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Tooth loss and cognitive decline in community dwelling older Irish adults: A cross-sectional cohort study

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ABSTRACT

Objectives: To investigate whether tooth loss and related loss of occluding tooth pairs, were associated with cognitive decline in a group of community dwelling older men and women from Ireland.
Methods: A group of 2508 men and women, aged 50–93 years, underwent a dental examination as part of The Irish Longitudinal Study of ageing (TILDA). Global cognitive function was assessed using the mini-mental state examination (MMSE). Analysis included multiple logistic regression with adjustment for various confounders.
Results: The mean age of participants was 65.5 years (SD 8.1) and 55.3% of the group were female. Three hundred and twenty-nine (13.1%) of the cohort were classified as having a low MMSE with a score ≤ 27. After adjustment for confounding variables, compared to subjects with ≥ 20 teeth, the odds ratio for a low MMSE amongst edentulous was 1.55 (95% CI 1.03–2.34) $p = 0.03$, and for those with 1–19 teeth was 1.38 (95% CI 1.03–1.84) $p = 0.04$. Having < 10 natural occluding pairs and < 4 posterior occluding pairs also associated with a low MMSE.
Conclusions: In this cross-sectional cohort study, tooth loss and related loss of occluding tooth pairs were associated with a low MMSE in a group of older adults from Ireland, independent of various known confounders.
Clinical Significance: Dentists should be aware of the potential systemic health implications of patients presenting with tooth loss. Tooth loss may be an important risk indicator for cognitive decline.

1. Introduction

The number of people living with dementia worldwide was estimated at 50 million in 2018, and is projected to rise 152 million by 2050 [1]. Mirroring global estimates and commensurate with its ageing population, the prevalence of dementia in Ireland is also projected to rise considerably. Ireland currently has over 55,000 people with dementia, with this figure expected to double by 2036 [2]. Mild cogitative impairment (MCI), represents a transitional state between normal ageing and dementia [3]. Prevalence of MCI amongst community-dwelling older adults, aged > 70, has been reported as high as 22% [4]. Both MCI and dementia are characterised by cognitive decline from a previously attained cognition level [5]. With few therapeutic options to reverse MCI/dementia, there is an emphasis on prevention through identification of modifiable risk factors utilising a life course approach [6].

A number of established risk factors have been identified which contribute to cognitive decline including: low education level; hypertension; obesity; smoking; depression; and physical inactivity [7]. Poor oral health, and more specifically tooth loss, has been reported to be a putative risk factor for cognitive decline [8]. Tooth loss has been shown to affect quality of life and self-esteem, as well as having socio-economic impacts and related healthcare costs [9,10]. Loss of all teeth (edentulism), is a particularly debilitating and challenging condition. Although global edentulism levels have decreased in recent decades, prevalence remains high amongst older individuals [11]. In Ireland, approximately 18% of adults aged ≥ 55 years are edentulous [12].

Several studies have been carried out to investigate tooth loss as a potential risk factor for cognitive decline. Results have been conflicting, however. Notable studies include a 10-year longitudinal cohort study involving 3166 adults aged >60 years in England. The study found that tooth loss (self-report edentulism) was independently associated with

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cognitive decline [13]. A larger, 5-year prospective cohort study involving 11,140 subjects aged 55–88 years with type 2 diabetes was conducted across multiple countries. Relative to the group with the greatest number of teeth, having no teeth was associated with the highest risk of both dementia and cognitive decline [14]. In contrast, a 5-year prospective cohort study in the USA involving 1053 participants age 70 to 79, found no clear association between either tooth loss or number of tooth contacts and cognitive decline [15]. Similarly, a well conducted case-control study in Spain involving 409 dentate adults (180 with cognitive impairment and 229 without) found that tooth loss was not associated with cognitive decline [16].

Despite inconsistencies across studies, several systematic reviews have tentatively supported an association between tooth loss and cognitive decline [17–20]. A recent meta-analysis based on 9 studies (6 cross-sectional cohort studies and 3 prospective cohort studies) found that subjects presenting with < 20 remaining teeth had an increased risk of cognitive decline with an odds ratio of 2.24 (95% confidence interval [CI] 1.73–2.90), $p < 0.001$ [18]. However, the review reported a low level of certainty in the evidence, with many studies failing to adequately adjust for confounding factors and only a limited few considering tooth loss related factors such as loss of occluding tooth contacts and impact on masticatory ability.

