey questionnaires to 140,459 participants in 24 municipalities, a total of 91,569 responded to the survey (response rate = 65.2 %). We excluded 318 participants who stated they had disabilities in activities of daily living in the baseline survey and 886 participants who received a certification of needed long-term care in the baseline survey. Therefore, eligible baseline participants were 90,365. The 2013 follow-up survey was filled out by 63,341 participants (follow-up rate = 70.1%). We excluded 1,008 participants who did not provide matching information on the self-reported sex between the baseline and the follow-up surveys. After the exclusions, a total of 62,333 participants were included in the present study. The median of the follow-up period was 707 days (1-3rd quartile: 694-1148). The baseline mean age was 73.0 years (standard deviation: 5.6). Table 1 shows the characteristics and the outcome of the participants (residential areas are shown in the supplemental Table 3). Participants with <20 teeth were older than participants with ≥20 teeth. In addition, participants with fewer remaining teeth had generally lower socio-economic status and poorer health behaviors. The percentage of missing values for each of the variables is shown in the supplemental Table 2.

Table 2 presents the results of the multiple linear regression. The multiple linear regression model after multiple imputation showed similar results with the results from

before multiple imputation. The variance inflation factors of the multiple linear regression before multiple imputation were 2.71, which is a generally acceptable level. After multiple imputation and adjusting for covariates, the multiple linear regression model analysis calculated the β of the change in higher-level functional capacity for having 10-19 teeth, or having 1-9 teeth, or being edentulous to be -0.035 (95%CI: -0.065, -0.005), -0.088 (95%CI: -0.119, -0.056), and -0.178 (95%CI: -0.221, -0.135), respectively, compared with having ≥20 teeth. Supplemental Table 4 lists the balancing of IPW in each of the 10 imputed data sets. As all of the standardized differences were close to zero (within ±0.1) and the variance ratios increased to close to one after being weighted, this confirms our ability to balance the propensity score. Table 3 shows the results of the ATE and the ATET calculated from the IPW. In the ATE models, the β of the treatment effects for tooth loss in all participants if they changed from being edentulous to having ≥20 teeth, or 10-19 teeth, or having 1-9 were 0.156 (95%CI: 0.103, 0.208), 0.115 (95%CI: 0.064, 0.165), and 0.065 (95%CI: 0.014, 0.115), respectively. In the ATET models, the β of the treatment effects for tooth loss if edentulous participants had ≥20 teeth, or 10-19 teeth, or 1-9 teeth were 0.170 (95%CI: 0.114, 0.227), 0.130 (95%CI: 0.080, 0.180), and 0.070 (95%CI: 0.022, 0.118), respectively.

DISCUSSIONS

The findings of this large population-based prospective cohort study indicate that

there was a dose-response association between number of remaining teeth and higher-level functional capacity over 2 years. To our surprise, table 2 showed that the impact of being edentulous on the outcome was between having a history of stroke and having a history of diabetes. Previous studies have reported that tooth loss were associated with a physical disability, and poor cognitive function.[5-7] In addition, oral health was also associated with the social communicative abilities such as speech ability,[8] smiling/laughing , and the ability to have conversations with family or friends.[9] The present study also indicated that tooth loss was potentially associated with not only physical and cognitive functions but also the ability and the activities necessary to live independently in a social community.

Inverse-Probability Weighting (IPW) with the Propensity Score

Our IPW models suggested that treatment effects for tooth loss are significantly attenuated with the decline in higher-level functional capacity in the ATE and the ATET estimation models. In this study, the ATE represented the treatment effects in all participants and the ATET represented the treatment effects in edentulous participants. The β values of ATE and ATET were similar. The treatment effects for tooth loss on higher-level functional capacity was essentially the same in each population.

