Archives of Gerontology and Geriatrics xxx (2014) xxx–xxx

Contents lists available at ScienceDirect

Archives of Gerontology and Geriatrics

journal homepage: www.elsevier.com/locate/archger

Influence of socio-demographic features and apolipoprotein E epsilon 4 expression on the prevalence of dementia and cognitive impairment in a population of 70–74-year olds: The InveCe.Ab study

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ARTICLE INFO

Article history:
Received 5 June 2014
Received in revised form 14 November 2014
Accepted 18 November 2014
Available online xxx

Keywords:
Dementia
Alzheimer's disease
Risk factors
Prevalence
Cognitive impairment
ApoE-ε4

ABSTRACT

The age-specific prevalence rates of dementia vary widely. Studies focusing on specific age groups are needed to provide reliable estimates for healthcare providers and policy makers.

We estimated the prevalence of dementia, dementia subtypes and cognitive impairment in "InveCe.Ab" (ClinicalTrials.gov, NCT01345110), a single-step multidimensional population-based study of 70–74-year olds living in Abbiategrasso (Milan, Italy). We also looked for associations with socio-demographic factors and the presence of the apolipoprotein E-ε4 allele.

The overall dementia prevalence was 3% (95%CI: 2.1–4.1%) [Alzheimer's disease (AD): 1.2% (95%CI 0.6–1.9%); vascular dementia (VD): 1.4% (95%CI: 0.8–2.2%)]. Being single was found to be a risk factor for vascular dementia; subjects born in southern Italy were shown to be at greater risk both of overall dementia and of vascular dementia. The prevalence of cognitive impairment, with or without subjective cognitive complaints (cognitive impairment, no dementia, CIND) was 7.8% (95%CI: 6.4–9.4%). As regards the CIND subgroups, the prevalence of subjects with subjective cognitive complaints (mild cognitive impairment, MCI) was 5.0% (95%CI 3.9–6.3%), while the prevalence of those without MCI (CIND-other) was 2.8% (95%CI: 1.9–3.8). The males had a higher risk of MCI and CIND-other; the older subjects were more likely to have MCI, and those born in north-eastern Italy to have CIND-other. The prevalence of AD was higher among the apolipoprotein E-ε4 carriers.

Our data highlight the importance of dementia and cognitive impairment in the transitional period from adulthood to old age, and reveal the presence of different associations with socio-demographic and genetic factors.

Abbreviations: MCI, mild cognitive impairment; CIND, cognitive impairment, no dementia; ApoE-ε4, apolipoprotein E- ε4; AD, Alzheimer's disease; VD, vascular dementia; DLB, dementia with Lewy bodies; FTD, frontotemporal dementia; DSM-IV-TR, Italian version of the Diagnostic and Statistical Manual of Mental Disorders IV; NINCDS/ADRDA, National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association; NINDS-AIREN, National Institute of Neurological Disorders and Stroke and Association Internationale pour la Recherché et l'Enseignement en Neurosciences; MMSE, mini-mental state examination; ISTAT, Italian National Institute of Statistics; MD, mixed dementia; PDD, Parkinson's disease dementia; Crude Prev., crude prevalence; Adj. Prev., adjusted prevalence; 95%CI, 95% confidence interval; OR, odds ratio.

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http://dx.doi.org/10.1016/j.archger.2014.11.006

Please cite this article in press as: Guaita, A., et al., Influence of socio-demographic features and apolipoprotein E epsilon 4 expression on the prevalence of dementia and cognitive impairment in a population of 70–74-year olds: The InveCe.Ab study. Arch. Gerontol. Geriatr. (2014), http://dx.doi.org/10.1016/j.archger.2014.11.006

1. Introduction

Dementia and cognitive impairment are among the leading causes of disability and dependence in the elderly and they constitute a major economic burden for public health systems (Gustavsson et al., 2011; Wimo, Jönsson, Bond, Prince, & Winblad, 2013).

In an aging population, reliable estimates of the prevalence of dementia and cognitive impairment are needed in order to guarantee efficient healthcare and social welfare policymaking, planning and resource allocation. Furthermore, identifying modifiable risk factors and diagnosing patients earlier could lead to more efficient screening and care and therefore lower health costs (Prince et al., 2013).

The prevalence of dementia worldwide shows slight variations, generally ranging between 5% and 7% (e.g. 5.57% in Asia and 6.92% in Western Europe) (Prince et al., 2013), which is in line with the 5.9–6.5% reported in the most of Italian prevalence studies in the over 60s (De Ronchi et al., 2005) and over 65s (Ravaglia et al., 2002; Tognoni et al., 2005). However, comparison of age-specific rates reported in the literature reveals marked differences between Italy and other countries. In Western Europe the prevalence of dementia in 70–74-year-olds has been found to be 4.3% (Prince et al., 2013), but in most of the Italian studies it was considerably lower: 1.4% (Tognoni et al., 2005), 1.6% (Cristina et al., 2001) and 1.8% (Ravaglia et al., 2002).

Cognitive impairment has been variously defined, but the most commonly used definitions are "cognitive impairment, no dementia" (CIND) and "mild cognitive impairment" (MCI). The broad definition of CIND includes demonstration of an objective cognitive impairment and excludes dementia (Chertkow et al., 2008), while MCI is defined by the presence of a subjective cognitive complaint and an objective demonstration of cognitive deficit in the absence of dementia and of dependence in activities of daily living (Petersen, 2004). Thus, providing the term is correctly applied, MCI can be considered a subgroup of CIND.

The prevalence of cognitive impairment, either CIND or MCI, reported in epidemiological studies varies considerably: in one systematic review, the prevalence of MCI ranged between 3% and 42% while that of CIND ranged between 5.1% and 35.9% (Ward et al., 2012). In Italian studies the prevalence of MCI in the over sixties ranged between 3.2% and 7.7%, and in 70–74-year-olds between 0% and 5.6% (Ravaglia et al., 2008; Solfrizzi et al., 2004); CIND had a prevalence of between 5.1% and 9.5% (De Ronchi et al., 2005; Di Carlo et al., 2007), with a rate of 4.2% recorded in 70–74-year olds (Di Carlo et al., 2007).

This heterogeneity in prevalence estimates is probably due to the use of different diagnostic tools and criteria, both for dementia and for cognitive impairment, different study designs and small sample sizes.

Although these limitations could be overcome by large multicentre studies, such studies can be difficult to implement for various reasons: difficulties conducting surveys across different centers, the risk of introducing diagnostic and information biases, and different prevalence rates between geographical areas. Single-center population studies would avoid these issues, providing the population studied was, as far as possible, homogeneous for age and residence (Launer, 2011; Misiak, Cialkowska-Kuzminska, Frydecka, Chladzinska-Kiejna, & Kiejna, 2013).

Aging is one of the main factors influencing prevalence estimates of dementia and MCI (DeCarli, 2003). Studies in the elderly generally focus on the over 65s, although single-age cohort studies often concentrate on70-year-olds (Persson, 1980; Sacuiu et al., 2010; Takata et al., 2012). Since people are now living longer and enjoying better health, with declining rates of disability, it has recently been suggested that the threshold age for studies in the elderly should be raised to 70–74 years (Waidmann & Liu, 2000). This five-year span may be considered a "transitional age" between late adulthood and old age, and a particularly useful period for the identification of risk factors for late-onset cognitive impairment and dementia (Andrieu et al., 2011).