The aim of this study, therefore, was to determine whether tooth loss and the related loss of occluding tooth pairs, were associated with cognitive decline in a group of community dwelling older adults from Ireland.

2. Methodology

2.1. Population

Subjects were recruited from the Irish Longitudinal Study of Ageing (TILDA), which is a nationally representative, large prospective cohort study on the social, economic, and health circumstances of community-dwelling adults aged 50 years and older in Ireland. Details of TILDA's design including survey methodology and weighting scheme have previously been published [21,22]. Briefly, the study comprises a clustered stratified random sample of the community-dwelling population aged ≥50 years old. There are three components to data collection: a computer-assisted personal interview administered by trained social interviewers in the participants' own homes; a self-completion questionnaire completed in the participants' own time; and a comprehensive health assessment in a dedicated health centre. Data on a broad range of domains including health status, healthcare utilisation, demographic, social and economic circumstances are all collected at successive 'waves' performed biennially.

Fieldwork at Wave 1 (2009–2011) yielded a sample of 8504 adults. At Wave 3 (2014–15), the response yielded a sample of 6902. Of the 6902, 4307 attended for the comprehensive health assessment at the TILDA health centre, Trinity College Dublin. Alongside the comprehensive health assessments, subjects were offered an optional oral health assessment of which 2508 participants took part. This study is based on a cross sectional analysis of the 2508 subjects aged ≥ 50 years of age that attended the oral health assessment at Wave 3 (**Fig. 1**).

Approval for the project was obtained from the Research Ethics Committee of the Faculty of Health Sciences, Trinity College Dublin. Participation was voluntary and all participants provided informed, written consent. Individuals were not eligible for inclusion if they reported a doctor's diagnosis of dementia. Furthermore, individuals who were not able to consent personally because of severe cognitive impairment (at interviewer's discretion) were also excluded.

2.2. Oral health assessment

The oral health assessment was based on World Health Organization (WHO) epidemiological survey methodology [23]. All oral health assessments were completed by one of four trained dentists who had been calibrated against a "gold standard" set by a senior clinical researcher prior to the study commencing. Regular meetings took place throughout the duration of the study to ensure inter- and intra-examiner consistency and reproducibility.

Tooth presence was recorded for each of the 32 teeth to calculate the number of natural teeth present in each adult. The examiners used clinical judgement regarding tooth morphology and took into account the respondent's previous dental history if doubt existed as to the correct notation for a particular missing tooth. Based upon the number of natural teeth present, participants were then categorised into three groups: ≥20 teeth; 1–19 teeth; & Edentulous.

Occluding tooth pairs were defined as pairs of maxillary and mandibular teeth that came into contact when the subjects closed in centric occlusion; this included fixed bridge abutments and pontics but excluded removable dentures, teeth indicated for extraction, and pontics indicated for removal (because of looseness of bridges or caries in abutments). A contact is scored as present (1) for pairs of incisors, canines, and premolars or half a molar tooth (mesial or distal) that was in contact [24]. Two variables were derived: natural occluding pairs (NOPs) based on all teeth (range 0 to 22 contacts); and posterior occluding pairs (POPs) based on pre-molar and molar teeth only (range 0 to 16 contacts).

The main exposure variable was of number of teeth category (≥ 20 teeth; 1–19 teeth; & Edentulous). Ancillary exposure variables considered were: number of teeth (continuous variable); NOPs (continuous variable); NOPs ≥ 10 or < 10 contacts; POPs (continuous variable); and POPs ≥ 4 or < 4 contacts.

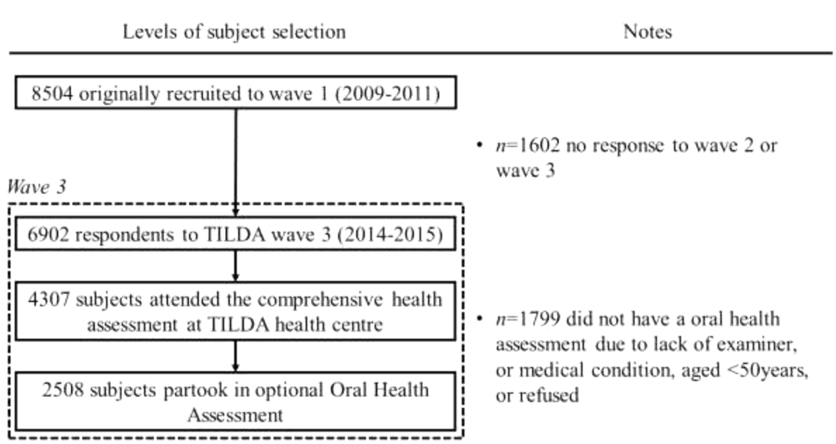

Fig. 1. Recruitment and enrolment of study participants.

