

# BMJ Open Measuring quality of life of people with predementia and dementia and their caregivers: a systematic review protocol

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## ABSTRACT

**Introduction** Dementia is the fastest growing major cause of disability globally and may have a profound impact on the health-related quality of life (HRQoL) of both the patient with dementia and those who care for them. This review aims to systematically identify and synthesise the measurements of HRQoL for people with, and their caregivers across the full spectrum of, dementia from its preceding stage of predementia to end of life.

**Methods and analysis** A systematic literature review was conducted in Medical Literature Analysis and Retrieval System Online, ExcerptaMedicadatabase, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, Database of Abstracts of Reviews of Effect, National Health Service Economic Evaluation Database and PsycINFO between January 1990 and the end of April 2017. Two reviewers will independently assess each study for inclusion and disagreements will be resolved by a third reviewer. Data will be extracted using a predefined data extraction form following best practice. Study quality will be assessed with the Effective Public Health Practice Project quality assessment tool. HRQoL measurements will be presented separately for people with dementia and caregivers by instrument used and, when possible, HRQoL will be reported by disease type and stage of the disease. Descriptive statistics of the results will be provided. A narrative synthesis of studies will also be provided discussing differences in HRQoL measurements by instrument used to estimate it, type of dementia and disease severity.

**Ethics and dissemination** This systematic literature review is exempt from ethics approval because the work is carried out on published documents. The findings of the review will be disseminated in a related peer-reviewed journal and presented at conferences. They will also contribute to the work developed in the Real World Outcomes across the Alzheimer's disease spectrum for better care: multimodal data access platform (ROADMAP).

**Trial registration number** CRD42017071416.

## INTRODUCTION

Dementia is a global disease with little prospect of a cure or means of preventing its progression. In 2014, it was estimated to affect 7.1% of people aged 65 and above worldwide.<sup>1</sup> It

## Strengths and limitations of this study

- This systematic literature review on quality of life of people with predementia and dementia and their caregivers is based on a detailed search strategy including studies from any country published in any language, covering the time frame from 1 January 1990 until 28 April 2017.
- The review follows robust guidelines and the quality of the papers included will be assessed using a validated tool.
- The heterogeneity in the way quality of life is measured and reported may not allow for direct comparisons between studies.

is a debilitating neurodegenerative condition which causes a progressive and irreversible decline in cognitive, social and physical function. There are several types of dementia and some people may present with a combination of types. Alzheimer's disease (AD) is the most common cause of dementia, accounting for 60%–80% of all cases.<sup>2</sup> Other causes include vascular dementia, frontotemporal dementia, dementia with Lewy bodies and others. Irrespective of the cause, dementia results in significant decline in intellectual abilities, such as memory and causes behavioural changes, insight and judgement, anxiety and depression, with eventual loss of physical functions and personality. This eventually becomes severe enough to interfere with a person's daily functioning and activities of daily living.

The cognitive and functional decline associated with dementia has a profound impact on the health-related quality of life (HRQoL) of both the patient and those that care for them. HRQoL, defined as the way health is empirically estimated to affect QoL, is a multidimensional concept that includes domains related



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to physical, mental, emotional and social functioning. HRQoL is now recognised as an increasingly valued health outcome measure in dementia. With no cure, the focus of attention in dementia care is to promote patient well-being and to maintain optimal HRQoL. As HRQoL refers to all aspects of a person's life, it can provide valuable information on the patient's self-perception of health and intervention impact. HRQoL measures attempt to evaluate directly the impact of dementia or interventions on people's ability to function in life. They have therefore become a key way in which to assess the effectiveness of health and social service interventions.

