The impact of social networks and APOE ε4 on dementia among older adults: tests of possible interactions

Jing Wu, Caroline Hasselgren, Anna Zettergren, Henrik Zetterberg, Kaj Blennow, Ingmar Skoog, and Björn Halleröd

Department of Sociology and Work Science, University of Gothenburg, Gothenburg, Sweden; Department of Psychiatry and Neurochemistry, Institute of Neuroscience and Physiology, Sahlgrenska Academy, Centre for Ageing and Health - AgeCap, University of Gothenburg, Möln达尔, Sweden; Clinical Neurochemistry Laboratory, Sahlgrenska University Hospital, Möln达尔, Sweden; Department of Molecular Neuroscience, UCL Institute of Neurology, London, UK; UK Dementia Research Institute, London, UK

ABSTRACT

Objectives: Emerging evidence suggests that social networks may protect against the development of dementia among older adults. In this study we analysed the association between social networks, the apolipoprotein E (APOE) ε4 allele, and dementia. We also investigated whether there were gender-specific patterns in this respect.

Method: The analyses used population-based longitudinal data from Gothenburg, Sweden: the H70 Birth Cohort Study and the Prospective Population Study on Women (PPSW). A total of 580 individuals born in 1930 underwent semi-structured neuropsychiatric examinations in 2000–2001. Follow-up examinations were carried out in 2005–2006 and 2009–2010. The timing of dementia onset was analysed using Cox proportional hazards regression.

Results: The presence of the APOE ε4 allele affected the risk of developing dementia in both genders. Among women, distant social networks had a protective effect on dementia, while among men the significant associations between close social networks and dementia did not remain after controlling for covariates. Significant interactions between social networks and the APOE ε4 allele were not found.

Conclusion: Strong social networks do not seem to moderate the increased risk of dementia implied by the APOE ε4 allele. Nevertheless, our results underline the importance of strong social networks in postponing dementia onset and indicate that their impact may differ among men and women.

Introduction

Are lonely people more likely to develop dementia? Conversely, can strong social networks protect individuals from developing dementia and reduce the impact of genetic risk factors? In this article we analyse the association between social networks, the apolipoprotein E (APOE) ε4 allele, and dementia. The question of interest is whether the impact of this well-known genetic risk factor could be reduced by the existence of strong social networks.

The APOE ε4 allele and dementia

Dementia is a formidable public health problem with an estimated prevalence of 6.2 percent among adults older than 60 years in Europe (Martínez et al., 2016). The most common form of dementia is Alzheimer’s disease. The APOE ε4 allele accounts for a large share of the genetic risk in sporadic Alzheimer’s disease (Blennow, de Leon, & Zetterberg, 2006; Corder et al., 1993; Poirier et al., 1993; Raber, Huang, & Ashford, 2004). Its effect on dementia is mediated by Alzheimer neuropathology (Mortimer, Snowdon, & Marksberry, 2009; Wang et al., 2012), and cerebral amyloid β pathology in particular (Jansen et al., 2015). Recent studies have further suggested that the APOE ε4 allele is also a genetic risk factor (albeit a weaker one) for other forms of dementia, such as vascular dementia (Liu et al., 2012; Martínez et al., 2017; Rohn, 2014) and dementias with synucleinopathy (Martínez et al., 2017; Tsuang et al., 2013), even if it is not settled to which degree such associations exist since patients with these disorders have concomitant cerebral amyloid β pathology (Lim et al., 1999; Lopez et al., 2002; Neuropathology Group of the Medical Research Council Cognitive Function and Aging Study, 2001). However, not all people carrying the APOE ε4 allele develop Alzheimer’s disease or dementia, whereas some people without the APOE ε4 allele do (Blennow, Hampel, Weiner, & Zetterberg, 2010; Blennow et al., 2006; Prince, Zetterberg, Andreasen, Marcusson, & Blennow, 2004). By extension, this might imply the existence of social and environmental characteristics that could either ‘buffer’ or ‘trigger’ the harmful effects of this genetic risk factor (Rizzuto & Frattigioni, 2014).

