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Midlife socioeconomic position and old-age dementia mortality: a large prospective register-based study from Finland

Kaarina Korhonen¹, Elina Einiö^{1,2,3}, Taina Leinonen⁴, Lasse Tarkiainen¹, Pekka Martikainen^{1,3,5}

¹ Population Research Unit, Faculty of Social Sciences, University of Helsinki, Helsinki, Finland

² Department of Social Policy, London School of Economics and Political Science, London, United Kingdom

³ Max Planck Institute for Demographic Research, Rostock, Germany

⁴ Finnish Institute of Occupational Health, Helsinki, Finland

⁵ Department of Public Health Sciences, Stockholm University, Stockholm, Sweden

Correspondence to:

Kaarina Korhonen

Faculty of Social Sciences

P.O. Box 18, 00014 University of Helsinki, Finland

+358 50 3199 388

kaarina.korhonen@helsinki.fi

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Abstract

Objectives To assess the association between multiple indicators of socioeconomic position and dementiarelated death, and to estimate the contribution of dementia to socioeconomic differences in overall mortality at older ages.

Design Prospective population-based register study.

Setting Finland.

Participants 11% random sample of men and women aged 70–87 resident in Finland at the end of 2000 (N=54 964).

Main outcome measure Incidence rates, Kaplan-Meier survival probabilities and Cox regression hazard ratios of dementia mortality in 2001–2016 by midlife education, occupational social class and household income measured at ages 53–57 years.

Results During the 528 387 person-years at risk, 11 395 individuals died from dementia (215.7 per 10 000 person-years). Lower midlife education, occupational social class and household income were associated with higher dementia mortality, and the differences persisted to the oldest old ages. Compared to mortality from all other causes, however, the socioeconomic differences emerged later and were altogether smaller. Dementia accounted for 30% of the difference between low and high education groups in overall mortality at age 70+, and for 25% of the difference between lowest and highest household income quintiles. All indicators of socioeconomic position were independently associated with dementia mortality, low household income being the strongest independent predictor (HR=1.24, 95% confidence interval 1.16–1.32), followed by basic education (HR=1.14, 1.06–1.23). Manual occupational social class was related to a 6% higher hazard (HR=1.06, 1.01–1.11) compared to white-collar social class. Adjustment for midlife economic activity, baseline marital status and chronic health conditions attenuated the excess hazard of low midlife household income, although significant effects remained.

Several indicators of socioeconomic position predict dementia mortality independently and these differences persist into the oldest old ages. The results demonstrate that dementia is among the most important contributors to socioeconomic inequalities in overall mortality at older ages.

Strengths and limitations of this study

- We used longitudinal registry data that permits a 15-year follow-up of dementia mortality with no attrition or recall bias.
- All indicators of socioeconomic position were measured in midlife in order to avoid selection to socioeconomic groups on the basis of cognitive decline.
- This is the first study to show the contribution of dementia to the socioeconomic inequalities in overall mortality at older ages.
- We used individual death records and could only identify dementia cases that were recorded on the death certificate.

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Introduction

Socioeconomic inequality in health and mortality is one of the most consistent findings in the demographic and social epidemiological literature. Lower education, occupational social class and income are strong predictors of all-cause and cause-specific mortality particularly among the working-age population, but inequalities are clear also at older ages (1–4). Among the ageing population, the key factors affecting morbidity and disability are Alzheimer's disease and other forms of progressive dementia. Globally, an estimated 47 million people lived with dementia in 2015, and the number is projected to triple by 2050 (5). In England and Wales, dementia has already become the leading cause of death (6). Despite the growing societal impact, however, no comprehensive understanding exists about the socioeconomic patterns of dementia mortality.

Educational inequalities in dementia mortality have previously been reported in studies following individuals from midlife or younger old ages (7,8) but also at the oldest ages (8,9). In a Norwegian health examination study, an educational pattern was present only among cohorts aged below 70 at baseline but not among those aged 70 and over. Similarly, among a Finnish cohort aged 90 and over, no statistically significant educational gradient in dementia mortality emerged (9). The lack of educational pattern among the oldest old may relate selective survival, indicating that people surviving to this age is more homogeneous in terms of health-related characteristics. However, the finding may also relate to the fact that the oldest cohorts are relatively homogeneous in terms of education and, thus, other indicators of socioeconomic position may be more suitable in identifying disadvantaged population subgroups among these cohorts (2,10). Moreover, previous studies suggest that among adults in general, overall mortality disparities are greater or have increased to a greater extent in terms of occupational social class (11) and income (12,13) than education. Among the Finnish cohort of nonagenarians (9), occupational social class was a strong predictor of dementia mortality with a 3-fold hazard of dementia death among the unskilled manual workers compared to upper non-manuals. Personal income in midlife was not related to dementia mortality among a cohort of Norwegian men (14). To our knowledge, no previous study has assessed

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inequalities in dementia mortality by household income, a socioeconomic indicator that is more directly related to material resources available to the individual and that more rigorously captures the living conditions of the most disadvantaged population subgroups.

This study contributes to the existing knowledge by assessing socioeconomic inequalities in dementia mortality using multiple indicators of socioeconomic position, including education, occupational social class and household income. More specifically, the aims of the study were to 1) investigate the magnitude of socioeconomic inequalities in dementia mortality in relation to age, and compare the patterns to those in mortality from all other causes of death, 2) to assess the contribution of dementia to the socioeconomic inequalities in overall mortality at older ages, and 3) to assess whether education, occupational social class and household income are independently related to dementia mortality once the other indicators are taken into account. This was because different indicators of socioeconomic position are correlated but each of them may have independent associations with mortality. In order to capture potential mediating pathways, we estimated models adjusted for marital status and various chronic health conditions. We used longitudinal registry data on a large population-based sample, which permits a 15-year follow-up of dementia-related deaths with no attrition or recall bias. All indicators of socioeconomic position were measured in midlife in order to avoid selection to socioeconomic groups on the basis of cognitive decline.

Methods

Sample

We used an 11% random sample of the Finnish population in 1987–2007 drawn from the Statistics Finland population register, which covers all permanent residents. Statistics Finland linked the sample with information from various administrative registers including the national Death Register and healthcare registers using unique personal identification numbers assigned to all permanent residents.

In the present study, we included men and women aged 70–87 at the end of 2000. For these cohorts, midlife socioeconomic characteristics could be identified using information from the Population Censuses

conducted in 1970, 1975, 1980 and 1985. Individuals with missing census information due to residing outside of Finland (n=920) and those with missing household income information due to institutional residence (n=401) were excluded. 7 individuals emigrated during the first year of follow-up and thus were excluded from the analyses. The analytic sample consisted of 54,964 individuals.

Mortality data

Dates and causes of death were obtained from the Death Register. Dementia-related deaths were identified using the International Classification of Diseases 10th revision (ICD-10) codes F00–03 and G30 as the underlying or any of the three contributory causes of death reported on the death certificate. We identified 11,395 persons who died from dementia and 30,637 persons who died from other causes during the follow-up in 2001–2016.

Indicators of socioeconomic position

The information of all indicators of socioeconomic position was derived from the quinquennial population censuses of 1970–1985. A particular census year was chosen on the basis of the study subject's age so that the indicators were measured at around the age of 55 (range 53–57) for all. Education was indicated as the highest achieved qualification, categorised as tertiary (generally 13+ years of education; International Standard Classification of Education ISCED-1997 codes 5–6), secondary (10–12 years, ISCED 3–4), and basic education (9 years, ISCED 0–2) or education unknown. Occupational social class comprised five groups, classified as white collar, manual, self-employed farmer, other self-employed, and unknown. For non-employed individuals in the census year, we tracked information from previous years. Household income indicated the taxable annual income of all household members. This includes all income received in money or monetary benefit subject to tax, therefore excluding tax-free income transfers such as child benefit, housing allowance and social assistance. The information was obtained from the Finnish Tax Administration and the Social Insurance Institution of Finland. We adjusted for household composition

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using the OECD-modified equivalence scale (15). Income quintiles were formed based on the household income distribution in the population census year.

Covariates

The analyses incorporated information of economic activity measured from the census year because being out of the labour market may indicate poor health and affect dementia risk independently but also lead to reduced household income. Economic activity was classified as being in the labour force, retired and other inactive. Marital status was measured at baseline (the end of 2000), classified as married, divorced, widowed and never married. Baseline chronic health conditions included indicators of vascular and lifestyle risk factors for dementia (16), and were identified from health registers in the five-year period before the baseline, covering 1996–2000. We used the diagnostic records of the hospital discharge register and patient censuses of the National Institute for Health and Welfare, and the records of prescription medicine purchases and of entitlement to special reimbursement for the medication expenses for certain chronic diseases maintained by the Social Insurance Institution of Finland. We included indicators for alcoholrelated diseases and accidental poisoning by alcohol (ICD-10 codes F10–19, G31.2, G40.51, G62.1, G72.1, I42.6, K29.2, K70, K86.0, O35.4, X45), asthma and other chronic obstructive pulmonary disease (COPD) (ICD-10 codes J43-46, Finnish disease category code 203), diabetes (ICD-10 codes E10-14, Anatomical Therapeutic Chemical (ATC) codes A10, Finnish disease category code 103), heart disease (ICD-10 codes 100-09 and 120-52, Finnish disease category codes 201, 206 and 207) and stroke (ICD-10 codes 160-66 and G45). To account for potential regional variance in socioeconomic characteristics and mortality, we included dummies for region of residence (Western Finland, Helsinki capital region, rest of Southern Finland, Eastern Finland, and Lapland). The variable accounting for the degree of urbanisation of the municipality of residence was based on the proportion of population living in urban settlements and the population of the largest urban settlement in the municipality (urban, semi-urban and rural).

Statistical analyses

We followed the study population for dementia mortality from 1 January 2001 until 31 December 2016. Individuals were censored on the date of death, the end of the year preceding emigration, or at the end of 2016, whichever came first.

For descriptive statistics, we calculated age-adjusted dementia mortality rates per 10,000 person-years by indicators of socioeconomic position, economic activity, marital status and chronic health conditions. In order to assess the magnitude of socioeconomic inequalities in relation to age, we estimated Kaplan–Meier survival functions by education, occupational social class and household income. In these analyses, we contrasted the survival functions of the highest and lowest education groups, white-collar employees and manual workers and the highest and lowest household income quintiles. The equality of survival functions was tested using log-rank tests. For the comparison between dementia mortality and the more general mortality patterns, separate Kaplan-Meier survival functions were estimated for mortality from all other causes of death.

To assess the contribution of dementia mortality to socioeconomic differences in overall mortality, we calculated absolute rate differences in dementia and total mortality between socioeconomic groups (basic vs. tertiary education, manual vs. white-collar occupational social class, lowest vs. highest household income quintile). The contribution was determined by the rate difference in dementia mortality as a percentage of the rate difference in total mortality. The rate differences by indicators of socioeconomic position and age are shown in Supplementary Table 1.

To estimate the independent associations between each indicator of socioeconomic position and dementia mortality, we used Cox regression models. Attained age in years was used as the time scale, and thus all analyses adjusted for the confounding effect of age (17). We first estimated crude associations between each indicator and dementia mortality, adjusting for calendar year dummies, gender, region of residence and the degree of urbanisation (model 1). Model 2 included education, occupational social class and household

income as covariates, thus showing mutually adjusted associations. Midlife economic activity was adjusted for in model 3. We further adjusted for baseline marital status and chronic health conditions in model 4 to assess the extent to which these factors attenuated the relative hazard attached to each socioeconomic indicator.

We tested for interactions between gender and each socioeconomic indicator using likelihood ratio test. Interactions were statistically nonsignificant (p>0.05), and thus we conducted all analyses for men and women combined. We also tested for interactions of all pairwise combinations of the socioeconomic indicators, adjusting for the covariates of model 1. These interactions were all statistically non-significant (p>0.05). All analyses were performed using Stata 15.1 (18).

Patient and public involvement

No patients were involved in setting the research question or the outcome measures, nor were they involved in developing plans for design or implementation of the study. No patients were asked to advise on interpretation or writing up of results. There are no plans to disseminate the results of the research to study participants or the relevant patient community.

Results

Table 1 shows the distribution of the study population by indicators of midlife socioeconomic position, economic activity and baseline characteristics. The vast majority of individuals (77.2%) had no higher than basic education, and manual employees formed the largest occupational social class (43.6%). Higher household income quintiles were over-represented among the study population due to greater mortality of the lower income groups between the time of measurement of midlife income and the baseline. During the 528 387 person-years at risk 11 395 individuals died from dementia, the average age-adjusted dementia mortality rate being 191.2 and 228.1 per 10,000 person-years among men and women, respectively. The rate was higher for those with lower education, occupational social class and household income, and also for the non-married and people with chronic health conditions apart from asthma and other COPD.

[Insert Table 1 about here]

Kaplan–Meier survival functions in Figure 1 show that dementia mortality differed by all indicators of socioeconomic position (log rank test, p<0.001 for each indicator), and that the age patterns differed between the indicators. The inequalities emerged at an earlier age when socioeconomic position was measured in terms of household income (Panel C) compared to education (Panel A) and occupational social class (Panel B). At the oldest old ages, by contrast, the differences were more pronounced when socioeconomic position was measured in terms of education and occupational social class. Nevertheless, inequalities in dementia mortality emerged substantially later in life compared to mortality from all other causes. Socioeconomic inequalities in mortality from other causes diminished after the age of 95, whereas inequalities in dementia mortality in terms of education persisted to the oldest old age and even increased after the age of 95.

[Insert Figure 1 about here]

Table 2 shows that dementia contributed to 25–30% of educational and household income differences in overall mortality at the age of 70+. Dementia contributed less to occupational social class differences (12%). The contribution of dementia to the excess mortality in the low educational and household income groups increased substantially with age.

[Insert Table 2 about here]

All indicators of midlife socioeconomic position were associated with dementia mortality in Cox regression models (Table 3, model 1). The associations were strongest for basic education (hazard ratio [HR]=1.23, 95% CI 1.15–1.32), unknown occupational social class (HR=1.20, 1.00-1.44), and the lowest household income quintile (HR=1.28, 1.20-1.35). Mutual adjustment of socioeconomic indicators in model 2 attenuated educational differences by about 40%, and unknown occupational social class (HR=1.06, 1.01-1.11) and three lowest household income quintiles (for the lowest quintile HR=1.24, 1.16-1.32) all

predicted dementia mortality independently of each other. Adjustment for midlife economic activity in model 3 attenuated the excess hazard particularly of the lower household income quintiles. Adjustment for baseline marital status and chronic health conditions in model 4 contributed to a small change in the estimates, the attenuation being largest for the lowest household income quintile. In this full model, basic education increased the hazard of dementia death by 14% (1.05-1.22), manual occupational social class by 5% (1.00-1.11) and the two lowest household income quintiles by 7-13% (HR=1.07, 1.00-1.14 to HR=1.13, 1.06-1.21).

[Insert Table 3 about here]

Discussion

Main findings and their interpretation

In this study we have shown that dementia mortality at older ages is socioeconomically patterned. People with lower education, occupational social class and household income have a higher risk of dementia death compared to those with higher socioeconomic position. These results add to the literature on socioeconomic inequalities in old-age mortality, which have previously shown a socioeconomic pattern in many other specific causes of death such as cardiovascular diseases, COPD and cancer (1). Our results indicate, moreover, that dementia is an important factor in overall socioeconomic inequalities in old-age mortality, contributing to 25–30% of educational and household income differences in total mortality among the population aged 70 and over. The contribution of dementia to overall socioeconomic inequalities in mortality with age, which relates to the fact that the proportion of deaths attributable to dementia also increases with age (19).

