

**Title:** Caregiver burden and quality of life two years after attendance at a memory clinic

**Running head:** Caregiver burden and quality of life over two years

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**Key points:**

- Evidence regarding the impact of memory assessment services (MASs) on informal caregivers' burden and health-related quality of life (HRQL) is limited.
- In a large multi-centre study, we show that caregiver burden increases slightly over two years but changes in HRQL are small.
- Most caregivers are satisfied with services, but low levels of satisfaction are associated with increased burden.

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## **ABSTRACT:**

**Objectives:** We aimed to describe 1) the burden and HRQL of informal caregivers of new patients attending a memory assessment service (MAS), 2) changes in these outcomes over two years and 3) satisfaction with services.

**Methods:** Informal caregivers of patients attending one of 73 MASs throughout England completed questionnaires at the patient's first appointment, and 6 and 12 months later. Participants from 30 of these MASs were also followed up at 24 months. Questionnaires covered caregivers' sociodemographic characteristics, Zarit Burden Interview, EQ-5D-3L and satisfaction with services. We used multivariable linear regression to assess relationships between burden, HRQL and caregiver and patient characteristics.

**Results:** Of 1020 caregivers at baseline, 569 were followed up at 6 months, 452 at 12 months and 187 at 24 months. There was a small increase in caregiver burden over two years (effect size 0.30 SD). These changes were not associated with most caregiver or patient characteristics, except socioeconomic deprivation which was associated with larger increases in burden at two years. Caregivers' HRQL was weakly associated with burden and showed a small reduction over time (0.2 SD). Most caregivers were satisfied with services but caregivers who were not satisfied with the services they received reported greater increases in burden.

**Conclusions:** Increases in caregiver burden and reductions in HRQL appear to be small over the first two years after attending a MAS. However, the longer-term impact on caregivers and those they care for needs investigating, as do strategies to reduce their burden.

## INTRODUCTION

Informal caregivers of older adults (unpaid caregivers who have a personal relationship with, and provide ongoing assistance for, an older person) are known to experience higher levels of stress and depression, poorer physical health and lower health-related quality of life (HRQL) than non-caregivers.<sup>1</sup> These differences are more pronounced among those who provide care for people with dementia.<sup>2,3</sup>

Conceptual models have proposed that the primary manifestations of dementia (cognitive impairment, functional dependency and behavioural problems) have an adverse impact on caregivers' HRQL through the burden it creates both in the time spent providing informal care and the physical and emotional burden.<sup>4-7</sup> This relationship may be mediated by factors such as the extent of social support, self-esteem and the use of formal services.<sup>7-9</sup>

Meanwhile contextual variables such as caregivers' sex, age, socioeconomic status and relationship to the care recipient also have an impact on the caregivers' burden and HRQL.<sup>10-13</sup>

The National Dementia Strategy in England<sup>14</sup> recognises the impact of dementia on the well-being of informal caregivers and the potential role of health services in alleviating the burden of care. It is envisaged that earlier diagnosis, better communication about diagnosis, and easier access to post-diagnostic support will improve the HRQL of people with dementia, and also reduce caregiver burden and improve their HRQL.

Memory assessment services (MASs) have been advocated as a key component in achieving the strategy's objectives. However, while recent findings have indicated that patients' HRQL improves in the first year after attendance at a MAS,<sup>15</sup> it is not clear what impact the services have on caregivers. Furthermore, the profile of informal caregivers using these

services is unknown. There is limited evidence from a pilot study in Australia which observed that attending a MAS was associated with an improvement in caregivers' HRQL over 12 months.<sup>16</sup> A trial in the Netherlands which studied the effects of follow-up care in MASs compared to care by general practitioners (GPs) did not find beneficial effects of MASs on informal caregivers' burden or HRQL,<sup>17</sup> but data on the actual changes in these scores over time were not available (communication with the authors, 20<sup>th</sup> July 2017).

Our aims were: to describe the burden and HRQL of informal caregivers when patients have their first appointment at a MAS; to determine the changes in caregivers' burden and HRQL following the first appointment and subsequent interventions; to examine the associations of any changes with caregivers' socio-demographic characteristics, their relationship to the patient, the patient's diagnosis and the patient's HRQL; and to examine the association of changes in caregivers' burden and HRQL with their satisfaction with formal services following a diagnosis of dementia.

## **METHODS**

### *Sample*

We randomly selected 80 MASs from all 212 clinics identified in England.<sup>18</sup> Of these, 73 took part in the study, which were representative of all MASs in terms of patient volume, waiting times and accreditation status.<sup>18</sup> All participating MASs were publicly-funded National Health Service (NHS) services. Patients referred for a first appointment between September 2014 and April 2015 and their informal caregivers were eligible for inclusion if they had sufficient English language to understand the consent process and questionnaires. In cases where a patient assented to take part in the study but was assessed by clinical staff as lacking capacity, the caregiver could act as a consultee (patient representative) and provide

consent on behalf of the patient. Each site recruited up to 25 consecutive new patients.<sup>19</sup>

Questionnaires were completed by patients (administered by trained interviewers) and their informal caregivers (self-administered) at the first appointment, and 6 and 12 months later.

