

D2.2 Report of systematic review of published and unpublished data identifying important and relevant outcomes in AD and criteria for disease progression

116020 - ROADMAP

Deliverable 2.2.1 (INTERIM REPORT)

WP2 – outcome definition

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Document history

Version	Date	Description
V0.5	15/10/2017	First draft of interim report
V1.0	17/11/2017	Updated interim report draft after internal UEDIN & ROCHE review
V1.1	01/12/2017	Updated interim report after formal internal review (Catherine Reed, Michele Potashman, Chi-Hun Kim) and Consortium review (no feedback)

Definitions

- Partners of the ROADMAP Consortium are referred to herein according to the following codes:
 - **UOXF.** The Chancellor, Masters and Scholars of the University of Oxford (United Kingdom) – **Coordinator**
 - **NICE.** National Institute for Health and Care Excellence (United Kingdom)
 - **EMC.** Erasmus University Rotterdam (Netherlands)
 - **UM.** Universiteit Maastricht (Netherlands)
 - **SYNAPSE.** Synapse Research Management Partners (Spain)
 - **IDIAP JORDI GOL.** Fundació Institut Universitari per a la Recerca a l'Atenció Primària de Salut Jordi Gol i Gurina (Spain)
 - **UCPH.** Københavns Universitet (Denmark)
 - **AE.** Alzheimer Europe (Luxembourg)
 - **UEDIN.** University of Edinburgh (United Kingdom)
 - **UGOT.** Goeteborgs Universitet (Sweden)
 - **AU.** Aarhus Universitet (Denmark)
 - **LSE.** London School of Economics and Political Science (United Kingdom)
 - **CBG/MEB.** Aagentschap College ter Beoordeling van Geneesmiddelen (Netherlands)
 - **IXICO.** IXICO Technologies Ltd (United Kingdom)
 - **RUG.** Rijksuniversiteit Groningen (Netherlands)
 - **Novartis.** Novartis Pharma AG (Switzerland) – **Project Leader**
 - **Eli Lilly.** Eli Lilly and Company Ltd (United Kingdom)
 - **BIOGEN.** Biogen Idec Limited (United Kingdom)
 - **ROCHE.** F. Hoffmann-La Roche Ltd (Switzerland)
 - **JPNV.** Janssen Pharmaceutica NV (Belgium)
 - **GE.** GE Healthcare Ltd (United Kingdom)
 - **AC Immune.** AC Immune SA (Switzerland)
- **Grant Agreement.** The agreement signed between the beneficiaries and the IMI JU for the undertaking of the ROADMAP project (116020).
- **Project.** The sum of all activities carried out in the framework of the Grant Agreement.
- **Work plan.** Schedule of tasks, deliverables, efforts, dates and responsibilities corresponding to the work to be carried out, as specified in Annex I to the Grant Agreement.
- **Consortium.** The ROADMAP Consortium, comprising the above-mentioned legal entities.
- **Consortium Agreement.** Agreement concluded amongst ROADMAP participants for the implementation of the Grant Agreement. Such an agreement shall not affect the parties' obligations to the Community and/or to one another arising from the Grant Agreement.

Publishable summary

A group of systematic literature reviews is under way to collate all available evidence on which outcomes of Alzheimer’s Disease (AD) are most important, and what constitutes a meaningful delay in its progression, from the perspectives of people with AD, their carers and healthcare professionals.

A series of distinct but internally consistent, sensitive searches were undertaken to capture a broad evidence base. Specific inclusion criteria were applied to refine this to a coherent, relevant subset of information which answers our research questions. ROADMAP members of WP2 have screened and are now quality appraising full-text papers in preparation for data extraction and synthesis.

This multi-disciplinary team continues to work collaboratively from bases in several European countries to achieve a common understanding of how the evidence can answer our questions. The interpretation and write up the report is on schedule for completion by the end of February 2018.

1. Introduction

Clinical trials involving people with Alzheimer’s Disease (AD) continue to try and identify disease modifying treatments. While trials are primarily designed to meet regulation and registration requirements, they may not provide convincing evidence for patients, payers or healthcare professionals. There has been criticism that some clinical trials use inappropriate or inadequately sensitive endpoints for this population and it is unclear how much stakeholder input (other than that of regulators) goes into clinical trial endpoint selection (Cano, 2010).

Understanding which ‘real world’ AD outcomes are most relevant to stakeholders, such as patients, carers and healthcare professionals, may help guide future AD research which will drive the development of relevant and effective treatments (Makady, 2017). Feedback on meaningful outcomes in both clinical trials and ‘real world’ assessments to all stakeholders is essential. Although large amounts of potentially valuable ‘real world’ data (which may be primarily related to symptomatic AD patients) are collected in healthcare settings, by insurance companies and other organisations, they are not well used in scientific research to support research and development.

In support of this goal, the international consortium Real world Outcomes across the AD spectrum for better care ([ROADMAP](#)) has planned a group of systematic literature reviews (SLR) of evidence of the prioritisation of AD outcomes and measures of disease progression from the perspective of key stakeholders. The review will include evidence from three stakeholder groups (patients, carers and healthcare professionals) and will cover the spectrum of AD. AD across the spectrum is interpreted as including all people affected by AD from subjective memory complaints and mild cognitive impairment (MCI), through preclinical and prodromal AD to confirmed AD dementia across disease severities.

2. Methods

The protocol for the combined reviews has been registered with PROSPERO ([CRD42017075722](https://www.crd42017075722)). For ease of reference in the rest of this report, the combined reviews will be referred to as ‘the SLR’.

The SLR is being conducted by members of the ROADMAP programme, co-ordinated by the Work Package 2 (WP2) co-lead Prof Cathie Sudlow and the University of Edinburgh team. Review tasks are being shared among WP2 partners at Roche, Alzheimer Europe, Universities of Oxford, Maastricht, Copenhagen & Aarhus, University Institute in Primary Care Research Jordi Gol, GE Healthcare, Takeda and Eli Lilly. Individuals involved in each stage are listed in Annexe I.

All contributors are employed by an organisation which is a member of the ROADMAP consortium and therefore have a professional interest in this topic. None of the systematic review authors has conflicts of interest which would confer undue influence on their judgement on this topic.

2.1. Research questions

The SLR is identifying research studies that have elicited information from stakeholders which answer one or both of the following research questions from their own perspective:

1. which outcomes of AD across the spectrum are prioritised by patients, carers and healthcare professionals?
2. What do patients, carers and healthcare professionals consider to be a meaningful delay in progression of AD across the spectrum?

Evidence to answer the research questions is being sought from a range of study types to include published primary or secondary research and unpublished ‘grey’ literature. The primary research evidence base comprises studies which collect and report quantitative, qualitative or mixed data based on research methods such as interviews, focus groups, surveys and Delphi or other consensus approaches.

The secondary research evidence base includes systematic reviews of relevant primary research (i.e. studies gathering views of stakeholders). Reviews of measurement tools or diagnostic instruments used in AD will not be included. Depending on the relevance of any included review, the content may be best included by accessing data in source research reports. Care will be taken not to give inappropriate additional weight to evidence from primary studies which also appear in systematic reviews.

Each included study must report data describing the views of one or more of the stakeholder groups with respect to the relative priority of outcomes of AD across the spectrum or what constitutes a meaningful delay in disease progression. Clarity on the phase of the disease will be crucial to apply the evidence to different portions of the spectrum.

Case studies, opinion pieces, commentaries and conference reports are not being included. Similarly RCTs or other clinical trials which report on the outcomes of interventions for AD without eliciting stakeholder priorities will not be included but such relevant information will be flagged for reference by ROADMAP colleagues if appropriate.

