Are sex and educational level independent predictors of dementia and Alzheimer’s disease? Incidence data from the PAQUID project

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Abstract

Objectives—To examine the age specific risk of Alzheimer’s disease according to sex, and to explore the role of education in a cohort of elderly community residents aged 65 years and older.

Methods—A community based cohort of elderly people was studied longitudinally for 5 years for the development of dementia. Dementia diagnoses were made according to the DSM III R criteria and Alzheimer’s disease was assessed using the NINCDS-ADRSA criteria. Among the 3675 non-demented subjects initially included in the cohort, 2881 participated in the follow up. Hazard ratios of dementia were estimated using a Cox model with delayed entry in which the time scale is the age of the subjects.

Results—During the 5 year follow up, 190 incident cases of dementia, including 140 cases of Alzheimer’s disease were identified. The incidence rates of Alzheimer’s disease were 0.8/100 person-years in men and 1.4/100 person-years in women. However, the incidence was higher in men than in women before the age of 80 and higher in women than in men after this age. A significant interaction between sex and age was found. The hazard ratio of Alzheimer’s disease in women compared with men was estimated to be 0.8 at 75 years and 1.7 at 85 years. The risks of dementia and Alzheimer’s disease were associated with a lower educational attainment (hazard ratio=1.8, p<0.001). The increased risk of Alzheimer’s disease in women was not changed after adjustment for education.

Conclusion—Women have a higher risk of developing dementia after the age of 80 than men. Low educational attainment is associated with a higher risk of Alzheimer’s disease. However, the increased risk in women is not explained by a lower educational level.

Keywords: dementia; sex; education; incidence

Several incidence studies on Alzheimer’s disease and other types of dementia in different countries and continents have shown a steady increase in the incidence of dementia according to age. This increase is essentially due to Alzheimer’s disease, which is the main cause of dementia. Several risk factors of dementia and Alzheimer’s disease have been studied, among them sex. Previous prevalence surveys have found an increased risk among women. Most of the incidence studies failed to confirm such a significant association until an analysis of incidence data from the Kungsholmen Project showed an association between Alzheimer’s disease and sex. This study, which was one of the first population based incidence studies to report such a result, was based on a cohort of subjects aged 75 years and older, living in an area in Stockholm (Sweden). Incident cases of dementia and Alzheimer’s disease were ascertained 3 years after the baseline assessment. Incidence of Alzheimer’s disease was higher in women than in men in all age groups. Age specific incidence increased in women, whereas the incidence was stable after the age of 80 in men. The risk of dementia was increased by 1.9 in women and the risk of Alzheimer’s disease by 3.1. A possible explanation is the biological differences between men and women but the possible influence of confounders such as social life or education cannot be ruled out.

The effect of education on the risk of dementia and Alzheimer’s disease is still controversial. Several prevalence surveys have reported an increased prevalence of Alzheimer’s disease in poorly educated people (Katzman), but several case-control or population based studies failed to confirm this association.

The main weakness of these cross sectional studies is the possible differential participation rate according to education. Highly educated people experiencing the early signs of dementia might refuse to participate, leading to an artificial increase of the proportion of poorly educated subjects among cases. Only prospective studies can reduce this bias. However, few results with incidence data are available. Stern et al found an increased risk of Alzheimer’s disease in subjects with less than 8 years of schooling, whereas Cobb et al failed to find such an association.

The effect of education could either be quantitative—that is, with a linear relation between the number of years of education and the risk of dementia, or qualitative—that is, with a threshold effect at a given level of education. If a threshold effect is demonstrated, it can be postulated that the important factor is intellectual ability rather than education itself. This hypothesis is supported by a study analysing data recorded in nuns reporting that low linguistic ability in early life was a
strong predictor of poor cognitive function and Alzheimer’s disease in late life.

This paper aims to examine the age specific risk of Alzheimer’s disease with special interest in the differential incidence in men and women according to age, and to explore the role of education in a cohort of elderly community residents aged 65 years and older.

Methods

SAMPLE

The PAQUID research programme was designed to study prospectively a representative random sample of people aged 65 years and over living in Gironde and Dordogne, two administrative areas in the south west of France. Subjects were randomly chosen from the electoral rolls of 75 parishes. Three criteria had to be met for subjects to be included in the study. They had: (1) to be at least 65 years of age by 31 December 1987, (2) to be living at home at the time of the initial data collection phase, (3) to have given their informed consent to participate in the study. A three step random procedure based on the electoral rolls stratified by age, sex, and size of the demographic unit was performed. This procedure led to a selection of 5554 elderly subjects living at home.

