Cost-effectiveness of memory assessment services for the diagnosis and early support of patients with dementia.

Abstract

Background

Policy makers in England advocate referral of patients with suspected dementia to Memory Assessment Services (MAS) but it is unclear how any improvement in patients' health-related quality of life (HRQL) compares with the associated costs.

Aims

To evaluate the cost-effectiveness of MAS for the diagnosis and follow-up care of patients with suspected dementia.

Method

We analysed observational data from 1318 patients referred to 69 MAS, and their lay carers (n=944), who completed resource use and HRQL questionnaires at baseline, three and six months. We reported mean differences in HRQL (disease-specific DEMQOL and generic EQ-5D-3L), quality-adjusted life years (QALYs) and costs between baseline and 6 months of referral to MAS. We also assessed cost-effectiveness of MAS across different patient subgroups and clinic characteristics.

Results

Referral to MAS was associated with gains in DEMQOL (mean gain 3.48, 95% confidence interval: 2.84 to 4.12), EQ-5D-3L (0.023, 0.008 to 0.038) and QALYs (0.006, 0.002 to 0.01). Mean total costs over six months, assuming a societal perspective, was £1,899 (£1277 to £2539). This yielded a negative incremental net monetary benefit, -£1724 (-£2388 to -£1085) assuming NICE's recommended willingness-to-pay threshold (£30,000 per QALY). These base case results were relatively robust to alternative assumptions about costs and HRQL. There was some evidence that patients aged 80 or older benefitted more from referral to MAS ($p<0.01$ from adjusted mean differences in net benefits) compared to younger patients. MAS with over 75 new patients a month or cost per patient less than £2500 were relatively more cost-effective ($p < 0.01$) than MAS with fewer new montly patients or higher cost per patient, respectively.

Conclusions

Diagnosis, treatment and follow-up care provided by MAS to patients with suspected dementia appears to be effective, but not cost-effective over the first six months after diagnosis. Longer-term evidence is required before drawing conclusions about the cost-effectiveness of MAS.

Introduction

Dementia is a major cause of disability and poor quality of life for older people and their families, and is associated with rising health care costs worldwide (1). In England, the number of people with dementia is growing fast and expected to reach 1 million in the next decade (2). The total costs associated with long-term care services for these patients have been estimated to be £19 billion per year, with an average cost of £28,000 per person, more than the costs of cancer or heart disease (3).

Timely diagnosis of dementia is key because it enables patients to receive early support and treatment if necessary, prepare for the future, and benefit from improvements in quality of life, while long-term health care costs might be reduced (4). However, many patients with dementia in England are not formally diagnosed. In addition, many of those diagnosed are not receiving adequate support and treatment to manage their condition. To address these deficiencies in dementia services, national policy makers advocate a model of care centred around Memory Assessment Services (MAS, (5)). These ambulatory care memory clinics provide an integrated multi-professional approach to diagnostic services and follow up dementia care. MAS have become the established and widely adopted model for providing services to diagnose and initiate treatment in those with cognitive impairment, although other approaches based within primary care have been proposed in a few areas (6, 7).

There is some limited evidence suggesting that patients referred to MAS in England have a better care experience (8) and improved health-related quality of life (HRQL) (9). On the other hand, clinical trials in France and Netherlands found few differences in health outcomes of patients receiving follow up care by MAS or GPs (10, 11). Importantly, the wide range of different models of memory services complicates any comparisons between studies – both

between and within countries - and may lead to misleading recommendations about the relative effectiveness of MAS (12).

Evidence on the relative costs of diagnostic and post-diagnosis services is also scarce. A previous study that focused on a single memory clinic (13) found no difference in costs of dementia services provided by MAS compared to community health services. The relative cost-effectiveness of MAS in England is not known. A previous modelling study (4) provided some cost projections for MAS based on published literature, and suggested that MAS needed to achieve only modest gains in patient's HRQL to be deemed cost-effective.