Dementia patients require long-term care and support, and the responsibility for caregiving most often falls on informal caregivers including family members, friends and neighbours. These caregivers provide a valuable resource for patients with dementia. There are over 700 000 informal caregivers of people with dementia estimated to be providing £12.4 billion of unpaid care in the UK per year.<sup>3</sup> The work of these caregivers is vital to support the growing number of people affected by dementia and without them, the formal care system would likely collapse. The National Dementia Strategy for England<sup>4</sup> recognises this and supporting caregivers is now a national and international policy priority.<sup>5</sup>

Given that caregivers of people with dementia are considered to be such an important resource, it is important to ensure that their own HRQoL is satisfactory. For many, the experience of caring for their loved ones provides personal satisfaction. However, the experience can also have a negative impact. Caregivers often have high levels of anxiety, stress and depression<sup>6</sup> as caring for people with dementia often places a heavy mental, physical, financial and social burden on them.<sup>7-11</sup> Great demands are placed on caregivers who are often elderly themselves.<sup>8,9</sup> As a result, caregivers might find themselves neglecting their own health and HRQoL. This could ultimately impact on the quality of the care that they provide for people with dementia. Therefore, addressing caregivers' HRQoL is an important challenge.

Shearer *et al*<sup>10</sup> conducted a systematic review of the literature on health value states for AD patients and their caregivers based on generic preference-based instruments.<sup>10</sup> Two recently published systematic reviews examined the factors associated with the HRQoL of dementia patients, either in all types of setting<sup>12</sup> or in long-term care facilities in particular.<sup>13</sup> A few reviews have identified HRQoL measures for dementia patients and their carers.<sup>14-16</sup> Caregiver burden has also been explored in a few systematic reviews, either identifying factors constituting caregiver burden on informal caregivers of dementia patients,<sup>7</sup> exploring the role of self-efficacy in HRQoL of family carers of dementia patients,<sup>8</sup> reviewing evidence for negative caregiver outcomes in mild cognitive impairment (MCI)<sup>9</sup> and synthesising risk factors or reviewing caregiver burden and interventions for familial caregivers of AD patients.<sup>11</sup> However, apart from Shearer *et al*,<sup>10</sup> none of these reviews report measurements for

HRQoL of these patients or caregivers. Furthermore, Shearer *et al*<sup>10</sup> did not consider dementia-specific HRQoL measures. This review therefore aims to address this gap in the literature by addressing the following questions:

1. What is the HRQoL for people with dementia across all stages of disease severity, from its preceding state of predementia (including preclinical AD—biomarker positive but presymptomatic, early symptoms, MCI or prodromal AD) through to diagnosed dementia and end of life?
2. What is the HRQoL for caregivers of people with dementia across all stages of disease severity, from its preceding stage of predementia to end of life?

## METHODS AND ANALYSIS

### Protocol and registration

The preparation of this protocol followed the reporting guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis for Protocols 2015 (PRISMA-P).<sup>17</sup> A completed PRISMA-P checklist is available in online supplementary file 1. The protocol was registered with the PROSPERO international prospective register of systematic reviews (registration number CRD42017071416). The systematic review manuscript will be prepared following the PRISMA statement.<sup>18-20</sup> In case of amendments to this protocol, they will be reported and published with the results of the review.

### Study selection criteria

#### Participants

The focus of this review is on adult populations reporting to have either predementia or dementia, irrespective of the type and stage of the disease and their caregivers. Our main interest is in AD, the most common cause of dementia, but given the lack of diagnostic accuracy and the recognised overlap between different causes of dementia, all causes will be considered.

#### Study design

This systematic literature review will include studies reporting measurements of HRQoL for adult onset predementia or dementia patients and their caregivers published in peer-reviewed journals or grey literature. We will only include primary studies that provide quantitative results. Qualitative studies will not be included.

The following study designs will be considered for inclusion: experimental studies, quasiexperimental studies, observational studies (either prospective or retrospective) and register-based studies. In cases where multiple studies used the same patient cohort, we will use the data from the study that presented the most detailed information on HRQoL. Case studies, series of case studies, studies with sample size of 30 or less patients, trial protocols, phase I clinical trials, news articles, interviews that do not use a structured quantitative questionnaire, patient education handouts, reviews, opinion or expert articles, editorials, letters to the editor, authors and editor's replies to comments will not be included.