2.2. Population of interest

The focus of the SLR is AD across the spectrum. As it is challenging to define what exactly is meant by AD across the spectrum and in order to avoid missing useful studies, this review will attempt to include all people affected by AD including those in the pre-dementia stage such as Mild Cognitive Impairment (MCI) and those described by terms such as prodromal, pre-clinical or pre-symptomatic. It is acknowledged that using the planned search strategy may not find studies including people with AD unless they are defined as ‘patients’. As previously noted, studies involving only people whose dementia or cognitive impairment was suspected to be caused by a condition other than AD will be excluded. As the definition of AD has changed over time, with more recent studies likely to have a more consistent definition, only studies published since 2008 will be included in this review. Although AD is defined by a combination of a clinical diagnosis and a biomarker diagnosis, for pragmatic reasons only the former is required to be considered in the person identification.

For simplicity, in the rest of this report the condition to be included is referred to as ‘AD across the spectrum’.

Each included study must provide evidence to answer one (or both) of the research questions from the perspective of one (or more) of the following groups:

1. people with AD across the spectrum;
2. people who care for individuals with AD across the spectrum in paid or voluntary roles, including but not limited to family members, caregivers, support workers and advocates;
3. healthcare professionals or clinicians who look after people with AD across the spectrum, including but not limited to neurologists, geriatricians, psychiatrists, family doctors, nurses, therapists and other professions allied to medicine.

2.3. Identifying the evidence

2.3.1. Searches

Relevant elements of existing search strategies developed by ROADMAP partners were brought together to achieve a consistent and comprehensive list of defining terms for condition, outcome, stakeholder and study types. Key papers identified by partners were examined using the [Yale MeSH analyser](#) to check for useful additional terms.

A search strategy for MEDLINE was developed in collaboration with WP2 partners and expert advice at the University of Edinburgh library to achieve a balance of sensitivity and specificity. This search is included in full in Annex II. It is based on the combination of grouped terms indicated in Table 1 to retrieve evidence for each review question for each stakeholder group in distinct but internally consistent searches.

Table 1 Grouped search terms and the combination in which they were searched to retrieve evidence

	Research question 1 outcome priority	Research question 2 delay in disease progression
AD across the spectrum: includes terms from search strategy developed by Alzheimer Europe & the Burden of Illness review (Kharawala, 2016)	x	x
Outcomes: keywords & MeSH terms based on the categories identified in WP2's "Universe of Outcomes" report (ROADMAP, 2017)	x	
Priority: developed from terms in Alzheimer Europe search strategy	x	
Meaningful delay of disease progression: includes MeSH terms identified from key papers and related keywords		x
Stakeholder group: patients & carers: developed from terms in AE search strategy healthcare professionals: using MeSH and keyword terms	x	x
Study method: developed from keywords in Roche and AE search strategies with relevant MeSH terms	x	x

The MEDLINE search terms were translated for additional databases to maximise relevant citation retrieval for each stakeholder group. These are included in Annex III.

- Patients & carers: PsycINFO (Ovid), CINAHL (EBSCO)
- Healthcare professionals (with European focus): EMBASE (Ovid)

As it was anticipated that studies relevant to a range of stakeholder groups would be identified in each of the databases, all citation lists were centrally collated and deduplicated before the first stage of screening. The combined results are summarised in Table 2 indicating the number removed by a two stage deduplication process, firstly automated deduplication during import to Endnote (matching on author, year, title and reference type), and secondly manual screening, allowing for variations in author name such as use of initials or full names.

Table 2 Combined citation numbers retrieved

	Citations
Medline	1,705
Embase	3,616
Cinahl	1,755
PsycInfo	670
Initial total	7,746
Post deduplication	5,383
Limit to 2008-2017	3,772

Further relevant studies will be gathered via expert recommendation throughout the SLR process. Relevant citations of key included papers will be checked using Web of Science. Additionally, sources which may provide formal, but non-peer reviewed, evidence (grey literature) to answer the research questions, such as charity and patient organisation websites are being searched. These include [Alzheimer Europe](#), [Alzheimer's Society](#), [James Lind Alliance](#) and [Alzheimer Scotland](#). Reports will be included provided they meet inclusion criteria and minimum quality thresholds consistent with other evidence. The process for this search is included in the Annex.

2.3.2. Inclusion criteria

A sensitive search strategy was agreed through consultation within WP2 and review by the ROADMAP executive committee. Through further consultation and in-depth discussion of a selection of papers by a WP2 sub-group, a set of specific inclusion and exclusion criteria were established to identify a coherent, useful body of evidence to answer our research questions. These will include all relevant studies which:

- elicit information from an included stakeholder group who either have the condition or work with/care for someone who has the condition, which answers one or both of the research questions
- use an appropriate and explicit research methodology
- meet a minimum quality threshold
- were published between 2008 and 2017 inclusive.

2.3.3. Exclusion criteria

This SLR will exclude research studies which:

- do not allow information related to AD across the spectrum to be distinguished from other conditions such as stroke, multiple sclerosis and epilepsy, or other causes of dementia and cognitive impairment, unless they occur as co-morbidities;

- only include information on people with dementia or cognitive impairment caused by a condition other than AD, or dementia of an undefined or non-specific aetiology;
- do not provide data which answers the research questions, such as commentaries and opinion pieces, conference papers or animal studies;
- fail to provide the required information (year of publication, title, abstract) for filtering when extracted from source;
- report on AD outcomes as measured by diagnostic tools or interventions without including the views of one of our stakeholder groups on their relative importance.

2.3.4. Screening

On completion of searching and de-duplicating, 3,772 titles and abstracts were uploaded to Covidence. Members of the team assessed each title and abstract for relevance to the research questions and trigger acquisition of full text papers. For excluded titles, one reason for exclusion is noted for reference.

Due to the challenging timeline, half of titles & abstracts were assessed by a second team member. Discrepancies between the two assessors were discussed with a third team member. All discrepancies were resolved simply. More details are provided in the results.

2.3.5. Full-text appraisal

Each article which passed screening by title and abstract will be reviewed in full text for relevance by two members of the team, with one or more other person involved to resolve any discrepancies. Papers which provide evidence on one of our research questions will be critically appraised using well-established, published tools from the [Critical Appraisal Skills Programme](#). An Excel spreadsheet was created for storing this information in standardised format.

Once the size and quality of the available, relevant literature is established, the team will agree a minimum quality threshold, above which studies will be included in the review and full data extraction undertaken. The optimal approach for this was discussed during a WP2 workshop at the 4th General Assembly Meeting.

2.3.6. Data extraction & synthesis

Detailed information will be extracted from all included papers on the citation, the research study, its subjects and its findings including approach to data analysis and synthesis.

The literature is expected to be based on a range of research methods with potentially heterogeneous findings, therefore the review output is likely to comprise a narrative synthesis based on common themes. If it is possible to group data in tabular or graphical format to assist interpretation, this will be included. Inter and intra-individual differences related to disease stage and other contextual issues are likely to be a challenge to synthesising findings in a meaningful way. Expertise among the broader WP2 programme team will be used to ensure a fair and meaningful summary is produced.

3. Results

Many papers of high relevance to ROADMAP were retrieved in the search but were found to be outside of this SLR's inclusion criteria during screening. They have been flagged and are being gathered for potential use elsewhere in the programme.

3.1. Health economists

The list of stakeholders identified during the development of the protocol included health economists. A comparable search was developed for the Centre for Reviews and Dissemination ([CRD](#)) database and is included in the Annex. Only two citations were retrieved, neither of which answered the research questions. The search strategy is provided in Table 7, Annex III.

It was agreed that a different approach to explore the perspectives of health economists would be appropriate. This includes stakeholder engagement work and a pragmatic review of the literature around decision making by HTA organisations and regulatory bodies which is being undertaken by ROADMAP members at the London School of Economics (LSE) for completion concurrently with this SLR.

