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Diabetes, Edentulism, and Cognitive Decline: A 12-Year Prospective Analysis

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Abstract

Diabetes mellitus (DM) is a recognized risk factor for dementia, and increasing evidence shows that tooth loss is associated with cognitive impairment and dementia. However, the effect of the co-occurrence of DM and edentulism on cognitive decline is understudied. This 12-y cohort study aimed to assess the effect of the co-occurrence of DM and edentulism on cognitive decline and examine whether the effect differs by age group. Data were drawn from the 2006 to 2018 Health and Retirement Study. The study sample included 5,440 older adults aged 65 to 74 y, 3,300 aged 75 to 84 y, and 1,208 aged 85 y or older. Linear mixed-effect regression was employed to model the rates of cognitive decline stratified by age cohorts. Compared with their counterparts with neither DM nor edentulism at baseline, older adults aged 65 to 74 y ($\beta = -1.12$; 95% confidence interval [CI], −1.56 to −0.65; $P < 0.001$) and those aged 75 to 84 y with both conditions ($\beta = -1.35$; 95% CI, −2.09 to −0.61; $P < 0.001$) had a worse cognitive function. For the rate of cognitive decline, compared to those with neither condition from the same age cohort, older adults aged 65 to 74 y with both conditions declined at a higher rate ($\beta = -0.15$; 95% CI, −0.20 to −0.10; $P < 0.001$). Having DM alone led to an accelerated cognitive decline in older adults aged 65 to 74 y ($\beta = -0.09$; 95% CI, −0.13 to −0.05; $P < 0.001$); having edentulism alone led to an accelerated decline in older adults aged 65 to 74 y ($\beta = -0.13$; 95% CI, −0.17 to −0.08; $P < 0.001$) and older adults aged 75 to 84 ($\beta = -0.10$; 95% CI, −0.17 to −0.03; $P < 0.01$). Our study finds the co-occurrence of DM and edentulism led to a worse cognitive function and a faster cognitive decline in older adults aged 65 to 74 y.

Keywords: cohort studies, dental health, epidemiology, gerontology, oral-systemic disease(s), public health

Introduction

Alzheimer's disease and related dementias (ADRDs) are among the most devasting diseases and pose great challenges to individuals, families, and health care systems. In 2021, over 6.2 million older adults in the United States were living with Alzheimer's disease, and the cost of ADRDs was $355 billion (Alzheimer's Association 2021). As cognitive decline is one of the main predictors of ADRDs, identifying risk factors and pathways underlying cognitive decline will inform interventions to prevent and delay ADRDs.

Diabetes mellitus (DM) is one of the most commonly recognized risk factors for cognitive decline (Gispen and Biessels 2000; Cukierman et al. 2005; Baumgart et al. 2015). However, current findings characterizing the relationships between DM and cognitive decline are inconsistent across different age groups (van Duinkerken and Ryan 2020): an insignificant relationship between DM and cognitive decline is detected in adults aged 85+ y (Gardner et al. 2013). Furthermore, there is increasing evidence of the association between tooth loss and cognitive decline and dementia (Li et al. 2017; Takeuchi et al. 2017; Dintica et al. 2018; Kato et al. 2019). Moreover, studies have found that periodontitis is a risk factor of DM (Ide et al. 2011), poor glycemic control contributes to the incidence of oral candidiasis (Lamster et al. 2008), and DM increases the risk of tooth loss (Borgnakke 2019). The relationship between DM and poor oral health is bidirectional in a chronic, "vicious" cycle (Borgnakke 2019).

Research on the longitudinal effect of co-occurring DM and edentulism on cognitive decline is rare, and few studies have investigated how age may modify the impact of these conditions on cognitive decline. Due to the prolonged nature of ADRDs, studies are needed to identify risk factors for accelerated cognitive decline. Given the bidirectional relationship between DM and poor oral health and both are risk factors for dementia (Ide et al. 2011; Baumgart et al. 2015; Li et al. 2017;

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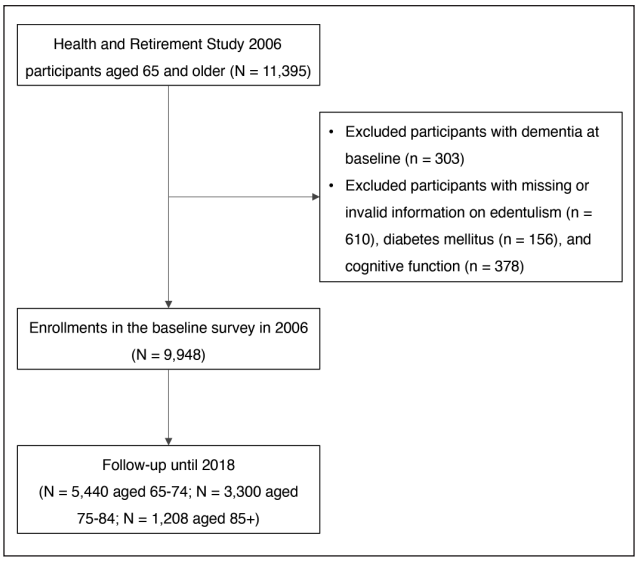

Figure 1. The flowchart of the participants for the analysis.

