Change in Health-related Quality of Life After Referral to Memory Assessment Services

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Title: Change in health-related quality of life after referral to Memory Assessment Services

Short title: Change in HRQL after referral to memory clinics

Authors: Min Hae PARK PhD[1], Sarah C. SMITH PhD[1], Theopisti Chrysanthaki PhD[2], Jenny Neuburger PhD[1], Craig W. RITCHIE MD PhD[3], A.A. Jolijn HENDRIKS PhD[1], Nick BLACK MD [1]

Affiliations: [1] Department of Health Services Research & Policy, London School of Hygiene & Tropical Medicine, 15-17 Tavistock Place, London WC1H 9SH, UK**;** [2] School of Health Sciences, Faculty of Health & Medical Sciences, University of Surrey, Guildford, Surrey GU2 7XH, UK**;** [3] Centre for Dementia Prevention, University of Edinburgh, Edinburgh EH10 5HF, UK

Corresponding author: Dr Min Hae Park, Department of Health Services Research & Policy, London School of Hygiene & Tropical Medicine, 15-17 Tavistock Place, London WC1H 9SH, UK. Telephone: +44(0)2079272714. Email: minhae.park@lshtm.ac.uk.

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ABSTRACT

Despite strong support for the provision of memory assessment services (MASs) in England and other countries, their effectiveness in improving patient outcomes is uncertain. We aimed to describe change in patients' health related quality of life (HRQL) six months after referral to MASs and to examine associations with patient characteristics and use of post-diagnostic interventions.

Data from 883 patients referred to 69 MASs and their informal caregivers (n=569) were collected at referral and 6 months later. Multivariable linear regression was used to examine associations of change in HRQL (DEMQOL, DEMQOL-Proxy) with patient characteristics (age, sex, ethnicity, socioeconomic deprivation and comorbidity) and use of post-diagnostic interventions (anti-dementia medications and non-pharmacological therapies).

Mean HRQL improved, irrespective of diagnosis: self-reported HRQL increased 3.4 points (95% CI 2.7 to 4.1), proxy-reported HRQL 1.3 points (95% CI 0.5 to 2.1). HRQL change was not associated with any of the patient characteristics studied. Patients with dementia (54%) receiving anti-dementia drugs reported greater improvement in their HRQL but those using non-pharmacological therapies reported less improvement than those not.

HRQL improves in the first 6 months after referral to MASs. Research is needed to determine longer-term sustainability of the benefits and the cost-effectiveness of MASs.

KEY WORDS: Dementia; Memory Assessment Services; Memory Clinics; Post-diagnostic interventions; Health-related Quality of Life

INTRODUCTION

Over the past decade, there has been a significant increase in the provision of memory assessment services (MASs) in England and in other countries.[1] MASs, frequently referred to as memory clinics, are ambulatory clinics that provide an integrated multi-professional approach.[2] Their activities include: diagnostic assessment of new referrals; provision of post-diagnostic support (both pharmacological and non-pharmacological); and follow-up.[3-6] By 2014, it was estimated that approximately £125m a year was spent on MASs in England.[1]

Despite strong support for their introduction, it has been recognised that the effectiveness of MASs in improving patient outcomes is uncertain.[7] In a recent review of the evidence, Banerjee concluded that there is a "lack of studies that have evaluated the absolute and relative impact of different models of diagnostic services or the impact of diagnosis and stage of illness at diagnosis."[8] This partly reflects the methodological challenges of evaluating a complex intervention that not only includes a wide range of diagnostic and therapeutic components but also one in which the components vary between MASs. Research has therefore either focused on single components,[9,10] on a single MAS [11] or have focused on patients' experiences and satisfaction.[12-16]

The aims of this study were: to describe the change in health related quality of life (HRQL) over the first 6 months after first referral to MAS; to assess whether patient characteristics, including diagnosis, are associated with changes in HRQL; and to determine if use of anti-dementia drugs and non-pharmacological post-diagnostic therapies are associated with improved HRQL among those patients diagnosed with dementia.

METHODS

Sampling

Initially, 80 MASs were randomly selected from 212 clinics identified by the Royal College of Psychiatrists in their national survey.[1] The survey is thought to have identified virtually all services in the country, through a review of existing registers, internet searches, and direct contact with NHS Trusts and key individuals from each Trust (clinical audit leads, chief executives and medical directors). Subsequently two MASs did not participate, five recruited fewer than six patients each and were excluded, and four sites did not take part in follow-up data collection at 6 months, leaving 69 MASs retained at 6 month follow up.[17] The selected services were representative of all MASs in England based on data from the national survey: number of new referrals per month (63 vs. 72 nationally); mean waiting time for first appointment (5.8 vs. 5.2 weeks); and accredited by the Royal College of Psychiatrists (26% vs. 30%).[1]

Patients referred for a first appointment between September 2014 and April 2015 and their informal caregivers (if present) were eligible for inclusion in the study, provided they had enough English language to understand the consent process and complete the questionnaires. Each site recruited consecutive referrals until 25 patients were included (maximum number of 25 patients per site chosen based on the sample size requirements). Details have been reported elsewhere.[17]

Data collection procedures

Questionnaires were completed by patients (interviewer administered) and their informal caregiver (self-administered) at the time of first referral and 6 months later. Data on patients' socio-demographic characteristics were collected at baseline, including: age (categorised as <75 years, 75-79 years, 80-84 years, ≥85 years); ethnicity (white or other);

socio-economic status (quintiles of the national ranking of Index of Multiple Deprivation scores based on patients' residential postcodes).[18]