A recent multi-centre observational study followed up a large number of patients attending a representative sample of MAS in England (14). Using data from this large observational study, we have previously reported detailed costs and outcomes associated with MAS (15, 16). Drawing on the same study, this paper assesses the cost-effectiveness of MAS for the diagnosis and follow up care of patients referred with suspected dementia in the first six months after diagnosis. We also examine whether the cost-effectiveness of MAS differs according to patient subgroups or clinic characteristics.

Methods

Study design

We recruited 80 MAS at random from the 212 memory clinics identified by the Royal College of Psychiatrists. Two sites subsequently withdrew, five sites were excluded for having recruited fewer than six patients, and four sites were excluded from this analysis after failing to collect outcome data at six months, leaving a final sample of 69 MAS. The sample was representative of MAS in England, both geographically and in terms of number of referrals, waiting times for first appointment and accreditation status. Further details on the

sample are reported elsewhere (14). The sample reflected the wide diversity of services provided by MASs in terms of size, staffing, provision of post-diagnostic support and follow-up regimes (17).

Patients with suspected dementia referred for a first appointment at one of the 69 clinics, between September 2014 and April 2015, were eligible for inclusion in the study. Patients or carers with insufficient English to understand the consent process or study materials (n=43) were excluded, resulting in a total sample of 1318 patients.

Data collection

Patients and carers completed questionnaires about HRQL of the patient, at the initial assessment and at 6-month follow-up. Data on patients' socio-demographic and clinical characteristics were recorded at baseline. Carers also completed a separate questionnaire about resource use at baseline, 3 months and 6 months. All eligible participants were followed up regardless of the diagnosis they received (whether or not they had dementia). MAS were also asked (by email) to complete an organisational survey, with telephone follow-up to maximise the response rate. This survey included data on clinic characteristics and resource use related to diagnosis, interventions, and follow-up care.

Health outcomes

The patient questionnaire included disease-specific (DEMQOL (18)) and generic (EQ-5D-3L (19)) HRQL instruments. DEMQOL is a 28-item instrument, where each item is scored on a four-point scale, with a higher score indicating better HRQL. Patients' informal carers completed a proxy-reported disease-specific instrument, DEMQOL-Proxy (18), which has 31 items with responses on the same 4-point scale as DEMQOL. Both DEMQOL and

DEMQOL-Proxy were scored using an improved scoring algorithm based on modern psychometric methods (20).

The EQ-5D-3L has five items covering different health domains: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. The EQ-5D-3L profiles were combined with health state preferences values from the UK general population (19) to give EQ-5D-3L utility index scores, anchored on a scale from 0 (death) and 1 (perfect health). Similar to DEMQOL, carers also completed a EQ-5D-3L-Proxy, with the same items as patient-reported EQ-5D-3L.

Quality-adjusted life years (QALYs) were calculated by valuing each patient's survival time (all patients included in the sample have survived for 6 months) by their EQ-5D-3L score at baseline and 6 months according to the 'area under the curve' approach. To construct QALYs based on DEMQOL, we have derived a preference-based score (DEMQOL-U and DEMQOL-Proxy-U) from the original DEMQOL measure, using a previously developed algorithm (21).

Resource use and costs

The cost analysis took a societal perspective, including costs incurred by health and social care providers, the MAS, the patient (out-of-pocket expenses), and the family and/or caregiver (informal care). Full details of the resource use and costing approach are reported elsewhere (16). Briefly, total MAS costs included diagnostic services, and half (6 months) of the annual MAS costs with interventions and follow up care. Patient's resource use reported by the carer included contacts with health care and social care professionals such as GPs, nurses, psychologists, psychiatrists and social workers (in the last four weeks). The unit cost of each contact was taken from national costs sources (22). Dementia drug costs were obtained from the British National Formulary (BNF, 2014). Psychosocial support services

such as cognitive stimulation, art and music therapies were costed per session, and unit costs taken from national sources and related literature (22). Following general guidance for valuing informal care in health economic evaluation (23), we included costs related to carer's time valued at £6 per hour based on the national minimum wage for 2013-2014.