Borgnakke 2019), a longitudinal study is warranted by investigating the effect of both conditions on the course of cognitive decline.

This study aimed to assess the joint effect of DM and edentulism on cognitive decline over a 12-y follow-up in US older adults from a nationally representative survey. We hypothesize that the co-occurrence of DM and edentulism contributes to poorer cognitive function and accelerated cognitive decline (H_1). We further hypothesize that the effects of the co-occurrence of both conditions on cognitive health vary by age (H_2).

Methods

Data were drawn from the 2006 to 2018 Health and Retirement Study (HRS). HRS is a biennial longitudinal survey of a nationally representative sample of community-dwelling middle-aged and older adults in the United States (Sonnega and Weir 2014), and it oversamples Blacks, Hispanics, and residents of Florida. HRS collects (by telephone or in person) detailed information on demographics, economics, work, family, health behaviors, and health conditions every 2 years. The HRS has high response rates (82%–90%) in each wave (Sonnega and Weir 2014).

Study Sample

HRS first collected information on edentulism in 2006 and every 6 years (i.e., every 3 waves). To construct an analytical sample, we identified a cohort of 11,395 older adults aged 65 y and older from the 2006 wave. Cognitive function was assessed every 2 years until 2018. We excluded participants with missing or invalid information about edentulism (n = 610), DM (n = 156), and cognition measurement in 2006 (n = 378). Participants with a self-reported diagnosis of dementia were also excluded (n = 303). We included a study sample of 9,948 participants. Among them, 5,440 were aged 65 to 74 y, 3,300 were aged 75 to 84 y, and 1,208 were aged 85+ y. During the period between 2006 and 2018, for older adults aged 65 to 74 y, 93.8% had time-repeated cognitive measures, and 41.2% completed the assessment in all waves; for the group aged 75 to 84 y, the percentage was 87.6% and 20.4%, respectively; and for those aged 85+ y, the percentage was 72.0% and 2.8%, respectively. A flowchart illustrates a sample selection process (Fig. 1). The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement guidelines were followed.

Measures

The primary outcome, cognitive function, was assessed biennially from 2006 to 2018 using the HRS version of the modified Telephone Interview for Cognitive Status (TICS-m) (Plassman et al. 2008). The HRS TICS-m assessed verbal memory, orientation, and executive functioning and attention. The instrument includes 1) immediate and delayed word recall (0–20 points), 2) serial 7-subtraction (0–5 points), 3) counting backward from 20 (0–2 points), and 4) orientation to time, naming an object, and president and vice president naming (0–8 points). The HRS TICS-m score ranges from 0 to 35, with a higher score indicating better cognition.

Edentulism was coded "yes" to the question on loss of all upper and lower natural permanent teeth. Self-reported edentulism is a robust measure of complete tooth loss as edentulism is irreversible (Tsakos et al. 2011). Participants were classified as having DM if they met at least 1 of the 3 criteria: 1) self-reported "yes" to the following question: Has a doctor ever told you that you have diabetes or high blood sugar? 2) are currently taking diabetes medication or insulin, or 3) have a hemoglobin A1c value of 6.5% or higher (measured via dried blood spot). This method for DM classification has been used in multiple studies (Whisman et al. 2014; Marden et al. 2017). Participants were accordingly grouped by exposure: group 1 (with neither condition), group 2 (with DM but not edentulous), group 3 (edentulous but without DM), and group 4 (with both DM and edentulism).

Covariates were selected according to prior research on the topic (Wu et al. 2016; Luo et al. 2021; Qi et al. 2021). Participants' demographic characteristics included sex (male/female), age, race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, and other), and marital status (married/unmarried). Socioeconomic status was measured by annual household income, years of schooling, and private insurance coverage. Health-related behaviors included physical exercise or workout (yes/no), alcohol abuse in the past 3 mo (yes/no) (Gunzerath et al. 2004), smoking status (current smoker, former smoker, or nonsmoker), and dental visits in the past 2 y (yes/no). Health conditions included body mass index (normal weight, underweight, overweight, and obesity), activities of daily living disability (yes/no), and depressive symptoms measured by the Center for Epidemiologic Studies Depression Scale–8. Participants were also asked whether they

ever had physician-diagnosed hypertension, heart disease (heart attack, coronary heart disease, or other heart problems), and stroke. Demographic characteristic variables were treated as time-invariant covariates; socioeconomic status, health-related behaviors, and health conditions variables were measured at each wave and regarded as time-varying variables. The detailed definition of each covariate is shown in Appendix Table 1.