Additionally at 24 months, participants from 30 of the original 73 MASs (selected on basis of largest sample sizes at baseline, to maximise sample size at follow-up) were followed up.

### *Outcomes*

Informal caregivers' burden was assessed using the 12-item short form Zarit Burden Interview (ZBI), which has similar properties to the full version when administered to caregivers of older adults with cognitive impairment.<sup>20</sup> Each item is scored on a 5-point scale, resulting in a total score ranging from 0 to 48 with higher score indicating greater burden. Although the scale comprises two domains (role strain and personal strain) only the overall ZBI score was used in this analysis. There have been preliminary attempts to establish a cut-off indicating "high" burden, but there is no established cut-off score.

Caregivers' HRQL was assessed using a generic measure of health status (EQ-5D-3L<sup>21</sup>) which covers five domains: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. A summary EQ-5D-3L index score was calculated using value sets derived from a UK general population survey to weight and combine responses, with a higher score indicating better quality of life.<sup>22</sup> A score of 0 represents death and 1 represents perfect health.

The outcomes of interest in this study were changes in caregivers' burden (ZBI score) and their HRQL (EQ-5D-3L index) between the patients' first appointment (baseline) and each follow-up (6, 12 and 24 months).

### *Caregiver characteristics*

Data on caregivers' sociodemographic characteristics were collected at baseline (age, sex, ethnicity, and socioeconomic deprivation based on residential postcode and national ranking of Index of Multiple Deprivation IMD scores<sup>23</sup>). Caregivers also reported their relationship to the patient (spouse, son/daughter, or other), living arrangements (whether or not they lived in the same household as the patient), the formal health and social care services used by the patient and caregiver, and their overall satisfaction with the post-diagnostic services they received (based on a single item, rated on a 4-point Likert scale: a lot, quite a bit, a little, not at all).

### *Patient characteristics*

Patients' disease-specific HRQL was both self-reported by the patient and proxy-reported by the caregiver using DEMQOL and DEMQOL-Proxy,<sup>24</sup> and scored using revised, equated scores<sup>25</sup> (higher score indicates better quality of life; scores transformed to range from 0 to 100). Interviewers also extracted data from the patient's case notes on their diagnosis (dementia; mild cognitive impairment (MCI); other; no diagnosis made) and on comorbid conditions from a pre-specified list (heart disease, high blood pressure, problems caused by stroke, leg pain due to poor circulation, lung disease, diabetes, kidney disease, diseases of the nervous system, liver disease, cancer within the last 5 years, depression or arthritis).<sup>26</sup>

### *Statistical analysis*

Caregiver characteristics were summarised as means and standard deviations (SDs) or percentages. We analysed cross-sectional relationships between caregiver burden and HRQL at each time point using linear regression analyses, both unadjusted and adjusted for

caregiver characteristics (age, sex, ethnicity, socioeconomic deprivation, relationship to patient) and patient diagnosis. We used cluster-robust standard errors to account for clustering of participants within MASs.

Changes in caregivers' burden and HRQL were assessed using paired t-tests to compare mean scores at baseline and at each follow up, for the whole sample and by the patient's diagnosis. For each longitudinal outcome, we used multivariable linear regression to examine the relationships of change scores with caregiver and patient characteristics, adjusting for all the characteristics listed above, score at baseline, patients' self-reported HRQL (DEMQOL) and using cluster-robust standard errors. For HRQL we additionally adjusted for caregiver burden to examine its effect on HRQL. For the subsample of caregivers caring for an individual diagnosed with dementia, we also modelled the relationships between change scores and caregivers' satisfaction with the post-diagnostic services the caregiver received, adjusting for the same variables above. Results are presented as adjusted differences in ZBI or EQ-5D-3L change score with 95% CIs (with Bonferroni adjustment for multiple testing; family-wise error rate of 0.05 per model divided by the number of tests).

All analyses were conducted using Stata V.14 (StataCorp, College station, Texas, USA).

#### *Missing data*

The 30 sites included in the study at 24 months were selected on the basis of largest sample sizes at baseline. Regression analyses indicated that none of the outcomes were associated with the sample size of the site, therefore data from the excluded sites were considered to be missing completely at random. To assess plausible mechanisms for missing data at



follow-up, we used logistic regression models to assess the relationships between missingness of outcomes at each time point and all the covariates of interest, plus earlier HRQL, caregiver burden and caregivers' satisfaction with services. Missingness at follow-up was predicted by some of the covariates included in the final analysis models (including carer's age, relationship to the patient and patient's diagnosis) but not earlier measures of HRQL (except at baseline, included as a covariate in analysis), burden or satisfaction with services. At each time point, a high proportion of participants (89-91%) had complete data on the covariates included in the final models. Based on these results, the assumption that outcomes were missing at random (MAR) given the covariates included in the analysis was considered to be plausible, and therefore a complete case analysis for each outcome was deemed valid for fully adjusted models.<sup>27</sup>

#### *Ethics approval*

The study protocol was approved by the National Research Ethics Service Committee London (reference: 14/LO/1146) and the London School of Hygiene & Tropical Medicine ethics committee (reference: 8418).