3.2. Grey literature

Searching for evidence from 'grey literature' sources was undertaken between 6th September and 1st November 2017 on the following sites:

- <http://www.greylit.org>
- <http://www.opengrey.eu>
- <http://explore.bl.uk>
- <http://www.alzscot.org>
- <https://www.google.co.uk>
- <https://www.alzheimers.org.uk>
- <http://www.alzheimer-europe.org/Research>
- <https://www.base-search.net/>
- <http://copac.jisc.ac.uk/search/form/main>
- <https://www.nice.org.uk/About/What-we-do/Evidence-Services/Evidence-Search>
- <https://scholar.google.com/>

Searches were performed using the keyword "Alzheimer" in combination with "outcome" or "progression", applying date limits of 2008 to 2017 where possible. On sites where there was no search facility or a very basic one, manual screening of all available publications by title was undertaken. Further details are provided in Annex IV.

If a search produced a list of websites, the first few paragraphs of each were screened in order to judge the suitability of the result for the research questions. Reports were screened based on table of content, summaries and relevant sections. In accordance with the SLR exclusion criteria, Ph.D. theses were not further screened. Published articles were not further screened but logged if they seemed relevant and were checked against the SLR's peer-reviewed literature search results list. The first ten result pages of google (which had several million hits for each search) were screened.

3.2.1. Evaluation of retrieved evidence

While some reports discussed the importance of involving patients and carers in decisions on meaningful and important outcomes, these were most often recommendations that did not translate into direct actions with implications for the SLR research questions (Alzheimer's Society 2012, Alzheimer's Disease Caregiving Advisory Board 2009). For each of the results which appeared to be relevant at first screen but subsequently excluded, the reason for exclusion is provided in Table 8 in Annex IV.

One study had some concrete results although it is not clear if the sample consists of people caring for people with AD or dementia in general so this may not fit with the rest of the evidence in the SLR (Alzheimer Europe 2006). Carers were asked which symptoms they find most problematic. They indicated that the ones which were the hardest to cope with were problems with activities of daily living, such as having a shower, incontinence and being left alone, and behavioural symptoms such as agitation or personality change.

3.3. Peer-reviewed literature search

3.3.1. Screening – inter-rater reliability

In advance of the SLR workshop at the 4th GAM (16th October 2017), 1,393 articles had been screened, 42 had passed the first screening stage with two independent decisions to include, 1,206 had been excluded by two decisions and 145 required a 3rd person to adjudicate because of disagreement between the first two independent decisions. This was an inter-rater agreement of 0.9. On discussion of the 145 conflicted decisions, most were found to be due to a desire by one of the two assessors to include a paper which was relevant to the programme in many ways but did not meet all the SLR inclusion criteria. Most often, study subjects had non-specific dementia or the paper was a clinical or scientific study of the outcomes of a particular intervention or treatment for AD. There were no papers which required revision of the inclusion criteria. This suggested that disagreement resulted from a tendency to be oversensitive, with low risk of excluding relevant material. On this basis, the team agreed to move forward to single screen for the remainder of the task. This work is now complete and 114 citations are being considered for full text review (Figure 1).

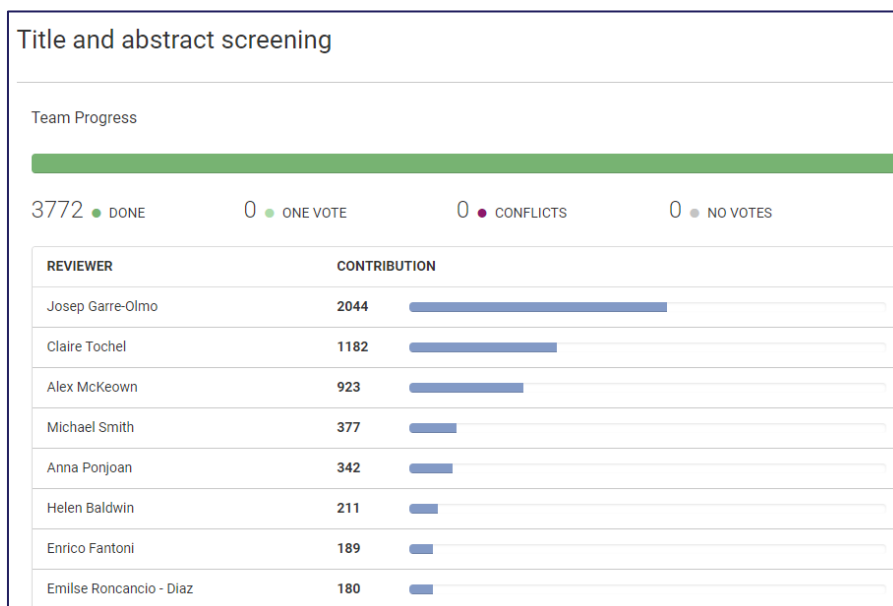


Figure 1 Screenshot from Covidence, the online tool used for screening

3.3.2. Critical appraisal

Full text versions of all 114 papers which passed the first screening phase were sought via Edinburgh University library, inter-library loan or direct contact with authors and have been retrieved in full-text. At the time of writing, 40 of the full text papers have been found to be of the wrong study type (mostly conference abstracts) and excluded. Following critical appraisal, other exclusions so far include seven papers which did not include people with AD across the spectrum, seven which did not provide answers to the research questions, two which did not include a stakeholder group of interest and one which was considered to be too low quality for its findings to be reliable. The interim PRISMA flow chart is shown in Figure 2. Note that the process of verification by a second member of the team may lead to some changes in these allocations.

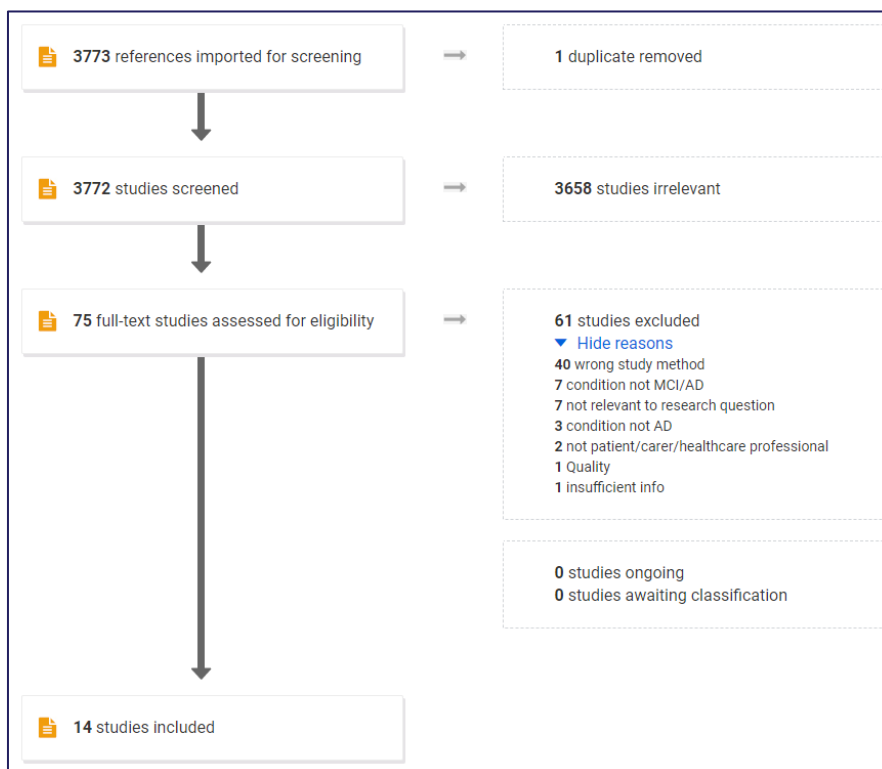


Figure 2 Interim PRISMA flowchart showing citation numbers in each stage at 15th November 2017

If time permits, where highly relevant, the authors of conference papers will be contacted to determine their study data is available in full.

3.3.3. Data extraction

At the time of writing, fourteen full text papers have passed forward for data extraction, references are included in Annexe V. A data extraction form was developed through consultation with WP2 partners and reference to existing work in similar projects. The team member who undertakes critical appraisal of full text articles will complete data extraction on each paper, with verification by a second member.

