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TITLE: Psychological interventions to improve psychological wellbeing in people with dementia or mild cognitive impairment: systematic review and meta-analysis protocol

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ABSTRACT

Introduction: Dementia and mild-cognitive impairment are associated with an increased risk of depression, anxiety, psychological distress and poor quality of life. However, there is a lack of evidence-based treatments to address such difficulties within this population. Furthermore, there is little research relating to the design of randomised controlled trials examining psychological interventions for dementia and mild cognitive impairment, such as effective recruitment techniques, trial eligibility, and appropriate comparators.

Methods and analysis: Systematic review of electronic databases (CINAHL; EMBASE; PsychInfo; Medline; ASSIA and CENTRAL), supplemented by expert contact, reference and citation checking and grey literature searches. Published and unpublished studies will be eligible for inclusion with no limitations placed on year of publication. Primary outcomes of interest will be standardised measurements of depression, anxiety, psychological distress or mental health related quality of life. Eligibility and randomisation proportions will be calculated as secondary outcomes. If data permits, meta-analytical techniques will examine: (1) overall effectiveness of psychological interventions for people with dementia or mild cognitive impairment in relation to outcomes of depression, anxiety, psychological distress or mental health related quality of life; (2) clinical and methodological moderators associated with effectiveness; (3) proportions eligible, recruited and randomised.

Ethics and dissemination: Ethical approval is not required for the present systematic review. Results will inform the design of a feasibility study examining a new psychological intervention for people with dementia and depression, with dissemination through publication in peer reviewed journals and presentations at relevant conferences.

PROSPERO registration number: CRD42015025177

Strengths and Limitations

- Review protocol adopts the following quality standards— independent study selection, data extraction, risk of bias assessments by two researchers—as informed by the Centre of Reviews and Dissemination (CRD) guidance and PRISMA-P guidelines.
- The first review to be conducted with a secondary aim of examining factors related to successful participant recruitment into psychological interventions trials for dementia and mild cognitive impairment.
- To increase quality of included studies and reduce methodological heterogeneity, studies with high risk of bias (following Cochrane Collaboration guidance) concerning method of random sequence generation and allocation concealment were excluded.
- Due to resource limitations selected studies were limited to those publically available in the English language; therefore language bias may be present.
- High levels of clinical heterogeneity may exist as a consequence of included studies adopting psychological interventions informed by variety of psychological approaches

INTRODUCTION

Whilst healthcare advances across the developed world have resulted in increased life expectancy,[1] increased numbers of people are also placed at risk of developing chronic health conditions.[2] As such, dementia, a common chronic condition associated with aging,[3] has become of significant concern. Current estimates of people living with dementia worldwide are in excess of 35 million, set to double by 2030, and more than triple by 2050.[4] In the absence of a cure for dementia, or identification of specific causal factors as targets for preventative interventions,[5] dementia care strategies are focused on providing appropriate psychological and psychosocial support, alongside the provision of physical care.[6] However, access to evidence based psychological therapies to improve the long-term psychological wellbeing and mental health related quality of life in people with dementia is currently limited.[7]

Elevated symptoms of depression in people with dementia are common with prevalence reported to be as high as 30%,[8, 9] compared to 13.2% of older adults without cognitive impairment.[10] However the prevalence of depression in people with dementia should potentially be considered with caution. Rates of depression vary across dementia type, with prevalence rates higher in patients experiencing dementia with Lewy bodies and vascular dementia, in comparison with Alzheimer's Disease.[8] Additionally, lower rates of depression (0.9% to 4.8%) have been found when a strict criterion is adopted with respect to meeting diagnosis of major depression.[11] In relation to mild cognitive impairment (MCI) rates of mild depressive symptoms have varied from 26.5%,[12] to 49.3%,[13] with 14% experiencing severe depressive symptoms.[13] Furthermore, prevalence of elevated symptoms of anxiety have been found to range from 8% to 71%,[14] with 5%-21% of people with a dementia meeting diagnostic criteria for a specific anxiety disorder.[15] However,

there is little consensus concerning how to define and measure anxiety experienced by people with a dementia.[9] Rates of anxiety symptoms have also been found to vary widely in MCI (10%-74%).[16]

Despite variability reported regarding the prevalence of depression and anxiety in people with dementia and MCI,[9] a clear need remains for evidence based psychological therapies to address these difficulties. However, only six studies were identified in a Cochrane review examining the effectiveness of psychological interventions specifically targeting depression or anxiety.[9] Other reviews have tended to focus on the effectiveness of non-pharmacological interventions for a variety of neuropsychiatric symptoms in severe or very severe dementia.[17] Furthermore, whilst depression and anxiety have a significant impact on the lives of people with dementia and MCI, the negative impact of these psychological difficulties extend beyond their symptomatology alone.[8] For depression and anxiety, symptoms have been associated with reduced quality of life,[8, 18] increased likelihood of being placed in a nursing home or other institution,[19, 20] and caregiver burden.[21, 22] Furthermore, specifically with respect to depression higher rates of cognitive decline have been reported,[23] with increased behavioural disturbances associated with anxiety.[24]

As such, the need to develop evidence based psychological interventions to support the long-term emotional needs of people experiencing dementia, and examine their impact on difficulties beyond those related solely depression and anxiety, is justified. Developing interventions that enable people with dementia to 'live well' is a priority with the UK National Dementia strategy,[25] with recent research focusing on improving general wellbeing and quality of life to facilitate people to 'live well' with dementia.[26] However, dementia research has previously adopted disease-focused rather than socially-orientated

perspectives.[27] Subsequently, previous reviews focusing on interventions targeting medicalised constructs such as depression or anxiety (for example,[9]) may have omitted the evidence base concerning psychological interventions targeting broader constructs relating to general psychological wellbeing. Indeed, there are currently no systematic reviews examining the evidence base of psychological interventions targeted at improving general psychological wellbeing or mental health related quality of life in people with dementia and MCI.[28]

As well as establishing the evidence base for psychological interventions targeting general psychological wellbeing in people with dementia or MCI, it may also be prudent to investigate clinical and methodological characteristics associated with these studies. A number of complexities have been identified when recruiting participants into pharmaceutical trials associated with dementia or MCI, including capacity to consent and the presence of physical or neuropsychiatric symptoms impacting on eligibility.[29] Furthermore, a number of known barriers exist regarding recruiting older adults into psychological intervention trials, including stigma concerning mental health difficulties experienced by older adults,[30-32] preoccupation with physical health symptoms,[33] and lack of healthcare professional recognition.[34] Participants and professionals have also been found to view participation in depression trials with greater caution for older rather than younger adults and for people with physical health conditions.[35] With respect to anxiety, symptoms are frequently unrecognised in older adults given they often do not conform to existing diagnostic criteria.[36] Additionally, elevated stigma exists concerning anxiety in older adults in comparison with other mental health conditions, including depression.[32]

Greater understanding of methodological factors may therefore help inform successful recruitment strategies into subsequent studies aiming to examine the effectiveness of psychological interventions for people with dementia and MCI to improve psychological wellbeing. A recent systematic review examining recruitment in pharmacological trails for Alzheimer's disease has suggested 10% of potential participants would take part in clinical drug trials if all those diagnosed were invited to participate.[29] However, currently, no reviews exist examining factors related to successful recruitment into psychological interventions for dementia. The present systematic review therefore aims to identify clinical and methodological moderators associated with effectiveness and recruitment strategies for trials involving people with dementia and MCI, alongside examining the overall effectiveness of psychological interventions to improve psychological wellbeing.

