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## **Cognitive functioning among cognitively intact dementia caregivers compared to matched self-selected and population controls**

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**Keywords:** Cognition, Caregiving, Stress, Alzheimer's, Sampling, Matching

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Researchers interested in using TILDA data may access the data for free from the following sites: Irish Social Science Data Archive (ISSDA) at University College Dublin

<http://www.ucd.ie/issda/data/tilda/>; Interuniversity Consortium for Political and Social

Research (ICPSR) at the University of Michigan

<http://www.icpsr.umich.edu/icpsrweb/ICPSR/studies/34315>

## Abstract

**Purpose of the Study:** Caregiving for a person with dementia is frequently used as a model for examining the impact of chronic stress on health, including cognitive functioning. However, the prevalence of self-selecting non-caregiving control groups, who are typically healthier than the general population, could contribute to a picture of poorer caregiver performance and overstate the negative effects of stress. We investigated differences in cognitive performance between dementia caregivers and two groups of non-caregivers recruited using different sampling methods.

**Design and Methods:** We compared cognitive function and psychological wellbeing among a sample of 252 spousal dementia caregivers with two demographically matched non-caregiving control groups drawn from (1) a population study and (2) a self-selecting sample. Comparable cognitive measures included immediate and delayed recall, processing speed reaction time and verbal fluency. Analysis of Covariance controlled for cognitive risk factors including demographics, medications, obesity, smoking, physical inactivity.

**Results:** Caregiver and non-caregiver performance was comparable on most cognitive domains. However, caregivers outperformed both control groups on processing speed ( $p \leq .05$ ) and reaction time ( $p \leq .05$ ), despite having higher levels of stress and depression ( $ps < .001$ ). Furthermore, caregivers had significantly better free recall than self-selecting controls ( $p < .001$ ).

**Implications:** Our results, overall, do not support the idea that caregiving is associated with stress-induced cognitive deficits. Rather, the trend toward better caregiver performance is consistent with the healthy caregiver hypothesis.

## Introduction

A large literature documents how the chronic stress associated with dementia care leads to psychological (Pinquart & Sorensen, 2003) and physical health problems (Vitaliano, Zhang, & Scanlan, 2003) among caregivers. Caregiving is seen as a chronic stressor that harms cognition through psychosocial (e.g., depression), behavioural (e.g., physical inactivity) and physiological (e.g., cortisol) mediating pathways (Pearlin, Mullan, Semple, & Skaff, 1990; Vitaliano et al., 2011). Potential implications are grave; caregiver cognitive dysfunction could affect caregivers' own quality of life and compromise their ability to provide care (de Vugt et al., 2006). Given our reliance on family caregivers as the main providers of dementia care, this could ultimately result in additional economic burden on health services.

As stress can affect cognition (Sandi, 2013), it has also been hypothesized that dementia caregivers are at an increased risk of cognitive dysfunction and decline compared to non-caregivers. Spousal caregivers are thought to be especially vulnerable due to their age and because they share risk factors e.g., socioeconomic status and associated behaviours like diet (Hughes & Ganguli, 2009) with their spouse who has dementia (Vitaliano, Murphy, Young, Echeverria, & Borson, 2011). Indeed, several studies report that spousal dementia caregivers perform more poorly than non-caregivers in cognitive domains including processing speed (de Vugt et al., 2006; Oken, Fonareva, & Wahbeh, 2011; Vitaliano et al., 2009), working memory (Mackenzie, Wiprzycka, Hasher, & Goldstein, 2009), and delayed recall (de Vugt et al., 2006; Mackenzie et al., 2009; Palma et al., 2011). Furthermore, caregivers' processing speed (Vitaliano et al., 2009) and vocabulary (Vitaliano et al., 2005) was found to decrease more rapidly over time compared to non-caregivers.

However, the view that caregiving invariably leads to stress, and thereby negative health outcomes, is increasingly being challenged. The healthy caregiver hypothesis contends that healthier individuals are more likely to become and remain caregivers and that factors related to caregiving, such as physical and cognitive caregiving demands, may serve to protect caregivers from stress and help to maintain their health as they age (Fredman et al., 2008; Fredman, Doros, Ensrud, Hochberg, & Cauley, 2009). Furthermore, caregivers may be more motivated to preserve their health (Fredman et al., 2009). This hypothesis is supported by population studies, which suggest that many caregivers are not stressed and that caregiving is actually associated with positive health outcomes (Roth, Fredman, & Haley, 2015). For example, prospective cohort studies indicate that caregivers have lower mortality risk than non-caregivers (Brown et al., 2009; O'Reilly, Connolly, Rosato, & Patterson, 2008). Furthermore, a large longitudinal study of women over 65 found no evidence that caregiving was associated with poorer physical functioning; indeed, low-frequency caregiving was associated with better grip-strength (Rosso et al., 2015).

Conflicting findings on caregiving and physical health has been attributed largely to methodological differences, in particular to sampling. Most existing studies were based on clinical or convenience samples, whereby caregivers and non-caregivers were recruited through entirely different procedures (Roth et al., 2015). Caregivers are generally recruited through dementia services and may therefore over-represent those with higher burden; while non-caregivers, typically recruited through the media, active retirement and social groups, comprise socially active volunteers who tend to be healthier than the general population (Pruchno et al., 2008). Consequently, observed differences may reflect better health among

the older adults who volunteer for research rather than the health effects of caregiver stress (Roth et al., 2015). This is supported by the finding that convenience samples of caregivers report poorer physical and mental health compared to non-caregivers than in population-based comparisons (Pinquart & Sorensen, 2003; Pruchno et al., 2008).