The patient questionnaire included disease-specific (DEMQOL [19]) and generic (EQ-5D-3L [20]) HRQL instruments. DEMQOL is a 28-item instrument developed for the UK population. Each item is scored on a four-point scale, with a higher score indicating better HRQL. We used a scoring algorithm based on modern psychometric methods (Rasch Measurement Theory) to generate scores.[21] For analysis, the scores derived using this algorithm (referred to as equated scores) were linearly transformed to range from 0 to 100. The EQ-5D-3L has five items, each covering one domain: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each item has three levels of response. A summary EQ-5D-3L index score was calculated using value sets derived from a UK general population survey to weight and combine responses.[22] A score of 0 represents death and 1 represents perfect health, with scores less than 0 permitted.

Informal caregivers completed a proxy-reported disease specific instrument of the patient's HRQL (DEMQOL-Proxy) and also a proxy-reported generic HRQL instrument (EQ-5D-3L proxy). DEMQOL-Proxy has 31 items with responses on the same four-point scale as DEMQOL; equated scores were derived using the revised scoring algorithm described above.[21] EQ-5D-3L proxy has the same items as self-reported EQ-5D-3L and is scored in the same way. Carers also completed questions on the patient's use of health and social care services in the past month.

Interviewers extracted data from the patient's record on whether the patient had any pre-specified comorbid conditions (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, based on an existing instrument [23]). The number of comorbidities was categorised as: 0, 1, 2 and 3 or more. In addition, data on cognitive function at baseline were extracted from the records and used to derive a three-category cognitive function variable based on tertiles of Mini-Mental State Examination (MMSE) score [24]: category 1 (lowest function) equivalent to MMSE score <24, category 2 MMSE score 24-27 and category 3 (highest function) MMSE score ≥28. The tertile cut offs were also justified on the basis of established cut offs supportive of a diagnosis of dementia at a score of <24.[25]

Additionally at 6 month follow up, interviewers extracted information on the patient's diagnosis, if one had been made, and informal caregivers provided information on the anti-dementia medications the patient had taken during the preceding four weeks and receipt of any non-pharmacological therapies, such as cognitive behaviour therapy, music and/or dance therapy, animal assisted therapies, social engagement groups, walking groups, life story work, peer support groups, befriending services, memory cafes and reminiscence therapy. At 6 months most interviews (96%) were conducted in the participant's home, with a small minority conducted at the MAS.

Statistical analysis

Chi-squared tests were used to compare baseline characteristics of respondents at 6 months with those of non-respondents. Patient characteristics were summarized as means and standard deviations (SDs) or percentages. Change in each measure of HRQL was assessed using paired *t*-tests to compare mean scores at baseline and 6 months. Changes in HRQL among patients with and without a diagnosis and by diagnostic category (dementia, MCI, other, none) were compared using *t*-tests for difference in means and linear regression.

Multivariable linear regression was used to examine the relationships between patient characteristics and change in HRQL (DEMQOL and DEMQOL-Proxy) at 6 months, with adjustment for patient characteristics (age, sex, ethnicity, socioeconomic status, comorbidities, diagnosis) and HRQL score at baseline to estimate adjusted differences in HRQL change. Clustering of patients within MASs was taken into account by using robust (clustered) standard errors. Linear regression was also used to assess the relationships between post-diagnostic service use (anti-dementia drugs and non-pharmacological therapies) and change in HRQL in patients diagnosed with dementia, adjusting for patient characteristics, cognitive function and HRQL at baseline, and each other (non-pharmacological therapies in the case of anti-dementia drugs and vice versa). Due to clustering of the use of non-pharmacological interventions in only around half of all sites, we adjusted for clinic as a random effect. Results of linear regression models are presented as adjusted differences in HRQL 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).

To assess the effects of early or late follow-up on outcomes, sensitivity analyses were conducted excluding data from 166 participants followed up at <5 or >9 months after baseline, or with unknown date of follow up.

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

Ethical 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

Recruitment and response

Participants recruited into the study at baseline were slightly younger and had a higher proportion of men when compared with referrals who did not take part in the study, but there was no significant difference in socio-economic status.[17] Comparison with cognitive function data from eight clinics for all new referrals over the study recruitment period (n=617 patients) also indicated that patients with lowest cognitive function were slightly underrepresented in our sample.

Of the 1318 patients eligible for follow up at six months (944 of whom had carers also recruited), 883 (67%) patients and 569 (60%) carers completed questionnaires at 6 months and form the main analysis sample in this study (flow chart showing sample sizes is presented in Supplemental Figure 1). Of these, 306 patients with a diagnosis of dementia and data on use of post-diagnostic interventions were included in sub-group analyses of patients with dementia.

