NEUROEPIDEMIOLOGY

Older age at retirement is associated with decreased risk of dementia

Carole Dufouil · Edwige Pereira · Geneviève Chêne · M. Maria Glymour · Annick Alpérovitch · Elodie Saubusse · Mathilde Risse-Fleury · Brigitte Heuls · Jean-Claude Salord · Marie-Anne Brieu · Françoise Forette

Received: 20 November 2013/Accepted: 18 April 2014 © Springer Science+Business Media Dordrecht 2014

Abstract To test the hypothesis that age at retirement is associated with dementia risk among self-employed workers in France, we linked health and pension databases of self-employed workers and we extracted data of those who were still alive and retired as of December 31st 2010. Dementia cases were detected in the database either through the declaration of a long-term chronic disease coded as Alzheimer's disease and other dementia (International Classification of Disease codes G30, F00, F01, F03) or through the claim for reimbursement of one of the anti-dementia drugs. Data were analyzed using Cox proportional hazard model adjusting for potential confounders. Among the 429,803 retired self-employed workers alive on December 31st 2010, prevalence of dementia was 2.65 %. Multivariable analyses showed that the hazard ratio of dementia was 0.968 [95 % confidence

interval = (0.962-0.973)] per each extra year of age at retirement. After excluding workers who had dementia diagnosed within the 5 years following retirement, the results remained unchanged and highly significant (p < 0.0001). We show strong evidence of a significant decrease in the risk of developing dementia associated with older age at retirement, in line with the "use it or lose it" hypothesis. Further evidence is necessary to evaluate whether this association is causal, but our results indicate the potential importance of maintaining high levels of cognitive and social stimulation throughout work and retiree life.

Keywords Dementia · Cognitive reserve · Prevention · Intellectual stimulation

C. Dufouil · E. Pereira · G. Chêne Centre INSERM U897-Epidemiologie-Biostatistique and CIC-EC7, INSERM, ISPED, 33000 Bordeaux, France

C. Dufouil · E. Pereira · G. Chêne · A. Alpérovitch Centre INSERM U897-Epidemiologie-Biostatistique, ISPED, Univ. Bordeaux, 33000 Bordeaux, France

C. Dufouil · G. Chêne Pôle de Santé Publique, CHU de Bordeaux, 33000 Bordeaux, France

C. Dufouil (🖂)

INSERM U897 and CIC-EC7, Bâtiment ISPED-Université de Bordeaux, 146 rue Léo Saignat, 33076 Bordeaux Cédex, France e-mail: carole.dufouil@isped.u-bordeaux2.fr

M. M. Glymour

Department of Epidemiology and Biostatistics, University of California, San Francisco, CA, USA

E. Saubusse Régime Social des Indépendants, 33000 Bordeaux, France

M. Risse-Fleury Régime Social des Indépendants, 93200 Saint-Denis, France

B. Heuls

Agence Nationale de sécurité du médicament et des produits de santé, 93200 Saint-Denis, France

J.-C. Salord · M.-A. Brieu · F. Forette International Longevity Centre-France, 75016 Paris, France

F. Forette University René Descartes, 75005 Paris, France

Background

There are strong arguments suggesting that intellectual stimulation could prevent dementia or delay its onset. The first set of evidence is derived from the consistently reported association between higher education level and lower risk of dementia [1, 2]. On the basis of this robust finding, the concept of "cognitive reserve" has been put forward, hypothesizing that higher education is protective against the biological effects of brain ageing either passively or actively [3–5]. Several other proxies for intellectual stimulation, besides education level, have also been shown to protect against the clinical manifestations of brain ageing [6]. These include occupations requiring complex mental activity [7-10], and also participation in leisure and stimulating cognitive activities [11, 12]. Globally, it is suggested that lifespan mental activity could be protective against dementia [13]. The impact of changes in mental activity across life on cognitive decline course has also been investigated. On one hand, some studies suggest that intensive cognitive training might be an effective intervention to delay/ slow cognitive decline [14–16]. On the other hand, few studies have investigated whether decreases in either mental engagement or cognitive stimulation during life are associated with dementia risk. One potentially important source of decrease in mental stimulation during life is retirement. The possibility that retirement increases risk of dementia has clinical and policy implications because state retirement and pension policies strongly influence retirement age [17]. Even if retirement age has only modest effects on the timing of dementia onset, the effect on financial and health burden of dementia could be tremendous [18]. To date, few studies have examined the link between retirement and dementia risk or cognitive decline. Most [19-21] but not all [17] of these studies report that retirement is associated with worse cognitive test scores. These results further suggest that retirement age could be associated with dementia risk, although the cognitive measures available in most studies were quite limited.

