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Shift work, long working hours, and later risk of dementia: A long-term follow-up of the Copenhagen Male Study

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The current study investigates the unresolved question about the effect of shift work and long working hours on dementia. We did not find an increased incidence of dementia among shift workers or employees with long working hours. Such working hours may lead to acute cognitive impairments but there is no strong evidence for a chronic effect eventually leading to dementia.

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Key terms: Alzheimer's disease; circadian disruption; Copenhagen Male Study; dementia; employee; long working hours; longitudinal; night work; shift work; work factor

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Original article

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Shift work, long working hours, and later risk of dementia: A long-term follow-up of the Copenhagen Male Study

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Objectives The aim of this study was to investigate the effect of shift work and long working hours in midlife on the risk of dementia in old age.

Methods The present study comprised 4766 participants from the Copenhagen Male Study. We used information on shift work (collected in 1970–1971 and 1985–1986), long working hours defined as >45 hours per week (collected in 1970–1971), socioeconomic status, sleep, stress, and cardiovascular risk factors. Information about dementia diagnoses was obtained from registers. Participants were followed until 2014 (mean length of follow-up was 17.8 years). We employed Poisson regression for the survival analyses and estimated incidence rate ratios (IRR) and their 95% confidence intervals (CI).

Results We found no statistically significant association between shift work (IRR 0.86, 95% CI 0.70–1.05) or long working hours (IRR 0.97, 95% CI 0.79–1.19) and dementia. Adjustment for potential confounders and mediators did not change the estimates. Working shifts at both time points of exposure assessment was not associated with a higher incidence of dementia compared with non-shift workers at both time points (IRR 0.99, 95% CI 0.69–1.42). The lowest incidence of dementia was observed among participants who reported shift work at one time point (only in 1985–1986: IRR 0.44, 95% CI 0.16–1.23 and only in 1970–1971: IRR 0.58, 95% CI 0.31–1.11).

Conclusion We did not find positive evidence of an association between shift work or long working hours and the incidence of dementia, but the negative findings may reflect the crude assessment of shift work and long working hours, which is a major limitation of the present study.

Key terms Alzheimer's disease; circadian disruption; employee; longitudinal; night work; work factor.

Dementia is strongly age-related with an incidence ranging from 3 per 1000 person-years among 60–64 year-olds to 122 per 1000 person-years among the ≥90-year olds (1). Despite the increased life expectancy, recent studies in Europe and the US suggest that the overall incidence of dementia is perhaps decreasing (2–5). Risk reduction throughout the life course, via improvements in living conditions, educational level, and lifestyle-related cardiovascular risk factors, has been suggested as a potential explanation of this decline (3, 4). Thus, some risk factors for dementia appear to be modifiable and therefore a suitable case for primary prevention targeting early or midlife risk factors (4, 6).

Shift work, especially night work and long working hours are among the possible modifiable risk factors that may influence the incidence of dementia through their effect on risk factors for dementia such as cardiovascular risk factors (7–10) and sleep (11–13). In addition, shift work may cause cortisol-induced atrophy of the hippocampus (14) as night work and jet-lag (causing circadian disruption) may elicit an activation of the hypothalamic-pituitary-adrenal axis as indicated by increased salivary

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cortisol levels (15, 16). Still, not all studies support that night work leads to elevated cortisol levels (17), and one study did not find that long working hours (>48 hours per week) was associated with higher cortisol levels (16). However, as reflected in two recent reviews of the literature on work-related factors, cognition and dementia, only few studies on shift work or long working hours and outcomes related to cognition have been published (18, 19).

Two previous studies based on data from the VIASAT cohort found indications of lower cognitive function among shift workers (20, 21), whereas two other studies found no association between shift work and cognitive function (22, 23). With dementia as the outcome, one study did not find an association with history of shift work (24), whereas one recent study reported that shift work was associated with mortality due to dementia (25). Lower cognitive function has been related to overtime work and long working hours (26, 27), but studies on the effect of long working hours on the incidence of dementia have yet to be published.

