BMJ Open Psychological interventions for depression among informal caregivers of older adult populations: protocol of a systematic review and meta-analysis of randomised controlled trials

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ABSTRACT

Introduction Increased life expectancy has led to an increased demand for family members to provide informal care for their older relatives in the home. Many studies suggest informal caregivers are at greater risk of experiencing symptoms of depression. However, there is a lack of research examining the effectiveness of psychological interventions targeting these symptoms alongside clinical and methodological moderators potentially associated with intervention effectiveness. This review aims to address this gap and will inform the development of a psychological intervention targeting depression among adult-child caregivers of older parents, given many studies show that among informal caregivers of older adults, adult children experience specific difficulties and needs for psychological support. Further, the lack of studies targeting adult children specifically necessitates conducting this review targeting caregivers of older adults in general.

Methods and analysis Randomised controlled trials of psychological interventions targeting symptoms of depression among informal caregivers will be identified via a systematic search of electronic databases (PubMed, Cumulative Index to Nursing and Allied Health Literature, Excerpta Medica DataBase, PsycINFO, Cochrane Library and Web of Science) and supplemented by handsearching of previous systematic reviews, reference and forward citation checking, and expert contact. If possible, a meta-analysis will be conducted to examine the: (1) effectiveness of psychological interventions for depression among informal caregivers of older adults, (2) effectiveness of psychological interventions for secondary outcomes such as anxiety, stress, caregiver burden, psychological distress, quality of life, well-being and self-efficacy and (3) moderating effects of clinical and methodological factors on effectiveness.

Ethics and dissemination Ethical approval will not be necessary for this study given primary data will not be collected. Results will inform the development of a psychological intervention for adult-child caregivers of older parents and will be disseminated through publication in peer-reviewed journals and conference presentations.

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Strengths and limitations of this study

- The first systematic review and meta-analysis of effectiveness of psychological interventions for depression among informal caregivers of an older adult population, including examination of clinical and methodological moderators associated with effectiveness.
- The reporting of this review protocol adopts quality standards informed by the Centre of Reviews and Dissemination guidance and Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols guidelines.
- To increase the quality of included studies and reduce methodological heterogeneity, only studies assessed as low or moderate risk of bias in terms of sequence generation and allocation concealment according to the Cochrane Collaboration's Risk of Bias tool 2.0 will be included.
- Selected studies will be limited to those publicly available in the English or Swedish language, which may lead to language bias in this review.
- Clinical heterogeneity may be high due to inclusion of psychological interventions informed by a variety of psychological approaches and including informal caregivers providing care to persons with a range of health conditions associated with ageing.

INTRODUCTION

Healthcare advances have resulted in global increases in life expectancy,¹ with people over the age of 65 being the fastest growing age group in the world.² Projections indicate that one in six people (16%) in the world will be over age 65 by 2050, compared with 1 in 11 (9%) in 2019.² One significant consequence of increases in an aged population is the concomitant reduction in proportion of working age populations, which leads to an additional strain on social and health-care systems.³ This, in combination with

reductions in residential care provision for older adults,⁴ has led to an increased reliance on family members, partners and friends to provide informal care to older adults (ie, as unpaid and untrained non-professionals).³ However, informal caregiving is associated with a number of negative impacts for the caregiver such as chronic stress,⁵ physical and emotional burden,^{6 7} sleep difficulties,⁸ role strain,^{9 10} loneliness¹¹ and financial problems.⁴ Furthermore, informal caregivers of older adults may experience specific difficulties related to the care recipient's older age, such as the care recipient being more socially isolated,¹² multimorbid (ie, suffering from more than one health condition),¹³ and/or neglected in terms of public support provision.^{4 14}

Given the increased stress and burden associated with the provision of informal care, informal caregivers are at greater risk of experiencing mental health difficulties, such as depression.¹⁵ However, the prevalence of depression among informal caregivers may vary depending on the health condition of the care recipient and its trajectory. For example, 23% of informal caregivers of people with dementia report a high level of depressive symptoms, compared with 11% of informal caregivers to persons with other health conditions.¹⁶ Other studies have found 30%–33% of informal caregivers of stroke survivors¹⁷ and 43% of informal caregivers of cancer patients experience depression.¹⁸ Not only is depression detrimental to informal caregivers' overall health,¹⁹ such as leading to a higher risk of mortality,⁷ but may also lead to lower quality of care provided.²⁰ Further, informal caregiving may lead to reductions in paid employment and engagement in social and recreational activities.^{21 22} As such, there are increased costs not only to the individual, but society in general. Given the increasing number of people providing informal care to older adults, and the long-term impact of informal caregiving on individuals and society, it is important to identify and develop effective psychological interventions for this population.