The timescale for this work and the distinct but overlapping working groups for each task means that they will continue in parallel, moving towards a deadline for the report at the end of February 2018.

4. Conclusion and next steps

The SLR continues to make progress by gathering high quality robust evidence from multiple sources on the outcomes of AD which matter most to a range of stakeholder groups and their perception of meaningful delay in disease progression.

The final report, including a summary of all findings and data synthesis, will be completed by the end of February 2018. It will feed directly into the final list of stakeholder-prioritised outcomes (D2.3) and other ROADMAP deliverables.

ANNEXES

Annex I. Working groups

Develop protocol	Amanda Ly (UEDIN) Anders Gustavsson (ROCHE) Anna Ponjoan (IDIAP JORDI GOL) Catherine Reed (Eli Lilly) Cathie Sudlow (UEDIN) Chi-Hun Kim (UOXF) Chris Edgar (ROCHE)	Christin Bexellius (ROCHE) Christophe Bintener (AE) Claire Tochel (UEDIN) Josep Garre-Olmo (IDIAP JORDI GOL) Julie Chandler (Eli Lilly) Lindsay Lee Lair (JPNV) Michele Potashman (BIOGEN)
Test and run search strategies	Claire Tochel Stephanie Cline (Takeda)	Maike Winters (Roche)
Develop inclusion & exclusion criteria	Alex McKeown (UOXF) Anders Gustavsson Anna Ponjoan Chi-Hun Kim	Claire Tochel Emilse Roncanciodiaz (GE) Josep Garre-Olmo Enrico Fantoni (GE)
Screen titles & abstracts	Alex McKeown Anna Ponjoan Helen Baldwin (UOXF) Michael Smith (UEDIN)	Claire Tochel Emilse Roncanciodiaz Josep Garre-Olmo Enrico Fantoni
Quality appraisal of full-text papers & data extraction	Alex McKeown Claire Tochel Buket Öztürk (AU) Emilse Roncanciodiaz Enrico Fantoni Helen Baldwin	Isabella Friis Jørgensen (UCPH) Josep Garre-Olmo Lars Pedersen (AU) Michael Smith Olin Janssen (UM) Stephanie Voß (UM)
Other	Grey literature Translation	Claire Tochel Christoph Jindra (UOXF) Filipa Landeiro (UOXF)

Annex II. Medline search strategy

Table 3 Medline search strategy with hits

	Search	Terms	Results
delay of disease progression	1	((delay or improv* or alleviat* or treat* or reduc* or lessen or prevent* or shorten or slow) and (symptom* or condition or effect or outcome)).ti,ab.	2,207,579
	2	disease progression/	135,023
	3	"disease progression".ab,ti.	51,644
	4	decline.ab,ti.	152,033
	5	1 or 2 or 3 or 4	2,460,864
patients & carers	6	Patients/	19,264
	7	Caregivers/	29,294
	8	patient*.ti,ab.	5,192,569
	9	(care?giver* or carer*).ti,ab.	49,283
	10	"support worker".ti,ab.	547
	11	6 or 7 or 8 or 9 or 10	5,230,365
healthcare professionals	12	Allied Health Personnel/	11,059
	13	exp Health Personnel/	452,821
	14	((doctor* or medical or nurs* or physi* or clinic* or geriatric* or psychiatrist* or "allied health" or neurolog* or health?care) and (prof* or practitioner)).ti,ab.	395,792
	15	12 or 13 or 14	799,266
AD across the spectrum	16	Alzheimer Disease/	81,153
	17	(alzheimer* adj (disease or dement*)).ti,ab.	94,179
	18	Dementia/	44,079
	19	dementia.ti,ab.	76,284
	20	((pre\$clinical or prodromal or pre?symptomatic) and (alzheimer * or dementia)).ti,ab.	1,621
	21	("mild cognitive impairment" or MCI or A\$MCI or M\$MCI or N\$MCI or CIND).ti,ab.	16,196
	22	pre?senile.ab,ti.	1,342
	23	16 or 17 or 18 or 19 or 20 or 21 or 22	174,946
Outcomes	24	"cost of illness".ab,ti.	1,177
	25	"Quality of Life"/	157,608
	26	("quality of life" or QOL or QALY or HRQOL or (health adj utili*)).ti,ab.	187,855
	27	(econom* and (burden or impact)).ti,ab.	36,107
	28	((cost* or resource) adj utili?ation) or hcru).ti,ab.	6,591
	29	((neuropsychiatr* or psychiatr* or behavi*) and symptom*).ti,ab.	94,932
	30	"dependency (psychology)"/	2,442
	31	dependen*.ab,ti.	1,329,162
	32	Health Resources/	11,033
	33	exp "Costs and Cost Analysis"/	213,357
	34	cost.ab,ti.	282,561

	35	diagnosis/ or early diagnosis/ or prodromal symptoms/	40,189
	36	(cognit* or memory or function* or depress* or anxiety or well?being or language or communicat*).ab,ti.	3,492,288
	37	(caregiver and (burden or impact)).ab,ti.	5,274
	38	"Activities of Daily Living"/	59,056
	39	activities of daily living.ab,ti.	18,269
	40	(caregiver and (burden or impact or stress or time)).ab,ti.	8,163
	41	outcome.ab,ti.	722,615
	42	Biomarkers/ or Amyloid/ or tau Proteins/	242,077
	43	(tau or biomarker or amyloid).ab,ti.	146,849
	44	24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43	5,734,100
Priorities	45	Health Priorities/	10,275
	46	(priorit* or importan* or valued or valuable or critical or wish or rank or relevan* or preferen* or meaningful).ti.	243,098
	47	45 or 46	250,069
Study method	48	(qualitative or delphi or "nominal group" or "priority setting" or "mixed method*" or multi?method or "patient?centred" or poll or consensus or "interpretive phenomenological analysis" or "thematic analysis" or "grounded theory" or "content analysis" or discours* or "lived experience*" or phenomenolog* or "conjoint analysis").ab,ti.	308,349
	49	"surveys and questionnaires"/ or delphi technique/ or health surveys/ or interviews as topic/ or focus groups/ or narration/ or qualitative research/	517,189
	50	((("semi-structured" or semistructured or unstructured or informal or "in-depth" or indepth or "face-to-face" or structured or guide) adj3 (interview* or discussion* or questionnaire* or survey*)) or (focus group* or qualitative or ethnograph* or fieldwork or "field work" or "key informant")).ti,ab.	226,399
	51	Humans/	17,026,907
	52	(48 or 49 or 50) and 51	724,698
	53	(23 and 11 and 44 and 47 and 52) or (23 and 15 and 44 and 47 and 52) or (23 and 11 and 5 and 52) or (23 and 15 and 5 and 52)	1,705

The final row above shows the grouped terms combined as indicated in table 1 in chapter 2 to answer each research question.