DATA COLLECTION

Baseline screening

Subjects were informed by mail that they had been chosen to participate in a study on the health status and living conditions of people aged 65 years and over. Then they were contacted by telephone or visited directly at home when they did not have a telephone. Subjects who agreed to participate were seen by a psychologist specially trained for home interviews. The baseline variables registered included sociodemographic factors, living conditions and habits, subjective and objective health measures, a comprehensive functional assessment, depressive symptomatology measured by the CES-D (Center for Epidemiological Study Depression) scale, personal medical history, current symptoms and diseases, and neurosensory deficiencies. A more complete description of the baseline data collected in the PAQUID study has been published previously. Among the socio-demographic data, we considered age in years, sex, and education with four levels: no schooling, primary school level (equivalent to 1 to 5 years of schooling), secondary school level (6 to 12 years of schooling), and university level (over 12 years of schooling). The higher diploma attained was also recorded.

Intellectual functioning was examined through a series of psychometric tests that were among the most sensitive for following cognitive decline in elderly people. The test battery included an evaluation of global mental status (mini mental state examination), visual memory (Benton’s visual retention test), verbal memory (Wechsler’s paired associates), verbal fluency (Isaacs set test), visuospatial attention (Zazzo’s cancellation test), and simple logical reasoning (Wechsler’s digit symbol test).

Diagnosis of dementia

After the psychometric evaluation, the psychologists systematically completed a standardized questionnaire designed to obtain the A (memory impairment), B (impairment of at least one other cognitive function) and C (interference with social or professional life) criteria for DSM-III R dementia. This questionnaire had been previously validated with a good interobserver reliability between the psychologist and the neurologist on the basis of the DSM-III criteria. In a second stage, subjects who met these first three DSM-III R criteria for dementia were seen by a senior neurologist who confirmed and completed the DSM-III R criteria for dementia, and filled in the NINCDS-ADRDA criteria and the Hachinski score to document the diagnosis of dementia and its aetiology: probable or possible Alzheimer’s disease or other type of dementia. An informant, when available, was consulted by the neurologist.

Follow up

Subjects were re-evaluated following the same procedure as for the baseline screening 1 year, 3 years, and 5 years after the initial visit in Gironde and 3 and 5 years after the initial visit in Dordogne. The case finding and the aetiological categorisation of incident cases of dementia followed the same procedure at each follow up assessment as for the baseline screening. However, to improve the sensitivity of the detection of incident cases, another criterion was added for the selection of subjects for the second stage (neurological examination). Subjects were selected for this stage if they met the criteria for DSM-III R dementia or if they had experienced a cognitive decline of more than two points at the MMSE score.

Statistical analysis

Two statistical methods were used to analyse the results. A descriptive approach using age specific incidence was carried out. In a second analysis, a Cox model with delayed entry was performed to estimate hazard ratios and to adjust for several covariates. To study the characteristics of people who refused to participate in the follow up or died before it, logistic regression analyses were performed.

Age specific incidence was estimated using the person-years method. The basic method used to estimate age specific incidence rates is to determine for each individual the amount of observation time contributed to a given age by calendar period category and to sum up those contributions for all cohort members so as to obtain the total number of person-years of observation in that category. For instance, a subject observed at age 74 years and followed up for 5 years, contributed for 1 year in the age group 65–74 years, and for 4 years in the age group 75–84 years. For subjects with more than one follow up evaluation, person-years were calculated as the time between the baseline visit and the last follow up examination if the subject remained non-demented. For a demented subject, we considered half of the time between the last visit in which the
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To a spurious association of the explanatory age may produce correlated residuals leading education are studied, a parametric model of the logarithm of the hazard is linear in age. When By contrast, if age is included as a covariate, the Cox model with delayed entry avoids making to the age of censorship or age of outcome. The this option, a subject participates to the cohort. This selection can be dealt with by the staggered entry or delayed entry using the staggered entry or delayed entry the sample is left truncated because subjects have not developed a dementia before entering the analysis only if they had not experienced dementia before their inclusion. The sample is left truncated because subjects are observed conditionally on the fact that they have not developed a dementia before entering the cohort. This selection can be dealt with using the staggered entry or delayed entry option available in most Cox model software. With this option, a subject participates to the “at risk set” from the age at entry in the cohort to the age of censoring or age of outcome. The Cox model with delayed entry avoids making parametric assumptions on the relation between age and the risk of Alzheimer’s disease. By contrast, if age is included as a covariate, the logarithm of the hazard is linear in age. When age related explanatory variables such as education are studied, a parametric model of age may produce correlated residuals leading to a spurious association of the explanatory variables and the risk of the disease. As for the person-years method, the age of onset of dementia was estimated by the mean age between the last visit when the subject was non-demented and the first visit when the subject was diagnosed as demented. This midpoint imputation is a reasonable procedure to estimate the HRs when interval widths are not too large.

