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Dental status and incident falls among older Japanese: a prospective cohort study

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Short title: Dental status and incident falls among older Japanese

ABSTRACT

Objective To examine if self reported number of teeth, denture use and chewing ability are associated with incident falls.

Design Longitudinal cohort study (the Aichi Gerontological Evaluation Study).

Setting 5 Japanese municipalities.

Participants 1 763 community dwelling individuals aged 65 and over without experience of falls within the previous year at baseline.

Main outcome measures Self-reported history of multiple falls during the past year at the follow-up survey about 3 years later. Baseline data on the number of teeth present and/or denture use and chewing ability were collected using self-administered questionnaires. Regression analyses controlled for sex, age, present illness related to falls, activities of daily living, functional disability during follow-up period, body mass index, use of sedatives, depression, self-rated health, exercise, frequency of outings, educational attainment and equivalized household income.

Results 86 (4.88%) subjects reported falls at the follow-up survey. Logistic regression models fully adjusted for all covariates showed that subjects having 19 or fewer teeth but not using dentures had a significantly increased risk for incident falls (odds ratio 2.98, 95% confidence interval 1.34 to 6.62; P=0.007) compared to those having 20 or more teeth. No significant association was observed between chewing ability and incident falls in the fully adjusted model.

Conclusion Having 19 or fewer teeth but not using dentures was associated with higher risk for the incident falls in older Japanese even after adjustment for multiple covariates. Dental care to prevent tooth loss and denture treatment for older people might prevent falls.

Article summary

Article focus

- An association has been reported between dental occlusion and physical function including lower extremity dynamic strength and balance.
- Whether number of teeth, denture use and chewing ability predict subsequent incidence of falls is unknown.
- The aim of this study is to examine if self reported number of teeth, denture use and chewing ability are associated with incident falls

Key messages

- Having 19 or fewer teeth but not using dentures was a strong independent predictor of incident falls in a community-dwelling older population.
- In addition to preventing tooth loss, denture treatment for older people might prevent falls.

Strengths and limitations of this study

- Strengths of this study include large sample size, population-based sampling, and control for many potential confounding factors.
- The following limitations should be considered: the information on dental status and falls was self-reported and misclassification of cases is possible.

INTRODUCTION

Falls occur frequently in older people and adversely affect their quality of life. More than one-third of persons aged 60 and older fall each year in Japan, [1] England [2] and USA, [3] and in half of cases, falls are recurrent. [3] The consequences of falls are severe: 6% of falls lead to a fracture and 24% lead to other serious injuries. [2] Thus falls impose a burden on the sustainability of health and long-term care in Japan and many other countries, where population is rapidly aging. [4] In Japan, the annual health and long-term care costs attributable to falls are about 730 thousand million Japanese yen in 2002, which amounts to roughly 5% of the entire health and long-term care costs. [5]

A number of studies [6] including those using Japanese data [7] have identified risk factors for falls, including female sex, older age, having a history of falls, arthritis, cerebrovascular disease, depression, and the impairment of muscle strength and/or balance. Although programs including exercise that challenge balance are effective, [8] multifactorial fall-prevention programs to address these risk factors have not been successful in reducing falls. [9] A recent systematic review concluded that there is limited evidence to suggest that multifactorial fall prevention programmes in primary care, community, or emergency care settings are effective in reducing the number of falls. [10] Therefore, identification of additional modifiable risk factors may be helpful to establish more effective programs for fall prevention.

Unhealthy dental status is a candidate risk factor for falls. [11 12] A longitudinal study showed that partial or complete loss of dental occlusion was associated with a decline in lower extremity dynamic strength and balance function. [13] One 1-year prospective longitudinal study using 146 demented older people reported the association between dental occlusion and subsequent physical health. [14] Researchers have argued that these potential links between dental health and physical health may be

because jaw position affects body posture. [11] However, whether or not dental occlusion and chewing ability actually predict the subsequent incidence of falls is largely unknown.

Therefore, this prospective study aimed to determine the association between dental health in terms of the number of teeth present, denture use, and chewing ability, and the incidence of falls in a large cohort of older Japanese people.

METHODS

Study population

Our analyses were based on data from the Aichi Gerontological Evaluation Study (AGES) Project, an on-going Japanese prospective cohort study. [15 16] The detailed protocol of AGES and baseline characteristics of the study participants have been published elsewhere. [15 17] In brief, AGES aims to investigate the factors related to the loss of healthy years, such as functional decline, cognitive impairment, or death among non-institutionalized elderly. The sample was restricted to those who did not already have a physical or cognitive disability at baseline, defined by not receiving public long-term care insurance benefits. In October 2003, a baseline survey was mailed to a random sample of 8 123 community-dwelling individuals aged 65 years or over residing in 5 municipalities in Aichi prefecture, Japan. Responses were obtained from 3 998 subjects (49.2%). The follow-up survey was conducted by mail between March 2006 and March 2007, and 3 471 subjects were responded and 2 640 subjects were connected with baseline data using ID. After excluding 166 and 545 subjects who experienced multiple and single falls, respectively, as well as 106 subjects without information of falls at baseline, we were left with 1 823 subjects who did not report experiencing falls at baseline. After excluding 56 subjects without information on falls at follow-up, 4 subjects without information on age, a total of 1 763 subjects formed the final analytic population of this study. The AGES protocol was reviewed and approved by the

Ethics Committee on Research of Human Subjects at Nihon Fukushi University.

Outcome variables

History of falls was ascertained by asking, "Have you had any falls over the past year?" with possible answers of "multiple times", "once" or "none". Multiple falls was used as an outcome and the last two categories were combined. [3]

Dental health variables

Dental status and chewing ability were assessed using a self-administered questionnaire. Respondents were asked to classify their dental status as having 20 or more teeth, having 19 or fewer teeth with dentures, having 19 or fewer teeth without dentures, having few teeth with dentures, or having few teeth without dentures.

Chewing ability was ascertained by asking, "How is your ability to chew?" with possible answers being "I can chew anything I want", "I can chew most foods with some exceptions", "I can eat limited foods as I cannot chew very well", "I can hardly chew anything", and "I have liquid foods as I cannot chew at all". Data from the last three categories were combined due to the small number of respondents.