We aimed at studying the relationship between age at retirement and dementia risk, using data from healthcare and pension databases of independent workers affiliated with a specific health and pension insurance plan.

The "Regime Social des Indépendants (RSI)" is an orga-

Data and methods

Study design and participants

medical claims (i.e., visits to general practitioners and other specialists, biological investigations, prescribed drugs). For each prescribed drug, the code [according to the anatomical therapeutic chemical (ATC) classification system], date of purchase and name of prescribers are entered in the database. The database does not include any clinical information other than, when it applies, the declaration of chronic diseases [named "affections de longue durée" (ALD) and coded according to the 10th revision of the International Classification of Disease] as well as, if any, its date of diagnosis. We only considered chronic diseases that had occurred prior to any dementia diagnosis. The pension database includes information allowing characterization of retirement (date, pension amount) and data on last professional occupation done prior to retirement. In this analysis, the source population was defined as all persons belonging to the RSI databases, receiving old age pension benefits at the date of December 31st 2010, and for whom healthcare data were available. Data were extracted in May 2011.

Outcome data

In France, 30 chronic diseases are classified as ALD and numbered 1-30, leading to a 100 % reimbursement of any medical expense. Among this list, dementia (Alzheimer's disease and related disorders) is ALD 15. Definition of dementia cases was based on [1] the purchase on anti-dementia drugs or [2] dementia diagnosis based on the request by a physician to diagnose the individual "dementia" ALD. Antidementia drugs used for case definition were either acetylcholinesterase inhibitors (ChEI) (donepezil, galantamine, rivastigmine) or N-methyl-D aspartate receptor partial antagonists (memantine). These drugs were routinely prescribed in France at mild to severe stages of the disease until recent updated recommendations (October 2011) from the French medical drugs regulation authorities. On the request of a patient's physician, the patient can be diagnosed as demented ("ALD" 15, ICD-10 codes "F00-F03" and "G30"), after validation by RSI. This validation may include either a medical record review, or, in special cases, a specific physical exam, by a physician working for RSI. Age at dementia diagnosis was defined as the lowest of age at first anti-dementia drug purchase or age at declaration of "ALD 15". Date of dementia diagnosis covered the entire retirement period of each individual; drug purchases are available only from January 1, 2008, and so can supplement diagnoses only if they occurred after that date.

Exclusions

The following exclusions were performed:

• Individuals belonging to occupations other than craftworkers or shopkeepers (e.g., self-employed attorneys) as they are likely to have other pension sources besides RSI

- Insurance beneficiaries other than the primary selfemployed individual (e.g., spouse, or children of the self-employed can be covered by RSI insurance for health costs reimbursed, but the related information was erased from the analytic database)
- Individuals taking anti-parkinsonism drugs or being diagnosed as "Parkinson disease" according to ALD declaration
- Individuals identified as still working despite receiving a pension
- Individuals identified as demented prior or concomitant to retirement

Covariates

Covariates extracted from the databases were: gender, area of residence, marital status (married vs. not married), number of semesters of work validated for RSI pension's level calculation, pension amount from RSI, last occupation category (craft workers and/or shopkeepers), type of retirement as classified by RSI (early, impairment, reduced rate, full rate, overvaluation), any medications claims in 2010, whether any of seven other ALDs had been declared and age of declaration for each ALD. Among the remaining 29 chronic diseases, we focused more specifically on the following: stroke ICD-10 "I60-I69, G81") diabetes (ICD-10 "E10-E14"), severe hypertension ("ICD-10 "I10"), coronary disease ("ALD 13"; ICD-10 codes "I20, I21, I25"), chronic arteriopathy (ICD-10 codes "I70-I74, I25"), severe cardiac failure ("I05-I06, I34-I35, I42, I48-I50, Q22–Q28), psychiatric disorders (ICD-10 codes "F10, F20, F22, F29, F31-F34, F401, F60, F79, F84). We categorized psychiatric disorder as such "absent", "present and diagnosed <1 year before or after retirement", "present and diagnosed between 1 and 5 years before or after retirement", "present and diagnosed more than 5 years before or after retirement". We also classified individuals as having a "Diagnosis of at least one chronic disease other than dementia" for any of the other "ALD" categories.