- Research question 1
 - patients and carers: 23 and 11 and 44 and 47 and 52
 - healthcare professionals: 23 and 15 and 44 and 47 and 52
- Research question 2
 - patients and carers: 23 and 11 and 5 and 52
 - healthcare professionals: 23 and 15 and 5 and 52

Annex III. Comparable search strategies for other databases

Table 4. Embase search strategy

Set	Search Statement
1	Alzheimer Disease/
2	(alzheimer* adj (disease or dement*)).ti,ab.
3	Dementia/
4	dementia.ti,ab.
5	((pre\$clinical or prodromal or pre?symptomatic) and (alzheimer* or dementia)).ti,ab.
6	("mild cognitive impairment" or MCI or A\$MCI or M\$MCI or N\$MCI or CIND).ti,ab.
7	pre?senile.ab,ti.
8	1 or 2 or 3 or 4 or 5 or 6 or 7
9	Patient/
10	Caregiver/
11	patient*.ti,ab.
12	(care?giver* or carer*).ti,ab.
13	support worker*.ti,ab.
14	9 or 10 or 11 or 12 or 13
15	paramedical personnel/
16	exp health care personnel/
17	((doctor* or medical or nurs* or physi* or clinic* or geriatric* or psychiatr* or "allied health" or neurolog* or health?care) and (prof* or practitioner)).ti,ab.
18	15 or 16 or 17
19	cost of illness.ab,ti.
20	quality of life/
21	("quality of life" or QOL or QALY or HRQOL or (health adj utili*)).ti,ab.
22	(econom* and (burden or impact)).ti,ab.
23	((cost* or resource) adj utili?ation) or hcru).ti,ab.
24	((neuropsychiatr* or psychiatr* or behavi*) and symptom*).ti,ab.
25	dependency (psychology)/
26	dependen*.ab,ti.
27	health care planning/
28	cost/ or "cost benefit analysis"/
29	cost.ab,ti.
30	diagnosis/ or "early diagnosis"/ or "prodromal symptom"/
31	(cognit* or memory or function* or depress* or anxiety or well?being or language or communicat*).ab,ti.
32	(caregiver and (burden or impact)).ab,ti.
33	daily life activity/
34	activities of daily living.ab,ti.
35	(caregiver and (burden or impact or stress or time)).ab,ti.

36	outcome.ab,ti.
37	biological markers/ or "amyloid"/ or "amyloid A protein"/ or "amyloid beta protein"/ or "tau Protein"/
38	(tau or biomarker or amyloid).ab,ti.
39	19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38
40	health care planning/
41	(priorit* or importan* or valued or valuable or critical or wish or rank or relevan* or preferen* or meaningful).ti.
42	40 or 41
43	(qualitative or delphi or "nominal group" or "priority setting" or "mixed method*" or multi?method or "patient?centred" or poll or consensus or "interpretive phenomenological analysis" or "thematic analysis" or "grounded theory" or "content analysis" or discours* or "lived experience*" or phenomenolog* or "conjoint analysis").ab,ti.
44	health care survey/ or "questionnaires"/ or "health survey"/ or "Delphi study"/ or "interview"/ or "information processing"/ or "narrative"/ or "qualitative research"/
45	((("semi-structured" or semistructured or unstructured or informal or "in-depth" or indepth or "face-to-face" or structured or guide) adj3 (interview* or discussion* or questionnaire* or survey*)) or (focus group* or qualitative or ethnograph* or fieldwork or "field work" or "key informant")).ti,ab.
46	human/
47	(43 or 44 or 45) and 46
48	((delay or improv* or alleviat* or treat* or reduc* or lessen or prevent* or shorten or slow) and (symptom* or condition or effect or outcome)).ti,ab.
49	disease course/
50	disease progression.ab,ti.
51	decline.ab,ti.
52	48 or 49 or 50 or 51
53	8 and 14 and 39 and 42 and 47
54	8 and 18 and 39 and 42 and 47
55	8 and 14 and 47 and 52
56	8 and 18 and 47 and 52
57	53 or 54 or 55 or 56

Table 5. Cinahl search strategy

#	Query
S1	Alzheimer's Disease/ OR (TI (alzheimer* N1 (disease or dement*)) or AB (alzheimer* N1 (disease or dement*))) OR Dementia/ OR dementia.ti,ab. OR (TI ((pre\$clinical or prodromal or pre?symptomatic) and (alzheimer * or dementia)) or AB ((pre\$clinical or prodromal or pre?symptomatic) and (alzheimer * or dementia))) OR (("mild cognitive impairment" or MCI or A\$MCI or M\$MCI or N\$MCI or CIND) or AB ("mild cognitive impairment" or MCI or A\$MCI or M\$MCI or N\$MCI or CIND)) OR (TI pre#senile or AB pre#senile)
S2	Patients/ OR Caregivers/ OR (TI patient* or AB patient*) OR (TI (care?giver* or carer*) or AB (care?giver* or carer*)) OR (TI "support worker*" or AB "support worker*")
S3	Allied Health Personnel/ OR exp Health Personnel/ OR (TI ((doctor* or medical or nurs* or physi* or clinic* or geriatric* or psychiatr* or "allied health" or neurolog* or health?care) and (prof* or practitioner)) or AB ((doctor* or medical or nurs* or physi* or clinic* or geriatric* or psychiatr* or "allied health" or neurolog* or health?care) and (prof* or practitioner)))
S4	"Economic Aspects of Illness"/ OR "Quality of Life"/ OR (TI "quality of life" or QOL or QALY or HRQOL or (health adj utili*)) or AB "quality of life" or QOL or QALY or HRQOL or (health adj utili*)) OR (TI (econom* and (burden or impact)) or AB (econom* and (burden or impact))) OR (TI (((cost* or resource) N1 utili?ation) or hcru) or AB (((cost* or resource) N1 utili?ation) or hcru)) OR (TI ((neuropsychiatr* or psychiatr* or behavi*) and symptom*) or AB ((neuropsychiatr* or psychiatr* or behavi*) and symptom*)) OR "dependency (psychology)"/ OR (TI dependen* or AB dependen*) OR Health Resource Utilization/ OR ("Costs and Cost Analysis"/) OR cost.ab,ti. OR (diagnosis/ or early diagnosis/)
S5	(AB (cognit* or memory or function* or depress* or anxiety or well?being or language or communicat*) or TI (cognit* or memory or function* or depress* or anxiety or well?being or language or communicat*)) OR (TI (caregiver and (burden or impact)) or AB (caregiver and (burden or impact))) OR "Activities of Daily Living"/ OR (TI activities of daily living OR AB activities of daily living) OR (TI (caregiver and (burden or impact or stress or time)) or AB (caregiver and (burden or impact or stress or time))) OR (TI outcome OR AB outcome) OR (Biological markers/ or Amyloid neuropathies/) OR (TI (tau or biomarker or amyloid) or AB (tau or biomarker or amyloid))
S6	S4 OR S5
S7	(Health Services Needs and Demand/) OR (TI (priorit* or importan* or valued or valuable or critical or wish or rank or relevan* or preferen* or meaningful))

S8	(TI (qualitative or delphi or "nominal group" or "priority setting" or "mixed method*" or multi?method or "patient?centred" or poll or consensus or "interpretive phenomenological analysis" or "thematic analysis" or "grounded theory" or "content analysis" or discours* or "lived experience*" or phenomenolog* or "conjoint analysis") or AB (qualitative or delphi or "nominal group" or "priority setting" or "mixed method*" or multi?method or "patient?centred" or poll or consensus or "interpretive phenomenological analysis" or "thematic analysis" or "grounded theory" or "content analysis" or discours* or "lived experience*" or phenomenolog* or "conjoint analysis")) OR ("surveys and questionnaires"/ or delphi technique/ or surveys/ or interviews/ or focus groups/ or narratives/ or qualitative studies/) OR (TI (((("semi-structured" or semistructured or unstructured or informal or "in-depth" or indepth or "face-to-face" or structured or guide) adj3 (interview* or discussion* or questionnaire* or survey*)) or (focus group* or qualitative or ethnograph* or fieldwork or "field work" or "key informant") or AB (((("semi-structured" or semistructured or unstructured or informal or "in-depth" or indepth or "face-to-face" or structured or guide) adj3 (interview* or discussion* or questionnaire* or survey*)) or (focus group* or qualitative or ethnograph* or fieldwork or "field work" or "key informant")))) AND Human/
S9	(TI ((delay or improv* or alleviat* or treat* or reduc* or lessen or prevent* or shorten or slow) and (symptom* or condition or effect or outcome)) or AB ((delay or improv* or alleviat* or treat* or reduc* or lessen or prevent* or shorten or slow) and (symptom* or condition or effect or outcome))) OR disease progression/ OR (TI "disease progression" or AB "disease progression") OR (TI decline or AB decline)
S10	S1 AND S2 AND S6 AND S7 AND S8
S11	S1 AND S3 AND S6 AND S7 AND S8
S12	S1 AND S2 AND S8 AND S9
S13	S1 AND S3 AND S8 AND S9
S14	S10 OR S11 OR S12 OR S13

Table 6. PsycInfo search strategy

Set	Search Statement
1	Alzheimer Disease/
2	(alzheim* adj (disease or dement*)).ti,ab.
3	Dementia/
4	dementia.ti,ab.
5	((pre\$clinical or prodromal or pre?symptomatic) and (alzheim* or dementia)).ti,ab.
6	("mild cognitive impairment" or MCI or A\$MCI or M\$MCI or N\$MCI or CIND).ti,ab.
7	pre?senile.ab,ti.
8	1 or 2 or 3 or 4 or 5 or 6 or 7
9	Patients/
10	Caregivers/
11	patient*.ti,ab.
12	(care?giver* or carer*).ti,ab.
13	"support worker*".ti,ab.