Statistical Analysis

We compared participants' baseline characteristics (including their DM and edentulism status) by different age cohorts. Chi-square tests or analysis of variance tests were used where appropriate. Sampling weights in HRS were accounted for in analyses.

We employed linear mixed-effect models for each age cohort to model participants' cognitive trajectories from 2006 to 2018. The mixed-effects model accounted for both *within*-individual and *between*-individual variance, assessed the intra-correlation of time-repeated measures for cognitive function within each individual, and addressed the unbalanced structure of the data (Fitzmaurice et al. 2011). First, we fitted a set of models, including the DM and edentulism groupings, as the exposures and the time variable to examine the *mean* differences in cognitive function at baseline, adjusting for all covariates. Second, to examine the *rate* of cognitive change over time, we fitted a set of models by adding the interaction terms between the exposure and the time (2006, 2012, and 2018) variables to the previous models. We ran separate models including the interaction term between edentulism and DM to assess the effects on cognitive function and rate of cognitive decline.

To account for sample attrition over the study period, we calculated inverse probability attrition weights (IPAW) by running a logistic regression model where the dependent variable was attrition (defined as dropping out, including death) from 2006 to 2018 and predictors are all the covariates mentioned before at baseline (Austin and Stuart 2015; Arce Rentería et al. 2019). For each participant, the final weight was the multiplication product of their IPAW and HRS's time-invariant sampling weights at baseline (Arce Rentería et al. 2019). The final weights were applied to the linear mixed-effect model, allowing for a random intercept and slope for time.

We also conducted 3 sets of sensitivity analyses. First, we added each participant's baseline cognitive function as an additional covariate to further account for the potential ex ante effects (prior to the baseline). Second, we limited the analytical sample to those whose exposure status did not change from 2006 to 2018. We reran the analyses described above using this subsample of participants (n = 2,870). Third, we conducted multiple imputations for missing values. We created 10 imputed data sets using multivariate imputation by chained equations (MICE), including all variables used, and analyses were conducted in these 10 data sets and the average estimates were calculated (White et al. 2011). A 2-tailed P value of <0.05 was considered statistically significant. Analyses were conducted in R (version 4.0.2; R Core Team) and Stata 15.1 (StataCorp LLC).

Results

As shown in Table 1, older adults aged 65 to 74 y had the highest cognitive scores (mean ± standard deviation [SD] = 23.07 ± 0.07), while those aged 85+ y had the lowest: 18.53 ± 0.17. The percentages having both DM and edentulism were 6.0%, 6.7%, and 5.0% for the older adults aged 65 to 74 y, 75 to 84 y, and 85+ y, respectively, and the percentages of those with neither condition were 63.5%, 60.4%, and 58.3% in these 3 age groups, respectively ($P < 0.001$).

Table 2 presents the results from linear mixed-effect regression with cognitive function as the outcome variable. For older adults aged 65 to 74 y, compared with those having neither condition, those having DM only, having edentulism only, and having both conditions had 0.28 points (95% confidence interval [CI], 0.03–0.53), 0.61 points (95% CI, 0.29–0.92), and 1.12 points (95% CI, 0.65–1.56) lower cognitive score, respectively. For the older adults aged 75 to 84 y, those with DM only would have an average of 0.53 points (95% CI, 0.14–0.92) lower cognitive score, and those with both conditions would have 1.35 points (95% CI, 0.61–2.09) lower cognitive score. For the older adults aged 85+ y, there were no significant differences in the mean cognitive scores across different exposure groups.

Table 3 presents the estimated coefficients from linear mixed-effect regressions modeling cognitive decline. Older adults aged 65 to 74 y having DM only, having edentulism only, or having both conditions all had an accelerated cognitive decline. Compared with their counterparts with neither condition, in older adults aged 65 to 74 y, those with DM only, with edentulism only, or with both conditions were found to have 0.09 (95% CI, 0.05–0.13), 0.13 (95% CI, 0.08–0.17), and 0.15 (95% CI, 0.10–0.20) points more decline each year, compared to an average decline of 0.29 points (95% CI, 0.25–0.33). In older adults aged 75 to 84 y, those with edentulism only had a 0.10 (95% CI, 0.03–0.17) additional rate of decline, in comparison to those with neither condition. However, there was no significant difference in decline rates by different exposures for older adults aged 85+ y.

Figure 2 depicts the cognitive function and cognitive decline rate during follow-up for the 3 age groups. On average, older adults aged 65 to 74 y had better cognitive function at baseline and a slower cognitive decline during follow-up. Having edentulism only contributed to a faster cognitive decline for older adults aged 65 to 74 y and 75 to 84 y. Having both DM and edentulism led to an accelerated cognitive decline for the group aged 65 to 74 y.

Separate analyses that included the interaction terms for edentulism and DM showed that edentulism and DM had a significant interactive effect on cognitive function for adults aged 65 to 74 y only ($P < 0.01$) but not for older adults in other groups and the interactive effects on cognitive decline were not significant in any age groups (P = 0.314 for those aged 65 to

Table 1. Descriptive Statistics of Baseline Characteristics by Age Group (*N* = 9,948).