The different dimensions of social networks

The complexity of an individual’s social network is difficult to capture. Kahn and Antonucci (1980) identified three dimensions of social networks: (1) structure, which includes...
network size, proximity and frequency of contact; (2) function, which refers to the exchange of different kinds of support between network members; and (3) subjective evaluations of quality, which provide insight into individuals’ experiences of their networks (Fiori, Smith, & Antonucci, 2007). Furthermore, social networks among men and women vary across the life span (Glass, de Leon Mendes, Seeman, & Berkman, 1997). In general, women have larger and more diverse social networks than men (Ajrouch, Blandon, & Antonucci, 2005), as well as a wider range of sources for emotional support (Fuhrer & Stansfeld, 2002). There are a number of studies focusing on the range of sources for emotional support (Fuhrer & Stansfeld, 2002; Crooks, Lubben, Petitti, Little, & Chiu, 2008; Anme et al., 2013; Beland, Zunzunegui, Alvarado, Otero, & del Ser, 2005; Crooks, Lubben, Petitti, Little, & Chiu, 2008; Fratiglioni, Wang, Ericsson, Maytan, & Winblad, 2000; Kuiper et al., 2015, 2016; Zunzunegui, Alvarado, del Ser, & Otero, 2003). For instance, structural aspects of social networks, such as larger network size (James, Boyle, Buchman, Barnes, & Bennett, 2011; Saczynski et al., 2006) and higher frequency of social contact (Crooks et al., 2008; Gureje et al., 2011; Saczynski et al., 2006; Scarmeas et al., 2001), have been found to decrease the risk of developing the disease. As to the quality of social networks, previous studies show divergent results. Amieva et al. (2010) reported an association between low satisfaction with social networks and incident dementia, while a meta-analysis by Kuiper et al. (2015) concluded that there was no association between these variables.

In general, the size of an individual’s network reflects his/her possibility to receive emotional and material support. A variety of behavioural, psychological, and physiological mechanisms have thus been investigated to explain the above-mentioned effects of social networks on dementia risk (Fratiglioni, Paillard-Borg, & Winblad, 2004; Qiu, Xu, & Fratiglioni, 2010). First, the support and intellectual stimulation provided by social networks is hypothesized to have a positive impact on the individual’s emotional state by, for instance, reducing stress (Fratiglioni et al., 2004) which in turn has been suggested to decrease disease susceptibility (Andel et al., 2012; Johansson et al., 2010, 2013), possibly because of its inverse relationship with vascular disorders and other risk factors linked to dementia and Alzheimer’s disease (Kivipelto et al., 2001, 2002; Launer et al., 2000; Skoog & Gustafson, 2002). Second, in line with the cognitive reserve hypothesis, the intellectual stimulation provided by social interaction is thought to impede degenerative brain changes by improving resilience and compensatory abilities in the neuronal networks (Kuiper et al., 2015; Stern, 2002, 2012).

### Social networks and the APOE ε4 allele

As discussed above, the impact of the APOE ε4 allele on dementia onset is well established and there are several studies that have investigated the relationship between social networks and the risk of developing dementia. However, studies that jointly examine the influence of the APOE ε4 allele and social networks are scarce (Heser et al., 2014; Saczynski et al., 2006; Salinas et al., 2017). Furthermore, to our knowledge there are relatively few studies that explicitly examine the possible interaction effect between aspects of social networks and genetic risk factors on the development of dementia. Among those, neither Brenowitz, Kukull, Beresford, Monsell, and Williams (2014), who investigated the incidence of mild cognitive impairment, nor Zuelsdorff et al. (2013), who examined a sample of individuals with a family history of AD, could verify interactions between aspects of social relationships and the APOE ε4 allele. In contrast, Poey, Burr, and Roberts (2017) found that living arrangements and perceived social support could moderate the association between the APOE ε4 allele and cognitive function. Moreover, Niti, Yap, Kua, Tan, and Ng (2008) found that different kinds of leisure activities (including social activities) protected against cognitive decline and that the protective impact was particularly strong among individuals carrying the APOE ε4 allele.

The overarching aim of the study was to analyse the association between social networks, the APOE ε4 allele and dementia. Special attention was paid to the question of whether strong social networks could moderate the effect of the APOE ε4 allele on dementia and, additionally, whether gender specific patterns existed in this respect.