## **RESULTS**

#### *Characteristics of sample*

For the 1420 patients recruited into the study, baseline questionnaires were also completed by 1020 caregivers. Of these, 569 (60% of eligible participants) completed questionnaires at 6 months, 452 (47%) at 12 months and 187 (40%) at 24 months (Supplementary Figure 1). Overall, 653 of 1020 caregivers (64%) contributed some longitudinal data.

Respondents who were followed up were similar to those who were not in terms of sex, ethnicity, socioeconomic deprivation and caregiver burden at baseline (Table 1). However, respondents were on average older, more likely to be a spouse of the patient and to be living with the patient, and had lower HRQL at baseline (EQ-5D-3L index score 0.79 v 0.82).

For the patients responding at follow-up, 91% had received a diagnosis by 24 months: 64% dementia, 24% MCI, 4% other diagnoses (Table 1). The rest had still received no diagnosis or were considered to have no cognitive impairment.

#### *Cross-sectional analysis of caregiver burden and HRQL*

Mean caregiver burden score at each time point ranged from 12 to 15 (Table 1; Supplementary Figure 2). Mean ZBI score at each time point was higher among those caring for someone with dementia compared to MCI or no diagnosis (Table 2). Caregivers' mean HRQL scores ranged from 0.74 at 24 months to 0.79 at baseline (Table 1). Scores did not vary by diagnosis at any of the time points (Table 2).

At each time point (except at 24 months, when no statistically significant relationship observed) higher caregiver burden was very weakly associated with lower HRQL: each point increase in ZBI score predicted a reduction in EQ-5D-3L index score of between 0.004 and 0.006 points (effect size 0.016 to 0.025 SD) (Table 3). This association was not affected by adjusting for caregiver characteristics and patient's diagnosis.

#### *Longitudinal changes in caregiver burden and HRQL*

Caregiver burden increased over time from 12.3 at baseline to 14.8 at 24 months (Table 2; Supplementary Figure 3). Linear regression analyses indicated that ZBI score increased by

0.1 points (95% CI 0.04 to 0.17) for each month from the first appointment, but the effect size over two years was moderate (0.30 SD).<sup>28</sup>

There was no statistically significant change in caregivers' HRQL from baseline to 6 or 12 months (Table 2), but a small decrease was observed at 24 months (from 0.79 to 0.74, effect size 0.22 SD).

#### *Longitudinal associations between caregiver and patient characteristics and outcomes*

In adjusted analyses, increases in caregiver burden were not associated with either the patients' diagnosis or most characteristics of caregivers, with the exception of socioeconomic deprivation at 24 months: caregivers from the most deprived areas reported a larger increase in burden compared to those in the least deprived areas (adjusted mean difference 7.2, 95% CI 0.09 to 14.3) (Table 4). However, we did not observe a consistent association between caregiver burden and socioeconomic deprivation over time or by level of deprivation.

The only caregiver or patient characteristic that was associated with the extent of change in HRQL in adjusted analyses was caregivers' age at 12 months (Table 5): older caregivers reported a greater reduction in their HRQL (0.004 lower per year increase in age).

#### *Longitudinal associations between caregiver burden and HRQL*

In adjusted analyses, change in caregivers' HRQL was associated with caregiver burden at 12 months, but not at 6 or 24 months (Table 5). At 12 months, higher caregiver burden was associated with a greater reduction in HRQL (one unit increase in ZBI score was associated with a reduction in 0.005 in EQ-5D change score).

### *Satisfaction with services for carers of those with dementia*

At 6 months, 88 (39%) caregivers of patients diagnosed with dementia reported that they were 'a lot' satisfied and 66 (29%) 'quite a bit' satisfied with the services they received. At 12 months the proportions were 28% and 32%, and at 24 months 16% and 21%. The proportions reporting not being at all satisfied was 14% at 6 months, 18% at 12 months and 29% at 24 months. Very few caregivers (n=9 at 6 months, 4 at 12 months, and 6 at 24 months) reported having made use of a carer support worker.

Compared to those who were most satisfied with services, those who reported that they were 'a little' or 'not at all' satisfied reported greater increases in burden at 12 months (but not at 6 or 24 months) after adjusting for all the other caregiver and patient characteristics (Table 6). Changes in caregivers' HRQL were not associated with caregivers' satisfaction with services.

## **DISCUSSION**

### *Main findings*

There was a small increase in caregiver burden over two years (effect size 0.3 SD), and a small reduction in HRQL (0.2 SD). In adjusted analyses these changes were not associated with most caregiver or patient characteristics, including patient diagnosis. Exceptions were socioeconomic deprivation, which was associated with larger increases in burden at two years, and older age, which was associated with greater reductions in HRQL over 12 months. Higher caregiver burden was associated with reductions in HRQL at 12 months, but this effect was small and was not observed at other time points. The majority of caregivers supporting people with dementia were satisfied with the services they received, but this

proportion declined over time. There was evidence to indicate that caregivers who were not satisfied with services reported greater increases in burden, but caregivers' HRQL was not associated with their level of satisfaction.