Thus, although there is some evidence in the literature that supports the hypothesis of a negative effect of shift work and long working hours on the incidence of dementia, this association is not empirically well established. The aim of the present study was therefore to investigate the effect of shift work and long working hours in midlife on the risk of dementia in old age using data on 4766 men from the Copenhagen Male Study combined with information on dementia diagnoses from Danish registers.

Methods

Study population, design, and exclusion criteria

We included participants from the Copenhagen Male Study (CMS). CMS was established in 1970 and included male employees from 14 large companies in the Copenhagen area. The companies included a number of public organizations (railways, public road construction, military, mail, telephone, customs, and the national bank) and the medical industry. All male employees aged 40–59 years were invited, and 5249 males participated (87%). The baseline data collection comprised a questionnaire, a short interview, and a clinical examination and lasted from October 1970 to September 1971. In 1985–1986, 3387 surviving males (75%) from the original cohort participated in a follow-up study (28).

When CMS was planned and initiated neither scientific committees nor data protection agencies existed in Denmark. The present study on shift work, long working hours and dementia is part of the MEMORIA project, which has the required permissions from the Danish Data Protection Agency and the local research ethics committee.

For the purpose of the present study, we started following individuals in the cohort five years after the completion date of exposure assessment to reduce the risk of reverse causation, ie, that early subclinical dementia could have affected the choice of working hours. Thus, only participants who were alive, not emigrated, and free of dementia during the first five years after reporting their exposure were eligible for inclusion. During follow-up, participants were censored if they died, were registered with a diagnosis of dementia or at end of follow-up (31 December 2014), whichever came first.

Dementia diagnoses – registered for the first time when the patients are ≥60 years old – have been shown to have good validity with a positive predictive value of 86% while those registered when the patients are younger have shown to be unreliable (29–31). Therefore, we made a further restriction and only included risk and dementia diagnoses from the date the participants turned 60 years old. These criteria implied that all participants aged ≤55 years at the time of exposure assessment started contributing with risk time when they turned 60 years; participants who were >55 years at the time of the exposure assessment were followed when five years had passed and these participants were, thus, >60 years old when they started contributing with risk time. Our final study population for the main analyses comprised 4766 participants, and 1597 participants were eligible for inclusion in the analyses using data from the 1985–1986 survey.

Outcome measure

We obtained information on dementia diagnoses from the Danish Psychiatric Central Research Register (PCRR), the Danish National Patient Register (NPR), and the Danish Register of Causes of Death (RCD). PCRR was established as an electronic database in 1969 and, from 1970, all mental hospitals and psychiatric departments were obliged to report to the register. From 1995, also outpatient treatment and emergency room contacts were included (32). The NPR was initiated in 1977 and covered inpatient contacts in somatic wards. From 1995 onwards, all outpatient activities, emergency room contacts, and activities in psychiatric wards were also recorded (33). The RCD was initiated in 1975 covering all deaths, and on a national level only 0.3–0.6% of all deaths are not fully reported (34). The earliest calendar year during which follow-up took place was 1975.

Dementia diagnoses were made based on WHO international classification of disease (ICD) criteria – ICD-8 in 1970–1993 and ICD-10 in 1994 onwards. The validity of dementia diagnoses in the NPR and PCRR has been shown to be good..." has been shown to be good with a positive predictive value of 86% in a random sample of patients with a mean age of 81 [standard deviation (SD) 9] years (29). The validity of the dementia diagnoses in the Danish RCD has not been examined.

In the current study, we did not differentiate between dementia subtypes for two reasons: First, the validity of the diagnoses of dementia subtypes has been shown to be low (29). Second, the different dementia subtypes may share a common cardiovascular pathway from exposure to disease because the majority of dementia subtypes involve an underlying small-vessel disease or cerebrovascular dysfunction at some point during disease progression (35). Accordingly, the dementia outcome was defined as being registered with one of the following diagnostic codes: Alzheimer's disease (ICD-8:290.09; ICD-10:F00.0-9, G30.0-9), vascular dementia (ICD-8:293.09-19; ICD-10:F01.0-9), fronto-temporal dementia (ICD-8:290.11; ICD-10:F02.0), dementia with Lewy bodies (ICD-10:G31.8), and dementia without specification (ICD-8:290.09-19; ICD-10:F03.9, G31.9).