Indeed, with reference to the life course conceptual model of epidemiology, these five years, while not "critical", could constitute a "sensitive" period for cognitive changes (Ben-Shlomo & Kuh, 2002). By profiling the status of 70–74-year olds, it could prove possible to identify factors potentially influencing successful or unsuccessful cognitive aging as people approach their eighties. Many risk factors for dementia and cognitive impairment that have been identified in this age range (such as education) indicate the need for preventive interventions at an earlier age. However, from the perspective of age-specific preventive intervention in dementia, they also provide pointers for planning interventions, mainly geared at enhancing protective factors like social activities or diet, that specifically target this age group (Fratiglioni, et al., 2004).

The influence of socio-demographic factors on dementia and cognitive impairment has been investigated in several studies, but the results are not univocal, and in some cases are even conflicting. This is true of data on widely studied factors such as education and occupation (Andel et al., 2007; Bonaiuto et al., 1995; Bosma et al., 2003; Helmer et al., 2001; Karp et al., 2004; Kröger et al., 2008; Marengoni, Fratiglioni, Bandinelli, & Ferrucci, 2011; Meng & D'Arcy, 2012; Ravaglia et al., 2002) and gender (Andersen et al., 1999; Katz et al., 2012). Interpreting these results can be difficult given that these factors may act differently at different ages (Schoenmaker & Van Gool, 2004). In previous studies, a gender difference in the prevalence both of dementia (Katz et al., 2012) and of cognitive impairment (Petersen et al., 2010; Ravaglia et al., 2002; Sharp & Gatz, 2011) was found only in the oldest subjects investigated. Due to the rapid technological advances of recent decades, it is possible that members of the youngest and oldest sections of the elderly population, despite having done the same job, had very different working experiences in terms of physical effort and mental engagement – two aspects that can influence the risk of developing dementia and cognitive impairment in old age (Andel et al., 2005, 2007; Bosma et al., 2003; Kröger et al., 2008; Smyth et al., 2004). Thus, consideration of a narrow age band, despite the unavoidable limitations of this approach, may allow better analysis (in the age class considered at least) of the association of these variables with dementia and cognitive impairment. Other socio-demographic factors, such as marital status (Håkansson et al., 2009) and place of birth, have rarely been considered. The latter could be a particularly interesting aspect to study in Italy, given the large number of people who migrated from all over Italy to the north-western part of the country after the Second World War. Several studies have highlighted a role, in dementia, of genetic risk factors; one of these is the presence of the apolipoprotein E-ε4(ApoE- ε4) allele (Sadigh-Eteghad, Talebi, & Farhoudi, 2012; Saunders et al., 1993). A relationship exists between ApoE and age: indeed, because the ApoE- ε4 allele is associated with increased mortality, coronary disease, atherosclerosis, the frequency of ApoE-ε4 homozygosity has been shown to decline with increasing age (McKay et al., 2011).

The heterogeneity in prevalence estimates of dementia and cognitive impairment is also due to the large number of studies that used a two-step methodology i.e. that adopted a screening test of global cognition to select subjects suitable for further in-depth neuropsychological and medical evaluation. The literature contains powerful arguments for one-step over two-step designs (McNamee, 2003; Prince, 2003). There is currently a need for well-designed, single-step, multidimensional, population-based studies involving homogeneous cohorts of people in order to provide

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unbiased estimates of dementia prevalence and a description of the factors influencing cognitive aging.

To address this need, the InveCe.Ab study, a two-part population-based study, was planned and conducted in Abbiategrasso, a northern Italian town on the outskirts of Milan (Guaita et al., 2013). The first part of the InveCe.Ab study was a cross-sectional study and the second was a prospective study focusing on the respondents in the previous cross-sectional study. The present paper concerns the first part.

The primary aim of the present work was to estimate the overall prevalence of dementia in an age-specific cohort of people living in Abbiategrasso, considering different dementia subtypes [Alzheimer's dementia (AD), vascular dementia (VD), dementia with Lewy bodies (DLB) and frontotemporal dementia (FTD)] as well as the rate of cognitive impairment and the influence of several potential risk factors (socio-demographic features). A secondary aim was to evaluate the association of ApoE-ε4 allele expression with the presence of dementia, its subtypes and cognitive impairment.

2. Materials and methods

In the present paper only data from the first part of the InveCe.Ab study (the cross-sectional phase) were evaluated, even though the follow-up was ongoing. The population eligible for the cross-sectional study consisted of all 1773 Abbiategrasso residents born between 1935 and 1939 and aged 70–74 years on the prevalence day (November 1st, 2009). Of these, 1644 were available for evaluation.

In this first part of InveCe.Ab, a multidimensional assessment (social, medical and neuropsychological) of all the participants was performed. However, as better specified in the following sections, only some of the variables collected were used for the purposes of the present work.

As already specified (Guaita et al., 2013), the InveCe.Ab study protocol was approved by the Ethics Committee of the University of Pavia. All the participants gave their written informed consent to the use of their personal data and agreed to provide a blood sample for biological analyses and DNA extraction. For participants with moderate or severe cognitive impairment, written informed consent was obtained from legal guardians, relatives or caregivers.

For the comparison between the participants (respondents) and those who refused to participate in the study (non-respondents), we used aggregated data collected by the local health authority from family practitioners and information obtained from the municipal registry office. These comparisons concerned gender, age, level of education, area of birth, marital status, dependence in activities of daily living and the presence of dementia.

2.1. Endpoints and diagnostic criteria

The primary endpoint of the study was overall dementia. The presence of dementia was ascertained by a geriatrician after clinical evaluation and multidimensional assessment using the Italian version of the Diagnostic and Statistical Manual of Mental Disorders IV (DSM IV-TR) (Andreoli, Cassano, & Rossi, 2007). Different dementia subtypes were diagnosed as follows:

- AD, using the NINCDS/ADRDA criteria for probable, possible and definite diagnoses (McKhann et al., 1984), and performing the diagnostic workup according to the European Federation of Neurological Societies guidelines (Hort et al., 2010);
- VD, applying the NINDS-AIREN criteria (Wiederkehr, Simard, Fortin, & van Reekum, 2008);
- DLB, using the criteria of the third report of the DLB Consortium (McKeith et al., 2005);
- FTD, applying the clinical criteria of the Manchester Royal Infirmary group, revised and confirmed by Rosen and co-workers (Rosen et al., 2002).

The presence of cognitive impairment was established on the basis of neuropsychological and clinical examinations as described elsewhere (Guaita et al., 2013). Briefly, participants were administered nine tests covering five domains (memory, attention, language, executive and visuospatial function), the MMSE and the Clock Drawing Test. A cognitive test score was considered "abnormal" when it fell under the threshold value of normality derived from Italian normative studies (Spinnler & Tognoni, 1987). For each test, regression analysis was used to define, using non-parametric techniques, the cut-off point of normality (i.e. the value corresponding to the level that, with a known risk of error (<5%), separates the bottom 5% of the population ranked by performance). This was done correcting for age, education and, when appropriate, gender. Scores below the cut-off level on two or more tests were taken as a criterion for the definition of CIND (Chertkow et al., 2008).