### *Strengths and limitations*

This is the first large study to describe burden and HRQL among the caregivers of patients at their first MAS appointment, and to explore changes over the following two years. The MASs that participated were representative of those across England and the sample of patients was largely representative of all those attending these services.<sup>19</sup> Mean EQ-5D Index score in our sample at baseline was similar to UK norms for people aged 65-74 years (mean 0.78)<sup>29</sup> and a previous study of caregivers of people with mild dementia (mean 0.78, SD 0.19).<sup>30</sup>

The study has four main limitations. The first is that we report findings from complete-case analysis based on those caregivers who contributed data at each time point. Our analyses of missing data indicated that adjusted analyses are appropriate and valid under the assumptions stated, but the mechanisms for non-response at follow-up are unknown and may be more complex than accounted for in our approach. At baseline, study participants were shown to be slightly younger, more likely to be male and had marginally better cognitive function than those patients who did not take part.<sup>19</sup> Consequently, the study findings may underrepresent caregivers of patients with the poorest cognitive function at referral.

The second limitation is that we cannot determine the absolute effect on caregivers' burden and HRQL of attending a MAS and any subsequent post-diagnosis support, as we have no

data on people who do not use such services to make a comparison. The increase in burden may have been greater without the help of the MAS and subsequent support. Such data are lacking because current policy is to refer all people with suspected dementia,<sup>31</sup> while in this study a control arm would not have been ethical due to lack of clinical equipoise regarding early assessment and treatment.

Third, although the EQ-5D-3L is frequently referred to as a measure of HRQL, it actually measures health status and assesses only one psychological characteristic (anxiety/depression). The EQ-5D-3L may not be sensitive to small changes in a relatively healthy caregiver population.<sup>32, 33</sup> Cross-sectional studies that have used other measures of quality of life, such as the SF-36<sup>12</sup> or a dementia-specific scale<sup>34</sup> have shown characteristics including sex, spousal relationship and care recipient's HRQL to be associated with caregivers' HRQL.

Fourth, information to support the interpretation of Zarit scores is lacking. There is some preliminary evidence that a score of 10 may be indicative of depressive symptomatology among informal caregivers.<sup>35</sup> The distribution of burden scores in our sample (upper quartile cut-off score >19) was similar to that reported in other caregiver populations,<sup>20</sup> but the clinical relevance of distribution-based cut-offs has not been established.

#### *Comparison with other studies*

Levels of caregiver burden at baseline were comparable to those among caregivers of patients with subjective memory complaint,<sup>36</sup> but were low relative to those reported by caregivers of patients with diagnosed dementia or MCI.<sup>20, 33, 36</sup> This suggests that at the first assessment at a memory clinic, most caregivers are experiencing quite low levels of burden,

which is perhaps expected given that the majority of patients have moderate to high cognitive function at their first appointment.<sup>19</sup> However, our study indicates that after two years, increases in caregiver burden are modest, even among those caring for patients who go on to receive a diagnosis of dementia or MCI. There have been two large longitudinal studies of caregivers of people with dementia, not specifically in relation to MASs, and these have reported contrasting findings of decreased burden over 12 months<sup>37</sup> and increased burden over 18 months,<sup>33</sup> with the latter study finding smaller increases among those caring for a person with severe dementia compared to mild or moderate dementia. Differences in study findings may therefore be explained by the differing stages of dementia of participants: reductions in caregiver burden observed in moderate to severe cases of dementia have been attributed to improvements in patients' behavioural symptoms as dementia becomes very severe.<sup>37</sup> In contrast, in earlier stages of dementia behavioural symptoms typically increase and these are associated with a considerable burden for informal caregivers.<sup>38-40</sup>

Changes in caregiver HRQL (as measured by EQ-5D) are extremely small and unrelated to diagnosis. Our results are consistent with those from a large cohort of caregivers of people with moderate to severe Alzheimer's disease in three European countries, which similarly reported a small, non-statistically significant decline in mean EQ-5D index score over 18 months which did not vary by dementia severity.<sup>33</sup> Whilst there are limitations of the EQ-5D as a measure for change in HRQL among caregivers (as described above), our results could also be explained in part by caregivers' increasing adoption of coping strategies (behavioural and cognitive) to mitigate the impact of increasing burden on HRQL,<sup>41</sup> including the use of formal and informal support.<sup>42, 43</sup>

Among caregivers of patients diagnosed with dementia, increases in caregiver burden were associated with greater dissatisfaction with the services the caregiver received. While this association may not be causal, it is plausible that better support for caregivers may reduce their level of burden. Studies indicate that educational and psychosocial interventions for caregivers can have beneficial effects on burden and psychological well-being.<sup>42, 44, 45</sup> It is known that uptake of services targeted at caregivers is low for reasons including a perceived lack of need or lack of awareness about services.<sup>46</sup>

### *Implications*

Despite a small increase in average burden over time, caregivers report only minor reductions in their EQ-5D-3L and most are satisfied with the support they receive. Further study to understand the attitudes and behaviour of informal caregivers is needed before an appropriate response can be made by policymakers and formal carers. One priority is to conduct studies using more specific HRQL instruments which can adequately capture the psychological and emotional effects of caring for a person with dementia. It is also important to understand whether the trends observed over the first two years following first attendance at a MAS continue or change subsequently, as patients' symptoms develop and other events such as initiation of formal care may take place.



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## **CONFLICTS OF INTEREST**

Authors have no conflicts of interest to declare.