Exposure measures

In 1970–1971, shift work was assessed with the question "Do you have shift work or frequent night work?" (yes/no), and the number of working hours was quantified through the question "How many hours do you work per week?" (Response options: less than 30, 30–35, 36–40, 41–45, >45 hours). In Denmark in 1970, the collective agreement defined the standard weekly working hours as 41.75 hours (36). In the present sample, the majority (69%) worked 41–45 hours per week, and long working hours was defined as ≥45 hours per week.

In 1985–1986, shift work was assessed with the question "Are your working hours (i) fixed day work, (ii) fixed evening work, (iii) fixed night work, or (iv) variable at different times of the 24-hour day?" In the sample eligible for inclusion in the analyses, the groups of fixed evening workers and fixed night workers were too small to be analyzed separately (N=6). Therefore, we applied a broad definition of shift work as work outside the conventional day time which thereby covers fixed evening and night work, roster work, and ordinary 3-shift work (37), and collapsed the last three categories (ii, iii, and iv) into one category. For our supplementary analyses, we combined the information on shift work from 1970–1971 and 1985–1986 and categorized the participants into four groups: shift work at both time points, shift work only in 1985-86, shift work only in 1970–1971, and no shift work at any time point (reference group). We did not have information on weekly working hours in 1985–1986.

Covariates

We included information about age in each calendar year (referred to as "current age"), time since exposure assessment in each calendar year, and calendar year in four groups (1975–1983, 1984–1993, 1994–2003, 2004–2014). In Denmark, ICD-10 replaced ICD-8 in 1994, thus this latter calendar year variable also took into account the change in diagnosing and registering dementia diagnoses. Socioeconomic status was measured by educational level and job position in terms of the number of subordinates (28).

From the questionnaires, we included information about psychological stress during work and leisure time, respectively (seldom/regularly), hours of sleep per night (dichotomized into <6 and ≥6 hours) and cardiovascular disease (treatment for heart disease or hypertension, having an acute myocardial infarction and/or experiencing chest pain). The participants were also asked whether they were smokers (yes/no), how much exercise they did during leisure-time (almost none/some/a lot), and how much alcohol they consumed (trichotomized into 0/1–2/≥3 units per day). We also included information from a clinical examination on body mass index (weight in kilograms divided by the square of height in meters) and systolic/diastolic blood pressure (BP) in mmHg.

Previous research has shown that day and shift workers differ on cardiovascular risk factors and exposure to job stressors (37, 38) and – importantly – that these differences may be present already before taking up shift work (39, 40). In addition, health-related selection of employees into shorter and longer working hours is likely to occur. Therefore, we conducted the analyses both with and without adjustment for the above-mentioned covariates. The adjusted analyses can be considered as conservative as these covariates may also constitute a pathway (ie, mediators) from exposure to disease (9, 10).

Statistical analyses

We stratified the individual follow-up time by age and calendar year into an event-time table and analyzed the association between exposure to shift work/long working hours and a later dementia diagnosis using Poisson regression (41, 42). The results are presented as incidence rate ratios (IRR) with their 95% confidence intervals (CI). In the first analyses, the estimates were only adjusted for current age, time since exposure measurement, and calendar year. In further analyses, we added covariates to the analyses in blocks in order to elucidate their influence on the estimated association between shift work/long working hours and dementia. Model 1 included shiftwork, long working hours, current age, time since exposure assessment, calendar year and socioeconomic status. Model 2 included covariates from Model 1 plus sleep length and psychological stress during work and leisure time. Model 3 included covariates from Model 1 plus cardiovascular disease and cardiovascular risk factors.