OBJECTIVES

1. To examine the effectiveness of psychological interventions targeted at improving psychological and emotional wellbeing and mental health related quality of life, compared with active and inactive control conditions, in adults with dementia or MCI.
2. To investigate clinical and methodological moderators associated with effectiveness.
3. To identify recruitment techniques and effectiveness of the techniques utilised across trials.

METHODS AND ANALYSIS

The Centre of Reviews and Dissemination (CRD) guidance for conducting systematic reviews,[37] will be followed, with results of the review reported in accordance with

PRISMA-P guidelines.[38] The review is registered with the PROSPERO International Prospective Register of Systematic Reviews (registration number CRDXXXXXXXXXXX).

Study Inclusion and Exclusion Criteria

Type of Studies

Randomised controlled trials (RCTs) and cluster RCTs, using a method of random sequence generation with allocation concealment assessed as having low or unclear risk of bias using the Cochrane Collaboration Risk of Bias tool,[39] will be eligible for inclusion. Quasi-RCTs and cross-over trials will not be eligible for inclusion.

Types of participants

Adults with diagnosis of a dementia or MCI identified by the DSM-IV (American Psychiatric Association,[40]) International Classification of Diseases-10 (ICD-10,[41]) alternative validated diagnostic criteria, or recorded in their medical records. Alzheimer's disease, vascular dementia, dementia with Lewy bodies, fronto-temporal dementia and MCI will be eligible for inclusion. No limitations will be placed on the severity of dementia, length of time since diagnosis, with dementia patients in both community and institutional settings eligible. No restrictions will be placed on severity of depression, anxiety, psychological distress or mental health related quality of life.

Types of interventions

The review will include any psychological therapy and includes specific interventions with no limitations placed on the psychological therapy informing the intervention. The intervention should target an improvement in general psychological wellbeing as identified

by measurement of depression, anxiety, psychological distress or mental health related quality of life. As long as the intervention is targeted at one of these outcome measures, interventions for the dementia patient and informal carer dyad will be eligible. Additionally, all intervention delivery modes (face-to-face, telephone, internet) and person supporting the intervention (professional, paraprofessional, unsupported) will be eligible for inclusion. Both inactive and active comparators will be considered eligible. However, the trial design must allow for the isolation of the effect of the psychological intervention of interest. Examples of appropriate designs are as follows:

1. Psychological intervention versus control (for example no-treatment control; wait-list control (WLC); treatment as usual (TAU));
2. Psychological intervention versus non-specific factor component control,[42] (for example where therapist time is equivalent to that provided in the experimental arm but only non-specific factors are provided as an intervention);
3. Psychological intervention plus medication versus medication;
4. Psychological intervention plus information versus information.

Types of settings

There will be no restriction placed on setting of intervention delivery. For example, studies where the intervention was delivered in primary care, secondary care, university based clinics, homes, residential care homes and community settings will all be included.

Types of outcome measures

Studies eligible for inclusion will have a self-report, clinician or proxy administered standardised measure of depression, anxiety, psychological distress or mental health-

related quality of life primary or secondary outcome measures, with a primary endpoint ≤ 6 months post-treatment. However, when adopted, longer-term outcomes will also be extracted from studies to enable a potential moderator analysis on length of follow-up.

Search methods for identification of studies

Electronic searches

The following electronic databases will be searched: Cumulative Index to Nursing and Allied Health Literature (CINAHL); Excerpta Medica DataBase (EMBASE); PsychInfo; Medline; Applied Social Sciences Index and Abstracts (ASSIA) and the Cochrane Central Register of Controlled Trials (CENTRAL). A comprehensive search strategy was developed using medical subject headings (MeSH). The Ovid MEDLINE search strategy can be found in online supplementary file 1. No limitations will be placed on year of publication and only studies with a publically available in the English language will be eligible for inclusion due to limited resources to fund translation services.

Searching other resources

The reference lists and citations of all included studies will be hand searched for further eligible studies. In addition, journals containing the highest numbers of included studies will be hand searched for recent potentially eligible publications (≤12 months). Experts in the field will also be contacted to identify any unpublished or ongoing trials.

Data collection and analysis

Selection of studies

Two researchers will act as reviewers and screen titles and abstracts. Full paper reviews will be conducted independently to determine inclusion with all discrepancies initially discussed. If consensus cannot be reached, a third member of the research team (PF) will be contacted. Degree of agreement in selecting studies in accordance with the exclusion/inclusion criteria will be examined with Cohen's Kappa. An Excel spreadsheet has been developed to manage all review data.

Data extraction and management

Following guidance,[37] data will be double extracted by the two reviewers (JW and MA) using a data extraction form developed in Excel for this review, with discrepancies discussed and the third member of the review team (PF) contacted if consensus is not reached. Study characteristics will be extracted from published papers, with study authors contacted in the event of missing data. In addition to the extraction of standard study information (study identification features, study characteristics, primary outcome measurements, statistical approaches and primary results) the following information will also be extracted:

1. *Participant characteristics:* dementia subtype (for example, Alzheimer's disease, vascular dementia, dementia with Lewy bodies, fronto-temporal dementia, MCI); how diagnosis of dementia or MCI was established (for example patient record check or in-trial procedures; validated diagnostic tool for dementia used (e.g., DSM-IV or ICD-10); global severity of dementia; severity of cognitive impairment; severity of behavioural and psychological symptoms of dementia; time since diagnosis; physical health comorbidities; neuropsychiatric comorbidities; age; gender; ethnicity; educational status; support from an informal carer (yes/no).