Sampling bias is also likely to be present in existing studies of caregiver cognitive functioning, which are typically based on small convenience samples of healthy older adult controls and caregivers recruited through dementia services. Thus it is not clear whether observed differences in cognition reflect stress-induced cognitive deficits from caregiving or cognitive advantages from being a socially active older adult. While population-based data compared dementia caregivers and non-caregivers on cognitive outcomes (Norton et al., 2010; Pertl, Lawlor, Robertson, Walsh, & Brennan, 2015), caregivers and controls in these comparisons were ill-defined. Neither study assessed caregiving; participants who had a spouse with dementia were categorised as 'caregivers', while those who did not comprised the controls. Therefore, it is unclear whether these samples are comparable to other studies in terms of the nature or extent of caregiving provided. While Norton et al. (2010) reported that spouses of persons with dementia are 1.62 times more likely to develop incident dementia than individuals whose spouses are dementia free, Pertl et al. (2015) did not find any significant differences between the groups across a range of cognitive domains.

Given the possible impact of sampling bias in research on caregiver cognition, we investigated whether differences between caregiver and non-caregiver cognitive performance would vary depending on the nature of the control group. We compared cognitive functioning in a large convenience sample of spousal dementia caregivers with two demographically matched non-caregiver groups: one drawn from a self-selecting sample of older adult volunteers, and the second from a population study of adults over 50. We hypothesized that caregiver cognitive performance would compare more favourably to the population than the self-selecting sample.

## **Methods**

### ***Participants***

#### *Caregivers*

Caregivers were recruited to a large national study of spousal dementia caregivers in Ireland, through media and local advertisements, community gatekeepers (e.g., public health nurses), and various organisations for caregivers, people with dementia, and/or older adults. All participants were aged over 50; able to engage in day-to-day activities like dressing, cleaning, shopping and managing finances unassisted; and were caring for and cohabiting with a spouse/partner with dementia. Exclusion criteria included a caregiver's diagnosis of dementia, visual or hearing impairment that would prevent neuropsychological evaluation and non-fluent English. Data were collected from 2013-2015 through a telephone health screening, a self-completion questionnaire, and a face-to-face assessment at the participant's home, the university or a community centre. Of the 370 eligible caregivers identified, 252 (68%) participated after giving written informed consent. Ethical approval was obtained from the University's School of Psychology Research Ethics committee.

### *Non-caregivers*

Two recent Irish studies were identified with similar profiles of health and cognitive data. First, data were available for 597 adults aged 50+ from the baseline cohort of the NeuroEnhancement for Independent Lives' Memory Research Unit (MRU), who self-identified as non-caregivers. This sample was self-selected (SS) and recruited [detailed by Hannigan, Coen, Lawlor, Robertson, and Brennan (2015)] via media campaigns and events provided or attended by the study team. Exclusion criteria were history of stroke, epilepsy, major psychiatric disorder, drug or alcohol abuse within the past 5 years, current anti-psychotic or anti-epileptic medication use, significant memory problems or dementia, or problems with vision or hearing that would prevent neuropsychological evaluation. Data were collected from 2012–2014 through a telephone health screening, a self-completion questionnaire, and face-to-face assessment in the university.

The second pool of 8,504 controls aged 50+ came from the baseline sample of The Irish Longitudinal Study of Ageing (TILDA) where data were collected from 2009–2011 (accessed via the Irish Social Science Data Archive; [www.ucd.ie/issda](http://www.ucd.ie/issda)). TILDA recruited via clustered sampling of addresses from the Irish GeoDirectory, a listing of residential addresses in Ireland [study and design described in Kenny et al. (2010) and Whelan and Savva (2013)]. Data collection occurred at three stages: a computer-aided participant interview in the respondent's home, a self-completion questionnaire, and a health assessment in the participant's home or a dedicated health centre. Participants were excluded if they had a severe cognitive impairment or a diagnosis of dementia.

### *Group Matching*

Two control groups were selected from the non-caregiver samples by (1) excluding participants who did not match the caregiver sample exclusion criteria and (2) matching control group participants with participants in the caregiver sample based on their demographic profile.

#### (1) Exclusion of controls for comparability with caregivers

MRU participants attended the university unaccompanied; therefore, we assumed no difficulty on Instrumental Activities of Daily Living (IADLs). As all caregivers were cohabiting with their spouse/partner, we excluded 169 MRU participants who identified as single. This left 428 participants available for matching, of whom 238 (56%) were female and 57 (15%) were educated to secondary level; the mean age was 63.4 years ( $SD = 6.2$ ; range = 50-82).

Complete non-caregiving TILDA spousal/partner dyads were selected by excluding: those not living with a spouse/partner (3,666 respondents); households with data from only one occupant (698 respondents); households providing care to relatives, friends or neighbours (1,728 respondents); households where one partner required help with ADLs (122 respondents) or IADLs (254 respondents). Finally, individuals were excluded if they were aged under 50 (124 respondents); aged 80 or over (50 respondents; the published data identified them as 80+ only) or did not complete the health assessment (433 respondents). This left 1,429 respondents (including 622 spousal pairs) of whom 731 (51%) were female and 718 (50%) had not completed second level education; the mean age was 61.9 years ( $SD =$

7.66; range 50-79). For the TILDA comparison 27 caregivers were thus also excluded as they were aged over 79 (caregiver sample n=225).