The mean duration of follow up was 6.5 months (SD 0.8; 98% between 5 and 9 months). Respondents at 6 months were similar to non-respondents for most characteristics measured at baseline (age, sex, ethnicity, co-morbidities, self-reported HRQL (DEMQOL and EQ-5D), proxy-reported HQL (EQ-5D Proxy), and whether or not they were accompanied by a carer who consented into the study). However, respondents were less likely to be from the most deprived areas (14% v 21%, $p<0.001$), less likely to have low cognitive function (MMSE score<24) (39% v 50%, $p=0.003$), and had higher DEMQOL-Proxy scores (44.2 v 41.8, $p=0.004$). Less than 7% of data were missing for all variables except cognitive function (20% missing). Cognitive function data were more likely to be missing among those with no

comorbidity (31% v 18% missing, *p*=0.001) and those who were not using non-pharmacological therapies (21% v 11% missing, *p*=0.021), but was not associated with any other patient characteristics including diagnosis and HRQL at baseline or 6 months (DEMQOL and DEQMOL-Proxy scores). Patients with a proxy in the study were more likely to be male (53% v 40%, *p*<0.001) and to have a diagnosis of dementia (58% v 42%, *p*<0.001) compared to those without a participating carer, but there was no difference in age, ethnicity, SES, comorbidity or cognitive function.

Patient characteristics

The socio-demographic characteristics of patients are described in Table 1. Six months after the initial referral to the MAS, 83% had received a diagnosis. About half had been diagnosed with dementia, a quarter with MCI and 5% with various other diagnoses (including depression, alcohol related diagnosis, cerebrovascular diseases, syndromic conditions and other psychiatric diagnoses).

Of those with dementia, 245 (55%) had Alzheimer's disease, 104 (24%) mixed or unspecified dementia, 73 (17%) vascular dementia, 8 (2%) dementia with Lewy bodies, 8 (2%) Parkinson's disease, and 3 (1%) fronto-temporal dementia.

Use of post-diagnosis interventions

Of 306 patients diagnosed with dementia and with data on use of post-diagnostic interventions, 186 (61%) were being treated with anti-dementia medications: donepezil (65%), memantine (19%), rivastigmine (11%), galantamine (2%) and unspecified (3%). Patients with a diagnosis of Alzheimer's disease were most likely to be taking anti-dementia drugs (77%), while the lowest proportion of use was among those diagnosed with vascular

dementia (14%) (p<0.001). Use of anti-dementia drugs was higher among patients without comorbidities (72%) than those with comorbid conditions (58%) (p=0.04). Of the patients who were not diagnosed with dementia (and had data on use of post-diagnostic interventions, n=218), 12 (6%) had been prescribed an anti-dementia drug: 1% (n=1) of those with MCI, 24% (n=5) of those with other diagnosis, and 8% (n=6) of those with no diagnosis.

Only 67 (22%) patients with dementia were using non-pharmacological interventions. Of these, 37 (55%) were also using anti-dementia drugs. Most (73%) patients using non-pharmacological interventions received one type of therapy or service, 21% two and 6% three or more. The most frequent were social engagement groups (used by 10%), memory cafes (4%), cognitive behaviour therapy (3%) and befriending services (3%). These interventions were also being used by 27 people (12%) who had not been diagnosed with dementia.

Change in health related quality of life

Patients on average reported their HRQL had improved between baseline and 6 months: mean DEMQOL score increased 3.4 points (95% CI 2.7 to 4.1), equivalent to an effect size of 0.28 SD; EQ-5D score rose 0.02 (effect size: 0.07 SD). Carers also reported patient HRQL had improved, according to DEMQOL-Proxy, though by a smaller amount (1.3 points; effect size: 0.14 SD) (Table 2).

The pattern of improvement in self-reported HRQL (DEMQOL) was similar for those diagnosed with dementia, with MCI or with no diagnosis. For self-reported EQ-5D improvement was only seen for those with a diagnosis of dementia. For proxy-reported

HRQL (DEMQOL-Proxy), carers reported improvement only for those with a diagnosis of dementia or no diagnosis, and did not report improvement for those with MCI.

Association between patient characteristics and change in HRQL

Overall, change in HRQL over time was not associated with any patient characteristics in unadjusted or adjusted analyses, for both self-reported (Table 3) and proxy-reported measures of HRQL (Table 4). Similarly, cognitive function was not associated with changes in self-reported HRQL (DEMQOL score) or proxy-reported HRQL (DEMQOL-Proxy score) in adjusted analyses (Supplemental Table 1).

Association between post-diagnostic interventions and change in HRQL in dementia

Among patients diagnosed with dementia, greater improvement in self-reported HRQL was associated with use of anti-dementia medications in unadjusted and adjusted analyses (Table 5): the adjusted change in DEMQOL score was 3.3 points (95% CI 1.4 to 5.3) greater among patients using anti-dementia medications (effect size: 0.27 SD). Although there was no significant effect of non-pharmacological therapies on self-reported HRQL in unadjusted analyses, after adjustment a significantly smaller improvement in DEMQOL score was observed compared to those who did not use these services: adjusted difference -2.4 points (95% CI -4.8 to -0.003; effect size: -0.20 SD). In both unadjusted and adjusted analyses, proxy-reported HRQL showed no significant association with either anti-dementia drugs or non-pharmacological therapies.

Sensitivity analyses excluding cognitive function as a covariate from the multivariable model resulted in a smaller but still positive association between use of anti-dementia drugs and

improvement in HRQL (2.3 points, 95% CI 0.4 to 4.2; effect size: 0.19), while the effect size for non-pharmacological interventions was unchanged.