In supplementary analyses, we investigated whether the incidence of dementia was associated with the amount and timing of shift work by using the exposure measure that combined information on shift work in 1970–1971 with the information on shift work in 1985–1986. In these analyses we adjusted for current age, time since exposure assessment, calendar year, and socioeconomic position.

Participants with missing data were excluded analysis by analysis. In the analyses, there was minimal loss to follow-up as the Danish national registers cover all participants.

All analyses were conducted using SAS version 9.2 (SAS Institute, Cary, NC, USA).

Results

In 1970–1971, 18.2% were categorized as having long working hours and 21.4% were categorized as shift workers. At follow-up in 1985–1986, 17.5% were categorized as shift workers. Table 1 illustrates that shift workers had a poorer dementia risk factor profile in terms of sleep, work stress, smoking, and BMI, and a better profile in term of leisure-time stress, cardiovascular disease, physical activity during leisure-time, and age. The most profound difference between the groups related to the lower socioeconomic position among shift workers, as only 7% belonged to the two highest socioeconomic groups, whereas for non-shift workers this number was 33%.

Participants with long working hours had a worse dementia risk factor profile in terms of sleep, work stress, and leisure-time stress, and a better profile in terms of smoking, physical activity during leisure-time, age, and BMI. Among participants with long working hours, 41% belonged to the two highest socioeconomic groups whereas this number was 24% for participants with shorter working hours.

In total, 634 participants (13.3%) were registered with dementia during a total number of 84 803 person-years (mean follow-up time was 17.8 years). The mean age at diagnosis was 80.0 (SD 6.7) years. The first analyses showed that the age-adjusted IRR was 0.89 (95% CI 0.73–1.10) for shift work and dementia and 0.91 (95% CI 0.74–1.11) for long working hours and dementia. Table 2 shows that when additionally adjusting for socioeconomic status the IRR for dementia among shift workers was 0.86 (95% CI: 0.70–1.05). The IRR for dementia among participants with long working hours was 0.97 (95% CI 0.79–1.19). Additional adjustment for stress, sleep and cardiovascular risk factors (ie, potential mediators) only changed these estimates marginally. In the current study only lower socioeconomic status (IRR 1.11, 95% CI 1.04–1.18), cardiovascular disease (IRR 1.25, 95% CI 1.03–1.53), and an alcohol consumption of ≥3 units per day (IRR 1.52, 95% CI 1.21–1.91) were significantly associated with a higher incidence of dementia during follow-up.

Our supplementary analyses (table 3) show that long-term exposure to shift work (ie, shift work at both time points of exposure assessment) was not associated with dementia. We also found that participants reporting shift work at only one time point had the lowest IRR of dementia. Categorizing fixed evening workers together with day workers or excluding them from the analyses did not change the results of the study.

Discussion

Main results

We found no association between long working hours and risk of dementia. When comparing shift and non-shift workers in the main analyses, the IRR was below unity indicating a negative association. However, in supplementary analyses, the risk of dementia for those who started or ceased working shifts were lower than the risk of dementia among those who either stayed in non-shift or shift work. Keeping in mind that the estimated differences were not statistically significant, the direction of the estimates (ie, below unity) may indicate a selection of healthy day workers into shift work in older ages and a selection of healthy shift workers into day work in older ages. We do not suggest that the estimate for those who start working shifts is indicative of a protective effect on the risk of dementia. In the present study, we cannot empirically determine whether the increased risk of dementia among those who reported shift work at both times of exposure assessment compared to those who report shift work only once is indicative of an increased risk of dementia associated with shift work or whether this finding is due to selection.

We conservatively adjusted for a range of covariates that could play a role as either confounders or mediators (stress, sleep and cardiovascular risk factors) which only slightly changed the estimates. Thus, in the present study these variables did not appear to play a major role for the investigated associations. Notably, a previous study in the same cohort did not find an association between shift work and cardiovascular disease (28), which may contribute to the null findings.