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**Table 1: Characteristics of caregivers who responded on at least one follow-up occasion (at 6, 12 or 24 months) compared to non-respondents**

| Caregiver characteristics            | Respondents<br>(n=653) | Non-respondents<br>(n=367) | p-value* |
|--------------------------------------|------------------------|----------------------------|----------|
| Mean age (SD)                        | 67.9 (12.8)            | 62.3 (14.3)                | <0.001   |
| Female (%)                           | 452 (69.2)             | 254 (69.2)                 | 0.998    |
| Black, Asian and minority ethnic (%) | 24 (3.7)               | 23 (6.5)                   | 0.055    |
| Missing                              | 7                      | 15                         |          |
| Deprivation quintile (%)             |                        |                            |          |
| 1 – least deprived                   | 185 (28.7)             | 93 (25.8)                  | 0.237    |
| 2                                    | 149 (23.1)             | 74 (20.6)                  |          |
| 3                                    | 129 (20.0)             | 81 (22.5)                  |          |
| 4                                    | 105 (16.3)             | 54 (15.0)                  |          |
| 5 – most deprived                    | 76 (11.8)              | 68 (16.1)                  |          |
| Missing                              | 9                      | 7                          |          |
| Relationship to patient (%)          |                        |                            |          |
| Spouse                               | 453 (69.9)             | 156 (44.2)                 | <0.001   |
| Son/daughter                         | 144 (22.2)             | 150 (42.5)                 |          |
| Other                                | 51 (7.9)               | 47 (13.3)                  |          |
| Missing                              | 5                      | 14                         |          |
| Living with patient (%)              | 489 (75.8)             | 188 (53.6)                 | <0.001   |
| Missing                              | 8                      | 16                         |          |
| Patient's diagnosis (%)              |                        |                            |          |
| Dementia                             | 406 (63.9)             | NA                         | NA       |
| Mild cognitive impairment            | 151 (23.8)             | NA                         | NA       |



|   |             |             |              |
|---|-------------|-------------|--------------|
| Other                                   | 23 (3.6)    | NA          | NA           |
| No diagnosis                            | 55 (8.7)    | NA          | NA           |
| Missing                                 | 18          |             |              |
| Zarit Burden Interview (ZBI) score (SD) |             |             |              |
| Baseline (n=629)                        | 12.5 (8.7)  | 13.2 (8.8)  | 0.203        |
| 6 months (n=544)                        | 12.7 (9.0)  | NA          | NA           |
| 12 months (n=436)                       | 13.1 (9.8)  | NA          | NA           |
| 24 months (n=185)                       | 14.7 (8.4)  | NA          | NA           |
| EQ-5D-3L index score (SD)               |             |             |              |
| Baseline (n=634)                        | 0.79 (0.24) | 0.82 (0.22) | <b>0.025</b> |
| 6 months (n=560)                        | 0.78 (0.25) | NA          | NA           |
| 12 months (n=440)                       | 0.78 (0.24) | NA          | NA           |
| 24 months (n=183)                       | 0.74 (0.26) | NA          | NA           |

\* from  $\chi^2$  test or t-test; NA = not available

**Table 2: Unadjusted change in caregiver burden and HRQL between baseline and follow-up (6, 12 and 24 months) by patient's diagnosis**