Results Of the 5554 contacted subjects, 3777 (68.0%) agreed to participate in the study. Non-responders did not differ from responders in age, sex, or educational level. Among the 3675 initially non-demented subjects in the cohort, 794 (21.6%) did not participate in the follow up because they died (n=365, 9.9%), or because they were lost to follow up (n=13, 0.4%) or refused the follow up screenings (n=416, 11.3%). At least one complete follow up evaluation was performed on 2881 subjects (78.4%).

Deaths A logistic regression analysis was performed, excluding subjects who refused to participate, in which being dead before the interview was the dependent variable. The results showed that at baseline, the deceased subjects were older (OR=1.09, 95% confidence interval (95% CI) 1.08–1.11), more often men (OR=1.99, 95% CI 1.57–2.53), and had a lower MMSE score (OR=1.08, 95% CI 1.05–1.12) than participants. Educational level was not different.

Refusals A logistic regression analysis was performed, excluding subjects who died before the interview, in which being a refusal was the dependent variable. The results showed that at baseline, the subjects who refused were younger (OR=0.95, 95% CI 0.94–0.97), more often women (OR=1.32, 95% CI 1.06–1.64), and had a lower education (OR=1.5, 95% CI 1.18–1.90) than participants. The MMSE score was not different.

Incidences of dementia, Alzheimer’s disease, and other dementias according to sex Of the 2881 reevaluated subjects, 190 were diagnosed with dementia during the follow up and 140 were diagnosed with Alzheimer’s disease; 76 met the criteria for probable Alzheimer’s disease and 64 the criteria for possible Alzheimer’s disease. Overall incidence of dementia and Alzheimer’s disease were estimated as 1.59/100 person-years and 1.17/100 person-years respectively. The incidence of dementia, Alzheimer’s disease, and other types of dementia according to sex are given in table 1. Among the 1203 men who had contributed to the follow up (4955 person-years), 64 cases of dementia and 42 cases of Alzheimer’s disease were diagnosed and 126 cases of dementia and 98 cases of Alzheimer’s disease were diagnosed among the 1678 women who had contributed to the follow up (6987 person-years). Hence, the overall incidence of dementia was estimated as 1.3/100 person-years in men and 1.8/100 person-years in women (0.8 and 1.4 for Alzheimer’s disease respectively). The incidence of Alzheimer’s disease was higher in men than women before 80 years, and higher in women than men after 80 years. The incidence rates of other dementias were similar according to sex. The risk of Alzheimer’s disease was assessed by a Cox model using age as the baseline time. Because a non-proportionality of the incidence rates with age was suspected, an interaction between sex and age was tested. Both sex and the interaction age by sex were significant (log likelihood ratio test=7, p=0.03). The hazard ratio of a woman developing Alzheimer’s disease was then estimated to be 0.82 at age 75, and to be 1.71 at age 85. When other dementias were studied, neither sex (p=0.47), nor the interaction between age and sex (p=0.49), were found to be significant (log likelihood ratio test=0.74, p=0.69).