A few individuals were considered cognitively impaired in the presence of just one abnormal result, when there was agreement between the doctor and the neuropsychologist. In cases of clinical instability and in the presence of serious language disorders no definite cognitive diagnosis was applied. People with major depression or psychosis were defined as affected by these conditions and remained in the study. To define the cognitive status of people with hearing and visual problems, only the tests that did not specifically involve the impaired function were considered. Among the subjects meeting the criteria for CIND, Petersen's criteria (Petersen, 2004) for MCI were applied to identify those with: objective cognitive impairment, self or informant reports of cognitive complaints, no dependence in basic and instrumental activities of daily living, no dementia. Finally, three diagnostic endpoints were computed based on these two definitions: "CIND" (with and without MCI), "CIND-other" (CIND without MCI), and "MCI". This approach has already been applied in other research (Brainerd et al., 2013).

2.2. Socio-demographic factors and apolipoprotein E-ε4

The socio demographic factors considered in this study were collected from municipal registry and from a social questionnaire administered by trained interviewers. The socio-demographic factors considered in this paper were gender (females vs males), birth cohort (1936, 1937, 1938, 1939 vs 1935) and area of birth in Italy [North East, center, South, islands vs North West, as defined according to the Italian National Institute of Statistics (ISTAT) classification], marital status (cohabiting, separated/divorced, widowed, single vs married), primary lifetime occupation (considering a series of categories–housewife, blue collar work, white collar work–adapted from the nine classes established by ISTAT) and years of education (≤5 years vs >5 years). Since basic education for this age cohort corresponds to primary schooling (i.e. when they were of school age the duration of compulsory schooling was five years), it was decided to compare people who had received primary schooling or less (up to five years of education) with those who had received a longer education (six years or more).

After a blood sample, the DNA of each participant was extracted and analysed using real-time PCR (Applied Biosystems) to ascertain the presence/absence of the ApoE-ε4 allele.

2.3. Statistical analysis

Subjects in whom a diagnosis could not be established were excluded from the prevalence analysis.

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Qualitative variables were expressed as percentages and quantitative variables as mean values with standard deviation. Differences in gender, age, level of education and area of birth between respondents and non-respondents were described using Pearson's chi-square test and an unpaired *t* test.

The crude prevalence with exact 95% confidence interval (95%CI) was estimated for the primary endpoint as well as the secondary endpoints. Prevalence was also estimated separately by socio-demographic characteristics. The crude association between these factors and outcomes was evaluated using Pearson's chi-square test or Fisher's exact test. The mutually adjusted prevalence of each endpoint for each socio-demographic factor was estimated by logistic regression and the effect of these factors was evaluated using the likelihood ratio test. The independent role of socio-demographic characteristics on outcomes was also verified, again by logistic regression analysis (Hosmer, et al., 2013).

In all cases a *p*-value less than 0.05 was considered significant. Statistical analyses were performed using Stata 12 (StataCorp. 2011. Stata Statistical Software: Release 12. College Station, TX: StataCorp, LP).

3. Results

3.1. The InveCe.Ab study participants

A total of 1321 subjects agreed to take part in the study, which corresponded to a response rate of 80.35%. The subjects who refused to participate, compared with the participants, were more often women (66.6% vs 54.0%; $p < 0.001$), but the two groups were similar in terms of mean age (71.68 ±1.43 years vs 71.69 ± 1.45 years), level of education (6.48 ± 2.78 years vs 6.75 ± 3.35 years), and birth area (as ascertained from registry office records). In 78.1% of the non-respondents, pooled data about functional, physical and cognitive status, collected by the local health authority from family practitioners, was available; in the other 21.9% this information was not available. Compared with the participants, the non-participating subjects showed similar rates of dementia (2.8% vs 3%) and of dependence in activities of daily living (3.6% vs 4.3%).

The respondents were mainly females and born in 1938–1939 (Table 1). Most of the respondents were born in north-western Italy, while a small number came from other parts of Italy; only ten were born abroad, and nine of these came from an Italian family (Table 1). Two-thirds (66.1%) of the respondents were married and a quarter widowed (24.6%). Almost 60% of the respondents had received five years of education or less. Almost all were living at home; only twenty-one (1.6%) were living in an institution.

Table 1
Socio-demographic features of the InveCe.Ab study participants.

		n	%
Gender	Males	607	45.9
	Females	714	54.1
Birth cohort	1935	236	17.8
	1936	219	16.6
	1937	264	20.0
	1938	305	23.1
	1939	297	22.5
Area of birth	North-western Italy	965	73.1
	North-eastern Italy	150	11.3
	Central Italy	20	1.5
	Southern Italy	109	8.3
	The Italian islands	66	5.0
	Foreign country	10	0.8
Marital status	Married	872	66.1
	Cohabiting	13	1.0
	Separated/Divorced	29	2.2
	Widowed	325	24.6
	Single	80	6.1
Primary lifetime occupation	Blue collar workers	666	50.6
	White collar workers	459	34.9
	Housewife	191	14.5
Years of education	≤5 years	754	57.2
	>5 years	565	42.8

3.2. The prevalence of dementia and cognitive impairment

Thirty-nine subjects were diagnosed with dementia, which therefore had a crude prevalence of 3.0% (95%CI: 2.1–4.1%). In particular, of the subjects with dementia, 15 (38.5%) were diagnosed with AD, 18 (46.1%) with VD, two (5.1%) with mixed dementia (MD) and four (10.3%) with other types of dementia [Parkinson's disease dementia (PDD), post-traumatic dementia, alcoholic dementia and advanced psychosis]. Mixed and other dementias are not outcomes of interest in the present study. No subject received a diagnosis of DLB or FTD. We therefore recorded the following prevalence rates for the different dementia subtypes: 1.2% (0.6–1.9%) for AD, 1.4% (95%CI: 0.8–2.2%) for VD, 0.2% (95%CI: 0.0–0.6%) for MD, and 0.1% (0.0–0.4%) for PDD.

One hundred and one subjects (7.8% [95%CI: 6.4–9.4%]) were classified as cognitively impaired (CIND with or without MCI). Of these subjects, 65 (5.0% [95%CI: 3.9–6.3%]) were affected by MCI and 36 (2.8% [95%CI: 1.9–3.8%]) by CIND-other (CIND without MCI).

3.3. Dementia prevalence and socio-demographic features

The crude prevalence of overall dementia was found to be significantly higher in the subjects who had received up to five years of education and in those who had been blue collar workers, while the slightly higher prevalence found in the males was not significant (Table 2).

Significantly higher overall dementia prevalence was also found in subjects born in southern Italy, while the lowest prevalence was found in those from the North East of the country. After adjustment, no socio-demographic feature was associated with overall dementia (Table 2).

A significantly higher crude prevalence of AD was calculated in people born in central Italy and in the islands, while no statistically significant difference in AD prevalence was found for education or gender (Table 2). After adjustment, no association between socio-demographic factors and AD was found.

The crude prevalence of VD was significantly higher both in people born in the South and in the blue collar workers, but these results were not confirmed after adjustment (Table 2). Again, there was no significant difference for education or gender (Table 2).

Finally, birth cohort and marital status were not found to influence the prevalence of any subtype of dementia.