| Zarit Burden Interview score | Mean score at baseline (SD) | Mean score at follow-up (SD) | Mean change (95% CI)           |
|------------------------------|-----------------------------|------------------------------|--------------------------------|
| Overall (6 months) (n=530)   | 12.3 (8.7)                  | 12.7 (9.0)                   | 0.38 (-.15 to .91)             |
| Dementia (n=291)             | 13.7 (8.8)                  | 14.2 (8.9)                   | 0.48 (-.27 to 1.22)            |
| MCI (n=114)                  | 10.9 (8.6)                  | 11.1 (8.9)                   | 0.21 (-.83 to 1.26)            |
| No diagnosis (n=74)          | 10.6 (9.0)                  | 10.1 (9.4)                   | -0.47 (-1.84 to .89)           |
| Overall (12 months) (n=420)  | 12.3 (8.8)                  | 13.1 (9.8)                   | <b>0.82 (.13 to 1.50) *</b>    |
| Dementia (n=271)             | 13.3 (9.0)                  | 14.3 (9.7)                   | <b>1.1 (.20 to 1.94) *</b>     |
| MCI (n=98)                   | 10.3 (8.4)                  | 11.4 (9.7)                   | <b>1.1 (.03 to 2.2) *</b>      |
| No diagnosis (n=34)          | 9.4 (7.6)                   | 9.0 (9.5)                    | -0.32 (-3.65 to 3.00)          |
| Overall (24 months) (n=178)  | 12.3 (8.3)                  | 14.8 (8.5)                   | <b>2.5 (1.4 to 3.6) *</b>      |
| Dementia (n=120)             | 13.0 (8.6)                  | 15.4 (7.9)                   | <b>2.4 (1.1 to 3.7) *</b>      |
| MCI (n=41)                   | 10.7 (7.4)                  | 13.9 (9.0)                   | <b>3.2 (0.8 to 5.6) *</b>      |
| No diagnosis (n=13)          | 10.5 (8.5)                  | 12.3 (11.6)                  | 1.8 (-2.3 to 5.8)              |
| <b>EQ-5D-3L Index</b>        |                             |                              |                                |
| Overall (6 months) (n=549)   | 0.78 (0.25)                 | 0.78 (0.25)                  | -0.006 (-.02 to .01)           |
| Dementia (n=303)             | 0.80 (0.22)                 | 0.79 (0.24)                  | -0.01 (-.03 to .006)           |
| MCI (n=117)                  | 0.77 (0.28)                 | 0.78 (0.24)                  | 0.005 (-.03 to .04)            |
| No diagnosis (n=76)          | 0.78 (0.27)                 | 0.75 (0.30)                  | -0.03 (-.09 to .03)            |
| Overall (12 months) (n=428)  | 0.79 (0.24)                 | 0.78 (0.23)                  | -0.01 (-.03 to .007)           |
| Dementia (n=274)             | 0.79 (0.24)                 | 0.78 (0.24)                  | -0.005 (-.03 to .02)           |
| MCI (n=103)                  | 0.80 (0.23)                 | 0.77 (0.22)                  | -0.03 (-.06 to .001)           |
| No diagnosis (n=33)          | 0.83 (0.24)                 | 0.78 (0.30)                  | -0.05 (-0.2 to .04)            |
| Overall (24 months) (n=178)  | 0.79 (0.23)                 | 0.74 (0.26)                  | <b>-0.05 (-.08 to -.02) *</b>  |
| Dementia (n=119)             | 0.80 (0.23)                 | 0.76 (0.26)                  | <b>-0.04 (-.08 to -.004) *</b> |
| MCI (n=42)                   | 0.79 (0.24)                 | 0.71 (0.27)                  | <b>-0.08 (-0.1 to -.03) *</b>  |
| No diagnosis (n=13)          | 0.79 (0.23)                 | 0.77 (0.23)                  | -0.02 (-.09 to .05)            |

\*Statistically significant change at 0.05 level

**Table 3: Cross-sectional associations between caregivers' burden and HRQL at baseline, 6, 12 and 24 months**

| Zarit Burden Interview SF score | EQ-5D-3L Index score             |                                |
|---------------------------------|----------------------------------|--------------------------------|
|                                 | Unadjusted difference † (95% CI) | Adjusted difference ‡ (95% CI) |
| Baseline                        | -0.005 (-.008 to -.003) *        | -0.006 (-.009 to -.004) *      |
| 6 months                        | -0.004 (-.006 to -.0009) *       | -0.004 (-.007 to -.002) *      |
| 12 months                       | -0.006 (-.009 to -.003) *        | -0.006 (-.009 to -.003) *      |
| 24 months                       | -0.003 (-.007 to .002)           | -0.002 (-.007 to .003)         |

\* Statistically significant at 0.05 level. † Difference in EQ-5D-3L index score per point increase in Zarit Burden Interview short form score; adjusted for clustering by clinic. ‡ Adjusted for age, sex, ethnicity, deprivation, relationship to patient and clustering by clinic, and at 6 and 12 months, adjusted for patient's diagnosis.

**Table 4: Mean change and adjusted difference in change in Zarit Burden Interview score between baseline and 6, 12 and 24 months by caregivers' and patients' characteristics**

