Socioeconomic status as a risk factor for dementia death

Socioeconomic Status as a Risk Factor for Dementia Death: An Individual Participant Meta-analysis of 86 508 Men and Women from the United Kingdom

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ABSTRACT

Background: Life-course socioeconomic factors may have a role in dementia aetiology but there is a current paucity of studies. Meta-analyses of individual participant data would considerably strengthen this evidence base.

Aims: To examine the association between socioeconomic status in early life and adulthood with later dementia death.

Method: Individual participant meta-analysis of eleven prospective cohort studies of the English population (1994-2004; N=86 508).

Results: Leaving full-time education at an earlier age was associated with an increased risk of dementia death in women (fully-adjusted hazard ratio [age≤14 vs age≥16]: 1.76, 95%CI 1.23-2.53) but not men. Occupational social class was not statistically significantly associated with dementia death in men or women.

Conclusions: Lower educational attainment in women was associated with an increased risk of dementia-related death independently of common risk behaviours and comorbidities.

Declaration of Interest: None

KEYWORDS: Socioeconomic Factors, Social Class, Education, Mortality, Dementia, Meta-Analysis

INTRODUCTION

Socioeconomic inequalities in cardiovascular disease[1] and selected cancers[2] are well recognised. More recently, research attention has focused upon such differentials in mental health, including depression[3] and other common mental disorders such as dementia.[4-6] There is a suggestion that socioeconomic factors may have a role in the aetiology of dementia including lifetime manual occupation[7] as well as various indicators of socioeconomic status in early life[8] and lower educational attainment.[8, 9] However, due to the paucity of large-scale, well-characterised studies, the extant evidence is discordant and there has been inconsistent control for confounding variables. Thus, the precise nature of the socioeconomic status-dementia relation remains unclear. While individual studies undoubtedly have value in improving this evidence base, the pooling of raw data from multiple studies, which would also represent an important technical advance in this context, has yet to be utilised. We therefore undertook the first individual participant meta-analysis using data from eleven large, community-based cohort studies which held data on socioeconomic status, covariates, and dementia death. The purpose of this paper is two-fold: first, as a proof of principle that this methodology can be applied to the study of the role of socioeconomic position in risk of dementia; and second, to add to the evidence base by further investigating the association between socioeconomic factors and dementia-related death.

METHODS

Study samples

Participants were taken from the Health Survey for England,[10] a representative general population-based health examination study sampling individuals living in households in that country. From 1994 to 2004, eleven independent, cross-sectional studies with identical methodologies were conducted on an annual basis. Consenting study members

(89.6%) were followed-up by linkage to the UK National Health Service mortality registry. Study participants gave full informed consent and ethical approval was obtained from the London Research Ethics Council.

Assessment of socioeconomic status

During a household visit, interviewers collected information using computer-assisted personal interviewing modules. Information on occupational social class was collected during the interview and coded according to the Registrar General classification (professional, intermediate, skilled non-manual, skilled manual, part-skilled, and unskilled), a standard approach in the UK.[11] Age upon leaving full-time education was recorded as <15, 15, 16, 17, 18, >18, never went to school, and still in full-time education. For this study occupational social class was coded into four groups: professional/intermediate (the referent), skilled non-manual, skilled manual, and part-skilled/unskilled. Educational attainment was coded into three groups: 14 years or younger, 15 years old, and 16 years or older (the referent).

Assessment of other risk factors and comorbidities

Smoking status (not a current smoker/<5 per day/5-10 per day/10-15 per day/15-20 per day/>20 per day), weekly alcohol consumption (converted to units of alcohol), and history of cardiovascular disease and diabetes (including hyperglycaemia) were collected by self-report at interview. Individuals drinking above safe limits of alcohol were identified using gender-specific safe limits (≤14 units per week for women and ≤21 units per week for men).[12]

Psychological distress was measured using the 12-item version of the General Health Questionnaire (GHQ-12), a widely-used measure in population studies.[13] A score of four

is often used as a threshold to denote psychological distress,[14] but since we have previously shown that even low levels of psychological distress – that is, scores below four – are associated with an increased risk of dementia in these cohort studies,[15] we adjusted for total GHQ-12 score as a continuous variable.

Ascertainment of Dementia

Causes of death recorded on death certificates were coded using the *International Classification of Diseases*, Ninth[16] (ICD-9) and Tenth[17] (ICD-10) Revisions. Any mention of dementia death was identified using codes 290.0 to 290.4, 294.9, 331.0 to 331.2, and 331.9 for ICD-9 and F01, F03, F09, G30 and G31 for ICD-10.

Statistical analyses

We ascertained that the proportional hazards assumption had not been violated by inspecting the log(-log(survival)) plot. We then used Cox proportional hazards models[18] to compute study-specific hazard ratios with accompanying 95% confidence intervals for the association between the measures of socioeconomic status and dementia death. Heterogeneity in the effect estimates between studies was examined using the I^2 statistic, which indicates the proportion of the total variation in the estimates that is due to between-studies variation. It varied between 0% and 36.9% depending on the measure of socioeconomic status used in the analysis. To obtain a conservative estimate, we pooled the study-specific effect estimates and their standard errors in random effects meta-analyses. Calendar time (days) was the time scale; for participants with no record of an event, the data were censored at the 15th February 2008.