Statistical methods

Dementia risk in relation to age at retirement was analysed with proportional hazards (Cox) regression models. In these models, the dependent time variable was the age at dementia for cases and age at December 31st 2010 for nondemented individuals (censored). In all analyses, we controlled for gender. In addition we controlled for area of residence, marital status, occupation category, type of retirement, pension amount, number of semesters worked as "craft workers or shopkeepers", diagnosis of hypertension, diabetes. We also performed stratified analyses by gender, occupation category and other disease's diagnosis (according to "ALD"). In a sensitivity analyses, we excluded all dementia cases that had occurred in the 5 years or in the 10 years following retirement to minimize reverse causation bias. As some individuals had worked a part of their career in other occupation(s) than "craftworkers or shopkeepers", we also ran the analysis in the restricted sample of those who had worked at least 20 years in this occupation (almost 70 % of the sample). As early retirement (prior to 60 years old) is potentially related to bad health conditions we also assessed the association between age at retirement and dementia risk in those who retired after 60 years old and in those who retired after 70 years old in order to assess the robustness of the findings. As the analyses are based only on individuals who had survived at December 31st 2010 (date of database extraction) we explored both whether survival bias and birth cohorts effect affected our findings by performing analyses stratified by categories of birth year [<1920, (1920-1930), (1930-1940), 1940 and above]. Psychiatric disorders (especially major depressive episodes) are more frequent in demented patients than in controls and could have led to early retirement. In order to control for a potential confounding effect or bias we performed sensitivity analyses by adjusting for delay between psychiatric disorders onset and retirement date and also excluding persons who had been diagnosed <1 year prior of after retirement.

Because the conditions of diagnosis of dementia have changed over time in France, we have also performed a stratified analysis by year of diagnosis (<2006, 2006, 2007, 2008, 2009, 2010).

Results

In total, 429,803 individuals were included in the study, of whom 11,397 were demented (2.65 %) by December 21st 2010. Dementia prevalence ranged from 0.07 % in individuals aged 65–69 years old to 10.2 % in individuals aged 85 years old and above. Dementia prevalence did not differ between men and women until the age of 80 years old. A marked difference was seen after 85 years of age as the prevalence almost doubled in women (12.8 %) compared to men (7.0 %). Of the 11,397 dementia cases, 88 % (n = 10,029) were categorized as such based on ALD declaration and 12 % were identified by prescription drug usage only.

Table 1 shows the sample characteristics at the time of database extraction by dementia status. On average, dementia cases were 10.9 years older than non-demented.

Table 1	Sample	characteristics	by	dementia	status	(N =	: 429,803)
---------	--------	-----------------	----	----------	--------	------	------------

	Non demented $N = 418,406$	Demented $N = 11,397$
Mean age in years (SD)	74.0 (8.6)	84.9 (6.8)
Male (%)	69.3	45.9
Married (%)	69.8	47.0
Craft workers (%)	44.9	34.0
Mean pension level in Euros (SD)	714 (412)	586 (344)
Mean number of semesters with occupation as craftworkers or shopkeepers (SD)	50.2 (20.3)	52.8 (21.7)
Declared chronic diseases other than dementia (%)	39.8	50.3
Severe hypertension (%) ^a	9.1	14.0
Diabetes (%) ^b	11.1	10.8
Stroke (%) ^c	2.3	4.3
Cardiovascular disease (%) ^d	23.5	34.7
Psychiatric disorder (%) ^e	1.1	1.8

^a ICD-10 codes "I10"

^b ICD-10 codes "E10-E14"

^c ICD-10 codes "I60-I69" and "G81"

^d Severe hypertension or coronary disease or severe cardiac failure or chronic arteriopathy or stroke : ICD-10 codes "I60–I69", "G81", "I10", "I20", "I21", "I25", "I70–I74", "I05–I06", "I34–I35", "I42", "I48–I50", "Q22–Q28"

^e ICD-10 codes "F10", "F20", "F22", "F29", "F31–F34", "F401", "F60", "F79", "F84"

Dementia cases were more often women, more often craft workers, and they overall more often had cardiovascular disease diagnoses, especially hypertension and stroke. Their mean pension level was smaller than that of nondemented.

Figure 1 shows the distribution of age at retirement. It shows two modes, one at 60 years old, and another one,

weaker, at 65 years old; these ages correspond to minimum mandatory retirement ages in French legislation (the statutory retirement age was dropped from 65 to 60 in 1982). Because self-employed individuals are not bound by the statutory retirement age, there is substantial variability around these modes. On average, individuals had retired for 12.5 years [standard deviation (SD) = 7.6] but demented individuals had been retired longer, consistent with their older age on average.