## (2) Matching participants

Three matching variables were employed: age, education (7 levels: some primary, primary completed, junior cert, secondary completed, diploma/cert, degree, postgraduate degree) and sex. Given our sample size, the adoption of a Mahalanobis distance metric was preferable to propensity matching (Zhao, 2004). The Mahapick procedure (Kantor, 2012) was employed for matching, and unique controls were identified using Selectmahaunique (Kantor, 2012).

A significantly higher prevalence of possible cognitive impairment (MoCA <24) among TILDA participants was found, which could bias the results in favour of caregivers (see Supplemental Tables S2-3 detailing the prevalence and comparing cognitive outcomes prior to applying cut-off). Therefore, both samples were restricted to those above the MoCA cut-off of 23 (caregiver sample n=183). Our iterative approach retained uniquely selected households thus eliminating the reduced variance that might occur if couples were included among controls. Three iterations were required to successfully match 179 caregivers with TILDA participants ('POP' control group).

One iteration of matching was performed for the MRU data. To mitigate a high prevalence of tertiary education in the MRU sample, the maximum allowed matching metric (Mahalanobis distance) was progressively lowered until no group significant differences were found on matching variables. The final level was 0.6. For consistency across the samples, caregivers and MRU controls with MoCA scores <24 were again excluded. The final MRU sample size ('SS' control group) was 155. The socio-demographic characteristics of the final groups are reported in Table 2 and the characteristics of the caregiving sample are shown in Supplemental Table S1.

## ***Measures***

### *Demographics and Covariates*

Data were collected on age, gender and seven main risk factors for dementia that could potentially confound differences in cognitive performance: 1) low educational attainment (secondary level not completed), 2) physical inactivity, 3) obesity, 4) being a current smoker, and a history of 5) hypertension, 6) diabetes, and 7) depression (Barnes & Yaffe, 2011). In addition, we included measures of frailty and verbal IQ (described later and in Table 1); frailty has been associated with accelerated cognitive decline (Kojima, Taniguchi, Iliffe, & Walters, 2016) and differences in IQ could contribute to differences in cognition. Table 1 lists how these confounds were assessed in each study. Physical inactivity and health-related measures are detailed below.

### Physical Inactivity

Activity levels were measured using the *International Physical Activity Questionnaire* short-form (IPAQ-SF; Craig et al., 2003). Total weekly physical activity was calculated by multiplying activity level metabolic equivalent (MET) energy expenditure values by the reported number of minutes per week spent per activity level (IPAQ, 2005). Physical

inactivity was operationalized in line with IPAQ recommendations as a total energy expenditure below 600 MET-minutes/week.

### Health-related covariates

Health screening in the three studies was not comparable; therefore, different approaches were used to control for health-related covariates. Participants in all studies self-reported medication use and this was included in lieu of measures of hypertension and history of depression. Anti-hypertensive medications were identified using the Anatomical Therapeutic Classification (ATC [[www.whooc.no/atc\\_ddd\\_index/](http://www.whooc.no/atc_ddd_index/)]; codes C02, C03, C07, C08, C09). The MRU classified psychotropic (anti-depressive or anxiolytic) medications using the ACT codes N05A, N05B, N06A, and N06CA' while TILDA coded only for anti-depressive use (N06A); caregiver data were therefore coded to match each group separately. In addition, the MRU and caregiver studies both included details of diabetes medication (A10) and this was used in lieu of a diabetes history measure. TILDA and caregiver data included a self-report item about diabetes history ("Has a doctor ever told you that you have diabetes or high blood sugar?").

### NART IQ

Caregivers' and MRU participants' premorbid cognitive function was assessed with the *National Adult Reading Test* (NART) (Nelson & Willison, 1991); participants read aloud a list of 50 irregularly pronounced words. WAIS-R IQ scores were estimated from verbal responses as per the manual. The NART has been shown to be highly stable over time and explain a significant proportion of the variance in IQ in later life (Barker-Collo *et al.*, 2008).

### *Cognitive outcomes*

Table 1 outlines the cognitive outcomes; these included all measures that were common between caregivers and at least one of the control group studies. The measures are described below:

### Montreal Cognitive Assessment (MoCA)

Global functioning was assessed using the MoCA, a widely-used rapid screening instrument for mild cognitive dysfunction (Nasreddine *et al.*, 2005). Scores of <24 (of a possible 30) indicate the presence of a cognitive impairment (Luis, Keegan, & Mullan, 2009).

### Choice Reaction Time (CRT) Test

The CRT Test is a 2-choice reaction time test. Participants pressed and held a start key on an Ergodex response board (DX1 input system, Ergodex Corporation, Mountain View, CA 94043) until either the word "yes" or "no" appeared on a screen; they then released the key and pressed a corresponding yes/no key before returning to the start key. The time (milliseconds) from the stimulus appearance to the release of the start key represents 'cognitive reaction time', our outcome measure.

### Colour Trails Test (CTT)

The CTT (D'Elia, Satz, Uchiyama, & White, 1996) was used to measure processing speed and executive functioning. The CTT is similar to the Trail Making Test but uses nonalphabetical stimuli. CTT-1 assesses processing speed, while CCT-2 incorporates

executive processes; the difference between the two scores is taken as an index of executive function. Times to completion (seconds) for each task and the difference scores were the outcome measures.

