Early parental death and psychosocial risk factors for dementia: A case-control study in Europe

Running title: Early parental death in dementia

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Abstract

Objectives: To assess the association between early parental death and the risk of dementia in adult life, and to examine the risk factors associated with early parental death in people with and without dementia.

Methods / Design: A population-based case-control study of a sample of 65,997 participants from the *Survey of Health, Ageing and Retirement in Europe* study. Early parental death was operationalized as parental death at the age of ≤ 16 years. Main analyses were conducted using bivariate and multivariate logistic regression analyses.

Results: The odds ratio (OR) for dementia in individuals who experienced early parental death (father or mother) at the age of ≤ 16 years was 1.83 (95%CI 1.61-2.09) and 1.54 (95%CI 1.35-1.76) adjusted for age, gender, and education. In the multivariate logistic regression analysis carried out with the whole sample, early parental death increased the risk of dementia (OR = 1.50, 95%CI 1.31-1.72), along with older age (OR = 5.92, 95%CI 4.86-7.17), neuroticism (OR = 2.94, 95%CI 2.61-3.31), low education level (OR = 1.84, 95%CI 1.64-2.05) and low income (OR = 1.49, 95%CI 1.34-1.67).

Discussion: Early parental death (≤ 16 years) was associated with an increased risk of dementia. We discuss the neurobiological markers associated with adverse childhood experiences (ACEs) and dementia as well as interventions to counteract the negative health effects on adults.

Key words: Dementia, Adverse childhood experiences, Early parental death, Biomarkers.

Key points

- Adverse childhood experiences (ACEs) have negative effects on adults' health.
- Early parental death (≤ 16 years) is an ACE with a relevant risk for dementia.
- Cortisol, telomeres, c-reactive protein (CRP), and interleukin-6 (IL-6) are biomarkers of ACEs.
- Interventions are needed to counter the negative effects of ACEs on health.

1 INTRODUCTION

It has been consistently documented [1-5] that adverse experiences in childhood and adolescence have negative repercussions on adult life and health and may affect between 23.5% and 35.0% of the population in Europe and the United States.[1]

The early death of parents has been one of the most studied adverse childhood experiences (ACEs) and has been shown to have negative effects on health throughout the life cycle.[6] It has been associated with a higher risk of depression[7,8] and suicide,[9] lower academic achievement,[10] lower occupational position,[11] higher separation rates [12] and a higher probability of psychosis.[13] In terms of physical health, early parental death has been associated with worse health perception[14] and more somatic symptoms,[15] as well as higher mortality,[16] cardiovascular disease, [4,5,17] self-harm[18] and an increased risk of dementia.[19-26]

Previous studies have identified certain mechanisms involved in the association between early parental death and the risk of dementia and other pathologies associated with older age: stress,[27, 28] increased inflammatory processes,[29] alterations of the hypothalamic-pituitary-adrenal axis [30] and shorter telomeres on chromosomes.[31,32]

Research into the relationship between early parental death and dementia and/or severe cognitive impairment in the elderly has confirmed a general increased risk (odds ratios (OR): 1.52 - 6.41) [19-26], although the results vary according to gender and age at the time of parental death. In a prospective longitudinal study, Persson and Skoog (1996)[19] found that the death of a parent before the age of 16 was associated with a relative risk (RR) of developing dementia of 6.3 (95% CI: 1.8-21.1). In contrast, in Fu's study (2020),[20] only the

death of the mother before the age of 16 was associated with severe cognitive decline in men (OR = 1.52, 95%CI: 1.01-2.28), though not in women.

Other authors have reported different age ranges. Conde-Sala (2003)[21] found that the death of the father before the age of 20 was associated with an increased risk of dementia in women. In Norton et al. (2009),[22] the father's death before the age of four resulted in a threefold increase in the dementia risk, without differences for gender and education and after adjustment for APOE-4. With a larger sample, the same authors (Norton et al., 2011)[23] also found a greater risk in the case of the father's death before the age of five and the mother's death between 11 and 17 years. In both cases, female gender, older age and APOE-4 were associated with a greater risk of dementia.

Whalley et al. (2013)[24] found an increased risk of dementia with the death of either parent before the age of 11, which was also associated with female gender, older age and APOE-4. In Wei et al. (2014),[25] early parental death was associated with an increased risk of dementia in the whole sample. In the study by Ravona-Springer et al. (2012)[26] which included data only on men (0-18 years), early parental death, either of the mother or the father, was associated with a higher risk of dementia.