2.3. Cognitive assessment

Global cognition was assessed using the Mini-Mental State Examination (MMSE) which is a 30-point questionnaire assessing orientation, memory, attention, language and visual-spatial skills [25]. The MMSE was delivered during the assisted personal interview. A threshold of $\leq$ 27 was categorised as 'Low MMSE' and $\geq$ 28 as 'High MMSE'. Using a threshold $\leq$ 27 has previously been validated as the optimal cut off point for screening for cognitive decline (MCI/dementia) with an AUC = 0.86, sensitivity 74% and specificity 88% in an Irish population of older adults [26].

2.4. Covariates

Covariates of theoretical, practical or previous empirical evidence of association with tooth loss or cognitive decline were included. Age was used in categorical form in descriptive tables ($\leq$ 59 years, 60–69 years, $\geq$ 70 years) and in continuous form in statistical modelling. Body weight and height were measured using standard procedures during the health assessment. BMI was calculated as weight/height^2 (kg/m^2). Smoking behaviour was divided into three categories: never smoked, former smoker and current smoker. Problematic alcohol intake was measured as a score of $\geq$ 2 on the Cut, Annoyed, Guilty, Eye-opener (CAGE) questionnaire [27]. Health status variables included a doctor's previous diagnosis of high blood pressure (yes/no), diabetes (yes/no), stroke or transient ischaemic attack (yes/no). Physical activity (PA) was measured with the International Physical Activity Questionnaire short form [28]. Participants were categorised as meeting or not meeting WHO physical activity guidelines (i.e., $\geq$ 150 min weekly of moderate PA or $\geq$ 75 min weekly of vigorous PA, or $\geq$ 600 metabolic equivalents. min of weekly moderate-to-vigorous PA) [29]. Education was classified as: primary (some primary / not complete; primary or equivalent); secondary (intermediate / junior / group certificate or equivalent; leaving certificate or equivalent); and tertiary (diploma / certificate; primary degree; postgraduate / higher degree). Social class was derived based on respondent's current occupation (or historic occupation—defined as the job title of the highest paying job they ever held—if they had retired). The coding of occupations followed the Irish Central Statistics Office social class schema: professional; managerial; non-manual; skilled manual; semi-skilled; unskilled; and all others gainfully occupied but unknown. These were then aggregated into 3 categories. Participant's level of access to health care was defined using the categories: those with a medical card only (a means tested state subsidy scheme for health care costs); those with private health insurance only; those with both a medical card and private health insurance (defined as dual cover); and those with neither (defined as 'no additional cover'). Loneliness was assessed by self-report and categorised as: rarely or never (< 1 day/week); some of the time (1–2 days / week); and moderate or all of the time (3–7 days/week). All covariate data utilised relates to data collected at Wave 3 (the time of the oral health assessment).

2.5. Statistical analysis

Comparisons of baseline characteristics were made based on category of number of teeth (Edentate; 1–19 teeth; $\geq$ 20 teeth). Comparisons were made using either analysis of variance (ANOVA) for continuous variables or chi-square test for categorical variables. Comparison of baseline characteristics were also made based on cognitive status (High MMSE or Low MMSE). Independent samples *t*-test for continuous variables or the chi-square test for categorical variables) were performed to evaluate potential associations.

Multiple logistic regression analysis was performed to determine odds ratios for the association between cognitive decline (Low MMSE) across categories of tooth loss utilising $\geq$ 20 teeth as the reference category. A series of models was fitted to adjust for potential confounding variables. Model 1 included adjustment for age, sex, and BMI; Model 2 included additional adjustment for smoking, alcohol, and physical activity; Model 3 further adjusted for the comorbidities of diabetes, hypertension, and stroke; finally Model 4 added adjustment for highest educational achievement, social class, access to health care, and loneliness. A test for trend in odds ratios (ORs) across categories of tooth loss was also performed. The same modelling was also carried out for other exposure variables including: tooth loss as a continuous variable, NOPs (< 10 units versus $\geq$ 10 units), NOPs as a continuous variable, POPs (< 4 units versus $\geq$ 4 units) and finally POPs as a continuous variable.