At the clinic level, staff use was valued using unit costs for health and social care professionals (22). The costs of imaging and other diagnostic tests were taken from NHS reference costs (24).

Cost-effectiveness

We assessed the cost-effectiveness of MAS by comparing the 6-month health outcomes (HRQL) and costs of patients attending MAS with those that would have occurred had these patients not received follow up care by MAS (baseline HRQL and costs). The implicit assumption here is that, without MAS attendance, patients' quality of life and costs would remain constant between baseline and 6 months.

We summarised cost-effectiveness of MAS at 6 months by reporting incremental net monetary benefits. These are calculated by valuing the incremental QALY by the willingness to pay threshold recommended by NICE (£30,000 per QALY), and subtracting from this the incremental cost. We investigated whether the cost-effectiveness of MAS differed according to patient subgroups: age, sex, ethnicity, deprivation, and number of comorbidities. Similarly, we also assessed cost-effectiveness by clinic characteristics: number of new patients per month, number of follow up appointments within the first year, cost of MAS per patient, and whether the clinic provided psychosocial support.

Statistical analysis

We estimated mean HRQL at baseline and 6 months across the different HRQL measures. Total costs at 6 months included patient-level costs related to health and social care and informal care, and clinic-level costs related to diagnostic services, interventions and follow up care. Confidence intervals around changes in HRQL, QALY and cost endpoints between baseline and 6 months were obtained using non-parametric bootstrapping (1000 replications). The base case analysis estimated incremental net benefits at 6 months, assuming that the cost and outcomes between baseline and 6 months would have remained the same had the patients not attended MAS. Mean differences in the net benefits between subgroups were adjusted for patient characteristics, baseline EQ-5D-3L and clustering by clinic (using a multilevel regression model). Uncertainty (95% CI) around adjusted differences in the net benefits was obtained from the bootstrap samples.

We conducted sensitivity analysis to assess whether the cost-effectiveness results were sensitive to key assumptions in the base case scenario. More specifically, we relaxed the assumption that patients' outcomes and costs would remain constant between baseline and 6 months without MAS attendance. For example, we estimated cost-effectiveness assuming that patients' HRQL was lower (due to ageing and deteriorating cognitive function) and costs were higher (at 6 months compared to baseline) had they not received follow up care by MAS. We considered decrements in HRQL of 0.1% (three times the age and gender-related HRQL decrement in the general population (25)), 5% and 10%; and patient-level cost increments of 5%, 10% and 20%.

Missing resource use and HRQL data were addressed using multiple imputation (MI) assuming that the data were 'missing at random' (26), that is conditional on the observed baseline patient and MAS characteristics, follow-up process measures and observed

endpoints. To ensure consistency with the analysis models, we considered a multilevel approach to MI (27) to recognise the clustering within clinics. Within each bootstrap iteration, we applied the analysis model to the multiple imputed datasets (M=20), combined the resultant estimates using Rubin's rules (26), and obtained uncertainty measures from the bootstrap samples as usual. All analyses were undertaken in R.

Results

1318 patients and 944 carers were recruited across the 69 MAS. Of those, 826 (63%) and 872 (66%) patients completed DEMQOL and EQ-5D-3L questionnaires, respectively (Table 1). Proxy outcomes (DEMQOL-Proxy and EQ-5D-3L-Proxy) and health and social care costs reported by carers were available for only about 50% of the patients partly because 374 (28%) did not have a carer. Patient and clinic characteristics were mostly complete (Table 1).

Table 2 reports the main cost components at baseline, 3 and 6 month follow-up. At 6 months, patients referred to MAS had higher monthly costs related to social care and informal care compared to baseline; mean differences were £53 (95% CI 15 to 96) and £59 (95% CI -36 to 148), respectively. At the clinic level, assessment costs corresponded to half of the total cost of MAS services. According to a societal perspective, the mean total cost up to 6 months was £1899 (95% CI 1277, 2539) per patient.