DISCUSSION

Main findings

Over half of patients who were referred to MASs for memory problems were diagnosed with dementia, and a further quarter were diagnosed with MCI. HRQL among patients improved in the first six months after referral, irrespective of diagnosis. The magnitude of change was smaller for proxy-reported measures of HRQL than self-reported measures. Improvement in HRQL measured using EQ-5D (self- and proxy-reported) was smaller than that measured using DEMQOL and DEMQOL-Proxy, but EQ-5D has been shown to have poor construct validity for dementia, and condition-specific measures such as DEMQOL are recommended.[26] Change in HRQL was not associated with any patient characteristics.

Among patients who were diagnosed with dementia, 61% were being treated with anti-dementia drugs and 22% were using non-pharmacological therapies. Anti-dementia drugs were associated with a greater improvement in self-reported HRQL whereas use of non-pharmacological therapies was associated with a smaller improvement. Change in proxy-reported HRQL did not show any association with use of pharmacological or non-pharmacological interventions. In adjusted analyses, cognitive function at baseline was not associated with improvement in HRQL.

Strengths and limitations

This is the largest published study of longitudinal change in HRQL among people referred to MASs. The sample is largely representative of MASs across the whole country and the patients attending them.[17]

However, the study has four main limitations which impact on the interpretation of the findings. First, it is not possible to attribute the observed improvement in HRQL to MASs (diagnosis and post-diagnosis support), since we do not have comparable information on those people who were not referred. Due to the lack of clinical equipoise concerning early assessment and treatment for dementia, a control arm was not considered to be ethical. Second, only two-thirds of participants were followed up at six months. Respondents at six months follow-up were more likely than non-respondents to be more affluent and have better baseline cognitive function and proxy-reported HRQL. This may have led to overestimation of the improvement in self-reported HRQL since higher cognitive function was associated with greater improvement in unadjusted analyses. Third, data on cognitive function were missing for a fifth of participants. However, the proportion of missing values was not associated with most patient characteristics, with the exception of the number of comorbidities and use of non-pharmacological interventions. Sensitivity analyses excluding cognitive function as a covariate from the multivariable model did not change the conclusions of our analyses. Fourth, data on the use of post-diagnostic interventions (pharmacological and non-pharmacological) were not available for patients without a carer participating in the study. As these patients were more likely to be female, women diagnosed with dementia are likely to be underrepresented in our analysis of post-diagnostic interventions.

Comparisons with other studies

A previous study found that referral to a MAS improved HRQL at six months, but the study was confined to one service so its generalizability is uncertain.[11] Based on their findings, Banerjee & Wittenberg modelled the likely cost-effectiveness of memory services which suggested a gain of 0.01-0.02 QALYs per person year would render the service cost-effective.[27] This is the approximate level of improvement reported over the first six months by patients and their carers in this study (based on EQ-5D index), suggesting referral to a MAS may be cost-effective. However, caution is required due to the study limitations described above, and the cost-effectiveness model only considered the benefit of preventing (delaying) admission to residential care and did not include direct costs of diagnostic investigations and post-diagnosis interventions.

The absence of an association with cognitive function at baseline could suggest that improvement in HRQL is feasible in any stage from mild to moderate dementia. However, patients with lower cognitive function at baseline were less likely to be followed up at 6 months, and it is possible that patients with the greatest deterioration in cognitive function are not represented in this sample.

The level of use of anti-dementia drugs in those diagnosed with dementia (61%) is higher than that reported from general practice (35%).[28] However, the latter includes both recently diagnosed patients and people with long-standing dementia in whom treatment may no longer be appropriate. There have been no studies of the frequency of uptake of non-pharmacological post-diagnosis therapies with which our findings can be compared.[29] The association between anti-dementia drug use and HRQL found in this study may be partly due to confounding by indications (or contraindications) for these medications; however, for those who are prescribed drugs, there appears to be a greater improvement in HRQL.

In experimental studies some non-pharmacological interventions have been shown to be effective in improving HRQL and other outcomes.[29-31] There are several possible reasons for the lack of observed benefit of non-pharmacological interventions in our study, which relate to the interventions (heterogeneity of interventions included; the fidelity with which they were provided may not have been as high as in trials; duration of treatment too short for an effect to be apparent) and the patients (lack of compliance; inappropriate expectations of benefit leading to disappointment). There is also the possibility of a reverse causality effect, with patients who have experienced poorer HRQL following diagnosis potentially being more likely to be referred for such interventions.

While our findings point to a potential role of both drugs and non-pharmacological interventions in affecting patients' HRQL, more work is needed to understand the processes underlying changes in HRQL and the other factors that may explain these changes. We are currently undertaking work to explore the associations between service-level factors and HRQL, which may lead to the identification of potential mediators of change and contribute to our understanding of the mechanisms involved.

Implications

Assuming the observed improvement in HRQL reflects the benefits of what can be achieved in normal clinical practice in MASs (rather than the natural history of HRQL in dementia without any intervention), then this study provides evidence of the value of the current policy in many countries to encourage detection and intervention for people with memory problems. Further evidence regarding the underlying mechanisms of change and the sustainability of the benefits beyond six months is needed. The sample in this study is

currently being followed up after 12 months with plans for a further extension to five years being drawn up.