In the Cox model adjusted for gender, we observed that an increase of 1 year in the age at retirement was associated with a 3.1 % lower risk of dementia (p = 0.0001). A further multivariable analysis adjusting for more potential confounders (marital status, area of residence, pension amount, duration of work as self-employed, occupation category, type of retirement, diabetes, hypertension) led to similar estimates [hazard ratio for an extra year of age at retirement = 0.968; 95 % CI = (0.962–0.973)]. The association between older age at retirement and decreased risk of dementia was stronger in men [hazard ratio = 0.956; 95 % CI = (0.947–0.964)] than in women [hazard ratio = 0.976; 95 % CI = (0.970–0.983)] (Table 2).

A series of stratified analyses by occupation category, retirement type, comorbidity were all consistent with the association between older age at retirement and a lower risk of dementia (Table 2). In sensitivity analyses excluding dementia cases that occurred <5 years after retirement (n = 517), the point estimate of the HR was even lower [HR = 0.95, 95 % CI = (0.944–0.956)]. Similarly, we estimated models excluding dementia cases that occurred within 10 years after retirement (n = 1549), the point estimate of the HR was 0.918, 95 % CI = (0.912–0.924). We also repeated analyses excluding individuals who retired after the age of 75 years in case of misclassification of retirement age; estimates were nearly identical (HR = 0.970). Analyses

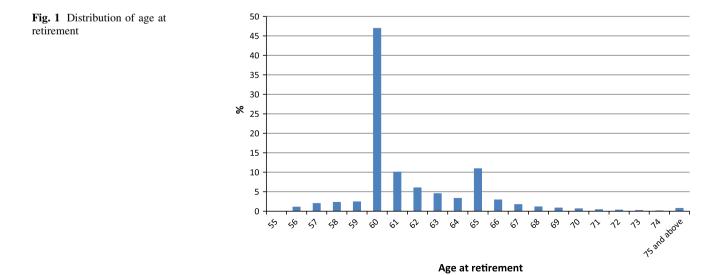


Table 2 Hazard ratio of dementia associated with age at retirement. Stratified analyses by gender, occupation category, retirement type, diagnosis of comorbidities

Characteristics	cs N with no dementia N with dementia		Hazard ratio for age of retirement ^a	95 % Confidence interval
Gender				
Male	295,368	5,225	0.956	0.947-0.964
Female	134,435	6,172	0.976	0.970-0.983
Occupation category				
Craft workers	191,613	3,868	0.941	0.929-0.953
Shopkeepers	213,713	6,928	0.975	0.968-0.981
Craft workers + shopkeepers	24,477	601	0.963	0.938-0.988
At least one chronic disease other	than dementia			
No	257,662	5,669	0.973	0.966-0.980
Yes	172,141	5,728	0.964	0.957-0.971
Severe hypertension ^b				
No	390,245	9,802	0.968	0.963-0.974
Yes	39,558	1,595	0.971	0.958-0.985
Diabetes ^c				
No	382,065	10,161	0.969	0.964-0.974
Yes	47,738	1,236	0.968	0.952-0.984
Stroke ^d				
No	419,825	10,909	0.970	0.964-0.975
Yes	9,978	488	0.944	0.918-0.970
Cardiovascular disease ^e				
No	327,736	7,447	0.971	0.964-0.977
Yes	102,067	3,950	0.964	0.955-0.973
Psychiatric disorder ^f				
No	424,854	11,194	0.969	0.964-0.974
Yes	4,949	203	0.937	0.894-0.982

ALD affections de longue durée (severe chronic disease)

^a Hazard ratio associated with an increase of 1 year in the age at retirement computed from Cox model adjusted for gender

^b ICD-10 codes "I10"

^c ICD-10 codes "E10–E14"

^d ICD-10 codes "I60–I69" and "G81"

^e Severe hypertension or coronary disease or severe cardiac failure or chronic arteriopathy or stroke : ICD-10 codes "I60–I69", "G81", "I10", "I20", "I21", "I25", "I70–I74", "I05–I06", "I34–I35", "I42", "I48–I50", "Q22–Q28"

f ICD-10 codes "F10", "F20", "F22", "F29", "F31-F34", "F401", "F60", "F79", "F84"

restricted to those who had worked more than 20 years as "shopkeepers or craftworkers" showed consistent findings for the association between age at retirement and dementia risk (HR = 0.965, 95 % CI = 0.959–0.972). We excluded persons who had retired prior to the age of 60 years as early retirement could be a sign of bad health conditions (n = 34,677 observations deleted) but results were unchanged [HR = 0.969, 95 %CI = (0.964–0.975)]. Major depression represented 80 % of psychiatric disorders diagnosed. Adjusting for delay between psychiatric disorder diagnosed with psychiatric disorder onset <1 year after of before retirement did not modify the main result

[HR = 0.969, 95 %CI = (0.964-0.974)]. Finally we excluded cases that were identified only based on anti-Alzheimer drug intake (n = 1,029); the estimate was almost unchanged [HR = 0.971, 95 % CI = (0.965-0.976)].