Models were initially unadjusted then a series of variables were added to the multivariable model: age, smoking status, alcohol consumption (units per week), baseline

cardiovascular disease (yes/no), diabetes (yes/no), psychological distress (GHQ-12 score), occupational social class, and educational attainment. Since, as described, the association between socioeconomic status and dementia has been reported to be different in men and women,[19] gender-specific analyses were conducted. We compared the effects of controlling for different covariates/mediators on the magnitude of the association by examining a change in the size of hazard ratio rather than a change in significance level.[20]

Individuals with data missing for one or more variable and those with no missing data were compared using Student's t-test for continuous variables and χ^2 tests for categorical variables. The main analysis was based on participants with no missing data. In the sensitivity analysis, missing values for covariates were imputed with PASW statistics version 18.0 using five imputations based on maximum likelihood estimates. All other analyses were conducted using R version 2.15.0 and the survival and metafor[21] packages. Figure 2 was constructed using the Rmeta package.[22] The reporting of this study conforms to the STROBE statement.[23]

RESULTS

The initial sample comprised 96,605 individuals. The derivation of the sample is shown in Figure 1. After removing individuals who declined linkage to mortality records (N=10,065) and for whom survival was incalculable or who had no cause of death recorded (N=32) the maximum analytic sample comprised 86 508 people (mean age=56.1 years, SD=14.4): 39,125 men and 47,383 women. Data were missing for occupational social class for 2325 individuals (analytic N=84,183) and for educational attainment for 61 individuals (analytic N=86,447). Table 1 shows the characteristics of study members from the eleven cohorts and pooled summaries.

Table 2 shows the baseline characteristics of the pooled sample according to occupational social class separately in men and women. Individuals from a lower occupational social class were older, were more likely to smoke, and had a somewhat greater likelihood of baseline cardiovascular disease, diabetes and psychological distress. There was little association between occupational social class and alcohol consumption. Individuals from a lower occupational social class were more likely, as anticipated, to have spent less time in full-time education (women r=0.41, p<0.001; men r=0.43, p<0.001). Similar patterns of association were seen with education as the exposure of interest (results not shown but available upon request).

Of the 12 952 deaths during a mean follow up of 8.6 years (SD=3.5), 622 were ascribed to dementia. Figure 2 shows the fully-adjusted hazard ratios for the association of occupational social class and educational attainment with dementia death for each cohort study, in addition to gender-specific totals and meta-analysed effects. Overall, relative to study members from professional/intermediate occupational social classes, there was no increase in the risk of dementia death among those belonging to the lower social classes in women (fully-adjusted HR, 95% CI; skilled non-manual: 0.88, 0.59-1.31; skilled manual: 0.61, 0.36-1.06; semi-skilled and unskilled manual: 0.92, 0.62-1.36) or men (skilled non-manual: 1.03, 0.53-2.00; skilled manual: 1.03, 0.63-1.69; semi-skilled/unskilled manual: 1.33, 0.80-2.21). Relative to study members who left school aged 16 or older, there was an increase in the risk of dementia death among those leaving school earlier in women (leaving school aged 15: 1.64, 1.02-2.65; leaving school aged 14 or younger: 1.76, 1.23-2.53) but not in men (leaving school aged 15: 0.98, 0.51-1.89; leaving school aged 14 or younger: 1.20, 0.77-1.87).

Table 3 shows the impact of controlling for covariates on the association between the two indicators of socioeconomic status and dementia in women and men. The association between occupational social class and dementia death seen in age-adjusted models was completely explained by covariates in women but was more robust to statistical adjustment in men.

The association between leaving full-time education at an earlier age and later dementia death observed in the age-adjusted models was fully attenuated on adjustment for covariates in men but remained in women.

Sensitivity and sub-group analyses

Data were missing for one or more variable in 32.8% (N = 28 375) of the sample. A supplementary table (eTable 1) shows a comparison of the characteristics of individuals with complete data for all variables versus individuals who were missing data for one or more variables. Individuals with complete data were more likely to be male, younger, drink more alcohol per week and were more likely to drink over recommended limits and a larger proportion were current smokers. They were less likely to have diabetes and cardiovascular disease at baseline. A slightly larger proportion of individuals with complete data belonged to a non-manual occupational social class and women were less likely to have left school early (the reverse was true of men). Therefore, individuals with missing data did not always have unfavourable levels of risk factors. Accounting for missing data by multiple imputation did not alter our conclusions (eTable 2). Similarly, excluding dementia-related deaths occurring within five years of follow up, to explore reverse causality in the case of current occupational social class, did not affect our results (eTable 3).

DISCUSSION

The purposes of the current study were to show that an individual-participant meta-analysis technique can be applied to a socioeconomic risk factor and also to investigate the association between socioeconomic status and dementia-related death. In order to achieve the former we used a convenience sample of eleven large UK population-based cohort studies. With regard to the latter, the main finding of this study was that educational attainment was associated with dementia death in women but not in men. In men, we also found that, relative to the highest two classes, belonging to the lowest two occupational social classes was associated with an elevated risk of dementia death; a relationship that did not reach statistical significance at conventional levels. There was no association between occupational social class and dementia death in women.