14	9 or 10 or 11 or 12 or 13
15	Allied Health Personnel/
16	exp Health Personnel/
17	((doctor* or medical or nurs* or physi* or clinic* or geriatric* or psychiatr* or "allied health" or neurolog* or health?care) and (prof* or practitioner)).ti,ab.
18	15 or 16 or 17
19	"cost of illness".ab,ti.
20	"Quality of Life"/
21	("quality of life" or QOL or QALY or HRQOL or (health adj utili*)).ti,ab.
22	(econom* and (burden or impact)).ti,ab.
23	((cost* or resource) adj utili?ation) or hcru).ti,ab.
24	((neuropsychiatr* or psychiatr* or behavi*) and symptom*).ti,ab.
25	"dependency (personality)"/
26	dependen*.ab,ti.
27	"Health Care Costs"/
28	exp "Costs and Cost Analysis"/
29	cost.ab,ti.
30	diagnosis/ or early diagnosis/ or prodromal symptoms/
31	(cognit* or memory or function* or depress* or anxiety or well?being or language or communicat*).ab,ti.
32	(caregiver and (burden or impact)).ab,ti.
33	"Activities of Daily Living"/
34	activities of daily living.ab,ti.
35	(caregiver and (burden or impact or stress or time)).ab,ti.
36	outcome.ab,ti.
37	Biomarkers/ or Amyloid/ or tau Proteins/
38	(tau or biomarker or amyloid).ab,ti.
39	19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38
40	Health Attitudes/
41	(priorit* or importan* or valued or valuable or critical or wish or rank or relevan* or preferen* or meaningful).ti.
42	40 or 41
43	(qualitative or delphi or "nominal group" or "priority setting" or "mixed method*" or multi?method or "patient?centred" or poll or consensus or "interpretive phenomenological analysis" or "thematic analysis" or "grounded theory" or "content analysis" or discours* or "lived experience*" or phenomenolog* or "conjoint analysis").ab,ti.
44	"surveys and questionnaires"/ or delphi technique/ or health surveys/ or interviews as topic/ or focus groups/ or narration/ or qualitative research/
45	((("semi-structured" or semistructured or unstructured or informal or "in-depth" or indepth or "face-to-face" or structured or guide) adj3 (interview* or discussion* or questionnaire* or survey*)) or (focus group* or qualitative or ethnograph* or fieldwork or "field work" or "key informant")).ti,ab.

46	43 or 44 or 45
47	limit 46 to human
48	((delay or improv* or alleviat* or treat* or reduc* or lessen or prevent* or shorten or slow) and (symptom* or condition or effect or outcome)).ti,ab.
49	disease course/
50	"disease progression".ab,ti.
51	decline.ab,ti.
52	48 or 49 or 50 or 51
53	(8 and 14 and 39 and 42 and 47) or (8 and 18 and 39 and 42 and 47) or (8 and 14 and 52 and 47) or (8 and 18 and 52 and 47)

Table 7. CRD search strategy

Item	Search terms in CRD database
1	(Alzheimer Disease) IN DARE, NHSEED, HTA
2	((alzheimer* ADJ (disease OR dement*)):ti,ab) IN DARE, NHSEED, HTA
3	(Dementia) IN DARE, NHSEED, HTA
4	(dementia:ti,ab) IN DARE, NHSEED, HTA
5	((pre-clinical OR preclinical OR prodromal OR pre-symptomatic OR presymptomatic) AND (alzheimer* OR dementia)):ti,ab) IN DARE, NHSEED, HTA
6	((mild cognitive impairment OR MCI OR AMCI OR MMCI OR NMCI OR CIND):ti,ab) IN DARE, NHSEED, HTA
7	((pre-senile OR presenile):ti,ab) IN DARE, NHSEED, HTA
8	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7
9	((cost of illness):ti,ab) IN DARE, NHSEED, HTA
10	(quality of life) IN DARE, NHSEED, HTA
11	((quality of life OR QOL OR QALY OR HRQOL OR (health ADJ utili*)):ti,ab) IN DARE, NHSEED, HTA
12	((econom* AND (burden OR impact)):ti,ab) IN DARE, NHSEED, HTA
13	((cost* OR resource) ADJ utilization) OR hcr):ti,ab) IN DARE, NHSEED, HTA
14	((neuropsychiatr* OR psychiatr* OR behavi*) AND symptom*):ti,ab) IN DARE, NHSEED, HTA
15	(dependency AND psychology) IN DARE, NHSEED, HTA
16	(dependen*:ti,ab) IN DARE, NHSEED, HTA
17	(Health Resources) IN DARE, NHSEED, HTA
18	(exp costs and cost analysis) IN DARE, NHSEED, HTA
19	(cost:ti,ab) IN DARE, NHSEED, HTA
20	(diagnosis OR early diagnosis OR prodromal symptoms) IN DARE, NHSEED, HTA
21	((cognit* OR memory OR function* Or depress* OR anxiety OR well-being OR wellbeing OR language OR communicat*):ti,ab) IN DARE, NHSEED, HTA

22	((caregiver AND (burden OR impact)):ti,ab) IN DARE, NHSEED, HTA
23	(activities of daily living) IN DARE, NHSEED, HTA
24	((activities of daily living):ti,ab) IN DARE, NHSEED, HTA
25	((caregiver AND (burden OR impact OR stress OR time)):ti,ab) IN DARE, NHSEED, HTA
26	(outcome:ti,ab) IN DARE, NHSEED, HTA
27	(biomarkers OR amyloid OR tau proteins) IN DARE, NHSEED, HTA
28	((tau OR biomarker OR amyloid):ti,ab) IN DARE, NHSEED, HTA
29	#9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29

Annex IV. Grey literature search strategy & results

Purpose: to seek evidence which answers our research questions from sources not captured by the main SLR searching process.

Goal: to demonstrate reasonable attempts to find information from organisations across Europe which represent, support or otherwise engage with people with AD. If they have undertaken qualitative research, interviews or focus groups with people with AD or their carers / supporters which answer our questions we want to try and find it – this may be available directly on their website or they may have a list of titles available on request by email. We will also include google which has a very broad reach for such documents.

Scope: although such reports are a different type of evidence (i.e. they are unlikely to be formal research studies) they still must be relevant to our research questions and meet our inclusion criteria. As it is impractical to achieve a comprehensive search given the number of potential sources, the goal is to demonstrate a systematic approach and reasonable effort to look for information in as unbiased a way as possible.

Process

1. Identify a range of relevant websites including generic grey literature sources, condition-specific organisations & generic search engines.
2. Where the site has a search facility use broad search terms below, otherwise scan report names for relevance to the research questions
 - a. “Alzheimer” and “outcome”
 - b. “Alzheimer” and “progression”
3. Where possible use the search to apply date limits or check for date before downloading
 - a. 2008 – 2017
4. Save details of all searches in the table below, no of hits, relevant report titles, efforts made to acquire full text.
5. On acquisition of full text report, read it and check whether it provides evidence to answer either of the research questions, and if so, save it and log citation details.
6. Read relevant full reports, extract useful information and synthesise.