3.4. Prevalence of MCI, CIND and socio-demographic features

More males than females were affected by cognitive impairment, whether considering CIND, MCI or CIND-other. After adjustment these associations were confirmed (Table 3). Although there emerged a higher crude prevalence of overall cognitive impairment and MCI among those born in 1935, of CIND-other among those born in north-eastern Italy, and of MCI among the blue collar workers, these associations were no longer significant after adjustment.

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Table 2
Crude prevalence and mutually adjusted prevalence for overall dementia, Alzheimer's disease, vascular dementia by socio-demographic features. In brackets 95% Confidence Interval was reported.

	Overall dementia [*n* 39 = 3.0% (2.1–4.1)]			Alzheimer's Disease [*n* 15 = 1.2% (0.6–1.9)]			Vascular Dementia [*n* 18 = 1.4% (0.8–2.2)]		
	n	Crude Prev.	Adj. Prev.	*n*	Crude Prev.	Adj. Prev.	*n*	Crude Prev.	Adj. Prev.
Gender		$p = 0.733$[a]	$p = 0.792$[b]		$p = 0.130$[a]	$p = 0.186$[b]		$p = 0.196$[a]	$p = 0.193$[b]
Males	19	3.2 (1.9–4.9)	2.3 (1.3–3.9)	4	0.7 (0.2–1.7)	0.4 (0.1–1.2)	11	1.8 (0.9–3.3)	1.0 (0.4–2.4)
Females	20	2.9 (1.8–4.4)	2.0 (1.2–3.5)	11	1.6 (0.8–2.8)	0.9 (0.3–2.1)	7	1.0 (0.4–2.0)	0.5 (0.2–1.3)
Birth cohort		$p = 0.788$[a]	$p > 0.900$[b]		$p = 0.096$[a]	$p > 0.900$[b]		$p = 0.423$[a]	$p > 0.900$[b]
1935	7	3.0 (1.2–6.1)	1.8 (0.7–4.2)	1	0.4 (0.0–2.4)	0.3 (0.0–2.2)	6	2.6 (1.0–5.5)	1.1 (0.4–3.2)
1936	8	3.8 (1.7–7.4)	2.9 (1.4–6.0)	5	2.4 (0.8–5.5)	1.6 (0.6–4.3)	2	1.0 (0.1–3.4)	0.6 (0.1–2.6)
1937	8	3.2 (1.3–5.9)	2.5 (1.2–5.0)	2	0.8 (0.1–2.7)	0.6 (0.1–2.3)	2	0.8 (0.1–2.7)	0.5 (0.1–2.1)
1938	6	2.0 (0.7–4.3)	1.4 (0.6–3.2)	1	0.3 (0.0–1.8)	0.2 (0.0–1.6)	5	1.7 (0.5–3.8)	0.9 (0.3–2.5)
1939	10	3.4 (1.6–6.2)	2.8 (1.4–5.3)	6	2.0 (0.8–4.4)	1.5 (0.6–3.8)	3	1.0 (0.2–3.0)	0.6 (0.2–2.2)
Area of birth		**p = 0.001**[a]	$p > 0.900$[b]		**p = 0.017**[a]	$p = 0.624$[b]		**p = 0.020**[a]	$p > 0.900$[b]
North-western Italy	22	2.3 (1.5–3.5)	2.2 (1.4–3.4)	9	0.9 (0.4–1.8)	0.6 (0.2–1.4)	10	1.1 (0.5–1.9)	0.6 (0.3–1.5)
North-eastern Italy	2	1.4 (0.2–4.9)	1.1 (0.3–4.6)	0	0.0 (0.0–2.5)	–	1	0.7 (0.0–3.8)	0.4 (0.1–3.2)
Central Italy	1	5.0 (0.1–24.9)	4.9 (0.7–29.0)	1	5.0 (0.1–24.9)	3.7 (0.4–26.1)	0	0.0 (0.0–16.8)	–
Southern Italy	10	9.4 (4.6–16.7)	2.2(1.4–3.4)	2	1.9 (0.2–6.6)	0.8 (0.2–4.2)	6	5.7 (2.1–11.9)	3.7 (1.4–9.5)
Italian islands	4	6.3 (1.7–15.2)	5.4 (2.1–15.4)	3	4.7 (1.0–13.1)	2.4 (0.6–9.0)	1	1.6 (0.0–8.4)	1.1 (0.1–8.3)
Marital status		$p = 0.348$[a]	$p > 0.900$[b]		$p = 0.459$[a]	$p > 0.900$[b]		$p = 0.093$[a]	$p = 0.876$[b]
Married	23	2.7 (1.7–4.0)	2.0 (1.2–3.2)	9	1.1 (0.5–2.0)	0.6 (0.2–1.4)	9	1.1 (0.5–2.0)	0.6 (0.3–1.4)
Cohabiting	0	0.0 (0.0–26.5)	–	0	0.0 (0.0–26.5)	–	0	0.0 (0.0–26.5)	–
Separated/Divorced	1	3.4 (0.1–17.8)	1.7 (0.2–12.4)	1	3.4 (0.1–17.8)	1.4 (0.1–11.4)	0	0.0 (0.0–11.9)	–
Widowed	10	3.2 (1.5–5.7)	2.3 (1.1–4.6)	4	1.3 (0.3–3.2)	0.5 (0.1–1.9)	5	1.6 (0.5–3.6)	0.8 (0.3–2.4)
Single	5	6.6 (2.2–14.7)	4.9 (1.8–12.9)	1	1.3 (0.0–7.1)	0.8 (0.1–6.3)	4	5.3 (1.5–12.9)	3.3 (0.1–10.7)
Primary lifetime occupation[c]		**p = 0.037**[a]	$p > 0.900$[b]		$p = 0.413$[a]	$p > 0.900$[b]		**p = 0.030**[a]	$p > 0.900$[b]
Blue collar workers	27	4.1 (2.7–5.9)	2.4 (1.5–4.0)	10	1.5 (0.7–2.8)	0.6 (0.2–1.7)	14	2.1 (1.2–3.6)	1.4 (0.7–2.8)
White collar workers	8	1.8 (0.8–3.4)	1.7 (0.8–3.7)	3	0.7 (0.1–1.9)	0.5 (0.1–1.9)	2	0.4 (0.1–1.6)	0.3 (0.1–1.6)
Housewife	3	1.6 (0.3–4.6)	2.4 (1.5–4.0)	2	1.1 (0.1–3.8)	0.6 (0.2–1.7)	1	0.5 (0.0–2.9)	0.4 (0.1–2.9)
Years of education		**p = 0.026**[a]	$p = 0.196$[b]		$p = 0.070$[a]	$p = 0.295$[b]		$p = 0.188$[a]	$p = 0.857$[b]
>5 years	10	1.8 (0.9–3.3)	1.5 (0.7–3.1)	3	0.5 (0.1–1.6)	0.4 (0.1–1.4)	5	0.9 (0.3–21.1)	0.6 (0.2–1.8)
≤5 years	29	3.9 (2.6–5.6)	2.8 (1.7–4.5)	12	1.6 (0.8–2.8)	0.8 (0.3–2.1)	13	1.8 (0.9–3.0)	0.7 (0.3–1.8)

[a] *p*-value from Pearson's chi-square test/Fisher's exact test when appropriate.
[b] *p*-value from the Likelihood Ratio test; bold text indicates a significant *p*-value (less than 0.05).
[c] One subject with no definite occupation.