A major difference in the patterns between dementia morality and mortality from all other causes of death was that socioeconomic inequalities in dementia mortality emerged later, were smaller and persisted in the same magnitude to the oldest old ages. Inequalities in mortality from other causes of death, instead, tended to diminish after the age of 95. The attenuation of socioeconomic inequalities with age is a general finding

(1,2), and may partly relate to selective survival, suggesting that people who survive to very old age have more similar health profiles across socioeconomic groups. Our results show, however, that even among people who survive to the oldest old age, socioeconomic groups differ in neurological health. This is a novel finding in that previous studies have identified consistent socioeconomic inequalities in dementia mortality only among the younger old (7,8) but the results have been mixed for the oldest old (8,9). Participation bias may at least partly explain the differences in findings; people of older age, lower socioeconomic position and health problems are less likely to participate in surveys and studies involving health examinations. Our study employed register data on a population-based cohort and thus is not affected by participation or attrition biases.

The age patterns in dementia mortality differed between indicators of socioeconomic position: while educational and occupational social class differences were more pronounced among the oldest old, the differences among the younger old were largest when socioeconomic position was measured in terms of household income. The lowest midlife household income quintiles represent the most disadvantaged population groups with multiple dementia risk factors. A low household income may be accompanied by impoverished living conditions and greater psychosocial stress, increasing the risk of chronic diseases directly or through less favourable health behaviours. Our findings show that the higher dementia mortality of the lowest midlife household income quintiles was strongly related to greater morbidity and early retirement of these groups. We cannot rule out the possibility, however, that people who died from dementia at younger old ages experienced cognitive decline already in midlife to the extent that affected their labour market participation and household income.

Education, in turn, may have particular benefits above and beyond physical health factors among the population surviving to the oldest old age. Our results show widening educational differences in dementia mortality after the age of 95, and the association was not related to chronic health conditions or marital status at baseline. Education is a well-established predictor of dementia incidence (20), although the exact mechanisms are still not known. Brain autopsy studies indicate, in line with the cognitive reserve hypothesis

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(21), that education is not associated with the burden of neuropathology at death but higher education enables individuals to compensate longer for the neuropathological changes before developing clinical symptoms of dementia (22). Thus, it is possible that the educational differences in dementia mortality we found in our study are due to competing risks; people with higher education died from other causes before they reached the phase of clinical dementia or died from other causes before dementia progressed to death. However, the empirical evidence for the cognitive reserve hypothesis remains open to debate. For example, multiple studies have not identified educational differences in survival time after dementia onset (23), which is among the key hypotheses in the cognitive reserve model (24). Therefore, it is plausible that higher education truly enhances brain health and protects against the development of neurodegenerative disorders. We used a unique population-representative sample of older adults in Finland with 11,395 dementia deaths identified from the National Death Register. The register-based sample was not affected by participation or attrition bias, which are common limitations of many cohort designs, particularly among the older population. The population register encompasses rich information on demographic and socioeconomic characteristics of individuals over the life course, and is not subject to bias from individuals' self-reports or recollection.

Despite the rich register data, our study also has some limitations. First, we could only identify cases that have been recorded on the death certificate. To minimise any bias arising from potential underreporting of dementia as the underlying cause of death, we applied the multiple-cause approach and included also cases where dementia was recorded as any of the three contributory causes (25). According to a validation study for identifying dementia and Alzheimer's disease in the Finnish national registers, the documentation of dementia as the cause of death has improved since the late 1990s, and the specificity is particularly high (26). Furthermore, we ran sensitivity analyses with interaction with calendar year, and found that the associations between the indicators of socioeconomic position and dementia mortality did not vary in time. Therefore, we believe our results are not biased by possible changes in documentation practices.

Second, the causal relationship between socioeconomic position and dementia is difficult to establish in observational studies. We therefore measured all socioeconomic characteristics 15–30 years before the mortality follow-up, and it is thus very unlikely that any symptoms of dementia affected the midlife socioeconomic attainment of individuals. Nevertheless, we cannot exclude the possibility that early cognitive decline may have affected midlife socioeconomic position, especially measured in term of occupational social class and household income.

Conclusions

This study provides new insight into the socioeconomic inequalities in old-age mortality by showing a consistent socioeconomic pattern in dementia mortality that persists to the oldest old ages. Low education, occupational social class and household income were all associated with higher risk of dementia death, although the socioeconomic differences emerged later and were smaller than in mortality from other causes. Household income differences in dementia mortality were more pronounced among the younger old, and the associations were largely attributable to other chronic health conditions such as diabetes and stroke. Educational inequalities, by contrast, were independent of chronic health conditions and became more pronounced at the oldest old age where mortality inequalities generally begin to attenuate. The findings suggest that dementia contributes to socioeconomic inequalities in overall mortality at older ages and, thus, dementia prevention is important also from the point of view of socioeconomic inequalities in mortality.

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Footnotes

Contributors: All authors participated in designing the study, generating hypotheses, interpreting the data and critically revised the manuscript for important intellectual content. KK analysed the data, conducted the literature review and wrote the first draft of the manuscript.

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Competing interests: None declared.

Data sharing statement: Statistics Finland, the National Institute for Health and Welfare and the Social Insurance Institution of Finland have collected and own the data. Due to data protection regulations, the authors are not allowed to make the data available to third parties. Researchers can apply for data access by contacting the register-holding institutions: Statistics Finland (http://stat.fi/index_en.html); National Institute for Health and Welfare (https://thl.fi/en); Social Insurance Institution of Finland (https://www.kela.fi/web/en).

Ethics approval: The study has been approved by Statistics Finland Board of Ethics (permit TK-53-339-13). The data were collected for routine administrative registration purposes and, therefore, informed consent of the participants was not obtained. These register data can be used for scientific purposes under the Personal Data Act and the Statistics Act. Statistics Finland anonymised the data prior to providing them to researchers. **Table 1.** Distribution of the study population, dementia deaths and age-adjusted dementia mortality rates (per 10,000 person-years) by indicators of socioeconomic position and other characteristics, Finnish men and women in 2001–2016

| | | | Dementia deaths | | | |
|---------------------------|------------|------|-----------------|-------|-------------|--|
| | N | % | n | Rate | 95% C | |
| Mean age at baseline (SD) | 76.4 (4.8) | | | | | |
| Gender | | | | | | |
| Men | 20100 | 36.6 | 3409 | 191.2 | 184.9–197.8 | |
| Women | 34864 | 63.4 | 7986 | 228.1 | 223.1–233.2 | |
| Education | | | | | | |
| Tertiary | 5445 | 9.9 | 1014 | 178.7 | 168.0–190.1 | |
| Secondary | 7074 | 12.9 | 1446 | 200.3 | 190.2–210.9 | |
| Basic | 42445 | 77.2 | 8936 | 223.7 | 219.1–228.4 | |
| Occupational social class | | | | | | |
| White-collar | 17015 | 31.0 | 3524 | 200.1 | 193.6–206.8 | |
| Manual | 23951 | 43.6 | 4882 | 216.8 | 210.8–223.0 | |
| Farmer | 10204 | 18.6 | 2211 | 242.0 | 232.1–252.3 | |
| Other self-employed | 3271 | 6.0 | 657 | 208.6 | 193.2–225.1 | |
| Unknown | 523 | 1.0 | 121 | 289.2 | 242.0-345.6 | |
| Household income | | | | | | |
| Highest quintile | 13667 | 24.9 | 2715 | 194.0 | 186.9–201.5 | |
| 2nd | 10522 | 19.1 | 2098 | 201.9 | 193.5-210.8 | |
| 3rd | 10110 | 18.4 | 2114 | 217.5 | 208.4–227.0 | |
| 4th | 10292 | 18.7 | 2183 | 224.3 | 215.1-233.9 | |
| Lowest quintile | 10373 | 18.9 | 2285 | 253.8 | 243.6-264.4 | |
| Economic activity | | | | | | |
| Active | 37266 | 67.8 | 7585 | 208.1 | 203.4-212.8 | |
| Retired | 8881 | 16.2 | 1742 | 219.2 | 209.1-229.7 | |
| Other inactive | 8817 | 16.0 | 2068 | 245.2 | 234.9–256.0 | |
| Marital status | | | | | | |
| Married | 24789 | 45.1 | 4471 | 175.5 | 170.4–180.7 | |
| Divorced | 4056 | 7.4 | 797 | 204.6 | 190.8-219.3 | |
| Widowed | 20997 | 38.2 | 5000 | 265.8 | 258.5-273. | |
| Never married | 5122 | 9.3 | 1127 | 242.3 | 228.6-256. | |
| | | | | | | |
| Chronic health conditions | | | | | 2004 | |
| Alcohol-related diseases | 308 | 0.6 | 68 | 329.9 | 260.1-418. | |
| Asthma and COPD | 4510 | 8.2 | 789 | 206.9 | 192.9–221. | |
| Diabetes | 6714 | 12.2 | 1240 | 243.7 | 230.5–257.0 | |
| Heart disease | 18094 | 32.9 | 3562 | 244.5 | 236.6–252.6 | |

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| | Stroke | 3180 | 5.8 | 685 | 328.3 | 304.6-353.8 |
|--------|-------------------------------------|-------|-------|-------|-------|-------------|
| | Region of residence | | | | | |
| | • | | | | | |
| | Western Finland | 25078 | 45.6 | 4979 | 206.0 | 200.3–211.8 |
| | Helsinki capital region | 7449 | 13.6 | 1582 | 218.0 | 207.5–229.0 |
| 0 | Rest of Southern Finland | 12056 | 21.9 | 2464 | 213.8 | 205.6–222.5 |
| 1 | Eastern Finland | 8458 | 15.4 | 1916 | 238.9 | 228.4–249.8 |
| 2 | Lapland | 1923 | 3.5 | 454 | 243.6 | 222.2–267.1 |
| 3 | | | | | | |
| 4 5 | Degree of urbanisation | | | | | |
| 5 6 | Urban | 29853 | 51.0 | 6401 | 221.3 | 215.9–226.8 |
| 7 | Semi-urban | 9285 | 17.7 | 1831 | 205.4 | 196.2–215.0 |
| 8 | Rural | 15826 | 31.3 | 3163 | 210.9 | 203.7–218.4 |
| 9 | Total | 54964 | 100.0 | 11395 | 215.7 | 211.7–219.7 |
| 0 | Alelene dettere CL seufisiones inte | | | | | |

Abbreviations: CI, confidence intervals; COPD, chronic obstructive pulmonary diseases

Table 2. The contribution (%) of dementia to socioeconomic differences in total mortality by indicator ofsocioeconomic position and age, Finnish men and women in 2001–2016

| | | | | All ages |
|--|-------|-------|------|----------|
| | 70-79 | 80-89 | 90+ | 70+ |
| Education ^a | 8.6 | 31.7 | 52.9 | 29.9 |
| Occupational social class ^b | 6.4 | 19.5 | 19.8 | 12.0 |
| Household income ^c | 13.3 | 22.2 | 35.0 | 24.0 |

^a Tertiary vs. basic education

^b White-collar vs. manual occupational social class

^c Highest vs. lowest household income quintiles

Table 2. Hazard ratios and 95% confidence intervals for dementia mortality by indicators of socioeconomicposition, Finnish men and women in 2001–2016, n=54,964

| Indicator of socioeconomic | Model 1ª | | N | Model 2 ^b | | Model 3 ^c | | Model 4 ^d | |
|----------------------------|----------|-----------|------|----------------------|------|----------------------|------|----------------------|--|
| position | HR | 95% CI | HR | 95% CI | HR | 95% CI | HR | 95% C | |
| Education | | | | | | | | | |
| Tertiary | 1.00 | | 1.00 | | 1.00 | | 1.00 | | |
| Secondary | 1.14 | 1.05-1.23 | 1.08 | 0.99–1.17 | 1.08 | 0.99–1.17 | 1.08 | 0.99–1.1 | |
| Basic | 1.23 | 1.15–1.32 | 1.14 | 1.06–1.23 | 1.14 | 1.05–1.22 | 1.14 | 1.05–1.2 | |
| Occupational social class | | | | | | | | | |
| White collar | 1.00 | | 1.00 | | 1.00 | | 1.00 | | |
| Manual | 1.14 | 1.09–1.20 | 1.06 | 1.01-1.11 | 1.05 | 1.00-1.11 | 1.05 | 1.00-1.1 | |
| Farmer | 1.08 | 1.02–1.15 | 0.96 | 0.90–1.03 | 0.97 | 0.91–1.04 | 0.98 | 0.92–1.0 | |
| Other self-employed | 1.05 | 0.96–1.14 | 0.98 | 0.90–1.07 | 0.99 | 0.91–1.08 | 1.00 | 0.92–1.0 | |
| Unknown | 1.20 | 1.00–1.44 | 1.04 | 0.87–1.25 | 0.94 | 0.78–1.14 | 0.94 | 0.78–1.1 | |
| Household income | | | | | | | | | |
| Highest quintile | 1.00 | | 1.00 | | 1.00 | | 1.00 | | |
| 2nd | 1.08 | 1.02-1.14 | 1.04 | 0.98–1.10 | 1.03 | 0.98–1.10 | 1.02 | 0.96–1.0 | |
| 3rd | 1.13 | 1.07-1.20 | 1.08 | 1.02-1.15 | 1.07 | 1.00-1.14 | 1.05 | 0.99–1.1 | |
| 4th | 1.17 | 1.10-1.24 | 1.13 | 1.06-1.20 | 1.10 | 1.03–1.17 | 1.07 | 1.00-1.1 | |
| | 1.28 | 1.20–1.35 | 1.24 | 1.16–1.32 | 1.18 | 1.10–1.26 | 1.13 | 1.06–1.2 | |

^aModel 1: each indicator of socioeconomic position separately

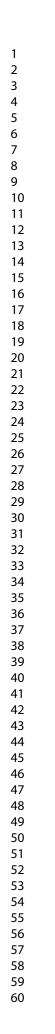
^bModel 2: indicators of socioeconomic position mutually adjusted

°Model 3: model 2 + midlife economic activity

^dModel 4: model 3 + baseline marital status and chronic health conditions (alcohol-related diseases, asthma and chronic obstructive pulmonary disease, diabetes, heart disease and stroke)

 Figure 1. Kaplan–Meier survival probabilities for dementia mortality and mortality from all other causes of death by a) education, b) occupational social class and c) household income quintile (Q1=highest, Q5=lowest), Finnish men and women in 2001–2012

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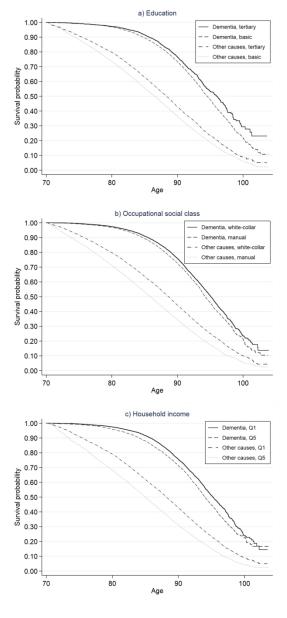


Figure 1. Kaplan–Meier survival probabilities for dementia mortality and mortality from all other causes of death by a) education, b) occupational social class and c) household income quintile (Q1=highest, Q5=lowest), Finnish men and women in 2001–2012

