Supplementary Material

Temporal Dementia and Cognitive Impairment Trends in the Very Old in the 21st Century

Evaluation of model assumptions

Differences in outcome with respect to missing values were tested using Pearson's χ^2 for variables with >5% missing values. A minimum of 10 events or non-events, whichever was smallest, per variable in a subgroup was required for logistic regression performance. Goodness-of-fit was tested for all models except those of MMSE score thresholds (as significance testing was not performed) using the Hosmer–Lemeshow test [1] and determination of whether χ^2 was nonsignificant at $\alpha = 0.05$. Linearity between continuous predictors (participation year and MMSE score) and log odds was tested using the Box-Tidwell test by including an interaction term between predictors and their natural logarithms and interpreting its significance at $\alpha = 0.05$/number of covariates [1]. Correlation between independent variables was tested using Spearman correlation, allowing $\rho < 0.3$. Outliers in the solution were evaluated using standardized residuals >3 in cases of poor model fit. Errors were independent by design.

The prevalence of cognitive impairment (MMSE score < 24) among 85-year-olds

The prevalence of cognitive impairment (MMSE score < 24) showed signs of non-linearity among 85-year-olds ($p = 0.004$), peaking in 2005–2007. Normalized time squared was entered to model non-linear associations with probability of MMSE score < 24 (odds $\text{ratio}_{\text{participation year}^2} = 0.742$, 95% confidence interval = 0.603–0.914, $p = 0.005$; odds $\text{ratio}_{\text{participation year}} = 0.726$, 95% confidence interval = 0.599–0.881, $p = 0.001$). The non-linear model was retained due to better fit (–2 log likelihood $\chi^2 = -7.995$, $p = 0.046$).

Differences between participants and those who declined participation

Participants and those who declined participation did not differ in terms of the distribution of sex (68.7% versus 66.5% women; $p = 0.287$, χ^2 test) or age groups (85 years: 35.5% versus 39.8%, 90 years: 35.8% versus 33.0%, ≥95 years: 28.7% versus 27.2%; $p = 0.139$, χ^2 test). No significant difference was found between visited participants and included participants who were

not visited in mean age or the prevalence of dementia, AD, VaD, or unclassified dementia. Men were overrepresented among visited participants (33.4% versus 23.4%, $p < 0.001$).

On average, followed participants were younger than included participants who were not followed (87.7 ± 3.49 versus 90.8 ± 4.70 years, $p < 0.001$). Men, people with dementia, and people with cognitive impairment were underrepresented in the followed sample (men: 27.2% versus 32.5%, $p < 0.022$, dementia: 13.0% versus 45.5%, $p < 0.001$, MMSE score < 24: 28.1% versus 59.7%, $p < 0.001$, MMSE score < 18: 5.3% versus 32.2%, $p < 0.001$).

Missing values

Proportions of missing values were investigated for all variables included in the statistical analyses. In the full sample, no value for sex was missing. In the subsample of visited participants, 59 (3.4%) education level, 57 (3.3%) MMSE score, 60 (3.5%) vision impairment, and 37 (2.2%) hearing impairment values were missing. As these proportions were ≤5%, they were not investigated further.

Among followed participants at risk of incident dementia, 26 (5.7%) educational level values were missing; this proportion did not differ between those who later did and did not develop dementia [$n = 14$ (8.1%) and $n = 12$ (4.3%), $p = 0.084$]. None of those followed with MMSE scores indicating a risk of cognitive impairment had missing information on education. Missing completely at random status was thus assumed also among followed participants.

REFERENCES

[1] Hosmer Jr DW, Lemeshow S, Sturdivant RX (2013) *Applied logistic regression*, vol. 398. John Wiley & Sons, Hoboken, NJ.

Supplementary Table 1. Number and proportions of dementia among persons with cognitive impairment

	Participation year/birth year							
	2000–02/ 1915–17		2005–07/ 1920–22		2010–12/ 1925–27		2015–17/ 1930–32	
	MMSE		MMSE		MMSE		MMSE	
	<24	<18	<24	<18	<24	<18	<24	<18
85 years								
Dementia, *n*	27	14	32	18	33	20	31	12
Dementia, %	58.7	100.0	57.1	90.0	62.3	95.2	83.8	100.0
90 years								
Dementia, *n*	32	25	49	36	56	34	70	37
Dementia, %	49.2	89.3	57.6	90.0	72.7	97.1	69.3	92.5
≥ 95 years								
Dementia, *n*	36	32	43	38	73	59	88	65
Dementia, %	67.9	94.1	55.8	90.5	79.3	98.2	81.5	98.5

MMSE, Mini-Mental State Examination.