### Data and operationalisation

#### Participants

The analyses are based on data from the H70 Birth Cohort Study and the Prospective Population Study on Women (PPSW), both conducted in Gothenburg, Sweden. All participants in the study were sampled from the Swedish population register and systematically selected on the basis of birth dates. Both persons living in private households and in residential care were included. The present analyses were based on a sample of 580 individuals born in 1930, all living in Sweden on 1 September 2000. When studying the relation between social networks and cognitive decline, the possibility of reverse causality needs to be taken into consideration (Kuiper et al., 2016). In order to minimize the possibility of such bias, respondents with cognitive impairments, i.e., dementia at baseline were excluded from the analysis (Amieva et al., 2008, 2010; Kuiper et al., 2015, 2016; Pillai & Verghese, 2009; Starkstein, Petracca, Chemerinski, & Kremer, 2001), leaving a total sample of 564 respondents. Information on the presence/absence of the APOE ε4 allele was available for 536 of these individuals. Follow-up examinations were carried out in 2005–2006 (n = 443) and in 2009–2010 (n = 368). Informed consent was obtained from all participants or their relatives, and the study was approved by the regional Ethics Review Board.

#### Table 1. Characteristics of the study population, n (%).

| Characteristics                      | All n (%)   | Men n (%)   | Women n (%) |
|--------------------------------------|-------------|-------------|-------------|
| Gender                               |             |             |             |
| Men                                  | 224 (39.72) |             |             |
| Women                                | 340 (60.28) |             |             |
| Cohabiting                           | 365 (65.18) | 177 (79.02) | 188 (55.95) |
| Socio-economic status                |             |             |             |
| Blue collar                          | 229 (42.43) | 140 (64.60) | 89 (39.91)  |
| Lower white collar                   | 139 (26.48) | 108 (35.64) | 31 (11.08)  |
| White collar and self-employed       | 158 (30.10) | 55 (18.15)  | 103 (41.93) |
| Education                            |             |             |             |
| Primary                              | 340 (60.82) | 215 (63.99) | 125 (36.01) |
| Secondary                            | 39 (19.40)  | 22 (9.82)   | 17 (5.18)   |
| Secondary/university                 | 39 (19.40)  | 22 (9.82)   | 17 (5.18)   |
| Presence of APOE ε4                  |             |             |             |
| Diagnosed with dementia 2000–2012    | 31 (9.12)   | 15 (4.91)   | 16 (5.18)   |

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| Diagnosed with dementia 2000–2012    | 31 (9.12)   | 15 (4.91)   | 16 (5.18)   |
Board for medical research in Gothenburg (Skoog et al., 2015). A more detailed description of the full baseline sample can be found in previous studies (see Karlsson et al., 2009, 2010). Table 1 shows the characteristics of the study population.

### Neuropsychiatric examinations, diagnoses, and genotyping

Clinical examinations were conducted at an outpatient department or in the participant’s home and included comprehensive social, functional, physical, neuropsychiatric and neuropsychological examinations. Semi-structured neuropsychiatric examinations were performed by trained psychiatric research nurses. These examinations included ratings of common symptoms and signs of dementia (e.g. assessments of memory, orientation, general knowledge, apraxia, visuospatial function, understanding proverbs, following commands, naming ability and language) and has been described in detail previously (Guo et al., 2007; Skoog et al., 1993). Close informant interviews were also performed as part of the clinical examinations. These interviews were semi-structured and contained questions about changes in behaviour and intellectual function, psychiatric symptoms, activities of daily living, and, in cases of dementia, age of onset and disease course (Karlsson et al., 2009; Skoog et al., 2015). Dementia was diagnosed by geriatric psychiatrists according to the Diagnostic and Statistical Manual of Mental Disorders, 3rd Edition Revised (DSM-III-R) (APA, 1987). The diagnoses were based both on symptoms rated during the neuropsychiatric examinations and on information from the close informant interviews. A more detailed description of the diagnostic procedures can be found in previous studies (see Guo et al., 2007; Skoog et al., 1993). For participants lost during follow-up, incident dementia cases (until 2012) were diagnosed based on information from medical records, and evaluated by geriatric psychiatrists, or from the Swedish Hospital Discharge Register (Guo et al., 2007). Information about the age of dementia onset was gathered from the Swedish Hospital Discharge Register, the neuropsychiatric examinations, or the close informant interviews. Blood samples were collected to establish genotyping for the single nucleotide polymorphisms (SNPs) rs7412 and rs429358 in APOE (gene map locus 19q13.2) using a KASPar® PCR SNP genotyping system (LG Genomics, Hoddesdon, Herts, UK), or by mini-sequencing (Blennow et al., 2000). Genotype data for these two SNPs were used to define ε2, ε3, and ε4 alleles. Statistical analyses focused upon ε4 as this is the only allelic variant clearly associated with and increased risk of Alzheimer’s disease.