| Characteristics                | 6 months         |  | 12 months        |  | 24 months        |  |
|--------------------------------|------------------|--|------------------|--|------------------|--|
|                                | Mean change (SD) | Adjusted difference in change (95% CI) † | Mean change (SD) | Adjusted difference in change (95% CI) † | Mean change (SD) | Adjusted difference in change (95% CI) † |
| Age (years)                    | 0.04             | 0.01 (-.06 to .09)                       | 0.05             | 0.05 (-.06 to 0.2)                       | 0.07             | 0.08 (-0.1 to 0.3)                       |
| Sex: Male                      | 0.18 (6.0)       | Reference                                | 0.83 (6.9)       | Reference                                | 3.6 (8.3)        | Reference                                |
| Female                         | 0.46 (6.3)       | 1.2 (-0.6 to 3.1)                        | 0.81 (7.2)       | 0.07 (-.03 to 0.2)                       | 2.0 (7.2)        | -0.3 (-3.2 to 2.8)                       |
| Ethnicity: White/White British | 0.51 (6.1)       | Reference                                | 0.87 (7.1)       | Reference                                | 2.7 (7.4)        | Reference                                |
| BAME ‡                         | -2.5 (8.6)       | -1.4 (-5.7 to 3.0)                       | -1.7 (7.1)       | -1.5 (-5.1 to 2.0)                       | -4.0 (9.2)       | -4.0 (-10.0 to 1.9)                      |
| Deprivation quintiles          |                  |  |                  |  |                  |  |
| 1 – least deprived             | 0.80 (6.0)       | Reference                                | 1.4 (6.7)        | Reference                                | 1.1 (6.4)        | Reference                                |
| 2                              | 0.67 (6.7)       | -0.4 (-2.8 to 1.9)                       | 0.97 (6.8)       | 0.2 (-2.6 to 2.9)                        | 2.9 (6.4)        | 4.1 (-0.7 to 9.0)                        |
| 3                              | 1.3 (6.3)        | 0.2 (-2.1 to 2.4)                        | 1.4 (8.0)        | 0.6 (-2.8 to 4.1)                        | 1.3 (8.5)        | 1.5 (-4.3 to 7.3)                        |
| 4                              | -0.71 (6.1)      | -1.2 (-4.0 to 1.6)                       | -1.0 (6.4)       | -2.1 (-4.8 to 0.7)                       | 2.4 (8.2)        | 1.3 (-5.7 to 8.3)                        |
| 5 – most deprived              | -1.1 (5.1)       | -1.9 (-4.5 to 0.7)                       | 1.1 (6.8)        | 0.2 (-3.9 to 4.4)                        | 8.0 (7.6)        | <b>7.2 (.09 to 14.3) *</b>               |
| Relationship to patient        |                  |  |                  |  |                  |  |
| Spouse                         | 0.44 (6.5)       | Reference                                | 0.80 (7.2)       | Reference                                | 2.7 (7.4)        | Reference                                |
| Son/daughter                   | -0.03 (5.8)      | 0.5 (-1.8 to 2.7)                        | 0.79 (7.3)       | 2.3 (-1.2 to 5.9)                        | 1.1 (8.3)        | 1.3 (-5.4 to 8.0)                        |
| Other                          | 0.97 (5.0)       | -0.4 (-3.1 to 2.3)                       | 1.1 (6.0)        | 1.2 (-2.1 to 4.5)                        | 3.9 (6.7)        | 1.9 (-3.0 to 6.7)                        |
| Patient's diagnosis            |                  |  |                  |  |                  |  |
| Dementia                       | 0.48 (6.5)       | Reference                                | 1.1 (7.3)        | Reference                                | 2.4 (7.3)        | Reference                                |
| MCI                            | 0.21 (5.7)       | -0.9 (-2.8 to 0.9)                       | 1.1 (5.4)        | -0.6 (-2.3 to 1.0)                       | 3.2 (7.7)        | 0.3 (-3.0 to 3.7)                        |
| No diagnosis                   | -0.47 (5.9)      | -1.7 (-3.5 to 0.2)                       | -0.32 (9.5)      | -2.0 (-6.7 to 2.7)                       | -2.7 (18.1)      | -0.9 (-8.4 to 6.6)                       |
| Patient's DEMQOL score §       | 0.005            | -0.03 (-0.1 to .03)                      | 0.007            | -0.05 (-0.1 to .04)                      | -0.03            | -0.05 (-0.2 to .07)                      |

Positive change score indicates increase in caregiver burden. \* Statistically significant at 0.05 level; † Adjusted for age, sex, ethnicity, deprivation, relationship to patient, patient's diagnosis, patient's HRQL and caregiver burden score at baseline and clustering by clinic (6 months: n=486; 12 months: n=400; 24 months: n=170); 95% confidence interval with Bonferroni correction. ‡ Black, Asian and minority ethnic; § Contemporaneous with outcome.

**Table 5: Mean change and adjusted differences in change in EQ-5D-3L Index between baseline and 6, 12 and 24 months by caregivers' and patients' characteristics**