2. *Intervention characteristics*: psychological model (for example; cognitive therapy, behaviour therapy, interpersonal therapy; psychoeducation; problem solving; psychosocial support; relaxation); mode of delivery (for example; individual, group, dyadic); type of support (for example; face-to-face, telephone, email); treatment setting (for example; community, care home, primary care, secondary care); clinician delivering treatment; intervention specific training of clinicians delivering the treatment; treatment duration; number of sessions; length of sessions; manualised treatment and measurement of treatment integrity.
3. *Recruitment characteristics*: patient or dyadic (patient and carer); type of consent (for example, informed, proxy); sampling method; recruitment setting (for example; clinical, community, mixed); type of recruitment (for example; mail-out, physician / healthcare professional referral, advertisement); number of participants invited, number of participants screened, number of participants eligible, number of participants randomised, reasons for non-eligibility, whether respondent characteristics match the target population defined as response rate ≥80% or appropriate analysis comparing respondent and non-respondent characteristics.[29]
4. *Statistical approaches and primary results*:

4.1 Consistent with the aims of intention-to-treat analysis, any outcome information available for patients excluded from the original analysis will also be extracted.

4.2 For cluster trials, estimates of intra-cluster correlation coefficients (ICC) and average cluster sizes will be gathered, which are potentially needed for revised analyses (see 'Unit of Analysis Issues').

4.3 Within-study correlations between different outcomes will be extracted, where available, to inform on the simultaneous effects of treatment on the outcomes of interest in the same participants.

Assessment of risk of bias

The methodological quality of included studies will be examined independently by the two reviewers using the Cochrane Collaboration's Risk of Bias tool.[39] Study quality ratings will be compared, discrepancies discussed and the third reviewer [PF] contacted if consensus is not reached. Specifically selection, performance, attrition and reporting bias will be examined. Reporting bias will be examined by making efforts to obtain study protocols (for example obtaining published protocols, checking trial databases or requesting from study authors) and comparing outcomes reported in the protocol with those reported in the paper. Additionally, comparisons will be made between outcomes reported in the methods and results sections of trial reports. Study authors will be contacted in the event of any discrepancy to identify potential changes to the study protocol and request any missing data. For cluster randomised trials, studies will be examined for 'unit-of-analysis' errors, [43, 44] whereby groups were randomised in the trial, but individuals were treated as the randomised units in analysis. Cluster trials will also be assessed for 'recruitment bias' in which individuals are recruited after cluster randomisation, with knowledge of cluster allocation [45].

Data synthesis and statistical analysis

Measures of treatment effect

If available data permits, a meta-analysis will be conducted using 'metafor' package in R.[46] Hedges' g will be calculated to determine the post-treatment between-group standardised mean effect size from outcomes relating to depression, anxiety, psychological distress and mental health related quality of life separately. In cases reporting multiple time points the longest follow-up time point will be adopted ≤ 6 months. Comparisons will be analysed separately with control condition sample size halved for studies where two treatments eligible for inclusion are compared with one control condition. Likewise, for studies comparing two control conditions with one treatment condition, comparisons will be analysed separately with the sample size in the treatment condition halved. A random effects model will be adopted as wide variations in treatment, participant characteristics and methodological factors are expected between the studies.[47, 48]

Unit of Analysis Issues

For cluster RCTs, if clustering was not appropriately considered in the original analysis, estimates of ICC and average cluster sizes will be used to increase the standard errors appropriately.[45] If the required information cannot be obtained from source, authors will be contacted directly, or values borrowed from similar studies if possible.

Summary proportions

To examine recruitment and data permitting, summary proportions will be calculated.[46] Effects will be reported as proportions but transformed to log(odds) for the purposes of the meta-analysis. Specifically, the following proportions will be included:

1. Proportion of participants invited into the trials and subsequently screened for eligibility;

2. Proportion of participants screened for eligibility in the trials and subsequently found to be eligible for inclusion;
3. Proportion of participants found eligible for study and subsequently randomised into the trials.

Dealing with missing data

Missing means and standard deviations of post-treatment measurement scores will be requested from authors. The intention-to-treat principle will be followed as far as possible, analysing all patients as they were randomised. Sensitivity analysis will be conducted by temporarily dropping studies with high attrition in at least one arm (≥30%) from the analysis.

Assessment of heterogeneity

The presence of statistically significant heterogeneity will be examined by calculating the Q statistic with the quantification of the degree of heterogeneity calculated using the I^2 statistic.[49, 50] If substantial heterogeneity is found (I^2 value ≥ 50%) possible causes will be examined through subgroup analyses.

Funnel asymmetry

To investigate sources of possible bias (publication bias, language bias, inclusion of small studies with poor methodological rigour, heterogeneity) funnel plot asymmetry will be examined using Egger's Test of the Intercept,[51] where a minimum of 10 studies are included within the analysis.[52] Separate funnel plots will be calculated for each of the main outcomes (depression, anxiety, psychological distress and mental health related

quality of life). Effect sizes for each outcome will also be calculated taking into account the potential of bias using the trim and fill procedure.[53]

Sensitivity analysis

Sensitivity analysis will be conducted by:

1. Temporarily dropping small studies (n≤20 across conditions)
2. Individually omitting each study from the meta-analysis to examine whether the effect size was biased by the inclusion of any particular study.
3. Selective outcome reporting bias,[54] will be examined using the maximum bias bound approach,[55, 56] with new treatment effects and confidence intervals calculated by the addition of the bias bound value to the original pooled effects.[55, 56]

Moderator analysis

Moderator analysis will be undertaken to examine intervention components, methodological components and participant characteristics of studies associated with effectiveness, when number of studies permits. Specifically, the following moderators will be examined:

1. Dementia subtype;
2. Baseline severity of cognitive impairment;
3. Psychological model intervention based on;
4. Mode of delivery (for example individual, dyadic or group);
5. Baseline severity of depression, anxiety, psychological distress or mental health related quality of life;

6. Treatment setting;
7. Recruitment setting;
8. Type of control condition;
9. Length of follow-up.

If sufficient data are available, subgroup analysis, or meta-regression[44] will be conducted to examine moderators. With heterogeneity being anticipated, random effects will be adopted with Q and I^2 reported as measures of heterogeneity.

DISCUSSION

Currently there is no comprehensive review of psychological interventions for people with dementia or MCI that systematically examines:

1. Several outcomes relating to psychological wellbeing, such as depression, anxiety, mental health related quality of life and psychological distress;
2. The quality of the available evidence;
3. Effectiveness of recruitment strategies utilised;
4. Effectiveness and clinical and methodological components associated with effectiveness.

This review will therefore examine the effectiveness of psychological interventions targeting psychological wellbeing for people experiencing dementia or MCI, identify clinical and methodological moderators of effect size alongside strategies associated with successful recruitment. With respect to these objectives this review seeks to meet important objectives within Phase I of the revised MRC guidance concerning the development of complex interventions.[57] It represents the first step towards developing a new psychological treatment for difficulties with psychological wellbeing in people with

dementia, identifying important methodological uncertainties (e.g., successful recruitment methods; appropriate comparator arms) to inform the design of a Phase II feasibility study.