### Assessment of social networks

Since the H70/PPSW studies did not include questions relating to functions of social networks (specifically support and reciprocity) during 2000–2001, the respondents were only asked about the structure and quality of their social networks (Table 2). With regard to structure the questions included the number of intimate person(s) as well as the frequency of visits to and from neighbours, greeting neighbours, and visits to and from acquaintances. Regarding network quality, the questions focused on whether the levels of contact with neighbours and acquaintances were perceived as satisfactory. Here we excluded the variables about family (e.g. contacts with children and grandchildren)
for two reasons. First, the beneficial association between social networks and survival among older people might be restricted to relationships with friends and confidants rather than with children and relatives (Giles, Glonek, Luszcz, & Andrews, 2005; Rizzuto & Fratiglioni, 2014). Moreover, it is common for childless old people to have more contact with friends and relatives (Albertini & Kohli, 2009; Deindl & Brandt, 2017). Second, since around 13 percent of the respondents reported that they had no children, information on the frequency and satisfaction of contact with children was missing for a large part of the study population. Consequently, these questions were not included in the factor analysis (see below); instead, ‘have no child/childless’ was added as a control variable.

**Covariates**

The socio-demographic variables (cohabiting, childlessness, occupational class, and education) were considered as potential confounding factors and controlled for in the analyses. The ‘cohabiting’ variable indicated whether an individual was either married or living together with someone without being formally married. Information on occupational class was recoded in accordance with the Swedish SEI standards for socioeconomic classification (MIS, 1982:4). Three socio-economic groups were categorized: blue collar, lower white collar, and white collar and self-employed. Blue collar corresponded to manual workers (unskilled, semi-skilled, and skilled). Lower white collar corresponded to assistant, non-manual employees, with or without subordinates, in occupations requiring a maximum of three years of post-comprehensive schooling. White collar and self-employed included intermediate/higher non-manual workers and professionals in occupations requiring three to six years of post-comprehensive education, as well as upper-level executives, self-employed persons, and farmers. In the present study, which was based on a sample gathered in an urban area, only one respondent reported ‘farmer’ to be their main occupation. Educational attainment was classified as primary, lower secondary, and secondary/university, based primarily on information obtained from the clinical examination in 2000–2001. Primary corresponded to elementary school/vocational school, lower secondary to girls’ school/junior secondary school/folk high school and secondary/university to high school/university. A more detailed description of the covariates can be found in the literature (see Hasselgren et al., 2018). While education and occupational class are often highly correlated, it has been suggested that these indicators could be linked to health via partly different mechanisms (Laahelma, Martikainen, Laaksonen, & Aittomaki, 2004; Torssander & Erikson, 2010). Additionally, while some studies propose that occupational class is associated with dementia only when education is not taken into account (Evans et al., 1997; Fratiglioni & Wang, 2007; Karp et al., 2004), others found that these variables have separate effects (Sattler, Toro, Schönknecht, & Schröder, 2012). Consequently, we controlled for occupational class and education separately in our models.

**Statistical methods**

Four of the seven social network variables were recoded as binary. The number of intimate persons was dichotomized on the basis of the question: ‘Do you have an intimate person with whom you can talk about anything?’ (Table 2). The responses ‘yes, spouse’, ‘yes, child’, ‘yes, relative’, ‘yes, friend’, ‘yes, another person’, ‘yes, combination’ were coded as ‘yes’, while ‘no’ was coded as ‘no’. The quality of contact with neighbours and people other than children or neighbours was dummy coded into ‘yes’ or ‘no’ on the basis of the questions: ‘Do you think you have enough, too much, or too little contact with your neighbours/people other than your children or neighbours?’ (Table 2). The response ‘enough’ was coded as ‘yes’, to indicate satisfaction, while ‘too little’ and ‘too much’ were coded as ‘no’ to reflect dissatisfaction. Due to overlapping response alternatives, the quantity of contact with people other than children or neighbours was dichotomized on the basis of the question: ‘How often do you receive visits from or visit people other than your children or neighbours?’ (Table 2). The responses ‘every day’, ‘at least once per week’, ‘once per week/once per month’, ‘once per month/once per quarter’, and ‘less than once per quarter’ were coded as ‘yes’, while ‘never’ was coded as ‘no’.

