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The incidence of dementia: relationship with educational attainment

by

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Abstract

Objectives: *To investigate whether educational attainment influences the development of dementia. The hypothesis is that higher educated persons have a lower incidence rate of dementia than persons with a lower educational attainment.*

Methods: *The project 'Epidemiology Research on Dementia in Antwerp' (ERDA) started in 1990 and had two follow-up periods in 1994 and 1996. It is a longitudinal population-based study using a general population in Antwerp (Heist-op-den-Berg), Belgium. Included in the analysis are 937 non-demented persons of 65 years and older at the time of the first follow-up period (1994).*

Incidence densities of dementia were calculated per age group and per sex. Dementia-free Kaplan Meier survival analyses and multivariate Cox Proportional Hazards models adjusted for risk factors are used to estimate relative risk for dementia.

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Results: *Overall incidence rates of dementia were 4.1/100 person years for men and 3.3/100 person years for women. Lower educated persons (primary education or less) were at higher risk to develop dementia compared to higher educated persons. The adjusted hazard risk is 2.9 (95%CI: 1.0-8.1).*

Conclusions: *Both men and women survived longer in good cognitive health when belonging to the higher educated group. Educational attainment could act upon the threshold of a cognitive reserve. The study indicates the importance of education at young ages.*

Keywords: *Dementia, educational attainment, general population, survival analysis, cognitive reserve.*

Introduction

Intensive investigation on dementia and Alzheimer's disease has been carried out for many years. The positive association between a low educational attainment and the development of dementia or Alzheimer's disease has been described in several prevalence studies (1-3) as well as some incidence studies (4-7). Other studies could not find a link with educational attainment (8,9).

The objective of this project is to study the impact of educational attainment on the occurrence of dementia, while accounting for potential confounding factors and to provide at the same time estimates of incidence rates of dementia. Survival analysis is used to test the hypothesis that dementia-free survival is higher among higher educated persons as compared to lower educated persons.

Methods

Study population

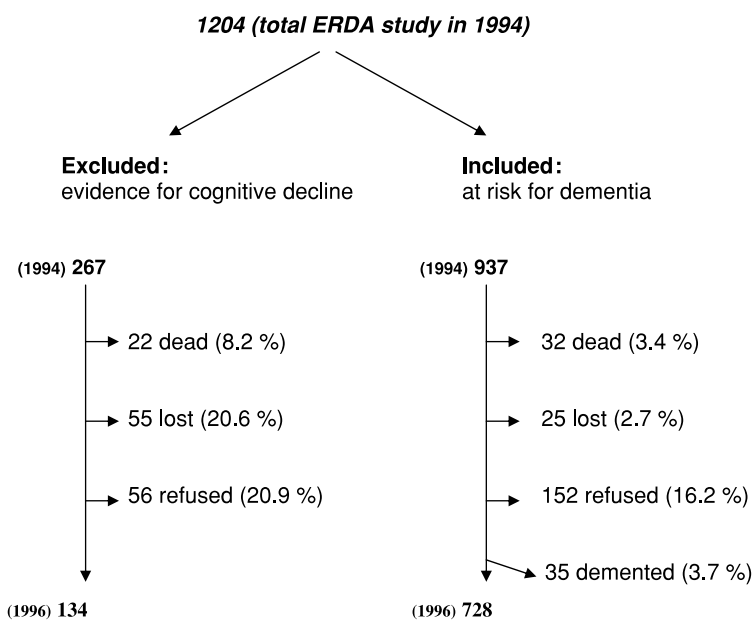
The project Epidemiology Research on Dementia in Antwerp (ERDA) included a random, population-based sample of persons 65 years and older (including the institutionalised population). The project was initiated in 1990 with a cross-sectional study by Mental Health Care, Province of Antwerp and the Service for 'Brain and Behaviour', Catholic University Leuven (10). Two follow-up studies were organised in 1994 and 1996 by the Service for 'Brain and Behaviour', Catholic University Leuven and the Unit of Epidemiology of the Scientific Institute of Public Health, Brussels. More details on the study population can be found in Van Oyen et al. (11).

