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Age, education and dementia related deaths. The Norwegian Counties Study and The Cohort of Norway

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ABSTRACT

An inverse relationship between educational level and dementia has been reported in several studies. In this study we investigated the relationship between educational level and dementia related deaths for cohorts of people all born during 1915–39. The cohorts were followed up from adulthood or old age, taking into account possible confounders and mediating paths. Our study population comprised participants in Norwegian health examination studies in the period 1974–2002; The Counties Study and Cohort of Norway (CONOR). Dementia related deaths were defined as deaths with a dementia diagnosis on the death certificate and linked using the Cause of Death Registry to year 2012. The study included 90,843 participants, 2.06 million person years and 2440 dementia related deaths. Cox regression was used to assess the association between education and dementia related deaths. Both high and middle educational levels were associated with lower dementia related death risk compared to those with low education when follow-up started in adulthood (35–49 years, high versus low education: HR = 0.68, 95% confidence interval (CI) 0.50–0.93; 50–69 years, high versus low education: HR = 0.52, 95% CI 0.34–0.80). However, when follow-up started at old age (70–80 years) there was no significant association between education and dementia related death. Restricting the study population to those born during a five-year period 1925–29 (the birth cohort overlapping all three age groups), gave similar main findings. The protective effects found for both high and middle educational level compared to low education were robust to adjustment for cardiovascular health and life style factors, suggesting education to be a protective factor for dementia related death. Both high and middle educational levels were associated with decreased dementia related death risk compared with low educational level when follow-up started in adulthood, but no association was observed when follow-up started at old age.

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1. Introduction

An inverse relationship between educational level and dementia has been reported in several epidemiological studies [1–9]. This education–dementia relationship is considered by some researchers to be robust [8]. Nevertheless, the conclusion in a recent updated systematic review by Sharp and Gatz, covering the last 25 years and including 71 studies, suggests that the education–dementia relationship may be more complex than earlier suggested, because the inverse relationship was found only in some studies [9]. Sharp and Gatz argue that sub-group analyses, such as analyses in different birth cohorts and age groups, are largely lacking. They also point out that education may have different value and may impact individuals' lives differently in different cultures and cohorts [9]. Furthermore, differences in methods and study samples make comparisons between studies difficult [9]. To our knowledge, no study of the relationship between educational level and dementia has been conducted in Norway. Furthermore, it is important to take into account a life-course perspective; Educational level might be influenced by childhood factors, and education might in turn influence environmental exposures and life style factors, which in turn affect dementia risk [9]. A number of mechanisms have been suggested to explain the education–dementia link, including brain and cognitive reserve [10] and biases, and that education is merely a marker for other variables linked to dementia [9]. To the latter point, several studies have reported that the education–dementia link is robust to adjustment for a broad range of health related factors, suggesting education to be a protective factor for dementia [6]. Clinical studies

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have shown that some people with extensive dementia pathology in the brain show no signs of cognitive impairment [11–13], which might imply there are some reserves in the brain which act as a buffer against this neuropathology. Brain reserve has been defined as the ability of a person to tolerate progressive brain pathology without expressing clinical cognitive symptoms [10,14]. Further, brain reserve is usually divided into two main features, brain reserve and cognitive reserve [10]. The former concept is quantitative, where higher reserve means larger brain volume, higher number of neurons or synapses [1], and has been defined by Stern as a passive model of brain reserve [15]. Cognitive reserve, on the other hand is thought to be a more active form of reserve, where the brain actively tries to cope with the dementia pathology [10]. Following the cognitive reserve hypothesis, two individuals with the same brain size, the one with higher cognitive reserve would tolerate more dementia brain pathology before it would manifest in a clinical diagnosis of dementia. Proxies of cognitive reserve include education, IQ and occupation [16]. These factors are often highly correlated — for example higher IQ might lead to higher education and higher occupational status. Nevertheless, a life-course study showed that all these factors independently had predictive power regarding cognitive decline [17]. Other cognitive activities such as participation in various leisure activities (for instance attending cultural events, listening to music, walking, visiting friends or relatives, reading, playing games) throughout the life course have been found to contribute to enhanced cognitive reserve and cognitive abilities [18–20].