Nearly all existing systematic reviews and meta-analyses of psychological interventions for depression among informal caregivers of older adults focus on caregivers to persons with specific health conditions or diagnoses, such as stroke^{23 24} and particularly dementia.^{25–27} Hence, it is difficult to gain an overview of the effectiveness of psychological interventions for depression among informal caregivers of older adults in general and how the health condition of the care recipient and types of psychological interventions may moderate effectiveness. Indeed, to the best of our knowledge, only one systematic review and meta-analysis has examined the effectiveness of interventions for depression among informal caregivers of older adults.²⁸ However, this review focused on interventions in general and the classifications of the included psychological interventions (ie, support based or psychotherapy) may have been too broad to allow an extensive examination of the moderating effects of type of intervention. Further, given the review was conducted in 2002, a more updated review is warranted.

As such, this review aims to extend on previous review findings²⁸ by providing a more detailed examination of psychological interventions only, and performing subgroup analyses for different psychological intervention types based on a commonly used classification of psychological interventions (ie, cognitive-behavioural therapy, CBT; non-directive supportive therapy, SUP; behavioural activation therapy, BA; psychodynamic therapy, DYN; problem-solving therapy, PST; third-wave CBT, TWCBT; interpersonal therapy, IPT; life review therapy, LRT).²⁹ In addition, this review aims to extend on the previous review by: (1) assessing the quality of included studies, (2) only including studies assessed as low or moderate risk of bias in terms of sequence generation and allocation concealment^{30 31} according to the Cochrane Collaboration's Risk of Bias tool 2.0,³² (3) including studies with any kind of comparator, with the intention to reduce the risk of inflated effect sizes due to only including no-treatment comparators³³ and (4) including studies conducted since the previous review was performed in 2002.²⁸

While it is important to identify effective interventions for depression among informal caregivers of older adults, comorbidity of depression with other mental health-related outcomes among informal caregivers suggests interventions should target these outcomes in addition to depression. Among informal caregivers, depression has been shown to be comorbid with anxiety,³⁴ stress,⁵ caregiver burden,³⁵ low quality of life,³⁶ low well-being and low self-efficacy.¹⁵ To our knowledge, the effectiveness of psychological interventions on these outcomes has not been examined for caregivers of older adults previously, and thus, they will be included as secondary outcomes in this review. In addition, recovery of depression (ie, no longer meeting diagnostic criteria for depression)³⁷ will be included as a secondary outcome.

Furthermore, research suggests symptoms of depression among informal caregivers are more prevalent among those providing care to a person with more severe health conditions,⁵ such as dementia¹⁵ or severe forms of stroke¹⁷ and cancer.³⁸ An examination into the moderating effects of the health condition of the care recipient and the severity of the health condition on the effectiveness of psychological interventions for depression among informal caregivers is thus warranted and will be undertaken in this study. Moreover, research suggests adult-child caregivers of older adults experience specific difficulties (eg, geographical distance to care recipients,³⁹ role strain,^{9 10} role reversal in terms of responsibility,⁴⁰ overall stress⁴¹ and lower quality of life).⁴² As such, adult-child caregivers of older adults may have specific needs for psychological support. Thus, the moderating effect of caregiver relationship on effectiveness of interventions will be investigated, measured as per cent adult children on study level. Similarly, research indicates gender differences in experiences of informal caregiving and needs for psychological support.⁴³ Thus, the moderating effect of gender, measured as per cent female on study level, on the

effectiveness of psychological interventions for depression among caregivers of older adults will be examined in the proposed review.

Other clinical and methodological factors found to moderate effectiveness of interventions for depression among informal caregivers in previous studies will be investigated. Such factors include severity of caregiver's depression at baseline,²⁷ intervention type (eg, CBT, IPT),^{44,45} individual versus dyadic intervention,^{44,46} method of delivery (face to face, group, internet administered or mixed),⁴⁷ multicomponent intervention or not,⁴⁶ and length of follow-up.⁴⁴ Other potential moderating factors of interest are type of support (eg, unsupported self-help, supported self-help or guided support),³¹ type of control condition and recruitment setting. Examining factors potentially associated with intervention effectiveness may contribute to the development of future interventions for informal caregivers of older adults. Particularly, investigating the moderating effect of caregiver relationship may inform the development of interventions targeting adult-child caregivers.