Contributors PF and JW conceived and designed the study protocol and wrote the manuscript. JM provided statistical expertise and contributed to the review design and assisted in the drafting of the manuscript. MA and CD made contributions to the design, critical evaluation of intellectual content and assisted with drafting the manuscript. All authors have approved the final manuscript.

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Competing Interests The authors declare that they have no competing interests.

Data Sharing Statement There is no unpublished data as this is a protocol paper

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Ovid MEDLINE Search Strategy

1. exp dementia/
2. exp Cognition Disorders/
3. (dement* or Alzheimer* or lewy* or frontotemporal or FTD or FTLD or tvFTD or OBS or OBD or demented).ti,ab.
4. (lewy* adj2 bod*).ti,ab.
5. (organic brain syndrome).ti,ab.
6. (organic brain disease).ti,ab.
7. (organic brain disorder*).ti,ab.
8. mild cognitive impairment/
9. (ADRD OR AAMI OR AACD OR MCI OR A-MCI N-MCI OR M-MCI or aMCI OR MCIa OR CIND OR MCD OR MNC OR MNCD or NCD).ti,ab.
10. (ag* associated cogniti* decline).ti,ab.
11. (ag* associated memory impairment).ti,ab.
12. (mild cognitive impairment).ti,ab.
13. (neurocognitive disorder).ti,ab.
14. (preclinical AD).ti,ab.
15. (pre-clinical AD).ti,ab.
16. (preclinical alzheimer*).ti,ab.
17. (pre-clinical Alzheime*).ti,ab.
18. (prodromal Alzheime*).ti,ab.
19. (prodrom* adj2 dement*).ti,ab.
20. neurocognitive disorder*.ti,ab.
21. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20
22. (non pharmacologic*).ti,ab.
23. (non-pharmacologic*).ti,ab.
24. nonpharmacologic*.ti,ab.
25. exp Counseling/
26. exp Behavior Therapy/
27. exp Psychotherapy/
28. exp Bibliotherapy/
29. cognitive restructuring.ti,ab.
30. cognitive reframing.ti,ab.
31. behavio* activation.ti,ab.
32. activity scheduling.ti,ab.
33. problem solving.ti,ab.
34. (cCBT or iCBT or ehealth or e-health or teletherapy or telehealth).ti,ab.
35. (self adj help).ti,ab.
36. (self adj manag*).ti,ab.
37. (self adj administer*).ti,ab.
38. (psycho* adj therapy).ti,ab.
39. (cognitive adj2 therap*).ti,ab.
40. (behavio* adj2 therap*).ti,ab.
41. (CBT OR psychotherapy OR psychodynamic OR counseling OR counselling OR psychoeducation* OR psychosocial OR psycho-social).ti,ab.
42. (group adj therap*).ti,ab.
43. (group adj treatment*).ti,ab.

44. (group adj intervention*).ti,ab.
45. (group adj support).ti,ab.
46. (psycho education*).ti,ab.
47. 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 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46
48. exp Depression/
49. exp Anxiety/
50. exp Anxiety Disorders/
51. exp Mood Disorders/
52. ("quality of life").ti,ab.
53. (mental adj health).ti,ab.
54. (mental adj distress).ti,ab.
55. (psycholo* adj distress).ti,ab.
56. (neuropsycholog* or neropsychiatric).ti,ab.
57. (mood OR emotion* OR affective OR wellbeing OR well-being OR distress).ti,ab.
58. (negative adj affect).ti,ab.
59. Depress*.ti,ab.
60. Melancholi*.ti,ab.
61. Dysphori*.ti,ab.
62. (anxiety OR anxious OR stress OR worry).ti,ab.
63. Affective symptoms/
64. (well adj being).ti,ab.
65. 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64
66. exp Randomized Controlled Trial/
67. exp Clinical Trial/
68. meta-analysis/
69. Random Allocation/
70. (randomi?ed controlled trial*).ti,ab.
71. (RCT OR Trial OR review OR meta-analysis).ti,ab.
72. (random* adj allocat*).ti,ab.
73. 66 or 67 or 68 or 70 or 71 or 72
74. 21 and 47 and 65 and 73

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Page
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	Page 1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	N/A
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	Page 2
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	Page 1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	Page 18
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	N/A
Support:			
Sources	5a	Indicate sources of financial or other support for the review	Page 18
Sponsor	5b	Provide name for the review funder and/or sponsor	
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	Page 4 - 7
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	Page 7
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	Page 8 - 10
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	Page 10
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	Supplementary File One

Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	Page 11
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	Page 10 - 11
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	Page 11 - 13
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	Page 8 - 12
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	Page 9 - 11
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	Page 13
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	Page 13 - 15
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	Page 13 - 15
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	Page 15 - 17
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	Page 15 - 17
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	N/A

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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Psychological interventions to improve psychological wellbeing in people with dementia or mild cognitive impairment: systematic review and meta-analysis protocol

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TITLE: Psychological interventions to improve psychological wellbeing in people with dementia or mild cognitive impairment: systematic review and meta-analysis protocol

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ABSTRACT

Introduction: Dementia and mild-cognitive impairment are associated with an increased risk of depression, anxiety, psychological distress and poor mental-health related quality of life. However, there is a lack of research examining the evidence base for psychological interventions targeting general psychological wellbeing within this population. Furthermore, there is little research relating to the design of randomised controlled trials examining psychological interventions for dementia and mild cognitive impairment, such as effective recruitment techniques, trial eligibility, and appropriate comparators.

Methods and analysis: Systematic review of electronic databases (CINAHL; EMBASE; PsychInfo; Medline; ASSIA and CENTRAL), supplemented by expert contact, reference and citation checking and grey literature searches. Published and unpublished studies will be eligible for inclusion with no limitations placed on year of publication. Primary outcomes of interest will be standardised measurements of depression, anxiety, psychological distress or mental health related quality of life. Eligibility and randomisation proportions will be calculated as secondary outcomes. If data permits, meta-analytical techniques will examine: (1) overall effectiveness of psychological interventions for people with dementia or mild cognitive impairment in relation to outcomes of depression, anxiety, psychological distress or mental health related quality of life; (2) clinical and methodological moderators associated with effectiveness; (3) proportions eligible, recruited and randomised.

Ethics and dissemination: Ethical approval is not required for the present systematic review. Results will inform the design of a feasibility study examining a new psychological intervention for people with dementia and depression, with dissemination through publication in peer reviewed journals and presentations at relevant conferences.