Strengths and limitations

To our knowledge, this study is the first to use an individual-participant meta-analysis methodology to examine the association between socioeconomic variables and dementia. In contrast to previous literature-based analyses, an individual participant meta-analysis has the advantage of providing precise estimates of risk marker-disease relationships, reliable information on the shape of a given risk factor-disease relationship (e.g., dose-response vs threshold), and a consistent approach to statistical control for plausible covariates and subgroup analyses. We used a large, well-characterised sample that is representative of the general population in England. This provided sufficient power to allow gender-specific analyses and allowed us to explore the role of a series of explanatory factors. By including two measures of socioeconomic status at different time points we offer some insights into the influence of life-course socioeconomic status on dementia risk.

This notwithstanding, the data have their limitations. Despite the large sample and over twelve thousand deaths during follow up, there were only 622 dementia-related deaths. This is due to the wide age range of individuals included in the survey at baseline—adults aged 35 and over. While this wide age-range increases the generalizability of the findings, it has resulted in a relatively small proportion of individuals dying with dementia and consequently wide confidence intervals, limiting the conclusions that can be drawn. The identified gender differentials should be viewed in the light of this question of power. The number of dementia-related deaths in this study is likely to have been additionally affected by the unavoidable problems of under-diagnosis of dementia in the community,[24] under-recording of dementia on death certificates,[25] and diagnoses being inaccurately coded. Non-recording of dementia on death certificates has been highlighted as an important issue but this seems to be improving. A recent study identified that 71.5% of a clinic sample diagnosed with probable Alzheimer disease had dementia correctly recorded on their death certificate.[26] There was no association in that sample between correct dementia certification and area deprivation or premorbid IQ estimated by the National Adult Reading Test (unpublished results available on request), suggesting that individuals reported as having dementia on their death certificate are representative of the population of people with diagnosed dementia in the community, at least in terms of intelligence and level of deprivation.

Comparison with previous studies

Dementia was estimated to affect over 24 million people globally in 2001 and this is expected to rise to over 80 million by 2040.[27] In England and Wales the prevalence of dementia is estimated to vary from approximately 1.5% at age 65-69 to approximately 25.3% over the age of 84.[28] Dementia incidence ranges from 7.4 (95% CI 3.6-16.1) per 1000 person-years at age 65-69 to 84.9 (95% CI 63.0-107.8) per 1000 person-years over

the age of 84.[29] However existing prospective studies of socioeconomic factors have generally been small in scale – only one analysis reported a combined sample larger than 10,000[19] – and few studies measure socioeconomic status at more than one timepoint.[8] On a related note, the association between education and dementia risk has been reported to be present in women but not in men;[19] it is therefore important that studies are sufficiently large to allow gender-specific analyses. In addition, for older participants – who are most likely to have died with dementia during follow-up – the social class may have been allocated to females on the basis of their husband's occupation, further muddying the waters.

Factors across the lifespan have been implicated in the aetiology of dementia. A series of studies confirm a link between early life socioeconomic status and dementia risk with early parental death – and, potentially, consequent socioeconomic hardship – being highlighted as an important risk factor.[30]

Fifty one of 88 studies included in a systematic review[6] reported a significant association between a basic education and dementia risk, the remainder reporting no effect. However, only two previous studies report gender-specific effects, showing an effect of education on dementia risk in women but not in men, as found in the current study.

In England, the Education Act (1918) raised the school leaving age from 12 to 14. It was further increased to 15 in 1947 and to 16 in 1973. Participants in the Health Survey for England came from all these educational eras and overall approximately half of men and women stayed on after completion of the compulsory period of education. However, individuals were much more likely to remain in education longer if they were born later: 86.7% women and 87.2% men born after 1956 (who therefore had to remain in school

until 16) compared to 17.8% women and 18.5% men born before 1906 and who could therefore leave school at 12. However the reference category used of individuals who remained in full-time education up to 16 years or later exactly matches those who remained in education after the compulsory school leaving age.

Since children scoring higher on IQ tests, as well as children from a higher occupational social class, are more likely to be given the opportunity to remain in education for longer, a number of studies have investigated the association between childhood mental ability and dementia. A Scottish study identified 50 participants in the 1932 Scottish Mental Survey who had developed dementia and ascertained that their scores on the Moray House Test in 1932 had been significantly lower than their peers in the same area who did not develop dementia.[31] However a larger subsequent study confirmed that this was the case for vascular dementia but not for Alzheimer's disease.[32] On the other hand, the Nun study identified that low linguistic ability at a mean age of 22 was associated with Alzheimer's disease in the 14 study participants aged 79 to 96 whose brains were neuropathologically examined post mortem.[33]

Occupation in adulthood has also been shown to be associated with dementia risk—high 'occupational attainment' is associated with lower dementia risk.[34] However, since the pathology of Alzheimer's disease and probably vascular dementia develops over a very long period of time[35] risk factors must be measured sufficiently early in life for them to have an effect and exposures immediately before retirement may have little or no effect on dementia risk.