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Supplementary Table 1 Differences in mortality rates (per 10,000 person-years) by cause of death, and the contribution of each cause of death (%) to differences in total mortality by indicator of socioeconomic position and age

| | 70- | -79 | 80- | -89 | 90 |)+ |
|--|-----------------|------------------|-----------------|------------------|-----------------|------------------|
| | Rate difference | Contribution (%) | Rate difference | Contribution (%) | Rate difference | Contribution (%) |
| Education ^a | | | | | | |
| Dementia | 9.1 | 8.6 | 40.4 | 31.7 | 152.4 | 52.9 |
| Other causes | 97.3 | 91.4 | 86.9 | 68.3 | 135.6 | 47.1 |
| Total mortality | 106.4 | 100.0 | 127.2 | 100.0 | 288.0 | 100.0 |
| Occupational social class ^b | | | | | | |
| Dementia | 7.8 | 6.4 | 33.0 | 19.5 | 49.1 | 19.8 |
| Other causes | 114.2 | 93.6 | 136.1 | 80.5 | 199.3 | 80.2 |
| Total mortality | 122.0 | 100.0 | 169.1 | 100.0 | 248.5 | 100.0 |
| Household income ^c | | | | | | |
| Dementia | 23.5 | 13.3 | 49.4 | 22.2 | 127.8 | 35.0 |
| Other causes | 152.9 | 86.7 | 173.3 | 77.8 | 237.4 | 65.0 |
| Total mortality | 176.4 | 100.0 | 222.7 | 100.0 | 365.2 | 100.0 |

^a Tertiary vs. basic education

^b White-collar vs. manual occupational social class

^c Highest vs. lowest household income quintiles

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

| | Item No | Recommendation | Page No | |
|------------------------|---|--|------------|--|
| Title and abstract | 1 | (a) Indicate the study's design with a commonly used term in the title or the | 1 | |
| | | abstract | | |
| | | (b) Provide in the abstract an informative and balanced summary of what was | at was 2-3 | |
| | | done and what was found | | |
| Introduction | | | 1 | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | 4 | |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | 5 | |
| Methods | | | I | |
| Study design | 4 | Present key elements of study design early in the paper | 5-6 | |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of | 5-6 | |
| | | recruitment, exposure, follow-up, and data collection | | |
| Participants | 6 | (a) Give the eligibility criteria, and the sources and methods of selection of | 5-6 | |
| I I I I I | | participants. Describe methods of follow-up | | |
| | | (b) For matched studies, give matching criteria and number of exposed and | | |
| | | unexposed | | |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and | 6-7 | |
| | | effect modifiers. Give diagnostic criteria, if applicable | | |
| Data sources/ | 8* | For each variable of interest, give sources of data and details of methods of | 6-7 | |
| measurement | assessment (measurement). Describe comparability of asses | | | |
| | | there is more than one group | | |
| Bias | 9 | Describe any efforts to address potential sources of bias | 8-9 | |
| Study size | 10 | Explain how the study size was arrived at | 5-6 | |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, | 6-9 | |
| | | describe which groupings were chosen and why | | |
| Statistical methods | 12 | (<i>a</i>) Describe all statistical methods, including those used to control for confounding | 8-9 | |
| | | (b) Describe any methods used to examine subgroups and interactions | 9 | |
| | | (c) Explain how missing data were addressed | 5-6 | |
| | | (d) If applicable, explain how loss to follow-up was addressed | 8 | |
| | | (<i>e</i>) Describe any sensitivity analyses | 13 | |
| Results | | | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially | 9 | |
| 1 articipants | 15 | eligible, examined for eligibility, confirmed eligible, included in the study, | - | |
| | | completing follow-up, and analysed | | |
| | | (b) Give reasons for non-participation at each stage | 9 | |
| | | (c) Consider use of a flow diagram | | |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) | 9 | |
| Descriptive data | 17 | and information on exposures and potential confounders | | |
| | | (b) Indicate number of participants with missing data for each variable of interest | | |
| | | (c) Summarise follow-up time (eg, average and total amount) | | |
| | | (c) Summarise follow up time (cg, average and total amount) | 9 | |

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| Main results | 16 | (<i>a</i>) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | 9-11 |
|------------------|-----|---|-----------|
| | | (b) Report category boundaries when continuous variables were categorized | |
| | | (c) If relevant, consider translating estimates of relative risk into absolute risk for a | |
| | | meaningful time period | |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | 9 |
| Discussion | | | |
| Key results | 18 | Summarise key results with reference to study objectives | 11- 12 |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 13- 14 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 11- 13 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | 13 |
| Other informati | ion | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if | 17 |
| - | | applicable, for the original study on which the present article is based | |

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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Midlife socioeconomic position and old-age dementia mortality: a large prospective register-based study from Finland

Kaarina Korhonen¹, Elina Einiö^{1,2,3}, Taina Leinonen⁴, Lasse Tarkiainen¹, Pekka Martikainen^{1,3,5}

¹ Population Research Unit, Faculty of Social Sciences, University of Helsinki, Helsinki, Finland

² Department of Social Policy, London School of Economics and Political Science, London, United Kingdom

³ Max Planck Institute for Demographic Research, Rostock, Germany

⁴ Finnish Institute of Occupational Health, Helsinki, Finland

⁵ Department of Public Health Sciences, Stockholm University, Stockholm, Sweden

Correspondence to:

Kaarina Korhonen

Faculty of Social Sciences

P.O. Box 18, 00014 University of Helsinki, Finland

+358 50 3199 388

kaarina.korhonen@helsinki.fi

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Abstract

Objectives To assess the association between multiple indicators of socioeconomic position and dementiarelated death, and to estimate the contribution of dementia to socioeconomic differences in overall mortality at older ages.

Design Prospective population-based register study.

Setting Finland.

Participants 11% random sample of the population aged 70–87 resident in Finland at the end of year 2000 (N=54 964).

Main outcome measure Incidence rates, Kaplan-Meier survival probabilities and Cox regression hazard ratios of dementia mortality in 2001–2016 by midlife education, occupational social class and household income measured at ages 53–57 years.

Results During the 528 387 person-years at risk, 11 395 individuals died from dementia (215.7 per 10 000 person-years). Lower midlife education, occupational social class and household income were associated with higher dementia mortality, and the differences persisted to the oldest old ages. Compared to mortality from all other causes, however, the socioeconomic differences emerged later. Dementia accounted for 28% of the difference between low and high education groups in overall mortality at age 70+, and for 21% of the difference between lowest and highest household income quintiles. All indicators of socioeconomic position were independently associated with dementia mortality, low household income being the strongest independent predictor (HR=1.24, 95% confidence interval 1.16–1.32), followed by basic education (HR=1.14, 1.06–1.23). Manual occupational social class was related to a 6% higher hazard (HR=1.06, 1.01–1.11) compared to non-manual social class. Adjustment for midlife economic activity, baseline marital status and chronic health conditions attenuated the excess hazard of low midlife household income, although significant effects remained.

Conclusion Several indicators of socioeconomic position predict dementia mortality independently and socioeconomic inequalities persist into the oldest old ages. The results demonstrate that dementia is among the most important contributors to socioeconomic inequalities in overall mortality at older ages.

Strengths and limitations of this study

- We used longitudinal registry data that permits a 15-year follow-up of dementia mortality with no attrition or recall bias.
- Dementia is documented in the national death register with high specificity.
- Due to the use of register data, traditional dementia risk factors such as smoking and physical activity could not be measured.
- All indicators of socioeconomic position were measured in midlife in order to avoid selection to socioeconomic groups on the basis of cognitive decline.
- This is the first study to show the contribution of dementia to the socioeconomic inequalities in overall mortality at older ages.

Introduction

Socioeconomic inequality in health and mortality is one of the most consistent findings in the demographic and social epidemiological literature. Lower education, occupational social class and income are strong predictors of all-cause and cause-specific mortality particularly among the working-age population, but inequalities are clear also at older ages.[1–4] Among the ageing population, the key factors affecting morbidity and disability are Alzheimer's disease and other forms of progressive dementia. Globally, an estimated 47 million people lived with dementia in 2015, and the number is projected to triple by 2050.[5] In England and Wales, dementia has already become the leading cause of death.[6] Despite the growing societal impact, however, no comprehensive understanding exists about the socioeconomic patterns of dementia mortality.

Educational inequalities in dementia mortality have previously been reported in studies following individuals from midlife or younger old ages[7,8] but not among the oldest old.[8,9] In a Norwegian health examination study, an educational pattern was present only among cohorts aged below 70 at baseline but not among those aged 70 and over.[8] Similarly, among a Finnish cohort aged 90 and over, no statistically significant educational gradient in dementia mortality emerged.[9] The lack of educational differentials among the oldest old may relate to selective survival. People with lower education experience higher mortality at younger ages, and those who survive to older ages do so because of their better health. Thus, the population surviving to older ages is more homogeneous in terms of health-related characteristics and, as a result, the socioeconomic differences in mortality are diminished. Another possible explanation for the lack of educational gradient in dementia mortality is the fact that the distribution of education in the oldest education, other indicators of socioeconomic position (SEP) may be more suitable for identifying high-risk population subgroups.[2,10] Previous studies suggest that among adults in general, overall mortality disparities are greater or have increased to a greater extent in terms of occupational social class[11] and income[12,13] than education. Among the Finnish cohort of nonagenarians,[9] occupational social class

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was a strong predictor of dementia mortality with a 3-fold hazard of dementia death among the unskilled manual workers compared to upper non-manuals. Personal income in midlife, however, was not related to dementia mortality among a cohort of Norwegian men.[14] To our knowledge, no previous study has assessed inequalities in dementia mortality by household income, a socioeconomic indicator that is more directly related to material resources available to the individual and that more rigorously captures the living conditions of the most disadvantaged population subgroups. A low household income may, in addition to material disadvantage, induce psychosocial stress, increasing the risk of dementia directly or through less favourable health behaviours. Disentangling the contributions of education, occupational social class and household income will thus provide important insights into the potential mechanisms how SEP shapes the risk of dementia death.

This study contributes to the existing knowledge by assessing socioeconomic inequalities in dementia mortality using multiple indicators of SEP, including education, occupational social class and household income. More specifically, the aims of the study were to 1) investigate the magnitude of socioeconomic inequalities in dementia mortality in relation to age, and compare the patterns to those in mortality from all other causes of death, 2) to quantify the contribution of dementia to the socioeconomic inequalities in overall mortality at older ages, and 3) to assess whether education, occupational social class and household income are independently related to dementia mortality once the other indicators are taken into account. This was because different indicators of SEP are correlated but each of them may have independent associations with dementia mortality. We further estimated models adjusting for other risk factors including marital status and various chronic health conditions. We used longitudinal registry data on a large population-based sample, which permits a 15-year follow-up of dementia-related deaths with no attrition or recall bias. All indicators of SEP were measured in midlife in order to avoid selection to socioeconomic groups on the basis of cognitive decline.

Methods

Sample

We used an 11% random sample of the Finnish population in 1987–2007 drawn from the Statistics Finland population register, which covers all permanent residents. Statistics Finland linked the sample with information from various administrative registers including the national Death Register and healthcare registers using unique personal identification numbers assigned to all permanent residents.

In the present study, we included men and women aged 70–87 at the end of year 2000. For these cohorts, midlife socioeconomic characteristics could be identified using information from the Population Censuses conducted in 1970, 1975, 1980 and 1985. Individuals with missing census information due to residing outside of Finland (n=920) and those with missing household income information due to not being part of the household population in the census year (n=401) were excluded. 7 individuals emigrated during the first year of follow-up and thus were excluded from the analyses. The analytic sample consisted of 54 964 individuals.

Mortality data

Dates and causes of death were obtained from the Death Register. Dementia-related deaths were identified using the International Classification of Diseases 10th revision (ICD-10) codes F00–03 and G30 as the underlying or any of the three contributory causes of death reported on the death certificate. We identified 11 395 persons who died from dementia and 30 637 persons who died from other causes during the follow-up in 2001–2016.

Indicators of socioeconomic position

The information of all indicators of SEP was derived from the quinquennial population censuses of 1970– 1985. A particular census year was chosen on the basis of the study subject's age so that the indicators were measured at around the age of 55 (range 53–57) for all. Education was indicated as the highest achieved qualification, categorised as tertiary (generally 13+ years of education; International Standard Classification of Education ISCED-1997 codes 5–6), secondary (10–12 years, ISCED 3–4), and basic education/no qualifications (9 years, ISCED 0–2). Occupational social class comprised five groups,

classified as non-manual, manual, self-employed farmer, other self-employed, and no occupation/unknown. Information of occupational social class in the census year was lacking for 10 465 individuals due to nonemployment at that time. For 9942 individuals, the information could nevertheless be obtained from previous years in which the individuals were employed. Household income indicated the taxable annual income of all household members, including all income received in money or monetary benefit subject to tax. The information was obtained from the Finnish Tax Administration and the Social Insurance Institution of Finland. We adjusted for household composition using the OECD-modified equivalence scale.[15] Income quintiles were formed based on the household income distribution in the population aged 15 and over in the census year.

Covariates

The analyses incorporated information of economic activity measured from the census year because being out of the labour market may indicate poor health and affect dementia risk independently but also lead to reduced household income. Economic activity was classified as being in the labour force, retired and other inactive. Marital status was measured at baseline (the end of 2000), classified as married, divorced, widowed and never married. Baseline chronic health conditions included indicators of vascular and lifestyle risk factors for dementia,[16] and were identified from health registers in the five-year period before the baseline, covering 1996–2000. We used the diagnostic records of the hospital discharge register and patient censuses of the National Institute for Health and Welfare, and the records of prescription medicine purchases and of entitlement to special reimbursement for the medication expenses for certain chronic diseases maintained by the Social Insurance Institution of Finland. We included indicators for alcoholrelated diseases and accidental poisoning by alcohol, asthma and other chronic obstructive pulmonary disease (COPD), diabetes, heart disease and stroke (for coding see Supplementary Table 1). To account for potential regional variance in socioeconomic characteristics and mortality, we included dummies for region of residence (Western Finland, Helsinki capital region, rest of Southern Finland, Eastern Finland, and Lapland) and the degree of urbanisation of the municipality of residence, a variable based on the proportion of population living in urban settlements and the population of the largest urban settlement in the municipality (urban, semi-urban and rural).

Statistical analyses

We followed the study population for dementia mortality from 1 January 2001 until 31 December 2016. Individuals were censored on the date of death, the end of the year preceding emigration, or at the end of 2016, whichever came first.

For descriptive statistics, we calculated age-adjusted dementia mortality rates per 10 000 person-years at risk by indicators of SEP and the covariates. In order to assess the magnitude of socioeconomic inequalities in relation to age, we estimated Kaplan–Meier survival functions by education, occupational social class and household income. In these analyses, we contrasted the survival functions of the highest and lowest education groups, non-manual and manual employees and the highest and lowest household income quintiles. The equality of survival functions was tested using log-rank tests. For the comparison between dementia mortality and the more general mortality patterns, separate Kaplan-Meier survival functions were estimated for mortality from all other causes of death. We also estimated hazard ratios and their 95% confidence intervals for low versus high socioeconomic groups at the age of 70–79, 80–89 and 90 years and over.

To quantify the contribution of dementia to socioeconomic differences in overall mortality at older ages, we calculated absolute rate differences in mortality between socioeconomic groups (basic vs. tertiary education, manual vs. non-manual occupational social class, lowest vs. highest household income quintile) by cause of death. The contribution was determined by the rate difference in dementia mortality as a percentage of the rate difference in total mortality. Because the level of dementia mortality increases substantially with age, we also assessed age-specific contributions (at the age of 70–79, 80–89 and 90+). To estimate the independent associations between each indicator of SEP and dementia mortality, we used Cox regression models. Attained age in years was used as the time scale, and thus all analyses adjusted for

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the confounding effect of age.[17] We first estimated crude associations between each indicator and dementia mortality, adjusting for calendar year dummies, gender, region of residence and the degree of urbanisation (model 1). Model 2 included education, occupational social class and household income as covariates, thus showing mutually adjusted associations. Midlife economic activity was adjusted for in model 3. We further adjusted for baseline marital status and chronic health conditions in model 4 to assess the extent to which these factors attenuated the relative hazard attached to each socioeconomic indicator.