The level of statistical significance was set at $p < 0.05$. Analyses were performed using SPSS version 27 (IBM Corp., Armonk, NY, USA).

3. Results

The mean age of participants was 65.5 years (SD 8.1) and 55.3% of the group were female. Two hundred and fifty (10.0%) participants were edentulous, 897 (35.8%) had 1–19 teeth and 1361 (54.3%) had $\geq$ 20 teeth. Three hundred and twenty-nine (13.1%) of the cohort were classified as having a low MMSE with a score $\leq$ 27.

Characteristics of participants by dentate status are reported in **Table 1**. Edentulous participants had a mean age of 71.9 years (SD 8.3), those with 1–19 teeth had a mean age of 68.0 years (SD 7.6), and those with $\geq$ 20 teeth had a mean age of 62.6 years (SD 7.1), $p < 0.001$. Significant differences were similarly reflected when reported by age category ($p < 0.001$). There was a significant difference across smoking categories with greater proportions of current and former smokers in those that had experienced more tooth loss (both edentulous and those with 1–19 teeth), $p < 0.001$. There were significant differences in the presence of co-morbidities across dentate categories with greater proportions of individuals with diabetes, hypertension, and stroke in the edentulous group, $p < 0.001$. Less than the recommended physical activity was more prevalent in the edentulous group at 51.2%, compared to 43.5% in the 1–19 teeth group, compared to 36.9% in the $\geq$20 teeth group, $p < 0.001$. Highest educational achievement was significantly different across dentate categories with 50.2% of participants reaching third level or higher in the $\geq$20 teeth group, compared to 31.5% in the 1–19 teeth group, and 23.3% in the edentulous group, $p < 0.001$. Similarly, social class structure was significantly different with a higher proportions of managerial / technical / professional occupations in the $\geq$20 teeth group at 43.9%, 32.2% in the 1–19 teeth group, and 20.8% in the edentulous group, $p < 0.001$. Participant's access to health care was significantly different across the different categories, with notable difference in the prorations of medical card only holders with 40.8% in the edentulous group, 31.4% in the 1–19 teeth group, and 15.9% in the $\geq$20 teeth group, $p < 0.001$.

Characteristics of participants by MMSE are reported in **Table 2**. Participants with a low MMSE were significantly older (68.7 versus 65.0 years) and were proportionally more likely to be male (50.2% versus 43.9%), $p < 0.001$. Participants with a low MMSE were also more likely to be diabetic ($p < 0.01$), have hypertension ($p = 0.02$), and have a history of stroke ($p < 0.001$). There was a significant difference across categories of highest educational achievement, $p < 0.001$; participants with a low MMSE were less likely to have reached third level education than those with a high MMSE (24.3% versus 43.4%). There were significant differences across categories of social class structure, $p < 0.001$; participants with a low MMSE were less likely to have been from a managerial / technical / professional occupation background (22.2% versus 39.7%). A similar trend was observed across categories related to access to health care access with a proportionally higher% of medical card only holders in the low MMSE group, $p < 0.001$. A significant difference was also observed across categories of reported loneliness, $p < 0.01$; participants with a low MMSE were more likely to have experienced loneliness at a 'moderate / all of the time' levels (12.0% versus 7.5%). Across number of teeth categories, participants with a low MMSE

Table 1
Characteristics of cohort by dentate status, $n = 2508$.