At 6 months, patients referred to MAS experienced better quality of life compared to baseline by reference to all HRQL measures (except EQ-5D-3L-Proxy) (Table 3). For example, mean difference in EQ-5D-3L was 0.023 (95% CI 0.008 to 0.038). The incremental net benefit based on $QALY_{EQ\text{-}5D\text{-}3L}$ was -£1724 (95% CI -2388 to -1085), suggesting that the QALY gain was relatively small compared to the additional costs. This led to a much higher cost per QALY (£374,164) compared to the NICE's recommended threshold (£30,000 per QALY gain). These base-case cost-effectiveness results appeared to be relatively robust to changes

in the assumptions related to costs and HRQL (Figure 1); the distribution of incremental costs and QALYs for most scenarios lay above the recommended willingness-to-pay threshold value for a QALY gain. MAS became cost-effective when the patients not referred to MAS were assumed to experience 20% higher health and social care costs and 10% lower HRQL at 6 months (compared to baseline).

Subgroup analyses according to patient and clinic characteristics are summarised in Figure 2 and Table 4, respectively. Incremental net benefits are relatively similar across the different patient subgroups, with the exception of age (Figure 2). Patients aged 80 or older achieved higher gains in QALYs and had lower costs, leading to a higher net monetary benefit (adjusted mean difference was £1379, p-value<0.01) compared to younger patients. Table 4 suggests that MAS with a higher number of new patients per month (more than 75), or lower clinic cost (below £2500) per new patient, were relatively more cost-effective (p-values<0.01), because these tended to be associated with a lower average total cost. In line with this, there was some evidence that MAS with a wider range of staff providing psychosocial support (reflecting larger MAS) were associated with higher net benefits (mean adjusted difference was £629, p-value=0.04).

Discussion

Main findings

Patients referred to MAS with suspected dementia had experienced an improvement in quality of life six months after diagnosis, according to both generic and disease-specific HRQL measures. However, over this short follow-up period the changes in HRQL were relatively small when compared to the costs associated with MAS meaning that this service was not cost-effective assuming that a QALY (based on EQ-5D-3L) is valued at £30,000. This assessment assumed that patients' HRQL and costs would have remained constant over

the 6-month period had they not attended MAS. The sensitivity analysis considered alternative assumptions, and suggested that MAS could be cost-effective if, without MAS attendance, patients' HRQL were to deteriorate by about 10% and health and social care costs were to increase 20% over the six-month period. Such changes would involve a decrease of 0.07 in the EQ-5D-3L score (0.71 to 0.64) and an increase in costs (£1543 to £1850) over the 6 months. These changes are unlikely given the changes observed for 'usual care' patients in recent clinical trials (10, 28, 29).

There was little evidence of differences in the cost-effectiveness of MAS between patient subgroups, although patients aged over 80 benefit more (greater change in HRQL) from referral to MAS. Large clinics (more than 75 new patients per month) appear to benefit from economies of scale, but these are not necessarily associated with better HRQL outcomes. There was strong evidence that MAS with lower cost per new patient (less than £2500) were relatively more cost-effective, regardless of their size.

Comparison with other studies

Only one previous study has attempted to determine the cost-effectiveness of MAS in England (4). Their model suggested that MAS could be cost-effective if QALY gains per person year were between 0.01 and 0.02. This is approximately the level of patient-reported QALY gains (based on both EQ-5D-3L and DEMQOL-U) reported in our study. However, for these levels of QALY improvement, our results suggest that MAS may not be cost-effective across alternative, plausible assumptions about the costs of MAS. Our sensitivity analysis suggests that QALY gains greater than 0.02 may be required to warrant the costs associated with MAS. The differences between the two studies may be related to assumptions about the costs. For example, Banerjee and Wittenberg's projections assumed that MAS would lead to cost savings from reduced use of residential care, something that we have not

considered, as that did not occur in the short time period we considered. In addition, their study did not include direct costs of diagnostic investigations, which can be relatively large.