We tested for interactions between gender and each socioeconomic indicator using likelihood ratio test. Interactions were statistically nonsignificant (p>0.05), and thus we conducted all analyses for men and women combined. We also tested for interactions of all pairwise combinations of the socioeconomic indicators, adjusting for the covariates of model 1. These interactions were all statistically nonsignificant (p>0.05). All analyses were performed using Stata 15.1.[18]

Patient and public involvement

No patients were involved in setting the research question or the outcome measures, nor were they involved in developing plans for design or implementation of the study. No patients were asked to advise on interpretation or writing up of results. There are no plans to disseminate the results of the research to study participants or the relevant patient community.

Results

Table 1 shows the distribution of the study population by indicators of midlife SEP, economic activity and baseline characteristics. The vast majority of individuals (77.2%) had no higher than basic education, and manual employees formed the largest occupational social class (43.6%). Higher household income quintiles were over-represented among the study population due to the higher incomes of the middle aged compared to the rest of the population and also partly because of greater mortality of the lower income groups between the time of measurement of midlife income and the baseline. During the 528 387 person-years at risk 11 395 individuals died from dementia, the average age-adjusted dementia mortality rate being 223.1 and

210.8 per 10 000 person-years among men and women, respectively. The rate was higher for those with lower education, occupational social class and household income, and also for the non-married and people with chronic health conditions apart from asthma and other COPD.

Kaplan–Meier survival functions in Figure 1 show that dementia mortality differed by all indicators of SEP (log rank test, p<0.001 for each indicator), and that the age patterns differed between the indicators (for 95% confidence intervals see Supplementary Table 2). The inequalities emerged at an earlier age when SEP was measured in terms of household income (Panel c) compared to education (Panel a) and occupational social class (Panel b). At the age of 90 years and above, by contrast, the differences were more pronounced when SEP was measured in terms of education. Nevertheless, inequalities in dementia mortality emerged substantially later in life compared to mortality from all other causes. Hazard ratios in Table 2 show that relative inequalities in mortality tended to diminish with age for all indicators of SEP regardless of cause of death. However, education differences in dementia mortality showed a different age pattern in that the point estimates indicated stable inequality with age.

Overall, dementia contributed to 28.1% of educational and 20.9% of household income differences in total mortality at the age of 70 and over (Table 2). The contribution to occupational social class differences was somewhat smaller (16.7%). The contribution of dementia to socioeconomic inequalities substantially increased from the age of 70–79 to 90 years and over.

Cox regression models in Table 3 show adjusted hazard ratios (HR) for dementia mortality across all ages from 70 years and over. Adjusted for calendar year, gender, region of residence and the degree of urbanisation in model 1, the associations were strongest for basic education (HR=1.23, 95% CI 1.15–1.32), unknown occupational social class (HR=1.20, 1.00-1.44), and the lowest household income quintile (HR=1.28, 1.20-1.35). Mutual adjustment of socioeconomic indicators in model 2 attenuated educational differences by about 40%, and unknown occupational social class (HR=1.06, 1.01-1.11) and three lowest household

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income quintiles (for the lowest quintile HR=1.24, 1.16–1.32) all predicted dementia mortality independently of each other. Adjustment for midlife economic activity in model 3 attenuated the excess hazard particularly of the lower household income quintiles. Adjustment for baseline marital status and chronic health conditions in model 4 contributed to a small change in the estimates, the attenuation being largest for the lowest household income quintile. In this full model, basic education increased the hazard of dementia death by 14% (1.05–1.22), manual occupational social class by 5% (1.00–1.11) and the two lowest household income quintiles by 7–13% (HR=1.07, 1.00–1.14 to HR=1.13, 1.06–1.21).

Discussion

Main findings and their interpretation

In this study we have shown that dementia mortality at older ages is socioeconomically patterned in terms of multiple indicators of SEP. People with lower education, occupational social class and household income have a higher risk of dementia death compared to those with higher SEP. These results add to the literature on socioeconomic inequalities in old-age mortality, which has previously shown a socioeconomic pattern in many other specific causes of death such as cardiovascular diseases, COPD and cancer.[1] Our results indicate, moreover, that dementia is an important factor in overall socioeconomic inequalities in old-age mortality, contributing to 21–28% of household income and educational differences in total mortality among the population aged 70 and over. The contribution of dementia to overall socioeconomic inequalities in mortality increased substantially with age, which relates to the increasing proportion of deaths attributable to dementia with advancing age.[19]

A major difference in the patterns between dementia morality and mortality from all other causes of death was that socioeconomic inequalities in dementia mortality emerged later and the inequalities in dementia mortality between high and low education groups persisted in the same magnitude to the oldest old ages (90 years and above). By contrast, inequalities in mortality from other causes of death tended to diminish with age. The attenuation of socioeconomic inequalities with age is a general finding,[1,2] and may partly

relate to selective survival, suggesting that people who survive to very old age have more similar health profiles across socioeconomic groups. Our results show, however, that even among people who survive to the oldest old age, education groups differ in neurological health. This is a novel finding in that previous studies have identified consistent socioeconomic inequalities in dementia mortality only among the younger old[7,8] but the results have been mixed for the oldest old.[8,9] Participation bias may at least partly explain the differences in findings; people of older age, lower SEP and with health problems are less likely to participate in surveys and studies involving health examinations. Our study employed register data on a population-based cohort and thus is not affected by participation or attrition biases.

The age patterns in dementia mortality differed between indicators of SEP: while educational differences were more pronounced among the oldest old (90 years and over), the differences among the younger old (70–79 years) were largest when SEP was measured in terms of household income. The lowest midlife household income quintiles represent the most disadvantaged population groups with potentially multiple dementia risk factors. Impoverished material conditions may affect dementia risk through, for example, psychological stress[20] and health-related behaviours and cardiovascular risk factors.[16] Our findings show that the higher dementia mortality of the lowest household income quintiles was strongly – although not fully – related to greater morbidity and early retirement of these groups. It is also possible that severe health problems that were present already in midlife affected labour market participation and household incomes and thus confounded the association between income and the risk of dementia death. Future studies are needed to establish the causal relationship between these factors using formal mediation analysis techniques.

Education, in turn, may have particular benefits above and beyond physical health factors among the population surviving to the oldest old age. Our results show persistent educational differences in dementia mortality, and the association was not related to chronic health conditions or marital status at baseline. Education is a well-established predictor of dementia incidence,[21] although the exact mechanisms are still not known. Brain autopsy studies indicate, in line with the cognitive reserve hypothesis,[22] that education

is not associated with the burden of neuropathology at death but higher education enables individuals to compensate longer for the neuropathological changes before developing clinical symptoms of dementia.[23] Thus, it is possible that the educational differences in dementia mortality we found in our study are due to competing risks; people with higher education died from other causes before they reached the phase of clinical dementia or died from other causes before dementia progressed to death. However, the empirical evidence for the cognitive reserve hypothesis remains open to debate. For example, several studies have not identified educational differences in survival time after dementia onset,[24] which is among the key hypotheses in the cognitive reserve model.[25] Therefore, it is plausible that higher education enhances brain health and protects against (or postpones) not only the clinical symptoms but also the development of neurodegenerative disorders.

Occupational social class differences in dementia mortality were modest following adjustment for education and household income. In particular, the high hazard among those with no occupation disappeared after these adjustments indicating that this group experienced multiple socioeconomic disadvantages. The results suggest, nevertheless, that higher social class occupations may involve greater cognitive demands and intellectual engagement, and thus enhance cognitive health.[26,27] In contrast, lower class occupations or long periods of economic inactivity due to unemployment or early retirement may reduce opportunities for cognitive investment. Overall, the results of this study suggest that all three indicators of SEP are important factors in bringing about socioeconomic differences in dementia mortality, also influencing inequalities in overall mortality among the older population.

We used a unique population-representative sample of older adults in Finland with 11 395 dementia deaths identified from the National Death Register. The register-based sample was not affected by participation or attrition bias, which are common limitations of many cohort designs, particularly among the older population. The population register encompasses rich information on demographic and socioeconomic characteristics of individuals over the life course, and is not subject to bias from individuals' self-reports or recollection.

Despite the rich register data, our study also has some limitations. First, we could only identify dementia cases that have been recorded on the death certificate. According to a validation study for identifying dementia in the Finnish national registers, the documentation of dementia as the cause of death has improved since the late 1990s, and the specificity is particularly high.[28] To minimise any bias arising from potential underreporting of dementia as the underlying cause of death, we applied the multiple-cause approach and included also cases where dementia was recorded as any of the three contributory causes.[29] Defined this way, we identified 21% of all deaths at the age of 70 and over to be attributable to dementia. This relatively high proportion is in line with that reported in England and Wales, where dementia accounted for 19% of all deaths at the age of 80 and over.[30] Furthermore, we ran sensitivity analyses with interaction with calendar year, and found that the associations between the indicators of SEP and dementia mortality did not vary in time. Therefore, we believe our results are not biased by overreporting or underreporting of dementia as the cause of death or by changes in documentation practices. Second, register data does not cover information of traditional risk factors related to health behaviours such as smoking and physical activity. However, we included indicators of chronic conditions to measure vascular and life style risk factors for dementia.

Third, the information of household income was based on taxable income and the variable thus excludes certain monetary transfers such as housing allowance and social assistance. These means-tested sources of income may be especially relevant for people with health problems and those outside the labour market. This might lead to overestimation of the income effect. Information of disposable income was not available for years 1970–1985, but we carried out a robustness check for the correlation between taxable and disposable household incomes (as continuous variables) using the population aged 15 and over in 1995 and found the correlation to be as high as 0.97. Therefore, it is unlikely that the use of disposable income would change the ranking of individuals in the household income distribution to the extent that it would affect our main findings.

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 Finally, the causal relationship between SEP and dementia is difficult to establish in observational studies. We therefore measured all socioeconomic characteristics 15–30 years before the mortality follow-up, and it is thus very unlikely that any symptoms of dementia affected the midlife socioeconomic attainment of individuals. Nevertheless, we cannot exclude the possibility that early cognitive decline may have affected midlife SEP, especially measured in term of occupational social class and household income. Also, given the small proportion of people with tertiary education in these cohorts (10%), it is possible that this forms a select group with multiple advantages including higher childhood SEP and early cognitive ability.

Conclusions

This study provides new insight into the socioeconomic inequalities in old-age mortality by showing a consistent pattern in dementia mortality by multiple indicators of SEP. Low education, occupational social class and household income were all associated with higher risk of dementia death, although the socioeconomic differences emerged later than in mortality from other causes. Household income differences in dementia mortality were more pronounced among the younger old, and the associations were largely attributable to other chronic health conditions such as diabetes and stroke. Educational inequalities, by contrast, were independent of chronic health conditions and became more pronounced at the oldest old age where mortality inequalities generally begin to attenuate. The results indicate that dementia mortality may be amenable to socioeconomic interventions in midlife. The findings also suggest that dementia contributes to socioeconomic inequalities in overall mortality at older ages and, thus, dementia prevention is important from the point of view of socioeconomic inequalities in total mortality.

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Footnotes

Contributors: KK, EE, TL, LT and PM participated in designing the study, generating hypotheses, interpreting the data and critically revised the manuscript for important intellectual content. KK analysed the data, conducted the literature review and wrote the first draft of the manuscript.

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Competing interests: None declared.

Data sharing statement: Statistics Finland, the National Institute for Health and Welfare and the Social Insurance Institution of Finland have collected and own the data. Due to data protection regulations, the authors are not allowed to make the data available to third parties. Researchers can apply for data access by contacting the register-holding institutions: Statistics Finland (http://stat.fi/index_en.html); National Institute for Health and Welfare (https://thl.fi/en); Social Insurance Institution of Finland (https://www.kela.fi/web/en).

Ethics approval: The study has been approved by Statistics Finland Board of Ethics (permit TK-53-339-13). The data were collected for routine administrative registration purposes and, therefore, informed consent of the participants was not obtained. These register data can be used for scientific purposes under the Personal Data Act and the Statistics Act. Statistics Finland anonymised the data prior to providing them to researchers. Table 1. Distribution of the study population, dementia deaths and age-adjusted dementia mortality rates (per 10 000 person-years) by indicators of midlife socioeconomic position and economic activity and baseline characteristics, Finnish men and women in 2001-2016

| | | | Dementi | a deaths | |
|--|-------|------|---------|----------|-----------|
| | N | % | n | Rate | 95% CI |
| | 76.4 | | | | |
| Mean age at baseline (SD) | (4.8) | | | | |
| Gender | | | | | |
| Men | 20100 | 36.6 | 3409 | 223.1 | 215.6–230 |
| Women | 34864 | 63.4 | 7986 | 210.8 | 206.3–215 |
| Education ^a | | | | | |
| Tertiary | 5445 | 9.9 | 1014 | 185.5 | 174.3–196 |
| Secondary | 7074 | 12.9 | 1446 | 205.7 | 195.4–216 |
| Basic | 42445 | 77.2 | 8936 | 221.8 | 217.3–226 |
| Occupational social class ^a | | | | | |
| Non-manual | 17015 | 31.0 | 3524 | 201.1 | 194.6-207 |
| Manual | 23951 | 43.6 | 4882 | 228.4 | 222.1–234 |
| Self-employed farmer | 10204 | 18.6 | 2211 | 215.7 | 206.9–224 |
| Other self-employed | 3271 | 6.0 | 657 | 212.2 | 196.3-228 |
| No occupation/unknown | 523 | 1.0 | 121 | 239.2 | 196.5–282 |
| Household income ^a | | | | | |
| Highest quintile | 13667 | 24.9 | 2715 | 196.9 | 189.7–204 |
| 2nd | 10522 | 19.1 | 2098 | 209.6 | 200.9–218 |
| 3rd | 10110 | 18.4 | 2114 | 217.3 | 208.2-220 |
| 4th | 10292 | 18.7 | 2183 | 223.2 | 214.0-232 |
| Lowest quintile | 10373 | 18.9 | 2285 | 241.5 | 231.8–25 |
| Economic activity ^a | | | | | |
| , Active | 37266 | 67.8 | 7585 | 208.1 | 203.6-212 |
| Retired | 8881 | 16.2 | 1742 | 257.1 | 245.2-269 |
| Other inactive | 8817 | 16.0 | 2068 | 212.7 | 203.7–222 |
| Marital status | | | | | |
| Married | 24789 | 45.1 | 4471 | 208.7 | 202.6-214 |
| Divorced | 4056 | 7.4 | 797 | 237.0 | 220.9-253 |
| Widowed | 20997 | 38.2 | 5000 | 214.3 | 208.4-220 |
| Never married | 5122 | 9.3 | 1127 | 240.9 | 200.4 220 |
| | 5122 | 5.5 | 116/ | 270.3 | 221.2-23 |
| Chronic health conditions | | | | | |
| Alcohol-related diseases | 308 | 0.6 | 68 | 505.3 | 381.2-629 |
| Asthma and COPD | 4510 | 8.2 | 789 | 232.9 | 216.9–248 |
| Diabetes | 6714 | 12.2 | 1240 | 275.0 | 259.8–290 |

| Z | | | | | | |
|----------|--------------------------|-------|-------|-------|-------|-------------|
| 3 | Heart disease | 18094 | 32.9 | 3562 | 237.1 | 229.5–244.7 |
| 4 5 | Stroke | 3180 | 5.8 | 685 | 330.5 | 306.4–354.6 |
| 6 | | | | | | |
| 7 | Region of residence | | | | | |
| 8 | Western Finland | 25078 | 45.6 | 4979 | 204.1 | 198.6–209.7 |
| 9 | Helsinki capital region | 7449 | 13.6 | 1582 | 208.3 | 198.3–218.4 |
| 10 11 | Rest of Southern Finland | 12056 | 21.9 | 2464 | 214.8 | 206.5-223.0 |
| 12 | Eastern Finland | 8458 | 15.4 | 1916 | 250.1 | 239.2–261.0 |
| 13 | Lapland | 1923 | 3.5 | 454 | 261.5 | 238.1–285.0 |
| 14 | | | | | | |
| 15 16 | Degree of urbanisation | | | | | |
| 10 | Urban | 29853 | 51.0 | 6401 | 217.2 | 212.0–222.4 |
| 18 | Semi-urban | 9285 | 17.7 | 1831 | 210.6 | 201.2-220.0 |
| 19 | Rural | 15826 | 31.3 | 3163 | 215.3 | 208.0-222.7 |
| 20 | Total | 54964 | 100.0 | 11395 | 215.7 | 211.7–219.7 |
| 21 | | | | | - | - |