Baseline characteristics	Aged 65–74 y (*n* = 5,440)	Aged 75–84 y (*n* = 3,300)	Aged 85+ y (*n* = 1,208)	*P* Value
Cognitive function, mean (SD)	23.07 (0.07)	20.94 (0.10)	18.53 (0.17)	<0.001
Exposure status, %				
Neither condition	63.5	60.4	58.3	<0.001
DM only	16.1	14.3	11.1	
Edentulism only	14.5	18.6	25.6	
Both conditions	6.0	6.7	5.0	
Female, %	44.8	40.1	35.6	<0.001
Age, mean (SD), y	69.47 (0.04)	78.99 (0.05)	88.23 (0.09)	<0.001
Race/ethnicity, %				<0.001
Non-Hispanic White	81.8	85.3	90.2	
Non-Hispanic Black	8.9	7.3	5.4	
Hispanic	7.2	5.7	3.8	
Other	2.1	1.7	0.6	
Married, %	64.9	54.4	31.1	
Years of schooling, mean (SD), y	12.49 (0.04)	12.17 (0.06)	12.01 (0.10)	<0.001
Household income, mean (SD), $	61,170.9 (2,636.8)	42,783.5 (1,259.0)	32,201.3 (1,288.6)	<0.001
Private health insurance, %	56.2	56.8	62.9	<0.001
Physical exercise, %	33.2	23.5	13.5	<0.001
Alcohol abuse, %	10.2	8.4	6.2	<0.001
Smoking status, %				<0.001
Current smoker	13.0	6.9	3.0	
Former smoker	37.1	34.9	45.6	
Nonsmoker	49.9	58.2	51.4	
Had dental visit, %	71.6	51.4	45.1	
BMI category, %				<0.001
Normal weight	29.0	37.1	51.3	
Underweight	1.1	2.8	4.8	
Overweight	39.4	38.6	33.4	
Obese	30.5	21.5	10.5	
ADL disability, %	15.6	17.8	22.9	<0.001
CES-D, mean (SD)	1.33 (0.03)	1.50 (0.04)	1.74 (0.06)	<0.001
Hypertension, %	57.3	62.6	61.9	<0.001
Heart disease, %	23.9	33.4	41.8	<0.001
Stroke, %	6.5	11.9	15.7	<0.001
Attrition, %	49.8	74.1	94.8	<0.001

Means were weighted by HRS 2006 sampling weights. *P* values were obtained from weighted χ^2 tests for categorical variables and weighted *F* tests for continuous variables.
ADL, activities of daily living; BMI, body mass index; CES-D, Center for Epidemiologic Studies Depression Scale; DM, diabetes mellitus; SD, standard deviation.

74 y, $P = 0.561$ for those aged 75 to 84 y, and $P = 0.124$ for those aged 85+ y).

Sensitivity Analyses Results

After controlling for baseline cognitive score, older adults with both DM and edentulism had significantly lower cognitive score and accelerated cognitive decline than their counterparts without either condition in older adults aged 65 to 74 y and 75 to 84 y (Appendix Table 2). When limiting the sample to older adults whose DM and edentulism status did not change from 2006 to 2018, older adults with both DM and edentulism or edentulism alone had a lower cognitive score than those without either condition in older adults aged 65 to 74 y (Appendix Table 3). Finally, results from the imputed data sets were consistent with the main results (Appendix Table 4).

Discussion

Using data on a nationally representative cohort of 9,948 older adults, we found that the effects of the co-occurrence of DM and edentulism or one of these conditions alone on cognitive decline varied across different age groups: for adults aged 65 to 74 y, co-occurring DM and edentulism was associated with worse cognitive function and an accelerated rate of cognitive decline compared with those with neither condition. In addition, edentulism is associated with diminished cognitive function for this group of 65 to 74 y and faster cognitive decline in both the group of 65 to 74 y and the group of 75 to 84 y. Yet, DM alone contributed to a faster cognitive decline only in the group 65 to 74 y. In summary, the results partially support the hypothesis (H_1) that co-occurrence of DM and edentulism led to a worse cognitive function and a faster cognitive decline.

Table 2. Linear Mixed-Effect Model Examining the Main Effects of the Co-occurrence of DM and Edentulism on Cognitive Function (*N* = 9,948).