### Category fluency

Verbal fluency was assessed using the *animal category fluency task*, a common measure of executive function. Participants named as many animals as possible in 60 seconds; the total score was the number of unique animals named in one minute (Lezak et al., 2004).

### Memory

The *Logical Memory* test from the *Wechsler Memory Scale-IV* (Wechsler, 2009) was used to assess immediate and delayed recall. Participants were read two stories and recited each story immediately afterwards and 20-30 minutes later. Age-adjusted immediate and delayed recall scaled scores were used as outcome measures.

The *Free and Cued Selective Reminding Test* (FCSRT) was used to measure free recall (Grober, Buschke, Crystal, Bang, & Dresner, 1988). Sixteen pictures are presented in four sets of four on successive cards. Participants initially identified each item pictured to control for encoding, the card is then removed and immediate cued recall of the four items is tested. The procedure was repeated until all 16 items were identified and retrieved in immediate recall. A brief numerical interference task was carried out before delayed free recall was assessed across three trials. Total free recall was used as a measure of delayed verbal memory.

### Working Memory

Working memory was assessed using the *Letter-Number Sequencing* (LNS) test from the WMS III (Wechsler, 1997); participants listened to a list of randomised numbers and letters of increasing lengths (from 2 to 8) and recited the numbers and letters from the lowest in each series, starting with the numbers. The span increased until the participant failed all three items of one length. The number of sequences recalled was used as the total score.

### *Additional measures*

#### Depression

We measured depression using the 20-item *Centre for Epidemiological Studies Depression* (CES-D) scale (Radloff, 1977); respondents rated the frequency of symptoms over the preceding week on 4-point Likert scales. Higher total summed scores (0- 60; with reverse scoring) indicate greater depressive symptomology.

#### Stress

We measured stress using the 4-item *Perceived Stress Scale* (PSS) (Cohen, Kamarck, & Mermelstein, 1983), a widely used instrument that assesses how unpredictable, uncontrollable, and overloaded participants find their lives. The total score ranges from 0–16, with higher scores indicating greater stress.

### ***Statistical Analysis***

We calculated descriptive statistics for gender, age, education and dementia risk factors and compared differences between groups using *t*-tests and Chi-square analyses. We used regression-based Analysis of Covariance (ANCOVA) models to test for differences in cognitive outcomes between caregivers and both non-caregiver groups, controlling for demographics and dementia risk factors and separately for NART IQ and frailty.

### **Results**

#### ***Participant characteristics***

Matching successfully created two sets of caregiver and non-caregiver groups; comparable in age, sex and education (Table 2). Few significant differences existed in risk factors between caregivers and POP controls; nearly five times fewer caregivers were physically inactive (4.5% vs. 26.38%;  $\chi^2(1)= 32.67, p <.001$ ) and caregivers were less frail ( $t(349) = 2.59, p =.01$ ). While, twice as many caregivers were currently using psychotropic medications this difference only approached significance (10.2% vs. 5.0%;  $\chi^2(1)= 3.30, p =.069$ ). Compared with SS controls, caregivers were more likely to smoke (8.5% vs. 1.3%;  $\chi^2(1)= 8.56, p =.003$ ), be obese (28.4% vs. 13.0%;  $\chi^2(1)= 11.16, p =.001$ ), and take psychotropic medications (16.2% vs. 3.2%;  $\chi^2(1)= 14.91, p <.001$ ), but were three times less likely to be physically inactive (3.2% vs. 11.0%;  $\chi^2(1)= 7.13, p =.008$ ). Caregivers reported significantly greater stress and depression than both non-caregiver groups (*p*'s <.001).

#### ***Cognitive functioning***

Caregivers had faster CRT than both control groups (POP:  $t(352)= 2.73, p =.007$ ; SS:  $t(283)= 2.03, p =.043$ ) and faster processing speed than POP controls ( $t(355)= 2.04, p =.042$ ); although the trend was the same with the SS group, the difference was non-significant (Table 2). Compared with SS controls, caregivers had better free recall ( $t(307)= 2.93, p =.004$ ) despite having significantly lower NART IQ ( $t(306) = 5.49, p <.001$ ).

Only the CRT comparison with POP controls was no longer significant (*p* = 0.07) when demographics and dementia risk factors were controlled in ANCOVA models (see beta values for caregivers from equivalent regression models in Table 3, Models 1). Otherwise, compared to POP controls, caregivers had faster processing speed; while compared to SS controls, caregivers had faster CRT and better free recall.

We examined whether differences in frailty might contribute to superior caregiver performance (Models 2). When frailty was included, processing speed was no longer related to caregiver-status ( $\beta= -.102, p =.056$ ) compared with POP controls; caregivers still performed better than SS controls on CRT and free recall.

Model 3 examined whether differences in IQ might contribute to better performance among SS controls by covarying for NART scores. When NART IQ was controlled, caregiver-status was associated with faster processing speed, and remained associated with faster CRT and better free recall.