3.5. Prevalence of dementia and cognitive impairment and apolipoprotein E-ε4

The crude prevalence of overall dementia did not differ between ApoE-ε4 carriers and non-carriers, while a significantly higher prevalence of AD was found in ApoE-ε4 carriers than in ApoE-ε4 non-carriers (Table 4). The prevalence of VD, like that of overall dementia, did not differ between ApoE-ε4 carriers and non-carriers (Table 4). After adjustment for socio-demographic characteristics, the results still failed to reach significance both for overall dementia and for VD, while the pattern for AD was confirmed (Table 4).

Finally, the adjusted prevalence did not differ significantly between ApoE-ε4 carriers and non-carriers, either for MCI (5.9% [3.5–9.6%] vs 3.8% [2.7–5.2%], $p = 0.142$) or for CIND-other (1.8% [0.8–4.2%] vs 2.0% [1.3–3.2%], $p = 0.775$).

3.6. Association of dementia and cognitive impairment with risk factors

On multivariate analysis, overall dementia was significantly associated only with area of birth (Table 5): subjects born in southern Italy had a higher risk of dementia than those born in the north-western part of the country, regardless of other factors. All that emerged for AD was a borderline significant effect of being born in the Italian islands (Table 5).

The risk of VD, like that of overall dementia was higher in subjects born in southern Italy. Furthermore, VD also showed an association with marital status, with the risk found to be higher in single than in married people (Table 5).

Gender was associated with cognitive impairment (Table 6), with the females showing a significantly lower risk of CIND, MCI and CIND-other.

Age was also associated with cognitive impairment. Indeed, younger individuals showed a significantly lower risk of MCI and CIND.

Moreover, the risk of CIND-other was found to be about three and a half times greater in subjects born in north-eastern Italy than in those born in the north-western part of the country.

No association was found between marital status and cognitive impairment.

Years of education and occupation not found to be associated with any of the endpoints (Tables 5 and 6).

4. Discussion

The main findings of this study can be summarized in the following points:

- The study population showed a 3% prevalence of dementia;
- We recorded prevalence rates of 1.2% for AD and 1.4% for VD;
- Single people were more likely than married ones to be affected by VD;
- The prevalence rates of CIND, MCI and CIND-other were greater in the men than in the women;
- Gender, birth cohort, duration of education and main lifetime occupation were not found to be associated with overall dementia;
- being born in southern Italy, as opposed to the North West, was associated with higher prevalence rates of overall dementia and VD;

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Table 3
Crude prevalence and mutually adjusted prevalence reported separately for CIND (with or without MCI), MCI and CIND-other (CIND without MCI) by socio-demographic features. In brackets 95% Confidence Interval was reported.

	CIND [*n* 101 = 7.8% (6.4–9.4)]			MCI [*n* 65 = 5.0% (3.9–6.3)]			CIND–other [*n* 36 = 2.8% (1.9–3.8)]		
	n	Crude Prev.	Adj. Prev	*n*	Crude Prev.	Adj. Prev	*n*	Crude Prev.	Adj. Prev.
Gender		**p < 0.001**[a]	**p = 0.0004**[b]		**p = 0.002**[a]	**p = 0.006**[b]		**p = 0.011**[a]	**p = 0.048**[b]
Males	66	11.4 (8.9–14.3)	10.6 (8.0–14.0)	42	7.3 (5.3–9.7)	6.5 (4.5–9.4)	24	4.1 (2.7–6.1)	3.2 (1.9–5.4)
Females	35	5.1 (3.6–7.1)	4.6 (3.2–6.6)	23	3.4 (2.2–5.0)	2.9 (1.8–4.5)	12	1.8 (0.9–3.1)	1.5 (0.8–2.7)
Birth cohort		**p = 0.017**[a]	p > 0.900[b]		**p = 0.018**[a]	p > 0.900[b]		p = 0.819[a]	p > 0.900[b]
1935	29	12.8 (8.8–17.9)	11.0 (7.9–15.0)	21	9.3 (5.8–13.9)	7.6 (5.1–11.1)	8	3.5 (1.5–6.9)	2.7 (1.4–5.1)
1936	19	9.4 (5.8–14.3)	11.0 (7.9–15.0)	12	5.9 (3.1–10.1)	7.6 (5.1–11.1)	7	3.5 (1.4–7.0)	2.7 (1.4–5.1)
1937	12	4.7 (2.5–8.1)	4.1 (2.3–7.3)	7	2.8 (1.1–5.6)	2.3 (1.1–4.5)	5	2.0 (0.6–4.6)	1.6 (0.6–3.9)
1938	22	7.4 (4.7–11.0)	6.5 (4.2–9.9)	13	4.4 (2.4–7.4)	3.6 (2.3–6.3)	9	3.0 (1.4–5.7)	2.4 (1.2–4.9)
1939	19	6.7 (4.1–10.3)	5.3 (3.3–8.5)	12	4.2 (2.2–7.3)	3.4 (1.9–6.1)	7	2.5 (1.0–5.0)	1.7 (0.7–3.9)
Area of birth		p = 0.099[a]	p > 0.900[b]		p = 0.116[a]	p = 0.195[b]		**p = 0.030**[a]	p > 0.900[b]
North-western Italy	68	7.3 (5.7–9.2)	6.5 (5.0–8.3)	46	4.9 (3.6–6.5)	4.2 (3.1–5.8)	22	2.4 (1.5–3.6)	1.9 (1.2–3.1)
North-eastern Italy	20	13.9 (8.7–20.6)	11.9 (7.5–18.2)	10	6.9 (3.4–12.4)	5.1 (2.6–9.7)	10	6.9 (3.4–12.4)	6.4 (3.3–12.0)
Central Italy	1	5.3 (0.1–26.0)	3.7 (0.5–22.8)	1	5.3 (0.1–26.0)	3.5 (0.5–22.2)	0	0.0 (0.0–17.6)	–
Southern Italy	9	9.4 (4.4–17.1)	8.1 (4.1–15.3)	8	8.3 (3.7–15.8)	6.5 (3.1–13.0)	1	1.0 (0.0–5.7)	1.0 (0.1–6.8)
Italian islands	3	5.0 (1.0–13.9)	4.1 (1.3–12.4)	0	0.0 (0.0–6.0)	–	3	5.0 (1.0–13.9)	4.6 (1.5–13.9)
Marital status		p = 0.639[a]	p > 0.900[b]		p = 0.544[a]	p > 0.900[b]		p = 0.773[a]	p > 0.900[b]
Married	70	8.3 (6.6–10.4)	6.7 (5.1–8.7)	46	5.5 (4.0–7.2)	4.3 (3.1–6.1)	24	2.9 (1.8–4.2)	1.9 (1.2–3.2)
Cohabiting	1	8.3 (0.2–38.5)	7.5 (1.0–39.4)	1	8.3 (0.2–38.5)	8.4 (1.1–42.7)	0	0.0 (0.0–26.5)	–
Separated/Divorced	3	10.7 (2.3–28.2)	8.8 (2.6–25.3)	2	7.1 (0.9–23.5)	5.4 (1.2–20.1)	1	3.6 (0.1–18.3)	2.6 (0.3–17.6)
Widowed	20	6.5 (4.0–9.8)	6.7 (4.2–10.4)	12	3.9 (2.0–6.7)	3.6 (2.0–6.5)	8	2.6 (1.1–5.0)	2.6 (1.3–5.4)
Single	7	9.9 (4.1–19.3)	7.7 (3.6–16.0)	4	5.6 (1.6–13.8)	4.4 (1.6–11.6)	3	4.2 (0.9–11.9)	3.1 (0.9–9.6)
Primary lifetime occupation		p = 0.116[a]	p > 0.900[b]		**p = 0.052**[a]	p > 0.900[b]		p = 0.164[a]	p > 0.900[b]
Blue collar workers	59	9.4 (7.2–11.9)	7.0 (8.3–9.2)	42	6.7 (4.9–8.9)	5.0 (3.6–7.0)	17	2.7 (1.6–4.3)	1.7 (0.9–2.9)
White collar workers	33	7.4 (5.1–10.2)	6.5 (4.4–9.6)	16	3.6 (2.1–5.8)	3.0 (1.7–5.3)	17	3.8 (2.2–6.0)	3.3 (1.8–6.1)
Housewife	9	4.9 (2.2–9.0)	7.0 (5.3–9.2)	7	3.8 (1.5–7.6)	5.0 (3.6–7.0)	2	1.1 (0.1–3.9)	1.7 (0.9–2.9)
Years of education		p = 0.295[a]	p = 0.372[b]		p = 0.172[a]	p = 0.610[b]		p > 0.900[a]	p = 0.487[b]
>5 years	39	7.1 (5.1–9.6)	6.0 (4.2–8.6)	23	4.2 (2.7–6.2)	3.9 (2.4–6.1)	16	2.9 (1.7–4.7)	1.8 (0.9–3.5)
≤5 years	62	8.7 (6.8–11.0)	7.5 (5.6–10.0)	42	5.9 (4.3–7.9)	4.5 (3.1–6.5)	20	2.8 (1.7–4.3)	2.4 (1.4–4.1)