This proposed review aims to provide a systematic review of psychological interventions for depression among informal caregivers of older adults. If data permit, a meta-analysis will be used to examine the effect on depression and secondary outcomes (ie, anxiety, stress, caregiver burden, psychological distress, quality of life, well-being and self-efficacy). To further inform future development of psychological interventions for caregivers of older adults, potential sources of heterogeneity will be examined in moderator analyses of clinical and methodological factors.

Objectives

To examine (1) the effectiveness of psychological interventions for depression among informal caregivers of older adults, (2) the effectiveness of psychological interventions on secondary outcomes such as anxiety, stress, caregiver burden, psychological distress, quality of life, well-being and self-efficacy among caregivers and (3) moderating effects of clinical and methodological factors on effectiveness.

METHODS AND ANALYSIS

This protocol has been developed in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA; see online supplementary appendix 1).⁴⁸

A systematic review will be performed to identify eligible studies following the Centre for Reviews and Dissemination (CRD) guidance on undertaking systemic reviews.⁴⁹ If data permit, meta-analysis, moderator analyses and sensitivity analyses will be performed in accordance with guidelines provided by Cochrane,⁵⁰ and reported in accordance with the PRISMA statement.⁵¹

Inclusion and exclusion criteria

Inclusion and exclusion criteria are categorised by population, interventions, comparators, outcomes and study design (PICOS).⁵² No limitations will be placed on year of publication and only studies available in the English or Swedish language will be eligible for inclusion due to limited resources for funding translation services.

Population

Adults (≥ 18 years) providing informal care, in the home, for at least one person who is ≥ 65 years of age will be included.⁵³ Because we anticipate that many older adults who receive informal care have age-related diseases,⁵⁴ the search strategy will include age-related diseases as a proxy for old age for cases in which care recipients' age is not conveyed in titles and abstracts. Age-related diseases are defined as diseases with incidence rates increasing quadratically with age among adults above 25 years of age.⁵⁴ Such diseases may include, but are not limited to, cardiovascular diseases, cerebrovascular diseases, chronic respiratory diseases, neoplasms, neurodegenerative disorders and sense organ disorders.⁵⁴ However, presence of an age-related disease in the care recipient is not required for study inclusion.

No constraints will be placed on the extent of informal caregiving in terms of time and effort or whether the informal caregiver is a family member or not. Studies including informal caregivers or care recipients with comorbid severe and enduring mental health difficulties (eg, post-traumatic stress disorder and psychosis) or with mood disorders other than depression (eg, bipolar affective disorder) will be excluded. Studies in which caregivers provide care during the palliative care stage will also be excluded.

Interventions

Any psychological intervention or combination of psychological interventions using specific therapeutic principles and techniques to target reductions in symptoms of depression (ie, CBT, SUP, BA, DYN, PST, TWCBT, IPT and LRT), alongside the use of measurement of depression as a primary outcome, will be included.⁵⁵ Interventions with more than one primary target (eg, mixed depression and anxiety) will be excluded. However, interventions are anticipated to additionally target secondary outcomes related to psychological well-being (eg, anxiety, psychological distress, caregiver burden and mental health-related quality of life). These interventions will also be eligible, as long as the primary target of the intervention is depression. No limitation will be placed on theories informing the intervention or setting (face to face, group, internet administered or mixed). There will be no limitations placed on professional background of the person supporting the intervention and self-guided interventions will be eligible. Interventions for the informal caregiver-care recipient dyad will be included as long as target of the intervention is caregiver's depression. Purely psychoeducational interventions will be excluded, such

as interventions focused on development of specific skills and competence in the caregiver (eg, management of behavioural and psychological symptoms of dementia).

Comparators

Both active and inactive comparators will be eligible, as long as the trial design allows for the isolation of the effect of the intervention of interest. Examples of eligible designs are: (1) intervention vs control (ie, no-treatment control, wait-list control, treatment as usual), (2) intervention versus non-specific factor component control³³ (eg, where therapist time is equivalent to that provided in the experimental arm but only non-specific factors are provided as an intervention), (3) intervention plus medication versus medication and (4) intervention plus information versus information. Trial designs that do not allow for the isolation of the effect (eg, intervention vs medication) will be excluded.