### **Discussion**

Contrary to our hypotheses, the inclusion of SS controls did not contribute to apparent deficits in spousal caregivers' cognitive performance; rather dementia caregiving was

associated only with better reaction time and processing speed in both group comparisons, as well as better free recall (SS controls only). There were no differences in tests of working memory, immediate and delayed recall, and speeded executive tasks. Observed differences remained significant after correction for demographics and dementia risk factors, and remained significant when differences in NART IQ (SS controls only) were controlled. In addition, the prevalence of possible cognitive impairment suggested lower impairment among caregivers than POP controls. Both the prevalence of lower impairment and the domain specific cognitive advantages for caregivers existed despite higher levels of stress and depression, and more prevalent psychotropic medication. Finally, our results suggest that caregivers were more physically active than both control groups and less frail than POP controls. Though caregivers were more likely to be obese and to smoke than SS controls, no differences in medication use were observed. Thus, these health and behavioural risk factors for dementia were not consistently more prevalent among caregivers than non-caregivers.

The cognitive results contradict previous studies suggesting that dementia caregiver cognition is poorer compared to non-caregivers (de Vugt et al., 2006; Mackenzie et al., 2009; Oken et al., 2011; Palma et al., 2011; Vitaliano et al., 2009). It is worth noting that the majority of these studies were based on small samples (of between 14–64 caregivers); only Vitaliano et al. (2009) included a comparatively large caregiver sample of 122. A recent review called for both greater sample sizes and the inclusion of population-based reference groups (Roth et al., 2015). Indeed, all these studies on relied on SS controls, except for de Vugt et al. (2006) who selected matched controls from a population study. However, no attempt was made to account for the reported differences in global cognition which we believe could introduce bias at the matching stage. Notably, in that study, the global cognition difference favoured better performance in the control group.

Our results are consistent with the idea that either healthier, more functionally-able people become caregivers or that the physical activities associated with caregiving lead to better caregiver health (Fredman et al., 2008; Fredman et al., 2009). An alternate explanation is that caregivers in our sample are not among the most highly stressed and instead experience moderate challenge raising arousal and vigilance to a more optimal level. There is some evidence that caring for others is associated with better cognition (Comijs, van den Kommer, Minnaar, Penninx, & Deeg, 2011; Rosnick, Small, McEvoy, Borenstein, & Mortimer, 2007). Ours is the first study, to our knowledge, to report these findings with spousal dementia caregivers; however, our findings are in line with those of Bertrand et al. (2012) who reported better caregiver than non-caregiver performance on delayed recall and processing speed. While we also found that caregivers had faster processing speed, as well as faster reaction times, than non-caregivers; we found no evidence of better caregiver delayed recall. Nevertheless, we found a strong effect of better caregiver memory on the FCSRT, though this could only be tested in the SS comparison. As the number of comparisons we carried out increased the possibility that observed differences were due to chance, our findings of better caregiver than non-caregiver cognitive functioning should be interpreted with caution. Nevertheless, correcting for multiple comparisons would not change our key finding – namely that there is no evidence from on our data that caregivers have poorer cognitive performance than non-caregivers.

Higher ratings on stress and depression measures, and higher prevalence of psychotropic medication use, among caregivers, comports with previous findings of poorer psychological wellbeing among caregivers compared to non-caregivers (Pinquart & Sorensen, 2003). Despite this, caregivers compared unfavourably to non-caregivers on only two domains related to physical health compared with SS controls: obesity and smoking. However, caregivers were comparable to POP controls on these factors. Furthermore, caregivers were less likely to be frail compared with POP controls, and physically inactive compared to both control groups using a measure capable of accounting for caregiving-related activities (Fredman, Bertrand, Martire, Hochberg, & Harris, 2006). No differences were observed between caregivers and non-caregivers in terms antihypertensive or diabetes medication use. However, as might be expected given higher caregiver depression ratings, psychotropic medication use was greater among caregivers compared with both control groups. Overall, our results support the contention (Roth et al., 2015) that a possible overreliance on convenience sampling methods for the recruitment of controls may have contributed to a picture of poorer caregiver health and health behaviour in the literature.

Recent evidence suggests that providing ongoing care for a spouse with dementia may increase caregivers' own risk of dementia (Norton et al., 2010). Multiple pathways within the stress model of caregiving have been identified as avenues of research into this finding (Vitaliano et al., 2011). Our study included seven dementia risk factors: low education, low activity, diabetes, obesity, hypertension, use of psychotropic medications and current smoking. However, we found that when matched on education level, the use of psychotropic medications/anti-depressants was the only risk more prevalent among caregivers than non-caregivers. It is noteworthy that the original study by Norton et al. did not account for medication use in the analysis; our data suggest further investigation of this pathway is warranted.

This paper was limited by testing protocol differences between the samples. For example, TILDA used a list recall paradigm to assess memory that was not employed in the other studies; therefore, caregiver memory could only be compared to SS controls. It is possible that we did not find differences in our study because of a selection bias in our caregiver group; healthier caregivers and caregivers with lower levels of burden and distress may have been more likely to self-select for and participate. However, recruitment was carried out in part through dementia and caregiver support services, and such convenience samples of caregivers may have poorer physical and mental health (Pruchno et al., 2008). Indeed, this possible self-selection bias also applies to our SS controls and all previous non-population-based studies that compared caregivers and non-caregivers, most of whom did report differences on at least some cognitive measures.

Despite these limitations this research has a number of advantages. We included two demographically matched comparison groups, recruited using different sampling methods; this builds on previous studies of caregiver cognition, which tended to rely on self-selection only for control purposes. Utilising different sampling methods allowed us to evaluate the potential effects of self-selection biases and, where consistent differences are seen across control groups, lessens the likelihood that observed effects are due to sampling. The finding of faster reaction times in caregivers was robust across the comparison groups. The cognitive batteries used covered a wide range of cognitive domains and our analyses took advantage of

a high degree of overlap in cognitive and psychological tests between the three studies. Also, we were able to match a large group of caregivers in both comparisons and the testing protocols were similar across the three groups.