Only in the 1994 survey, the determinants of dementia were considered. For that reason, only a subsample of 937 dementia-free persons was extracted for follow-up (1994). Figure 1 gives an overview of the study population at risk for dementia in the ERDA study in the period of 1994.

Cognitive evaluation

Dementia-free persons who have been included for analysis (1994), were selected through the following procedure. First, every person was screened for cognitive decline by means of the Mini-Mental State Examination (MMSE), a widely used clinically validated screening for dementia, using its 30-item version and a cutting point of 23/24 (12). As such, persons with an initial MMSE score of $\geq$ 24/30 are included for analysis. Most non-dement elderly people rarely score below 24 (13). Persons scoring $\leq$ 23, and a control group (random sample, stratified for age and sex) of 10% of the persons with a score $\geq$ 24, were referred for diagnosis of dementia using the 'Cambridge Examination for Mental Disorders of the Elderly' (CAMDEX) (14). This standardized diagnostic procedure provides computerized diagnostic algorithms, which meet ICD-9 criteria. A team of two psychiatrists and a psychologist made the final diagnosis in case of non-conformities. Different levels of dementia

Figure 1:
Study population at risk for dementia in the ERDA study



were defined according to the DSM III-R criteria, as there are minimal, light, moderate to severe dementia (15). As such, two other groups of dementia-free persons have been included for analysis: persons with an initial MMSE score of ≥ 24/30 and diagnosed as non-dement by the CAMDEX, and also persons with an initial MMSE score of < 24/30 but diagnosed as non-dement using the CAMDEX. During the second follow-up period, an incident dement case was diagnosed using the CAMDEX (1996).

Evaluation of co-variables (1994)

In order to adjust for possible confounding factors, co-variables were selected because of their association with cognitive decline, as there are socio-demographic variables, socially related and lifestyle variables (8,16) and health status indicators (16). Educational attainment was measured using the number of years of education followed. A lower educational attainment is defined as ≤ 7 years of education. Those persons belong to the group with primary education or less. A higher educational attainment is defined as > 7 years of education. Depressive mood was measured by the Centre for Epidemiologic Studies Depression Scale (CES-D Scale) (17). A score of 0-15 has been defined as the absence of depression mood, a score of 16-60 as the presence of depressive mood. The General Health Questionnaire (GHQ-12) (18) was used to screen mental well-being. Persons with a score of 3-12 were considered as potential psychiatric cases, persons with a score 0-2 as free from non-psychotic psychiatric disorders. A modified OECD Long-Term Disability Questionnaire measured physical limitations (19). The different answer categories were merged into two: no physical limitations on the one hand, and mild to serious difficulty for at least one item on the other hand.

Statistical analysis

In order to estimate incidence densities of dementia, calculation of person years is carried out using the following method. As change in cognitive status was studied in function of time, new cases of dementia were expressed in relation to the total survival time. Whereas deceased persons counted up to the exact time of death, people who refused to participate and respondents that dropped out along the way counted up to halfway between the 2 points of measurement, using calculated means by municipality in order to adjust for socio-demographical factors. Persons who developed dementia were considered to add only half of the observation time between two points of measurement. Survival times are expressed in years.

Next, Kaplan Meier dementia-free survival analysis is used to analyse the mean survival time and plot the unadjusted survivor function from normal cognitive function to incident dementia according to education attainment and other covariates. Survival curves are tested for equality of survival distributions by the log-rank test (results not presented).

Finally, Cox proportional hazards regression is used to investigate the relation between the incidence of dementia and educational attainment. To calculate hazard ratios of incident dementia associated with years of education, adjustment of the final Cox model was performed by the successive inclusion of age, sex and other co-variables significant around the 5% level in the bivariate analysis. Possible effect modifications were investigated. To find out whether the hazards were independent of time, log(-log(survival) curves were examined for each age group, for sex and other co-variables. Only those variables significantly contributing are kept and finally presented into the model. Analysis is performed using SPSS, version 8.