When discussing the associations between oral health and general health, we need to consider a possibility that there are bidirectional relationships between dental status and general health.[23] Compared to conventional multiple regression models, IPW was used to

minimize the differences in the covariates of participants to reduce potential confounding and bias, and to directly estimate the treatment effects.[14, 24] Therefore, the IPW analysis could show more clearly the association between tooth loss and changes in higher-level functional capacity and the treatment effects for tooth loss. We found a significant impact of the treatment effects for tooth loss on higher-level functional capacity in IPW. Therefore the present study has provided robust evidence on the association between tooth loss and higher-level functional capacity and has demonstrated the possibility that the treatment to replace missing natural teeth could attenuate a decline in the higher-level functional capacity.

Mechanism

There are several possible pathways that could be responsible for the association between tooth loss and the decline in higher-level functional capacity. First, an inflammation pathway could be a candidate for it. Tooth loss reflects history of periodontal disease and accumulation of caries.[25] Oral inflammation has been shown to be associated with biological markers of inflammation such as increased C reactive protein (CRP) and fibrinogen through poor oral health behaviors.[26] Chronic inflammation was also associated with physical and cognitive disability.[27] Second, psychosocial aspects of oral health might affect higher-level functional capacity, because TMIG-IC includes the social communicative ability such as visiting friends and talking to someone. The human face is

an important tool for social communication.[28] Thus, oral health affects the facial esthetic and social communicative ability.[8, 9] Third, there might be a nutritional pathway to explain the link between tooth loss and higher-level functional capacity. Severe tooth loss is a risk factor for poorer nutritional status, because the number of natural teeth play an important role in chewing ability.[29] People with poor nutritional status tend to have physical and cognitive decline, but also a decline in higher-level functional capacity.[16]

Limitations

There were some limitations in the present study. The first limitation involved the self-reporting of the number of remaining teeth and TMIG-IC in the questionnaire. This opens the possibility of a self-reporting bias. However, previous studies that have been performed in the JAGES project have documented the validity of using self-reported questionnaires.[30] Second, the follow-up period was fairly short (median: 707 days). However, the findings of our present study did show a significant decline in the higher-level functional capacity, especially in the older participants. In relation to oral health, we did find that there was a dose-response association between tooth loss and the decline in the higher-level functional capacity. Therefore, this suggests that the present results are robust. Third, we observed some variability in the follow-up period for each municipality. To exclude the effect of the diverse follow-up period, we included a fixed-effect term for the municipalities. Therefore, since we were able to adequately

address this problem, the follow-up period could not affect the association between tooth loss and the decline in higher-level functional capacity. Fourth, some of the participants (N= 27,024) were lost in the follow-up. The lost participants were older, had a lower score of higher-level functional capacity, and poorer oral health than those who were successfully followed. These differences could have biased the association.

Implications

The results of this study indicate the importance of maintaining number of teeth in later life to maintain functional capacity. It is therefore essential that adults and older people are given appropriate support to maintain good oral health self-care practices and clinical dental teams need to provide high quality evidence based care to ensure teeth are retained into older age.

Generalisability

Although the present study was conducted among Japanese, other previous studies in worldwide investigated similar associations between oral health and general health. Therefore, this current study results might be acceptable internationally.

CONCLUSION

The findings of this prospective cohort study highlight that tooth loss was associated with a future decline in higher-level functional capacity amongst a large cohort

of older people.

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Conflict of Interest Disclosures:

Elements of Financial/Personal Conflicts	*Author 1 Yukihiro Sato and Jun Aida and Katsunori Kondo and Toru Tsuboya and Richard G Watt and Tatsuo Yamamoto and Shihoko Koyama and Yusuke Matsuyama and Ken Osaka (all authors)		Author 2		Author 3		Etc.	
	Yes	No	Yes	No	Yes	No	Yes	No
Employment or Affiliation		x						
Grants/Funds		x						
Honoraria		x						
Speaker Forum		x						
Consultant		x						
Stocks		x						
Royalties		x						

Expert Testimony		**x**						
Board Member		**x**						
Patents		**x**						
Personal Relationship		**x**						