Characteristic	Aged 65–74 y		Aged 75–84 y		Aged 85+ y	
Sample size	5,440		3,300		1,208	
Person-wave observation	28,398		13,796		3,229	
Variable	Coefficient	(95% CI)	Coefficient	(95% CI)	Coefficient	(95% CI)
Exposure status (reference: neither)						
DM only	−0.28*	(−0.53, −0.03)	−0.53*	(−0.92, −0.14)	−0.72	(−1.63, 0.19)
Edentulism only	−0.61***	(−0.92, −0.29)	−0.26	(−0.66, 0.14)	−0.66	(−1.34, 0.02)
Both	−1.12***	(−1.56, −0.65)	−1.35***	(−2.09, −0.61)	−0.78	(−2.16, 0.60)
Time	−0.30***	(−0.31, −0.29)	−0.56***	(−0.58, −0.53)	−0.89***	(−0.97, −0.82)
Age	−0.16***	(−0.18, −0.14)	−0.22***	(−0.28, −0.17)	−0.19***	(−0.28, −0.10)
Female	−1.17***	(−1.38, −0.96)	−0.78***	(−1.10, −0.46)	0.23	(−0.44, 0.91)
Race/ethnicity (reference: non-Hispanic White)						
Non-Hispanic Black	−2.92***	(−3.45, −2.39)	−2.96***	(−3.50, −2.42)	−2.50***	(−3.48, −1.52)
Hispanic	−1.14***	(−1.44, −0.84)	−0.44	(−1.10, 0.22)	−1.01	(−2.42, 0.40)
Other	−1.36***	(−2.05, −0.66)	−2.45***	(−3.61, −1.29)	−5.11***	(−8.04, −2.18)
Married	−0.16	(−0.39, 0.07)	−0.62***	(−0.96, −0.28)	−1.12**	(−1.80, −0.44)
Years of schooling	0.48***	(0.44, 0.52)	0.50***	(0.45, 0.55)	0.56***	(0.45, 0.66)
Household income	0.27***	(0.19, 0.36)	0.38***	(0.25, 0.51)	0.24	(0.00, 0.48)
Private insurance coverage	0.41***	(0.21, 0.61)	0.27*	(0.12, 0.42)	0.66*	(0.04, 1.29)
Regular physical exercise	0.14	(−0.07, 0.34)	0.50**	(0.18, 0.81)	0.33	(−0.41, 1.06)
Alcohol abuse	0.29	(−0.01, −0.58)	0.04	(−0.37, 0.45)	0.31	(−0.86, 1.49)
Smoking status (reference: nonsmoker)						
Former smoker	0.00	(−0.31, 0.31)	0.04	(−0.07, 0.15)	0.05	(−0.14, 0.24)
Current smoker	−0.17*	(−0.31, −0.03)	−0.48*	(−0.92, −0.03)	0.49	(−1.24, 2.23)
Dental visits	0.17	(−0.09, 0.43)	0.25	(0.00, 0.50)	0.11	(−0.05, 0.26)
BMI (reference: normal weight)						
Underweight	0.50	(−0.63, 1.60)	−1.34*	(−2.22, −0.46)	−0.54	(−1.94, 0.86)
Overweight	0.47***	(0.23, 0.72)	0.50**	(0.17, 0.83)	0.59	(−0.04, 1.22)
Obese	0.54***	(0.27, 0.80)	0.94***	(0.54, 1.33)	1.59***	(0.65, 2.53)
ADL disability	−0.41***	(−0.61, −0.21)	−0.54***	(−0.77, −0.31)	−0.57***	(−0.85, −0.29)
CES-D	−0.24***	(−0.30, −0.18)	−0.18***	(−0.27, −0.09)	−0.13	(−0.28, 0.03)
Hypertension	−0.09	(−0.28, 0.11)	0.03	(−0.27, 0.33)	0.37	(−0.21, 0.96)
Heart disease	−0.03	(−0.27, 0.20)	0.11	(−0.21, 0.42)	−0.01	(−0.60, 0.58)
Stroke	−1.04***	(−1.47, −0.61)	−0.93***	(−1.43, −0.44)	−0.39	(−1.23, 0.45)
Constant	21.60***	(20.50, 22.70)	25.31***	(21.81, 28.81)	27.38***	(18.72, 36.03)

Robust standard errors clustered within each individual in parentheses. Estimates were weighted to adjust for differential probabilities of selection and nonresponse of Health and Retirement Study participants. Longitudinal attrition was handled through inverse probability of attrition weights.
ADL, activities of daily living; BMI, body mass index; CES-D, Center for Epidemiologic Studies Depression Scale; CI, confidence interval; DM, diabetes mellitus.
*$P < 0.05$. **$P < 0.01$. ***$P < 0.001$.

The results also support the hypothesis (H_2) that the co-occurrence of DM and edentulism had different effects on cognitive decline across different age groups.

To our knowledge, this is the first study examining the longitudinal association of the co-occurrence of DM and edentulism with cognitive decline. An earlier study examined the association of poor oral health and DM with dementia/cognitive decline, but they did not investigate the effects of the co-occurrence of DM and poor oral health (Batty et al. 2013).