Exploratory factor analysis was performed in order to identify potential latent constructs in the data and hence enable a better conceptual understanding of correlations among the seven social network variables (Fabrigar et al., 1999). In our study as all seven manifest variables were categorical (binary or ordinal scale) we began by computing a polychoric correlation matrix which is suitable for factor analysis with discrete data (Kolenikov & Angeles, 2004). From this matrix, two factors were retained (both with

| Table 3. Factor loadings of the seven manifest indicators on the two factors representing social networks at baseline. |
|---------------------------------------------------------------|
| **Variable** | **Factor 1 (distant social networks)** | **Factor 2 (close social networks)** | **Uniqueness** |
|----------------|---------------------------------|
| Intimate(s) (1) | 0.241 | 0.839 | 0.238 |
| Intimate(s) (2) | 0.019 | 0.823 | 0.322 |
| Neighbours (1) | 0.612 | 0.092 | 0.617 |
| Neighbours (2) | 0.522 | 0.298 | 0.639 |
| Neighbours (3) | 0.682 | 0.184 | 0.501 |
| Acquaintances (1) | 0.586 | 0.133 | 0.639 |
| Acquaintances (2) | 0.737 | 0.176 | 0.426 |

Extraction method: Principal-factor. Rotation: Varimax orthogonal.

Abbreviations: Intimate(s) (1): Do you have an intimate person with whom you can talk about anything? Intimate(s) (2): Do you have more than one intimate person? Neighbours (1): Do you and your neighbours visit each other to say hello? Neighbours (2): Do you stop and talk with your neighbours when you meet? Neighbours (3): Do you think you have enough contact with your neighbours? Acquaintances (1): Do you think you have enough contact with people other than your children or neighbours? Acquaintances (2): Do you receive visits from or visit people other than your children or neighbours?
eigenvalues >1). Furthermore, following Ledesma, Valero-Mora, and Macbeth (2015), we also took the factor loadings, the percentage of variance accounted for by the factors, and the factors’ theoretical interpretability into consideration in the selection process. The first retained factor could be defined as presence of one or more intimate person(s) (close social networks) and the second as frequency of, and satisfaction with, contact with neighbours and acquaintances (distant social networks). The factors were rotated using varimax orthogonal rotation, and accordingly constrained from being correlated (Table 3). Subsequently, the factor scores were saved as covariates in the regression; for ease of interpretation, they were standardized to have a mean of zero and a standard deviation of one.

The timing of dementia onset was estimated using Cox regression (Guo, 2010, p. 73). The continuous component of the dependent variable measured years-at-risk for dementia from baseline (i.e. from age 70) while the dichotomous component indicated whether the participant had developed dementia during the study period (up to 2012). The Cox proportional hazards model is a distribution-free model which assumes that the hazard for any individual in a sample is a fixed proportion of the hazard for any other individual; that is, that the ratio of the two hazards is constant over time (Guo, 2010, pp. 73–75). A post-estimation test based on Schoenfeld residuals was conducted for all models in order to assess the proportionality of hazards (Allison, 2014). The tests showed no signs of violations (test statistics not shown here but can be requested from the first author). The analysis was conducted using partial-likelihood estimation in version 14.0 of the Stata software package (Stata Corp LP, College Station, TX). We report hazard ratios and 95 percent confidence intervals, and also mark 0.01 and 0.05 significance levels for two-tailed test for the variables included.