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CONFLICTS OF INTEREST

None

REFERENCES

1. Royal College of Psychiatrists & NHS England. *Second English National Memory Clinics Audit Report.* London2015.
2. Department of Health. *Case for change - memory service for people with dementia. Evidence. Accessed from: http://webarchive.nationalarchives.gov.uk/20130107105354/http:/www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_128580.pdf. Access date July 2016.* London, Crown Copyright2011.
3. Lindesay J, Marudkar M, van Diepen E, et al. The second Leicester survey of memory clinics in the British Isles. *International Journal of Geriatric Psychiatry.* 2002;17(1):41-47.
4. Kelly C. Memory clinics. *Psychiatry and Clinical Neurosciences.* 2007;7:61-63.
5. Jolley D, Moniz-Cook E. Memory clinics in context. *Indian Journal of Psychiatry* 2009;51(Suppl1):S70-S76.
6. Department of Health. *Living well with dementia: a national dementia strategy.* London, Crown Copyright: Department of Health; 9 February 2009 2009.
7. Melis RJ, Meeuwsen EJ, Parker SG, et al. Are memory clinics effective? The odds are in favour of their benefit, but conclusive evidence is not yet available. *J R Soc Med.* 2009;102(11):456-457.
8. Banerjee S. A narrative review of evidence for the provision of memory services. *Int Psychogeriatr.* 2015;27(10):1583-1592.
9. Knapp M, Iemmi V, Romeo R. Dementia care costs and outcomes: a systematic review. *International Journal of Geriatric Psychiatry.* 2013;28(6):551-561.

10. McLaren AN, Lamantia MA, Callahan CM. Systematic review of non-pharmacologic interventions to delay functional decline in community-dwelling patients with dementia. *Aging Ment Health.* 2013;17(6):655-666.

11. Banerjee S, Willis R, Matthews D, et al. Improving the quality of care for mild to moderate dementia: an evaluation of the Croydon Memory Service Model. *International Journal of Geriatric Psychiatry.* 2007;22(8):782-788.

12. Lee L, Hillier LM, Stolee P, et al. Enhancing dementia care: a primary care-based memory clinic. *J Am Geriatr Soc.* 2010;58(11):2197-2204.

13. Abley C, Manthorpe J, Bond J, et al. Patients' and carers' views on communication and information provision when undergoing assessments in memory services. *J Health Serv Res Policy.* 2013;18(3):167-173.

14. Dodd E, Cheston R, Fear T, et al. An evaluation of primary care led dementia diagnostic services in Bristol. *BMC Health Services Research.* 2014;14(1):1-11.

15. Dodd E, Cheston R, Cullum S, et al. Primary care-led dementia diagnosis services in South Gloucestershire: Themes from people and families living with dementia and health care professionals. *Dementia (London).* 2015.

16. Hailey E, Hodge S, Burns A, et al. Patients' and carers' experiences of UK memory services. *International Journal of Geriatric Psychiatry.* 2016;31(6):676-680.

17. Park MH, Smith SC, Neuburger J, et al. Sociodemographic characteristics, cognitive function, and health-related quality of life of patients referred to Memory Assessment Services in England *Alzheimer Dis Assoc Disord.* In Press.

18. Department for Communities and Local Government. *English Indices of Deprivation 2010.* 2011.

19. Smith SC, Lamping DL, Banerjee S, et al. Measurement of health-related quality of life for people with dementia: development of a new instrument (DEMQOL) and an evaluation of current methodology. *Health Technology Assessment.* 2005;9(10):1-93, iii-iv.

20. EuroQol Group. *EQ-5D-3L Health Questionnaire: English version for the UK.* 1990.

21. Smith SC, Hendriks AAJ, Chrysanthaki T, et al. How can we interpret proxy reports of HRQL when it is no longer possible to obtain a self-report? ISOQOL 22nd Annual Conference; 2015; Vancouver, Canada.

22. EuroQol Group. *User Guide: Basic information on how to use EQ-5D.* Rotterdam: EuroQol Research Foundation;2015.

23. Chard J, Kuczawski M, Black N, et al. Outcomes of elective surgery undertaken in independent sector treatment centres and NHS providers in England: audit of patient outcomes in surgery. *BMJ.* 2011;343.

24. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research.* 1975;12(3):189-198.

25. Tombaugh TN, McIntyre NJ. The mini-mental state examination: a comprehensive review. *Journal of the American Geriatrics Society.* 1992;40(9):922-935.

26. Ara R, Duarte A, Harnan S, et al. *Supporting the routine collection of patient reported outcome measures in the National Clinical Audits for assessing cost-effectiveness. Work Package 1: What patient reported outcome measures should be used in the 13 health conditions specified in the 2013/14 National Clinical Audit programme? Economic Evaluation of Health and Social Care Interventions Policy Research Unit. Research Report RR0029.* 2015.

27. Banerjee S, Wittenberg R. Clinical and cost effectiveness of services for early diagnosis and intervention in dementia. *Int J Geriatr Psychiatry.* 2009;24(7):748-754.

28. Donegan K, Fox N, Black N, et al. Secular trends in patterns of diagnosis and treatment for people with dementia in the UK, 2005-2015. *(submitted).* 2016.

29. Knapp M, Black N, Dixon J, et al. *Independent assessment of improvements in dementia care and support since 2009. Report from the Policy Innovation Research Unit and the NIHR School for Social Care Research. Accessed at: http://socialwelfare.bl.uk/subject-areas/services-client-groups/older-adults/policyinnovationresearchunit/1761132014-9AssessingDementiaReport.pdf.* 2014.

30. Olazarán J, Reisberg B, Clare L, et al. Nonpharmacological Therapies in Alzheimer's Disease: A Systematic Review of Efficacy. *Dementia and Geriatric Cognitive Disorders.* 2010;30(2):161-178.