Poor oral health, DM, and cognitive decline are connected (Lamster et al. 2008; Ide et al. 2011; Noble et al. 2013). For example, complete tooth loss (edentulism) could lead to loss of masticatory function, which in turn leads to changes in dietary intake and diversity (De Marchi et al. 2008); DM-related impaired glucose tolerance and insulin sensitivity (Ojo and Brooke 2015) could partially contribute to a nutritional deficiency—all of which are risk factors for cognitive impairment and dementia (Chew et al. 2015). One could argue that edentulous older adults should even have less systemic burden as they no longer have periodontal inflammation. However, multiple studies have shown that edentulous older adults exhibited higher levels of inflammation (e.g., C-reactive protein, white blood cells, fibrinogen) than those who are dentate. Furthermore, in the United States, more than 75% of edentulous older adults wear dentures (Dai et al. 2022), and it is known that biofilm that forms on dentures can house bacteria, yeasts, and fungus that result in inflammatory response in the oral tissues (Barros et al. 2013). Thus, being edentulous is not free from the risk of elevated inflammation. Therefore, the inflammatory processes shared in common between DM or edentulism and diminished cognitive function may explain the poorer cognitive health for older adults with both DM and edentulism (Meisel et al. 2012; Barros et al. 2013; Li et al. 2021). In our study, 29.8% of participants with DM

Table 3. Linear Mixed Effects Model Examining the Rate of Cognitive Decline by DM and Edentulism Exposure Status (*N* = 9,948).

Characteristic	Aged 65–74 y		Aged 75–84 y		Aged 85+ y	
Sample size	5,440		3,300		1,208	
Person-wave observation	28,398		13,796		3,229	
Variable	Coefficient	(95% CI)	Coefficient	(95% CI)	Coefficient	(95% CI)
Exposure status (reference: neither)						
DM only	−0.10	(−0.30, 0.10)	−0.41*	(−0.72, −0.10)	−0.76	(−1.37, −0.15)
Edentulism only	−0.31*	(−0.53, −0.09)	−0.10	(−0.52, −0.32)	−0.61	(−1.29, 0.07)
Both	−0.81***	(−1.20, −0.42)	−1.36**	(−2.15, −0.57)	−0.51	(−2.01, 0.99)
Time	−0.29***	(−0.33, −0.25)	−0.53***	(−0.56, −0.50)	−0.89***	(−0.98, −0.80)
Exposure status × time						
DM only × time	−0.09***	(−0.13, −0.05)	−0.05	(−0.12, 0.02)	0.25	(−0.01, 0.50)
Edentulism only × time	−0.13***	(−0.17, −0.08)	−0.10**	(−0.17, −0.03)	−0.17	(−0.49, 0.83)
Both × time	−0.15***	(−0.20, −0.10)	−0.05	(−0.18, 0.07)	−0.33	(−0.88, 0.22)
Age	−0.17***	(−0.20, −0.14)	−0.22***	(−0.28, −0.17)	−0.20***	(−0.30, −0.10)
Female	−1.07***	(−1.28, −0.86)	−0.72***	(−1.10, −0.34)	0.33	(−0.24, 0.90)
Race/ethnicity (reference: non-Hispanic White)						
Non-Hispanic Black	−3.02***	(−3.35, −2.70)	−2.95***	(−3.49, −2.41)	−2.50***	(−3.48, −1.51)
Hispanic	−1.03***	(−1.46, −0.61)	−0.44	(−1.10, 0.23)	−1.00	(−2.41, 0.40)
Other	−1.35***	(−2.05, −0.66)	−2.45***	(−3.62, −1.27)	−5.34***	(−8.10, −2.58)
Married	−0.15	(−0.38, 0.07)	−0.62***	(−0.96, −0.28)	−1.12**	(−1.80, −0.44)
Years of schooling	0.48***	(0.44, 0.52)	0.50***	(0.44, 0.55)	0.56***	(0.45, 0.66)
Household income	0.27***	(0.19, 0.36)	0.38***	(0.26, 0.51)	0.24	(−0.00, 0.48)
Private insurance coverage	0.41***	(0.21, 0.62)	0.27	(−0.03, 0.56)	0.65*	(0.02, 1.27)
Regular physical exercise	0.14	(−0.07, 0.34)	0.50**	(0.18, 0.81)	0.33	(−0.41, 1.07)
Alcohol abuse	0.29*	(0.00, 0.58)	0.04	(−0.36, 0.45)	0.30	(−0.87, 1.48)
Smoking status (reference: nonsmoker)						
Former smoker	0.14	(−0.03, 0.31)	0.04	(−0.07, 0.15)	0.09	(−0.24, 0.42)
Current smoker	−0.00	(−0.31, 0.31)	0.17	(0.02, 0.32)	0.12	(−0.21, 0.45)
Dental visits	0.17	(−0.09, 0.43)	0.25	(0.00, 0.50)	0.11	(−0.05, 0.26)
BMI (reference: normal weight)						
Underweight	0.47	(−0.54, 1.49)	−1.31*	(−2.53, −0.09)	−0.55	(−1.95, 0.86)
Overweight	0.47***	(0.23, 0.72)	0.50**	(0.17, 0.83)	0.59	(−0.04, 1.22)
Obese	0.54***	(0.27, 0.81)	0.94***	(0.54, 1.34)	1.58***	(0.64, 2.52)
ADL disability	−0.44***	(−0.61, −0.27)	−0.54***	(−0.77, −0.31)	−0.57***	(−0.85, −0.29)
CES-D	−0.24***	(−0.30, −0.18)	−0.18***	(−0.27, −0.09)	−0.13	(−0.28, 0.02)
Hypertension	−0.09	(−0.28, 0.11)	0.03	(−0.27, 0.33)	0.37	(−0.22, 0.96)
Heart disease	−0.04	(−0.27, 0.19)	0.11	(−0.21, 0.42)	−0.02	(−0.60, 0.57)
Stroke	−1.05***	(−1.47, −0.62)	−0.93***	(−1.43, −0.44)	−0.39	(−1.23, 0.46)
Constant	23.77***	(20.96, 26.58)	29.32***	(24.78, 33.87)	28.54***	(19.87, 37.20)