### **Conclusion**

Overall, our results do not support the idea that caregiving is associated with stress-induced cognitive deficits. On the majority of comparisons, no statistically significant differences were observed between caregiver and non-caregiver cognitive performance. These findings were consistent in both comparisons with SS and POP non-caregivers. Rather, our results are consistent with the healthy caregiver hypothesis for domain specific cognitive outcomes since better processing speed and reaction times were observed among caregivers compared to both control groups. In line with the healthy caregiver hypothesis, these results may reflect an element of self-selection among caregivers, as healthier and more functionally-able persons may be more likely to take on and maintain a caregiving role. While our cross-sectional findings cannot speak to the possibility that ongoing distress among caregivers leads to accelerated cognitive decline, we found no evidence that caregivers have poorer cognitive functioning than non-caregivers, despite significantly higher levels of stress and depression.

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Table 1. Measures used in each study group to assess covariates and cognitive outcomes

| Measure                      | Caregivers:   | Self-selected control sample                                       | Population control sample                |
|------------------------------|---|--|--|
| <b>Covariates</b>            |   |  |  |
| Low education                | Self-report item; not completing second level education were coded as having low education  | ✓  | ✓  |
| Current smoking              | Single self-report item   | ✓  | ✓  |
| Obesity                      | Height (cm; stadiometer) and weight (kg; standard clinical weighing scales) used to calculate Body Mass Index (BMI) (weight in kg / height in m <sup>2</sup> ); BMI > 30 coded as obese | ✓  | ✓  |
| Physical inactivity          | 'Low' activity category based on the International Physical Activity Questionnaire (IPAQ-SF) short form   | ✓  | ✓  |
| Hypertension                 | Use of anti-hypertensive medication defined by ACT codes: 'C02, C03, C07, C08, C09'   | ✓  | ✓  |
| Depression                   | Coded to compare to both control groups   | Defined by the ATC classifications 'N05A, N05B, N06A, and N06CA'   | Defined by the ATC classification 'N06A' |
| Diabetes                     | Coded to compare to both control groups   | Use of diabetes medication defined by the ATC classification 'A10' | Doctor diagnosis of diabetes             |
| Frailty                      | Average of two measures of grip strength taken with dominant hand   | ✓  | ✓  |
| NART IQ                      | National Adult Reading Test (NART)  | ✓  | X  |
| <b>Cognitive functioning</b> |   |  |  |
| Global functioning           | Montreal Cognitive Assessment (MoCA)  | ✓  | ✓  |
| Processing speed             | Choice Reaction Time (CRT) <sup>a</sup>   | ✓  | ✓  |
|                              | Color Trails Test (CTT)-1 <sup>a</sup>  | ✓  | ✓  |
| Executive functioning        | Color Trails Test (CTT)-2 (Time for CCT-2 and difference between CTT1 and CTT2) <sup>a</sup> ;  | ✓  | ✓  |
| Verbal fluency               | Animal Category Fluency   | x <sup>b</sup>   | ✓  |
| Memory                       | Logical Memory test from the Wechsler Memory Scale-IV   | ✓  | X  |
|                              | Free and Cued Selective Reminding Test (FCSRT)  | ✓  | X  |
| Working memory               | Letter-Number Sequencing (LNS)  | ✓  | X  |

*Note.* In instances where the MRU and TILDA control groups used different pre-processing procedures for the data, the caregiver data were processed to match each control group separately for comparability. ✓s indicate that the same measures were used consistently across all groups. Xs indicate that a study did not include a given comparable measure. <sup>a</sup> preprocessing regimes of caregiver data matched to each control sample; <sup>b</sup> Verbal Fluency

was assessed in the participant's home in TILDA prior to the health and cognitive assessment and was excluded on this basis. ATC = Anatomical Therapeutic Classification.

Table 2. Participant characteristics and comparisons between caregivers and non-caregivers on each variable assessed.