Covariates

Studies suggest that falls are associated with sex, [7 18] age, [2 7] stroke, [7] severe foot problems, [2] impaired vision and impaired hearing, [2] activities of daily living (ADL), [3 6 18] body mass index (BMI), [18] use of sedatives, [2] depression, [2] self-rated health, [18] exercise, [2] mobility, [2] and socioeconomic status. [19] Therefore, our regression analyses controlled for sex, age, present illness related to falls, ADL, BMI, use of sedatives, depression, self-rated health, exercise (how much they walked in minutes per day), frequency of outings, educational attainment

and equivalized household income. Self-reported current medical treatment of stroke, osteoporosis, joint disease/ neuralgia, injury/ fracture, impaired vision and/or impaired hearing was used as a variable for present illness related to falls. To evaluate functional status, the survey asked whether the respondents had difficulty or needed someone's assistance in performing any of the following ADL: basing, walking, and using the toilet. [20] Subjects without difficulty for all three ADL items were categorized into ADL without limitation and those with at least one ADL item with difficulty into ADL without limitation. BMI was categorized into three groups (less than 18.5, 18.5-24.9, 25.0 or more). Depression was assessed with the short version of the Geriatric Depression Scale (GDS) -15 developed for self-administration in the community using a simple yes/no format, [21] and was categorized into three groups: 0-4 (no), 5-9 (mild) and 10-15 (moderate to severe). To adjust household income for household size, equivalized income was calculated by dividing the household income by the square root of the number of household members, and grouped into one of three categories (1,999,999 yen or less, 2,000,000-3,999,999 yen, or 4,000,000 yen or higher). In addition to these covariates, data on functional disability during follow-up period were collected from the public long-term care insurance database maintained by each participating municipality and used as a covariate. Incidence of functional disability was determined based on when a person newly qualified for the insurance benefit; new registrations to the public long-term care insurance data base. [22] The distribution of each covariate at baseline for the overall AGES 2003 cohort (n=32 891) has been reported elsewhere. [15]

Statistical analysis

Logistic regression models were used to calculate the odds ratio (OR) and 95% confidence intervals (CI) for the incident falls at the follow-up. First, univariate ORs were calculated

for each dental health variable and each covariate. Then, logistic regression analysis was performed for each dental variable after including sex, age, present illness related to falls, ADL, functional disability during follow-up period, BMI, use of sedatives, depression, self-rated health, exercise, frequency of outings, educational attainment and equivalent income as covariates. All statistical analyses were conducted using IBM SPSS Statistics 19 (International Business Machines Co., New York, NY, USA).

RESULTS

A total of 86 (4.9%) out of 1 763 respondents reported the incidence of multiple falls at the follow-up survey. Table 1 shows the rates of fallers for the incident falls according to dental health variables and covariates.

Table 2 presents the non-adjusted and adjusted ORs for reporting multiple falls at the follow up survey according to dental status at baseline. Univariate models showed that poor dental status, chewing ability, male sex, older age, lower functional disability during follow-up period, depression, poor self-rated health and low educational attainment were each associated with incident falls. In the fully adjusted model, subjects with 19 or fewer teeth without dentures had a 2.98 (95% CI 1.34 to 6.62)-fold increased risk for incident falls compared with those having 20 or more teeth. No significant association was observed between incident falls and chewing ability after adding all covariates in the logistic regression model. When the two dental health variables were entered simultaneously into the same model with full adjustment for all covariates, there was no change in the ORs for any of the dental status variables.

DISCUSSION

Results of the present study showed that subjects with 19 or fewer teeth without dentures had

a significantly higher risk for incident falls than those with 20 or more teeth, even after adjusting for multiple potential confounding factors including demographics, physical and mental health status, health behavior, and socioeconomic status. These findings are consistent with those of a 1-year longitudinal study using 146 older patients with severe dementia, showing that patients with functionally inadequate dental status had significantly more-frequent falls than those with functionally adequate occlusion composed of natural teeth, dentures, or both. [14] Interestingly, among subjects with few teeth, their risk of falls was not significantly elevated so long as they wore dentures. These results suggest that the poor dental occlusion due to not using dentures after losing teeth is a strong risk factor for falls among subjects with 19 or fewer teeth.

There are several possible pathways between not using dentures after losing teeth and incident falls. One possibility is that the loss of occlusion due to not using dentures may result in a decrease in functional balance and these functional declines lead to falls. A cross-sectional study suggests that dental occlusal condition is associated with balance function. [12] An 8-year longitudinal study showed that partial or complete loss of occlusion was associated with a decrease in balance function. [13] Because balance deficit is a well-known risk factor for falls, [6] it is plausible that poor balance may explain the increased risk of falls among subjects with poor dental occlusion. Clinical studies suggest that dental occlusion affects postural and gaze stabilization, [23] and denture use improves postural swaying. [24]

The second possibility is that there are some confounding factors affecting the association between the loss of teeth not using dentures and incident falls. In fact, in the present study depression was significantly associated with falls in the fully adjusted logistic regression model in table 2. These results suggest that depression in part confounded the association between loss of teeth without dentures and falls. A study suggests an increased

risk for impaired dental health including self-perceived dental treatment needs among subjects with depressive symptoms. [25] Another study suggests that decayed and missing teeth influence depression. [26] Because depression is a well-known risk factor for falls, [6] it is possible that residual confounding by depressive symptomatology may account for the association between tooth loss and risk of falls. In the present study, self-reported chewing ability was not associated with the incident falls in the present study. This result disagreed with those from a cross-sectional study showing a significant association between chewing ability judged from number of foods chewable, and one-leg standing time. [27] Because self-reported mastication can be modified by cooking (*e. g.*, cooking soft meal helps chewing ability) and is more subjective than self-reported number of teeth present and denture use, this might dilute the association between self-reported chewing ability and the incident falls. A study using 5 643 subjects aged 40-89 showed that number of functional teeth which differentiate subjects with and without subjective dysphagia, defined as suffering any kind of subjective impairment to eating function including biting difficulty, declined with age. [28] Additional studies using objective measures for chewing ability are required to clarify the relationship between chewing ability and the incident falls.