Robust standard errors clustered within each individual in parentheses. Estimates were weighted to adjust for differential probabilities of selection and nonresponse of Health and Retirement Study participants. Longitudinal attrition was handled through inverse probability of attrition weights.
ADL, activities of daily living; BMI, body mass index; CES-D, Center for Epidemiologic Studies Depression Scale; CI, confidence interval; DM, diabetes mellitus.
*$P < 0.05$. **$P < 0.01$. ***$P < 0.001$.

were edentulous, and 27.4% of edentulous individuals also had diabetes. Our study found that the co-occurrence was strongly related to worse cognitive health at baseline and over time; thus, this research conveys important information regarding the progression of cognitive decline for individuals with both conditions.

We found that while having DM led to worse cognitive function for older adults aged 65 to 74 y and 75 to 84 y, it only contributed to a faster rate of cognitive decline for those aged 65 to 74 y. Our findings are consistent with prior studies that showed that although DM is generally associated with worse cognitive function among older adults, the findings are inconclusive with regard to the accelerated rate of cognitive decline, especially for those older adults aged 85+ y (van den Berg et al. 2006; Formiga et al. 2014; van Duinkerken and Ryan 2020). Presumably, individuals aged 85+ y are less susceptible to the adverse effects of DM (van den Berg et al. 2006), and they may have DM under control with a prolonged treatment history. With respect to the relationship between DM and cognition, our findings reveal that the relationship varied by age groups. Future studies are warranted to further examine these complex relationships across age groups.

We found that, compared with dentate older adults, edentulism could contribute to a faster cognitive decline in older adults aged 65 to 74 y and 75 to 84 y. These finding are consistent with our recent meta-analysis, which concluded that tooth