Table 8. Summary of results

Date	Source	Search terms	Hits	details
06/09/2017	http://www.greylit.org	Alzheimer & outcome 2008 - 2017	0	
		Alzheimer & progression 2008 - 2017	1	2014-2015 Alzheimer's disease progress report : advancing research toward a cure, Rodgers, Anne Brown, National Institute on Aging – broken link on website – see follow up below
26.10.2017	http://www.greylit.org	Alzheimer + outcome 2008 - 2017	0	
26.10.2017	http://www.greylit.org	Alzheimer + outcome	9	<p>2014-2015 Alzheimer's disease progress report : advancing research toward a cure, Rodgers, Anne Brown, National Institute on Aging (http://www.questri.com/wp-content/uploads/2016/09/2014-2015_alzheimers-disease-progress-report.pdf)</p> <ul style="list-style-type: none"> Only section CATEGORY E. CARE AND CAREGIVER SUPPORT was potentially interesting. However, the section did neither discuss which outcomes should be prioritised, nor did it discuss meaningful delay. The report is thus not of further interest
26.10.2017	http://www.greylit.org	Alzheimer + progression 2008 - 2017	3	None relevant

Date	Source	Search terms	Hits	details
26.10.2017	http://www.greylit.org	Alzheimer + progression (year was taken into account manually)	52	<p>ALZHEIMER'S DISEASE CAREGIVING ADVISORY GROUP - Convened by the National Alliance for Caregiving (http://www.caregiving.org/data/AlzhADPilotCaregiverAdBrd.pdf)</p> <ul style="list-style-type: none"> While the report has a section on how to involve caregivers in research so that guidelines can include evidence that reflects the caregiving experience, the report does not go beyond the recommendation of doing so and does not provide evidence on priorities from family caregivers or discusses meaningful delay <p>National Plan to Address Alzheimer's Disease: 2013 Update (https://aspe.hhs.gov/system/files/pdf/102516/NatlPlan2013.pdf)</p> <ul style="list-style-type: none"> Item "Action 2.D.2: Identify and review measures of high-quality dementia care" is aimed at identifying measures for high-quality dementia care and emphasises consensus. However, it is a goal and project, thus no further information can be found in the report.
06/09/2017	https://www.nia.nih.gov/ National Institute on Aging (follow up from above as broken link to this document)	Email to National Institute on Aging	0	Response from NIAIC (7 th Sep): "Unfortunately, the "2014-2015 Alzheimer's Disease Progress Report: Advancing Research Toward a Cure" is no longer available on our website."
	Comment on above			Available online see link above
06/09/2017	http://www.opengrey.eu	Alzheimer & outcome 2008 - 2017	3	All theses - excluded
		Alzheimer & progression 2008 - 2017	53	All theses - excluded
26.10.2017	http://www.opengrey.eu	Alzheimer & outcome 2008 - 2017	0	
26.10.2017	http://www.opengrey.eu	Alzheimer & outcome	9	All theses - excluded

Date	Source	Search terms	Hits	details
26.10.2017	http://www.opengrey.eu	Alzheimer & progression 2008 - 2017	0	
26.10.2017	http://www.opengrey.eu	Alzheimer & progression	53	All theses - excluded
06/09/2017	http://explore.bl.uk British library	Alzheimer & outcome 2008 - 2017	13 books 6 theses 3 audio recordings	Lay perspectives of medicines for dementia: a qualitative study Taylor, Denise Ann, University of Bath 2009 – thesis but relevant for elsewhere in WP2?
		Alzheimer & progression 2008 - 2017	20 theses 17 books 6 audio recordings	None answer review questions
26.10.2017	http://explore.bl.uk British library	Alzheimer & outcome (restricted to start and end date)	23, 3 audio 6 theses 14 books	Taylor, D. A., 2009. <i>Lay Perspectives of Medicines for Dementia: a Qualitative Study</i> . Thesis (Doctor of Philosophy (PhD)). University of Bath <i>as above</i> Intellectual disability and dementia : research into practice / edited by Karen Watchman ; foreword by Diana Kerr. London : Jessica Kingsley Publishers, 2014. <i>Not grey literature.</i>
26.10.2017	http://explore.bl.uk British library	Alzheimer & progression (restricted to start and end date)	43, 20 theses 17 books 6 audio	MacQuarrie, C. R. (2008). <i>Mid-Life Transitions: Spousal Experiences of Coping with Dementia of the Alzheimer Type</i> . In H. S. Jeong (Ed.), <i>Alzheimer's Disease in the Middle-Aged</i> (pp. 225-253). New York: Nova Science Publishers, Inc. <i>Not grey literature.</i>
06/09/2017	http://www.alzscot.org	Alzheimer & outcome 2008 - 2017	35	Perspectives on outcomes for early stage support See below

Date	Source	Search terms	Hits	details
26.10.2017	http://www.alzscot.org	Alzheimer & outcome	36	Perspectives on outcomes for early stage support <i>Trying to retrieve the site on 30.10.2017 lead to "Page not found error". I made an inquiry (info@alzscot.org). No reply 1.11.2017</i>
26.10.2017	http://www.alzscot.org	Alzheimer & outcome 2008 - 2017	1	Scotland's National Dementia Strategy 2017-2020 <ul style="list-style-type: none"> Is a strategy paper and as such does not address outcome priorities beyond those being decided upon in some, non-disclosed way
26.10.2017	http://www.alzscot.org	Alzheimer & progression 2008 - 2017	1	Scotland's National Dementia Strategy 2017-2020 Is a strategy paper and as such does not address outcome priorities beyond those being decided upon in some, non-disclosed way
26.10.2017	http://www.alzscot.org	Alzheimer + progression	56	National Dementia Dialogue events 2015 <i>Only events, but results would be interesting. I got in touch with Alzheimer Scotland (info@alzscot.org) and made an inquiry whether results are published somewhere. No reply by 1.11.2017</i>
06/09/2017	gcolston@alzscot.org email to request info related to Practitioner Research Older People programme		0	Response from Lindsay Kinnaird (25 th Sep): "To my knowledge none of the projects would contribute to the questions below".

06/09/2017	https://www.google.co.uk	Alzheimer & outcome 2008 - 2017	<p>Outcomes from the James Lind Alliance priority setting partnership – 2013</p> <ul style="list-style-type: none"> • Brought together a wide range of organisations that collectively represent the views of people affected by dementia, practitioners and clinicians to try to agree on priorities regarding the care, treatment, diagnosis and prevention of dementia → result is list of top 10 priorities for research • The report discusses questions that were submitted via a questionnaire. While these questions can be interpreted as giving evidence of what seems important to carers and other stakeholders, it is not the main focus of the report and thus, without making the step to organise the information into priorities, the report cannot answer questions of the systematic review. <ul style="list-style-type: none"> ○ Also independence made it on top 1 question • They also only refer to dementia really, not AD <p>Consultation on Commissioning Outcomes Framework February 2012</p> <ul style="list-style-type: none"> • The report is a response to the Commissioning Outcomes Framework which seems to be an initiative that tries to find indicators for outcome measures for people dementia across the health and social care system. As such, it proposes indicators that measure outcomes at an aggregate level but does not provide evidence beyond that on priorities of outcomes by patients, carer or healthcare professionals. It mentions quality of life but as the abstract fuzzy concept <p>Outcomes measures in a decade of dementia and mild cognitive impairment trials – Harrison, 2016 (already included in main search)</p> <p>Priority of Treatment Outcomes for Caregivers and Patients with Mild Cognitive Impairment: Preliminary Analyses, Gonzalez-Barrios, 2016 (already included in main search)</p> <p>Outcomes Assessment in Clinical Trials of Alzheimer’s Disease and its Precursors: Ready for Short-term and Long-term Clinical Trial Needs <i>Not grey literature (see below)</i></p>
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Date	Source	Search terms	Hits	details
				<p data-bbox="1084 357 1713 384">Scotland's National Dementia Strategy 2017-2020</p> <ul data-bbox="1137 395 1989 451" style="list-style-type: none"> • Is a strategy paper and as such does not address outcome priorities beyond those being decided upon in some, non-disclosed way <p data-bbox="1084 491 2051 555">Beyond barriers. Developing a palliative care approach for people in the later stages of dementia. An Alzheimer Scotland Partnership Project – 2010?</p> <ul data-bbox="1137 560 2056 770" style="list-style-type: none"> • Objective of the “Beyond barriers” project were the development, implementation and evaluation of an educational programme that focusses on communication, to provide relatives with an equal opportunity to participate in the programme, to enable staff to fully participate, to enable care home staff and relative to influence the practice of other staff within their care home and so on. The project didn't try to elicit information on patient priorities or meaningful delays and is thus nor relevant <p data-bbox="1084 810 1966 874">Dementia outcome measures: charting new territory. Report of a JPND working group on longitudinal cohorts, 2015</p> <p data-bbox="1084 879 1619 906">(http://www.neurodegenerationresearch.eu/)</p> <ul data-bbox="1137 911 2033 1034" style="list-style-type: none"> • Study involves experts to identify the best dementia outcome measures. • Report does not distinguish between types of dementia • It is more a review and ranking of diagnostic and measurement instruments <p data-bbox="1084 1114 2018 1177">World Alzheimer Report 2016 Improving healthcare for people living with dementia coverage, Quality and costs now and in the future</p> <ul data-bbox="1137 1182 2033 1268" style="list-style-type: none"> • Mentions importance of eliciting individual preferences but seems to not handle the issue themselves and thus does not answer the research question