Results

937 persons were included for analysis. The majority, namely 877 dementia-free persons who have been included, had an initial MMSE score of $\geq$ 24/30. Thirty-nine persons had an initial MMSE score of $\geq$ 24/30 and were diagnosed as non-dement by the CAMDEX. 21 persons had an initial MMSE score of < 24/30 but were diagnosed as non-dement using the CAMDEX. Men (n=509) contributed 507 person years; women (n=428) contributed 430 person years. The maximum personal length of the follow-up was 2.98 years with a median of 1.02 (percentile 75 and 95: 1.15 and 1.68 years respectively). Mean age for men and women in the study period of 1994 was 75 years. Table 1 gives an overview of the investigated co-variables by sex for the whole dementia-free study population. Educational attainment was known for a total of 931 persons. The majority of this population belonged to the group with an educational attainment of $\leq$ 7 years (70%). More men belong to the group with a lower educational attainment.

Table 2 shows the incidence rates of dementia per age group and per sex. A total of 35 persons became dement; none of them were categorized in the severe dementia group. Overall incidence rates for dementia were 4.1/100 person years for men and 3.3/100 person years for women. Incidence rates of dementia moved upward with increasing age with a peak in age group 85 years and older.

TABLE 1
Co-variables for the dementia-free study population

Variable	Men (n=509) (%)	Women (n=428) (%)	Total (n=937) (%)
Age			
65-69 year	126 (24.8)	93 (21.7)	219 (23.4)
70-74 year	135 (26.5)	133 (31.1)	268 (28.6)
75-79 year	115 (22.6)	96 (22.4)	211 (22.5)
80-84 year	88 (17.3)	68 (15.9)	156 (16.6)
≥ 85 year	45 (8.8)	38 (8.9)	83 (8.9)
Educational attainment [a]			
≤ 7 years	376 (74.6)	279 (65.3)	655 (70.4)
> 7 years	128 (25.4)	148 (34.7)	276 (29.6)
Occupational level [b]			
White-collar work	113 (22.4)	78 (19.3)	191 (21.0)
Manual work	390 (77.4)	165 (40.7)	555 (61.1)
Housewives	1 (0.2)	162 (40.0)	163 (17.9)
Marital status			
Married	364 (71.5)	214 (50.2)	578 (61.8)
Divorced/widow/not married	145 (28.5)	212 (49.8)	357 (38.2)
Living alone			
Living with partner, children, in home or other	391 (76.8)	280 (65.4)	671 (71.6)
Living alone	118(23.2)	148 (34.6)	266 (28.4)
Children alive			
≥ 1 child alive	434 (87.9)	373 (89.2)	807 (88.5)
No children alive	60 (12.1)	45 (10.8)	105 (11.5)
Satisfaction with contact children			
Very satisfied	368 (86.2)	320 (87.7)	688 (86.9)
Not to fairly satisfied	59 (13.8)	45 (12.3)	104 (13.1)
Having friends			
≥ 1 friend	394 (79.0)	317 (74.9)	711 (77.1)
No friends	105 (21.0)	106 (25.1)	211 (22.9)
Satisfaction with contact friends			
Very satisfied	357 (91.5)	281 (89.5)	638 (90.6)
Not to fairly satisfied	33 (8.5)	33 (10.5)	66 (9.4)
Close family members			
≥ 1 family member	448 (88.9)	379 (90.0)	827 (89.4)
No family	56 (11.1)	42 (10.0)	98 (10.6)
Satisfaction with contact family			
Very satisfied	353 (79.1)	300 (78.9)	653 (79.1)
Not to fairly satisfied	93 (20.9)	80 (21.1)	173 (20.9)
Having a person of trust			
Yes	447 (88.3)	397 (93.0)	844 (90.5)
No	59 (11.7)	30 (7.0)	89 (9.5)
Ever smoked			
Yes, sometimes or daily	268 (70.3)	27 (6.9)	295 (38.1)
No	113 (29.7)	366 (93.1)	479 (61.9)
Alcohol consumption			
Intake > 1 week up to 1 year ago	219 (44.8)	311 (78.7)	530 (60.0)
Intake ≤ 1 week ago	270 (55.2)	84 (21.3)	354 (40.0)