Abbreviations: CI, confidence intervals; COPD, chronic obstructive pulmonary diseases

^a Information from the population censuses of 1970–1985, the study population being aged 53-57 years

 Table 2. Relative and absolute differences in mortality between high and low socioeconomic groups^a by cause of death and age, and contribution (%) of dementia

 and other causes of death to socioeconomic differences in total mortality by age, Finnish men and women in 2001–2016

| | 70-79 | 9 years | | | 80-89 | 9 years | | | 90+ y | 90+ years | | | All ages 70+ | |
|------------------------|----------------------|-----------|--------------------|---------------------|-------|-----------|--------------------|---------------------|-------|-----------|--------------------|---------------------|---------------------|--|
| | HR | 95% CI | Rate difference | Contribution (%) | HR | 95% CI | Rate difference | Contribution (%) | HR | 95% CI | Rate difference | Contribution (%) | Contribution (%) | |
| Education ^b | | | | | | | | | | | | | | |
| Dementia | 1.24 | 0.97–1.58 | 8.7 | 8.3 | 1.19 | 1.09–1.29 | 40.4 | 33.5 | 1.24 | 1.10-1.40 | 157.9 | 51.8 | 28.1 | |
| Other causes | 1.38 | 1.26-1.50 | 96.1 | 91.7 | 1.11 | 1.06-1.17 | 83.0 | 68.9 | 1.13 | 1.03-1.24 | 146.9 | 48.2 | 71.8 | |
| Total mortality | 1.36 | 1.25–1.48 | 104.8 | 100.0 | 1.13 | 1.09–1.18 | 120.4 | 102.4 | 1.17 | 1.09–1.26 | 304.8 | 100.0 | 100.0 | |
| Occupational socia | l class ^c | | | | | | | | | | | | | |
| Dementia | 1.22 | 1.03-1.44 | 7.7 | 6.3 | 1.17 | 1.10-1.23 | 35.3 | 20.3 | 1.09 | 1.00-1.17 | 63.5 | 22.8 | 16.7 | |
| Other causes | 1.44 | 1.36–1.53 | 114.2 | 93.8 | 1.24 | 1.20-1.29 | 138.7 | 79.7 | 1.19 | 1.12-1.27 | 215.0 | 77.2 | 83.3 | |
| Total mortality | 1.41 | 1.34–1.49 | 121.8 | 100.1 | 1.22 | 1.19–1.26 | 173.9 | 100.0 | 1.15 | 1.09–1.21 | 278.4 | 100.0 | 100.0 | |
| Household income | d | | | | | | | | | | | | | |
| Dementia | 1.63 | 1.32-2.01 | 22.4 | 12.9 | 1.22 | 1.14–1.31 | 46.3 | 21.4 | 1.19 | 1.08–1.32 | 135.6 | 35.2 | 20.9 | |
| Other causes | 1.54 | 1.43-1.66 | 151.0 | 87.1 | 1.24 | 1.19–1.30 | 169.7 | 78.6 | 1.19 | 1.10-1.28 | 249.1 | 64.8 | 79.2 | |
| Total mortality | 1.55 | 1.44–1.67 | 173.3 | 100.0 | 1.24 | 1.19–1.29 | 216.0 | 100.0 | 1.19 | 1.12–1.26 | 384.7 | 100.0 | 100.0 | |

Abbreviations: CI, confidence interval; HR, hazard ratio

Hazard ratios adjusted for calendar year. Age-adjusted incidence rates calculated as dementia deaths per 10,000 person-years at risk. Contribution of dementia determined by the rate difference in dementia mortality as a percentage of the rate difference in total mortality

^a Information from the population censuses of 1970–1985, the study population being aged 53–57 years

^b Tertiary vs. basic education

 ^c Non-manual vs. manual occupational social class

^d Highest vs. lowest household income quintiles

Table 3. Hazard ratios and 95% confidence intervals for dementia mortality by indicators of midlife socioeconomic position^a, Finnish men and women in 2001–2016, n=54,964

| Indicator of socioeconomic | N | 1odel 1 ^ь | Ν | /lodel 2° | N | 1odel 3 ^d | N | /lodel 4ª |
|----------------------------|------|----------------------|------|-----------|------|----------------------|------|-----------|
| position | HR | 95% CI | HR | 95% CI | HR | 95% CI | HR | 95% CI |
| Education | | | | | | | | |
| Tertiary | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| Secondary | 1.14 | 1.05-1.23 | 1.08 | 0.99–1.17 | 1.08 | 0.99–1.17 | 1.08 | 0.99–1.1 |
| Basic | 1.23 | 1.15–1.32 | 1.14 | 1.06–1.23 | 1.14 | 1.05–1.22 | 1.14 | 1.05–1.2 |
| Occupational social class | | | | | | | | |
| Non-manual | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| Manual | 1.14 | 1.09-1.20 | 1.06 | 1.01-1.11 | 1.05 | 1.00-1.11 | 1.05 | 1.00-1.1 |
| Farmer | 1.08 | 1.02–1.15 | 0.96 | 0.90-1.03 | 0.97 | 0.91-1.04 | 0.98 | 0.92–1.0 |
| Other self-employed | 1.05 | 0.96–1.14 | 0.98 | 0.90-1.07 | 0.99 | 0.91-1.08 | 1.00 | 0.92–1.0 |
| No occupation/unknown | 1.20 | 1.00–1.44 | 1.04 | 0.87–1.25 | 0.94 | 0.78–1.14 | 0.94 | 0.78–1.1 |
| Household income | | | | | | | | |
| Highest quintile | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| 2nd | 1.08 | 1.02-1.14 | 1.04 | 0.98–1.10 | 1.03 | 0.98-1.10 | 1.02 | 0.96–1.0 |
| 3rd | 1.13 | 1.07-1.20 | 1.08 | 1.02-1.15 | 1.07 | 1.00-1.14 | 1.05 | 0.99–1.1 |
| 4th | 1.17 | 1.10-1.24 | 1.13 | 1.06-1.20 | 1.10 | 1.03-1.17 | 1.07 | 1.00-1.1 |
| Lowest quintile | 1.28 | 1.20–1.35 | 1.24 | 1.16–1.32 | 1.18 | 1.10–1.26 | 1.13 | 1.06-1.2 |

Abbreviations: CI, confidence interval; HR, hazard ratio

All models used age as time scale and adjusted for calendar year, gender, region of residence and the degree of urbanisation

^a Information from the population censuses of 1970–1985, the study population being aged 53–57 years

^b Model 1: each indicator of socioeconomic position separately

^c Model 2: indicators of socioeconomic position mutually adjusted

^d Model 3: model 2 + midlife economic activity

^e Model 4: model 3 + baseline marital status and chronic health conditions (alcohol-related diseases, asthma and chronic obstructive pulmonary disease, diabetes, heart disease and stroke)

Figure 1. Kaplan–Meier survival probabilities for dementia mortality and mortality from all other causes of death by a) education, b) occupational social class and c) household income quintile (Q1=highest, Q5=lowest), Finnish men and women in 2001-2016. Information of midlife socioeconomic position obtained from the population censuses of 1970–1985, the study population being aged 53–57 years

. 1970-1985, the

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a) Education

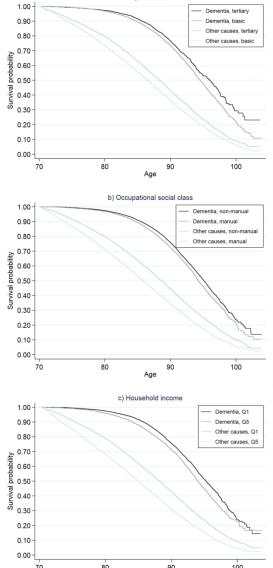
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Figure 1. Kaplan-Meier survival probabilities for dementia mortality and mortality from all other causes of death by a) education, b) occupational social class and c) household income quintile (Q1=highest, Q5=lowest), Finnish men and women in 2001-2016. Information of midlife socioeconomic position obtained from the population censuses of 1970–1985, the study population being aged 53–57 years

122x265mm (300 x 300 DPI)

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Supplementary Table 1. Classification of chronic health conditions used as covariates in the study

| | | Prescription medication | Special reimbursement category |
|---|----------------------------------|-------------------------|--------------------------------|
| Condition | Hospital diagnoses (ICD-10) | (ATC) | (Finnish disease code) |
| Alcohol-related diseases and accidental | F10–19, G31.2, G40.51, G62.1, | | |
| poisoning by alcohol | G72.1, I42.6, K29.2, K70, K86.0, | | |
| | O35.4, X45 | | |
| Asthma and other COPD | J43–46 | | 203 |
| Diabetes | E10-14 | A10 | 103 |
| Heart disease | 100–09, 120–52 | | 201, 206, 207 |
| Stroke | 160–66, G45 | | |

Abbreviations: ATC, Anatomical Therapeutic Chemical; COPD, chronic obstructive pulmonary diseases; ICD, International Classification of Diseases

Supplementary Table 2. Kaplan-Meier survival probabilities at specific ages by midlife a) education, b) occupational social class and c) household income quintile (Q1=highest, Q5=lowest), Finnish men and women in 2001–2016

| | | Dementia | | Other caus | ses |
|----------------------|----------|----------|-----------|------------|----------|
| | | Survivor | | Survivor | |
| | Age | function | 95% CI | function | 95% CI |
| a) Education | | | | | |
| Tertiary | 70 | 1.00 | | 1.00 | |
| | 75 | 0.99 | 0.99–1.00 | 0.91 | 0.89–0.9 |
| | 80 | 0.97 | 0.97–0.98 | 0.80 | 0.78–0.8 |
| | 85 | 0.92 | 0.90–0.92 | 0.63 | 0.61–0.6 |
| | 90 | 0.76 | 0.75–0.78 | 0.43 | 0.41-0.4 |
| | 95 | 0.53 | 0.50-0.56 | 0.23 | 0.22-0.2 |
| | 100 | 0.29 | 0.24–0.35 | 0.09 | 0.07–0.1 |
| Basic | 70 | 1.00 | | 1.00 | |
| | 75 | 0.99 | 0.99–1.00 | 0.88 | 0.87–0.8 |
| | 80 | 0.97 | 0.97–0.97 | 0.74 | 0.73-0.7 |
| | 85 | 0.89 | 0.89–0.90 | 0.56 | 0.55-0.5 |
| | 90 | 0.73 | 0.73–0.74 | 0.36 | 0.36-0.3 |
| | 95 | 0.48 | 0.47–0.49 | 0.19 | 0.18-0.2 |
| | 100 | 0.22 | 0.20-0.24 | 0.06 | 0.05–0.0 |
| b) Occupational soci | al class | | | | |
| Non-manual | 70 | 1.00 | | 1.00 | |
| | 75 | 1.00 | 0.99–1.00 | 0.92 | 0.90-0.9 |
| | 80 | 0.97 | 0.97–0.98 | 0.80 | 0.79–0.8 |
| | 85 | 0.91 | 0.90–0.92 | 0.64 | 0.63–0.6 |
| | 90 | 0.76 | 0.75–0.77 | 0.44 | 0.43-0.4 |
| | 95 | 0.51 | 0.49–0.52 | 0.25 | 0.24–0.2 |
| | 100 | 0.24 | 0.21-0.27 | 0.10 | 0.09–0.2 |
| Manual | 70 | 1.00 | | 1.00 | |
| | 75 | 0.99 | 0.99–0.99 | 0.87 | 0.85–0.8 |
| | 80 | 0.97 | 0.96–0.97 | 0.71 | 0.70-0.7 |
| | 85 | 0.89 | 0.89–0.90 | 0.53 | 0.52-0.5 |
| | 90 | 0.73 | 0.72-0.73 | 0.34 | 0.34–0.3 |
| | 95 | 0.46 | 0.45-0.47 | 0.17 | 0.17-0.1 |
| | 100 | 0.21 | 0.18-0.24 | 0.06 | 0.05-0.0 |

| | | Dementia | | Other causes | | |
|--------------------|-----|----------|-----------|--------------|-----------|--|
| | | Survivor | | Survivor | | |
| | Age | function | 95% CI | function | 95% CI | |
|) Household income | | | | | | |
| Q1 | 70 | 1.00 | | 1.00 | | |
| | 75 | 0.99 | 0.99–1.00 | 0.91 | 0.90–0.92 | |
| | 80 | 0.97 | 0.97–0.98 | 0.79 | 0.78–0.80 | |
| | 85 | 0.92 | 0.91–0.92 | 0.62 | 0.61–0.63 | |
| | 90 | 0.75 | 0.74–0.76 | 0.43 | 0.42-0.44 | |
| | 95 | 0.51 | 0.49–0.53 | 0.24 | 0.22-0.25 | |
| | 100 | 0.24 | 0.20-0.28 | 0.09 | 0.08–0.11 | |
| Q5 | 70 | 1.00 | | 1.00 | | |
| | 75 | 0.99 | 0.99–1.00 | 0.85 | 0.83–0.87 | |
| | 80 | 0.96 | 0.95–0.97 | 0.68 | 0.67–0.70 | |
| | 85 | 0.88 | 0.87–0.89 | 0.50 | 0.48–0.51 | |
| | 90 | 0.71 | 0.70-0.72 | 0.31 | 0.30-0.32 | |
| | 95 | 0.45 | 0.43-0.47 | 0.15 | 0.14–0.16 | |
| | 100 | 0.23 | 0.19–0.26 | 0.04 | 0.04–0.06 | |

90 0.71 0.70-0.72 0.31 0.30-0.32 95 0.45 0.43-0.47 0.15 0.14-0.16 100 0.23 0.19-0.26 0.04 0.04-0.06