26.10.2017	Google.com	Alzheimer & outcome 2008 - 2017	2,690,000 only first 10 pages checked	<p>2011 Alzheimer Europe Survey: The Value of Knowing (http://www.alzheimer-europe.org/Research/Value-of-Knowing)</p> <ul style="list-style-type: none"> I went over the questionnaire and the questions are all related to knowledge about AD or whether or not somebody would want use a diagnostic tool to learn about the likelihood of a future diagnosis. The research does not contribute to answering the review question <p>Who cares? The state of dementia care in Europe (http://www.alzheimer-europe.org/Publications/Alzheimer-Europe-Reports)</p> <ul style="list-style-type: none"> Reports results of survey of people caring for AD patients. There is one question that asks for the most problematic symptoms but that's about it <p>Rotpacki et al 2017: Clinically Meaningful Outcomes in Early Alzheimer Disease - A Consortia-Driven Approach to Identifying What Matters to Patients. <i>Therapeutic Innovation & Regulatory Science</i> 51(3). <i>Not grey literature.</i></p> <p>Dementia 2012: A national challenge (https://www.alzheimers.org.uk/download/downloads/id/1389/alzheimers_society_dementia_2012- full_report.pdf)</p> <ul style="list-style-type: none"> Does not itself prioritise outcomes but instead uses those from Dementia Action Alliance National Dementia Declaration, which seems to be participatory. It thus uses priorities defined elsewhere and does not elicit information themselves. One should however look at the report they are citing <p>Women and Dementia A Global Challenge (https://www.gadaalliance.org/wp-content/uploads/2017/02/Women-Dementia-A-Global-Challenge_GADAA.pdf)</p> <ul style="list-style-type: none"> This report provides a brief overview of the key dementia-related issues facing women around the globe, highlighting more comprehensive literature on the subject. It then considers the next steps urgently needed to address these challenges. It identifies where national dementia strategies have begun to take gender perspectives; and analyses which
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Date	Source	Search terms	Hits	details
				<p>international policy frameworks must be used to construct gendersensitive responses. The time is now for gender-equality advocates and those involved in dementia policy and practice to put women at the front and centre of global dementia action</p> <ul style="list-style-type: none"> • It is a systematic review and thus does not explicitly elicit information on outcomes that are not included via the publications it includes. • It also focuses on national dementia plans and strategies <p>Sorensen et al 2008: Early counselling and support for patients with mild Alzheimer's disease and their caregivers: A qualitative study on outcome. <i>Aging and Mental Health</i> 2008 12(4) <i>Not grey literature.</i></p> <p>Harisson et al 2016: Outcomes measures in a decade of dementia and mild cognitive impairment trials. <i>Alzheimer's Research & Therapy</i> 2016 8:48. <i>Not grey literature.</i></p> <p>Posner et al 2017: Outcomes Assessment in Clinical Trials of Alzheimer's Disease and its Precursors: Readying for Short-term and Long-term Clinical Trial Needs. <i>Innovations in Clinical Neuroscience</i> 14(1-2) <i>Not grey literature.</i></p>
26.10.2017	Google.com	Alzheimer & progression 2008 - 2017	9,450,000, only first 10 pages checked	None answer review questions
26.10.2017	https://www.alzheimers.org.uk	Alzheimer & outcome 2008 - 2017	3	None answer review questions

Date	Source	Search terms	Hits	details
26.10.2017	https://www.alzheimers.org.uk	Alzheimer & progression 2008 - 2017	6	<p>End of life care (https://www.alzheimers.org.uk/info/20091/position_statements/139/end_of_life_care)</p> <ul style="list-style-type: none"> • Mentions some relevant outcomes, however, it is not a systematic report but just a piece on the website and does not itself elicit the information but, if at all, quotes other publications
30.10.2017	http://www.alzheimer-europe.org/Research	Alzheimer & outcome 2008 - 2017	910	<p><i>Only first 10 result page were screened and only first few paragraphs were screened to assess suitability</i></p> <p>Working group explores views of people with dementia and carers about outcome measures (http://www.alzheimer-europe.org/News/EU-developments/Wednesday-24-June-2015-Working-group-explores-views-of-people-with-dementia-and-carers-about-outcome-measures/(language)/eng-GB)</p> <ul style="list-style-type: none"> • Not itself a report but just a brief news story
30.10.2017	http://www.alzheimer-europe.org/Research	Alzheimer & progression 2008 - 2017	1247	<p><i>Only first 10 result page were screened and only first few paragraphs were screened to assess suitability</i></p> <p>None answer review questions</p>
1.11.2017	https://www.base-search.net/	Alzheimer & outcome 2008 - 2017	29	None answer review questions
1.11.2017	https://www.base-search.net/	Alzheimer & progression 2008 - 2017	51	<p>Caring for elders with Alzheimer's disease: experiences of family caregivers</p> <ul style="list-style-type: none"> • Link https://www.revistas.ufg.br/fen/article/view/46488 could not be accessed from my website and I couldn't find anything else on it <p>Olivetti, L et al 2017 Better Journeys for People with Dementia in Northern Sydney. International Journal of Integrated Care, 17(3): A116, pp. 1-8, DOI: dx.doi.org/10.5334/ijic.3228</p> <p><i>Not grey literature (but also only two pages with not much information)</i></p>

Date	Source	Search terms	Hits	details
1.11.2017	http://copac.jisc.ac.uk/search/form/main	Alzheimer & outcome (year had to be taken out, search in title field)	4	None answer review questions
1.11.2017	http://copac.jisc.ac.uk/search/form/main	Alzheimer & progression (year had to be taken out, search in title field)	16	None answer review questions
1.11.2017	https://www.nice.org.uk/About/What-we-do/Evidence-Services/Evidence-Search	Alzheimer & outcome 2008 - 2017	0	
1.11.2017	https://www.nice.org.uk/About/What-we-do/Evidence-Services/Evidence-Search	Alzheimer & progression 2008 - 2017	0	
1.11.2017	https://scholar.google.com/scholar?hl=en&as_sdt=0,5	Alzheimer & outcome 2008 - 2017	82900 only first 10 pages checked	All published results and none seems to answer research questions
1.11.2017	https://scholar.google.com/scholar?hl=en&as_sdt=0,5	Alzheimer & progression 2008 - 2017	135,000 only first 10 pages checked	All published results and none seems to answer research questions

Annex V. References

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