Few studies measure socioeconomic status across the whole lifespan. One study to do so identified early parental death, manual work and physical illness in the spouse or serious

illness in a child, both after the age of 65 to be independent risk factors for dementia.[8] However, many of the socioeconomic factors measured in studies are closely linked and disentangling their individual effects can be extremely difficult.

Mechanisms of effect

The role of education and mental ability as potential risk factors for dementia has been linked to the hypothesis of cognitive reserve – that certain individuals' brains are structurally or functionally more resilient to disease or injury. This sprang from the observation that there was no clear relationship between the extent of brain pathology and the clinical manifestations of dementia in an individual. Cognitive reserve might relate to a person's intrinsic makeup or could result from external experience, i.e. education and occupation. Indeed there is evidence that occupation is associated with differences in parietal blood flow in Alzheimer disease which could be a marker of reserve.[36]

Criticisms of the cognitive reserve hypothesis include the suggestion that the effect merely reflects performance on cognitive tests[37] or that the effect is mediated by lifestyle factors and cerebrovascular risk.[38] The present study used clinical diagnoses of dementia recorded on death certificates and two measures of socioeconomic status at different stages of life. This allows us to demonstrate that the observed association between education and dementia in women was not mediated by adult occupation.

Since an individual with more cognitive reserve would have more advanced pathological changes at the time of diagnosis, it has been suggested that this could be linked with a swifter decline and poorer survival. Some studies have found that individuals with Alzheimer's disease and higher educational and occupational attainment declined faster

in their performance on cognitive tests.[39] This aspect of the cognitive reserve hypothesis was not examined by the current study.

Implications

An association between lower educational attainment and dementia in women but not men has a number of implications. First, the mechanism of this association, currently hypothesised to relate to cognitive reserve, must be clarified. Second, the reason that the association is observed only in women should be investigated. It may be that fewer women entered further education and that those who did had to be very intelligent to do so. Thus length of education in these cohorts could be confounded by intelligence in women to a greater extent than men. However the identified gender difference may also potentially hold the clue to an intervention to decrease the risk of dementia in women, if a modifiable risk (or protective) factor could be identified. Lastly, if this association were to reflect a causative link between education and dementia risk, promoting higher and further education, especially for women, could have important public health consequences for a common and serious condition.

Conclusion

This large prospective study shows an association between leaving full-time education at a younger age and dementia death in women, but not in men. This relationship remained after adjustment for alcohol, smoking, cardiovascular disease, diabetes, psychological distress, and occupational social class. An association between lower occupational social class and dementia death which did not reach statistical significance at conventional levels was also observed in men but not in women.

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Table 1. Characteristics of participants[1] according to cohort study: the Health Survey for England 1994-2004

Year		1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	Overall
Number		10,599	10,905	11,344	5,875	11,058	5,522	8,684	11,283	5,399	10,887	5,049	**96,605**
Household response (%)		77	78	79	76	74	76	75	74	74	73	72	**—**
Estimated adult interview response (%)		71	73	75	71	69	70	68	67	67	66	66	**—**
Age	56.1 (14.4)	56.2 (14.3)	56.0 (14.3)	55.6 (14.0)	56.1 (14.3)	55.7 (14.3)	65.8 (18.5)	56.0 (14.3)	55.4 (14.4)	56.3 (14.3)	57.0 (14.3)	**56.9 (15.0)**	**56.9 (15.0)**
	35-97	35-100	35-102	35-95	35-97	35-96	35-107	35-97	35-97	35-97	35-96	**35-107**	**35-107**
Female (%)		54.9	54.1	54.3	54.6	55.0	54.3	62.1	55.5	56.3	55.6	57.6	**55.7**
Occupational social class (% I-IIINM)		53.8	55.3	55.2	54.8	54.6	56.5	56.4	56.6	57.8	57.7	59.7	**53.2**
Current smoker (%)		23.5	23.2	24.2	23.3	23.2	22.6	17.7	21.6	22.5	21.2	19.3	**22.2**
Drinks more than recommended alcohol limit[2] (%)		18.8	19.6	20.1	20.0	21.3	19.1	13.1	21.2	20.5	—[3]	—[3]	**19.4**
Cardiovascular disease at baseline[4] (%)		4.8	5.0	4.9	4.5	4.5	4.9	7.6	5.0	4.2	4.4	4.5	**5.0**
Diabetes, including hyperglycaemia, at baseline (%)		2.6	3.0	3.1	3.5	3.0	3.7	4.7	4.3	4.1	4.7	5.5	**3.7**
GHQ-12 score	mean (SD)	1.5 (2.6)	1.7 (2.8)	—[5]	1.5 (2.7)	1.5 (2.7)	1.7 (2.8)	1.6 (2.8)	1.3 (2.5)	1.6 (1.7)	1.3 (2.5)	1.3 (2.6)	**1.5 (2.7)**
Consented to mortality linkage (%)		95.2	93.5	93.5	94.1	94.5	93.8	68.2	88.4	88.4	87.2	85.5	**89.6**
Median follow-up (years)		13.5	12.5	11.5	10.5	9.5	8.5	7.4	6.6	5.6	4.6	3.5	**8.4**
Deaths from any cause		2320	2193	2023	892	1591	697	1364	867	337	503	165	**12952**
Dementia deaths		106	104	88	43	83	30	101	34	11	17	5	**622**