Educational level The distribution of educational level is given in table 2. We studied the risk of Alzheimer’s disease in subjects with no schooling and in subjects with a primary school level, taking subjects with a secondary or university level as the referent category. We found a higher risk of developing dementia in subjects with no schooling (HR=1.93, p=0.04) and in subjects...
Table 1 Age specific incidence of dementia, Alzheimer’s disease, and other dementias according to sex. PAQUID 1989–95. n=2881

<table>
<thead>
<tr>
<th>Age</th>
<th>Men (person-years)</th>
<th>Incidence 100 person-years</th>
<th>Women (person-years)</th>
<th>Incidence 100 person-years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dementia:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65–69</td>
<td>3</td>
<td>0.35</td>
<td>2</td>
<td>0.18</td>
</tr>
<tr>
<td>70–74</td>
<td>10</td>
<td>0.63</td>
<td>7</td>
<td>0.36</td>
</tr>
<tr>
<td>75–79</td>
<td>24</td>
<td>1.90</td>
<td>29</td>
<td>1.70</td>
</tr>
<tr>
<td>80–84</td>
<td>16</td>
<td>1.93</td>
<td>43</td>
<td>3.30</td>
</tr>
<tr>
<td>85–89</td>
<td>8</td>
<td>2.45</td>
<td>26</td>
<td>3.73</td>
</tr>
<tr>
<td>90+</td>
<td>3</td>
<td>3.18</td>
<td>19</td>
<td>7.03</td>
</tr>
<tr>
<td>Alzheimer’s disease:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65–69</td>
<td>2</td>
<td>0.23</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>70–74</td>
<td>5</td>
<td>0.31</td>
<td>6</td>
<td>0.31</td>
</tr>
<tr>
<td>75–79</td>
<td>15</td>
<td>1.19</td>
<td>18</td>
<td>1.06</td>
</tr>
<tr>
<td>80–84</td>
<td>11</td>
<td>1.33</td>
<td>32</td>
<td>2.46</td>
</tr>
<tr>
<td>85–89</td>
<td>7</td>
<td>2.14</td>
<td>24</td>
<td>3.44</td>
</tr>
<tr>
<td>90+</td>
<td>2</td>
<td>2.12</td>
<td>18</td>
<td>6.66</td>
</tr>
<tr>
<td>Other dementias:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65–69</td>
<td>1</td>
<td>0.12</td>
<td>2</td>
<td>0.18</td>
</tr>
<tr>
<td>70–74</td>
<td>5</td>
<td>0.31</td>
<td>6</td>
<td>0.31</td>
</tr>
<tr>
<td>75–79</td>
<td>9</td>
<td>0.71</td>
<td>11</td>
<td>0.65</td>
</tr>
<tr>
<td>80–84</td>
<td>5</td>
<td>0.60</td>
<td>11</td>
<td>0.84</td>
</tr>
<tr>
<td>85–89</td>
<td>1</td>
<td>0.31</td>
<td>2</td>
<td>0.31</td>
</tr>
<tr>
<td>90+</td>
<td>1</td>
<td>1.06</td>
<td>1</td>
<td>0.37</td>
</tr>
</tbody>
</table>

Table 2 Distribution of educational level and diploma. PAQUID 1989–95. n=2881

<table>
<thead>
<tr>
<th>Education</th>
<th>n (%)</th>
<th>Men (%)</th>
<th>Women (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No education</td>
<td>120 (4.2)</td>
<td>42 (3.5)</td>
<td>78 (4.7)</td>
</tr>
<tr>
<td>Primary school without diploma</td>
<td>812 (28.2)</td>
<td>291 (24.2)</td>
<td>521 (31.0)</td>
</tr>
<tr>
<td>Primary school with diploma</td>
<td>1286 (44.6)</td>
<td>546 (45.4)</td>
<td>740 (44.1)</td>
</tr>
<tr>
<td>Secondary school without diploma</td>
<td>346 (12.0)</td>
<td>144 (12.0)</td>
<td>202 (12.0)</td>
</tr>
<tr>
<td>Secondary school with diploma</td>
<td>171 (5.9)</td>
<td>79 (6.5)</td>
<td>92 (5.5)</td>
</tr>
<tr>
<td>University level</td>
<td>146 (5.1)</td>
<td>101 (8.4)</td>
<td>45 (2.7)</td>
</tr>
</tbody>
</table>

who attained only a primary school level (HR=1.49, p=0.02). However, this categorisation does not seem to be the best one. Most of the subjects only have a primary school level (table 2), and among these subjects, 61% (1286 of 2098) passed the primary school diploma. Among subjects who only have a secondary school level, 33% (171 of 517) passed the secondary school diploma. We performed a series of analyses to determine the best cut off and found that the model with the highest log likelihood was one in which subjects with no education or without a primary school diploma were considered as having a low education.