In view of the heterogeneity of the results of previous studies and also bearing in mind the small size of some samples, the present study aimed to explore the association between early parental death and the risk of dementia according to age ranges, gender of parents and participants, schooling and income, using a large representative sample of older Europeans.

We hypothesized that individuals with early parental death would have a higher prevalence of dementia.

The specific objectives of the present study were: 1. To determine the frequency of early parental death in childhood and adolescence and its association with the risk of dementia in adult life; and 2. To examine the risk factors associated with early parental death in people with and without dementia.

2. MATERIAL AND METHODS

2.1 Study design

Data for this population-based case-control study came from the seventh wave of the "Survey of Health, Ageing and Retirement in Europe" (SHARE), corresponding to the year 2017 and including people born between 1912 and 1967. The SHARE study provided information on sociodemographic aspects and on physical and mental health status.[33]

The seventh wave collected data from people over 50 years of age from 27 European countries: Austria, Germany, Sweden, Spain, Italy, France, Denmark, Greece, Switzerland, Belgium, Israel, Czechia, Poland, Luxembourg, Hungary, Portugal, Slovenia, Estonia, Croatia, Lithuania, Bulgaria, Cyprus, Finland, Latvia, Malta, Romania, and Slovakia. Average rates of individual response were around 69.6%, ranging from 39.01% in Slovakia to 89.05% in Greece.[33]

SHARE wave 7 comprised 76,250 individuals. The main sample of the present study, i.e., those for whom data on the year of parents' deaths were available, totalled 65,997 (86.8%)

people; 3,754 (4.9%) people with both parents alive and 6,249 (8.2%) people for whom no data on parental death were available were not included in the study. The research was approved by the Ethics Committee of Girona Biomedical Institute.

2.2 Measures

• *Periods of parental death.* The year of parental death and the year of the participants' birth were used to establish participants' age periods at time of parental death: 0-5, 6-10, 11-16, 17-20 and > 21 years. The analysis of the risk of dementia focused on the period of early parental death, i.e., when the participants were aged ≤ 16 years. Previous authors have established this age as the most relevant for assessing the effect of early parental death (≤ 16 years) on the health of the elderly.[11,15,19,34]

• *Sociodemographic data.* The following data were recorded: age (<65 / ≥65 years), gender (male / female), marital status (married, widowed, separated-divorced or never married), mean years of schooling (<11 / ≥11 years), economic difficulties (yes/no) and income in percentiles (≤50 />50).

• *Functional state.* Five basic daily life activities (dressing, bathing, eating, cutting up food, walking across a room and getting in or out of bed) and five instrumental activities (telephone calls, taking medication, managing money, shopping for groceries and preparing a hot meal) were examined by assessing the presence or absence of the activity (0 / ≥ 1 deficit). Four items were used to determine fragility (falling down, fear of falling down, dizziness and fatigue). On all scales, the higher the score, the greater the difficulty.

• *Cognition.* The items of recent memory (range = 0-10) and deferred memory (range = 0 -10) were used. The variable was dichotomized based on the mean of the scores (<9 / ≥9).

• *Diseases*. A total of 18 self-reported diseases were recorded, in response to the following question: "Has a doctor ever told you that you had [or do you currently have] any of the conditions listed on this sheet? By this we mean that a doctor has told you that you have this condition, and that you are either currently being treated for or bothered by this condition. The conditions are heart attack, hypertension, cholesterol, stroke, diabetes, chronic lung disease, cancer, stomach or duodenal ulcer, Parkinson disease, cataracts, hip or femoral fracture, other fractures, emotional disorders, rheumatoid arthritis, osteoarthritis, chronic kidney disease and dementia". The sum of the 18 diseases was also used as a variable.

• *Personality traits*. The short version of the Big Five Inventory (BFI-10) comprising 10 items was used to identify traits of Extraversion, Agreeableness, Conscientiousness, Neuroticism and Openness.[35]

2.3 Statistical analysis

The presence in adulthood of a total of 18 diseases was analysed according to the presence or absence of parental death in each age range. The frequency (mean and standard deviation) was examined and a Student's t-test was applied. A multivariate binomial logistic regression analysis was performed to analyse the degree of association between the adulthood diseases and parental death (≤ 16 years).

To establish the periods in which parental death presented significant results with respect to dementia, we performed a frequency analysis using the Chi-square test (χ^2) to calculate the differences in each of the age groups. The analysis was performed for the death of the father, the mother, the father or mother, and for the two together. A logistic regression analysis was performed for each of the age groups with parental death, indicating the crude and adjusted values for the variables age, gender and years of schooling.