Strengths and limitations

We note some strength of the present study including large sample size, population-based sampling, and control for many potential confounding factors. However, the present study has a number of limitations. First, measurements of dental status were not based on clinical examination. However, validity and reliability of self-reported number of teeth is established by multiple studies and widely used in epidemiological surveys. [29] For example, validation studies in the United States and Japan have reported a high agreement between

self-reported and examined number of teeth (Pearson's correlation coefficient: r=0.97, and 0.93, respectively) in 50 community-dwelling individuals aged 70 or older and 2 496 subjects with a mean age of 59. [30 31] Second, self-report of falls may not be perfectly accurate. [32] However, the associations with demographic factors and other covariates are in the generally expected direction, suggesting that there may be sufficient value in this outcome. Third, although subjects having 19 or fewer teeth but not using dentures had significantly higher risk for incident falls, those having few teeth but not using dentures did not. The non-significance might be ascribed to small number of subjects. Additional study using increased number of subjects is needed to confirm the results.

Conclusion

The primary implication of this study is the importance of maintaining the dental occlusion in order to prevent falls among older adults. The loss of teeth might be an independent risk factor for incident falls but it could be prevented by using dentures. Promoting dental care including proper use of denture might be an additional option for the prevention of falls in addition to current interventions targeting conventional risk factors, which warrants further interventional studies testing the effects of dental care and denture use on the prevention of falls

Contributors: TY and YH had the idea for the study, participated in its design, performed the statistical analysis, and drafted the manuscript, and YH is guarantor. KK is coordinator of Aichi Gerontological Evaluation Study (AGES) Project, helped develop the idea of the study, participated in acquiring the data and with design, and edited the manuscript. JM participated in design of study and edited manuscript. HH and MN participated in acquiring the data and with design, and critically revised the manuscript. JA, NK and IK participated

in the design of the study, deciding on statistical methods used, helped in interpreting the results, and revising the manuscript.

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Competing interests: All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare (1) No financial support for the submitted work from anyone other than their employer; (2) No financial relationships with commercial entities that might have an interest in the submitted work; (3) No spouses, partners, or children with relationships with commercial entities that might have an interest in the submitted work; (4) No non-financial interests that may be relevant to the submitted work.

Ethical approval: The Aichi Gerontological Evaluation Study (AGES) protocol including the present study was reviewed and approved by the Ethics Committee on Research of

Human Subjects at Nihon Fukushi University.

Data sharing: No additional data available.

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Table 1 Associations of dental health variables and covariates with incident falls

		Total	Fallers	
		n	n	%
Dental status	≥20 teeth	586	17	2.9
	≤19 teeth with dentures	521	19	3.6
	≤19 teeth without dentures	148	13	8.8
	Few teeth with dentures	437	30	6.9
	Few teeth without dentures	50	4	8.0
	Missing	21	3	14.3
Chewing ability	Can chew anything	719	30	4.2
	Can chew most foods	935	47	5.0
	Cannot chew very well	97	9	9.3
	Missing	12	0	0.0
Sex	Female	853	32	3.8
	Male	910	54	5.9
Age (years)	65-69	707	23	3.3
	70-74	569	27	4.7
	75-79	325	18	5.5
	80-84	120	12	10.0
	≥85	42	6	14.3
Present illness related to falls [a]	No	1224	58	4.7
	Yes	539	28	5.2
Activities of daily living	Without limitation	1669	81	4.9
	With limitation or missing	94	5	5.3
Functional disability during follow-up period	No	1734	81	4.7
	Yes	29	5	17.2
Body mass index	≤18.4	113	8	7.1
	18.5-24.9	1196	52	4.3
	≥25.0	380	21	5.5
	Missing	74	5	6.8
Use of sedatives	No	1602	80	5.0
	Yes	161	6	3.7
Depression	No	1143	39	3.4
	Mild	311	21	6.8
	Moderate to severe	77	8	10.4
	Missing	232	18	7.8
Self-rated health	Excellent	162	6	3.7
	Good	1192	50	4.2
	Fair	321	21	6.5
	Poor	59	9	15.3
	Missing	29	0	0.0

Exercise (minute-walk per day)	≥60	430	20	4.7
	30-59	569	16	2.8
	<30	564	38	6.7
	Missing	200	12	6.0
Frequency of outings	Almost everyday	843	37	4.4
	2-3 times a week	532	27	5.1
	Once a week or less	335	20	6.0
	Missing	53	2	3.8
Educational attainment (years)	≥13	184	4	2.2
	10-12	506	23	4.5
	6-9	953	49	5.1
	<6	53	4	7.5
	Missing	67	6	9.0
Equivalized household income (yen)	<500,000	53	0	0.0
	500,000-999,999	108	7	6.5
	1,000,000-1,499,999	139	7	5.0
	1,500,000-1,999,999	262	15	5.7
	2,000,000-2,999,999	429	16	3.7
	3,000,000-3,999,999	263	15	5.7
	≥4,000,000	164	5	3.0
	Missing	345	21	6.1

[a] Stroke, osteoporosis, joint disease/ neuralgia, injury/ fracture, impaired vision and/or impaired hearing.

Table 2 Logistic regression models for dental health variables and incident falls

		Univariate models				Fully adjusted models [b]							
		OR	95% CI		p	OR	95% CI		p	OR	95% CI		p
Dental status	≥20 teeth	1.00				1.00							
	≤19 teeth with dentures	1.27	0.65	2.46	0.486	1.06	0.53	2.11	0.870				
	≤19 teeth without dentures	3.22	1.53	6.80	0.002	2.98	1.34	6.62	0.007				
	Few teeth with dentures	2.47	1.34	4.53	0.004	1.88	0.96	3.65	0.064				
	Few teeth without dentures	2.91	0.94	9.01	0.064	1.91	0.56	6.50	0.300				
	Missing	5.58	1.50	20.76	0.010	7.23	1.36	38.48	0.020				
Chewing ability	Can chew anything	1.00								1.00			
	Can chew most foods	1.22	0.76	1.94	0.414					1.05	0.64	1.74	0.840
	Cannot chew very well	2.35	1.08	5.11	0.031					1.70	0.71	4.04	0.231
	Missing	0.00	0.00		0.999					0.00	0.00		0.999
Sex	Female	1.00				1.00				1.00			
	Male	1.62	1.03	2.53	0.035	1.84	1.12	3.02	0.016	1.84	1.13	3.01	0.014
Age (years)	65-69	1.00				1.00				1.00			
	70-74	1.48	0.84	2.61	0.175	1.31	0.72	2.38	0.371	1.42	0.79	2.55	0.247
	75-79	1.74	0.93	3.28	0.084	1.43	0.72	2.86	0.306	1.69	0.86	3.32	0.129
	80-84	3.30	1.60	6.84	0.001	3.07	1.35	6.99	0.008	3.64	1.62	8.18	0.002
	≥85	4.96	1.90	12.93	0.001	4.04	1.27	12.82	0.018	5.17	1.69	15.82	0.004