|   | Caregivers<br>(n = 179) | Population<br>control group<br>(TILDA) | Caregivers<br>(n = 155) | Self-selected<br>control group<br>(MRU) |
|---|-------------------------|--|-------------------------|---|
| <b>Covariates</b>                         |                         |  |                         |   |
| Age                                       | 67.53 (68.6)            | 67.06 (6.61)                           | 67.02 (7.20)            | 66.29 (6.47)                            |
| Gender (% female)                         | 125 (69.8%)             | 127 (71.0%)                            | 103 (66.5%)             | 103 (66.5%)                             |
| Education (% low level)                   | 58 (32.4%)              | 59 (33.0%)                             | 40 (26.0%)              | 41 (26.5%)                              |
| Current smoker                            | 12 (6.8%)               | 17 (9.5%)                              | 13 (8.5%)               | 2 (1.3%)**                              |
| Obesity                                   | 56 (32.3%)              | 52 (29.0%)                             | 44 (28.4%)              | 20 (13.0%)**                            |
| Physical inactivity                       | 8 (4.5%)                | 47 (26.3%***)                          | 5 (3.2%)                | 17 (11.0%)**                            |
| Antihypertensive medication               | 67 (40.1%)              | 66 (36.9%)                             | 53 (34.4%)              | 42 (27.1%)                              |
| Psychotropic medication                   | 17 (10.2%)              | 9 (5.0%)                               | 25 (16.2%)              | 5 (3.2%***)                             |
| Diabetes/- medication                     | 13 (7.3%)               | 11 (6.2%)                              | 4 (2.6%)                | 4 (2.6%)                                |
| Frailty (grip strength)                   | 26.29 (9.62)            | 23.73 (8.82) **                        | 25.99 (9.07)            | 27.2 (10.07)                            |
| NART IQ                                   |                         |  | 111.85 (7.07)           | 115.72<br>(5.10)***                     |
| <b>Psychological wellbeing</b>            |                         |  |                         |   |
| Perceived Stress                          | 6.01 (3.30)             | 3.27 (3.03) ***                        | 6.01 (3.19)             | 2.70 (2.36)***                          |
| Depression                                | 14.80 (10.01)           | 3.75 (5.08) ***                        | 14.68 (9.61)            | 5.91 (5.71)***                          |
| <b>Cognitive Outcomes</b>                 |                         |  |                         |   |
| MoCA                                      | 26.83 (1.90)            | 26.55 (1.83)                           | 26.94 (1.91)            | 27.10 (1.85)                            |
| CRT (ms)                                  | 474 (98)                | 506 (125)**                            | 473 (92)                | 502 (143)*                              |
| Color Trails Test-1 (s)                   | 50.47 (18.29)           | 54.66 (20.46) *                        | 50.25 (18.91)           | 52.09 (18.20)                           |
| Color Trails Test-2 (s)                   | 103.84<br>(29.03)       | 104.74 (31.69)                         | 103.90 (31.56)          | 104.67 (28.64)                          |
| Color Trails Test<br>Difference Score (s) | 53.37 (21.41)           | 50.17 (23.31)                          | 53.65 (22.00)           | 52.58 (24.32)                           |
| Verbal Category Fluency                   |                         |  | 21.78 (4.97)            | 21.59 (5.61)                            |
| Logical Memory:                           |                         |  |                         |   |
| Immediate Recall                          |                         |  | 9.31 (2.66)             | 9.80 (3.01)                             |
| Delayed Recall                            |                         |  | 9.23 (2.71)             | 9.51 (3.04)                             |
| FCSRT: Free recall                        |                         |  | 36.10 (4.85)            | 34.30 (5.88)**                          |
| Letter-Number<br>Sequencing               |                         |  | 10.52 (2.25)            | 10.80 (2.69)                            |

\* $p < .05$ , \*\*  $p < .01$ , \*\*\*  $p < .001$

Note. CRT = Choice Reaction Time; FCSRT = Free and Cued Selective Reminding Test; MoCA = Montreal Cognitive Assessment, ms = milliseconds, NART = National Adult Reading Test, s = seconds

Table 3. Differences in cognitive outcomes between caregivers and controls. Standardised beta values and significance levels from ANCOVA equivalent regressions.

|  | Population control group |         | Self-selected control group |         |         |
|--|--------------------------|---------|-----------------------------|---------|---------|
|  | Model 1                  | Model 2 | Model 1                     | Model 2 | Model 3 |
|  | $\beta$                  | $\beta$ | $\beta$                     | $\beta$ | $\beta$ |
| MoCA                                   | .054                     | .047    | .009                        | .008    | .098    |
| Choice Reaction Time (ms)              | -.102                    | -.087   | -.174**                     | -.175** | -.211** |
| Color Trails Test-1 (s)                | -.102*                   | -.102   | -.106                       | -.120   | -.183** |
| Color Trails Test-2 (s)                | -.048                    | -.050   | -.069                       | -.069   | -.137*  |
| Color Trails Test Difference Score (s) | .020                     | .017    | -.004                       | .004    | -.034   |
| Verbal Category Fluency                | -                        | -       | .047                        | .044    | .096    |
| Logical Memory:                        |                          |         |                             |         |         |
| Immediate Recall                       | -                        | -       | .088                        | .111    | .063    |
| Delayed Recall                         | -                        | -       | .064                        | .105    | .045    |
| FCSRT Free recall                      | -                        | -       | .227***                     | .238*** | .297*** |
| Letter-Number Sequencing               | -                        | -       | -.031                       | -.046   | -.057   |

Note: Caregivers coded as 1, controls as 0. Negative beta values indicate a lower score (faster time) for caregivers. Model 1 included the following covariates Age, Low Education, Gender, Obesity, Diabetes, Antihypertensives, Psychotropics, Low Activity, Current Smoking; Model 2 included Grip Strength; Model 3 included NART IQ as a covariate (available for MRU only). FCSRT = Free and Cued Selective Reminding Test; MoCA = Montreal Cognitive Assessment

Supplemental Table S1. Characteristics of Spousal Caregiver Groups selected for comparison with Self-Selected and Population control groups.