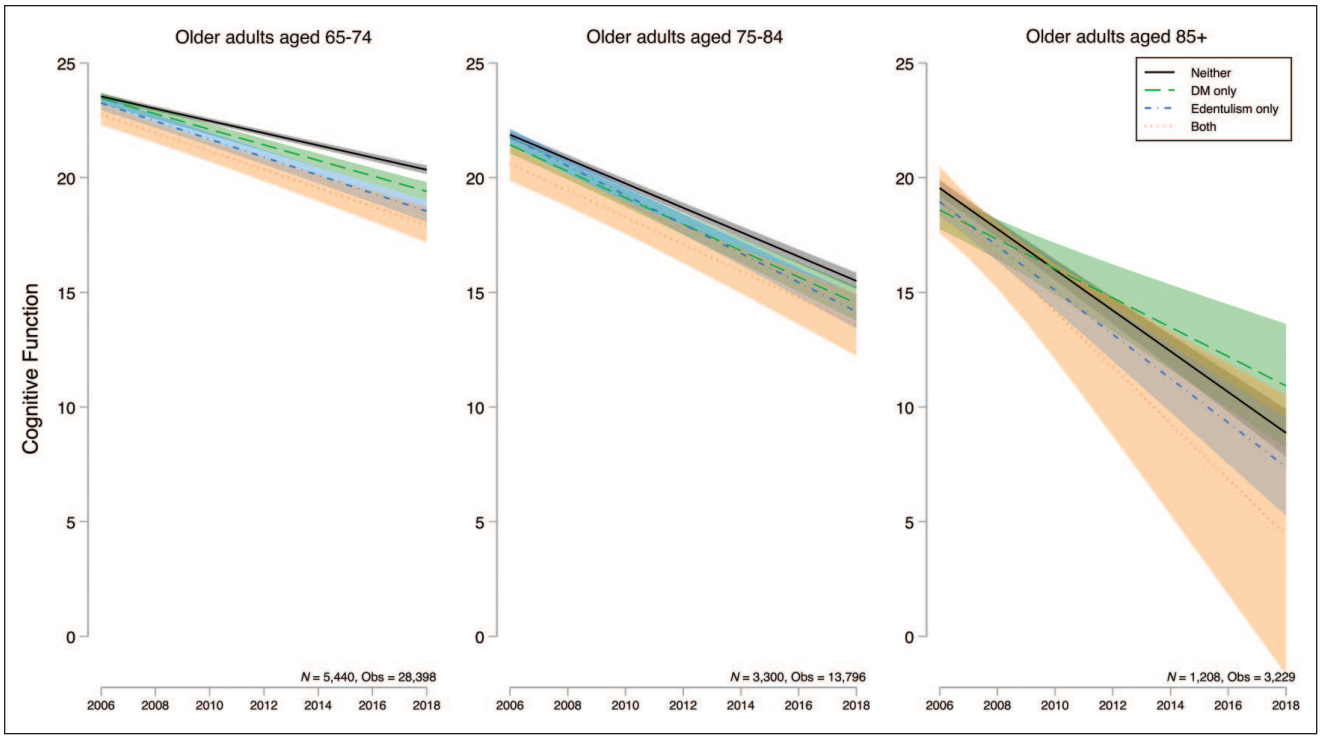

Figure 2. Trajectories of cognitive decline over time by baseline diabetes mellitus (DM) and edentulism status. Solid line, with neither condition; dashed line, with DM only; dashed and dotted line, with edentulism only; dotted line, with both conditions. Shaded areas are 95% confidence intervals (CIs). Estimated rates of cognitive decline: older adults aged 65 to 74 y (panel 1): neither = −0.29 (95% CI, −0.33 to −0.25), DM only = −0.38 (95% CI, −0.46 to −0.30), edentulism only = −0.42 (95% CI, −0.50 to −0.33), both = −0.44 (95% CI, −0.53 to −0.35). Older adults aged 75 to 84 y (panel 2): neither = −0.53 (95% CI, −0.56 to −0.50), DM only = −0.58 (95% CI, −0.68 to −0.48), edentulism only = −0.63 (95% CI, −0.73 to −0.53), both = −0.58 (95% CI, −0.74 to −0.57). Older adults aged 85+ y (panel 3): neither = −0.89 (95% CI, −0.98 to −0.80), DM only = −0.64 (95% CI, −0.99 to −0.30), edentulism only = −1.06 (95% CI, −1.47 to 0.03), both = −1.22 (95% CI, −1.86 to −0.68).

loss was associated with higher risks of cognitive impairment and dementia (Qi et al. 2021); however, it is noted that the results of the present study show that the relationship was not significant among the older adults aged 85+ y. Further studies are needed to examine the impact of tooth loss on cognitive decline using longitudinal and clinical measures of oral health. From a public health perspective, our study demonstrates the importance of improving access to dental health care and integrating primary dental and medical care in older adults.

This study has the following limitations. First, the status of DM and edentulism was self-reported. Future studies should use clinical diagnosis for measuring the onset of DM and edentulism. Second, since a limited number of participants developed both DM and edentulism from neither condition between waves (e.g., there were only 25 participants who had neither condition in 2006 but had both conditions in 2012), we used the baseline exposure and did not account for older adults who developed a new condition in the follow-up waves. In our sensitivity analysis, in which we excluded participants with changes in DM and/or edentulism status, the results remained consistent. Third, we were not able to incorporate the duration of complete tooth loss into our analysis as data on the onset of complete tooth loss was not available. Fourth, oral health or dental treatment data (e.g., dentures used) are not available in HRS. Therefore, we may suffer from omitted variable bias. Finally, participants' attrition is an issue, as those who remained in the sample were generally healthier compared to those who dropped out. We used IPAW to address the survival bias.

In summary, our study demonstrated that the co-occurrence of DM and edentulism can lead to worse cognitive function and accelerated cognitive decline for older adults aged 65 to 74 y. The findings have important policy and clinical implications for preventing cognitive decline among older adults, especially those with DM and poor oral health. For individuals with both poor oral health and DM, regular dental visits should be encouraged in addition to adherence to the diabetes self-care protocol. Regular cognitive screening may be needed in the primary care setting for older adults with poor oral health and DM. Furthermore, the link between oral health and cognition should be emphasized during routine cleanings; dental care and programs are needed to reduce the societal cost of ADRDs.

Author Contributions

B. Wu, contributed to conception and design, data acquisition, analysis, and interpretation, drafted and critically revised the manuscript; H. Luo, C. Tan, contributed to conception and design, and data interpretation, drafted and critically revised the manuscript;

X. Qi, A.R. Kamer, Schwartz, M. Martinez, contributed to data interpretation, critically revised the manuscript; F.A. Sloan, B.L. Plassman, contributed to conception and design, data interpretation, critically revised the manuscript. All authors gave their final approval and agreed to be accountable for all aspects of the work.

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