Modelling studies will be excluded but studies informing the model parameters will be considered for inclusion. Similarly, existing reviews of HRQoL of people with dementia and their caregivers will not be included but their reference lists will be screened for additional studies. Conference abstracts will not be included. However, the abstracts will be screened to determine whether the work presented has been published in a peer-reviewed journal or thesis. If this is the case, then the published study will be considered for inclusion.

### Outcomes

The outcomes of interest are:

- ▶ The HRQoL of people with either predementia or dementia;
- ▶ The HRQoL of caregivers of people with either predementia or dementia.

Where possible, the HRQoL of people with dementia and their caregivers will be detailed by stage of the disease: preclinical dementia (biomarker positive but presymptomatic), early symptoms (memory and other behavioural changes), MCI, prodromal AD, mild dementia, moderate dementia, severe dementia and end of life to understand how HRQoL evolves throughout disease progression.

### Quality of life

A wide range of instruments have been developed to measure HRQoL. These include both generic and disease-specific instruments. Whereas generic HRQoL measures are universal and cover general health aspects, regardless of the presence or absence of a disease, disease-specific HRQoL measures target individual diseases and aim to emphasise the problems specific to patients with a specific disease, such as dementia. These generic and disease-specific instruments can be further subdivided into preference or non-preference depending on whether the index has been derived by using preference weights obtained from patients or the general public or using simple summation of item scores.

In this review, we will include any study reporting a quantitative measurement of HRQoL, regardless of the instrument used to estimate it.

### Intervention

All types of interventions related to dementia, either symptomatic or disease modifying, will be included. We will also include studies that have not assessed any intervention.

### Language

No language restrictions were applied to the search.

### Setting

No geography restrictions were applied to the search.

### Search strategy

#### Electronic databases

The selection of the electronic databases used was carried out with the assistance of an information specialist.

The search terms were devised in conjunction with an information specialist based on the search strategy of a previous literature review.<sup>10</sup> Medical Literature Analysis and Retrieval System Online, Excerpta Medica database, Cochrane Database of Systematic Reviews, Central Register of Controlled Trials, Database of Abstracts of Reviews of Effects, National Health Service Economic Evaluation Database and PsycINFO were searched for studies published between 1 January 1990 and 28 April 2017. Online supplementary file 2 provides a description of the search terms used in each database.

### Manual searches

The reference list of the studies included in this review, as well as those of previous literature reviews on HRQoL across the full spectrum of dementia, will be searched to identify additional potentially relevant studies. The studies informing the model parameters in identified modelling studies will be considered for inclusion. Conference abstracts identified through the electronic searches will be screened and manuscripts of relevant abstracts will be manually searched for.

### Study selection

ENDNOTE V.X7 (Thomson Reuters) will be used for reference management. Database results will be imported to ENDNOTE where duplicates will be removed by one reviewer (KW) based on title and first author name. Subsequently, two reviewers (FL and KW) will independently assess the titles and abstract of the studies to determine whether full-text review is needed, with disagreement being resolved by a third reviewer (HW). Full text will be sought for potentially relevant studies and assessed for final inclusion by two reviewers (FL and KW) with disagreements being resolved by a third reviewer (HW). The full selection process will be presented in a flow diagram according to PRISMA guidelines.<sup>18</sup>

### Data extraction

Two of the following reviewers (SM, EN, FL, AG and JW) will extract the data from the final set of studies onto a data extraction form (see online supplementary file 2) with disagreements being solved by a third reviewer. Two native or fluent speakers will review and extract the data for the non-English references. The following information will be extracted:

- ▶ Study details: title, author, publication details, language of the study, countries of the study;
- ▶ Study design: aim of the study, type of study, type of analysis, duration, outcomes measured, instruments used to measure them, administration mode;
- ▶ Participant information: type of participant, setting, inclusion and exclusion criteria, sample size, sociodemographic information, self or proxy rating;
- ▶ Disease-specific information: type of dementia, level of severity, instrument used to measure level of severity;
- ▶ Outcomes: outcomes measured, time points measured, subgroup analysis conducted;

- ▶ Results: HRQoL of patients by disease severity, HRQoL of caregivers by disease severity of the patients (where studies report HRQoL using different instruments or report the same instrument in different ways, data will be extracted for each of them);
- ▶ Conclusions: author's conclusions.