Present illness related to falls [a]	No	1.00					1.00					1.00				
	Yes	1.10	0.69	-	1.75	0.682	0.83	0.49	-	1.41	0.492	0.78	0.47	-	1.32	0.359
Activities of daily living	Without limitation	1.00					1.00					1.00				
	With limitation or missing	1.10	0.44	-	2.79	0.838	0.71	0.23	-	2.23	0.556	0.95	0.33	-	2.77	0.928
Functional disability during follow -up period	No	1.00					1.00					1.00				
	Yes	4.25	1.58	-	11.43	0.004	2.46	0.74	-	8.20	0.143	2.32	0.71	-	7.53	0.163
Body mass index	≤18.4	1.68	0.78	-	3.62	0.189	1.25	0.54	-	2.91	0.602	1.28	0.55	-	2.96	0.570
	18.5-24.9	1.00					1.00					1.00				
	≥25.0	1.29	0.77	-	2.17	0.342	1.44	0.83	-	2.50	0.199	1.45	0.84	-	2.52	0.182
	Missing	1.59	0.62	-	4.12	0.336	1.10	0.37	-	3.32	0.862	1.06	0.35	-	3.19	0.921
Use of sedatives	No	1.00					1.00					1.00				
	Yes	0.74	0.32	-	1.72	0.478	0.51	0.20	-	1.28	0.151	0.51	0.21	-	1.27	0.148
Depression	No	1.00					1.00					1.00				
	Mild	2.05	1.19	-	3.54	0.010	2.03	1.11	-	3.70	0.022	2.02	1.11	-	3.68	0.021
	Moderate to severe	3.28	1.48	-	7.29	0.004	2.54	1.01	-	6.41	0.049	2.55	1.02	-	6.36	0.044
	Missing	2.38	1.34	-	4.24	0.003	2.43	1.20	-	4.96	0.014	2.12	1.04	-	4.29	0.038
Self-rated health	Excellent	1.00					1.00					1.00				
	Good	1.14	0.48	-	2.70	0.769	1.16	0.47	-	2.86	0.752	1.12	0.46	-	2.74	0.808
	Fair	1.82	0.72	-	4.60	0.206	1.50	0.54	-	4.13	0.437	1.44	0.52	-	3.95	0.482
	Poor	4.68	1.59	-	13.80	0.005	2.78	0.80	-	9.63	0.106	2.80	0.82	-	9.60	0.101
	Missing	0.00	0.00	-		0.998	0.00	0.00	-		0.998	0.00	0.00	-		0.998
Exercise (minute-walk per day)	≥60	1.00					1.00					1.00				
	30-59	0.59	0.30	-	1.16	0.126	0.57	0.28	-	1.16	0.121	0.57	0.28	-	1.13	0.109
	<30	1.48	0.85	-	2.58	0.167	1.29	0.71	-	2.36	0.407	1.30	0.72	-	2.36	0.385
	Missing	1.31	0.63	-	2.73	0.474	1.31	0.58	-	2.95	0.511	1.41	0.63	-	3.13	0.405

Frequency of outings	Almost everyday	1.00					1.00					1.00				
	2-3 times a week	1.17	0.70	-	1.94	0.557	1.04	0.60	-	1.80	0.898	0.97	0.57	-	1.67	0.924
	Once a week or less	1.38	0.79	-	2.42	0.256	0.85	0.46	-	1.58	0.614	0.80	0.43	-	1.49	0.484
	Missing	0.85	0.20	-	3.65	0.831	0.45	0.10	-	2.14	0.317	0.47	0.10	-	2.28	0.350
Educational attainment (years)	≥13	1.00					1.00					1.00				
	10-12	2.14	0.73	-	6.28	0.165	2.77	0.89	-	8.59	0.078	2.90	0.94	-	8.93	0.064
	6-9	2.44	0.87	-	6.84	0.090	2.33	0.78	-	6.99	0.130	2.61	0.88	-	7.73	0.084
	<6	3.67	0.89	-	15.22	0.073	1.99	0.38	-	10.40	0.414	2.57	0.52	-	12.74	0.247
	Missing	4.43	1.21	-	16.21	0.025	3.15	0.68	-	14.53	0.141	3.52	0.77	-	16.06	0.104
Equivalized household income (yen)	<500,000	0.00	0.00	-		0.997	0.00	0.00	-		0.997	0.00	0.00	-		0.997
	500,000-999,999	1.00					1.00					1.00				
	1,000,000-1,499,999	0.77	0.26	-	2.25	0.627	0.91	0.28	-	2.93	0.874	0.90	0.28	-	2.83	0.850
	1,500,000-1,999,999	0.88	0.35	-	2.21	0.780	1.31	0.47	-	3.64	0.602	1.17	0.43	-	3.16	0.762
	2,000,000-2,999,999	0.56	0.22	-	1.39	0.213	0.95	0.35	-	2.59	0.926	0.85	0.32	-	2.25	0.737
	3,000,000-3,999,999	0.87	0.35	-	2.20	0.773	1.58	0.56	-	4.43	0.388	1.41	0.52	-	3.87	0.501
	≥4,000,000	0.45	0.14	-	1.47	0.187	0.65	0.18	-	2.32	0.512	0.60	0.17	-	2.10	0.428
	Missing	0.94	0.39	-	2.26	0.882	0.92	0.33	-	2.52	0.868	0.98	0.37	-	2.62	0.967

[a] Stroke, osteoporosis, joint disease/ neuralgia, injury/ fracture, impaired vision and/or impaired hearing.

[b] Adjusted for sex, age, present illness related to falls, activities of daily living, functional disability during follow-up period, body mass index, use of sedatives, depression, self-rated health, exercise, frequency of outings, educational attainment and equivalized household income.