PROSPERO registration number: CRD42015025177

Strengths and Limitations

- Review protocol adopts the following quality standards— independent study selection, data extraction, risk of bias assessments by two researchers—as informed by the Centre of Reviews and Dissemination (CRD) guidance and PRISMA-P guidelines.
- The first review to be conducted with a secondary aim of examining factors related to successful participant recruitment into psychological interventions trials for dementia and mild cognitive impairment.
- To increase quality of included studies and reduce methodological heterogeneity, studies with high risk of bias (following Cochrane Collaboration guidance) concerning method of random sequence generation and allocation concealment were excluded.
- Due to resource limitations selected studies were limited to those publically available in the English language; therefore language bias may be present.
- High levels of clinical heterogeneity may exist as a consequence of included studies adopting psychological interventions informed by variety of psychological approaches and including participants with different dementia types and levels of cognitive impairment.

INTRODUCTION

Whilst healthcare advances across the developed world have resulted in increased life expectancy,[1] increased numbers of people are also placed at risk of developing chronic health conditions.[2] As such, dementia, a common chronic condition associated with aging,[3] has become of significant concern. Current estimates of people living with dementia worldwide are in excess of 35 million, set to double by 2030, and more than triple by 2050.[4] In the absence of a cure for dementia, or identification of specific causal factors as targets for preventative interventions,[5] dementia care strategies are focused on providing appropriate psychological and psychosocial support, alongside the provision of physical care.[6] However, access to evidence based psychological therapies to improve the long-term psychological wellbeing and mental health related quality of life in people with dementia is currently limited.[7]

Elevated symptoms of depression in people with dementia are common with prevalence reported to be as high as 30% [8, 9] to 50%, [10] compared to 13.2% of older adults without cognitive impairment.[11] However the prevalence of depression in people with dementia should potentially be considered with caution. Rates of depression may vary across dementia type, with a small number of studies indicating prevalence rates higher in patients experiencing dementia with Lewy bodies and vascular dementia, in comparison with Alzheimer's Disease.[8] Large variations in rates of depression in Alzheimer's Disease have also been found when a stricter criterion is adopted with respect to meeting a diagnosis of major depression.[12] Studies adopting ICD-10 criteria have found rates of 5% [13] to 14% using DSM-IV criteria [14] and 38% [15] to 44% [14] when using the National Institutes of Mental Health (NIMH) proposed standardised diagnostic criteria for depression in Alzheimer's Disease (NIMH-dAD).[16] Such wide variations in prevalence rates may be

due to the differences in depressive symptom presentation in people with dementia and variation diagnostic criterion utilised in these tools.[12] In relation to mild cognitive impairment (MCI) rates of mild depressive symptoms have varied from 26.5%,[17] to 49.3%,[18] with 14% experiencing severe depressive symptoms.[18] Furthermore, prevalence of elevated symptoms of anxiety have been found to range from 8% to 71%,[19] with 5%-21% of people with a dementia meeting diagnostic criteria for a specific anxiety disorder.[20] However, there is little consensus concerning how to define and measure anxiety experienced by people with a dementia.[9] Rates of anxiety symptoms have also been found to vary widely in MCI (10%-74%).[21]

Despite variability reported regarding the prevalence of depression and anxiety in people with dementia and MCI,[9;12] a clear need remains for evidence based psychological therapies to address these difficulties. However, only six studies were identified in a Cochrane review examining the effectiveness of psychological interventions specifically targeting depression or anxiety.[9] Other reviews have tended to focus on the effectiveness of non-pharmacological interventions for a variety of neuropsychiatric symptoms in severe or very severe dementia.[22] Furthermore, whilst depression and anxiety have a significant impact on the lives of people with dementia and MCI, the negative impact of these psychological difficulties extend beyond their symptomatology alone.[8] For depression and anxiety, symptoms have been associated with reduced quality of life,[8, 23] increased likelihood of being placed in a nursing home or other institution,[24, 25] and caregiver burden.[26, 27] Furthermore, specifically with respect to depression higher rates of cognitive decline have been reported,[28] with increased behavioural disturbances associated with anxiety.[29]

As such, the need to develop evidence based psychological interventions to support the long-term emotional needs of people experiencing dementia, and examine their impact on difficulties beyond those related solely depression and anxiety, is justified. Developing interventions that enable people with dementia to 'live well' is a priority with the UK National Dementia strategy,[30] with recent research focusing on improving general wellbeing and quality of life to facilitate people to 'live well' with dementia.[31] However, dementia research has previously adopted a disease-focused model, rather than a focus on longer-term wellbeing and quality of life.[32] Indeed, a limitation of existing literature is that interventions tend to overlook outcomes relating to quality of life and general psychological well-being.[33] This is of particular importance considering the elevated stigma associated with mental health difficulties in older adult physical health populations [34] and associated low levels of help-seeking regarding mental health support.[35,36] One reason for low levels of help-seeking behaviour may relate to the greater identification of physical health populations with the experience of general distress as a response to illness,[37] as opposed to a specific mental health difficulty, such as depression or anxiety. Subsequently, previous reviews focusing on interventions targeting medicalised constructs such as depression or anxiety (for example,[9]) may have omitted the evidence base concerning psychological interventions targeting broader constructs relating to general psychological distress and wellbeing.

Currently, there are no systematic reviews examining the evidence base of psychological interventions targeted at improving general psychological wellbeing or mental health related quality of life in people with dementia and MCI.[38] Whilst a recent review [9] has examined the effectiveness of psychological interventions for people with dementia and MCI targeting depression and anxiety, this current review protocol widens the scope by

also including interventions targeting general psychological distress and quality of life. Further, results of this review will allow the independent triangulation of results obtained by this previous review [9].

As well as establishing the evidence base for psychological interventions targeting general psychological wellbeing in people with dementia or MCI, it may also be prudent to investigate clinical and methodological characteristics associated with these studies. A number of complexities have been identified when recruiting participants into pharmaceutical trials associated with dementia or MCI, including capacity to consent and the presence of physical or neuropsychiatric symptoms impacting on eligibility.[38] Furthermore, a number of known barriers exist regarding recruiting older adults into psychological intervention trials, including stigma concerning mental health difficulties experienced by older adults,[39-41] preoccupation with physical health symptoms,[42] and lack of healthcare professional recognition.[43] Participants and professionals have also been found to view participation in depression trials with greater caution for older rather than younger adults and for people with physical health conditions.[44] With respect to anxiety, symptoms are frequently unrecognised in older adults given they often do not conform to existing diagnostic criteria.[45] Additionally, elevated stigma exists concerning anxiety in older adults in comparison with other mental health conditions, including depression.[41]

Greater understanding of methodological factors may therefore help inform successful recruitment strategies into subsequent studies aiming to examine the effectiveness of psychological interventions for people with dementia and MCI to improve psychological wellbeing. A recent systematic review examining recruitment in pharmacological trails for Alzheimer's disease has suggested 10% of potential participants

would take part in clinical drug trials if all those diagnosed were invited to participate.[38] However, currently, no reviews exist examining factors related to successful recruitment into psychological interventions for dementia. The present systematic review therefore aims to identify clinical and methodological moderators associated with effectiveness and recruitment strategies for trials involving people with dementia and MCI, alongside examining the overall effectiveness of psychological interventions to improve psychological wellbeing.