Two small clinical trials in the Netherlands compared costs and outcomes of post-diagnostic care to patients with dementia between MAS and GP services. One study (10) found that MAS were not effective or cost-effective compared to GP care. Conversely, the other (single-centre) trial (29) reported that MAS were cost-effective compared to GP care at 1 year (QALY gain was 0.05, incremental cost was €65). However, this was partly related to the fact that MAS assessment costs were not included and randomised patients had poor prognosis (average baseline EQ-5D-3L was about 0.5), benefitting relatively more from MAS compared to 'usual care'.

Strengths and limitations

This study reports a cost-effectiveness analysis of the largest observational study of patients referred to MAS in England. Unlike previous studies focussing on a single memory clinic (9, 13, 28), our results are representative of MAS across all regions in the country (14). This economic evaluation is based on rigorous collection of data on different measures of effectiveness (both disease-specific and generic HQRL measures reported by patients and carers), and costs to the NHS, social care, carers and patients (adopting a societal perspective). In addition, this is the first study assessing the relative cost-effectiveness of MAS of different 'types' of memory services.

A major limitation of this study is the lack of a comparator, i.e. what would have been patients' costs and outcomes had they not been referred to MAS. Our base case assumption was that these patients would have, at 6 months, the same HRQL and costs as they had at baseline (first appointment at MAS) had they not been referred. This is plausible as these patients were likely to have remained undiagnosed and, hence, received the same level of

care as before. The literature suggests that there is no change in people's HRQL over 6-12 months (30-32). However, in sensitivity analysis we explored departures from this assumption. For example assuming higher costs or lower HRQL if patients had not attended a MAS suggested that MAS would only be cost-effective over the first six months if implausible assumptions are made.

Our study was prone to missing data, which is typical in studies using self-reported and proxy-reported HRQL and resource use questionnaires. We have considered a principled approach (multiple imputation) to address the missing values, rather than relying on ad-hoc assumptions. This approach assumed that the missing data were unrelated to unobserved values, conditional on the observed data, such as baseline patient and MAS characteristics, follow-up process measures and observed endpoints.

Given the large number of MAS included in the study, it was not feasible to undertake a micro-costing of each clinic. Instead, the costs were mostly based on staff use in these clinics, which crucially depended on the quality of reporting by MAS. This was thoroughly checked with local sites and the mean whole-time equivalent (WTE) staff observed was similar to the assumption of 10 WTE considered in Banerjee and Wittenberg's projections (4). In addition, our sensitivity analysis suggested that the cost-effectiveness of MAS was relatively robust to alternative assumptions about costs.

An additional limitation was that potential cost savings following referral to MAS, for example delayed admission to a care home, were not included in this study. The positive cost-effectiveness of MAS presented by Banerjee and colleagues (9) included a 10% reduction in care home use. While ignoring such cost savings may have underestimated the cost-effectiveness of MAS, such impact was unlikely to occur within the first 6 months after

diagnosis (we also noted that less than 1% of our sample were care home residents at baseline).

Policy implications and conclusion

Early diagnosis and treatment of dementia is a priority in many countries. The model of care based on MAS improves the HRQL of patients, but the gains over the first six months may not be sufficient to warrant the costs involved. Patients in this study are being followed up to 24 months, which will allow us to examine whether HRQL gains are maintained and/or costs reduced in the longer term. In such analyses, assumptions about HRQL deterioration of patients not referred to MAS and potential cost savings due to delayed care home admission will play an important role in establishing the cost-effectiveness of MAS. The relative cost-effectiveness of MAS differed according to clinic characteristics, including the number of new patients per month, clinic costs per new patient, and availability of psychosocial support. One policy challenge is, therefore, to learn from these observed associations so as how to improve the efficiency of MAS, particularly those with high average cost.