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Dental status and incident falls among older Japanese: a prospective cohort study

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Short title: Dental status and incident falls among older Japanese

ABSTRACT

Objective To examine if self reported number of teeth, denture use and chewing ability are associated with incident falls.

Design Longitudinal cohort study (the Aichi Gerontological Evaluation Study).

Setting 5 Japanese municipalities.

Participants 1 763 community dwelling individuals aged 65 and over without experience of falls within the previous year at baseline.

Main outcome measures Self-reported history of multiple falls during the past year at the follow-up survey about 3 years later. Baseline data on the number of teeth present and/or denture use and chewing ability were collected using self-administered questionnaires. Logistic regression analyses controlled for sex, age, functional disability during follow-up period, depression, self-rated health and educational attainment.

Results 86 (4.88%) subjects reported falls at the follow-up survey. Logistic regression models fully adjusted for all covariates showed that subjects having 19 or fewer teeth but not using dentures had a significantly increased risk for incident falls (odds ratio 2.50, 95% confidence interval 1.21 to 5.17; P=0.013) compared to those having 20 or more teeth. Among subjects with 19 or fewer teeth, their risk of falls was not significantly elevated so long as they wore dentures (odds ratio 1.36, 95% confidence interval 0.76 to 2.45; P=0.299). No significant association was observed between chewing ability and incident falls in the fully adjusted model.

Conclusion Having 19 or fewer teeth but not using dentures was associated with higher risk for the incident falls in older Japanese even after adjustment for multiple covariates. Dental care to prevent tooth loss and denture treatment for older people might prevent falls, although we cannot exclude the possibility that the association is due to residual confounding.

Article summary

Article focus

- An association has been reported between dental occlusion and physical function including lower extremity dynamic strength and balance.
- Whether number of teeth, denture use and chewing ability predict subsequent incidence of falls is unknown.
- The aim of this study is to examine if self reported number of teeth, denture use and chewing ability are associated with incident falls

Key messages

- Having 19 or fewer teeth but not using dentures was a strong independent predictor of incident falls in a community-dwelling older population.
- In addition to preventing tooth loss, denture treatment for older people might prevent falls.

Strengths and limitations of this study

- Strengths of this study include large sample size, population-based sampling, and control for many potential confounding factors.
- The following limitations should be considered: the information on dental status and falls was self-reported and misclassification of cases is possible. Moreover, we cannot exclude the possibility that the association is due to residual confounding.

INTRODUCTION

Falls occur frequently in older people and adversely affect their quality of life. More than one-third of persons aged 60 and older fall each year in Japan, [1] England [2] and USA, [3] and in half of cases, falls are recurrent. [3] The consequences of falls are severe: 6% of falls lead to a fracture and 24% lead to other serious injuries. [2] Thus falls impose a burden on the sustainability of health and long-term care in Japan and many other countries, where population is rapidly aging. [4] In Japan, the annual health and long-term care costs attributable to falls are about 730 thousand million Japanese yen in 2002, which amounts to roughly 5% of the entire health and long-term care costs. [5]

A number of studies [6] including those using Japanese data [7] have identified risk factors for falls, including female sex, older age, having a history of falls, arthritis, cerebrovascular disease, depression, and the impairment of muscle strength and/or balance. Although exercise programs including balance training are effective, [8] multifactorial fall-prevention programs to address these risk factors have not been successful in reducing falls. [9] A recent systematic review concluded that there is limited evidence to suggest that multifactorial fall prevention programmes in primary care, community, or emergency care settings are effective in reducing the number of falls. [10] Therefore, identification of additional modifiable risk factors may be helpful to establish more effective programs for fall prevention.

Unhealthy dental status is a candidate risk factor for falls. [11 12] A longitudinal study showed that partial or complete loss of dental occlusion was associated with a decline in lower extremity dynamic strength and balance function. [13] One 1-year prospective longitudinal study using 146 demented older people reported the association between dental occlusion and subsequent physical health. [14] Researchers have argued that these potential links between dental health and physical health may be

because jaw position affects body posture. [11] Proprioceptive receptors of the masticatory muscular system and dentoalveolar ligaments provide sensory afferent input, [15] and hence poor dental occlusion may decrease that proprioception, thereby interfering with the stability of head posture (and increasing the risk of falling). However, whether or not dental occlusion and chewing ability actually predict the subsequent incidence of falls is largely unknown.

Therefore, this prospective study aimed to determine the association between dental health in terms of the number of teeth present, denture use, and chewing ability, and the incidence of falls in a large cohort of older Japanese people.

METHODS

Study population

Our analyses were based on data from the Aichi Gerontological Evaluation Study (AGES) Project, an on-going Japanese prospective cohort study. [16 17] The detailed protocol of AGES and baseline characteristics of the study participants have been published elsewhere. [16 18] In brief, AGES aims to investigate the factors related to the loss of healthy years, such as functional decline, cognitive impairment, or death among non-institutionalized elderly. The sample was restricted to those who did not already have a physical or cognitive disability at baseline, defined by not receiving public long-term care insurance benefits and self-reported dependence in walking, toileting, and bathing.

The sampling frame for the AGES cohort was selected as follows. In 2003, the residential registers of 5 municipalities in Aichi prefecture were obtained with the cooperation of city officials. From these comprehensive registers, we selected a random sample of one in three citizens aged 65 years or over in 4 towns (1 281, 1 537, 1 766 and 1 873) and a random sample 1 666 of in a city. They (N=8 123) were then mailed the baseline

questionnaire, inviting them to participate in the AGES cohort study. Responses were obtained from 3 998 subjects (49.2%) and 3 981 subjects were identified using ID. We mailed a follow-up survey between March 2006 and March 2007 to the 3 471 subjects after excluding 510 subjects who died or started receiving insurance benefits due to certified disability (N=472), or could not be traced (N=38). 2 640 subjects responded to the follow-up survey (76%), and formed the analytic sample for our study. After excluding 166 and 545 subjects who experienced multiple and single falls, respectively, as well as 106 subjects without information of falls at baseline, we were left with 1 823 subjects who did not report experiencing falls at baseline. After excluding 56 subjects without information on falls at follow-up, 4 subjects without information on age, a total of 1 763 subjects formed the final analytic population of this study. The AGES protocol was reviewed and approved by the Ethics Committee on Research of Human Subjects at Nihon Fukushi University.