In analyses stratified by "generation" (Table 3), we noted similar patterns for all birth cohorts. The HR was furthest from the null among subjects born after 1940, for whom survival bias is likely to be least pronounced.

Finally, in analyses stratified by year of diagnosis (Table 4), the HR for age of retirement was statistically significant and protective for every stratum; the hazard ratio ranged from 0.942 for individuals diagnosed in 2010 to 0.984 for individuals diagnosed in 2006.

Discussion

In a large sample of retired self-employed workers, we found strong evidence of an inverse relationship between the risk of developing dementia and older age at retirement. The evidence was consistent in analyses stratified by work type and by presence of comorbidities (especially cardio-vascular conditions and psychiatric disorders). These findings are unlikely to be due to reverse causation, given that the results were consistent and even stronger when excluding all dementia cases that had occurred over 5 or 10 years following retirement. The findings were also robust to potential "generation/cohort" or "trends in diagnosis" biases: the results remained consistent in sensitivity analyses stratifying on year of birth or on year of dementia diagnosis.

An older age at retirement for these self-employed individuals reflects both a longer working life but also a personal choice to work above the mandatory ages for retiring that are applicable to other French workers. Our data, however, do not allow us to distinguish between the effects of delaying retirement due to personal choice, or working law consequences.

Only one prior study has reported on the association of retirement age with dementia risk. Lupton et al. [20], in a study of 1,320 probable AD cases, found that later age at retirement, as reported by an informant, was associated with older age at onset of AD. However, the sampling was based on AD cases only, and hence the generalization of the findings is weak.

Other studies have reported on the link between retirement and cognitive functions rather than full-blown dementia and their findings are overall inconsistent, variously reporting harmful, beneficial or no effects. Survey data from the Health and Retirement study [19] were analysed using an econometric approach. From a sample of 14,710 respondents, a decrease in cognitive performances was reported after the age of 62 years (minimum age at which social security benefits can be claimed). Using a subsample (n = 11,311) of the same survey, Coe et al. [17] compared cognitive decline trajectories of early retirees (at age 55 years) to those of late retirees (at age 62 years) using offers of early retirement as an instrumental variable in a US sample. They found no evidence for an inverse association between retirement duration and cognitive functions and a suggestion that among blue-collar workers, early retirement might be beneficial.

Rohwedder et al. [22] used cross-national (in the USA and 11 European countries) differences in policy incentives for retirement as an instrumental variable for the effect of retirement on memory scores and found large adverse effects on memory. However, this analysis was based on cross-sectional memory assessments and had no way to account for other sources of cross-national difference in memory scores, such as educational history. In an ancillary analysis of the Whitehall II study that included 2,031 male civil servants, average cognitive performances over 5 years follow-up increased but the slope of increase was found to be smaller in those who had retired compared to those who were still working [21]. The effect of age at retirement has also been studied largely in relation to other health outcomes. Reports are mostly in favor of the detrimental effect of early retirement or late job loss on health outcomes including mortality and cardiovascular outcome [23–25].

Several explanations of why older age at retirement could prevent cognitive decline and dementia have been proposed, including changes in financial conditions due to limited pension income or deterioration of health at retirement. However, one possible hypothesis is that work itself has cognitive benefits. Such benefits may arise from mental exercise in that employed individuals encounter more cognitively challenges than retirees. Additionally, some occupations may entail more frequent social interactions and higher level of physical activity than maintained by retirees. The finding of cognitive benefits of work is consistent with the "use it or lose it" concept as well as with the cognitive reserve hypothesis, according to which complex mental activity protects against the clinical consequences of brain insults due to dementing process [26, 27]. In line with this hypothesis, studies have demonstrated that demanding or socially engaging work during adulthood are associated with better cognitive performances later in life [10]. In our study, we have no information to disentangle what aspect of work may be beneficial.

Whether this apparent protective effect of older age at retirement on dementia risk stands for any job category should be further explored as all jobs do not require the same level of mental activity complexity and one could expect the effect of retirement to therefore be specific to the occupation. Other databases should be used to investigate that hypothesis.