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

| | Item No | Recommendation | Pag No |
|------------------------|------------|---|-----------|
| Title and abstract | 1 | (<i>a</i>) Indicate the study's design with a commonly used term in the title or the abstract | 1 |
| | | (<i>b</i>) Provide in the abstract an informative and balanced summary of what was done and what was found | 2-3 |
| Introduction | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | 4 |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | 5 |
| Methods | | | |
| Study design | 4 | Present key elements of study design early in the paper | 5-6 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 5-6 |
| Participants | 6 | (<i>a</i>) Give the eligibility criteria, and the sources and methods of selection of | 5-6 |
| | | participants. Describe methods of follow-up | |
| | | (b) For matched studies, give matching criteria and number of exposed and | |
| | | unexposed | |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 6-7 |
| Data sources/ | 8* | For each variable of interest, give sources of data and details of methods of | 6-7 |
| measurement | | assessment (measurement). Describe comparability of assessment methods if | |
| | | there is more than one group | |
| Bias | 9 | Describe any efforts to address potential sources of bias | 8-9 |
| Study size | 10 | Explain how the study size was arrived at | 5-6 |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 6-9 |
| Statistical methods | 12 | (<i>a</i>) Describe all statistical methods, including those used to control for | 8-9 |
| Statistical methods | 12 | confounding | |
| | | (b) Describe any methods used to examine subgroups and interactions | 9 |
| | | (c) Explain how missing data were addressed | 5-6 |
| | | (d) If applicable, explain how loss to follow-up was addressed | 8 |
| | | (<i><u>e</u></i>) Describe any sensitivity analyses | 13 |
| | | (<u>e)</u> Describe any sensitivity analyses | |
| Results | 12* | | 9 |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially | |
| | | eligible, examined for eligibility, confirmed eligible, included in the study, | |
| | | completing follow-up, and analysed | 9 |
| | | (b) Give reasons for non-participation at each stage | |
| Descriptive data | 14* | (c) Consider use of a flow diagram | 9 |
| DESCLIDITVE (1818 | 14" | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | Í |
| | | and mormation on exposures and potential comounders | |
| | | | |
| | | (b) Indicate number of participants with missing data for each variable of interest(c) Summarise follow-up time (eg, average and total amount) | |

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| Main results | 16 | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their | 9-11 |
|------------------|-----|---|-----------|
| | | precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | |
| | | (b) Report category boundaries when continuous variables were categorized | |
| | | (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | 9 |
| Discussion | | | |
| Key results | 18 | Summarise key results with reference to study objectives | 11- 12 |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 13- 14 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 11- 13 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | 13 |
| Other informati | ion | | • |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if | 17 |

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

applicable, for the original study on which the present article is based

BMJ Open

Midlife socioeconomic position and old-age dementia mortality: a large prospective register-based study from Finland

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| Midlife socioeconomic position | and | old-age | dementia | mortality: | a | large | prospec | tive |
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| register-based study from Finla | ınd | | | | | | | |

Kaarina Korhonen¹, Elina Einiö^{1,2,3}, Taina Leinonen⁴, Lasse Tarkiainen¹, Pekka Martikainen^{1,3,5}

¹ Population Research Unit, Faculty of Social Sciences, University of Helsinki, Helsinki, Finland

² Department of Social Policy, London School of Economics and Political Science, London, United Kingdom

³ Max Planck Institute for Demographic Research, Rostock, Germany

⁴ Finnish Institute of Occupational Health, Helsinki, Finland

⁵ Department of Public Health Sciences, Stockholm University, Stockholm, Sweden

Correspondence to:

Kaarina Korhonen

Faculty of Social Sciences

P.O. Box 18, 00014 University of Helsinki, Finland

+358 50 3199 388

kaarina.korhonen@helsinki.fi

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Abstract

Objectives To assess the association between multiple indicators of socioeconomic position and dementiarelated death, and to estimate the contribution of dementia to socioeconomic differences in overall mortality at older ages.

Design Prospective population-based register study.

Setting Finland.

Participants 11% random sample of the population aged 70–87 resident in Finland at the end of year 2000 (N=54 964).

Main outcome measure Incidence rates, Kaplan-Meier survival probabilities and Cox regression hazard ratios of dementia mortality in 2001–2016 by midlife education, occupational social class and household income measured at ages 53–57 years.

Results During the 528 387 person-years at risk, 11 395 individuals died from dementia (215.7 per 10 000 person-years). Lower midlife education, occupational social class and household income were associated with higher dementia mortality, and the differences persisted to the oldest old ages. Compared to mortality from all other causes, however, the socioeconomic differences emerged later. Dementia accounted for 28% of the difference between low and high education groups in overall mortality at age 70+, and for 21% of the difference between lowest and highest household income quintiles. All indicators of socioeconomic position were independently associated with dementia mortality, low household income being the strongest independent predictor (HR=1.24, 95% confidence interval 1.16–1.32), followed by basic education (HR=1.14, 1.06–1.23). Manual occupational social class was related to a 6% higher hazard (HR=1.06, 1.01–1.11) compared to non-manual social class. Adjustment for midlife economic activity, baseline marital status and chronic health conditions attenuated the excess hazard of low midlife household income, although significant effects remained.

Conclusion Several indicators of socioeconomic position predict dementia mortality independently and socioeconomic inequalities persist into the oldest old ages. The results demonstrate that dementia is among the most important contributors to socioeconomic inequalities in overall mortality at older ages.

Strengths and limitations of this study

- We used longitudinal registry data that permits a 15-year follow-up of dementia mortality with no attrition or recall bias.
- Dementia is documented in the national death register with high specificity.
- Due to the use of register data, traditional dementia risk factors such as smoking and physical activity could not be measured.
- All indicators of socioeconomic position were measured in midlife in order to avoid selection to socioeconomic groups on the basis of cognitive decline.
- This is the first study to show the contribution of dementia to the socioeconomic inequalities in overall mortality at older ages.

Introduction

Socioeconomic inequality in health and mortality is one of the most consistent findings in the demographic and social epidemiological literature. Lower education, occupational social class and income are strong predictors of all-cause and cause-specific mortality particularly among the working-age population, but inequalities are clear also at older ages.[1–4] Among the ageing population, the key factors affecting morbidity and disability are Alzheimer's disease and other forms of progressive dementia. Globally, an estimated 47 million people lived with dementia in 2015, and the number is projected to triple by 2050.[5] In England and Wales, dementia has already become the leading cause of death.[6] Despite the growing societal impact, however, no comprehensive understanding exists about the socioeconomic patterns of dementia mortality.

Educational inequalities in dementia mortality have previously been reported in studies following individuals from midlife or younger old ages[7,8] but not among the oldest old.[8,9] In a Norwegian health examination study, an educational pattern was present only among cohorts aged below 70 at baseline but not among those aged 70 and over.[8] Similarly, among a Finnish cohort aged 90 and over, no statistically significant educational gradient in dementia mortality emerged.[9] The lack of educational differentials among the oldest old may relate to selective survival. People with lower education experience higher mortality at younger ages, and those who survive to older ages do so because of their better health. Thus, the population surviving to older ages is more homogeneous in terms of health-related characteristics and, as a result, the socioeconomic differences in mortality are diminished. Another possible explanation for the lack of educational gradient in dementia mortality is the fact that the distribution of education in the oldest education, other indicators of socioeconomic position (SEP) may be more suitable for identifying high-risk population subgroups.[2,10] Previous studies suggest that among adults in general, overall mortality disparities are greater or have increased to a greater extent in terms of occupational social class[11] and income[12,13] than education. Among the Finnish cohort of nonagenarians,[9] occupational social class

was a strong predictor of dementia mortality with a 3-fold hazard of dementia death among the unskilled manual workers compared to upper non-manuals. Personal income in midlife, however, was not related to dementia mortality among a cohort of Norwegian men.[14] To our knowledge, no previous study has assessed inequalities in dementia mortality by household income, a socioeconomic indicator that is more directly related to material resources available to the individual and that more rigorously captures the living conditions of the most disadvantaged population subgroups. A low household income may, in addition to material disadvantage, induce psychosocial stress, increasing the risk of dementia directly or through less favourable health behaviours. Disentangling the contributions of education, occupational social class and household income will thus provide important insights into the potential mechanisms how SEP shapes the risk of dementia death.

This study contributes to the existing knowledge by assessing socioeconomic inequalities in dementia mortality using multiple indicators of SEP, including education, occupational social class and household income. More specifically, the aims of the study were to 1) investigate the magnitude of socioeconomic inequalities in dementia mortality in relation to age, and compare the patterns to those in mortality from all other causes of death, 2) to quantify the contribution of dementia to the socioeconomic inequalities in overall mortality at older ages, and 3) to assess whether education, occupational social class and household income are independently related to dementia mortality once the other indicators are taken into account. This was because different indicators of SEP are correlated but each of them may have independent associations with dementia mortality. We further estimated models adjusting for confounders including marital status and chronic health conditions. We used longitudinal registry data on a large population-based sample, which permits a 15-year follow-up of dementia-related deaths with no attrition or recall bias. All indicators of SEP were measured in midlife in order to avoid selection to socioeconomic groups on the basis of cognitive decline.

Methods

Sample

We used an 11% random sample of the Finnish population in 1987–2007 drawn from the Statistics Finland population register, which covers all permanent residents. Statistics Finland linked the sample with information from various administrative registers including the national Death Register and healthcare registers using unique personal identification numbers assigned to all permanent residents.

In the present study, we included men and women aged 70–87 at the end of year 2000. For these cohorts, midlife socioeconomic characteristics could be identified using information from the Population Censuses conducted in 1970, 1975, 1980 and 1985. Individuals with missing census information due to residing outside of Finland (n=920) and those with missing household income information due to not being part of the household population in the census year (n=401) were excluded. 7 individuals emigrated during the first year of follow-up and thus were excluded from the analyses. The analytic sample consisted of 54 964 individuals.

Mortality data

Dates and causes of death were obtained from the Death Register. Dementia-related deaths were identified using the International Classification of Diseases 10th revision (ICD-10) codes F00–03 and G30 as the underlying or any of the three contributory causes of death reported on the death certificate. We identified 11 395 persons who died from dementia and 30 637 persons who died from other causes during the follow-up in 2001–2016.

Indicators of socioeconomic position

The information of all indicators of SEP was derived from the quinquennial population censuses of 1970– 1985. A particular census year was chosen on the basis of the study subject's age so that the indicators were measured at around the age of 55 (range 53–57) for all. Education was indicated as the highest achieved qualification, categorised as tertiary (generally 13+ years of education; International Standard Classification of Education ISCED-1997 codes 5–6), secondary (10–12 years, ISCED 3–4), and basic education/no qualifications (9 years, ISCED 0–2). Occupational social class comprised five groups,

classified as non-manual, manual, self-employed farmer, other self-employed, and no occupation/unknown. Information of occupational social class in the census year was lacking for 10 465 individuals due to nonemployment at that time. For 9942 individuals, the information could nevertheless be obtained from previous years in which the individuals were employed. Household income indicated the taxable annual income of all household members, including all income received in money or monetary benefit subject to tax. The information was obtained from the Finnish Tax Administration and the Social Insurance Institution of Finland. We adjusted for household composition using the OECD-modified equivalence scale.[15] Income quintiles were formed based on the household income distribution in the population aged 15 and over in the census year.

Covariates

The analyses incorporated information of economic activity measured from the census year because being out of the labour market may indicate poor health and affect dementia risk independently but also lead to reduced household income. Economic activity was classified as being in the labour force, retired and other inactive. Marital status was measured at baseline (the end of 2000), classified as married, divorced, widowed and never married. Baseline chronic health conditions included indicators of vascular and lifestyle risk factors for dementia,[16] and were identified from health registers in the five-year period before the baseline, covering 1996–2000. We used the diagnostic records of the hospital discharge register and patient censuses of the National Institute for Health and Welfare, and the records of prescription medicine purchases and of entitlement to special reimbursement for the medication expenses for certain chronic diseases maintained by the Social Insurance Institution of Finland. We included indicators for alcoholrelated diseases and accidental poisoning by alcohol, asthma and other chronic obstructive pulmonary disease (COPD), diabetes and heart disease (for coding see Supplementary Table 1). These chronic conditions may confound the association between midlife SEP and dementia mortality as the diseases usually develop over a long period of time and thus reflect health behaviours or health problems already present in midlife. To account for potential regional variance in socioeconomic characteristics and mortality, we included dummies for region of residence (Western Finland, Helsinki capital region, rest of Southern Finland, Eastern Finland, and Lapland) and the degree of urbanisation of the municipality of residence, a variable based on the proportion of population living in urban settlements and the population of the largest urban settlement in the municipality (urban, semi-urban and rural).

Statistical analyses

We followed the study population for dementia mortality from 1 January 2001 until 31 December 2016. Individuals were censored on the date of death, at the end of the year preceding emigration, or at the end of 2016, whichever came first.

For descriptive statistics, we calculated age-adjusted dementia mortality rates per 10 000 person-years at risk by indicators of SEP and the covariates. In order to assess the magnitude of socioeconomic inequalities in relation to age, we estimated Kaplan–Meier survival functions by education, occupational social class and household income. In these analyses, we contrasted the survival functions of the highest and lowest education groups, non-manual and manual employees and the highest and lowest household income quintiles. The equality of survival functions was tested using log-rank tests. For the comparison between dementia mortality and the more general mortality patterns, separate Kaplan-Meier survival functions were estimated for mortality from all other causes of death. We also estimated hazard ratios and their 95% confidence intervals for low versus high socioeconomic groups at the age of 70–79, 80–89 and 90 years and over.

To quantify the contribution of dementia to socioeconomic differences in overall mortality at older ages, we calculated absolute rate differences in mortality between socioeconomic groups (basic vs. tertiary education, manual vs. non-manual occupational social class, lowest vs. highest household income quintile) by cause of death. The contribution was determined by the rate difference in dementia mortality as a percentage of the rate difference in total mortality. Because the level of dementia mortality increases substantially with age, we also assessed age-specific contributions (at the age of 70–79, 80–89 and 90+).

To estimate the independent associations between each indicator of SEP and dementia mortality, we used Cox regression models. Attained age in years was used as the time scale, and thus all analyses adjusted for the confounding effect of age.[17] We first estimated crude associations between each indicator and dementia mortality, adjusting for calendar year dummies, gender, region of residence and the degree of urbanisation (model 1). Model 2 included education, occupational social class and household income as covariates, thus showing mutually adjusted associations. Midlife economic activity was adjusted for in model 3. We further adjusted for baseline marital status and chronic health conditions in model 4 to assess the extent to which these confounding factors attenuated the relative hazard attached to each socioeconomic indicator.

We tested for interactions between gender and each socioeconomic indicator using likelihood ratio test. Interactions were statistically nonsignificant (p>0.05), and thus we conducted all analyses for men and women combined. We also tested for interactions of all pairwise combinations of the socioeconomic indicators, adjusting for the covariates of model 1. These interactions were all statistically nonsignificant (p>0.05). All analyses were performed using Stata 15.1.[18]

Patient and public involvement

No patients were involved in setting the research question or the outcome measures, nor were they involved in developing plans for design or implementation of the study. No patients were asked to advise on interpretation or writing up of results. There are no plans to disseminate the results of the research to study participants or the relevant patient community.

Results

Table 1 shows the distribution of the study population by indicators of midlife SEP, economic activity and baseline characteristics. The vast majority of individuals (77.2%) had no higher than basic education, and manual employees formed the largest occupational social class (43.6%). Higher household income quintiles were over-represented among the study population due to the higher incomes of the middle aged compared

to the rest of the population and also partly because of greater mortality of the lower income groups between the time of measurement of midlife income and the baseline. During the 528 387 person-years at risk 11 395 individuals died from dementia, the average age-adjusted dementia mortality rate being 223.1 and 210.8 per 10 000 person-years among men and women, respectively. The rate was higher for those with lower education, occupational social class and household income, and also for the non-married and people with chronic health conditions apart from asthma and other COPD.