#### Risk of bias (quality) assessment

The Effective Public Health Practice Project 'Quality assessment tool for quantitative studies'<sup>21</sup> recommended by the Cochrane Public Health Group will be used to assess the quality of the studies included in this review as it covers a wide range of study designs.<sup>22</sup> Two of above-mentioned reviewers will independently assess each study and two native or fluent speakers will independently assess the quality of each of the non-English studies.

#### Description of studies and analysis

We expect to find a diverse range of HRQoL measures for both patients and caregivers. The HRQoL measurements will be presented separately for patients and caregivers by instrument used and, if possible, graphically. When described, distinction will be made between the different types of dementia but with a special emphasis on AD, the most common cause. If possible, HRQoL will be reported for each stage of the disease and if the HRQoL was self-rated or proxy rated informed by a caregiver or care/research professional. Descriptive statistics of the results will be provided.

A narrative synthesis of all relevant studies will be provided discussing differences in HRQoL measurements by instrument used to estimate it, type of dementia, disease severity, setting and describing study and participants' characteristics, results and author's conclusions.

In case the study does not provide all the necessary data for our analysis, we will contact the authors of the studies included in this review to attempt to retrieve it.

If feasible, a meta-analysis of the findings will be conducted.

## DISCUSSION

This systematic literature review will identify and synthesise the measurements of QoL, both preference and non-preference based, for patients across the full spectrum of dementia from MCI, predementia and dementia to end of life and their caregivers. HRQoL is increasingly seen as an important outcome in dementia research, and this level of detailed measurements of HRQoL will be useful and help to better inform disease progression and cost-effectiveness models of dementia.

We will present HRQoL measurements separately by disease type when the information is available. The main focus of our research is on AD, the most common cause of dementia, but given the lack of diagnostic accuracy and the recognised overlap between different causes of dementia, all causes of dementia will be considered.

Even though HRQoL as a measurement of the health status of individuals has been used since the second half of the 20th century, it was only in the 1990s that its use increased with the introduction of instruments such as EQ-5D-3L<sup>23</sup> and SF-6D.<sup>24</sup> As such, this review will include published studies on HRQoL since 1990. Furthermore, no languages or geographic restrictions were applied to the searches.

In conclusion, the results of this review could inform models assessing interventions on dementia for both patients and their caregivers by providing information about patient's and caregiver's perspective on treatment benefits. Additionally, this synthesis of HRQoL measurements for dementia patients and their caregivers can help policy-makers better understand the impact of this staggering clinical condition.

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**Collaborators** Novartis Pharma AG, GE Healthcare, Biogen and Eli Lilly and Company Limited are industry partners in the ROADMAP Project.

**Contributors** FL designed the study and is the guarantor of the review. FL, KW, IG, SM, EN and HW wrote the protocol. FL, NR, RW, JW, RH, MHP, AT-H and AMG devised the search strategy. PL, RW, JW, RH, ER-D, MHP, AT-H and AMG critically appraised the protocol and also contributed to its development by revising different versions. All authors read and approved the final version of the manuscript.

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**Competing interests** PL is employed by, owns stock in and has stock options in Novartis Pharma AG. RH has received consulting fees from Roche, Nutricia and Piramal; research grants from private/public collaborations: IMI2-ROADMAP; Alzheimer Netherlands Flutemetamol; CTMM LEARN Grant 02 N-101 and public grants from: JPND Actifcare and JPND BIOMARKAPD. ERD is employed by GE Healthcare. MHP is an employee of Biogen and owns stock in Biogen. She owns stock in a variety of companies that at times include other pharmaceutical and healthcare-related companies. ATH is an employee of Eli Lilly and Company Limited and owns stock in Eli Lilly and Company Limited. Novartis Pharma AG, GE Healthcare, Biogen and Eli Lilly and Company Limited are industry partners in the ROADMAP Project.

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