That later retirement could protect against dementia through ongoing stimulation is also supported by the results of randomized controlled trials that have demonstrated the beneficial cognitive effect of cognitive exercise interventions compared to "wait and see" control conditions [28]. Our results could reflect that it might important to consider not to have a mandatory age for retirement but rather to leave some freedom to people regarding when they wish to retire. However data extracted from administrative database did not allow us to explore that hypothesis further.

The cohort comprised only craft workers and shopkeepers and we cannot infer whether these results would be replicated in the general population but our results encourage further studies other studies on the is topic to be undertaken. We can suspect there are two main differences

Table 3 Hazard ratio of dementia associated with age at retirement

Year of birth	Ν	Dementia cases	Hazard ratio ^a	95 % Confidence interval
Prior to 1920	12,469	1,694	0.986	0.974–0.999
(1920–1930)	89,986	6,732	0.985	0.979–0.991
(1930–1940)	152,689	2,630	0.986	0.973-0.999
1940 and later	174,659	341	0.904	0.848-0.965

Stratified analysis by birth cohorts

^a Hazard ratio associated with an additional 1 year in the age at retirement computed from Cox model adjusted for gender

Table 4 Hazard ratio of dementia associated with age at retirement.

 Stratified analysis by year of diagnosis

Year of diagnosis	Ν	Dementia cases	Hazard ratio ^a	95 % Confidence interval
<2006	316,575	8,514	0.955	0.949-0.962
2006	337,078	1,252	0.984	0.969-1.000
2007	365,009	1,155	0.974	0.958-0.990
2008	393,393	1,500	0.960	0.946-0.974
2009	405,046	2,099	0.974	0.963-0.986
2010	411,501	2,408	0.942	0.930-0.954

^a Hazard ratio associated with an increase of 1 year in the age at retirement computed from Cox model adjusted for gender

between self-employed craft workers and shopkeepers and people having other occupations that could modify the relationship between age at retirement and dementia risk: firstly compared to other occupations, they have more freedom choosing when they retire (no mandatory age) and secondly there might be differences in the intellectual demands of the type of occupations covered here. Although the greater autonomy in determining age of retirement is a potential limitation in that it introduces potential reverse causation, it is also an advantage in that variation in age of retirement is essential in a study of the effects of retirement age. Because retirement age is nationally mandated in France, it would be difficult to conduct this study in the full population; such a study could only be based on the rare statutory changes in retirement age and would therefore have other limitations.

However in this sample almost 30 % of individuals are likely of having other occupations than being "craft workers of shopkeepers" during a large part their working life (<20 years as self-employed) and our data do not suggest that this could be neither a confounding factor nor a bias as adjusting for work duration as self-employed did not affect the findings and similarly analysis restricted to those who had worked more than 20 years showed similar patterns.

Dementia prevalence reported in our study is very close to that of the general population in France as published recently from a very large representative database of individuals covered by the national insurance plan [29] but is lower that reported in the general population from epidemiological studies [30]. In the Paquid study [30], a population-based study in southern France, prevalence of dementia was 23.9 % in men and 38.4 in women after the age of 85 years old. The difference may be due to early stage cases (mild dementia) who are not yet registered as "chronic diseases" as they do not require any care and are not prescribed any anti-dementia drugs. We do not think this misclassification is related to the exposure and we anticipate the main consequence was to reduce statistical power because we have fewer cases.

We could only obtain information on individuals who were retired and still alive on December 31st 2010. We have assessed the impact of this data truncation on our findings by performing age-stratified analyses, because if there were substantial truncation bias, this bias should have the most influence on parameter estimates from the oldest cohorts (born before 1920) and the least influence on parameter estimates in the youngest cohort (born after 1940). The results were very consistent across cohorts, with effect estimates furthest from the null in the youngest. This pattern suggests that truncation, if anything, attenuated our effect estimates and the actual benefit of delaying retirement is even larger. The similarity in effect estimates across age groups also indicates that birth cohort effects are unlikely.

From Table 3, crude calculations suggest a trend towards a lower prevalence of dementia among persons born after 1940 (0.2 %) compared to those born between 1930 and 1940 (1.7 %) that could corroborate recent reports from the CFAS study [31]. However, this observation could likely be the confounding of age and cohort i.e. the older cohort was actually older for much of the outcome assessment years, whereas the more recent cohorts were younger. So the younger people (more recent cohorts) have a lower absolute dementia risk and any relative effects appear to be much more extreme. Other studies than ours will be necessary to assess the hypothesis for a temporal trend towards a decrease in dementia incidence.