| Characteristics                | 6 months         |  | 12 months        |  | 24 months        |  |
|--------------------------------|------------------|--|------------------|--|------------------|--|
|                                | Mean change (SD) | Adjusted difference in change (95% CI) † | Mean change (SD) | Adjusted difference in change (95% CI) † | Mean change (SD) | Adjusted difference in change (95% CI) † |
| Age (years)                    | -0.001           | -0.003 (-.006 to .001)                   | -0.0007          | <b>-0.004 (-.006 to -.001) *</b>         | 0.001            | -0.001 (-.005 to .003)                   |
| Sex: Male                      | -0.01 (0.24)     | Reference                                | -0.01 (0.21)     | Reference                                | -0.03 (0.23)     | Reference                                |
| Female                         | -0.003 (0.19)    | 0.005 (-.05 to .06)                      | -0.01 (0.20)     | 0.005 (-.05 to .06)                      | -0.06 (0.20)     | -0.03 (-0.1 to .07)                      |
| Ethnicity: White/White British | -0.009 (0.21)    | Reference                                | -0.01 (0.20)     | Reference                                | -0.05 (0.21)     | Reference                                |
| BAME ‡                         | 0.03 (0.18)      | 0.05 (-.03 to 0.1)                       | -0.04 (0.34)     | -0.06 (-0.3 to 0.2)                      | -0.06 (0.07)     | 0.1 (-0.1 to 0.4)                        |
| Deprivation quintiles          |                  |  |                  |  |                  |  |
| 1 – least deprived             | -0.02 (0.15)     | Reference                                | -0.05 (0.19)     | Reference                                | -0.04 (0.17)     | Reference                                |
| 2                              | -0.02 (0.21)     | -0.02 (-.09 to .05)                      | -0.02 (0.16)     | 0.004 (-.06 to .07)                      | -0.02 (0.20)     | 0.02 (-.09 to 0.1)                       |
| 3                              | -0.02 (0.26)     | -0.01 (-.09 to .06)                      | -0.005 (0.17)    | 0.04 (-.03 to 0.1)                       | -0.08 (0.22)     | -0.07 (-0.2 to .04)                      |
| 4                              | 0.005 (0.23)     | -0.03 (-0.1 to .04)                      | 0.07 (0.23)      | 0.07 (-.02 to 0.2)                       | 0.005 (0.24)     | 0.002 (-0.2 to 0.2)                      |
| 5 – most deprived              | 0.04 (0.21)      | 0.003 (-.06 to .07)                      | 0.0002 (0.27)    | 0.02 (-.09 to 0.1)                       | -0.16 (0.26)     | -0.1 (-0.3 to .06)                       |
| Relationship to patient        |                  |  |                  |  |                  |  |
| Spouse                         | -0.001 (0.21)    | Reference                                | -0.01 (0.20)     | Reference                                | -0.03 (0.21)     | Reference                                |
| Son/daughter                   | -0.01 (0.20)     | -0.05 (-0.1 to .05)                      | -0.03 (0.21)     | -0.06 (-0.1 to .01)                      | -0.1 (0.21)      | -0.09 (-0.3 to .08)                      |
| Other                          | -0.03 (0.22)     | -0.04 (-0.2 to .07)                      | 0.04 (0.17)      | 0.01 (-.06 to .09)                       | -0.005 (0.18)    | 0.03 (-.09 to 0.2)                       |
| Patient's diagnosis            |                  |  |                  |  |                  |  |
| Dementia                       | -0.01 (0.18)     | Reference                                | -0.005 (0.20)    | Reference                                | -0.04 (0.21)     | Reference                                |
| MCI                            | 0.005 (0.19)     | 0.002 (-.05 to .06)                      | -0.03 (0.16)     | -0.04 (-0.1 to .02)                      | -0.08 (0.17)     | -0.03 (-0.1 to .08)                      |
| No diagnosis                   | -0.03 (0.27)     | -0.03 (-0.1 to .04)                      | -0.05 (0.25)     | -0.07 (-0.2 to .07)                      | 0.21 (0.43)      | 0.009 (-0.1 to 0.1)                      |
| ZBI score §                    | 0.001            | -0.001 (-.005 to .003)                   | -0.003           | <b>-0.005 (-.008 to -.0007) *</b>        | -0.003           | -0.002 (-.007 to .003)                   |

|                                     |        |                         |        |                        |        |                        |
|-------------------------------------|--------|-------------------------|--------|------------------------|--------|------------------------|
| Patient's DEMQOL score <sup>§</sup> | -0.001 | -0.0006 (-.002 to .001) | 0.0004 | 0.0004 (-.001 to .002) | 0.0005 | 0.0008 (-.003 to .005) |
|-------------------------------------|--------|-------------------------|--------|------------------------|--------|------------------------|

Positive change score indicates improvement in HRQL. \*Statistically significant at 0.05 level; † Adjusted for age, sex, ethnicity, deprivation, relationship to patient, patient's diagnosis, contemporaneous caregiver burden score, patient's HRQL score and EQ-5D-3L Index at baseline and clustering by clinic (6 months: n=485; 12 months: n=398; 24 months: n=169); 95% confidence interval with Bonferroni correction. ‡ Black, Asian and minority ethnic; § Contemporaneous with outcome.

**Table 6: Adjusted differences in changes in Zarit Burden Interview (ZBI) score and EQ-5D-3L Index at 6,12 and 24 months by caregiver's satisfaction with services, among those caring for a patient diagnosed with dementia.**

| Satisfaction with services | ZBI Adjusted difference in change (95% CI) † |                           |                    | EQ-5D-3L Adjusted difference in change (95% CI) † |                     |                   |
|----------------------------|--|---------------------------|--------------------|---|---------------------|-------------------|
|                            | 6 months                                     | 12 months                 | 24 months          | 6 months  | 12 months           | 24 months         |
| A lot                      | Reference                                    | Reference                 | Reference          | Reference   | Reference           | Reference         |
| Quite a bit                | -0.9 (-3.7 to 1.9)                           | 1.7 (-2.2 to 5.6)         | 3.0 (-9.2 to 15.2) | 0.07 (-0.003 to 0.1)                              | 0.01 (-.08 to 0.1)  | 0.2 (-.02 to 0.5) |
| A little                   | 2.2 (-1.9 to 6.3)                            | <b>4.0 (0.4 to 7.6) *</b> | 3.6 (-5.6 to 12.7) | -0.02 (-0.1 to .09)                               | 0.03 (-.09 to 0.1)  | 0.2 (-.02 to 0.4) |
| Not at all                 | 2.2 (-0.7 to 5.2)                            | <b>5.4 (1.5 to 9.3) *</b> | 2.5 (-7.6 to 12.5) | -0.002 (-0.1 to 0.1)                              | -0.03 (-0.1 to 0.1) | 0.1 (-0.1 to 0.4) |

Positive change in ZBI score indicates increase in caregiver burden. Positive change in EQ-5D-3L score indicates improvement in HRQL.

\*Statistically significant at 0.05 level. † Adjusted for age, sex, ethnicity, deprivation, relationship to patient, patient's HRQL and score at baseline and clustering by clinic; HRQL outcome additionally adjusted for contemporaneous burden score