Outcome variables

History of falls was ascertained by asking, "Have you had any falls over the past year?" with possible answers of "multiple times", "once" or "none". Multiple falls was used as an outcome and the last two categories were combined because previous studies have found that single fallers are more similar to nonfallers than to recurrent fallers on a range of medical, physical and psychological risk factors. [3 19 20]

Dental health variables

Dental status and chewing ability were assessed using a self-administered questionnaire. Respondents were asked to classify their dental status as having 20 or more teeth, having 19 or fewer teeth with dentures, having 19 or fewer teeth without dentures, having few teeth

with dentures, or having few teeth without dentures. Data from having 19 or fewer teeth with dentures and those from having few teeth with dentures were combined. Data from having 19 or fewer teeth without dentures and those from having few teeth without dentures were also combined.

Chewing ability was ascertained by asking, "How is your ability to chew?" with possible answers being "I can chew anything I want", "I can chew most foods with some exceptions", "I can eat limited foods as I cannot chew very well", "I can hardly chew anything", and "I have liquid foods as I cannot chew at all". Data from the last three categories were combined due to the small number of respondents.

Covariates

Studies suggest that falls are associated with sex, [7 21] age, [2 7] stroke, [7] severe foot problems, [2] impaired vision and impaired hearing, [2] activities of daily living (ADL), [3 6 21] body mass index (BMI), [21] use of sedatives, [2] depression, [2] self-rated health, [21] exercise, [2] mobility, [2] and socioeconomic status. [22] Therefore, associations of incident fall with sex, age, present illness related to falls, ADL, BMI, use of sedatives, depression, self-rated health, exercise (how much they walked in minutes per day), frequency of outings, educational attainment and equivalized household income were analyzed. Self-reported current medical treatment of stroke, osteoporosis, joint disease/ neuralgia, injury/ fracture, impaired vision and/or impaired hearing was used as a variable for present illness related to falls. To evaluate functional status, the survey asked whether the respondents had difficulty or needed someone's assistance in performing any of the following ADL: basing, walking, and using the toilet. [23] Subjects without difficulty for all three ADL items were categorized into ADL without limitation and those with at least one ADL item with difficulty into ADL without limitation. BMI was categorized into three groups (less than 18.5, 18.5-24.9, 25.0 or more).

[24] Depression was assessed with the short version of the Geriatric Depression Scale (GDS) -15 developed for self-administration in the community using a simple yes/no format, [25] and was categorized into three groups: 0-4 (no), 5-9 (mild) and 10-15 (moderate to severe). To adjust household income for household size, equivalized income was calculated by dividing the household income by the square root of the number of household members, and grouped into one of three categories (1,999,999 yen or less, 2,000,000-3,999,999 yen, or 4,000,000 yen or higher). In addition to these covariates, data on functional disability during follow-up period were collected from the public long-term care insurance database maintained by each participating municipality and used as a covariate. Incidence of functional disability was determined based on when a person newly qualified for the insurance benefit; new registrations to the public long-term care insurance data base. [26] The distribution of each covariate at baseline for the overall AGES 2003 cohort (n=32 891) has been reported elsewhere. [16]

Statistical analysis

Categorical variables that included missing data were recorded by reassigning missing values to separate "missing" categories in order to maximize the number of subjects included in the statistical analysis and thereby maximize statistical power. Logistic regression models were used to calculate the odds ratio (OR) and 95% confidence intervals (CI) for the incident falls at the follow-up. First, univariate ORs were calculated for each dental health variable and each covariate. Variables that were marginally significant ($p<0.10$) in the univariate analyses were selected as covariates for subsequent multivariate analysis. Then, logistic regression analysis was performed for each dental variable after including sex, age, functional disability during follow-up period, depression, self-rated health and educational attainment as covariates. All statistical analyses were conducted using IBM SPSS Statistics 19

(International Business Machines Co., New York, NY, USA).

RESULTS

A total of 86 (4.9%) out of 1 763 respondents reported the incidence of multiple falls at the follow-up survey. Table 1 shows the rates of fallers and non-adjusted ORs for reporting multiple falls at the follow up survey according to dental health variables and covariates. Univariate models showed that poor dental status, chewing ability, male sex, older age, lower functional disability during follow-up period, depression, poor self-rated health and low educational attainment were each associated with incident falls.

In the fully adjusted model, subjects with 19 or fewer teeth without dentures had a 2.50 (95% CI 1.21 to 5.17)-fold increased risk for incident falls compared with those having 20 or more teeth. No significant association was observed between incident falls and chewing ability after adding all covariates in the logistic regression model. When the two dental health variables were entered simultaneously into the same model with full adjustment for all covariates, there was no change in the ORs for any of the dental status variables.

DISCUSSION

Results of the present study showed that subjects with 19 or fewer teeth without dentures had a significantly higher risk for incident falls than those with 20 or more teeth, even after adjusting for multiple potential confounding factors including demographics, physical and mental health status, and socioeconomic status. These findings are consistent with those of a 1-year longitudinal study using 146 older patients with severe dementia, showing that patients with functionally inadequate dental status had significantly more-frequent falls than those with functionally adequate occlusion composed of natural teeth, dentures, or both. [14] Interestingly, among subjects with 19 or fewer teeth, their risk of falls was not significantly

elevated so long as they wore dentures. These results suggest that the poor dental occlusion due to not using dentures after losing teeth is a strong risk factor for falls among subjects with 19 or fewer teeth.

There are several possible pathways between not using dentures after losing teeth and incident falls. One possibility is that the loss of occlusion due to not using dentures may result in a decrease in functional balance and these functional declines lead to falls. A cross-sectional study suggests that dental occlusal condition is associated with balance function. [12] An 8-year longitudinal study showed that partial or complete loss of occlusion was associated with a decrease in balance function. [13] Because balance deficit is a well-known risk factor for falls, [6] it is plausible that poor balance may explain the increased risk of falls among subjects with poor dental occlusion.

A clinical study showed that dental occlusion affects postural and gaze stabilization because proprioceptive receptors of the masticatory muscular system and dentoalveolar ligaments provide sensory afferent input, and hence poor dental occlusion may decrease that proprioception and interfere with the stability of head posture. [15] Another clinical study showed that denture use improves postural swaying. [27] Because using dentures reduced the OR for incident falls in the present study, proprioceptive receptors of the masticatory muscular system might be more strongly associated with balance function and falls than those of dentoalveolar ligaments.