OBJECTIVES

1. To examine the effectiveness of psychological interventions targeted at improving psychological and emotional wellbeing and mental health related quality of life, compared with active and inactive control conditions, in adults with dementia or MCI.
2. To investigate clinical and methodological moderators associated with effectiveness.
3. To identify recruitment techniques and effectiveness of the techniques utilised across trials.

METHODS AND ANALYSIS

The Centre of Reviews and Dissemination (CRD) guidance for conducting systematic reviews,[46] will be followed, with results of the review reported in accordance with PRISMA-P guidelines.[47] The review is registered with the PROSPERO International Prospective Register of Systematic Reviews (registration number CRD42015025177).

Study Inclusion and Exclusion Criteria

Type of Studies

Randomised controlled trials (RCTs) and cluster RCTs, using a method of random sequence generation with allocation concealment assessed as having low or unclear risk of bias using the Cochrane Collaboration Risk of Bias tool,[48] will be eligible for inclusion. This is to help minimise the inclusion of studies of low quality with high of selection bias known to inflate effect sizes (for example,[49,50]) and is a technique used in a number of other systematic reviews and meta-analyses.[51-53] Quasi-RCTs and cross-over trials will not be eligible for inclusion.

Types of participants

Adults with diagnosis of a dementia by the DSM-IV or DSM-5 (American Psychiatric Association (APA,[54,55]) International Classification of Diseases-10 (ICD-10,[56]) alternative validated diagnostic criteria, or recorded in their medical records. Alzheimer's disease, vascular dementia, dementia with Lewy bodies and fronto-temporal dementia and will be eligible for inclusion. In addition, adults with a diagnosis of MCI, a term used to describe a person experiencing problems with cognitive function but with such difficulties not being severe enough to currently attract a diagnosis of dementia, will be eligible for inclusion. Valid methods of diagnosis adopted for MCI will include: DSM-5 criteria [55], Petersen's criteria (P-MCI,[57]), alternative validated diagnostic criteria, or where recorded in medical records. No limitations will be placed on the severity of dementia, length of time since diagnosis, with dementia patients in both community and institutional settings eligible. No restrictions will be placed on severity of depression, anxiety, psychological distress or mental health related quality of life.

Types of interventions

The review will include any psychological therapy and includes specific interventions with no limitations placed on the psychological therapy model informing the intervention. Psychological therapies eligible for inclusion will utilise specific therapeutic principles and techniques hypothesised to target an improvement in psychological wellbeing or a reduction in symptoms associated with psychological difficulties. Psychological therapies eligible for inclusion may include, but is not restricted to: cognitive-behavioural therapies; behavioural interventions; social skills training; relaxation therapy; psychodynamic; humanistic / counselling approaches; and interpersonal therapies. The intervention should target an improvement in general psychological wellbeing as identified by measurement of depression, anxiety, psychological distress or mental health related quality of life. As long as the intervention is targeted at improving psychological wellbeing in the person with dementia or MCI, dyadic interventions that may additionally target the informal carer will also be eligible. Additionally, all intervention delivery modes (individual, group, or dyadic) and methods of support (face-to-face, telephone, internet) will be eligible for inclusion. There will be no limitations placed on the professional background of the person supporting the intervention; additionally unsupported (self-guided/self-administered) interventions will also be eligible for inclusion.

Both inactive and active comparators will be considered eligible. However, the trial design must allow for the isolation of the effect of the psychological intervention of interest. Examples of appropriate designs are as follows:

1. Psychological intervention versus control (for example no-treatment control; wait-list control (WLC); treatment as usual (TAU));

2. Psychological intervention versus non-specific factor component control,[58] (for example where therapist time is equivalent to that provided in the experimental arm but only non-specific factors are provided as an intervention);
3. Psychological intervention plus medication versus medication;
4. Psychological intervention plus information versus information.

Types of settings

There will be no restriction placed on setting of intervention delivery. For example, studies where the intervention was delivered in primary care, secondary care, university based clinics, homes, residential care homes and community settings will all be included.

Types of outcome measures

Studies eligible for inclusion will use one or more of the following self-report, clinician or proxy administered primary outcome measurements: (1) standardised measurement of depression (for example the Beck Depression Inventory, BDI-II,[59]); (2) standardised measurement of anxiety,(for example the Beck Anxiety Inventory, BAI[60]); (3) standardised measurement of psychological distress, defined as a measurement of general psychiatric distress including domains of mental health related symptoms such as depression, anxiety, insomnia and somatic complaints (for example, the General Health Questionnaire, GHQ[61]) or (4) standardised measurement of quality of life if they include a mental health specific subscale or domain (for example, the SF-36[62]) or the Alzheimer Disease Related Quality of Life.(ADRQL[63]) Where multiple time points are reported a primary endpoint ≤ 6 months post-treatment will be adopted to minimise the likelihood bias associated with examining short-term post-treatment effects only that are likely to result in higher effect

sizes.[64,51,65] However, outcomes for all time points reported in the included studies will be extracted to enable a potential moderator analysis on length of follow-up.

Search methods for identification of studies

Electronic searches

The following electronic databases will be searched: Cumulative Index to Nursing and Allied Health Literature (CINAHL); Excerpta Medica DataBase (EMBASE); PsychInfo; Medline; Applied Social Sciences Index and Abstracts (ASSIA) and the Cochrane Central Register of Controlled Trials (CENTRAL). A comprehensive search strategy was developed using medical subject headings (MeSH). The Ovid MEDLINE search strategy can be found in online supplementary file 1. No limitations will be placed on year of publication and only studies with a publically available in the English language will be eligible for inclusion due to limited resources to fund translation services.

Searching other resources

The reference lists and citations of all included studies will be hand searched for further eligible studies. In addition, journals containing the highest numbers of included studies will be hand searched for recent potentially eligible publications (≤12 months). Experts in the field will also be contacted to identify any unpublished or ongoing trials.