	Edentulous $n = 250$	1–19 teeth $n = 897$	≥ 20 teeth $n = 1361$	p
Age, mean (SD)	71.9 (8.3)	68.0 (7.6)	62.6 (7.1)	< 0.001
Age, categories, n (%)				
≤ 59 years	19 (7.6%)	129 (14.4%)	529 (38.9%)	< 0.001
60–69 years	78 (31.2%)	400 (44.6%)	603 (44.3%)	
≥ 70 years	153 (61.2%)	368 (41.0%)	229 (16.8%)	
Gender, female, n (%)	159 (63.6%)	458 (51.1%)	769 (56.5%)	< 0.01
BMI, mean (SD)	27.0 (4.4)	27.4 (4.8)	26.9 (4.7)	0.04
Smoking, *n* (%)				
Never	105 (42.0%)	388 (43.3%)	713 (52.4%)	< 0.001
Former	118 (47.2%)	413 (46.0%)	542 (39.8%)	
Current	27 (10.8%)	96 (10.7%)	106 (7.8%)	
Problem drinking (Cage ≥ 2), *n* (%)	11 (5%)	84 (10.6%)	183 (15.2%)	< 0.001
Diabetes, *n* (%)	29 (11.6%)	85 (9.5%)	74 (5.4%)	< 0.001
Hypertension, *n* (%)	97 (38.8%)	336 (37.5%)	411 (30.2%)	< 0.001
Stroke, *n* (%)	13 (5.2%)	54 (6.0%)	40 (2.9%)	< 0.01
Physical Activity (< 150 min/week), n (%)	128 (51.2%)	390 (43.5%)	502 (36.9%)	< 0.001
Highest educational achievement, *n* (%)				
Primary / none	97 (38.8%)	228 (25.4%)	153 (11.3%)	< 0.001
Secondary	95 (38.0%)	386 (43.0%)	524 (38.5%)	
Third / higher	58 (23.2%)	283 (31.5%)	683 (50.2%)	
Social Class, *n* (%)				
Routine, manual, other	125 (50%)	374 (41.7%)	393 (28.9%)	< 0.001
Intermediate	73 (29.2%)	234 (26.1%)	370 (27.2%)	
Managerial, technical, & professional	52 (20.8%)	289 (32.2%)	598 (43.9%)	
Access to Health Care				
Medical Card only	102 (40.8%)	282 (31.4%)	217 (15.9%)	< 0.001
Private Health Insurance only	56 (22.4%)	334 (37.2%)	790 (58.0%)	
Dual Cover	84 (33.6%)	209 (23.3%)	225 (16.5%)	
No additional cover	8 (3.2%)	72 (8.0%)	129 (9.5%)	
Loneliness, *n* (%)				
Rarely or never	200 (80.6%)	713 (79.5%)	1108 (81.5%)	0.32
Some of the time	24 (9.7%)	115 (12.8%)	143 (10.5%)	
Moderate or all of the time	24 (9.7%)	69 (7.7%)	109 (8.0%)	

were more likely to have been edentulous (18.2% versus 8.7%) or have experienced greater tooth loss by presenting with 1–19 teeth (45.6% versus 34.3%), $p < 0.001$. Participants with a low MMSE were also more likely to have presented with < 10 NOPs or < 4 POPs; both $p < 0.001$.

Multiple logistic regression, with adjustment for age, sex, body mass index, smoking, alcohol, physical activity, hypertension, diabetes, stroke, education, social class, access to health care, and loneliness, showed that subjects with a low MMSE were more likely to be edentulous (OR = 1.55, 95% CI 1.03–2.34) or have a reduced dentition of 1–19 teeth (OR = 1.38, 95% CI 1.03–1.84) (Table 3). Having < 10 NOPs (OR = 1.36, 95% CI 1.03–1.81) and <4 POPs (OR = 1.43 95% CI 1.08–1.88) were also associated with a low MMSE in similar fully adjusted models (Table 4). Utilising number of teeth (borderline significant $p = 0.05$) or

Table 2
Characteristics of cohort by cognitive status, $n = 2508$.