Comparison with previous findings

Our finding of no significant association between shift work and dementia is partly in line with previous research. In the Nurses' Health Study, Devore et al (22) found no substantial longitudinal association between night work and cognition and, in a recent study, Bokenberger et al (23) found no longitudinal association between shift work and cognitive aging. In contrast, using cross-sectional data from the VISAT study, Roach et al found indications of lower cognitive efficiency, in terms of immediate free recall, with increasing duration of shift work among males but not among females (20). In a later follow-up of the same cohort, Marquié et al (21) found that shift work was associated with lower global cognitive performance and poorer memory and the effect increased with increasing duration of exposure to shift work. Importantly, the potential effect of shift work on cognitive function seemed to be reversible when ceasing shift work. When it comes to a dementia

Table 1. Characteristics of the study population. If nothing else is mentioned, all information is obtained from the 1970–1971 survey (N=4766; 35 participants had missing values on shift work and 2 participants had missing values on long working hours).

	No shift work (N=3720)			Shift work (N=1011)			≤45 hours/week (N=3895)			>45 hours/week (N=869)		
	%	Mean	SD	%	Mean	SD	%	Mean	SD	%	Mean	SD
Shift work												
No shift work	NA			NA			79.8			73.4		
Shift work	NA			NA			20.2			26.6		
Working hours												
≤45 hours/week	83.0			77.4			NA			NA		
>45 hours/week	17.0			22.7			NA			NA		
Socioeconomic position												
1 (highest)	21.0			3.6			14.9			27.9		
2	11.5			3.0			9.0			13.1		
3	11.9			44.5			19.4			15.9		
4	42.4			35.9			42.3			35.6		
5 (lowest)	13.2			13.1			14.5			7.6		
Hours of sleep per night												
≥6	94.9			93.1			95.5			90.2		
<6	5.1			6.9			4.6			9.8		
Work stress												
No	79.1			73.7			80.9			65.3		
Yes	20.9			26.3			19.1			34.7		
Leisure-time stress												
No	92.6			95.2			94.6			86.7		
Yes	7.4			4. 8			5.4			13.3		
Cardiovascular diseases												
No	80.8			82.6			81.5			79.9		
Yes	19.2			17.4			18.5			20.1		
Smoking												
No	30.2			25.3			28.3			33.5		
Yes	69.8			74.7			71.7			66.5		
Physical activity during leisure-time												
A lot	10.4			13.0			9.9			15.8		
Some	72.1			72.3			72.7			69.0		
Almost nothing	17.6			14.7			17.4			15.2		
Alcohol consumption (units per day)												
0	34.2			34.1			34.6			31.6		
1–2	48.1			44.7			47.3			48.2		
≥3	17.7			21.1			18.1			20.3		
Shift work in 1985–1986 (N=1597)												
Day work	95.5			34.1								
Shift work	4.5			65.9								
Age at exposure assessment		49.1	5.4		48.4	5.2		49.1	5.4		48.4	5.2
Age at start of follow-up		60.9	1.0		60.7	0.8		60.8	1.0		60.8	0.9
Body mass index		33.3	5.0		34.2	4.8		33.6	5.0		33.1	4.6
Blood pressure												
Systolic		134.6	19.1		135.5	19.4		135.1	19.4		133.2	17.8
Diastolic		82.9	11.4		83.0	11.6		83.0	11.6		82.6	11.0

Table 2. The association between shift work, long working hours and dementia. [IRR=incidence rate ratio. 95% CI=95% confidence intervals.