***Authors can be listed by abbreviations of their names.**

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REFERENCES

1. Rowe JW, Kahn RL. Successful aging 2.0: Conceptual expansions for the 21st century. J Gerontol B Psychol Sci Soc Sci 2015;70: 593-596.
2. Koyano W, Shibata H, Nakazato K et al. Measurement of competence: Reliability and validity of the tmig index of competence. Arch Gerontol Geriatr 1991;13: 103-116.
3. Ogata S, Hayashi C, Sugiura K et al. Association between subjective memory complaints and impaired higher-level functional capacity in people aged 60 years or older. Arch Gerontol Geriatr 2015;60: 201-205.
4. Marcenes W, Kassebaum NJ, Bernabe E et al. Global burden of oral conditions in 1990-2010: A systematic analysis. J Dent Res 2013;92: 592-597.
5. Kaye EK, Valencia A, Baba N et al. Tooth loss and periodontal disease predict poor cognitive function in older men. J Am Geriatr Soc 2010;58: 713-718.
6. Tsakos G, Watt RG, Rouxel PL et al. Tooth loss associated with physical and cognitive decline in older adults. J Am Geriatr Soc 2015;63: 91-99.
7. Yamamoto T, Kondo K, Hirai H et al. Association between self-reported dental health status and onset of dementia: A 4-year prospective cohort study of older japanese adults from the aichi gerontological evaluation study (ages) project. Psychosom Med 2012;74: 241-248.
8. Knipfer C, Riemann M, Bocklet T et al. Speech intelligibility enhancement after maxillary denture treatment and its impact on quality of life. Int J Prosthodont 2014;27: 61-69.
9. Sato Y, Aida J, Takeuchi K et al. Impact of loss of removable dentures on oral health after the great east japan earthquake: A retrospective cohort study. J Prosthodont 2015;24: 32-36.
10. Aida J, Kondo K, Hirai H et al. Association between dental status and incident disability in an older japanese population. J Am Geriatr Soc 2012;60: 338-343.
11. Ohara Y, Hirano H, Yoshida H et al. Prevalence and factors associated with xerostomia and hyposalivation among community-dwelling older people in japan. Gerodontology 2013.
12. Moriya S, Tei K, Yamazaki Y et al. Relationships between higher-level functional capacity and dental health behaviors in community-dwelling older adults. Gerodontology 2013;30: 133-140.
13. Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. Multivariate Behav Res 2011;46: 399-424.
14. McCaffrey DF, Griffin BA, Almirall D et al. A tutorial on propensity score estimation for multiple treatments using generalized boosted models. Statistics in Medicine 2013;32: 3388-3414.
15. Yamamoto T, Kondo K, Misawa J et al. Dental status and incident falls among older japanese: A prospective cohort study. BMJ Open 2012;2.
16. Imai E, Tsubota-Utsugi M, Kikuya M et al. Animal protein intake is associated with higher-level functional capacity in elderly adults: The ohasama study. J Am Geriatr Soc 2014;62: 426-434.
17. Ogata S, Tanaka H, Omura K et al. Association between intake of dairy products and short-term memory with and without adjustment for genetic and family environmental factors: A twin study.

Clin Nutr 2015.

18. Ogata S, Hayashi C, Sugiura K et al. Associations between depressive state and impaired higher-level functional capacity in the elderly with long-term care requirements. PLoS One 2015;10: e0127410.

19. Burke WJ, Roccaforte WH, Wengel SP. The short form of the geriatric depression scale: A comparison with the 30-item form. J Geriatr Psychiatry Neurol 1991;4: 173-178.

20. Marmot M, Bell R. Social determinants and dental health. Adv Dent Res 2011;23: 201-206.

21. Summary report of comprehensive survey of living conditions 2010. Comprehensive Survey of Living Conditions. Ministry of Health, Labour and Welfare. Available at: *http://www.mhlw.go.jp/english/database/db-hss/cslc-report2010.html*. Accessed February 17, 2016.

22. van Buuren S, Boshuizen HC, Knook DL. Multiple imputation of missing blood pressure covariates in survival analysis. Statistics in Medicine 1999;18: 681-694.

23. Al-Jewair TS, Al-Jasser R, Almas K. Periodontitis and obstructive sleep apnea's bidirectional relationship: A systematic review and meta-analysis. Sleep Breath 2015.