One limitation of the use of this type of database is that we do not record all variables that would generally be considered as potential confounders in this type of analyses. Therefore education level was not available but we adjusted for RSI pension's amount a proxy of education. It should be noted that had some persons subscribed to complementary retirement benefit, we did not have the information. Despite these limitations, we have been able to fully rule out many of the potential biases that arise in studies assessing the effect of retirement on health, most critically reverse causality. Because true randomized studies of this research question are not feasible, observational evidence such as this is critical to build an evidence base on the effects of retirement. Key strengths of this study are the large size and the fact that we have been able to control for several potential confounders that were available from the database. Future research should consider issues of generalizability and attempt to identify exogenous sources of variation in retirement age for quasiexperimental designs.

Finally, professional activity may be an important determinant of mental exercise and social integration. Our data show strong evidence of a significant decrease in the risk of developing dementia associated with older age at retirement. This health perspective should be taken into consideration when the age of cessation of professional activity is discussed.

As countries across the world respond to population aging with changes in policies that shape retirement age and the life circumstances of older adults, these findings highlight the potentially immense health implications of such policy changes.

Dementia presents a very high burden of disease for patients, caregivers, and society, but there are very few established prevention or treatment options. If large scale social policies, such as retirement and pension arrangements, influence population dementia risk even slightly, the population health consequences—whether beneficial or adverse—could be dramatic. However, there is at this point limited convincing evidence on the effects of retirement on dementia, although there are both theoretical reasons and some empirical evidence supporting the idea that continued employment may benefit cognitive health.

Our results thus highlight the importance of maintaining high levels of cognitive and social stimulation throughout work and retiree life and emphasize the need for interventions and policies to help older individuals achieve such cognitive and social engagement.

Acknowledgments This study was initiated by ILC-France and supported by funds provided by Ipsen Pharma, Van Dyck Health Care, Groupe PREVOIR, Lündbeck SAS, Nutricia Nutrition Clinique (groupe Danone), HSBC France. The funding sources had no role in study design, data collection, analysis, interpretation, or writing of the report.

Conflict of interest The authors declare that no competing interests exist.

References

- 1. Ngandu T, von Strauss E, Helkala EL, Winblad B, Nissinen A, Tuomilehto J, et al. Education and dementia: What lies behind the association? Neurology. 2007;69(14):1442–50.
- 2. Cohen CI. Education, occupation, and Alzheimer's disease. JAMA. 1994;272:Letters 1405.

- Stern Y. Cognitive reserve and Alzheimer disease. Alzheimer Dis Assoc Disord. 2006;20(Suppl 2):S69–74.
- Cummings JL, Vinters HV, Cole GM, Khachaturian ZS. Alzheimer's disease: etiologies, pathophysiology, cognitive reserve, and treatment opportunities. Neurology. 1998;51(Suppl 1):S2–17.
- 5. Staff RT, Murray AD, Deary IJ, Whalley LJ. What provides cerebral reserve? Brain. 2004;127:1191–9.
- 6. Stern Y. What is cognitive reserve? Theory and research application of the reserve concept. J Int Neuropsychol Soc. 2002;8(3):448–60.
- Stern Y, Albert S, Tang MX, Tsai WY. Rate of memory decline in AD is related to education and occupation—Cognitive reserve? Neurology. 1999;53(9):1942–7.
- Valenzuela MJ, Sachdev P. Brain reserve and dementia: a systematic review. Psychol Med. 2006;36(4):441–54. doi:10.1017/ S0033291705006264.
- Kroger E, Andel R, Lindsay J, Benounissa Z, Verreault R, Laurin D. Is complexity of work associated with risk of dementia? The Canadian Study of Health and Aging. Am J Epidemiol. 2008;167(7):820–30.
- Potter GG, Helms MJ, Plassman BL. Associations of job demands and intelligence with cognitive performance among men in late life. Neurology. 2008;70(19 Pt 2):1803–8.
- Wilson RS, Bennett DA, Bienias JL, Aggarwal NT, de Leon CFM, Morris MC, et al. Cognitive activity and incident AD in a population-based sample of older persons. Neurology. 2002;59(12):1910–4.
- Boyle PA, Buchman AS, Wilson RS, Yu L, Schneider JA, Bennett DA. Effect of purpose in life on the relation between Alzheimer disease pathologic changes on cognitive function in advanced age. Arch Gen Psychiatry. 2012;69(5):499–505. doi:10. 1001/archgenpsychiatry.2011.1487.
- Valenzuela MJ, Sachdev P, Wen W, Chen X, Brodaty H. Lifespan mental activity predicts diminished rate of hippocampal atrophy. PLoS One. 2008;3(7):e2598. doi:10.1371/journal.pone. 0002598.
- 14. Gates NJ, Valenzuela M, Sachdev PS, Singh NA, Baune BT, Brodaty H, et al. Study of Mental Activity and Regular Training (SMART) in at risk individuals: a randomised double blind, sham controlled, longitudinal trial. BMC Geriatr. 2011;11:19. doi:10. 1186/1471-2318-11-19.
- Sitzer DI, Twamley EW, Jeste DV. Cognitive training in Alzheimer's disease: a meta-analysis of the literature. Acta Psychiatr Scand. 2006;114(2):75–90. doi:10.1111/j.1600-0447.2006.00789. x.
- Unverzagt FW, Guey LT, Jones RN, Marsiske M, King JW, Wadley VG, et al. ACTIVE cognitive training and rates of incident dementia. J Int Neuropsychol Soc. 2012;18(4):669–77. doi:10.1017/S1355617711001470.
- 17. Coe NB, von Gaudecker HM, Lindeboom M, Maurer J. The effect of retirement on cognitive functioning. Health Econ. 2012;21(8):913–27. doi:10.1002/hec.1771.
- Brookmeyer R, Gray S, Kawas C. Projections of Alzheimer's disease in the United States and the public health impact of delaying disease onset. Am J Public Health. 1998;88(9):1337–42.
- Bonsang E, Adam S, Perelman S. Does retirement affect cognitive functioning? J Health Econ. 2012;31(3):490–501. doi:10. 1016/j.jhealeco.2012.03.005.
- Lupton MK, Stahl D, Archer N, Foy C, Poppe M, Lovestone S, et al. Education, occupation and retirement age effects on the age of onset of Alzheimer's disease. Int J Geriatr Psychiatry. 2010;25(1):30–6. doi:10.1002/gps.2294.
- Roberts BA, Fuhrer R, Marmot M, Richards M. Does retirement influence cognitive performance? The Whitehall II Study. J Epidemiol Community Health. 2011;65(11):958–63. doi:10.1136/ jech.2010.111849.