Data collection and analysis

Selection of studies

Two researchers will act as reviewers and screen titles and abstracts. Full paper reviews will be conducted independently to determine inclusion with all discrepancies initially discussed.

If consensus cannot be reached, a third member of the research team (PF) will be contacted. An Excel spreadsheet has been developed to manage all review data.

Data extraction and management

Following guidance,[46] data will be double extracted by the two reviewers (JW and MA) using a data extraction form developed in Excel for this review, with discrepancies discussed and the third member of the review team (PF) contacted if consensus is not reached. Study characteristics will be extracted from published papers, with study authors contacted in the event of missing data. In addition to the extraction of standard study information (study identification features, study characteristics, primary outcome measurements, statistical approaches and primary results) the following information will also be extracted:

1. *Participant characteristics:* dementia subtype (for example, Alzheimer's disease, vascular dementia, dementia with Lewy bodies, fronto-temporal dementia, MCI); how diagnosis of dementia or MCI was established (for example patient record check or in-trial procedures; validated diagnostic tool for dementia used (e.g., DSM-IV, DSM-V or ICD-10); global severity of dementia; severity of cognitive impairment; severity of behavioural and psychological symptoms of dementia; time since diagnosis; physical health comorbidities; neuropsychiatric comorbidities; age; gender; ethnicity; educational status; support from an informal carer (yes/no).
2. *Intervention characteristics*: psychological model (for example; cognitive therapy, behaviour therapy, interpersonal therapy; psychoeducation; problem solving; psychosocial support; relaxation); mode of delivery (for example; individual, group, dyadic); type of support (for example; face-to-face, telephone, email); treatment setting (for example; community, care home, primary care, secondary care); clinician delivering

treatment; intervention specific training of clinicians delivering the treatment; treatment duration; number of sessions; length of sessions; manualised treatment and measurement of treatment integrity.

3. *Recruitment characteristics*: patient or dyadic (patient and carer); type of consent (for example, informed, proxy); sampling method; recruitment setting (for example; clinical, community, mixed); type of recruitment (for example; mail-out, physician / healthcare professional referral, advertisement); number of participants invited, number of participants screened, number of participants eligible, number of participants randomised, reasons for non-eligibility, whether respondent characteristics match the target population defined as response rate ≥80% or appropriate analysis comparing respondent and non-respondent characteristics.[38]
4. *Statistical approaches and primary results*:

4.1 Consistent with the aims of intention-to-treat analysis, any outcome information available for patients excluded from the original analysis will also be extracted.

4.2 For cluster trials, estimates of intra-cluster correlation coefficients (ICC) and average cluster sizes will be gathered, which are potentially needed for revised analyses (see 'Unit of Analysis Issues').

4.3 Within-study correlations between different outcomes will be extracted, where available, to inform on the simultaneous effects of treatment on the outcomes of interest in the same participants.

Assessment of risk of bias

The methodological quality of included studies will be examined independently by the two reviewers using the Cochrane Collaboration's Risk of Bias tool.[48] Study quality ratings will

be compared, discrepancies discussed and the third reviewer [PF] contacted if consensus is not reached. Specifically selection, performance, attrition and reporting bias will be examined. Reporting bias will be examined by making efforts to obtain study protocols (for example obtaining published protocols, checking trial databases or requesting from study authors) and comparing outcomes reported in the protocol with those reported in the paper. Additionally, comparisons will be made between outcomes reported in the methods and results sections of trial reports. Study authors will be contacted in the event of any discrepancy to identify potential changes to the study protocol and request any missing data. For cluster randomised trials, studies will be examined for 'unit-of-analysis' errors, [66, 67] whereby groups were randomised in the trial, but individuals were treated as the randomised units in analysis. Cluster trials will also be assessed for 'recruitment bias' in which individuals are recruited after cluster randomisation, with knowledge of cluster allocation.[68]

Data synthesis and statistical analysis

Measures of treatment effect

If available data permits, a meta-analysis will be conducted using 'metafor' package in R.[69] Hedges' g will be calculated to determine the post-treatment between-group standardised mean effect size from outcomes relating to depression, anxiety, psychological distress and mental health related quality of life separately. In cases reporting multiple time points the longest follow-up time point will be adopted ≤ 6 months. Comparisons will be analysed separately with control condition sample size halved for studies where two treatments eligible for inclusion are compared with one control condition. Likewise, for studies comparing two control conditions with one treatment condition, comparisons will be

analysed separately with the sample size in the treatment condition halved. A random effects model will be adopted as wide variations in treatment, participant characteristics and methodological factors are expected between the studies.[70, 71]

Unit of Analysis Issues

For cluster RCTs, if clustering was not appropriately considered in the original analysis, estimates of ICC and average cluster sizes will be used to increase the standard errors appropriately.[68] If the required information cannot be obtained from source, authors will be contacted directly, or values borrowed from similar studies if possible.

Summary proportions

To examine recruitment and data permitting, summary proportions will be calculated.[69] Effects will be reported as proportions but transformed to log(odds) for the purposes of the meta-analysis. Specifically, the following proportions will be included:

1. Proportion of participants invited into the trials and subsequently screened for eligibility;
2. Proportion of participants screened for eligibility in the trials and subsequently found to be eligible for inclusion;
3. Proportion of participants found eligible for study and subsequently randomised into the trials.

Dealing with missing data

Missing means and standard deviations of post-treatment measurement scores will be requested from authors. The intention-to-treat principle will be followed as far as possible,

analysing all patients as they were randomised. Sensitivity analysis will be conducted by temporarily dropping studies with high attrition in at least one arm (≥30%) from the analysis.

Assessment of heterogeneity

The presence of statistically significant heterogeneity will be examined by calculating the Q statistic with the quantification of the degree of heterogeneity calculated using the I^2 statistic.[72,73] If substantial heterogeneity is found (I^2 value ≥ 50%) possible causes will be examined through subgroup analyses.

Funnel asymmetry

To investigate sources of possible bias (publication bias, language bias, inclusion of small studies with poor methodological rigour, heterogeneity) funnel plot asymmetry will be examined using Egger's Test of the Intercept,[74] where a minimum of 10 studies are included within the analysis.[75] Separate funnel plots will be calculated for each of the main outcomes (depression, anxiety, psychological distress and mental health related quality of life). Effect sizes for each outcome will also be calculated taking into account the potential of bias using the trim and fill procedure.[76]

Sensitivity analysis

Sensitivity analysis will be conducted by:

1. Temporarily dropping small studies (n≤20 across conditions)
2. Individually omitting each study from the meta-analysis to examine whether the effect size was biased by the inclusion of any particular study.