24. Margaritis V, Mamai-Homata E, Koletsi-Kounari H. Novel methods of balancing covariates for the assessment of dental erosion: A contribution to validation of a synthetic scoring system for erosive wear. J Dent 2011;39: 361-367.

25. Nicolau B, Thomson WM, Steele JG et al. Life-course epidemiology: Concepts and theoretical models and its relevance to chronic oral conditions. Community Dent Oral Epidemiol 2007;35: 241-249.

26. de Oliveira C, Watt R, Hamer M. Toothbrushing, inflammation, and risk of cardiovascular disease: Results from scottish health survey. BMJ 2010;340: c2451.

27. Brinkley TE, Leng X, Miller ME et al. Chronic inflammation is associated with low physical function in older adults across multiple comorbidities. J Gerontol A Biol Sci Med Sci 2009;64: 455-461.

28. Jack RE, Schyns PG. The human face as a dynamic tool for social communication. Curr Biol 2015;25: R621-634.

29. Sheiham A, Steele JG, Marcenes W et al. The relationship among dental status, nutrient intake, and nutritional status in older people. J Dent Res 2001;80: 408-413.

30. Yamamoto T, Kondo K, Fuchida S et al. Validity of self-reported oral health variables: Aichi gerontological evaluation study (ages) project. Health Science and Health Care 2012;12: 4-12.

GRAPHICS

TABLES

Table 1. Characteristics and the outcome of the participants for each of the number of remaining teeth categories (n=62,333)

		All participants (n=62,333)		Having ≥20 teeth (n=22,257)	Having 10-19 teeth (n=15,953)	Having 1-9 teeth (n=15,016)	Being edentulous (n=7,306)
Characteristics of the participants		n	%	%	%	%	%
Sex	Female	33,512	53.8	52.6	52.9	55.8	52.6
	Male	28,821	46.2	47.4	47.1	44.2	47.5
Age	65-69	20,797	33.4	42.8	37.7	25.2	14.3
	70-74	19,051	30.6	32.7	31.3	30.3	23.7
	75-79	13,687	22.0	17.2	20.6	26.4	28.7
	80-84	6,650	10.7	6.1	8.2	13.6	22.7
	≥85	2,148	3.5	1.2	2.1	4.5	10.6
Medical history	Heart disease	7,024	14.9	13.9	14.0	15.5	17.9
	Stroke	753	1.6	1.4	1.5	1.7	2.0
	Diabetes	7,731	16.4	14.9	16.4	17.6	18.0
	Respiratory disease	1,937	4.1	3.6	4.1	4.6	4.7
Equalized household income	≥JPY 4 million	5,885	11.5	13.6	11.1	9.7	8.9
	JPY 2-3.99 million	20,632	40.1	45.1	40.8	35.7	31.6
	<JPY 2 million	24,897	48.4	41.3	48.1	54.6	59.5
Years of education	≥13 years	10,989	18.4	23.1	18.2	14.6	11.9
	10-12 years	20,960	35.1	39.1	36.6	32.2	26.2
	6-9 years	26,766	44.8	37.1	44.0	50.8	57.2