In the Cambridge City over 75 Cohort Study, cognitive decline in the period before death of the participants was investigated [21]. It was reported that those with high education had delayed the onset of terminal cognitive decline compared to their less educated peers [21]. Other studies have also reported educational level to be associated with a delayed onset of accelerated memory decline [18], mild cognitive impairment and Alzheimer's disease [22]. In line with the cognitive reserve hypothesis, it has been argued that education could be a protective factor against dementia onset [14]. Among persons with so called high cognitive reserve, a more rapid cognitive decline has been found after clinical manifestation of Alzheimer's disease than among those with lower reserve [23]. Furthermore, survival has been found to be poorer among dementia patients with higher education compared to those with lower education [24]. Stern's theoretical explanation for this is that when those with high cognitive reserve reaches the point where cognitive function is affected, they have so much brain pathology that it overwhelms function, and therefore these patients have a more rapid cognitive decline [15]. Following this line of thought, we hypothesised that for individuals followed up from adulthood for dementia related deaths there would be an inverse association with educational level because high education (higher cognitive reserve) would be related to later onset. However, when follow-up starts at old age we hypothesised there would be no educational gradient, or even a reversed gradient, as at old age there would be a more rapid cognitive decline, and earlier death, in the groups of dementia patients with the highest levels of education [24].

Thus, the aim of this study was to investigate the association of educational attainment with subsequent dementia related deaths followed up from adulthood or old age. Further, our aim was to examine whether any such association could be explained by other known risk factors for dementia, such as history of cardiovascular disease, smoking, physical inactivity, adiposity, high cholesterol level and elevated blood pressure.

2. Methods

2.1. Sample

Sub-sets from two prospective cohort studies were included: The Norwegian Counties Study (NCS) – a health examination study of men and women in Oppland, Sogn og Fjordane and Finnmark counties during 1974–1988 [25] – and The Cohort of Norway (CONOR) — a joint study of several regional Norwegian cohort studies performed during 1994–2002 [26]. Included in these analyses are participants born during 1925–1939 (35–49 years at baseline) or during 1915–39 (50–80 years at baseline). Only the first measurement was included for persons participating in more than one study. Age at health examination was grouped in three categories: 35–49 years (born 1925–1939), 50–69 years (also born 1925–1939), and 70–80 years (born 1915–1929). Thus, the two youngest age groups could reach a maximum age of 87 years at the end of follow-up, while the oldest group could reach 97 years. The birth cohort 1925–29 overlapped all the three age at health examination groups (35–49, 50–69 and 70–80 years). The final study population included 90,843 participants, 2.06 million person years and 2440 dementia deaths (Tables 1 and 2).

2.2. Dementia related deaths

Dementia related deaths were linked to the participants using the Norwegian Cause of Death Registry, and defined as deaths with a dementia diagnosis (ICD-9: 331.0, 294.10, 290.0–290.4; ICD-10: F00–F03 and G30) recorded on the death certificate, either as the underlying cause of death or as a contributory cause. Study members were followed from the date of the health examination until death, emigration or until 01.01.2012, whichever occurred first.

2.3. Education

Attained educational level was linked to the participants using the National Education Data Base. The youngest age group (35–49 years) attended the health examination studies in the period 1974–87. For this age group, highest educational level in 1970 or 1980 was classified into three groups: university degree and equivalents (high), advanced secondary qualifications (middle), and basic (public school/elementary school) (low). Low education corresponds to 7 years of schooling, middle education corresponds to 10 years and, high corresponds to 13 or more years of schooling. The same classification was applied to the two oldest age groups (50–80 years). For these two oldest age groups (50–69, and 70–80 years) educational level in 1990 was used, as these were screened in the period 1994–2002.

2.4. Vascular conditions and risk factors

The health examination procedures in the various sub studies were similar and included measurements of height, weight, and blood pressure. In addition, a non-fasting blood sample was drawn for serum analyses of cholesterol and glucose, and participants were asked to fill in a questionnaire assessing health related variables such as cardiovascular disease, diabetes, physical activity and smoking habits. Participants who reported current or previous diabetes were categorised as having diabetes. Participants in the Norwegian Counties Study reporting cardiovascular disease (CVD), medical treatment of CVD, or symptoms of such a disease, were categorised as having a history of CVD. Participants in the CONOR sub-studies were categorised as having a history of CVD if they reported having suffered a heart attack, angina or stroke. Smoking was grouped either as daily smoker or not daily smoker. Leisure time physical activity was dichotomized as physically inactive (watching television mostly) or physically active (light walking, intermediate exercise activities, or intensive exercise). For the CONOR sub-studies two extra questions about physical activity in leisure time were used: one on hard activity (sweating or out of breath) and one on light activity (not sweating or out of breath). Those performing none or less than one activity per week were classified as physically inactive, while those having more than one activity per week were classified as physically active. Body mass index (BMI) was defined as weight in kilogrammes divided by square metres (kg/m^2), and grouped in four categories as: <20 kg/m^2, 20–24.9 kg/m^2,

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