Finally, a bivariate analysis was performed to identify the degree of association between the different variables and the groups with or without dementia. This was completed with a multivariate binomial logistic regression analysis with dementia status as dependent variable.

We also calculated the effect size, using Cohen's d for the continuous variables (weak <0.5; moderate 0.5-0.8 or strong > 0.8), and Cramer's V for the categorical variables (weak <0.10, moderate 0.30 or strong 0.50).[36] For odds ratios, we used the values consistent with Cohen's d (<0.2 vs OR <1.5; 0.5 vs OR 1.5-4.9; >0.8 vs OR >5.0).[37]

The level of statistical significance for contrasting the hypotheses was <0.05 with 95.0% confidence intervals according to the different analyses. The statistical analysis was performed using SPSS v24.0 for Windows (IBM SPSS Corp., Amonk, NY).

3. RESULTS

3.1 Sample description

The sample with data on parental death consisted of 65,997 people, of whom 1431 (2.2%) had a diagnosis of dementia. Only 3754 subjects had two living parents, and only six (0.3%) of these had dementia. Data on parental death were not available in 6249 subjects, and 410 (6.6%) had a diagnosis of dementia (see Figure 1).

In all variables, the group with living parents had the most favourable data (younger, more education and cognition, less disease), and the group who had lost their parents had the least favourable. The complete data of the three groups can be found in supplementary Table 1.

Figure 1

In the main sample (n = 65,997), the mean age was 68.65 ± 9.4 years, with 43.1% men and 56.9% women. A total of 68.8% were married and 16.8% were widows/widowers. With regard to education, 59.5% had more than 11 years of schooling, and the average score for recent and deferred memory was 8.85 ± 3.6 on a scale of 20 points.

Medical conditions were recorded in 79.9% of the sample, as follows: hypertension (45.1%), cholesterol (25.3%), osteoarthritis (19.7%), diabetes (14.0%), heart attacks (12.8%) and rheumatoid arthritis (10.2%). In relation to the five personality traits (range 0-5), Extraversion had an average score of 3.49 ± 0.9, Agreeableness 3.66 ± 0.8, Conscientiousness 4.12 ± 0.8, Neuroticism 2.66 ± 0.9 and Openness 3.29 ± 0.9.

In the main sample the deceased parents were father (n = 62096, 94.1%), mother (n = 55635, 84.3%), father or mother (n = 65997, 100.0%), and both (n = 51734, 78.4%). In terms

of parental death in the participant age range of ≤ 16 years: the father had died (n = 6034, 9.7%), mother (n = 2181, 3.9 %), father or mother (n = 8024, 12.2%) or both (n = 191, 0.4%).

3.2 Presence of disease in adulthood according to the age at parental death

A first analysis was performed to verify the presence of disease in adulthood in relation to early parental death. Using the variable "sum of the 18 diseases", a higher number of diseases were recorded in the ≤ 16 years age range (2.18 ± 1.7 vs 1.87 ± 1.6; t = 15.2, p <0.001). In the 17-20 age range the differences were not significant. From the age of 21 onwards, the mean number of diseases was lower (1.88 ± 1.6 vs 2.07 ± 1.7; t = 10.7, p <0.001). The complete data set is shown in Table 1.

Table 1

A multivariate binomial logistic regression was performed with parental death at participant age ≤ 16 years as a dependent variable, and with the 18 diseases as covariates. Dementia had the highest odds ratio (OR = 1.63, 95% CI = 1.42-1.86), with a moderate effect size (>1.5). The complete data are shown in Table 2.

Table 2

3.3 Dementia according to the age of participants at time of parental death

Previous analyses (Table 2) justify focusing the study on the association of early parental deaths on dementia. Supplementary Table 2 shows the frequencies of the presence/absence of dementia in each of the age groups, differentiating between the deaths of the father,

mother, either of the two, or both. Looking at the early deaths of the father or mother (third column), it can be seen that the rates of dementia compared to no dementia are higher until the age of 16 years. The data at the age of 0-5 years are: Dementia, n= 95, 6.6%; No dementia, n = 2596, 4.0%; χ^2 = 24.5, p <0.001. At participant age 10-11 the data are: Dementia n = 82, 5.7%; No dementia, n = 2137, 3.3%; χ^2 = 25.2, p <0.001. At participant age 11-16 the data are: Dementia n = 109, 7.6%; No dementia, n = 3005, 4.7%; χ^2 = 27.3, p <0.001. And in the set of 0 to 16 years the data are: Dementia n = 286, 20.0%; No dementia, n = 7738, 12.0%; χ^2 = 83.9, p <0.001.