	<6 years	1,048	1.8	0.7	1.3	2.3	4.8
Marital status	Married	44,329	74.0	79.9	75.1	69.7	63.6
	Widowed	12,377	20.7	15.4	19.2	24.7	31.5
	Divorced	1,958	3.3	2.7	3.5	3.9	3.2
	Never married	1,214	2.0	2.1	2.2	1.8	1.7
Family member	Live alone	7,006	11.7	9.8	11.5	13.3	13.9
	Only with spouse	23,286	38.8	43.6	39.6	35.3	29.9
	With spouse and child(ren)	15,819	26.4	28.6	27.1	24.7	23.1
	With only child(ren)	7,887	13.2	9.8	12.3	15.8	19.9
	Other	5,953	9.9	8.2	9.5	10.9	13.2
Depression (GDS-15)	No depression (0-4)	38,442	74.5	79.7	74.6	69.5	68.9
	Depressive tendency (5-9)	10,082	19.6	16.4	19.7	22.4	23.3
	Depression (10-15)	3,048	5.9	4.0	5.8	8.1	7.8
Falls over the past year	None	42,506	71.5	76.4	71.8	67.5	64.7
	Once	13,422	22.6	19.7	22.8	24.7	26.2
	More than once	3,515	5.9	3.9	5.4	7.8	9.1
Smoking status	Never smoker	33,873	60.4	63.8	59.2	58.8	54.6
	Former smoker	16,139	28.8	28.8	29.5	27.8	30.6
	Current smoker	6,036	10.8	7.5	11.4	13.4	14.8
Drinking alcohol status	Current drinker	21,296	36.4	41.4	38.3	32.2	27.6
	Former drinker	1,839	3.2	2.6	3.3	3.7	3.5
	Never drinker	35,304	60.4	55.9	58.4	64.2	69.0
BMI (m^2/kg)	≥25	13,174	22.3	20.6	22.9	23.4	24.3
	18.5-24.9	42,067	71.3	73.8	71.4	69.3	67.5
	<18.5	3,770	6.4	5.6	5.7	7.3	8.2

TMIG-IC score at baseline	mean	11.7	12.0	11.8	11.5	11.2
	SD	1.7	1.5	1.6	1.9	2.2
Changes in higher-level functional capacity	mean	-0.247	-0.173	-0.212	-0.306	-0.447
	SD	1.45	1.28	1.40	1.55	1.78

Abbreviations: GDS-15, geriatric depression scale 15; BMI, body mass index; TMIG-IC, the Tokyo Metropolitan Institute of Gerontology Index of Competence.

Change in higher-level functional capacity was calculated by the total TMIG-IC score at the follow-up minus the total TMIG-IC score at the baseline.

Missing values of number of remaining teeth categories (n=1,801).

Residential areas were shown in supplemental Table 3.

Table 2. Associations between the number of remaining teeth and changes in higher-level functional capacity determined by multiple regression models

		Before multiple imputation			After multiple imputation		
		Multiple regression model Fully adjusted model[a] (n=25,658)			Multiple regression model Fully adjusted model[a] (n=62,333)		
		β	95%CI	P-value	β	95%CI	P-value
Number of remaining teeth (reference: having ≥20 teeth)	Having 10-19 teeth	-0.040	-0.081, 0.001	0.058	-0.035	-0.065, -0.005	0.024
	Having 1-9 teeth	-0.063	-0.108, -0.019	0.006	-0.088	-0.119, -0.056	<0.001
	Being edentulous	-0.149	-0.211, -0.087	<0.001	-0.178	-0.221, -0.135	<0.001
Sex (reference: female)	Male	-0.091	-0.142, -0.041	<0.001	-0.117	-0.152, -0.081	<0.001
Age (reference: 65-69)	70-74	-0.077	-0.118, -0.037	<0.001	-0.106	-0.135, -0.077	<0.001
	75-79	-0.189	-0.236, -0.141	<0.001	-0.257	-0.290, -0.224	<0.001
	80-84	-0.530	-0.595, -0.466	<0.001	-0.578	-0.622, -0.534	<0.001
	≥85	-1.212	-1.323, -1.101	<0.001	-1.133	-1.205, -1.062	<0.001
Medical history (reference: none)	Heart disease	-0.020	-0.067, 0.027	0.398	-0.023	-0.061, 0.015	0.229
	Stroke	-0.220	-0.358, -0.082	0.002	-0.183	-0.301, -0.065	0.003
	Diabetes	-0.076	-0.121, -0.032	0.001	-0.067	-0.109, -0.026	0.002
	Respiratory disease	-0.138	-0.224, -0.053	0.001	-0.102	-0.172, -0.031	0.005
Equalized household income (reference: ≥JPY 4 million)	JPY 2-3.99 million	-0.017	-0.072, 0.037	0.533	-0.008	-0.052, 0.035	0.700
	<JPY 2 million	-0.067	-0.123, -0.010	0.020	-0.063	-0.109, -0.016	<0.001
Years of education (reference: ≥13 years)	10-12 years	-0.060	-0.106, -0.015	0.010	-0.028	-0.062, 0.005	0.100
	6-9 years	-0.167	-0.215, -0.118	<0.001	-0.168	-0.205, -0.130	<0.001
	<6 years	-0.805	-0.963, -0.646	<0.001	-0.523	-0.621, -0.424	<0.001
Marital status (reference: married)	Widowed	0.044	-0.052, 0.139	0.369	0.015	-0.045, 0.075	0.629
	Divorced	0.037	-0.093, 0.167	0.579	-0.038	-0.125, 0.050	0.399
	Never married	-0.118	-0.264, 0.028	0.113	-0.102	-0.205, 0.001	0.053