Kaplan–Meier survival functions in Figure 1 show that dementia mortality differed by all indicators of SEP (log rank test, p<0.001 for each indicator), and that the age patterns differed between the indicators (for 95% confidence intervals see Supplementary Table 2). The inequalities emerged at an earlier age when SEP was measured in terms of household income (Panel c) compared to education (Panel a) and occupational social class (Panel b). At the age of 90 years and above, by contrast, the differences were more pronounced when SEP was measured in terms of education. Nevertheless, inequalities in dementia mortality emerged substantially later in life compared to mortality from all other causes. Hazard ratios in Table 2 show that relative inequalities in mortality tended to diminish with age for all indicators of SEP regardless of cause of death. However, education differences in dementia mortality showed a different age pattern in that the point estimates indicated stable inequality with age.

Overall, dementia contributed to 28.1% of educational and 20.9% of household income differences in total mortality at the age of 70 and over (Table 2). The contribution to occupational social class differences was somewhat smaller (16.7%). The contribution of dementia to socioeconomic inequalities substantially increased from the age of 70–79 to 90 years and over.

Cox regression models in Table 3 show adjusted hazard ratios (HR) for dementia mortality across all ages from 70 years and over. Adjusted for calendar year, gender, region of residence and the degree of urbanisation in model 1, the associations were strongest for basic education (HR=1.23, 95% CI 1.15–1.32), unknown occupational social class (HR=1.20, 1.00–1.44), and the lowest household income quintile

(HR=1.28, 1.20–1.35). Mutual adjustment of socioeconomic indicators in model 2 attenuated educational differences by about 40%, and unknown occupational social class to a non-significant level. Basic education (HR=1.14, 1.06–1.23), manual occupational social class (HR=1.06, 1.01–1.11) and three lowest household income quintiles (for the lowest quintile HR=1.24, 1.16–1.32) all predicted dementia mortality independently of each other. Adjustment for midlife economic activity in model 3 attenuated the excess hazard particularly of the lower household income quintiles. Adjustment for baseline marital status and chronic health conditions in model 4 contributed to a small change in the estimates, the attenuation being largest for the lowest household income quintile. In this full model, basic education increased the hazard of dementia death by 14% (1.06–1.23), manual occupational social class by 5% (1.00–1.10) and the two lowest household income quintiles by 7–13% (HR=1.07, 1.00–1.14 to HR=1.13, 1.06–1.22).

Discussion

Main findings and their interpretation

In this study we have shown that dementia mortality at older ages is socioeconomically patterned in terms of multiple indicators of SEP. People with lower education, occupational social class and household income have a higher risk of dementia death compared to those with higher SEP. These results add to the literature on socioeconomic inequalities in old-age mortality, which has previously shown a socioeconomic pattern in many other specific causes of death such as cardiovascular diseases, COPD and cancer.[1] Our results indicate, moreover, that dementia is an important factor in overall socioeconomic inequalities in old-age mortality, contributing to 21–28% of household income and educational differences in total mortality among the population aged 70 and over. The contribution of dementia to overall socioeconomic inequalities in mortality increased substantially with age, which relates to the increasing proportion of deaths attributable to dementia with advancing age.[19]

A major difference in the patterns between dementia mortality and mortality from all other causes of death was that socioeconomic inequalities in dementia mortality emerged later and the inequalities in dementia

mortality between high and low education groups persisted in the same magnitude to the oldest old ages (90 years and above). By contrast, inequalities in mortality from other causes of death tended to diminish with age. The attenuation of socioeconomic inequalities with age is a general finding,[1,2] and may partly relate to selective survival, suggesting that people who survive to very old age have more similar health profiles across socioeconomic groups. Our results show, however, that even among people who survive to the oldest old age, education groups differ in neurological health. This is a novel finding in that previous studies have identified consistent socioeconomic inequalities in dementia mortality only among the younger old[7,8] but the results have been mixed for the oldest old.[8,9] Participation bias may at least partly explain the differences in findings; people of older age, lower SEP and with health problems are less likely to participate in surveys and studies involving health examinations. Our study employed register data on a population-based cohort and thus is not affected by participation or attrition biases.

The age patterns in dementia mortality differed between indicators of SEP: while educational differences were more pronounced among the oldest old (90 years and over), the differences among the younger old (70–79 years) were largest when SEP was measured in terms of household income. Individuals in the lowest income quintile represent the most disadvantaged population subgroups with multiple potential dementia risk factors. Our findings show that the higher dementia mortality of the lowest household income quintiles was strongly — although not fully — confounded by greater morbidity of these groups. Severe health problems that were already present in midlife have potentially affected both household incomes and the risk of dementia death. However, we cannot rule out the possibility of mediation, especially because chronic health conditions were measured after midlife income; impoverished material conditions may also affect dementia risk through, for example, health-related behaviours, cardiovascular risk factors[16] and psychological stress.[20] In the presence of mediation, our estimates would be conservative as they would overadjust part of the effect of socioeconomic disadvantage. Future studies are needed to establish the causal relationship between mediating factors and dementia mortality using mediation analysis techniques.

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Education, in turn, may have particular benefits above and beyond physical health factors among the population surviving to the oldest old age. Our results show persistent educational differences in dementia mortality, and the association was not confounded by chronic health conditions, economic activity or marital status. Education is a well-established predictor of dementia incidence,[21] although the exact mechanisms are still not known. Brain autopsy studies indicate, in line with the cognitive reserve hypothesis,[22] that education is not associated with the burden of neuropathology at death but higher education enables individuals to compensate longer for the neuropathological changes before developing clinical symptoms of dementia.[23] Thus, it is possible that the educational differences in dementia mortality we found in our study are due to competing risks; people with higher education died from other causes before they reached the phase of clinical dementia or died from other causes before dementia progressed to death. However, the empirical evidence for the cognitive reserve hypothesis remains open to debate. For example, several studies have not identified educational differences in survival time after dementia onset,[24] which is among the key hypotheses in the cognitive reserve model.[25] Therefore, it is plausible that higher education enhances brain health and protects against (or postpones) not only the clinical symptoms but also the development of neurodegenerative disorders.

Occupational social class differences in dementia mortality were modest following adjustment for education and household income. In particular, the high hazard among those with no occupation disappeared after these adjustments indicating that this group experienced multiple socioeconomic disadvantages. The results suggest, nevertheless, that higher social class occupations may involve greater cognitive demands and intellectual engagement, and thus enhance cognitive health.[26,27] In contrast, lower class occupations or long periods of economic inactivity due to unemployment or early retirement may reduce opportunities for cognitive investment. Overall, the results of this study suggest that all three indicators of SEP are important factors in bringing about socioeconomic differences in dementia mortality, also influencing inequalities in overall mortality among the older population.

Methodological considerations

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We used a unique population-representative sample of older adults in Finland with 11 395 dementia deaths identified from the National Death Register. The register-based sample was not affected by participation or attrition bias, which are common limitations of many cohort designs, particularly among the older population. The population register encompasses rich information on demographic and socioeconomic characteristics of individuals over the life course, and is not subject to bias from individuals' self-reports or recollection.

Despite the rich register data, our study also has some limitations. First, we could only identify dementia cases that have been recorded on the death certificate. According to a validation study for identifying dementia in the Finnish national registers, the documentation of dementia as the cause of death has improved since the late 1990s, and the specificity is particularly high.[28] To minimise any bias arising from potential underreporting of dementia as the underlying cause of death, we applied the multiple-cause approach and included also cases where dementia was recorded as any of the three contributory causes.[29] Defined this way, we identified 21% of all deaths at the age of 70 and over to be attributable to dementia accounted for 19% of all deaths at the age of 80 and over.[30] Furthermore, we ran sensitivity analyses with interaction with calendar year, and found that the associations between the indicators of SEP and dementia mortality did not vary in time. Therefore, we believe our results are not biased by overreporting or underreporting of death or by changes in documentation practices.

Second, the information of household income was based on taxable income and the variable thus excludes certain monetary transfers such as housing allowance and social assistance. These means-tested sources of income may be especially relevant for people with health problems and those outside the labour market. This might lead to overestimation of the income effect. Information of disposable income was not available for years 1970–1985, but we carried out a robustness check for the correlation between taxable and disposable household incomes (as continuous variables) using the population aged 15 and over in 1995 and found the correlation to be as high as 0.97 (among the population aged 53–57 in 1995 the correlation was

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0.98). Therefore, it is unlikely that the use of disposable income would change the ranking of individuals in the household income distribution to the extent that it would affect our main findings.

Finally, the causal relationship between SEP and dementia is difficult to establish in observational studies. We therefore measured all socioeconomic characteristics 15–30 years before the mortality follow-up, and it is thus very unlikely that any symptoms of dementia affected the midlife socioeconomic attainment of individuals. Nevertheless, we cannot exclude the possibility that early cognitive decline may have affected midlife SEP, especially measured in term of occupational social class and household income. Also, given the small proportion of people with tertiary education in these cohorts (10%), it is possible that this forms a select group with multiple advantages including higher childhood SEP and early cognitive ability. Because register data does not cover information of traditional risk factors related to health behaviours such as smoking and physical activity, we included indicators of chronic conditions to measure cardiovascular and life style risk factors for dementia that may confound the association between SEP and dementia mortality.

Conclusions

This study provides new insight into the socioeconomic inequalities in old-age mortality by showing a consistent pattern in dementia mortality by multiple indicators of SEP. Low education, occupational social class and household income were all associated with higher risk of dementia death, although the socioeconomic differences emerged later than in mortality from other causes. Household income differences in dementia mortality were more pronounced among the younger old, and the associations were largely attributable to other chronic health conditions such as diabetes and alcohol-related diseases. Educational inequalities, by contrast, were independent of chronic health conditions and became more pronounced at the oldest old age where mortality inequalities generally begin to attenuate. The results indicate that dementia mortality may be amenable to socioeconomic interventions in midlife. The findings also suggest that dementia contributes to socioeconomic inequalities in overall mortality at older ages and,

thus, dementia prevention is important from the point of view of socioeconomic inequalities in total mortality.

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Footnotes

Contributors: KK, EE, TL, LT and PM participated in designing the study, generating hypotheses, interpreting the data and critically revised the manuscript for important intellectual content. KK analysed the data, conducted the literature review and wrote the first draft of the manuscript.

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Competing interests: None declared.

Data sharing statement: Statistics Finland, the National Institute for Health and Welfare and the Social Insurance Institution of Finland have collected and own the data. Due to data protection regulations, the authors are not allowed to make the data available to third parties. Researchers can apply for data access by contacting the register-holding institutions: Statistics Finland (http://stat.fi/index_en.html); National Institute for Health and Welfare (https://thl.fi/en); Social Insurance Institution of Finland (https://www.kela.fi/web/en).

Ethics approval: The study has been approved by Statistics Finland Board of Ethics (permit TK-53-339-13). The data were collected for routine administrative registration purposes and, therefore, informed consent of the participants was not obtained. These register data can be used for scientific purposes under the Personal Data Act and the Statistics Act. Statistics Finland anonymised the data prior to providing them to researchers.

 Table 1. Distribution of the study population, dementia deaths and age-adjusted dementia mortality rates (per 10 000 person-years) by indicators of midlife socioeconomic position and economic activity and baseline characteristics, Finnish men and women in 2001-2016

| | | | Dementi | a deaths | |
|--|-------|------|---------|----------|-----------|
| | Ν | % | n | Rate | 95% CI |
| | 76.4 | | | | |
| Mean age at baseline (SD) | (4.8) | | | | |
| Gender | | | | | |
| Men | 20100 | 36.6 | 3409 | 223.1 | 215.6–230 |
| Women | 34864 | 63.4 | 7986 | 210.8 | 206.3–215 |
| Education ^a | | | | | |
| Tertiary | 5445 | 9.9 | 1014 | 185.5 | 174.3–196 |
| Secondary | 7074 | 12.9 | 1446 | 205.7 | 195.4–216 |
| Basic | 42445 | 77.2 | 8936 | 221.8 | 217.3–226 |
| Occupational social class ^a | | | | | |
| Non-manual | 17015 | 31.0 | 3524 | 201.1 | 194.6–207 |
| Manual | 23951 | 43.6 | 4882 | 228.4 | 222.1–234 |
| Self-employed farmer | 10204 | 18.6 | 2211 | 215.7 | 206.9–224 |
| Other self-employed | 3271 | 6.0 | 657 | 212.2 | 196.3–228 |
| No occupation/unknown | 523 | 1.0 | 121 | 239.2 | 196.5–282 |
| Household income ^a | | | | | |
| Highest quintile | 13667 | 24.9 | 2715 | 196.9 | 189.7–204 |
| 2nd | 10522 | 19.1 | 2098 | 209.6 | 200.9–218 |
| 3rd | 10110 | 18.4 | 2114 | 217.3 | 208.2-226 |
| 4th | 10292 | 18.7 | 2183 | 223.2 | 214.0-232 |
| Lowest quintile | 10373 | 18.9 | 2285 | 241.5 | 231.8-251 |
| Economic activity ^a | | | | | |
| Active | 37266 | 67.8 | 7585 | 208.1 | 203.6-212 |
| Retired | 8881 | 16.2 | 1742 | 257.1 | 245.2-269 |
| Other inactive | 8817 | 16.0 | 2068 | 212.7 | 203.7-221 |
| Marital status | | | | | |
| Married | 24789 | 45.1 | 4471 | 208.7 | 202.6-214 |
| Divorced | 4056 | 7.4 | 797 | 237.0 | 202.0 21- |
| Widowed | 20997 | 38.2 | 5000 | 214.3 | 208.4-220 |
| Never married | 5122 | 9.3 | 1127 | 214.3 | 208.4-220 |
| | 2122 | 5.5 | 112/ | 240.9 | 221.2-232 |
| Chronic health conditions | | | | | |
| Alcohol-related diseases | 308 | 0.6 | 68 | 505.3 | 381.2-629 |
| Asthma and COPD | 4510 | 8.2 | 789 | 232.9 | 216.9–248 |
| Diabetes | 6714 | 12.2 | 1240 | 275.0 | 259.8–290 |

| Heart disease | 18094 | 32.9 | 3562 | 237.1 | 229.5–244.7 |
|--------------------------|-------|-------|-------|-------|-------------|
| Region of residence | | | | | |
| Western Finland | 25078 | 45.6 | 4979 | 204.1 | 198.6–209.7 |
| Helsinki capital region | 7449 | 13.6 | 1582 | 208.3 | 198.3–218.4 |
| Rest of Southern Finland | 12056 | 21.9 | 2464 | 214.8 | 206.5–223.0 |
| Eastern Finland | 8458 | 15.4 | 1916 | 250.1 | 239.2–261.0 |
| Lapland | 1923 | 3.5 | 454 | 261.5 | 238.1–285.0 |
| Degree of urbanisation | | | | | |
| Urban | 29853 | 51.0 | 6401 | 217.2 | 212.0–222.4 |
| Semi-urban | 9285 | 17.7 | 1831 | 210.6 | 201.2–220.0 |
| Rural | 15826 | 31.3 | 3163 | 215.3 | 208.0-222.7 |
| Total | 54964 | 100.0 | 11395 | 215.7 | 211.7–219.7 |
| | | | | | |

Abbreviations: CI, confidence intervals; COPD, chronic obstructive pulmonary diseases

^a Information from the population censuses of 1970–1985, the study population being aged 53–57 years