31. Livingston G, Kelly L, Lewis-Holmes E, et al. A systematic review of the clinical effectiveness and cost-effectiveness of sensory, psychological and behavioural interventions for managing agitation in older adults with dementia. *Health Technol Assess.* 2014;18(39):1-226, v-vi.

Table 1: Baseline characteristics and diagnosis of patients followed up at 6 months (n=883)

Characteristic	Mean (SD) or n (%)
Age (years)	77.6 (8.3)
<75	274 (31.0%)
75-79	198 (22.4%)
80-84	232 (26.3%)
≥85	179 (20.3%)
Sex	
Male	436 (49.4%)
Female	447 (50.6%)
Ethnicity	
White/White British	833 (94.8%)
Other ethnicity	46 (5.2%)
Missing	4
Deprivation quintiles	
1 – least deprived	243 (27.9%)
2	189 (21.7%)
3	162 (18.6%)
4	159 (18.3%)
5 – most deprived	117 (13.5%)
Missing	13
Number of comorbidities	
0	183 (20.7%)
1	242 (27.4%)
2	216 (24.5%)
≥3	241 (27.3%)
Missing	1
Diagnosis	
Dementia *	441 (53.5%)
MCI	202 (24.5%)
Other diagnosis	44 (5.3%)
No diagnosis took place	138 (16.7%)
Missing	58
Cognitive function	
1 – lowest function	272 (38.7%)
2	222 (31.6%)
3 – highest function	209 (29.7%)
Missing	180

* Alzheimer's disease, vascular dementia, dementia with Lewy bodies, frontotemporal dementia, mixed or unspecified dementia, dementia in Parkinson's disease

Table 2: Change in self- (n=883) and proxy-reported (n=569) patient HRQL in all patients with both baseline and 6 month scores and by diagnosis

	Score at baseline Mean (SD)	Score at 6 months Mean (SD)	Mean change* (95% CI)
DEMQOL equated score (n=875)	65.4 (12.3)	68.8 (12.7)	**3.4 (2.7 to 4.1)**
Dementia (n=436)	66.5 (12.8)	69.8 (12.7)	**3.3 (2.3 to 4.3)**
MCI (n=202)	65.7 (12.0)	68.7 (12.6)	**3.0 (1.7 to 4.4)**
No diagnosis (n=137)	64.1 (12.0)	67.0 (12.7)	**2.9 (1.1 to 4.8)**
EQ-5D-3L Index score (n=861)	0.71 (0.28)	0.73 (0.28)	**.02 (.01 to .04)**
Dementia (n=428)	0.75 (0.25)	0.77 (0.24)	**.02 (.01 to .05)**
MCI (n=199)	0.70 (0.28)	0.71 (0.31)	.01 (-.02 to .04)
No diagnosis (n=136)	0.67 (0.32)	0.68 (0.33)	.01 (-.04 to .06)
DEMQOL-Proxy equated score (n=563)	57.1 (9.4)	58.4 (10.6)	**1.3 (0.5 to 2.1)**
Dementia (n=308)	55.5 (9.1)	57.0 (10.4)	**1.5 (0.5 to 2.5)**
MCI (n=123)	59.6 (9.6)	59.8 (10.6)	0.2 (-1.4 to 1.9)
No diagnosis (n=80)	58.7 (9.5)	61.2 (10.9)	**2.5 (0.6 to 4.5)**
EQ-5D-3L Proxy Index score (n=538)	0.62 (0.31)	0.60 (0.32)	-.02 (-.04 to .003)
Dementia (n=293)	0.60 (0.30)	0.57 (0.32)	-.03 (-.06 to .004)
MCI (n=117)	0.68 (0.30)	0.65 (0.31)	-.03 (-.08 to .02)
No diagnosis (n=75)	0.62 (0.33)	0.63 (0.32)	.01 (-.05 to .08)

*Positive change score indicates improvement in HRQL. Figures in **bold** $p<0.05$.

Table 3: Change in DEMQOL equated score by patient characteristics (linear regression analyses)

Patient characteristics	Number	DEMQOL equated score at 6 months Mean (SD)	Change (SD) in DEMQOL equated score	Unadjusted difference in change *	Adjusted difference in change †	(95% CI with Bonferroni correction)
Age (years)						
<75	273	65.8 (12.7)	3.5 (9.8)	Reference	Reference	
75-79	197	69.9 (13.2)	5.1 (10.6)	1.5	2.2	(-0.6 to 5.0)
80-84	229	70.2 (12.6)	2.3 (10.5)	-1.2	0.04	(-2.6 to 2.7)
≥85	177	70.6 (11.7)	2.7 (10.3)	-0.8	0.7	(-2.0 to 3.3)
Sex						
Male	433	68.3 (12.9)	3.2 (10.3)	Reference	Reference	
Female	442	69.4 (12.5)	3.6 (10.3)	0.4	1.0	(-1.3 to 3.3)
Ethnicity						
White/White British	826	68.9 (12.8)	3.3 (10.4)	Reference	Reference	
Other ethnicity	46	68.1 (11.9)	5.0 (9.3)	1.8	0.5	(-3.6 to 4.7)
Deprivation (quintiles of IMD)						
1 – least deprived	239	70.1 (12.2)	2.7 (10.2)	Reference	Reference	
2	188	68.6 (13.1)	3.5 (10.2)	0.8	0.2	(-3.1 to 3.4)
3	161	69.6 (12.0)	3.9 (9.9)	1.2	1.1	(-1.6 to 3.8)
4	157	66.7 (13.0)	3.9 (10.2)	1.2	-.001	(-2.9 to 2.9)
5 – most deprived	117	68.8 (13.6)	3.3 (10.9)	0.6	0.4	(-3.1 to 3.9)
Number of comorbidities						
0	181	69.1 (12.5)	2.9 (11.2)	Reference	Reference	
1	242	70.3 (11.6)	4.4 (9.7)	1.5	1.5	(-1.5 to 4.4)
2	214	69.5 (13.0)	3.2 (10.4)	0.3	0.3	(-2.9 to 3.7)
3 or more	238	66.5 (13.6)	2.8 (10.1)	-0.1	-0.8	(-4.4 to 2.7)