The data for ages 17, 18, 19 and 20, analysed individually, did not differ significantly and so they were combined in a single age group (17-20 years). No significant differences were found here either: Dementia n = 72, 5.0%; No dementia, n= 2844, 4.4%; χ^2 = 1.3, p = 0.254. In the age group of 21 years and over, the proportions were reversed as there were significantly more cases without dementia: Dementia n = 1,073, 75.0%; No dementia, n= 53984, 83.6%; χ^2 = 75.3, p <0.001.

Table 3 shows the binary logistic regressions with the odds ratios for the different age groups. The crude ORs of the deaths of the father or mother together (third column), for age groups 0-5, 6-10, 11-16 and 0-16, were relatively high: 1.70, 1.77, 1.69 and 1.83 (p <0.05) respectively. When the regressions were adjusted with the variables age, gender and years of schooling they continued to be significant, although their values were slightly lower: 1.32, 1.51, 1.56, and 1.54 (p <0.05) respectively. In the data for "both parents" (fourth column), the results were not significant due to the small sample size, and older age it was the

variable that made the father's death non-significant in the adjusted model (0-5b years). The complete data are shown in Table 3.

Table 3

3.4 Factors associated with early parental death in people with and without dementia

In the bivariate analysis, the most notable differences between participants with and without dementia with regard to early parental death (≤ 16 years) were found in deficits in active daily living (4.21 ± 3.6 vs 0.49 ± 1.4, d = 1.34), Cognition (3.83 ± 3.1 vs 8.35 ± 3.6, d = 1.32), Age (81.7 ± 7.8 vs 71.7 ± 9.8, d = 1.20), Sum of diseases (3.86 ± 2.1 vs 2.12 ± 1.6, d = 0.89), Frailty (1.69 ± 1.3 vs 0.73 ± 1.0, d = 0.78), Neuroticism (3.07 ± 0.8 vs. 2.66 ± 0.9, d = 0.45) and Emotional disorders (57.7% vs 27.3, V = 0.12). The complete data are shown in Table 4.

Table 4

A multivariate logistic analysis was performed with the whole sample, with the variable No-dementia / Dementia as the dependent variable and with the deaths of the father or mother (≤ 16 years) as a covariate, to rank it hierarchically with respect to the possible confusion covariates: age, neuroticism, years of schooling, income and gender. The covariate early parental death continued to be significant (OR = 1.50, 95%CI = 1.31-1.72, p <0.001), as did older age (OR = 5.92), greater neuroticism (OR = 2.94), fewer years of schooling (OR = 1.84), and lower income (OR = 1.49). Gender was not significant. The complete results are shown in Table 5.

Table 5

4 DISCUSSION

4.1 Prevalence of early parental death

Demographic studies provide some data on the magnitude of early parental death. The study by Parsons (2011),[34] which analysed a British cohort of 1970, placed parental death at the age of 16 at 4.7%. In a cohort study in the Netherlands, Van Poppel et al. (2013)[38] found that the prevalence of parental death at 15 years of age ranged from 13.4% in the 1900-1922 cohort to 3.0% in the 1975-1985 cohort. In our sample, the rates of early parental death at participant age 16 years were higher (11.8%); however, we also observed reductions in the more recent cohorts: 1912-1949 (14.1%) and 1950-1967 (7.8%).

4.2 Early parental death and diseases

Many studies have linked parental death with depression.[7,8] However, our data also confirm the negative effects on adult physical health.[6, 14-18] The study by Neeleman et al. (2002)[15] analysed 20 chronic diseases and found a higher risk in adults whose parents had died before they were 16 years old.

We have not found any references that establish a hierarchy among physical illnesses in relation to early parental death. Most studies analyse the diseases individually, and the diseases most commonly studied are dementia[19-26] and cardiovascular disease. [4,5,17]

4.3 Early parental death and dementia

In our study, in all age groups up to 16 years, parental death (death of the father, mother, or either father or mother) is associated with an increased risk of dementia, with moderate odds ratios. These results corroborate those of other studies;[19,25] however, in other studies a greater risk was only observed in some age groups [22-24, 26] or for the death of the mother[20] or the father[22], with higher odds ratios than in our analysis. This heterogeneity in the results may be due to small sample sizes.