Some subjects with 20 or more teeth may have had dentures in the present study; however, the information was not obtained. Subjects with 20 or more teeth without dentures may be more appropriate than those with 20 or more teeth with/without dentures as a reference, and lack of the information might underestimate the association between dental status and incident falls. However, studies show that

people having at least 20 teeth usually can eat anything even they do not ware dentures. [28 29] Therefore, the lack of the information of with/without dentures in subjects having 20 or more teeth may be negligible.

We excluded individuals with past history of falls because we wanted to examine prospectively the risk of incident falls. In addition, there is a theoretical possibility that past history of falls might confound the association between number of teeth and risk of future falls, *i.e.* history of falls in the past can be a prior common cause of (a) number of teeth (because some people may break teeth when they fall) and (b) past falls predict future falls. For these reasons, we felt it was justified to exclude those with fall history at baseline.

In the present study, self-reported chewing ability was not associated with the incident falls in the present study. This result disagreed with those from a cross-sectional study showing a significant association between chewing ability judged from number of foods chewable, and one-leg standing time. [30] Because self-reported mastication can be modified by cooking (*e. g.*, cooking soft meal helps chewing ability) and is more subjective than self-reported number of teeth present and denture use, this might dilute the association between self-reported chewing ability and the incident falls. A study using 5 643 subjects aged 40-89 showed that number of functional teeth which differentiate subjects with and without subjective dysphagia, defined as suffering any kind of subjective impairment to eating function including biting difficulty, declined with age. [31] Additional studies using objective measures for chewing ability are required to clarify the relationship between chewing ability and the incident falls.

Using dentures does not always recover chewing ability. For example, a cross-sectional study showed that biting forces among removable partial and complete denture wearers were 35 and 11% respectively, when expressed as a percentage of the subjects with natural dentition. [32] These results may explain the different associations of

dental status and chewing ability with incident falls in the present study. When both dental status and chewing ability were simultaneously entered in the fully adjusted logistic regression model, only dental status was still significantly associated with incident falls (data not shown).

Males were at increased risk of falls in the present study, which disagrees with a meta analysis [7] based on people aged 60 or older showing that female sex was a risk factor. On the other hand, our study result is also similar to another large study of 12 684 individuals aged 85 or older. [21] We feel that the association between sex and risk of falls might vary according to the study population. Indeed current clinical guidelines for the prevention of falls do not include sex as a risk factor, [6 33] and thus it may not be a settled question.

Strengths and limitations

We note some strength of the present study including large sample size, population-based sampling, and control for many potential confounding factors. However, the present study has a number of limitations. First, measurement of dental status was based on self-report, not based on clinical examination. However, the validity and reliability of self-reported number of teeth has been established by multiple studies and widely used in epidemiological surveys. [34] For example, validation studies in the United States and Japan have reported a high agreement between self-reported and examined number of teeth (Pearson's correlation coefficient: r=0.97, and 0.93, respectively) in 50 community-dwelling individuals aged 70 or older and 2 496 subjects with a mean age of 59. [35 36] Second, self-report of falls may not be perfectly accurate. [37] However, the associations with demographic factors and other covariates are in the generally expected direction, suggesting that there may be sufficient value in this outcome.

Conclusion

The primary implication of this study is the importance of maintaining the dental occlusion, especially with natural teeth, in order to prevent falls among older adults. The loss of teeth might be an independent risk factor for incident falls but it could be prevented by using dentures. Promoting dental care including proper use of denture might be an additional option for the prevention of falls in addition to current interventions targeting conventional risk factors, which warrants further interventional studies testing the effects of dental care and denture use on the prevention of falls

Contributors: TY and YH had the idea for the study, participated in its design, performed the statistical analysis, and drafted the manuscript, and YH is guarantor. KK is coordinator of Aichi Gerontological Evaluation Study (AGES) Project, helped develop the idea of the study, participated in acquiring the data and with design, and edited the manuscript. JM participated in design of study and edited manuscript. HH and MN participated in acquiring the data and with design, and critically revised the manuscript. JA, NK and IK participated in the design of the study, deciding on statistical methods used, helped in interpreting the results, and revising the manuscript.

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Ethical approval: The Aichi Gerontological Evaluation Study (AGES) protocol including the present study was reviewed and approved by the Ethics Committee on Research of Human Subjects at Nihon Fukushi University.

Data sharing: No additional data available.

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Table 1 Univariate associations of dental health variables and covariates with incident falls

		Total	Fallers		OR	95% CI			p
		n	n	%					
Dental status	≥20 teeth	586	17	2.9	1.00				
	≤19 teeth with dentures	958	49	5.1	1.80	1.03	-	3.16	0.039
	≤19 teeth without dentures	198	17	8.6	3.14	1.57	-	6.28	0.001
	Missing	21	3	14.3	5.58	1.50	-	20.76	0.010
Chewing ability	Can chew anything	719	30	4.2	1.00				
	Can chew most foods	935	47	5.0	1.22	0.76	-	1.94	0.414
	Cannot chew very well	97	9	9.3	2.35	1.08	-	5.11	0.031
	Missing	12	0	0.0	0.00	0.00	-		0.999
Sex	Female	853	32	3.8	1.00				
	Male	910	54	5.9	1.62	1.03	-	2.53	0.035
Age (years)	65-69	707	23	3.3	1.00				
	70-74	569	27	4.7	1.48	0.84	-	2.61	0.175
	75-79	325	18	5.5	1.74	0.93	-	3.28	0.084
	80-84	120	12	10.0	3.30	1.60	-	6.84	0.001
	≥85	42	6	14.3	4.96	1.90	-	12.93	0.001
Present illness related to falls [a]	No	1224	58	4.7	1.00				
	Yes	539	28	5.2	1.10	0.69	-	1.75	0.682
Activities of daily living	Without limitation	1669	81	4.9	1.00				
	With limitation or missing	94	5	5.3	1.10	0.44	-	2.79	0.838
Functional disability during follow-up period	No	1734	81	4.7	1.00				
	Yes	29	5	17.2	4.25	1.58	-	11.43	0.004
Body mass index	≤18.4	113	8	7.1	1.68	0.78	-	3.62	0.189
	18.5-24.9	1196	52	4.3	1.00				