[1] All participants in the surveys are represented in this table, irrespective of consent to mortality linkage. All subsequent tables and figures only represent individuals who consented to linkage and were therefore included in the present study.
[2] Calculated using gender-specific safe limits: ≤14 units per week for women and ≤21 units for men
[3] Alcohol intake was recorded in a different format to other years in the Health Surveys for England in 2003 and 2004
[4] History of cardiovascular disease including angina, myocardial infarction or stroke (haemorrhagic or thrombotic)
[5] GHQ-12 was not administered in the Health Survey for England in 1996

Table 2. Study members' baseline characteristics according to occupational social class: the Health Survey for England 1994-2004

Women

	Occupational Social Class						Total N
	I	**II**	**IIINM**	**IIIM**	**IV**	**V**	
N	754	11663	15956	4079	8954	4081	45487
Age mean (SD)	49.1 (12.5)	53.4 (13.7)	56.0 (14.4)	59.0 (15.3)	56.6 (14.6)	60.8 (14.6)	45487
Left school <16 years (%)	4.4	23.7	43.2	65.8	63.7	39.6	45455
Current smoker (%)	12.1	18.0	19.9	26.8	28.2	29.7	45469
Drinks more than recommended alcohol limit[1] (%)	19.1	15.7	12.9	9.7	8.6	7.8	37752
Cardiovascular disease at baseline[2] (%)	1.6	2.7	3.5	5.1	4.9	6.4	45487
Diabetes, including hyperglycaemia, at baseline (%)	0.9	2.1	2.6	4.2	3.5	4.2	45487
GHQ-12 score[3] mean (SD)	1.5 (2.7)	1.6 (2.7)	1.5 (2.7)	1.8 (2.9)	1.8 (2.9)	1.8 (3.0)	38162

Men

	Occupational Social Class						Total N
	I	**II**	**IIINM**	**IIIM**	**IV**	**V**	
N	2987	12272	3759	12835	5163	1680	38696
Age mean (SD)	54.7 (13.5)	54.3 (13.5)	56.2 (14.6)	56.4 (13.9)	56.7 (14.1)	57.2 (13.7)	38696
Left school <16 years (%)	11.5	27.8	40.0	64.1	64.2	71.4	38667
Current smoker (%)	9.2	16.1	19.8	28.6	31.2	37.6	38672
Drinks more than recommended alcohol limit[1] (%)	22.8	25.7	21.1	23.0	20.6	22.8	32554
Cardiovascular disease at baseline[2] (%)	2.8	4.5	6.4	6.8	6.7	6.7	38696
Diabetes, including hyperglycaemia, at baseline (%)	2.7	4.0	4.8	4.6	5.4	4.5	38696
GHQ-12 score[3] mean (SD)	1.1 (2.2)	1.2 (2.3)	1.2 (2.4)	1.3 (2.5)	1.5 (2.7)	1.6 (2.9)	32560

[1] Calculated using gender-specific safe limits: ≤14 units per week for women and ≤21 units for men
[2] History of cardiovascular disease including angina, myocardial infarction or stroke (haemorrhagic or thrombotic)
[3] GHQ-12 was not administered in the Health Survey for England 1996

Table 3. Hazard ratio (95% confidence interval) for the association between occupational social class and educational attainment with dementia death: the Health Survey for England 1994-2004