The greater risk was maintained in the models adjusted for age, gender and education. In the multivariate regression, risk associated with early parental death remained significant even after adding the possible confounding variables age, neuroticism, years of schooling and income. Neuroticism has already been documented as a risk factor for dementia[39] and the loss of a parent may be associated with lower academic achievement and income.[10] Some studies have found differences in relation to participant gender; [20,23] however, gender was not relevant in our analysis.

4.4 Biomarkers of adverse childhood experiences

A recent review[40] identified the biomarkers related to adverse childhood experiences: inflammatory processes (IL-6, interleukin; CRP, C-reactive protein), cardio-metabolic systems (blood pressure), genetics (length of telomeres) and endocrine systems (cortisol).

Norton et al. (2017)[29] found that people with two or more family deaths in childhood were 79% more likely to have high CRP in old age, emphasizing the relationship between childhood stress and inflammatory processes in old age. Multiple adverse childhood experiences, including parental death, have also been associated with higher blood pressure,[3] higher levels of IL-6 and shorter telomeres.[41] Mitchell et al. (2017)[31] found that children who had lost their father before nine years of age had the shortest telomeres. Early life stress, including parental death, has been associated with cell aging, with shorter telomeres and high copy numbers of mitochondrial DNA (mtDNA).[32] Regarding endocrine systems, early parental death has been related to changes in the HPA (hypothalamic-pituitary-adrenal) axis, with increased cortisol.[30]

A review on dementia [27] found that there is sufficient proven evidence to consider adverse childhood experiences as a risk factor for this condition. Early life stress has been associated with deficits in various cognitive functions[42] and with an increased risk of dementia.[28] In addition, shorter telomeres were identified as a risk factor for dementia.[43]

4.5 Clinical implications: interventions in adverse childhood experiences

A recent review of the prevalence of adverse childhood experiences (ACE)[1] reported that 23.5% of people in Europe had had one ACE and 18.7% two or more, while in North America

23.4% had had one ACE and 35.0% two or more. The authors emphasized the need for programmes and interventions to prevent ACEs or to mitigate their effects.

The recognition of this need has generated a wide variety of interventions for reducing the negative health consequences of ACEs, in both childhood and adulthood. The interventions for modifying the biological markers associated with stress,[44] such as cortisol,[45] telomeres[46] and interleukin-IL6 [47] stand out. Certain interventions have been specifically designed for early parental death,[48,49] and have varying orientations: some are centred on increasing resilience[47,48,50] and others focus on implementing coping strategies.[51]

In general, interventions are directed at people who have had adverse childhood experiences, including adults, children and adolescents. In the last case, the programmes incorporate parents or caregivers into the treatment, highlighting the importance of warmth and supportiveness and a positive family upbringing.

4.6 Strengths and limitations

A strength of this study is the sample size (65,997 participants and 1431 cases of dementia). This sample size is the largest in the studies carried out to date on early parental death and dementia. However, the study has some limitations that should be mentioned. First, we found few data on parents' backgrounds, especially with regard to health and illness. Second, we could not rule out an information bias, because information on medical diagnoses was self-referred. Third, the number of lost cases with dementia and without data on parental death was relatively high (6.6%). A fourth limitation is the impossibility of

analysing the coexistence of other ACEs with early parental death (such as abuse, neglect, drug addiction, etc.).

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Conflict of Interest: None declared

Availability of data: These data were derived from the following resources available in the public domain: Survey of Health, Ageing and Retirement in Europe (SHARE). http://www.share-project.org/home0.html

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TABLE 1 Age of the subject at the death of the parents and diseases

		Number of diseases				
		Age	Other ages	Differences		
Age at time of parental death	**N groups**	**Mean (D)**	**Mean (SD)**	***t***	***p***	***d***
0-5 / Other	2691 / 63306	2.29 (1.7)	1.89 (1.6)	11.4	**<0.001**	0.23
6-10 / Other	2219 / 63778	2.20 (1.7)	1.90 (1.6)	8.1	**<0.001**	0.18
11-16 / Other	3114 / 62883	2.10 (1.7)	1.90 (1.6)	6.3	**<0.001**	0.11
0-16 / Other	8024 / 57973	2.18 (1.7)	1.87 (1.6)	15.2	**<0.001**	0.18
17-20 / Other	2916 / 63081	1.93 (1.6)	1.91 (1.6)	0.9	0.358	0.01
≥ 21 / Other	55057 / 10940	1.88 (1.6)	2.07 (1.7)	10.7	**<0.001**	0.11

Note. Dependent variable: Sum of 18 diseases

t, Student's t-test; d, Cohen's d, small = <0.5); $p < 0.05$ are shown in bold.