Variable	Men (n=509) (%)	Women (n=428) (%)	Total (n=937) (%)
Depressive mood (CES-D score)			
Present	43 (8.6)	47 (11.1)	90 (9.7)
Absent	459 (91.4)	377 (88.9)	836 (90.3)
Mental well-being (GHQ-12)			
Poor mental health	51 (10.2)	46 (11.0)	97 (10.6)
Good mental health	448 (89.8)	373 (89.0)	821 (89.4)
Physical limitation			
Mild to serious difficulty	262 (52.7)	279 (66.7)	541 (59.1)
No limitation	235 (47.3)	139 (33.3)	374 (40.9)
Cardiovascular risk [c]			
≥ 1 cardiovascular related disease	51 (10.0)	58 (13.6)	109 (11.6)
No cardiovascular related disease	458 (90.0)	370 (86.4)	828 (88.4)

a Mean number of years of education is 8 years with median of 7 years.
b Occupational level has been determined using the Statistics Belgium (NIS91) coding of occupations, consequently recoded into the EGP10 coding of occupational level.
c Cardiovascular risk results from the combination of all reported diseases related to cardiovascular disease.

TABLE 2
Incidence rate (per 100 person years) of dementia by age group for men and women

	Age	N	Person years	# cases	ID (per 100 PY)	95 % CI
Men	65-69	126	124	1	0.81	0.02-4.49
	70-74	135	148	7	4.73	1.90-9.74
	75-79	115	113	3	2.65	0.55-7.76
	80-84	88	81	6	7.41	2.72-16.12
	≥85	45	41	4	9.76	2.66-24.98
	Total	***509***	***507***	***21***	***4.14***	***2.56-6.33***
Women	65-69	93	85	1	1.18	0.03-6.55
	70-74	133	139	2	1.44	0.17-5.19
	75-79	96	102	2	1.96	0.24-7.08
	80-84	68	67	3	4.48	0.92-13.08
	≥85	38	37	6	16.22	5.95-35.29
	Total	***428***	***430***	***14***	***3.25***	***2.66-6.90***

Influence of co-variables on the development of dementia

Table 3 provides stratified specific incidence rates and crude hazard ratios of dementia for the follow-up period 1994-1996. Co-variables with a significant log rank test (5% level) in Kaplan Meier survival analyses

are shown. Hazard ratios of dementia were higher with increasing age and a lower educational attainment showing a significant 3 times higher risk to become dement when belonging to the lower educated group (education ≤ 7 years). A potentially bad mental well-being is associated with a significant threefold increase of developing dementia. The

TABLE 3
Factors associated with incidence rate of dementia (1994-1996)

	N	Person years	# cases	ID per 100 PY	Crude HR (95 % CI)
Age at entrance study					
65-69	219	209	2	0.96	1.00
70-74	268	287	9	3.14	3.29 (0.71-15.25)
75-79	211	215	5	2.32	2.43 (0.47-12.52)
80-84	156	148	9	6.09	6.39 (1.38-29.59)
≥85	83	78	10	12.79	13.57 (2.97-61.95)
Sex					
Women	428	431	14	3.25	0.79 (0.40-1.55)
Men	509	507	21	4.14	1.00
Educational attainment					
≤ 7 years	655	656	31	4.73	3.35 (1.18-9.48)
> 7 years	276	276	4	1.45	1.00
Occupation					
Manual work	555	561	26	4.64	2.75 (0.83-9.08)
White-collar work	191	179	3	1.67	1.00
Housewives	163	172	5	2.91	1.79 (0.43-7.48)
Depressive mood					
Present	90	99	7	7.04	2.27 (0.99-5.22)
Absent	836	831	28	3.37	1.00
Mental well-being					
Poor mental health	97	105	10	9.48	3.32 (1.59-6.92)
Good mental health	821	820	25	3.05	1.00
Has person of trust					
No	89	89	7	7.91	2.48 (1.08-5.68)
Yes	844	845	28	3.31	1.00
Physical limitations					
Mild to serious	541	542	24	4.43	1.69 (0.81-3.53)
No limitation	374	369	10	2.71	1.00
Ever smoked					
Sometimes or daily	295	287	10	3.49	0.83 (0.39-1.77)
Never	479	483	20	4.14	1.00
Married					
Not, divorced, widow	357	368	17	4.61	1.43 (0.74-2.79)
Married	578	567	18	3.17	1.00
Children alive					
None	105	105	6	5.73	1.72 (0.71-4.16)
≥ 1 child	807	810	28	3.46	1.00
Cardiovascular risk					
Risk patient	109	118	6	5.11	1.46 (0.61-3.53)
No risk patient	828	820	29	3.54	1.00