	Low MMSE$n = 329$	High MMSE$n = 2179$	p
Age, mean (SD)	68.7 (8.6)	65.0 (7.9)	< 0.001
Age, categories, n (%)			
≤ 59 years	50 (15.2%)	627 (28.8%)	< 0.001
60–69 years	127 (38.6%)	954 (43.8%)	
≥ 70 years	152 (46.2%)	598 (27.4%)	
Gender, female, n (%)	164 (49.8%)	1222 (56.1%)	0.03
BMI, mean (SD)	27.0 (4.7)	27.1 (4.7)	0.71
Smoking, *n* (%)			
Never	157 (47.7%)	1049 (48.1%)	0.24
Former	134 (40.7%)	939 (43.1%)	
Current	38 (11.6%)	191 (8.8%)	
Problem alcohol intake (Cage ≥ 2), *n* (%)	21 (7.6%)	257 (13.3%)	0.01
Diabetes, *n* (%)	38 (11.6%)	150 (6.9%)	< 0.01
Hypertension, *n* (%)	130 (39.5%)	714 (32.8%)	0.02
Stroke, *n* (%)	28 (8.5%)	79 (3.6%)	< 0.001
Physical Activity (< 150mins/week), *n* (%)	144 (43.8%)	876 (40.2%)	0.22
Highest educational achievement, *n* (%)			
Primary / none	122 (37.1%)	356 (16.3%)	< 0.001
Secondary	127 (38.6%)	878 (40.3%)	
Third / higher	80 (24.3%)	944 (43.3%)	
Social Class, *n* (%)			
Routine, manual, other	175 (53.2%)	714 (32.9%)	< 0.001
Intermediate	81 (24.6%)	596 (27.4%)	
Managerial, technical, & professional	73 (22.2%)	866 (39.7%)	
Access to Health Care			
Medical Card only	126 (38.3%)	475 (21.8%)	< 0.001
Private Health Insurance only	80 (24.3%)	1100 (50.5%)	
Dual Cover	97 (29.5%)	421 (19.3%)	
No additional cover	26 (7.9%)	183 (8.4%)	
Loneliness, *n* (%)			
Rarely or never	245 (75.2%)	1776 (81.5%)	< 0.01
Some of the time	42 (12.9%)	240 (11.0%)	
Moderate or all of the time	39 (12.0%)	163 (7.5%)	
Number of teeth, *n* (%)			
≥ 20 teeth	119 (36.2%)	1242 (57.0%)	< 0.001
1–19 teeth	150 (45.6%)	747 (34.3%)	
Edentulous	60 (18.2%)	190 (8.7%)	
Natural occluding pairs, *n* (%)			
≥ 10 occluding contacts	109 (33.1%)	1173 (53.8%)	< 0.001
< 10 occluding contacts	220 (66.9%)	1006 (46.2%)	
Posterior occluding pairs, *n* (%)			
≥ 4 occluding contacts	128 (38.9%)	1301 (59.7%)	< 0.001
< 4 occluding contacts	201 (61.1%)	878 (40.3%)	

NOPs ($p = 0.02$) as continue variables gave similar results (Table 4).

4. Discussion

The main finding of this cross-sectional cohort study was that tooth loss and the related loss of occluding pairs of teeth, were associated with a lower cognitive function in a group of community dwelling older adults in Ireland. After adjustment for potential confounders, participants who were edentulous had a 55% increased odds of a low MMSE and participants with 1–19 teeth had a 38% increased odds of a low MMSE, compared to those ≥ 20 teeth. A trend test across the three categories (≥ 20 teeth, 1–19 teeth, and edentulous) was significant, which suggests a dose-dependent response relationship in the odds of a low MMSE. Having less than < 10 NOPs was associated with a 36% increased odds of a low MMSE, and having <4 POPs was associated with a 43% increased odds of a low MMSE.

The results of this study corroborate previously published findings that have shown independent associations between tooth loss and cognitive decline [17–19]. Tooth loss was considered in three categories

Table 3
Multiple logistic regression analysis for risk of low MMSE with number of teeth category before and after adjustment for confounders in 2444* subjects with complete data.

	Crude modelOR (95% CI)	Model 1OR (95% CI)	Model 2OR (95% CI)	Model 3OR (95% CI)	Model 4OR (95% CI)
Number of teeth (ref. ≥ 20 teeth)					
1–19 teeth	2.12 (1.63–2.76)	1.69 (1.28–2.24)	1.66 (1.25, 2.20)	1.66 (1.25, 2.19)	1.38 (1.03–1.84)
edentulous	3.22 (2.26–4.59)	2.26 (1.53–3.32)	2.20 (1.49, 3.25)	2.23 (1.51, 3.30)	1.55 (1.03–2.34)
p for trend	< 0.001	< 0.001	< 0.001	< 0.001	0.02

Notes.
OR, odds ratio; CI, confidence interval.
Model 1 = adjusted for age, sex, and body mass index.
Model 2 = Model 1 + smoking, alcohol, and physical activity.
Model 3 = Model 2 + diabetes, hypertension, and stroke.
Model 4 = Model 3 + highest educational achievement, social class, access to health care, and loneliness.
[*] 64 cases excluded due to missing confounder data.

Table 4
Summary table of multiple logistic regression analysis for risk of low MMSE by various dentate status measures, before and after adjustment for confounders in 2444* subjects with complete data.