Before drawing conclusions from these findings it is also important to recognise that referral to MAS is a gateway to a wide range of different consequences. Whilst about 61% of patients are likely to receive anti-dementia medication and 22% may take part in psychosocial interventions, there is a proportion of patients for whom no discrete action is taken and also some (17%) for whom no diagnosis is given (15). Against this background, measures of HRQL may not encompass all the potential benefits that patients may obtain from MAS. For example, users of these services may welcome and value the reassurance and support that staff provide and the knowledge that they are not alone in having to deal with the challenges that their dementia symptoms present. Despite the widespread use of EQ-5D-3L and DEMQOL, they are designed to measure health-related outcomes (HRQL) rather than other

experiential benefits or broader wellbeing. In addition, the results reported here do not include any HRQL gains for carers, which would have improved the cost-effectiveness of MAS (33). We plan to consider the impact of such benefits in future analyses.

In conclusion, this study adds important evidence to the debate on the relative value for money of MAS for early diagnosis, treatment and follow-up care of patients with suspected dementia. Our findings suggest that the relative gains in HRQL may be modest when compared to the additional costs of MAS but longer-term evidence is required before drawing conclusions about the cost-effectiveness of MAS.

References

1. Wimo A, Winblad B, Jonsson L. The worldwide societal costs of dementia: Estimates for 2009. Alzheimers Dement. 2010;6(2):98-103.
2. Prince M, Knapp M, Guerchet M, McCrone P, Comas-Herrera A, Wittenberg R, et al. Dementia UK: Second edition - Overview. Alzheimer's Society. 2014.
3. Department of Health. A state of the nation report on dementia care and support in England https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/262139/Dementia.pdf2013 [cited 2016 October].
4. Banerjee S, Wittenberg R. Clinical and cost effectiveness of services for early diagnosis and intervention in dementia. Int J Geriatr Psychiatry. 2009;24(7):748-54.
5. Department of Health. Memory assessment service specifications http://dementia.dh.gov.uk/memory-assessment-service-specifications/2011 [cited 2017 April].
6. Greening L, Greaves I, Greaves N, Jolley D. Positive thinking on dementia in primary care: Gnosall Memory Clinic. Community Pract. 2009;82(5):20-3.
7. Lee L, Hillier LM, Stolee P, Heckman G, Gagnon M, McAiney CA, et al. Enhancing dementia care: a primary care-based memory clinic. J Am Geriatr Soc. 2010;58(11):2197-204.
8. Hailey E, Hodge S, Burns A, Orrell M. Patients' and carers' experiences of UK memory services. Int J Geriatr Psychiatry. 2016;31(6):676-80.
9. Banerjee S, Willis R, Matthews D, Contell F, Chan J, Murray J. Improving the quality of care for mild to moderate dementia: an evaluation of the Croydon Memory Service Model. Int J Geriatr Psychiatry. 2007;22(8):782-8.
10. Meeuwsen E, Melis R, van der Aa G, Goluke-Willemse G, de Leest B, van Raak F, et al. Cost-effectiveness of one year dementia follow-up care by memory clinics or general practitioners: economic evaluation of a randomised controlled trial. PLoS One. 2013;8(11):e79797.
11. Nourhashemi F, Andrieu S, Gillette-Guyonnet S, Giraudeau B, Cantet C, Coley N, et al. Effectiveness of a specific care plan in patients with Alzheimer's disease: cluster randomised trial (PLASA study). BMJ. 2010;340:c2466.
12. Banerjee S. A narrative review of evidence for the provision of memory services. Int Psychogeriatr. 2015;27(10):1583-92.
13. Rubinsztein JS, van Rensburg MJ, Al-Salihy Z, Girling D, Lafortune L, Radhakrishnan M, et al. A memory clinic v. traditional community mental health team service: comparison of costs and quality. BJPsych Bull. 2015;39(1):6-11.