Family member (reference: live alone)	Only with spouse	-0.115	-0.220, -0.010	0.032	-0.149	-0.215, -0.083	<0.001
	With spouse and child(ren)	-0.173	-0.280, -0.066	0.002	-0.170	-0.240, -0.100	<0.001
	With only child(ren)	-0.246	-0.321, -0.171	<0.001	-0.239	-0.288, -0.189	<0.001
	Other	-0.155	-0.256, -0.055	0.002	-0.161	-0.225, -0.097	<0.001
Depression (GDS-15) (reference: No depression (0-4))	Depressive tendency (5-9)	-0.188	-0.231, -0.145	<0.001	-0.240	-0.272, -0.207	<0.001
	Depression (10-15)	-0.315	-0.389, -0.240	<0.001	-0.369	-0.422, -0.317	<0.001
Falls over the past year (reference: none)	Once	0.018	-0.022, 0.059	0.370	-0.002	-0.031, 0.026	0.880
	More than once	-0.093	-0.167, -0.018	0.015	-0.118	-0.171, -0.064	<0.001
Smoking status (reference: never smoker)	Former smoker	-0.045	-0.094, 0.003	0.067	-0.027	-0.064, 0.011	0.168
	Current smoker	-0.112	-0.177, -0.048	0.001	-0.134	-0.180, -0.088	<0.001
Drinking alcohol status (reference: current drinker)	Former drinker	-0.069	-0.160, 0.021	0.134	-0.098	-0.170, -0.026	0.008
	Never drinker	-0.055	-0.094, -0.015	0.007	-0.062	-0.090, -0.034	<0.001
BMI (m2/kg) (reference: ≥25)	18.5-24.9	0.022	-0.017, 0.061	0.262	0.034	0.004, 0.063	0.024
	<18.5	-0.145	-0.225, -0.066	<0.001	-0.084	-0.137, -0.031	0.002
TMIG-IC score at baseline		-0.241	-0.251, -0.230	<0.001	-0.264	-0.271, -0.256	<0.001

[a] Residential areas were adjusted, but the results were not shown in the table.

Abbreviations: GDS-15, geriatric depression scale 15; BMI, body mass index; TMIG-IC, the Tokyo Metropolitan Institute of Gerontology Index of Competence.

Table 3. The treatment effects for tooth loss on changes in higher-level functional capacity determined by inverse-probability weighting models

	IPW model					
	ATE[a] (n=62,333)			ATET[b] (n=62,333)		
Number of remaining teeth (reference: being edentulous)	β	95%CI	P-value	β	95%CI	P-value
Having ≥20 teeth	0.156	0.103, 0.208	0.012	0.170	0.114, 0.227	0.004
Having 10-19 teeth	0.115	0.064, 0.165	<0.001	0.130	0.080, 0.180	<0.001
Having 1-9 teeth	0.065	0.014, 0.115	<0.001	0.070	0.022, 0.118	<0.001

[a] The average treatment effect (ATE) represented the β of the treatment effects for tooth loss in all participants if they changed from being edentulous to having ≥20 teeth, or 10-19 teeth, or having 1-9.

[b] The average treatment effect on the treated (ATET) represented the β of the treatment effects for tooth loss if edentulous participants had ≥20 teeth, or 10-19 teeth, or 1-9 teeth.

Abbreviations: IPW, inverse-probability weighting.