WOMEN	Occupational Social Class								Age Upon Leaving Full-Time Education						
	Dementia Deaths	N	I-II	IIINM		IIIM		IV-V		Dementia Deaths	N	≥16	15		≤14	
			HR	*HR*	I^2	*HR*	I^2	*HR*	I^2			*HR*	*HR*	I^2	*≤14*	I^2
Unadjusted model	358	45487	1 (ref.)	1.34 (0.97, 1.86)	0.0	2.27 (1.49, 3.44)	0.0	2.18 (1.59, 2.98)	0.0	411	47351	1 (ref.)	1.32 (0.90, 1.95)	5.4	9.87 (7.67, 12.7)	0.0
Adjusted for age (basic model)	358	45487	1	1.05 (0.75, 1.48)	5.9	0.96 (0.63, 1.47)	0.0	1.33 (0.97, 1.83)	0.0	411	47351	1	1.54 (0.96, 2.47)	28.4	1.61 (1.25, 2.08)	0.0
+ risk factors[1]	343	37998	1	1.07 (0.75, 1.53)	8.5	0.94 (0.61, 1.46)	0.0	1.30 (0.94, 1.79)	0.0	393	39612	1	1.46 (0.88, 2.43)	36.9	1.56 (1.18, 2.07)	6.6
+ somatic comorbidities[2]	358	45487	1	1.05 (0.74, 1.49)	8.5	0.96 (0.63, 1.46)	0.0	1.34 (0.98, 1.84)	0.0	411	47351	1	1.57 (0.98, 2.53)	29.3	1.65 (1.28, 2.13)	0.0
+ psychological distress	275	38553	1	0.99 (0.69, 1.43)	0.0	0.81 (0.49, 1.35)	0.0	1.23 (0.86, 1.75)	0.0	317	40035	1	1.60 (1.04, 2.48)	3.3	1.61 (1.20, 2.16)	0.0
+ age upon leaving full-time education	358	45487	1	0.93 (0.67, 1.31)	2.7	0.74 (0.48, 1.15)	0.0	1.01 (0.72, 1.42)	0.0	-	-	-	-	-	-	-
+ occupational social class	-	-	-	-	-	-	-	-	-	358	45465	1	1.57 (1.02, 2.43)	6.2	1.68 (1.24, 2.28)	0.0
Fully Adjusted	264	31343	1	0.88 (0.59, 1.31)	4.1	0.61 (0.36, 1.06)	0.0	0.92 (0.62, 1.36)	0.0	264	31343	1	1.64 (1.02, 2.65)	0.0	1.76 (1.23, 2.53)	0.0
MEN	**Dementia Deaths**	**N**	**I-II**	**IIINM**		**IIIM**		**IV-V**		**Dementia Deaths**	**N**	**≥16**	**15**		**≤14**	
			HR	*HR*	I^2	*HR*	I^2	*HR*	I^2			*HR*	*HR*	I^2	*HR*	I^2
Unadjusted model	210	36880	1 (ref.)	1.51 (0.88, 2.59)	0.0	1.43 (0.95, 2.15)	21.8	1.81 (1.23, 2.67)	4.3	211	37263	1 (ref.)	0.77 (0.44, 1.33)	0.0	8.89 (6.38, 12.4)	0.0
Adjusted for age (basic model)	210	36880	1	1.13 (0.66, 1.94)	0.0	1.29 (0.88, 1.89)	11.5	1.52 (1.01, 2.29)	10.3	211	37263	1	1.03 (0.59, 1.80)	0.0	1.44 (1.03, 2.02)	0.0
+ risk factors[1]	204	32596	1	1.07 (0.62, 1.85)	0.0	1.29 (0.85, 1.95)	19.8	1.38 (0.86, 2.22)	24.8	205	32939	1	0.96 (0.54, 1.72)	0.0	1.30 (0.92, 1.84)	0.0
+ somatic comorbidities[2]	210	36880	1	1.14 (0.66, 1.96)	0.0	1.28 (0.86, 1.90)	16.8	1.49 (0.97, 2.30)	16.4	211	37263	1	1.05 (0.60, 1.84)	0.0	1.38 (0.99, 1.94)	0.0
+ psychological distress	158	30899	1	1.15 (0.60, 2.19)	0.0	1.24 (0.83, 1.85)	1.3	1.72 (1.12, 2.64)	0.0	158	31215	1	1.05 (0.56, 1.97)	0.0	1.45 (0.98, 2.14)	0.0
+ age upon leaving full-time education	210	36854	1	1.06 (0.61, 1.84)	0.0	1.12 (0.72, 1.74)	20.8	1.38 (0.90, 2.12)	6.1	-	-	-	-	-	-	-
+ occupational social class	-	-	-	-	-	-	-	-	-	210	36854	1	0.94 (0.53, 1.67)	0.0	1.29 (0.88, 1.88)	0.0
Fully Adjusted	155	26790	1	1.03 (0.53, 2.00)	0.0	1.03 (0.63, 1.69)	13.0	1.33 (0.80, 2.21)	6.4	155	26790	1	0.98 (0.51, 1.89)	0.0	1.20 (0.77, 1.87)	0.0

[1] Risk factors comprise smoking and alcohol consumption
[2] Somatic comorbidities comprise cardiovascular disease and diabetes

Figure 1. Flow chart of participants from initial pooled sample through to analytic sample showing subsequent mortality: the Health Survey for England 1994-2004