TABLE 2 Multivariate logistic regression. Diseases and early parental death (≤16 years)

Method: Forward Wald	**OR**	**95% CI**	***p***
Diseases			
Dementia	1.63	1.42-1.86	**<0.001**
Chronic kidney	1.44	1.26-1.64	**<0.001**
Cataracts	1.37	1.27-1.48	**<0.001**
Heart attack	1.36	1.27-1.45	**<0.001**
Rheumatoid arthritis	1.18	1.09-1.27	**<0.001**
Stroke	1.18	1.06-1.31	**0.003**
Hypertension	1.16	1.10-1.21	**<0.001**
Stomach and duodenal ulcer	1.14	1.02-1.27	**0.016**
Other diseases	1.08	1.02-1.15	**0.009**
Osteoarthritis	0.91	0.86-0.97	**0.003**

Note. Dependent variable: death of parents at ≤ 16 years. 0 = Other ages (*n* = 57973); 1 = ≤ 16 years (*n* = 8024).
OR, Odds ratio; CI, Confidence interval; $p < 0.05$ are shown in bold.
Effect size for OR: small = <1.5, medium = 1.5-4.9, strong = > 5.0

TABLE 3 Multivariate binary logistic regression. Odds ratio for dementia in adulthood according to the age of the subject at the death of the parents

	Father Dementia, n = 1336		**Mother Dementia, n = 1345**		**Father or Mother Dementia, n = 1431**		**Both parents Dementia, N = 1250**	
Years of death	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*
0-5[a]	1.49 (1.16-1.92)	**0.002**	2.00 (1.40-2.87)	**<0.001**	1.70 (1.37-2.10)	**<0.001**	1.24 (0.30-5.08)	0.762
0-5[b]	1.18 (0.92-1.53)	0.188	1.73 (1.21-2.49)	**0.003**	1.32 (1.07-1.63)	**0.010**	1.11 (0.27-4.58)	0.879
6-10[a]	1.69 (1.29-2.21)	**<0.001**	1.85 (1.25-2.73)	**0.002**	1.77 (1.41-2.23)	**<0.001**	2.64 (0.82-8.49)	0.104
6-10[b]	1.47 (1.12-1.93)	**0.005**	1.67 (1.13-2.47)	**0.010**	1.51 (1.20-1.89)	**<0.001**	2.18 (0.67-7.07)	0.195
11-16[a]	1.62 (1.29-2.05)	**<0.001**	1.49 (1.04-2.14)	**0.031**	1.69 (1.38-2.06)	**<0.001**	.....	.....
11-16[b]	1.54 (1.22-1.95)	**<0.001**	1.46 (1.01-2.11)	**0.042**	1.56 (1.28-1.91)	**<0.001**	.....	.....
0-16[a]	1.67 (1.43-1.94)	**<0.001**	1.79 (1.44-2.23)	**<0.001**	1.83 (1.61-2.09)	**<0.001**	1.08 (0.44-2.64)	0.856
0-16[b]	1.44 (1.23-1.67)	**<0.001**	1.64 (1.32-2.04)	**<0.001**	1.54 (1.35-1.76)	**<0.001**	0.95 (0.39-2.33)	0.920
17-20[a]	1.21 (0.92-1.59)	0.169	0.82 (0.51-1.34)	0.437	1.15 (0.90-1.46)	0.254	.....	.....
17-20[b]	1.26 (0.96-1.66)	0.095	0.82 (0.50-1.33)	0.415	1.13 (0.89-1.44)	0.301	.....	.....