	Crude ModelOR (95% CI)	*p*	Fully adjusted model [a]OR (95% CI)	*p*
Number of teeth, (per tooth increase)	0.95 (0.94–0.97)	< 0.001	0.98 (0.97–1.00)	0.05
NOPs, (per contact increase)	0.93 (0.91–0.95)	< 0.001	0.98 (0.95–0.99)	0.04
NOPs (ref ≥ 10 contacts)				
< 10 contacts	2.33 (1.81–2.99)	< 0.001	1.36 (1.03–1.81)	0.03
POPs, (per contact increase)	0.89 (0.86–0.92)	< 0.001	0.96 (0.92–0.99)	0.02
POPs (ref ≥ 4 contacts)				
< 4 contacts	2.37 (1.86–3.03)	< 0.001	1.43 (1.08–1.88)	0.01

Notes.
OR: odds ratio; CI: confidence interval; NOPs: Naturally occluding pairs; POPs: Posterior occluding pairs.
[a] Fully adjusted model = adjusted for age, sex, body mass index, smoking, alcohol, physical activity, diabetes, hypertension, stroke, highest educational achievement, social class, access to health care, and loneliness.
[*] 64 cases excluded due to missing confounder data.

of ≥ 20 teeth as the reference group, 1–19 teeth, and edentulous. From a functional point of view having 20 or more teeth is considered a useful threshold and has been consistently applied in studies as a measure of a 'functioning' dentition [30]. To increase sensitivity in relation to function and chewing capacity, occluding pairs of teeth (NOPs and POPs) were additionally considered as ancillary exposure variables. Ten NOPs, similar to 20 natural teeth, are considered to represent a minimal functioning dentition [31]. Chewing efficiency is particularly related to posterior occluding pairs [32]. Four POPs was chosen as a threshold that would represent a shortened dental arch situation, again considered a minimum for a functioning dentition [33]. NOPs and POPs were both significantly associated with cognitive decline when analysed utilising these threshold values or as a continuous variable.

There are a number of proposed mechanisms which may explain an association between tooth loss and the related loss of occluding pairs of teeth with cognitive decline. Firstly, tooth loss may be associated with an impaired chewing ability, potentially affecting food choices and leading to a poorer nutritional status [34]. Deterioration in nutritional status is associated with chronic illnesses and may be a risk factor for cognitive decline [35]. However, severe masticatory impairment causing a significant shift in food selection is generally only observed when few teeth or no teeth remain and subjects fail to adapt to dentures [36]. In the current study, all participants in the edentulous group wore complete dentures which limits the ability to draw conclusion regarding severe masticatory impairment. Furthermore, we included analysis of both NOPs and POPs as proxies of chewing efficiency, however, as a static measure based on tooth contact only, these variables are crude estimators of actual chewing efficiency. Chewing efficiency can be measured more accurately through specialised testing [37], but its application at a population level is currently limited. A recent review concluded that evidence relating to the effect of tooth loss on diet and nutrition is weak, with inconsistent results among the few studies identified [38]. Secondly, tooth loss and the associated loss of occluding pairs of teeth may impact important somatosensory feedback to the central nervous system resulting in cognitive decline [39]. However, whether input from the stomatognathic apparatus can affect the central nervous system is questionable, with supportive evidence predominantly drawn from animal research. Thirdly, periodontitis as one of the main causes of tooth loss in older adults [40], has been previously associated with cognitive decline [41,42]. This could be the direct action of specific periodontal pathogens such as *Porphyromonas gingivalis* [43], or alternatively through common inflammatory pathways affecting the central nervous system. There is strong evidence that periodontitis represents a source of chronic low-grade inflammation, which contributes to the cumulative systemic inflammatory burden [44,45]. Persistent inflammation in the systemic immune system can impose detrimental effects on the central nervous system [46]. However, directly linking periodontitis as the cause of tooth loss in context of the current study is problematic as reasons for tooth loss can be multiple. In addition to periodontitis; dental caries, dental trauma, congenitally missing teeth, and oral cancer, may all be reasons for individuals presenting with missing teeth. Finally, rather than a causal relationship between tooth loss and cognitive decline, a 'life course' model has recently been proposed to explain the association between tooth loss and cognitive decline [47]. In this model, people with better childhood cognitive function have better oral health and access to routine dental care as they go through life, therefore losing fewer teeth. They are also more likely to have better cognitive function in old age. Conversely, children with less cognitive ability will experience higher disease rates and poorer access to care, resulting in greater tooth loss. The lack of clarity on a potential mechanism between tooth loss and cognitive decline highlights the need for further studies in this area. Until this is clarified the question as to whether dental intervention, through for example periodontal treatment to prevent tooth loss or prosthodontic rehabilitation to restore tooth loss, will limit or restore cognitive capacity is tenuous.