Analytic approach

Our analysis began by testing the basic bivariate associations between the APOE ε4 allele and the risk of dementia, and by examining whether weak social networks were associated with increased risk of dementia. As expected (see Table 4), gender differences were observed in this respect. Even though no significant interaction between gender and social networks could be detected in the full sample, presumably due to lack of power, the observed tendency of a difference was similar to that revealed in the stratified analyses (results not shown here but can be requested from the author). Thus, in the continued analysis, we presented separate results for men and women in addition to those obtained from the full sample. In the second step, we analysed whether the expected positive association between dementia and social networks remained after controlling for the effect of the APOE ε4 allele. Finally, we explored whether strong social networks could ‘buffer’ the negative effect of the APOE ε4 allele. Our main focus was on this final analysis, and we hypothesized that strong social networks would decrease the impact of the APOE ε4 allele on the risk of dementia. Thus, we assumed that the negative effect of the APOE ε4 allele on dementia would be lower among individuals with strong social networks.

Results

Table 4 shows the bivariate relationships between social networks (close and distant), the APOE ε4 allele, and dementia. In the total sample, close and distant social networks were negatively associated with dementia (HR = 0.781, 95% CI = [0.621–0.981]; HR = 0.760, 95% CI = [0.593–0.974]), whereas the APOE ε4 allele had a positive relationship with dementia (HR = 2.327, 95% CI = [1.334–4.059]). Close social networks were significantly associated with dementia among men (HR = 0.678, 95% CI = [0.483–0.952]), while distant social networks had a significant relationship with dementia among women (HR = 0.683, 95% CI = [0.493–0.946]). The risk of developing dementia was more than double among carriers of the APOE ε4 allele compared to non-carriers. However, the estimated effect was only significant in the total sample and among women.

Table 5 shows Cox regression models for the impact of the APOE ε4 allele, social networks, and their interaction on dementia in the total sample as well as among men and women, respectively. Models 1–3 gave estimates for close social networks. With regards to the total sample, the estimates for close social networks were statistically significant except in Model 2, and the hazard ratios for the APOE ε4 allele were above 2. Among men, the estimate for close social networks was significant only in Model 1, but none of the estimates for the APOE ε4 allele was found to be significant. Among women, the hazard ratios for close social networks were non-significant. The APOE ε4 allele, on the other hand, had a strong effect with estimated hazard ratios above 2.7. The estimates for the interaction effects were non-significant in all groups (Model 3).

Models 4–6 gave the corresponding estimates for distant social networks. While the APOE ε4 allele had a strong effect with estimated hazard ratios above 2, the estimates for distant social networks in the total sample were non-significant. Among men, there were no significant effects found for distant social networks. This held true also for the effect of the APOE ε4 allele. Among women, a strong distant social network had an inverse relationship with dementia in all three models. Increasing the distant social network index by one standard deviation decreased the hazard rate by about one third. Meanwhile, the APOE ε4 allele had estimated hazard ratios above 3 in model 4. The estimates for the interaction effects were again non-significant in all groups (Model 6).

In order to draw the correct substantial conclusions from the interaction models (models 3 and 6) we also computed and compared the marginal effects of APOE ε4 allele at different values for social networks (Brambor, Clark, & Golder, 2006). However, no such effects were detected (results not shown here but can be requested from the first author).

Table 4. Bivariate analysis between social networks, APOE ε4, and dementia.

| Social Networks          | All (n=1122) | Men (n=595) | Women (n=527) |
|--------------------------|--------------|------------|---------------|
| Close social networks    | 0.781*       | 0.678*     | 0.869         |
|                          | [0.621–0.981] | [0.483–0.952] | [0.631–1.197] |
| Distant social networks  | 0.760*       | 0.861      | 0.683*        |
|                          | [0.593–0.974] | [0.580–1.279] | [0.493–0.946] |
| APOE ε4                  | 2.327***     | 2.087      | 2.522**       |
|                          | [1.334–4.059] | [0.879–4.954] | [1.217–5.225] |

*<p<0.05, **p<0.01.
author). We also tested the inclusion of confounders in the interaction models, but the results did not change in any substantial way.

Discussion

The aim of this study was to examine whether social networks and the APOE e4 allele were associated with dementia onset. Special attention was paid to the question of whether strong social networks could moderate the effect of the APOE e4 allele on dementia and, additionally, whether gender specific patterns existed in this respect.