≥ 21[a]	0.63 (0.55-0.72)	**<0.001**	0.66 (0.54-0.80)	**<0.001**	0.58 (0.52-0.66)	**<0.001**	1.24 (0.51-3.02)	0.629
≥ 21[b]	0.70 (0.61-0.80)	**<0.001**	0.70 (0.57-0.86)	**0.001**	0.64 (0.57-0.73)	**<0.001**	1.34 (0.55-3.27)	0.515

Note. Dependent variable: 0 = No dementia, 1 = Dementia. Co-variables: Years of death. OR, Odds ratio; CI, Confidence interval; $p < 0.05$ are shown in bold.
[a] Crude value, [b] Adjusted for age, gender and years of schooling. Effect size for OR, small = <1.5, medium = 1.5-4.9, strong = >5.0

TABLE 4 Clinical and sociodemographic data. Dementia vs No-Dementia in death of parents (≤ 16 years)

	Dementia	**No-Dementia**	**Differences**		
	***n* = 286**	***n* = 7738**	***t* / χ^2**	***p***	***d* / *V***
Death of parents (≤ 16 years), *n (%)*	286 (20.0)	7738 (12.0)	83.9	**<0.001**	0.04
Age, mean (SD)	81.87 (7.8)	71.17 (9.8)	22.4	**<0.001**	**1.20**
> 65 years, *n (%)*	279 (97.6)	5625 (72.7)	87.6	**<0.001**	0.10
Gender (female), *n (%)*	166 (58.0)	4474 (57.8)	0.0	0.940	0.00
Marital status, *n (%)*					
Married	134 (47.2)	4935 (63.8)	50.5	**<0.001**	0.08
Widowed	110 (38.7)	1679 (21.7)			
Divorced	20 (7.0)	710 (9.2)			
Single	20 (7.0)	406 (5.3)			
Years of schooling, mean (SD)	8.88 (4.1)	10.35 (4.0)	6.0	**<0.001**	0.36
<11 years, *n (%)*	182 (63.6)	3649 (47.2)	30.0	**<0.001**	0.06
Economic difficulties, *n (%)*	144 (50.3)	3437 (44.4)	3.9	**0.047**	0.02
Income (10-50 perc.), *n (%)*	133 (46.8)	2845 (36.8)	11.7	**0.001**	0.04
ADL deficits, mean (SD)	4.21 (3.6)	0.49 (1.4)	17.3	**<0.001**	**1.34**
≥ 1, *n (%)*	216 (75.5)	1363 (17.6)	585.1	**<0.001**	**0.27**
Frailty, mean (SD)	1.69 (1.3)	0.73 (1.0)	11.5	**<0.001**	**0.78**
Cognition (recall), mean (SD)	3.83 (3.1)	8.35 (3.6)	23.8	**<0.001**	**1.32**
0-8 points, *n (%)*	269 (94.1)	3984 (44.6)	200.6	**<0.001**	**0.16**
Personality, mean (SD					
Extraversion	3.36 (0.9)	3.50 (0.9)	1.9	0.055	0.15
Agreeableness	3.61 (0.8)	3.67 (0.8)	0.8	0.387	0.07
Conscientiousness	3.96 (0.9)	4.13 (0.8)	2.4	**0.014**	0.19
Neuroticism	3.07 (0.8)	2.66 (0.9)	7.9	**<0.001**	0.45
>2.5, *n (%)*	207 (72.4)	3717 (48.0)	65.4	**<0.001**	0.09
Openness	3.04 (0.8)	3.29 (0.9)	3.7	**<0.001**	0.27
Depression (≥ 4 EURO-D)	165 (57.7)	2112 (27.3)	125.3	**<0.001**	**0.12**
Diseases, *n (%)*					
Emotional disorders	67 (23.4)	530 (6.8)	110.0	**<0.001**	**0.12**
Parkinson	17 (5.9)	70 (0.9)	65.3	**<0.001**	0.09
Stroke	44 (15.4)	407 (5.3)	53.2	**<0.001**	0.08
Cataracts	59 (20.6)	883 (11.4)	22.6	**<0.001**	0.05
Fracture (hip, femoral)	15 (5.2)	155 (2.0)	13.9	**<0.001**	0.04
Heart attack	69 (24.1)	1310 (16.9)	10.0	**0.002**	0.03
Chronic lung	30 (10.5)	491 (6.3)	7.8	**0.005**	0.03
Diabetes	63 (22.0)	1229 (15.9)	7.7	**0.005**	0.03
Rheumatoid arthritis	50 (17.5)	949 (12.3)	6.8	**0.009**	0.03
Sum of 18 diseases, mean (SD)	3.86 (2.1)	2.12 (1.6)	13.2	**<0.001**	**0.89**
Parents' critical events *, *n (%)*					
Father	125 (43.7)	2839 (36.7)	5.8	**0.016**	0.03

Mother	55 (19.2)	1166 (15.1)	3.7	0.054	0.02
Years of schooling, mean (SD)					
Father	8.23 (3.3)	8.70 (2.9)	1.8	0.061	0.14
Mother	7.41 (2.2)	7.97 (2.4)	3.1	**0.002**	0.23