presence of depressive mood is associated with a two times increase of developing dementia. 'Not having a person of trust' led to a significant 2.5 times greater risk of developing dementia.

The incidence of dementia in relation to educational attainment

Table 4 provides the multivariate Cox model for the follow-up period of 1994-1996. Lower educated persons still have a significant 3 times higher risk to develop dementia (HR 2.86; 95%CI 1.01-8.11). The interactions between age and educational attainment were not significant at the 10% level. Figure 2 displays the incidence of dementia by educational attainment adjusted for age and mental well-being. Subjects survive longer in good cognitive health if they belong to the higher educated group (number of years of education > 7 years).
Log (-log (survival) curves showed a good overall model fit.

TABLE 4.
Factors associated with dementia-free survival and their Hazard Ratios, multivariate Cox Proportional Hazard regression model (1994-1996). N=937 subjects at risk for dementia

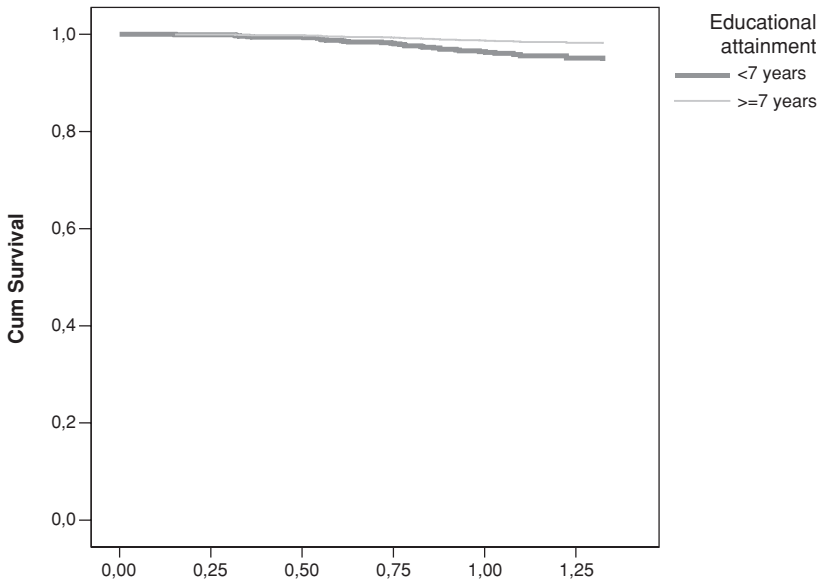
Variable	HR (95 % CI)
Educational attainment (≤ 7 years vs > 7 years)	2.86 (1.01-8.11)
Age at entrance study (per 5-year age group)	1.69 (1.29-2.24)
Mental well-being (potentially bad vs good)	2.89 (1.39-6.04)

Discussion

The ERDA study was the first population-based investigation allowing us to estimate the incidence and determinants of dementia in Belgium. A positive association between a low educational level and the development of dementia has been described in several studies. Somehow, the strength of a longitudinal study and a survival analysis provides a higher methodological quality. In 1994, the questionnaires included a whole set of potential risk factors such as lifestyle factors and health status indicators. Therefore, it was far more interesting to analyse the shorter time period as it gave us the opportunity for more effective multivariate analyses.

A stringent method of the calculation of the total survival time (person years) is used in order to avoid overestimation and underestimation of the dementia incidence rates.