3. Selective outcome reporting bias,[77] will be examined using the maximum bias bound approach,[78, 79] with new treatment effects and confidence intervals calculated by the addition of the bias bound value to the original pooled effects.[78, 79]

Moderator analysis

Moderator analysis will be undertaken to examine intervention components, methodological components and participant characteristics of studies associated with effectiveness, when number of studies permits. Specifically, the following moderators will be examined:

1. Dementia subtype;
2. Baseline severity of cognitive impairment;
3. Psychological model intervention based on;
4. Mode of delivery (for example individual, dyadic or group);
5. Baseline severity of depression, anxiety, psychological distress or mental health related quality of life;
6. Treatment setting;
7. Recruitment setting;
8. Type of control condition;
9. Length of follow-up.

If sufficient data are available, subgroup analysis, or meta-regression[67] will be conducted to examine moderators. With heterogeneity being anticipated, random effects will be adopted with Q and I^2 reported as measures of heterogeneity. It should be noted

moderator analysis only provides correlational, not casual, data.[80]. Any significant findings should be examined through further primary research.[81]

DISCUSSION

Currently there is no comprehensive review of psychological interventions for people with dementia or MCI that systematically examines:

1. Several outcomes relating to psychological wellbeing, such as depression, anxiety, mental health related quality of life and psychological distress;
2. The quality of the available evidence;
3. Effectiveness of recruitment strategies utilised;
4. Effectiveness and clinical and methodological components associated with effectiveness.

This review will therefore examine the effectiveness of psychological interventions targeting psychological wellbeing for people experiencing dementia or MCI, identify clinical and methodological moderators of effect size alongside strategies associated with successful recruitment. With respect to these objectives this review seeks to meet important objectives within Phase I of the revised MRC guidance concerning the development of complex interventions.[82] It represents the first step towards developing a new psychological treatment for difficulties with psychological wellbeing in people with dementia, identifying important methodological uncertainties (e.g., successful recruitment methods; appropriate comparator arms) to inform the design of a Phase II feasibility study.

Contributors PF and JW conceived and designed the study protocol and wrote the manuscript. JM provided statistical expertise and contributed to the review design and

assisted in the drafting of the manuscript. MA and CD made contributions to the design, critical evaluation of intellectual content and assisted with drafting the manuscript. All authors have approved the final manuscript.

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Competing Interests The authors declare that they have no competing interests.

Data Sharing Statement There is no unpublished data as this is a protocol paper

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Ovid MEDLINE Search Strategy

1. exp dementia/
2. exp Cognition Disorders/
3. (dement* or Alzheimer* or lewy* or frontotemporal or FTD or FTLD or tvFTD or OBS or OBD or demented).ti,ab.
4. (lewy* adj2 bod*).ti,ab.
5. (organic brain syndrome).ti,ab.
6. (organic brain disease).ti,ab.
7. (organic brain disorder*).ti,ab.
8. mild cognitive impairment/
9. (ADRD OR AAMI OR AACD OR MCI OR A-MCI N-MCI OR M-MCI or aMCI OR MCIa OR CIND OR MCD OR MNC OR MNCD or NCD).ti,ab.
10. (ag* associated cogniti* decline).ti,ab.
11. (ag* associated memory impairment).ti,ab.
12. (mild cognitive impairment).ti,ab.
13. (neurocognitive disorder).ti,ab.
14. (preclinical AD).ti,ab.
15. (pre-clinical AD).ti,ab.
16. (preclinical alzheimer*).ti,ab.
17. (pre-clinical Alzheime*).ti,ab.
18. (prodromal Alzheime*).ti,ab.
19. (prodrom* adj2 dement*).ti,ab.
20. neurocognitive disorder*.ti,ab.
21. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20
22. (non pharmacologic*).ti,ab.
23. (non-pharmacologic*).ti,ab.
24. nonpharmacologic*.ti,ab.
25. exp Counseling/
26. exp Behavior Therapy/
27. exp Psychotherapy/
28. exp Bibliotherapy/
29. cognitive restructuring.ti,ab.
30. cognitive reframing.ti,ab.
31. behavio* activation.ti,ab.
32. activity scheduling.ti,ab.
33. problem solving.ti,ab.
34. (cCBT or iCBT or ehealth or e-health or teletherapy or telehealth).ti,ab.
35. (self adj help).ti,ab.
36. (self adj manag*).ti,ab.
37. (self adj administer*).ti,ab.
38. (psycho* adj therapy).ti,ab.
39. (cognitive adj2 therap*).ti,ab.
40. (behavio* adj2 therap*).ti,ab.
41. (CBT OR psychotherapy OR psychodynamic OR counseling OR counselling OR psychoeducation* OR psychosocial OR psycho-social).ti,ab.
42. (group adj therap*).ti,ab.
43. (group adj treatment*).ti,ab.

44. (group adj intervention*).ti,ab.
45. (group adj support).ti,ab.
46. (psycho education*).ti,ab.
47. 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 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46
48. exp Depression/
49. exp Anxiety/
50. exp Anxiety Disorders/
51. exp Mood Disorders/
52. ("quality of life").ti,ab.
53. (mental adj health).ti,ab.
54. (mental adj distress).ti,ab.
55. (psycholo* adj distress).ti,ab.
56. (neuropsycholog* or neropsychiatric).ti,ab.
57. (mood OR emotion* OR affective OR wellbeing OR well-being OR distress).ti,ab.
58. (negative adj affect).ti,ab.
59. Depress*.ti,ab.
60. Melancholi*.ti,ab.
61. Dysphori*.ti,ab.
62. (anxiety OR anxious OR stress OR worry).ti,ab.
63. Affective symptoms/
64. (well adj being).ti,ab.
65. 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64
66. exp Randomized Controlled Trial/
67. exp Clinical Trial/
68. meta-analysis/
69. Random Allocation/
70. (randomi?ed controlled trial*).ti,ab.
71. (RCT OR Trial OR review OR meta-analysis).ti,ab.
72. (random* adj allocat*).ti,ab.
73. 66 or 67 or 68 or 70 or 71 or 72
74. 21 and 47 and 65 and 73

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Page
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	Page 1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	N/A
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	Page 2
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	Page 1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	Page 18
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	N/A
Support:			
Sources	5a	Indicate sources of financial or other support for the review	Page 18
Sponsor	5b	Provide name for the review funder and/or sponsor	
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	Page 4 - 7
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	Page 7
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	Page 8 - 10
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	Page 10
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	Supplementary File One

Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	Page 11
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	Page 10 - 11
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	Page 11 - 13
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	Page 8 - 12
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	Page 9 - 11
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	Page 13
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	Page 13 - 15
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	Page 13 - 15
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	Page 15 - 17
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	Page 15 - 17
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	N/A

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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