* Positive change score indicates improvement in HRQL. Adjusted for clustering by clinic; † Adjusted for age, sex, ethnicity, deprivation, number of comorbidities, diagnosis, DEMQOL score at baseline and clustering by clinic, n=804 with complete data on all variables.

Table 4: Change in DEMQOL-Proxy equated score by patient characteristics (linear regression analyses)

Patient characteristics	Number	DEMQOL-Proxy equated score at 6 months. Mean (SD)	DEMQOL-Proxy equated score change (SD)	Unadjusted difference in change *	Adjusted difference in change †	(95% CI with Bonferroni correction)
Age (years)						
<75	172	59.0 (11.0)	2.2 (9.3)	Reference	Reference	
75-79	142	58.4 (9.5)	1.3 (8.2)	-0.9	-0.9	(-3.8 to 2.1)
80-84	148	57.4 (10.6)	-0.4 (9.5)	-2.6	-2.1	(-6.6 to 2.4)
≥85	104	58.9 (11.4)	2.2 (10.8)	-0.01	-0.06	(-4.5 to 4.3)
Sex						
Male	307	59.2 (10.5)	1.3 (9.0)	Reference	Reference	
Female	256	57.5 (10.7)	1.3 (9.8)	0.03	-0.5	(-3.0 to 1.9)
Ethnicity						
White/White British	540	58.5 (10.6)	1.2 (9.3)	Reference	Reference	
Other ethnicity	23	56.0 (11.8)	4.4 (10.8)	3.2	1.4	(-5.2 to 7.9)
Deprivation (quintiles of IMD)						
1 – least deprived	154	58.7 (9.4)	0.6 (7.3)	Reference	Reference	
2	121	58.0 (9.2)	1.0 (8.4)	0.4	0.1	(-2.6 to 2.9)
3	108	59.0 (10.6)	0.7 (10.6)	0.1	1.0	(-2.4 to 4.4)
4	104	58.5 (13.2)	2.3 (11.1)	1.7	0.9	(-2.2 to 4.0)
5 – most deprived	69	57.7 (11.5)	2.9 (10.6)	2.3	1.2	(-2.8 to 5.2)
Number of comorbidities						
0	111	59.6 (10.5)	0.5 (9.3)	Reference	Reference	
1	146	58.0 (10.3)	1.6 (8.6)	1.1	0.2	(-2.8 to 3.2)
2	148	59.2 (10.4)	1.1 (9.0)	0.6	0.2	(-2.8 to 3.2)
3 or more	158	57.3 (11.1)	1.8 (10.6)	1.2	0.2	(-3.6 to 4.1)