Supplementary Table 2. Cumulative incidence of dementia during 5-year intervals among 454 followed, initially dementia-free, participants

	Index participation year/birth year			Sex-adjusted		Fully adjusted	
85 y	2000–02/ 1915–17	2005–07/ 1920–22	2010–12/ 1925–27	OR (95% CI)	*p*	OR (95% CI)	*p*
Persons at risk, *n* (% of followed)	83 (92.2)	79 (87.8)	106 (86.9)				
Cum. 5-y dementia incidence, *n* (%)	36 (43.4)	20 (25.3)	31 (29.2)	0.73 (0.53–0.99)	0.045	0.76 (0.55–1.06)	0.105
90 y	2000–02/ 1910–12	2005–07/ 1915–17	2010–12/ 1920–22	OR (95% CI)	*p*	OR (95% CI)	*p*
Persons at risk, *n* (% of followed)	43 (93.5)	53 (84.1)	53 (84.1)				
Cum. 5-y dementia incidence, *n* (%)	15 (34.9)	23 (43.4)	25 (47.2)	1.26 (0.83–1.90)	0.277	1.28 (0.84–1.97)	0.254
≥95 y	2000–02/ ≤1905–07	2005–07/ ≤1910–12	2010–12/ ≤1915–17	OR (95% CI)	*p*	OR (95% CI)	*p*
Persons at risk, *n* (% of followed)	8 (80.0)	11 (78.6)	18 (75.0)				
Cum. 5-y dementia incidence, *n* (%)	5 (62.5)	5 (45.5)	12 (66.7)	1.25 (0.54–2.88)	0.608	1.23 (0.53–2.86)	0.625

ORs and *p* values for the probability of events with increasing participation year were calculated using multiple logistic regression, adjusted for sex or sex and education.
The fully-adjusted analyses of dementia data were performed for the visited participants.
OR, odds ratio; CI, confidence interval.

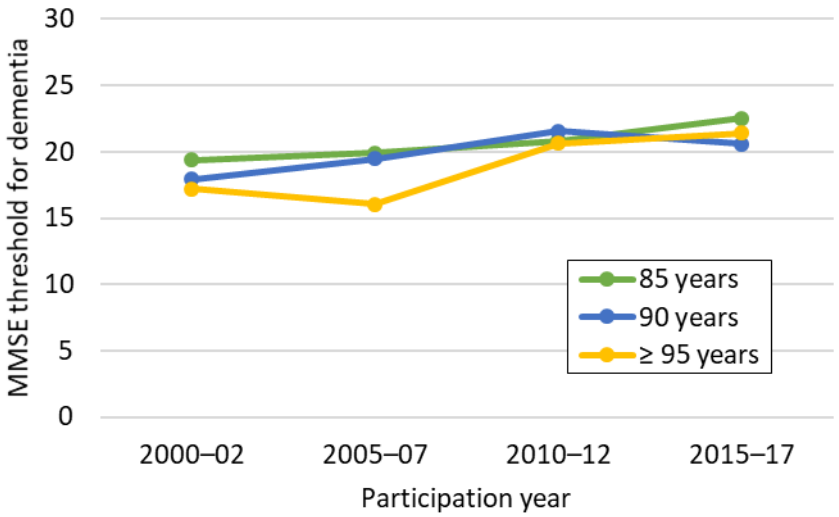
Supplementary Table 3. Cumulative incidence of cognitive impairment during 5-year intervals among 258 followed, visited participants with MMSE scores ≥ 24

	Index participation year/birth year			Sex-adjusted		Fully adjusted	
85 years	2000–02/ 1915–17	2005–07/ 1920–22	2010–12/ 1925–27	OR (95% CI)	*p*	OR (95% CI)	*p*
Persons at risk, *n* (% of followed)	53 (84.1)	42 (71.2)	60 (81.1)				
Cum. incidence of decline to MMSE <24, *n* (%)	29 (54.7)	13 (31.0)	22 (36.7)	0.69 (0.47–1.02)	0.063	0.69 (0.47–1.02)	0.062
Cum. incidence of decline to MMSE <18, *n* (%)	11 (20.8)	4 (9.5)	4 (6.7)	-*	-*	-*	-*
90 years	2000–02/ 1910–12	2005–07/ 1915–17	2010–12/ 1920–22	OR (95% CI)	*p*	OR (95% CI)	*p*
Persons at risk, *n* (% of followed)	27 (79.4)	29 (58.0)	28 (75.7)				
Cum. incidence of decline to MMSE <24, *n* (%)	20 (74.1)	12 (41.4)	13 (46.4)	0.51 (0.28–0.91)	0.022	0.53 (0.29–0.95)	0.034
Cum. incidence of decline to MMSE <18, *n* (%)	7 (25.9)	7 (24.1)	5 (17.9)	-*	-*	-*	-*
≥95 years	2000–02/ ≤1905–07	2005–07/ ≤1910–12	2010–12/ ≤1915–17	OR (95% CI)	*p*	OR (95% CI)	*p*
Persons at risk, *n* (% of followed)	2 (40.0)	5 (71.4)	12 (80.0)				
Cum. incidence of decline to MMSE <24, *n* (%)	2 (100.0)	2 (40.0)	9 (75.0)	-*	-*	-*	-*
Cum. incidence of decline to MMSE <18, *n* (%)	1 (50.0)	2 (40.0)	4 (33.3)	-*	-*	-*	-*

ORs and *p* values for the probability of events with increasing participation year were calculated using multiple logistic regression, adjusted for sex and education. MMSE <24 or <18 denotes achieved points on the assessment, irrespective of dementia status.

*Analysis not performed due to insufficient sample.

OR, odds ratio; CI, confidence interval; MMSE, Mini-Mental State Examination.



Supplementary Figure 1. Mean estimated Mini-Mental State Examination (MMSE) score thresholds for the diagnosis of dementia.
The estimated MMSE threshold was defined as the MMSE score under which 50% of participants had received a diagnosis of dementia, as indicated by sex- and education-adjusted logistic regression analyses performed separately for each age group. Only visited participants were included in this analysis.