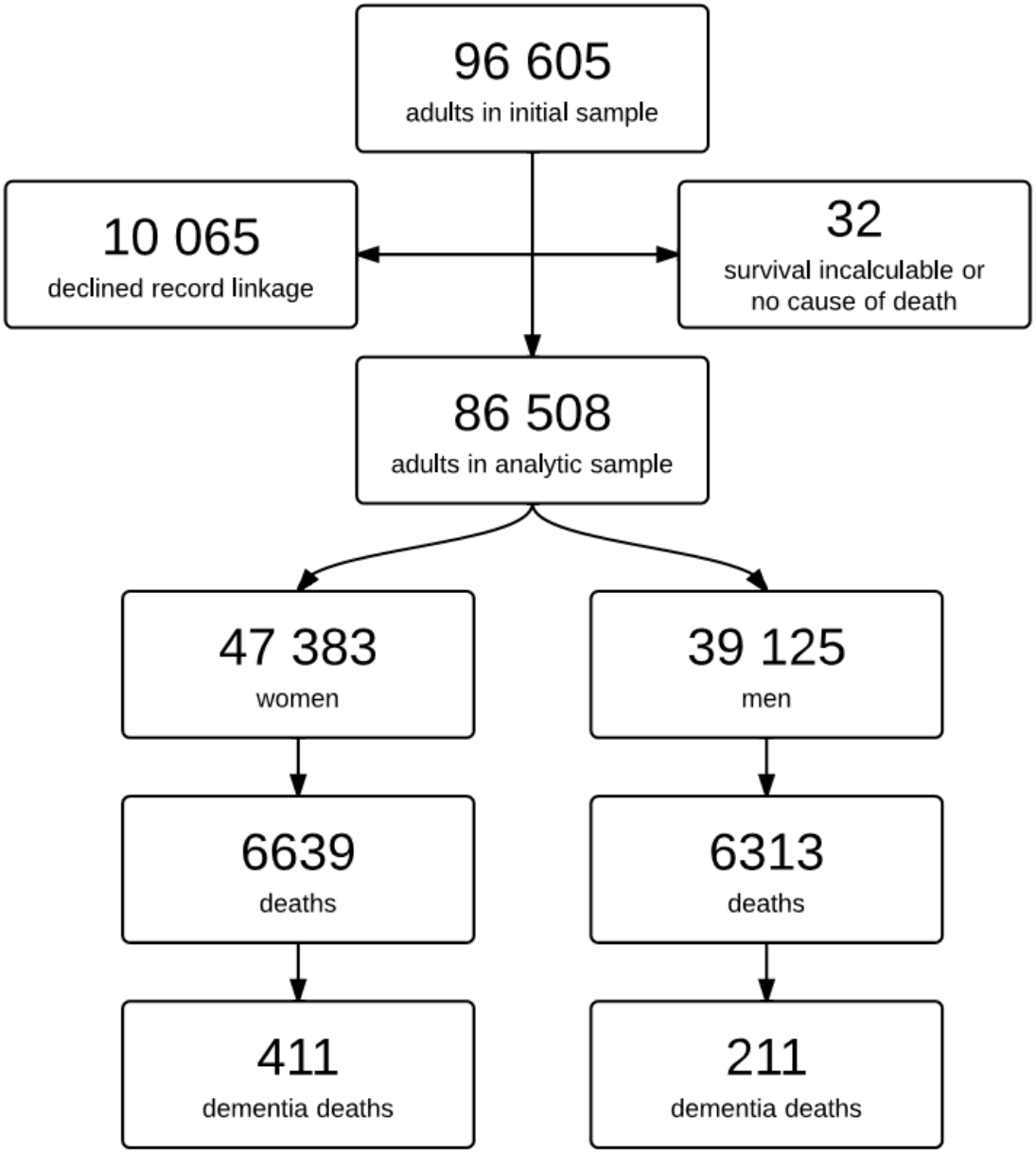
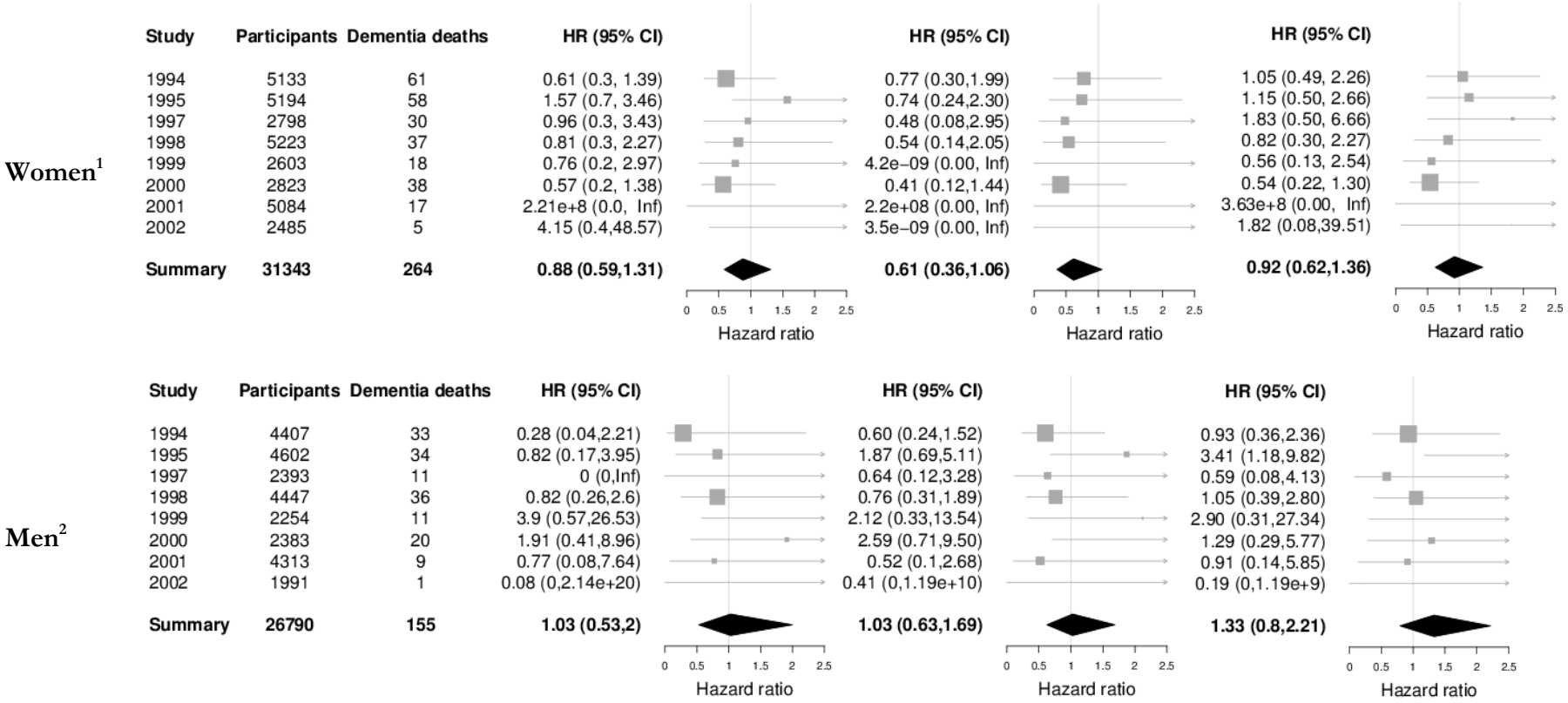