As expected, and in line with previous research, we found that individuals carrying the APOE e4 allele had an increased risk of developing dementia (e.g. Blennow et al., 2006; Corder et al., 1993; Mortimer et al., 2009; Poirier et al., 1993; Raber et al., 2004; Skoog et al., 2015; Wang et al., 2012). Moreover, we observed that the impact of the APOE e4 allele on dementia increased in the total sample and among women, after controlling for all covariates, including occupational class and education, which might imply that these factors moderate its effect (Ferrari et al., 2012). Moreover, we observed that the slightly lower estimate for the APOE e4 allele among men (Hasselgren et al., 2018) may therefore partially explain our results. It has also been shown that although women generally have larger networks and more close friends compared to men, women also to a higher extent report that they are lonely and perceive loneliness as a problem (Halléröd, 2009; Halléröd & Seldén, 2013).

Our bivariate analysis in Table 4 and multivariate analysis in Table 5 showed that close and distant social networks had an inverse relationship with dementia in the total sample, which generally supported the main assumption that weak social networks are associated with an increased risk of dementia. Thus, in line with previous findings, the present study indicates that strong social networks may have a positive influence on cognition and a protective function in relation to disease development (Crook et al., 2005; Beland et al., 2005; Crooks et al., 2008; Skoog et al., 2015). It is also likely that the effect size for the APOE e4 allele would have been higher for individuals with Alzheimer’s disease, or positive for cerebral amyloidosis.

We chose to distinguish between close and distant social networks. In line with earlier results (Caetano, Silva, & Vettore, 2013; McLaughlin, Vagenas, Pachana, Begum, & Dobson, 2010), our bivariate analyses in Table 4 indicated that there could be gender-specific patterns in the effect of social networks on dementia among older adults. Previous studies have pointed out that older women have more confidants, while older men rely mainly on their spouses for emotional intimacy (Bildtgård & Öberg, 2017; McLaughlin et al., 2010). This is also in line with studies of bereavement that show spousal loss emotionally affects men more than women, while women suffer more economically (Halléröd, 2013). It has also been shown that although women generally have larger networks and more close friends compared to men, women also to a higher extent report that they are lonely and perceive loneliness as a problem (Halléröd, 2009; Halléröd & Seldén, 2013).

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Our study indicates that for women, distant social networks (i.e. those involving frequent and satisfying contact with neighbours and acquaintances) are important for preventing or postponing dementia onset. This is in line with

### Table 5. Cox regression models for the impact of social networks and APOE e4 on dementia.

| Model | Social Networks | All Male | All Female | p | p Adjusted |
|-------|----------------|----------|------------|---|------------|
| Model 1* | Close social networks | 0.778* [0.617–0.981] | 0.684* [0.475–0.987] | 0.855 [0.618–1.181] | 0.001 |
| | APOE e4 | 2.345** [1.279–4.299] | 1.599 [0.616–4.148] | 3.064** [1.356–6.921] | 0.001 |
| | N | 452 | 192 | 260 | 0.001 |
| Model 2b | Close social networks | 0.831 [0.656–1.054] | 0.757 [0.518–1.105] | 0.910 [0.659–1.257] | 0.001 |
| | APOE e4 | 2.315** [1.296–4.134] | 2.023 [0.791–5.172] | 2.780** [1.317–5.865] | 0.001 |
| | N | 479 | 191 | 286 | 0.001 |
| Model 3c | Close social networks | 0.688* [0.500–0.946] | 0.605 [0.357–1.025] | 0.733 [0.485–1.110] | 0.001 |
| | APOE e4 | 2.388** [1.333–4.278] | 1.778 [0.663–4.774] | 2.765** [1.305–5.858] | 0.001 |
| | Close social networks/APOE e4 | 1.322 [0.846–2.064] | 1.239 [0.626–2.454] | 1.484 [0.778–2.833] | 0.001 |
| | N | 479 | 193 | 286 | 0.001 |
| Model 4* | Distant social networks | 0.808 [0.618–1.056] | 0.999 [0.625–1.598] | 0.653 [0.468–0.911] | 0.001 |
| | APOE e4 | 2.418** [1.327–4.407] | 1.890 [0.751–4.762] | 3.159** [1.404–7.105] | 0.001 |
| | N | 452 | 192 | 260 | 0.001 |
| Model 5b | Distant social networks | 0.813 [0.624–1.059] | 0.921 [0.572–1.484] | 0.695 [0.507–0.952] | 0.001 |
| | APOE e4 | 2.357** [1.325–4.195] | 2.148 [0.853–5.411] | 2.897** [1.375–6.102] | 0.001 |
| | N | 479 | 191 | 286 | 0.001 |
| Model 6c | Distant social networks | 0.843 [0.568–1.252] | 1.016 [0.512–2.017] | 0.730 [0.446–1.195] | 0.001 |
| | APOE e4 | 2.221** [1.245–3.960] | 1.845 [0.745–4.571] | 2.649* [1.229–5.710] | 0.001 |
| | Distinct social networks/APOE e4 | 0.900 [0.536–1.513] | 0.968 [0.384–2.436] | 0.844 [0.446–1.598] | 0.001 |
| | N | 479 | 193 | 286 | 0.001 |