	Number of cases	Person-years	Model I [a]		Model II [b]		Model III [c]	
			IRR	95% CI	IRR	95% CI	IRR	95% CI
Shift work								
No shift work (reference)	514	66 868	1.00		1.00		1.00	
Shift work	115	17 337	0.86	0.70–1.05	0.87	0.70–1.07	0.83	0.68–1.03
Working hours								
No long working hours (reference)	516	68 511	1.00		1.00		1.00	
Long working hours	118	16 257	0.97	0.79–1.19	0.96	0.77–1.18	0.97	0.79–1.19
Age (continuous, 5 years increase)			1.69	1.55–1.83	1.69	1.55–1.83	1.63	1.50–1.78
Socioeconomic position (1 level decrease)			1.11	1.04–1.18	1.11	1.04–1.18	1.08	1.01–1.15
Sleep length (hours)								
>6 (reference)	601	80 394			1.00			
<6	33	4378			1.02	0.71–1.48		
Work stress								
No	489	65 416			1.00			
Yes	141	19 176			0.96	0.78–1.17		
Leisure-time stress								
No	577	78 697			1.00			
Yes	55	5793			1.30	0.96–1.75		
Smoking								
No	236	28 391					1.00	
Yes	398	56 375					1.05	0.89–1.25
Physical activity during leisure-time								
A lot (reference)	72	9218					1.00	
Some	451	61 717					0.95	0.74–1.23
Almost nothing	110	13 793					1.08	0.80–1.46
Alcohol consumption (units/day)								
0	235	29 873					1.15	0.96–1.37
1–2 (reference)	280	41 668					1.00	
≥3	117	12 994					1.52	1.21–1.91
Body mass index							1.01	0.99–1.03
Cardiovascular diseases								
No	490	69 094					1.00	
Yes	144	15 709					1.25	1.03 –1.53
Blood pressure (5 mmHg increase)								
Diastolic							1.01	0.95–1.06
Systolic							1.02	0.99–1.05

[a] Shift work, long working hours, current age, time since exposure assessment, calendar year and socioeconomic status
[b] Model I + sleep, work stress, leisure-time stress
[c] Model I + smoking, physical activity during leisure-time, alcohol consumption, BMI, cardiovascular disease, diastolic and systolic BP

Table 3. The association between number of time points with reported shift work and the incidence dementia adjusted for current age, time since exposure assessment, calendar year and socioeconomic status [IRR=incidence rate ratio. 95% CI=95% confidence intervals.]

	Number of cases	Person-years	IRR	95% CI
Never shift work (reference) [a]	202	18 085	1.00	
Shift work only in 1985–1986 [b]	4	867	0.44	0.16–1.23
Shift work only in 1970–1971 [c]	10	1725	0.58	0.31–1.11
Shift work in 1970–1971 and 1985–1986 [d]	36	3388	0.99	0.69–1.42

[a] Stayed in non-shift work (N=1201, 75.2%).
[b] Started working shifts (N=56, 3.5%).
[c] Ceased working shifts (N=116, 7.3%).
[d] Stayed in shift work (N=224, 14.0%).

diagnosis, Seidler et al (24) reported no association with history of shift work. In contrast, one recent study on mortality patterns among day and shift workers found that evening and rotating shift workers had a higher mortality rate due to dementia (25). This finding may be due to a poorer survival with dementia among shift workers and does not necessarily support a higher incidence in this group.

Our finding of no association between long working hours measured at one time point and dementia is not in line with the results of previous studies on long working hours and cognitive function: Proctor et al (26) found that overtime work was associated with poorer attention and executive function. In addition, Virtanen et al (27) reported that working long hours was associated with having a lower score on a vocabulary test and with a decline in performance on the reasoning test. No previous studies investigated the effect of long working hours on the incidence of dementia.

Strengths and limitations

The strengths of the present study lie in the longitudinal design with prospective exposure measurement and objectively measured dementia diagnoses as the outcome. To reduce the risk of reverse causation, follow-up started five years after the exposure measurement. In addition, we were able to adjust for stress, sleep, and cardiovascular risk factors.

The main limitation of the present study is the crude measurement of shift work (at two time points) and long working hours (only at one time point) which, furthermore, increased the risk of exposure misclassification during follow-up. In particular, the inclusion of shift workers without night work (eg, fixed evening workers) into the exposed group may contribute to our null findings, as evening work is not associated with substantial disturbance of diurnal rhythms. Still, our sensitivity analyses revealed that categorizing the fixed evening workers as non-shift workers or excluding them from the analyses did not change the results of the study.