**CONFOUNDING EFFECT OF EDUCATIONAL ATTAINMENT**

The association between dementia and sex might be explained by a confounding effect of education as there were more women than men in the lower education group (35.7% vs 27.7%). To test this hypothesis, we ran three successive models including sex and the age by sex interaction (model 1), education alone (model 2), and both variables (model 3) (table 3). The hazard ratios of sex and education were unchanged when sex was adjusted for education. Thus a confounding effect of education seems unlikely to explain the excess risk of dementia or Alzheimer’s disease in older women. No interaction between educational level and age was found, suggesting that the relation between educational level and Alzheimer’s disease does not vary according to age.

**INTERACTION OF SEX AND EDUCATION**

To determine if the higher rate of Alzheimer’s disease in women could be modified by education, a model with sex, education, interaction between sex and age, and interaction between sex and education was tested. Sex and the interaction between sex and age remained significant, whereas the interaction between sex and education was not significant (p=0.72). Thus, education is not an effect modifier for sex.

**Discussion**

Several conclusions can be drawn from this study. Firstly, incidence of Alzheimer’s disease is higher in women than men after 80, whereas the incidence is higher in men before the age of 80. The different progression of the incidence according to sex is not found when other dementias are analysed. In addition, incidence of other dementias seems to decrease in both sexes after 85 years. Secondly, this incidence study confirms that subjects with a lower educational level are at higher risk of developing Alzheimer’s disease. Thirdly, adjusting for education does not change the association between sex and risk of Alzheimer’s disease.

In women, an increased risk of dementia and Alzheimer’s disease has been reported in several incidence studies, but without significant differences. Other studies also reported a higher incidence of dementia in women, but the significance of the results was not given. Two studies reported a significantly higher incidence of dementia or Alzheimer’s disease in women, but both samples were studying subjects over 85 years and 75 years of age respectively. In the Framingham study, Bachman et al did not find any difference of incidence according to sex. Finally, two studies

Table 3 Study of the independent effect of sex and educational attainment on dementia and Alzheimer’s disease. PAQUID 1989–95. n=2881

<table>
<thead>
<tr>
<th></th>
<th>Dementia</th>
<th>Alzheimer’s disease</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>p Value</td>
</tr>
<tr>
<td>Model 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex (female vs male)</td>
<td>0.396 (0.99–0.90)</td>
<td>0.033</td>
</tr>
<tr>
<td>Age by sex</td>
<td>1.072 (1.014–1.132)</td>
<td>0.013</td>
</tr>
<tr>
<td>Model 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td>1.83 (1.37–2.44)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Model 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex (female vs male)</td>
<td>0.376 (0.082–0.857)</td>
<td>0.027</td>
</tr>
<tr>
<td>Age by sex</td>
<td>1.072 (1.014–1.132)</td>
<td>0.013</td>
</tr>
<tr>
<td>Education</td>
<td>1.82 (1.36–2.42)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*The hazard ratio is given for a woman aged 65. The hazard ratio of developing Alzheimer’s disease for a woman aged 85 years is*: 0.395(0.06–1.17) = 0.71
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occurrence of dementia in women. Several

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v erent genetic and hormonal

women might be related to biological di

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er-

studies have reported a negative association

between oestrogen replacement therapy and

studies reported a significant modification

part of confounders in our results. Educational

characteristics are also important and may play

the part of confounders in our results. Educational

level is one of these confounders. We showed

an association between dementia or

Alzheimer's disease with lower educational

attainment in men and women. We defined low

educated people as subjects with no education

or subjects with a primary school level without

diploma. In our sample, most subjects had

attained a primary school level. Among the

generations studied, it was usual to stop train-

ing at this stage. However, this did not mean

that people who stopped were not able to reach

a secondary level. Thus the primary school

level itself does not seem to be the best indica-

tor of their cognitive capabilities and the

achievement or not of the primary school

diploma seems to provide a more adequate

threshold for a dichotomy. Several studies have

reported an association between low education

or low occupational history and an increased

risk of developing dementia or Alzheimer's dis-
ease in prevalent cases51–53 or in incident

cases.7,12 However, Cobb et al22 did not find an

association between education and incident

cases of Alzheimer's disease in the Framing-

ham study, although an association was found

between non-Alzheimer's disease dementias

and low educational attainment. Mortimer and

Graves48 suggested that education could induce
dendritic growth in the brain and that people

with high levels of education would be

protected to some degree against Alzheimer's
disease. Another hypothesis was expressed by