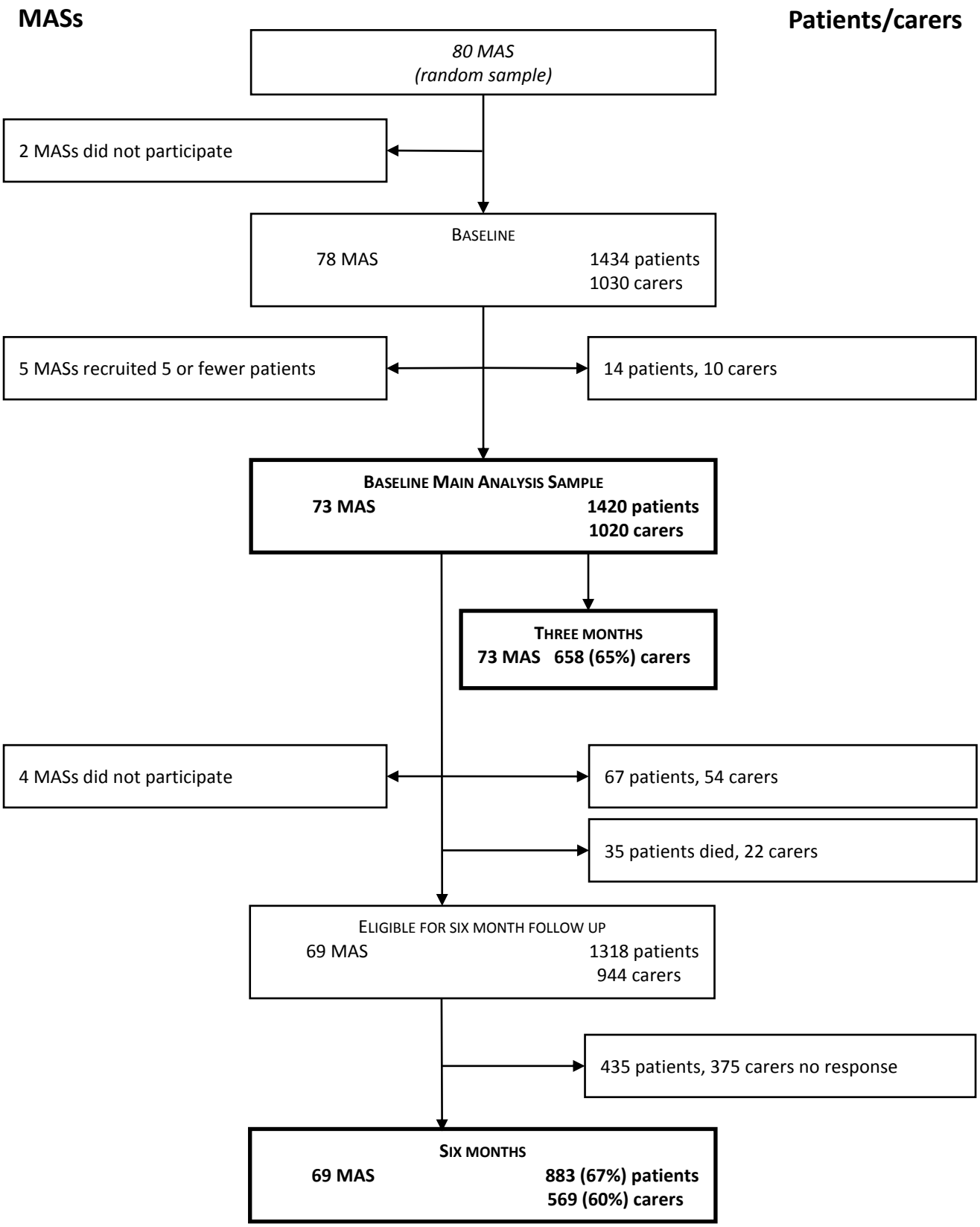
* Positive change score indicates improvement in HRQL. Adjusted for clustering by clinic; † Adjusted for age, sex, ethnicity, deprivation, number of comorbidities, diagnosis, DEMQOL-Proxy score at baseline and clustering by clinic, n=524.

Table 5: Change in HRQL among patients with dementia diagnosis by post-diagnosis interventions (random effects model)

	Number with outcome	Score at 6 months (SD)	DEMQOL equated score change (SD)	Unadjusted difference in change *	Adjusted difference in change †	(95% CI)
Self-reported DEMQOL						
Anti-dementia medications						
No	116	68.8 (12.1)	2.2 (10.7)	Reference	Reference	
Yes	187	70.3 (13.2)	4.6 (10.0)	**2.4**	**3.3**	**(1.4 to 5.3)**
Non-pharmacological therapies						
No	238	70.9 (13.0)	3.8 (11.0)	Reference	Reference	
Yes	67	65.4 (11.5)	2.4 (7.5)	-1.4	**-2.4**	**(-4.8 to -.003)**
Proxy-reported DEMQOL						
Anti-dementia medications						
No	111	56.8 (11.1)	0.8 (9.5)	Reference	Reference	
Yes	182	57.6 (10.0)	2.1 (8.9)	1.3	1.4	(-1.1 to 3.9)
Non-pharmacological therapies						
No	234	57.8 (10.6)	1.8 (9.6)	Reference	Reference	
Yes	61	55.5 (9.4)	1.5 (7.4)	-0.3	-0.3	(-2.8 to 2.2)

Positive change score indicates improvement in HRQL. * Adjusted for clustering by clinic; † Adjusted for age, sex, ethnicity, deprivation, number of comorbidities, cognitive function, HRQL at baseline and clinic as a random effect. (In addition, medications adjusted for non-pharmacological therapies and vice versa). Coefficients in **bold** $p<0.05$.

Supplemental Figure 1. Flow chart showing sample sizes in MAS Study at baseline, three- and six-month follow up



Supplemental Table 1: Change in HRQL among patients with dementia diagnosis by cognitive function at baseline (random effects model)

	Cognitive function		
	1 – lowest	2- mid	3 – highest
DEMQOL equated score			
Number	203	111	45
Change (SD)	2.0 (11.4)	4.7 (8.8)	3.6 (9.5)
Unadjusted difference in change * (95% CI)	Reference	**2.7 (0.3 to 5.1)**	1.5 (-1.8 to 4.9)
Adjusted difference in change † (95% CI)	Reference	1.5 (-1.0 to 4.0)	-0.7 (-4.8 to 3.5)
DEMQOL-Proxy equated score			
Number	144	80	29
Change (SD)	1.7 (10.1)	1.9 (9.2)	0.1 (5.7)
Unadjusted difference in change *(95% CI)	Reference	0.2 (-2.4 to 2.8)	-1.6 (-5.4 to 2.2)
Adjusted difference in change † (95% CI)	Reference	-0.003 (-2.7 to 2.7)	-2.5 (-5.1 to 0.1)

Positive change score indicates improvement in HRQL. * Adjusted for clustering by clinic; † Adjusted for age, sex, ethnicity, deprivation, number of comorbidities, medications, use of non-pharmacological therapies, HRQL score at baseline and clinic as a random effect. Coefficients in **bold** $p<0.05$.