[a] *p*-value from Pearson's chi-square test/Fisher's exact test when appropriate.
[b] *p*-value from the Likelihood Ratio test; bold text indicates a significant *p*-value (less than 0.05).

- Female gender exerted a protective effect for CIND, MCI and CIND-other, while belonging to the younger birth cohorts was a protective factor only for CIND and MCI;
- The prevalence of AD was higher in the ApoE-ε4 carriers than in the non-carriers.

4.1. Dementia

Our findings on the prevalence of dementia are in partial agreement with literature data, but also show some important differences. In most of the previous Italian studies the prevalence of dementia in people aged 70–74 years was under 2% (De Ronchi et al., 2005; Ravaglia et al., 2002; Tognoni et al., 2005), which is lower than the rate reported in our study. However, these previously reported rates were based on small samples and very small numbers (from three to six) of dementia sufferers in the age group of interest. De Ronchi et al. (2005), analysing a larger number of individuals, found a 2.6% prevalence of dementia in the 70–74-year olds, which is closer to the 3% prevalence of our study. The chosen study design is another possible reason for the discrepancy between our study and others. Most of the previous Italian studies used a two-step assessment protocol, which included use of the MMSE as a screening test to identify the population subsequently submitted to comprehensive medical-neuropsychological assessment. The MMSE has well-known limitations as regards its ability to distinguish cognitively healthy individuals from demented subjects (particularly those with mild dementia) (Larner, 2013). Nevertheless the prevalence rate of dementia in our study was still lower than the 4.3% prevalence reported for regions like Western Europe (Prince et al., 2013), which seems to confirm that, compared with people of other nationalities, 70–74-year old Italians have less dementia.

The present study, confirming data from the Conselice study (Ravaglia et al., 2002), showed a higher prevalence of VD but a lower prevalence of AD with respect to previous studies (Tognoni et al., 2005). This may be explained by the diagnostic criteria used: our study and the Conselice study were the only ones to use the NINDS-AIREN criteria for diagnosing VD. In agreement with other studies (Ravaglia et al., 2002), none of the InveCe.Ab subjects with dementia had DLB or FTD.

Our data showed no gender difference for prevalence rate of AD. This finding is line with published data from Italian and European studies in which a considerably higher prevalence of AD was generally reported only in women older than those included in our study (Andersen et al., 1999; De Ronchi et al., 2005; Ravaglia et al., 2002; Rocca et al., 1990; Tognoni et al., 2005).

Table 4
Crude prevalence and mutually adjusted prevalence reported separately for type of dementia by ApoE-ε4. In brackets 95% Confidence Interval was reported.

	n	Crude Prev. (95%CI)	Adj. Prev. (95%CI)
Overall dementia		p = 0.334[a]	p = 0.267[b]
ApoE-ε4 carriers	9	3.8 (1.8–7.1)	2.6 (1.3–5.4)
ApoE-ε4 non carriers	28	2.7 (1.8–3.8)	1.7 (1.0–2.8)
Alzheimer's disease		**p = 0.029**[a]	**p = 0.019**[b]
ApoE-ε4 carriers	6	2.5 (0.9–5.5)	1.4 (0.5–3.9)
ApoE-ε4 non carriers	8	0.8 (0.3–1.5)	0.3 (0.1–0.9)
Vascular dementia		p = 0.752[a]	p = 0.527[b]
ApoE-ε4 carriers	2	0.8 (0.1–3.0)	0.4 (0.1–1.9)
ApoE-ε4 non carriers	15	1.4 (0.8–2.3)	0.6 (0.3–1.4)

[a] *p*-value from Pearson's chi-square test/Fisher's exact test when appropriate.
[b] *p*-value from the Likelihood Ratio test; bold text indicates a significant *p*-value (less than 0.05).

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Table 5
Mutually adjusted association[a] of dementia, Alzheimer's disease and vascular dementia.

	Overall dementia			Alzheimer's disease			Vascular dementia		
	OR	95%CI	*p*-value	OR	95%CI	*p*-value	OR	95%CI	*p*-value
Gender									
Females vs Males	0.90	0.43–1.89	0.78	2.15	0.61–7.55	0.23	0.49	0.15–1.57	0.23
Year of birth									
1936 vs 1935	1.65	0.55–4.95	0.37	5.69	0.64–50.36	0.12	0.50	0.09–2.69	0.42
1937 vs 1935	1.40	0.47–4.18	0.55	1.93	0.17–21.82	0.59	0.46	0.08–2.47	0.37
1938 vs 1935	0.78	0.24–2.52	0.68	0.76	0.05–12.40	0.85	0.88	0.24–3.27	0.85
1939 vs 1935	1.57	0.55–4.49	0.40	5.69	0.66–49.20	0.11	0.58	0.13–2.56	0.47
Area of birth									
North-eastern Italy vs north-western Italy	0.51	0.12–2.24	0.37	–	–	–	0.64	0.08–5.30	0.68
Central Italy vs north-western Italy	2.31	0.28–18.72	0.43	6.34	0.67–60.11	0.11	–	–	–
Southern Italy vs north-western Italy	4.06	1.76–9.34	**0.001**	1.39	0.27–7.22	0.70	6.36	1.98–20.43	**0.002**
Italian islands vs north-western Italy	2.79	0.89–8.70	0.08	3.98	0.96–16.57	0.06	1.88	0.22–15.92	0.56
Marital status									
Cohabiting vs married	–	–	–	–	–	–	–	–	–
Separated/divorced vs married	0.87	0.10–7.18	0.90	2.42	0.25–23.03	0.44	–	–	–
Widowed vs married	1.17	0.51–2.68	0.71	1.05	0.29–3.78	0.94	1.79	0.52–6.19	0.36
Single vs married	2.52	0.81–7.81	0.11	1.31	0.15–11.04	0.80	5.63	1.33–23.80	**0.02**
Primary lifetime occupation									
Housewife vs blue collar workers	0.46	0.13–1.68	0.24	0.58	0.11–3.06	0.52	0.41	0.05–3.60	0.42
White collar workers vs blue collar workers	0.71	0.27–1.91	0.50	0.75	0.15–3.67	0.73	0.28	0.50–1.55	0.14
Years of education									
≤5 years vs >5 years	1.84	0.71–4.73	0.21	2.52	0.53–12.02	0.25	1.12	0.29–4.28	0.87