Also, selection into and out of shift work are often mentioned as major methodological obstacles in shift work research (43). It is unclear, however, exactly how these selection mechanisms operate. In a subpopulation that was still occupationally active at follow-up, we had access to updated information about working hours approximately 15 years after the first exposure assessment. In this subpopulation, 4.5% of the non-shift workers had changed to shift work and 34.1% of the shift workers had changed to day work during follow-up. In our study, we observed the highest risk of dementia among those with the same type of working hours at both time point of exposure assessment (ie, either non-shift or shift work in both 1970–1971 and 1985–1986). Regarding selection out of the study, the register-based outcome assessment implied minimal loss to follow-up among those who initially participated in the study. Thus, later non-participation in the survey did not affect these analyses. Those, who remained occupationally active for 15 years (until the 1985–1986 survey), can be considered as a more selected group of healthy workers. Importantly, however, we found that among the initial non-shift workers, 1257 (33.8%) were included in the follow-up analyses and among the initial shift workers 340 (33.8%) were included in the follow-up analyses. Thus, reporting shift work at the time of the first exposure assessment was not associated with inclusion/exclusion from the analyses of the follow-up data.

Registration of dementia appears to have changed over time, eg, in the RCD there has been a remarkable increase in the registration of dementia as the underlying cause of death since the beginning of the 2000s (34). Furthermore, the hospital registers currently only capture approximately two-thirds of the estimated number of people with dementia in Denmark (44). The number of cases might be particularly underestimated until 1995, from which year outpatient visits were also registered (44). Despite the lower coverage of the registers, we also included risk time and diagnoses from the 20-years' period from 1975–1994 and, during this early period, 97 participants (15% of the total number of cases) were registered with dementia. The incidence of dementia steeply increases already from the age of 65 years and even more from the age of 70 (45). Starting follow-up in 1995 would imply that 72% of the original sample would have turned at least 70 years and 41% would have turned at least 75 years before start of follow-up. Therefore, we decided also to include risk time in the calendar years before 1995, despite that a larger proportion of cases might have been misclassified as non-cases.

Apart from lack of registration of outpatient visits until 1995, another overarching reason for low completeness of case identification is that some people with dementia will not be seen at the hospital-based outpatient clinics or hospitalized and would thus miss being diagnosed and registered as such. In particular, differences in the diagnostic rate associated with socioeconomic status may have influenced our results. On the one hand, higher education is associated with a higher cognitive reserve and thereby a lower chance of being diagnosed with dementia given the same absolute decrease in cognitive functioning (45, 46). Furthermore, the overall morbidity is decreasing with increasing socioeconomic status making it less likely that dementia is diagnosed in connection with a hospital contact due to another disease. One the other hand, individuals with a higher socioeconomic status may in general make more optimal use of the health care system and seek advanced medical help and treatment if deemed needed. In addition, one empirical study suggests that some disadvantage groups (in this case older ethnic minorities) are particularly underdiagnosed when it comes to dementia (30). However, ethnic minorities are not represented in the present study and make up only a small percentage in Denmark. In the current study, lower socioeconomic status was associated with a higher incidence of dementia, but adjustment for this variable did not influence the association between the investigated exposures and dementia.

The generalizability of the current findings is limited to male employees from occupational groups similar to the groups included in the present study. Still, work-related exposures, living conditions, and cardiovascular risk profiles may have changed to an extent that it has influenced the degree to which our results can be generalized from employees working in the 1970s and 1980s to individuals who have started their working life decades later. The methodological limitations of the present study and its limitations related to the generalizability point to a need for studies using more contemporary data, including both gender, and relying on a more detailed measure of shift work.

Concluding remarks

We did not find associations between shift work or long working hours and the risk of dementia. Thus, the current study does not support the hypothesis that employees working shifts or long hours have a higher incidence of dementia in old age. However, given the limitations of the study, in particular with respect to the assessment of long working hours and short-term and long-term shift work and the contradictory findings in the literature, further studies of shift work, long working hours, and the risk of dementia are warranted..

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