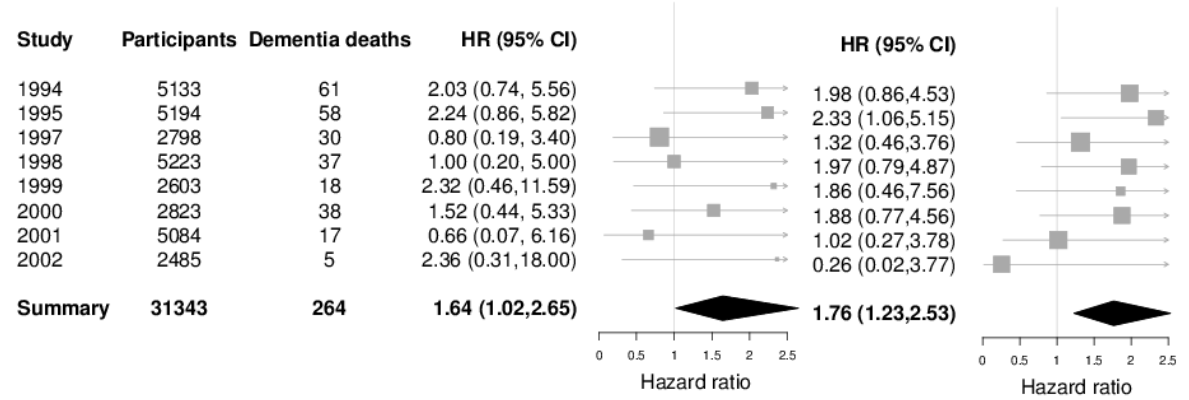
Figure 2a. Fully-adjusted hazard ratios with 95% confidence intervals of dementia death by survey year for individuals from (i) skilled non-manual, (ii) skilled manual, and (iii) semi-skilled/unskilled manual occupational social classes compared to professional/intermediate: the Health Survey for England 1994-2004



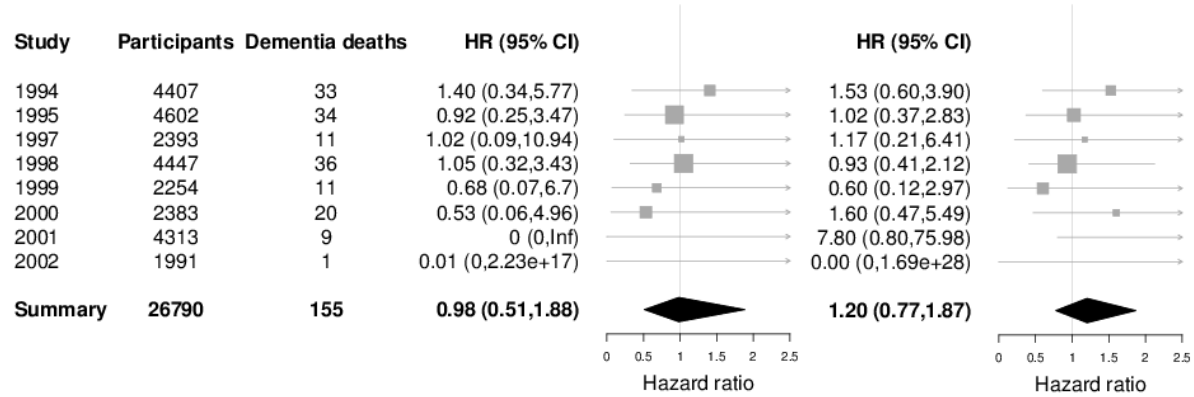
[1] I^2 values for these models are 4.1%, 0.0%, and 0.0%
[2] I^2 values for these models are 0.0%, 12.9%, and 6.4%

Figure 2b. Fully-adjusted hazard ratios with 95% confidence intervals of dementia death by survey year for individuals who left full-time education aged (i) 15 years, and (ii) 14 years or younger compared to those who left full-time education aged 16 years or older: the Health Survey for England 1994-2004

Women[3]



Men[4]



[3] I^2 values for these models are 0.0% and 0.0%
[4] I^2 values for these models are 0.0% and 0.0%