- 22. Rohwedder S, Willis RJ. Mental retirement. J Econ Perspect. 2010;24(1):119–38. doi:10.1257/jep.24.1.119.
- Bamia C, Trichopoulou A, Trichopoulos D. Age at retirement and mortality in a general population sample: the Greek EPIC Study. Am J Epidemiol. 2008;167(5):561–9. doi:10.1093/aje/kwm337.
- Hammerman-Rozenberg R, Maaravi Y, Cohen A, Stessman J. Working late: the impact of work after 70 on longevity, health and function. Aging Clin Exp Res. 2005;17(6):508–13.
- 25. Gallo WT, Teng HM, Falba TA, Kasl SV, Krumholz HM, Bradley EH. The impact of late career job loss on myocardial infarction and stroke: a 10 year follow up using the health and retirement survey. Occup Environ Med. 2006;63(10):683–7. doi:10.1136/oem.2006.026823.
- Stern Y. Cognitive reserve in ageing and Alzheimer's disease. Lancet Neurol. 2012;11(11):1006–12. doi:10.1016/S1474-4422(12)70191-6.
- Driscoll I, Troncoso J. Asymptomatic Alzheimer's disease: A prodrome or a state of resilience? Curr Alzheimer Res. 2011;8(4): 330–5.

- Valenzuela M, Sachdev P. Can cognitive exercise prevent the onset of dementia? Systematic review of randomized clinical trials with longitudinal follow-up. Am J Geriatr Psychiatry. 2009;17(3):179–87. doi:10.1097/JGP.0b013e3181953b57.
- Bertrand M, Tzourio C, Alperovitch A. Trends in recognition and treatment of dementia in France. Analysis of the 2004–2010 database of the national health insurance plan. Alzheimer Dis Assoc Disord. 2013;27(3):213–7. doi:10.1097/WAD.0b013e3182695a3b.
- Ramaroson H, Helmer C, Barberger-Gateau P, Letenneur L, Dartigues JF. Prevalence of dementia and Alzheimer's disease among subjects aged 75 years or over: updated results of the PAQUID cohort. Rev Neurol (Paris). 2003;159(4):405–11.
- 31. Matthews FE, Arthur A, Barnes LE, Bond J, Jagger C, Robinson L, Brayne C. Medical Research Council Cognitive Function and Ageing Collaboration. A two-decade comparison of prevalence of dementia in individuals aged 65 years and older from three geographical areas of England: results of the Cognitive Function and Ageing Study I and II. Lancet. 2013;382(9902):1405–12. doi:10.1016/S0140-6736(13)61570-6.