Note. t, Student's t-test; χ2, Pearson Chi-Square; Effect size: d, Cohen's d (small = 0.2, medium = 0.5, large = 0.8); V = Cramer's (df1 = small: ≤0.10, medium: 0.11–0.49, large: ≥0.50); ADL: activities of daily living; *p*-values <0.05 are shown in bold. *Critical events: Imprisonment, labour camp, concentration camp, deportation, engaged in combat, serious damage to health or injury, deaths

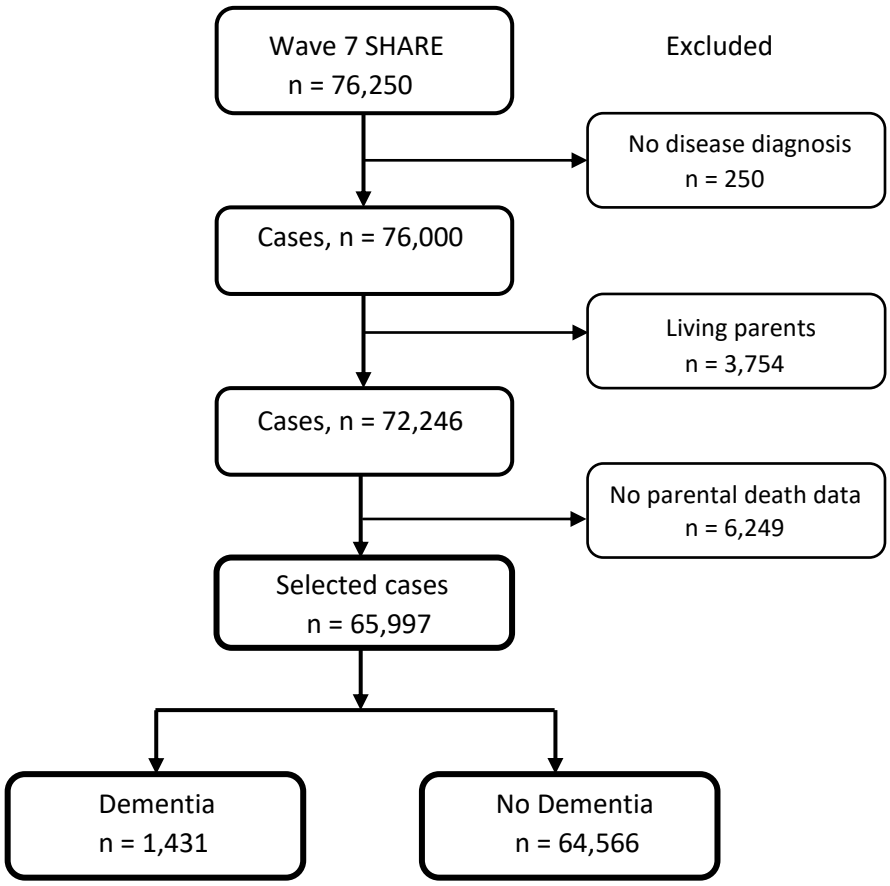
TABLE 5 Multivariate binary logistic regression. No dementia vs Dementia

Method: Enter together		OR	95% CI	p
Age	(≥ 65)	5.92	4.86-7.17	**<0.001**
Neuroticism	(>2.6)	2.94	2.61-3.31	**<0.001**
Years of schooling	(< 11 years)	1.84	1.64-2.05	**<0.001**
Death of parents	(≤ 16 years)	1.50	1.31-1.72	**<0.001**
Income	(10-50 perc.)	1.49	1.34-1.67	**<0.001**
Gender	(male)	1.10	0.99-1.23	0.079

Note. Dependent variable: 0 = No dementia (*n* = 64566), 1 = Dementia (*n* = 1431). Odds ratio; CI, Confidence interval; $p < 0.05$ are shown in bold. Effect size for OR, small = <1.5, medium = 1.5-4.9; strong = >5.0. Collinearity, Tol: 0.94-0.99; VIF: 1.00-1.06; Index of Condition: 17.5

Figure captions

FIGURE 1 Flowchart describing the analysed sample


Wave 7 SHARE
n = 76,250
Excluded
No disease diagnosis
n = 250
Cases, n = 76,000
Living parents
n = 3,754
Cases, n = 72,246
No parental death data
n = 6,249
Selected cases
n = 65,997
Dementia
n = 1,431
No Dementia
n = 64,566