Figure 2:
Dementia-free survival by educational attainment
(1994-1996)



(Hazard ratio = 2.86; 95% CI: 1.01-8.11; P = 0.0158 by the log-rank test)

A weakness of the study is that due to the short time of follow-up intervals, rather a low number of persons became dement. None of the newly detected cases became severe dement. This can be explained by an early detection of the disease. It could also be an indication that possible severe dement persons did not further participate in the study (deceased, refusal or loss to follow-up).

Incidence of dementia in relation to age and sex

One consistent finding is the dramatic increase of dementia with age (20) (Table 2). Age is highly related to the incidence of dementia (21,22). Hebert (21) and Kokmen's (22) studies pointed out the exponential increase of dementia by age. We find similar results.

The overall incidence rate for dementia within the study period of 2 years (1994 to 1996) was similar for men (4.1/100 person years; 95%CI: 2.6-6.3) and women (3.3/100 person years; 95%CI: 2.7-6.9). Because of small numbers for each age category resulting in wide and overlapping confidence intervals it is difficult to draw conclusions. As reported in other studies, we did not find age-specific incidence rates that differ significantly by sex (23,24).

Incidence of dementia in relation to educational attainment

The final model presents the variables that contribute significantly, as there are educational attainment, age and mental well-being. Depressive mood may increase the risk of developing dementia (25); on the other hand, a number of persons may develop depression as part of a dementia process (26). A possible effect of 'having a person of trust' remains unclear. In our final model, the effect of depressive mood and 'having a person of trust' disappeared.

The data of this study suggest that a lower educational attainment is associated with a higher risk to develop dementia. Dementia-free survival was significantly higher in elderly people with more years of education. All the results point in the same direction. The association between a low educational attainment and the development of dementia or Alzheimer's disease has been described in several prevalence studies (1-3;27-30) as well as some incidence studies (4,5). Other studies (8,9) could not find a link with educational attainment (31).

A lower educational attainment is defined as $\leq$ 7 years of education. This educational attainment is for most persons equivalent to the maximum achievement of primary school level. However, educational attainment is not always a good proxy of one's personal capacity to study as the generation which our study population stems from used to or may even have been obliged to quit school at an early age. Therefore, educational attainment refers to a certain set of knowledge achieved at a young age.

This effect of educational attainment may support the theory of a 'cognitive reserve', favouring persons with more years of education. Well-educated persons can easier 'mask' dementia on examination in the earlier stages of dementia. This cognitive reserve enables them to better answer the questionnaires. Stern et al. (4) supported the hypothesis that an achieved set of skills (practical and theoretical knowledge) enables persons to delay the clinical expression of Alzheimer's disease (32). Innate intelligence may supply reserve (33). This hypothesis supports the *threshold theory* that states that cognitive decline becomes noticeable if one falls below a certain threshold. This threshold would be exceeded faster in lower educated persons, who could not build up enough cognitive reserve. In this way it is possible that, due to the short-term of follow-up (2 years), a group of people did not yet show the clinical manifestation of dementia.

On one hand, the threshold theory offers a nuance in the expected increase of dementia in view of a shift of the overall population to a

higher educational attainment. On the other hand, the threshold could be higher in the future due to the increasing complexity of our society. This study contains persons of age 65+ in 1994. Younger generations most probably have a larger cognitive reserve and will probably, due to the *cohort effect* (effect of longer study), reach the threshold later. Moreover, a modest delay of Alzheimer's disease onset has an important impact on public health (34).

The threshold theory suggests an important influence of the educational system. Basic education could delay the onset of dementia. The question remains: could the cohort effect all by itself increase life expectancy in good cognitive health, leading to the fact that younger cohorts be better protected? Thus, one can expect a shift of the age of onset, and possibly the degree of cognitive decline.

Conclusions

Lower educated persons are at higher risk to develop dementia. The study indicates the importance of education at young ages. Both men and women survive longer in good cognitive health when belonging to the higher educated group. How the mechanism through which educational attainment has a preventive effect works, remains one of the unanswered questions. Educational attainment could act upon the threshold of a cognitive reserve. Professional health workers and the general population should be aware of the advantages of educational attainment on cognitive health.

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