[a] For each endpoint, the associations were estimated by logistic regression analysis with all the covariates included in the model. Odds ratio with 95% confidence interval and *p*-value are also indicated; bold text indicates a significant *p*-value (less than 0.05).

Age did not influence dementia prevalence and no association between age and dementia was found within the narrow age range considered in our study (70–74 years). All the previous studies that have reported significant age-related differences in dementia prevalence analysed people aged from 65 to over 80 years, usually grouped in five-year age brackets (De Ronchi et al., 2005; Lobo et al., 2000; Prencipe et al., 1996; Ravaglia et al., 2002). Thus, it can be concluded that age-related increases in dementia prevalence can be seen only when comparing subjects of more widely differing ages.

The present study, which focused on a population of 70–74-year olds resident in north-western Italy, is the first to report, after mutual adjustment for socio-demographic factors, an increased risk of dementia, including the vascular subtype, in people born in southern Italy. This result may be related to the higher prevalence of dementia recorded in southern Italian communities (Azzimondi,

Table 6
Mutually adjusted association[a] of CIND (with or without MCI), MCI and CIND-other(CIND without MCI) by socio-demographic features.

	CIND			MCI			CIND-other		
	OR	95%CI	*p*-value	OR	95%CI	*p*-value	OR	95%CI	*p*-value
Gender									
Females vs Males	0.41	0.25–0.69	**0.001**	0.42	0.22–0.79	**0.008**	0.44	0.19–1.01	**0.05**
Year of birth									
1936 vs 1935	0.70	0.37–1.31	0.27	0.65	0.30–1.38	0.26	0.93	0.33–2.66	0.89
1937 vs 1935	0.35	0.17–0.71	**0.004**	0.29	0.12–0.71	**0.007**	0.57	0.18–1.81	0.34
1938 vs 1935	0.56	0.31–1.02	0.06	0.45	0.22–0.94	**0.03**	0.90	0.33–2.42	0.83
1939 vs 1935	0.46	0.25–0.86	**0.01**	0.42	0.20–0.89	**0.02**	0.63	0.22–1.80	0.39
Area of birth									
North-eastern Italy vs north-western Italy	1.95	1.11–3.41	**0.02**	1.23	0.59–2.56	0.59	3.48	1.54–7.84	**0.003**
Central Italy vs north-western Italy	0.56	0.07–4.33	0.58	0.84	0.11–6.59	0.86	–	–	–
Southern Italy vs north-western Italy	1.28	0.60–2.73	0.52	1.57	0.69–3.57	0.28	0.50	0.06–3.85	0.51
Italian Islands vs north-western Italy	0.62	0.19–2.09	0.44	–	–	–	2.47	0.69–8.77	0.16
Marital status									
Cohabiting vs married	1.12	0.14–9.06	0.91	1.87	0.23–15.49	0.56	–	–	–
Separated/divorced vs married	1.33	0.37–4.77	0.66	1.29	0.28–5.92	0.74	1.35	0.17–10.88	0.78
Widowed vs married	1.00	0.57–1.77	0.98	0.82	0.40–1.65	0.57	1.39	0.57–3.40	0.47
Single vs married	1.16	0.50–2.70	0.73	0.95	0.32–2.81	0.93	1.58	0.45–5.58	0.48
Primary lifetime occupation									
Housewife vs blue collar workers	0.81	0.36–1.83	0.62	0.96	0.37–2.46	0.93	0.57	0.12–2.79	0.49
White collar workers vs blue collar workers	0.94	0.55–1.61	0.83	0.59	0.29–1.17	0.13	2.03	0.86–4.76	0.10
Years of education									
≤5 years vs >5 years	1.27	0.76–2.12	0.37	1.24	0.66–2.32	0.50	1.34	0.57–3.12	0.50

[a] For each endpoint, the associations were estimated by logistic regression analysis with all the covariates included in the model. Odds ratio with 95% confidence interval and *p*-value are also indicated; bold text indicates a significant *p*-value (less than 0.05).

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D'Alessandro, Pandolfo, & Feruglio, 1998; Prencipe et al., 1996), to social stress associated with migration from the South to the North of Italy (Editorial staff, 2012), or to both. Moving for economic reasons from small villages to cities, and thus from a rural to an industrial society, they had to deal with a very different way of life, diet and even language (given the prevalent use of dialect by Italians of the generation considered in this study). All these are factors liable to induce the kind of social stress that is associated with migration from other countries (Bhugra & Becker, 2005). Unknown genetic factors as well as social aspects may have influenced the higher prevalence of dementia in the individuals originating from other parts of Italy, but more studies are needed to better understand this poorly recognized aspect.

Our study revealed that being married protects against VD, a finding that supports a previously reported association between married status and better cognitive performances (Moraes, Pinto, Lopes, Litvoc, & Bottino, 2010).

Even though duration of education was not found to be significantly related to dementia, there nevertheless emerged a trend toward higher prevalence rates of AD and VD in subjects with a lower educational level. This result, not reaching significance, is unable to confirm current thinking and some published evidence on the protective effect exerted by higher education on dementia (Meng & D'Arcy, 2012); others, too, have failed to demonstrate such an effect (Sharp & Gatz, 2011). Published Italian studies have shown a significantly higher prevalence of dementia only in very low educated people (i.e. those with 0–3 years of schooling), a finding that could indicate a link with illiteracy rather than with educational level (De Ronchi et al., 1998; Prencipe et al., 1996; Ravaglia et al., 2002).

In agreement with some previous Italian prevalence surveys (De Ronchi et al., 1998; Ravaglia et al., 2002), but not with others (Bonaiuto et al., 1995), our study, after mutual adjustment for socio-demographic factors, revealed no significant relationship between occupation and dementia. Most evidence in the international literature shows that the relationship between dementia and occupation actually depends on education (Fritsch et al., 2007; Helmer et al., 2001; Karp et al., 2004); indeed, autopsy-confirmed AD was not related to occupation (Munoz, Ganapathy, Eliasziw, & Hachinski, 2000). These varying findings with regard to the role of occupation in dementia may be explained by the nature of the occupation, in particular by the risk associated with work-related stress (Andel et al., 2012) and the protection against dementia associated with socially and mentally stimulating work (Karp et al., 2009; Potter, Helms, & Plassman, 2008).