14. Park M, Smith SC, Neuburger J, Chrysanthaki T, Hendriks J, Black N. Socio-demographic characteristics, cognitive function and health-related quality of life of patients referred to Memory Assessment Services in England Alzheimer Disease and Associated Disorders. 2016;(In press).
15. Park M, Smith SC, Chrysanthaki T, Neuburger J, Ritchie C, Hendriks J, et al. Change in health-related quality of life of patients at 6 months after referral to Memory Assessment Services. Alzheimer Disease and Associated Disorders. 2016;(In press).
16. Pennington M, Gomes M, Chrysanthaki T, Hendriks J, Wittenberg R, Knapp M, et al. The cost of diagnosis and early support in patients with cognitive decline. (In press). 2016.
17. Chrysanthaki T, Fernandes B, Smith S, Black N. Can Memory Assessment Services (MAS) in England be categorized? A national survey. J Public Health (Oxf). 2017:1-13.
18. Smith SC, Lamping DL, Banerjee S, Harwood R, Foley B, Smith P, 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 Technol Assess. 2005;9(10):1-93, iii-iv.
19. EuroQol Group. EuroQol-a new facility for the measurement of health-related quality of life. Health Policy. 1990;16(3):199-208.
20. Smith SC, Hendriks J, Chrysanthaki T, Cano S, Black N. How can we interpret proxy reports of HRQL when it is no longer possible to obtain a self-report? ISOQOL. 2015; 22nd Annual conference:Vancouver, Canada.
21. Mulhern B, Rowen D, Brazier J, Smith S, Romeo R, Tait R, et al. Development of DEMQOL-U and DEMQOL-PROXY-U: generation of preference-based indices from DEMQOL and DEMQOL-PROXY for use in economic evaluation. Health Technol Assess. 2013;17(5):v-xv, 1-140.
22. Curtis L. Unit costs of health and social care http://www.pssru.ac.uk/project-pages/unit-costs/2014/: Personal Social Services Research Unit; 2014 [cited 2016 October].
23. Koopmanschap MA, van Exel JN, van den Berg B, Brouwer WB. An overview of methods and applications to value informal care in economic evaluations of healthcare. Pharmacoeconomics. 2008;26(4):269-80.
24. Department of Health. NHS Reference Costs 2013 to 2014 https://www.gov.uk/government/publications/nhs-reference-costs-2013-to-20142014 [cited 2016 October].
25. Ara R, Brazier JE. Populating an economic model with health state utility values: moving toward better practice. Value Health. 2010;13(5):509-18.
26. Rubin DB. Multiple Imputation for Nonresponse in Surveys. New York: Wiley; 1987.
27. van Buuren S. Multiple Imputation of Multilevel Data. In: Hox J, Roberts K, editors. The Handbook of Advanced Multilevel Analysis. Milton Park, UK: Routledge; 2010.
28. Tanajewski L, Franklin M, Gkountouras G, Berdunov V, Harwood RH, Goldberg SE, et al. Economic Evaluation of a General Hospital Unit for Older People with Delirium and Dementia (TEAM Randomised Controlled Trial). PLoS One. 2015;10(12):e0140662.
29. Wolfs CA, Dirksen CD, Kessels A, Severens JL, Verhey FR. Economic evaluation of an integrated diagnostic approach for psychogeriatric patients: results of a randomized controlled trial. Arch Gen Psychiatry. 2009;66(3):313-23.
30. Hoe J, Hancock G, Livingston G, Woods B, Challis D, Orrell M. Changes in the quality of life of people with dementia living in care homes. Alzheimer Dis Assoc Disord. 2009;23(3):285-90.
31. Selwood A, Thorgrimsen L, Orrell M. Quality of life in dementia--a one-year follow-up study. Int J Geriatr Psychiatry. 2005;20(3):232-7.
32. Sheehan B, Lall R, Gage H, Holland C, Katz J, Mitchell K. A 12-month follow-up study of people with dementia referred to general hospital liaison psychiatry services. Age Ageing. 2013;42(6):786-90.
33. Al-Janabi H, Flynn TN, Coast J. QALYs and carers. Pharmacoeconomics. 2011;29(12):1015-23.