* Adjusted for cohabiting, childlessness, and socio-economic status.  
** Adjusted for cohabiting, childlessness, and education.  
* Adjusted for covariates.  
* p < 0.05, ** p < 0.01.
previous studies that report an association between social networks and incident dementia (Amieva et al., 2010; Crooks et al., 2008; Gureje et al., 2011; James et al., 2011; Saczynski et al., 2006; Scarmeas et al., 2001). Additionally, our findings show that the positive effect of having strong social networks remains even after controlling for the APOE ε4 allele (Heser et al., 2014; Saczynski et al., 2006; Salinas et al., 2017). For men, we found significant associations between close social networks and dementia onset. This result held true also after controlling for the APOE ε4 allele and other covariates but not after controlling for education. In our analysis, close social networks consist of the presence and the number of intimate person(s) to whom the older adults can talk about everything. Here, talking with an intimate person(s) is not only related to the structural dimension of social networks but is also characterized as emotional support which can be included in the functional aspects of social networks. Taken together, this might imply that there are gender-specific patterns of social networks that need to be taken into consideration when studying the effect of social networks on dementia and health in general (Fuhrer & Stansfeld, 2002).

Contrary to our expectations social networks and the APOE ε4 allele were unrelated and no interactions between them were found to be significantly associated with dementia. Hence, in line with the results presented by Brenowitz et al. (2014) and Zuelsdorff et al. (2013), but in contrast to those of Niti et al. (2008) and Poey et al. (2017), strong social networks do not seem to moderate the increased risk of dementia implied by the APOE ε4 allele.

The main contribution of the present study is twofold. First, it adds to the current state of knowledge by underlining the importance of social interaction in postponing dementia onset. Second, it highlights the fact that there might be gender-specific patterns in this respect. By extension, this suggests that special attention should be paid to individuals’ social settings in preventive efforts undertaken by healthcare professionals and others.

**Limitations**

The limitations of the measures must be considered in relation to the findings of the study. It was impossible to include more functional aspects of social networks, especially social support, emotional closeness, and instrumental reciprocity, since the H70/PPSW studies did not ask about these aspects in 2000–2001. Due to both theoretical reasons and missing data, neither social networks with children and/or grandchildren nor social networks with acquaintances were included in the analysis. Another limitation was lack of biomarker data on cerebral β-amyloidosis and neurodegeneration (cerebrospinal fluid- or positron emission tomography-based markers) on the included individuals. Moreover, reverse causality is an important issue in terms of the association between social networks and dementia as dementia may result in poorer or more restricted social networks (Rizzuto & Fratiglioni, 2014). Although we excluded the respondents who were diagnosed with dementia before baseline in order to limit such bias, it is difficult to exclude the possibility of reverse causality, and this may still play a role in the relation between social networks and cognitive decline (Gallacher, Bayer, & Ben-Shlomo, 2005; Kuiper et al., 2016). Furthermore, other non-genetic confounders, such as mid-life hypertension, more severe late-life cardiovascular disease and obesity, which could also give rise to reverse causality, were not included in our study. Finally, as the sample size was relatively small and a significant interaction effect between gender and social networks could not be corroborated, the observed gender differences must be interpreted with caution.

**Conclusions**

The present study offers insight into the relationship between social networks and dementia onset. Our results provide further evidence to support the idea that gender-specific patterns in social networks exist in older adulthood and that social networks could play a different role in dementia among men and women. Future research should therefore take into consideration how social networks influence dementia through social support, emotional closeness, and instrumental help, and investigate whether this influence varies between genders.

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**ORCID**

Jing Wu http://orcid.org/0000-0002-4941-3370

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