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Table 2. Relative and absolute differences in mortality between high and low socioeconomic groups^a by cause of death and age, and contribution (%) of dementia

 and other causes of death to socioeconomic differences in total mortality by age, Finnish men and women in 2001–2016

| | 70-79 | 9 years | | | 80-89 |) years | | | 90+ y | ears | | | All ages 70+ |
|------------------------|----------------------|-----------|--------------------|---------------------|-------|-----------|--------------------|---------------------|-------|-----------|--------------------|---------------------|---------------------|
| | HR | 95% CI | Rate difference | Contribution (%) | HR | 95% CI | Rate difference | Contribution (%) | HR | 95% CI | Rate difference | Contribution (%) | Contributior (%) |
| Education [⊾] | | | | | | | | | | | | | |
| Dementia | 1.24 | 0.97–1.58 | 8.7 | 8.3 | 1.19 | 1.09–1.29 | 40.4 | 33.5 | 1.24 | 1.10-1.40 | 157.9 | 51.8 | 28.1 |
| Other causes | 1.38 | 1.26-1.50 | 96.1 | 91.7 | 1.11 | 1.06-1.17 | 83.0 | 68.9 | 1.13 | 1.03-1.24 | 146.9 | 48.2 | 71.8 |
| Total mortality | 1.36 | 1.25-1.48 | 104.8 | 100.0 | 1.13 | 1.09–1.18 | 120.4 | 102.4 | 1.17 | 1.09–1.26 | 304.8 | 100.0 | 100.0 |
| Occupational socia | l class ^c | | | | | | | | | | | | |
| Dementia | 1.22 | 1.03-1.44 | 7.7 | 6.3 | 1.17 | 1.10-1.23 | 35.3 | 20.3 | 1.09 | 1.00-1.17 | 63.5 | 22.8 | 16.7 |
| Other causes | 1.44 | 1.36–1.53 | 114.2 | 93.8 | 1.24 | 1.20–1.29 | 138.7 | 79.7 | 1.19 | 1.12–1.27 | 215.0 | 77.2 | 83.3 |
| Total mortality | 1.41 | 1.34-1.49 | 121.8 | 100.1 | 1.22 | 1.19–1.26 | 173.9 | 100.0 | 1.15 | 1.09–1.21 | 278.4 | 100.0 | 100.0 |
| Household income | d | | | | | | | | | | | | |
| Dementia | 1.63 | 1.32-2.01 | 22.4 | 12.9 | 1.22 | 1.14–1.31 | 46.3 | 21.4 | 1.19 | 1.08–1.32 | 135.6 | 35.2 | 20.9 |
| Other causes | 1.54 | 1.43–1.66 | 151.0 | 87.1 | 1.24 | 1.19–1.30 | 169.7 | 78.6 | 1.19 | 1.10-1.28 | 249.1 | 64.8 | 79.2 |
| Total mortality | 1.55 | 1.44–1.67 | 173.3 | 100.0 | 1.24 | 1.19–1.29 | 216.0 | 100.0 | 1.19 | 1.12-1.26 | 384.7 | 100.0 | 100.0 |

Abbreviations: CI, confidence interval; HR, hazard ratio

Hazard ratios adjusted for calendar year. Age-adjusted incidence rates calculated as dementia deaths per 10,000 person-years at risk. Contribution of dementia determined by the rate difference in total mortality

^a Information from the population censuses of 1970–1985, the study population being aged 53–57 years

^b Tertiary vs. basic education

^c Non-manual vs. manual occupational social class

^d Highest vs. lowest household income quintiles

Table 3. Hazard ratios and 95% confidence intervals for dementia mortality by indicators of midlife socioeconomic position^a, Finnish men and women in 2001–2016, n=54,964

| Indicator of socioeconomic | N | lodel 1 ^b | N | odel 2° | N | 1odel 3 ^d | Model 4 ^e | | |
|----------------------------|------|----------------------|------|-----------|------|----------------------|----------------------|----------|--|
| position | HR | 95% CI | HR | 95% CI | HR | 95% CI | HR | 95% CI | |
| Education | | | | | | | | | |
| Tertiary | 1.00 | | 1.00 | | 1.00 | | 1.00 | | |
| Secondary | 1.14 | 1.05-1.23 | 1.08 | 0.99–1.17 | 1.08 | 0.99–1.17 | 1.08 | 0.99–1.1 | |
| Basic | 1.23 | 1.15–1.32 | 1.14 | 1.06–1.23 | 1.14 | 1.05–1.22 | 1.14 | 1.06-1.2 | |
| Occupational social class | | | | | | | | | |
| Non-manual | 1.00 | | 1.00 | | 1.00 | | 1.00 | | |
| Manual | 1.14 | 1.09-1.20 | 1.06 | 1.01-1.11 | 1.05 | 1.00-1.11 | 1.05 | 1.00-1.1 | |
| Farmer | 1.08 | 1.02-1.15 | 0.96 | 0.90-1.03 | 0.97 | 0.91-1.04 | 0.98 | 0.92–1.0 | |
| Other self-employed | 1.05 | 0.96–1.14 | 0.98 | 0.90-1.07 | 0.99 | 0.91-1.08 | 1.00 | 0.92–1.0 | |
| No occupation/unknown | 1.20 | 1.00-1.44 | 1.04 | 0.87–1.25 | 0.94 | 0.78–1.14 | 0.94 | 0.78–1.1 | |
| Household income | | | | | | | | | |
| Highest quintile | 1.00 | | 1.00 | | 1.00 | | 1.00 | | |
| 2nd | 1.08 | 1.02-1.14 | 1.04 | 0.98-1.10 | 1.03 | 0.98–1.10 | 1.02 | 0.96–1.0 | |
| 3rd | 1.13 | 1.07-1.20 | 1.08 | 1.02-1.15 | 1.07 | 1.00-1.14 | 1.05 | 0.99–1.1 | |
| 4th | 1.17 | 1.10-1.24 | 1.13 | 1.06-1.20 | 1.10 | 1.03–1.17 | 1.07 | 1.00-1.1 | |
| Lowest quintile | 1.28 | 1.20–1.35 | 1.24 | 1.16-1.32 | 1.18 | 1.10-1.26 | 1.13 | 1.06-1.2 | |

Abbreviations: CI, confidence interval; HR, hazard ratio

All models used age as time scale and adjusted for calendar year, gender, region of residence and the degree of urbanisation

^a Information from the population censuses of 1970–1985, the study population being aged 53–57 years

^b Model 1: each indicator of socioeconomic position separately

^c Model 2: indicators of socioeconomic position mutually adjusted

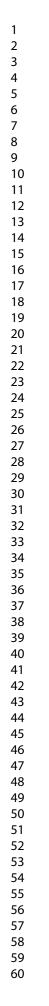
^d Model 3: model 2 + midlife economic activity

^e Model 4: model 3 + baseline marital status and chronic health conditions (alcohol-related diseases, asthma and chronic obstructive pulmonary disease, diabetes and heart disease)

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Figure 1. Kaplan–Meier survival probabilities for dementia mortality and mortality from all other causes of death by a) education, b) occupational social class and c) household income quintile (Q1=highest, Q5=lowest), Finnish men and women in 2001-2016. Information of midlife socioeconomic position obtained from the population censuses of 1970–1985, the study population being aged 53–57 years

.el ela 2001–2016. .f 1970–1985, the



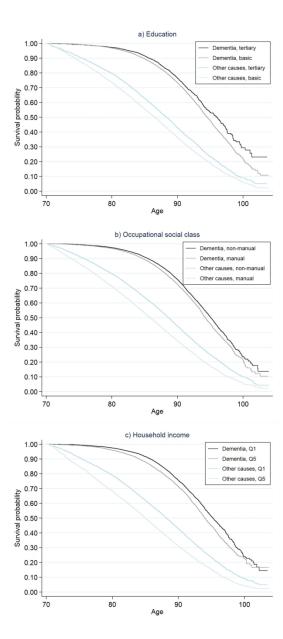


Figure 1. Kaplan–Meier survival probabilities for dementia mortality and mortality from all other causes of death by a) education, b) occupational social class and c) household income quintile (Q1=highest, Q5=lowest), Finnish men and women in 2001–2016. Information of midlife socioeconomic position obtained from the population censuses of 1970–1985, the study population being aged 53–57 years

122x265mm (300 x 300 DPI)

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Supplementary Table 1. Classification of chronic health conditions used as covariates in the study

| (105, 10) | Prescription medication | Special reimbursement category |
|----------------------------------|--|---|
| Hospital diagnoses (ICD-10) | (ATC) | (Finnish disease code) |
| F10–19, G31.2, G40.51, G62.1, | | |
| G72.1, I42.6, K29.2, K70, K86.0, | | |
| O35.4, X45 | | |
| J43–46 | | 203 |
| E10-14 | A10 | 103 |
| 100–09, 120–52 | | 201, 206, 207 |
| | G72.1, I42.6, K29.2, K70, K86.0, O35.4, X45 J43–46 E10–14 | Hospital diagnoses (ICD-10) (ATC) F10–19, G31.2, G40.51, G62.1, G72.1, I42.6, K29.2, K70, K86.0, O35.4, X45 J43–46 E10–14 A10 |

Abbreviations: ATC, Anatomical Therapeutic Chemical; COPD, chronic obstructive pulmonary diseases; ICD, International Classification of Diseases

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Supplementary Table 2. Kaplan-Meier survival probabilities at specific ages by midlife a) education, b) occupational social class and c) household income quintile (Q1=highest, Q5=lowest), Finnish men and women in 2001–2016

| | | Dementia | | Other caus | ses |
|----------------------|-----------|----------|-----------|------------|----------|
| | | Survivor | | Survivor | |
| | Age | function | 95% CI | function | 95% CI |
| a) Education | | | | | |
| Tertiary | 70 | 1.00 | | 1.00 | |
| | 75 | 0.99 | 0.99–1.00 | 0.91 | 0.89–0.9 |
| | 80 | 0.97 | 0.97–0.98 | 0.80 | 0.78–0.8 |
| | 85 | 0.92 | 0.90-0.92 | 0.63 | 0.61–0.6 |
| | 90 | 0.76 | 0.75–0.78 | 0.43 | 0.41-0.4 |
| | 95 | 0.53 | 0.50-0.56 | 0.23 | 0.22-0.2 |
| | 100 | 0.29 | 0.24–0.35 | 0.09 | 0.07–0.1 |
| Basic | 70 | 1.00 | | 1.00 | |
| | 75 | 0.99 | 0.99–1.00 | 0.88 | 0.87–0.8 |
| | 80 | 0.97 | 0.97–0.97 | 0.74 | 0.73–0.7 |
| | 85 | 0.89 | 0.89–0.90 | 0.56 | 0.55-0.5 |
| | 90 | 0.73 | 0.73-0.74 | 0.36 | 0.36-0.3 |
| | 95 | 0.48 | 0.47-0.49 | 0.19 | 0.18-0.2 |
| | 100 | 0.22 | 0.20-0.24 | 0.06 | 0.05–0.0 |
| b) Occupational soci | ial class | | | | |
| Non-manual | 70 | 1.00 | | 1.00 | |
| | 75 | 1.00 | 0.99–1.00 | 0.92 | 0.90-0.9 |
| | 80 | 0.97 | 0.97–0.98 | 0.80 | 0.79–0.8 |
| | 85 | 0.91 | 0.90-0.92 | 0.64 | 0.63–0.6 |
| | 90 | 0.76 | 0.75-0.77 | 0.44 | 0.43-0.4 |
| | 95 | 0.51 | 0.49–0.52 | 0.25 | 0.24-0.2 |
| | 100 | 0.24 | 0.21-0.27 | 0.10 | 0.09–0.1 |
| Manual | 70 | 1.00 | | 1.00 | |
| | 75 | 0.99 | 0.99–0.99 | 0.87 | 0.85-0.8 |
| | 80 | 0.97 | 0.96–0.97 | 0.71 | 0.70–0.7 |
| | 85 | 0.89 | 0.89–0.90 | 0.53 | 0.52-0.5 |
| | 90 | 0.73 | 0.72-0.73 | 0.34 | 0.34–0.3 |
| | 95 | 0.46 | 0.45-0.47 | 0.17 | 0.17–0.1 |
| | | | | | |

| | | Dementia | | Other caus | ses |
|---------------------|-----|----------|-----------|------------|---------|
| | | Survivor | | Survivor | |
| | Age | function | 95% CI | function | 95% C |
| c) Household income | | | | | |
| Q1 | 70 | 1.00 | | 1.00 | |
| | 75 | 0.99 | 0.99–1.00 | 0.91 | 0.90–0. |
| | 80 | 0.97 | 0.97–0.98 | 0.79 | 0.78–0. |
| | 85 | 0.92 | 0.91–0.92 | 0.62 | 0.61–0. |
| | 90 | 0.75 | 0.74–0.76 | 0.43 | 0.42–0. |
| | 95 | 0.51 | 0.49-0.53 | 0.24 | 0.22–0. |
| | 100 | 0.24 | 0.20-0.28 | 0.09 | 0.08-0. |
| | | | | | |
| Q5 | 70 | 1.00 | | 1.00 | |
| | 75 | 0.99 | 0.99–1.00 | 0.85 | 0.83–0. |
| | 80 | 0.96 | 0.95–0.97 | 0.68 | 0.67–0. |
| | 85 | 0.88 | 0.87–0.89 | 0.50 | 0.48–0. |
| | 90 | 0.71 | 0.70-0.72 | 0.31 | 0.30-0. |
| | 95 | 0.45 | 0.43-0.47 | 0.15 | 0.14–0. |
| | 100 | 0.23 | 0.19–0.26 | 0.04 | 0.04–0. |
| | | | | | |

0.43 0.43-0.47 0.15 0.14-0.16 100 0.23 0.19-0.26 0.04 0.04-0.06

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

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

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| Main results16(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time periodOther analyses17Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analysesDiscussionKey results18Summarise key results with reference to study objectivesLimitations19Discuss limitations of the study, taking into account sources of potential bias imprecision. Discuss both direction and magnitude of any potential biasInterpretation20Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidenceOther information21Discuss the generalisability (external validity) of the study resultsFunding22Give the source of funding and the role of the funders for the present study and, if | | | | |
|---|------------------|----|---|---|
| (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period Other analyses 17 Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses Discussion Key results 18 Summarise key results with reference to study objectives Limitations 19 Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias Interpretation 20 Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Generalisability 21 Discuss the generalisability (external validity) of the study results | Main results | 16 | precision (eg, 95% confidence interval). Make clear which confounders were adjusted for | 1 |
| meaningful time period Other analyses 17 Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses Discussion Key results 18 Summarise key results with reference to study objectives Limitations 19 Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias Interpretation 20 Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Generalisability 21 Discuss the generalisability (external validity) of the study results | | | | |
| Other analyses 17 Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses Discussion Key results 18 Summarise key results with reference to study objectives Limitations 19 Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias Interpretation 20 Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Generalisability 21 Discuss the generalisability (external validity) of the study results Other information External validity External validity | | | | |
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| Limitations 19 Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias Interpretation 20 Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Generalisability 21 Discuss the generalisability (external validity) of the study results Other information 20 | Discussion | | | |
| imprecision. Discuss both direction and magnitude of any potential bias Interpretation 20 Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Generalisability 21 Discuss the generalisability (external validity) of the study results Other information 20 | Key results | 18 | Summarise key results with reference to study objectives | 1 |
| Interpretation 20 Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Generalisability 21 Discuss the generalisability (external validity) of the study results Other information 20 | Limitations | 19 | | 1 |
| Other information | Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, | 1 |
| | Generalisability | 21 | Discuss the generalisability (external validity) of the study results | 1 |
| Funding22Give the source of funding and the role of the funders for the present study and, if | Other informatio | n | | |
| applicable, for the original study on which the present article is based | Funding | 22 | | 1 |

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.