Despite the lack of clarity in a causal relationship between tooth loss and cognitive decline, the finding of a significant association does not preclude the usefulness of tooth loss as a risk indicator for cognitive decline. Tooth loss is considered an effective marker of population oral health and is therefore monitored in many countries [11]. Furthermore, the ease and validity of self-reported number of teeth without need for a dedicated oral health assessment may additionally merit its usefulness in inaccessible population groups [13,48].

Strengths of the study include the large sample size (n = 2525), which ranks comparatively as one of the larger studies investigating tooth loss and cognitive decline [18]. All participants were objectively examined by a calibrated dental examiner utilising a standardised protocol and had the MMSE carried out by a trained interviewer. Due to the design of the TILDA study, with its main aim to investigate factors associated with population ageing, we were able to make use of a range of relevant data on potential confounding factors. The initial logistic regression models indicated strong effects of tooth loss and loss of occluding pairs on cognitive capacity. As expected, these estimates were considerably attenuated in subsequent adjustment stages; controlling for social class, access to health care, and highest education achievement resulted in a large attenuation. This highlights the importance of the broader determinants of health in explaining the association between tooth loss and cognitive decline.

Limitations with this study include firstly, that the study is a cross-sectional study and as such, it is not possible to determine whether tooth loss contributed to cognitive decline or was a consequence of it. Although a statistically significant result was achieved after adjusting for confounders, the cross-sectional design precludes assessment of any temporal relationships between tooth loss and cognitive decline though the temporality is biologically plausible. To investigate temporality and direction of an association, the observations in this study would need to be confirmed in future prospective studies. Secondly, there is selection bias based in the recruitment strategy of participants into the study. Although the TILDA study used a nationally representative sampling strategy, the health assessments including oral health assessments required participants to attend a dedicated research centre in Trinity College, Dublin. Participants who were not mobile or well enough would not likely have attended the oral health assessments. A further form of selection bias relates to the inclusion criteria used for entry into the study. Individuals were not eligible if they reported a doctor's diagnosis of dementia or were not able to consent because of severe cognitive impairment. Previous research has found higher levels of tooth loss and edentulism in such cohorts in Ireland [49]. Therefore, if a causal link exists between tooth loss and cognitive decline there may in fact be a stronger association than what we have reported in the current study. Thirdly, although a training and calibration exercise was carried out at the outset of the study, this focused on reliability measures of caries and periodontal indices and not on number of teeth / tooth contacts. Although number of teeth / tooth contacts represents a more objective measurement, ideally in the context of the current study corresponding reliability measures for number of teeth / tooth contacts would also have been included. Finally, in common with all observational studies, the possibility of residual confounding such as ageing, or the failure to account for other relevant confounders such as common risk factors for both conditions (early life circumstances).

5. Conclusion

In conclusion, tooth loss and related loss of occluding tooth pairs were associated with a lower MMSE in a group of community dwelling older adults from Ireland. This relationship was independent of known confounders and as such could reflect the possibility that tooth loss may be a risk indicator for cognitive decline. Alternatively, there may be shared biological pathways leading to both tooth loss and cognitive decline. Further, longitudinal type studies should be aimed at specifically investigating potential causality and the mechanistic process linking tooth loss and cognitive decline. Additionally, randomised controlled trails are also required to investigate whether treatment of the causes of tooth loss (eg. periodontitis), or treatment of the consequences of tooth loss (eg. prosthodontic rehabilitation) might have a beneficial impact on cognitive status.

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CRediT authorship contribution statement

Lewis Winning: Formal analysis, Writing – original draft. **Amara Naseer:** Investigation, Writing – review & editing. **Céline De Looze:** Formal analysis, Writing – review & editing. **Silvin P. Knight:** Formal analysis, Writing – review & editing. **Rose Anne Kenny:** Funding acquisition, Writing – review & editing. **Brian O'Connell:** Funding acquisition, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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