Snowdon et al51 who studied linguistic ability

among nuns. They found that low linguistic

ability in early life was a strong predictor of

poor cognitive function and Alzheimer's dis-
ease in late life and suggested that low linguis-
tic ability may be an early expression of

Alzheimer's disease neuropathology. Plassman

et al50 found similar results when they corre-

lated a general learning ability test adminis-
tered to inductees into the United States armed

forces with cognitive tests performed in late

life. They showed that cognitive performances

in late life were related to cognitive ability

measured in early adult life. These results were

supported by two studies which used brain

imaging to assess the association between

cerebral blood flow and education51 or between

cerebral metabolism and premorbid measures

of intelligence52 in subjects with similar levels

of severity of clinical dementia. Both studies

showed that greater cerebral metabolic deficits

were associated with higher level of education

or premorbid ability, indicating that

Alzheimer's disease was more advanced in

these subjects.

Our results are consistent with these studies

as obtaining a primary school diploma may be

considered as an indicator of premorbid intelli-
gence. Our findings also suggest that increasing

the number of years of education does not

decrease the risk of developing dementia. It

rather suggests that people who reached a

threshold (who passed a relatively difficult

diploma) have a lower risk, whether they

continued to go to school or not. However, it is

not possible to strictly show that untrained or

unsuccessful pupils have a higher risk of devel-
opment of dementia in later life. Subjects who failed

the examination might be involved later in less

demanding cognitive tasks, leading to lower

brain stimulation and a more limited cognitive

reserve. These subjects might also be more

likely to be exposed to toxic substances as they

were practising rural and manual occupations

more often.

Although in our sample women were less

educated on average, the association between

low education and Alzheimer's disease was

seen both in men and women. Thus, the differ-

eence in incidence found according to sex could

not be explained by a confounding effect or a

modification effect of education.

Another confounder that has been analysed

in this cohort is wine consumption. In a previ-

ous article,13 we showed that moderate wine

consumption was associated with a lower risk

developing Alzheimer's disease. As wine

consumption is higher in men than in women,
it could act as a confounder. However, after

adjustment for wine consumption, the associa-
tion between Alzheimer's disease and sex

remained unchanged. Both sex and the age by

sex interaction were still significant.

Several other points need to be discussed.
The number of refusals may bias our results.

Refusals were younger, more often women,

and were on average less educated. On the one

hand, this could lead to an underestimation of

the incidence of dementia in women younger

than 80. However, when the analysis was

limited to subjects aged 80 years and older at

baseline (647 subjects and 83 with dementia),
the hazard ratio of Alzheimer's disease in

women was close to significance (HR=1.72,
95% CI 0.97–3.04, p=0.06) and the magni-

tude of the association remained unchanged.

On the other hand, as it is expected that low

educated people would have a higher incidence

of dementia, the higher rate of lower educated

subjects among refusals might result in a loss of
power, but is unlikely to bias the negative association between education and incidence of dementia.

The problem of underdiagnosis of dementia in subjects with a higher educational level is more of concern. In our study, some of the subjects were selected to be seen by the neurologist if they experienced a decline in ability in the neuropsychological tests during the follow up. Although there is some variability in the test scores, the performance of a non-demented subject should remain stable throughout the period of study. The diagnosis of dementia at follow up implies a substantial decline from the initial performance and the ontological link of the decline of cognitive performances reduces the chance of misdiagnosing a demented individual. Actually, in our sample, low educated subjects lost on average 5.02 points on the MMSE score before being diagnosed as demented, whereas subjects with higher education lost on average 4.96 points.

Another problem is the lack of independence between the data collection on educational level and the diagnosis of dementia. In a prospective cohort study such as this, it is not realistic to try to interpret the evolution of cognitive performances without taking into account the educational level of the subject. It is likely that knowing the results of the initial prevalence study of PAQUID, the senior neurologists who validated the incident cases were more restrictive in making the diagnosis of dementia in subjects with lower education. Even though impossible to document or quantify, this bias could have only lowered the rate of diagnosis of dementia in this higher risk group.

In conclusion, the present findings confirm the higher rate of Alzheimer’s disease in older women. We also confirmed that the incidence was higher in men before 80 years. This association did not display a different adjustment for education. Our results on education are consistent with previous studies showing that premorbid measures of intelligence in early life were predictors of cognitive impairment in late life.

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