|  | <b>Caregivers<br/>Compared with<br/>Population<br/>Controls<br/>N (%)</b> | <b>Caregivers<br/>Compared with Self-<br/>Selected Controls<br/>N (%)</b> |
|--|---|---|
| Cohabiting with Spouse                   | 179 (100%)  | 155 (100%)  |
| No. of years giving care to spouse       |   |   |
| Less than 2                              | 20 (11.2%)  | 15 (9.7%)   |
| 2-4                                      | 81 (45.2%)  | 71 (45.8%)  |
| 5-6                                      | 38 (21.2%)  | 33 (21.3%)  |
| 7- 9                                     | 18 (10.1%)  | 18 (11.61%)   |
| 10 or more                               | 20 (11.7%)  | 17 (11.0%)  |
| Not available                            | 2 (1.1%)  | 1 (0.7%)  |
| Diagnosis of Spouse (Care Recipient)     |   |   |
| Alzheimer's Disease                      | 83 (46.4%)  | 69 (44.5%)  |
| Corticobasal Degeneration                | 2 (1.1%)  | 2 (1.3%)  |
| Dementia non-specific                    | 22 (12.3%)  | 17 (11%)  |
| Frontotemporal Dementia                  | 23 (12.9%)  | 20 (12.9%)  |
| Lewy Body Dementia                       | 5 (2.8%)  | 5 (3.2%)  |
| Mixed                                    | 7 (3.9%)  | 6 (3.9%)  |
| Other                                    | 5 (2.8%)  | 4 (2.6%)  |
| Parkinson's Disease                      | 3 (1.7%)  | 4 (2.6%)  |
| Primary Progressive Aphasia              | 2 (1.1%)  | 2 (1.3%)  |
| Unknown                                  | 8 (4.5%)  | 7 (4.5%)  |
| Vascular Dementia                        | 19 (10.6%)  | 19 (12.3%)  |
| Hours in Paid Employment                 |   |   |
| Not in Paid Employment                   | 145 (81%)   | 122 (78.7%)   |
| 1-14                                     | 7 (3.9%)  | 6 (3.9%)  |
| 15-28                                    | 10 (5.6%)   | 10 (6.5%)   |
| 29-40                                    | 10 (5.6%)   | 10 (6.5%)   |
| Above 40                                 | 3 (1.7%)  | 2 (1.3%)  |
| Not Available                            | 4 (2.2%)  | 5 (3.2%)  |
| Average per day spent giving care? (Hrs) |   |   |
| Less than 4                              | 23 (12.9%)  | 22 (14.2%)  |
| 4-8                                      | 36 (20.1%)  | 33 (21.3%)  |
| 9-13                                     | 18 (10.1%)  | 15 (9.7%)   |
| 14-18                                    | 76 (42.5%)  | 62 (40%)  |
| More than 19                             | 20 (11.2%)  | 16 (10.3%)  |
| Not Available                            | 6 (3.4%)  | 7 (4.5%)  |

Note. All variables were self-reported, in the case of Spouse's Diagnosis, participants reported a doctor's diagnosis.

Supplemental Table S2: Prevalence of MOCA scores less than 24 in Caregivers and Control Group Prior to exclusion on this basis.

|               | N    | MOCA < 24<br>N (%) | Test comparing with caregivers |
|---------------|------|--------------------|--------------------------------|
| Caregivers    | 225  | 42 (18.5%)         | -                              |
| Population    | 1429 | 407 (28.5%)        | $\chi^2(1) = 9.47, p < .01$    |
| Self-Selected | 428  | 32 (7.5%)          | $\chi^2(1) = 18.38, p < .001$  |

Note: Significance tests suggest that cognitive impairment defined by a score of less than 24 in the Montreal Cognitive Assessment (MOCA) was more prevalent in caregivers than self-selected controls but more prevalent in population controls than caregivers.

Supplemental Table S3: Means and Standard Deviations of cognitive outcomes prior to exclusion of participants with MOCA scores below 24.

|   | Caregivers<br>(n = 200) | Population<br>control group<br>(TILDA) | Caregivers<br>(n = 181) | Self-selected<br>control group<br>(MRU) |
|---|-------------------------|--|-------------------------|---|
| <b>Cognitive Outcomes</b>                 |                         |  |                         |   |
| MoCA                                      | 25.56 (2.97)            | 24.77 (3.77)**                         | 26.14 (2.70)            | 26.54 (2.4)                             |
| CRT (ms)                                  | 488 (113)               | 553 (186)***                           | 484 (112)               | 508 (180)                               |
| Color Trails Test-1 (s)                   | 54.65 (20.74)           | 64.12 (33.95)***                       | 52.27 (20.18)           | 52.47 (19.20)                           |
| Color Trails Test-2 (s)                   | 113.54 (35.18)          | 112.88 (36.05)                         | 107.88 (24.48)          | 106.61 (32.53)                          |
| Color Trails Test<br>Difference Score (s) | 59.17 (27.93)           | 54.22 (24.78)*                         | 55.61 (24.48)           | 54.66 (27.98)                           |
| Verbal Category<br>Fluency                |                         |  | 21.22 (5.1)             | 21.63 (5.75)                            |
| Logical Memory:                           |                         |  |                         |   |
| Immediate Recall                          |                         |  | 9.14 (2.87)             | 9.58 (2.97)                             |
| Delayed Recall                            |                         |  | 9.04 (2.92)             | 9.19 (3.07)                             |
| FCSRT: Free recall                        |                         |  | 35.67 (4.68)            | 34.18 (5.99)**                          |
| Letter-Number<br>Sequencing               |                         |  | 10.31 (2.35)            | 10.67 (2.73)                            |

\* $p < .05$ , \*\* $p < .01$ , \*\*\* $p < .001$

Note. CRT = Choice Reaction Time; FCSRT = Free and Cued Selective Reminding Test; MoCA = Montreal Cognitive Assessment, ms = milliseconds, s = seconds