Our finding of a significantly increased prevalence (both crude and adjusted) of AD in the ApoE-ε4 carriers compared with the non-carriers is consistent with published evidence, which identifies the ε4 variant as the largest known genetic risk factor for late-onset familial and sporadic AD (Sadigh-Eteghad et al., 2012; Saunders et al., 1993). Instead, we did not detect any association of the ApoE-ε4 allele with the prevalence of either overall dementia or VD. The question of whether the presence of the ApoE-ε4 allele is a risk factor for VD is still debated in several studies (Baum et al., 2006; Chuang et al., 2010; Davidson et al., 2006; Kim et al., 2008; Lin, Lai, Tai, Lin, & Liu, 2004).

4.2. Cognitive impairment

The prevalence rates of MCI found in our study are lower than those found, for the same age group, by a Mayo Clinic survey (10.3%) (Petersen et al., 2010), even though these authors, like us, defined cognitive impairment using a multidimensional approach, based on neuropsychological scores and clinical evaluation. Conversely, the prevalence of MCI reported in our study is greater than that found in 70–74-year olds in other Italian studies, in which it ranges from 0.0% to 4.0% (Ravaglia et al., 2008; Solfrizzi et al., 2004; Tognoni et al., 2005) and similar to the 5.6% reported by Ravaglia and colleagues (Ravaglia et al., 2008). As already suggested by DeCarli (2003), these contrasting findings are probably due to differences in the methods used to detect cognitive impairment.

The prevalence of CIND, MCI and CIND-other was found to be significantly higher in our male participants. The lower odds ratio (OR) for CIND, MCI and CIND-other in the females remained significant after adjusting for all the other factors in the study. These results are consistent with some previous observations (Ganguli, Dodge, Shen, & DeKosky, 2004; Koivisto et al., 1995; Petersen et al., 2010; Ravaglia et al., 2008) but not with others (De Ronchi et al., 2005; Tognoni et al., 2005). Our finding of a lower prevalence of cognitive impairment in females, despite the absence of a gender difference in dementia prevalence, seemed to confirm the hypothesis formulated by Petersen: "If the higher prevalence [of MCI] in men is confirmed, it may suggest the interplay of sex-specific risk factors, sex-specific disease course, and sex-specific survival. For example, men may experience cognitive decline earlier in life but more gradually, whereas women may transition from normal cognition directly to dementia at a later age but more abruptly." (Petersen et al., 2010).

The older members of our study population (the 1935 birth cohort) showed a higher crude prevalence of CIND and of MCI, but the adjusted prevalence did not confirm this difference. Moreover, in our study, a younger age emerged as a protective factor against MCI and CIND. Most previous studies comparing younger people with the over 80s reported an increasing prevalence of cognitive impairment with age, however they did not evaluate the 70–74-year age group separately (Petersen et al., 2010; Ravaglia et al., 2008; Tognoni et al., 2005). Unlike what is documented in dementia, even a slightly younger age can be associated with less cognitive decline.

Since no previous studies have investigated the impact of area of birth on cognitive impairment, the significant association we found between this factor and CIND-other as well as CIND is a new finding that, awaiting corroboration in further investigations, should be interpreted with caution.

Similarly, although most previous studies on cognitive impairment in aging did not examine the possible association with marital status, it has to be noted that our results fail to confirm a previously reported higher prevalence of MCI in single people (Håkansson et al., 2009; Petersen et al., 2010).

The findings of our study do not confirm the previously reported role of educational level in cognitive impairment. This discordance may be due not only to the methodology we used but also to the cohort we investigated (people born in the period 1935–1939): indeed, the participants in our study attended school during and in the immediate aftermath of World War II, which was a period of great social change in our country. They are therefore likely to have experienced negative situations (death, hunger, destructions and poverty) but also, in subsequent years, to have experienced the benefits, such as more education for everyone, associated with the general spirit of reconstruction that characterized the period. This is a peculiarity not shared by previously investigated Italian cohorts (De Ronchi et al., 1998; Ravaglia et al., 2008; Solfrizzi et al., 2004).

Few studies seeking to establish the prevalence of MCI have considered the possible association with main lifetime occupation. A higher crude prevalence of MCI was seen in the blue collar workers but these data were not confirmed after adjustment. CIND was not found to be associated with occupation in our study, confirming the negative findings of other studies with regard to the influence of occupation on CIND prevalence (Atti et al., 2010; Fei et al., 2009). In the "InCHIANTI" study, manual work was found to

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be associated with CIND (Marengoni et al., 2011), but the InCHIANTI study population had a broad age range (from 60 to 98 years) and included a high proportion of farmers. Ultimately the influence of occupation on cognitive impairment, either CIND or MCI, remained weak or unproven.

The prevalence rate of MCI was not significantly different between the ApoE-ε4 carriers and non-carriers. This finding fails to support the idea that the ApoE-ε4 allele, in addition to being a genetic risk factor for AD, could also influence the rate of conversion from normal cognition to MCI (although not to CIND) (Brainerd et al., 2013). However, our data, drawn from a cross-sectional study, cannot be considered conclusive, since only longitudinal data can reject or confirm this hypothesis.

4.3. Strengths and limitations

In this study we tried to avoid selection bias by considering a population that was homogeneous in terms of age and area of residence. Second, unlike most previous studies in this field, every participant in the present study underwent a single-step multidimensional assessment. Third, the information collected about the physical, functional and cognitive status of the non-participants showed that the prevalence of dementia was similar between the participants and the non-participants and thus provided a guarantee that the results were not influenced by the response rate.

A possible limitation of this study is the difficulty in comparing its findings with those of differently designed studies. Another limitation is the failure to include biomarker analysis among the diagnostic criteria for AD (Dubois et al., 2007). This limitation may have led to underrepresentation of AD subjects, although this risk was partially offset by the use of diagnostic criteria developed by expert geriatricians and psychologists.

5. Conclusions

This study, showing prevalence rates higher than those previously reported in other Italian studies, confirmed the importance of dementia and cognitive impairment in the transitional age from adulthood to old age, albeit with the emergence of different associations with socio-demographic and genetic factors. Being born in southern Italy was associated both with overall dementia and with VD, and being single with a higher prevalence of VD, while ApoE-ε4 carrier status was associated with AD; however, the study failed to confirm an influence of age, gender, education and occupation in dementia. Older age, male gender and being born in north-eastern Italy were instead associated with a higher prevalence of different types of cognitive impairment, while education, occupation and marital status showed no such association.

Cognitive impairment and dementia screening programs developed for people on the threshold of old age should perhaps target, in particular, certain individuals who, according to the findings of the present study, could have a particularly high-risk profile.

Given the limitations of the cross-sectional data herein reported, it is hoped that data from forthcoming longitudinal observations will clarify the influence of socio-demographic and genetic factors on the incidence of dementia and cognitive impairment in the aging population.

Conflict of interest statement

The authors declare that they have no competing interests.

Acknowledgements

The authors are deeply indebted to "Federazione Alzheimer Italia", Milan, for supporting the InveCe.Ab study and for overseeing the correct execution of the study.

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