	≥25.0	380	21	5.5	1.29	0.77	-	2.17	0.342
	Missing	74	5	6.8	1.59	0.62	-	4.12	0.336
Use of sedatives	No	1602	80	5.0	1.00				
	Yes	161	6	3.7	0.74	0.32	-	1.72	0.478
Depression	No	1143	39	3.4	1.00				
	Mild	311	21	6.8	2.05	1.19	-	3.54	0.010
	Moderate to severe	77	8	10.4	3.28	1.48	-	7.29	0.004
	Missing	232	18	7.8	2.38	1.34	-	4.24	0.003
Self-rated health	Excellent	162	6	3.7	1.00				
	Good	1192	50	4.2	1.14	0.48	-	2.70	0.769
	Fair	321	21	6.5	1.82	0.72	-	4.60	0.206
	Poor	59	9	15.3	4.68	1.59	-	13.80	0.005
	Missing	29	0	0.0	0.00	0.00	-		0.998
Exercise (minute-walk per day)	≥60	430	20	4.7	1.00				
	30-59	569	16	2.8	0.59	0.30	-	1.16	0.126
	<30	564	38	6.7	1.48	0.85	-	2.58	0.167
	Missing	200	12	6.0	1.31	0.63	-	2.73	0.474
Frequency of outings	Almost everyday	843	37	4.4	1.00				
	2-3 times a week	532	27	5.1	1.17	0.70	-	1.94	0.557
	Once a week or less	335	20	6.0	1.38	0.79	-	2.42	0.256
	Missing	53	2	3.8	0.85	0.20	-	3.65	0.831
Educational attainment (years)	≥13	184	4	2.2	1.00				
	10-12	506	23	4.5	2.14	0.73	-	6.28	0.165
	6-9	953	49	5.1	2.44	0.87	-	6.84	0.090
	<6	53	4	7.5	3.67	0.89	-	15.22	0.073
	Missing	67	6	9.0	4.43	1.21	-	16.21	0.025
Equivalized household income (yen)	<500,000	53	0	0.0	0.00	0.00	-		0.997
	500,000-999,999	108	7	6.5	1.00				

1,000,000-1,499,999	139	7	5.0	0.77	0.26	-	2.25	0.627
1,500,000-1,999,999	262	15	5.7	0.88	0.35	-	2.21	0.780
2,000,000-2,999,999	429	16	3.7	0.56	0.22	-	1.39	0.213
3,000,000-3,999,999	263	15	5.7	0.87	0.35	-	2.20	0.773
≥4,000,000	164	5	3.0	0.45	0.14	-	1.47	0.187
Missing	345	21	6.1	0.94	0.39	-	2.26	0.882

[a] Stroke, osteoporosis, joint disease/ neuralgia, injury/ fracture, impaired vision and/or impaired hearing.

Table 2 Multivariate adjusted OR and 95% CI for the association of dental status and chewing ability with incident falls

		OR	95% CI		p	OR	95% CI		p
Dental status	≥20 teeth	1.00							
	≤19 teeth with dentures	1.36	0.76	-	2.45	0.299			
	≤19 teeth without dentures	2.50	1.21	-	5.17	0.013			
	Missing	5.75	1.23	-	26.78	0.026			
Chewing ability	Can chew anything					1.00			
	Can chew most foods					0.97	0.59	- 1.59	0.910
	Cannot chew very well					1.47	0.64	- 3.37	0.361
	Missing					0.00	0.00	-	0.999
Sex	Female	1.00				1.00			
	Male	1.86	1.16	-	2.96	0.010	1.86	1.16 - 2.96	0.009
Age (years)	65-69	1.00				1.00			
	70-74	1.31	0.73	-	2.34	0.366	1.36	0.76 - 2.42	0.302
	75-79	1.42	0.74	-	2.74	0.290	1.57	0.82 - 3.02	0.178
	80-84	2.51	1.17	-	5.39	0.018	2.84	1.34 - 6.04	0.007
	≥85	3.78	1.27	-	11.19	0.017	4.63	1.59 - 13.49	0.005
Functional disability during follow-up period	No	1.00				1.00			
	Yes	2.30	0.75	-	7.06	0.144	2.11	0.70 - 6.37	0.184
Depression	No	1.00				1.00			
	Mild	1.82	1.01	-	3.26	0.046	1.82	1.01 - 3.26	0.045
	Moderate to severe	2.47	1.02	-	5.97	0.045	2.49	1.03 - 6.02	0.042
	Missing	2.14	1.09	-	4.17	0.026	2.07	1.06 - 4.04	0.032
Self-rated health	Excellent	1.00				1.00			
	Good	1.14	0.47	-	2.77	0.767	1.07	0.44 - 2.59	0.877

	Fair	1.43	0.54	-	3.78	0.474	1.33	0.50	-	3.54	0.568
	Poor	2.71	0.83	-	8.77	0.097	2.60	0.81	-	8.34	0.109
	Missing	0.00	0.00	-		0.998	0.00	0.00	-		0.998
Educational attainment (years)	≥13	1.00					1.00				
	10-12	2.49	0.83	-	7.45	0.102	2.59	0.87	-	7.72	0.089
	6-9	2.21	0.77	-	6.33	0.140	2.50	0.87	-	7.12	0.087
	<6	1.77	0.37	-	8.56	0.476	2.24	0.49	-	10.27	0.299
	Missing	2.78	0.68	-	11.38	0.156	3.17	0.77	-	13.01	0.110

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1, 3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5-6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	6-7
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-7
Bias	9	Describe any efforts to address potential sources of bias	6-9
Study size	10	Explain how the study size was arrived at	6-7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-9
		(*b*) Describe any methods used to examine subgroups and interactions	NA
		(*c*) Explain how missing data were addressed	9
		(*d*) If applicable, explain how loss to follow-up was addressed	6-7
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10, Tab. 1
		(b) Indicate number of participants with missing data for each variable of interest	Tab. 1,2
		(c) Summarise follow-up time (eg, average and total amount)	NA
Outcome data	15*	Report numbers of outcome events or summary measures over time	Tab. 1

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Tab. 2
		(*b*) Report category boundaries when continuous variables were categorized	Tab. 1,2
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10-13
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for exposed and unexposed groups.