Outcomes

Studies eligible for inclusion will use one or more self-report, clinician or proxy administered standardised measurements of depression, such as the Patient Health Questionnaire (PHQ-9),⁵⁶ the Beck Depression Inventory (BDI-II),⁵⁷ Hamilton Depression Rating Scale,⁵⁸ the Depression Anxiety Stress Scale (DASS-D),⁵⁹ the Centre for Epidemiological Depression Scale (CES-D),⁶⁰ the Montgomery-Åsberg Depression Rating Scale (MADRS)⁶¹ or the Clinical Global Impression Improvement Scale.⁶²

A secondary outcome of interest is recovery from depression, which will be operationalised as the participant (1) no longer meeting primary diagnosis of depression according to the Structured Clinical Interview for DSM-IV Axis I Disorders⁶³ or Mini-International Neuropsychiatric Interview⁶⁴ and/or (2) scoring below a clinical cut-off score on the PHQ-9,⁵⁶ BDI-II,⁵⁷ DASS-D,⁵⁹ CES-D,⁶⁰ MADRS⁶¹ and Hospital Anxiety and Depression Scale.⁶⁵

Other secondary outcomes of interest are self-report, clinician or proxy administered standardised measurements of

- ▶ Anxiety (eg, Beck Anxiety Inventory).⁶⁶
- ▶ Stress (eg, the perceived stress scale,⁶⁷ the Trier inventory for chronic stress).⁶⁸
- ▶ Caregiver burden (eg, the Burden Interview,⁶⁹ the Caregiver Strain Index).⁷⁰
- ▶ Psychological distress (eg, Kessler 6,⁷¹ the psychological distress manifestations measurement scale).⁷²
- ▶ Quality of life (eg, the Quality of Life scale).⁷³
- ▶ Well-being (eg, the satisfaction with life scale).⁷⁴
- ▶ Self-efficacy (eg, the generalised self-efficacy scale).⁷⁵

All postintervention outcomes will be included regardless of time frame variability. For the sake of consistency, for studies in which multiple measurements are used for primary or secondary outcomes (eg, two scales that assess depressive symptomatology, the measurement which is most frequently used within our sample of included studies will be used in the analyses.

Study designs

To increase internal and external validity of results from this review, only randomised controlled trials assessed as low or moderate risk of bias in terms of sequence generation and allocation concealment according to the Cochrane Collaboration's Risk of Bias tool 2.0³² will be included. Excluding studies with high risk of bias in terms of sequence generation and allocation concealment has been used in previous systematic reviews and meta-analyses^{30 31 76} to minimise the risk of including low quality studies which may inflate effect sizes.^{77 78}

Information sources

The following electronic databases will be systematically searched for relevant studies: PubMed, Cochrane Library, Excerpta Medica DataBase, Cumulative Index to Nursing and Allied Health Literature, PsycINFO and ISI Web of Science. All databases were searched in September 2019, with an update search planned in the end of the review process (ie, at data analysis stage). Other information sources include reference lists of other systematic reviews, reference lists and forward citation checks of studies eligible for inclusion in the present review and expert contact. Reference lists of systematic reviews will only be searched if they (1) search at least one database, (2) report selection criteria, (3) include a quality assessment of included studies and (4) provide a synthesis of included studies.⁷⁹ Studies from grey literature will be included if they fulfil inclusion criteria. Specifically, conference abstracts captured in the electronic databases which fulfil criteria will be included and grey literature will be searched in OpenGrey (<http://www.opengrey.eu/>), a database for grey literature. Due to time constraints, full dissertations will not be included.

Search strategy

Electronic databases will be searched using controlled vocabulary and text words in titles and abstracts (see online supplementary appendix 2). Search strategies were developed for each electronic database alongside librarian Agnes Kotka from Uppsala University and were reviewed by professor Mariët Hagedoorn and information specialist Truus van Ittersum from University of Groningen using the PRESS Peer Review of Electronic Search Strategies guidelines⁸⁰ (see online supplementary appendix 3).

Study records

Data management

Articles retrieved from initial database searches will be transferred to EndNote X8 and duplicate record will be removed. Titles and abstracts will be screened in Rayyan.⁸¹ Included studies will be assessed in full text and evaluation of eligibility based on the PICOS will be documented using an eligibility database developed in Microsoft Excel, including reasons for exclusion. Included studies which have generated multiple publications will be regarded as single studies when counting the number

of studies included, regardless of the number of publications each such study has generated. Data on study participant characteristics from included studies which have generated multiple publications will be extracted from the publication reporting results for the primary follow-up time point (ie, the longest follow-up period ≤ 6 months post-treatment). Data from eligible studies will be extracted using an extraction database in Microsoft Excel. Data analyses will be performed in Comprehensive Meta-Analysis (V.3).

Selection process

Two reviewers will independently screen study titles and abstracts retrieved from searches, and perform full paper checks of identified potentially eligible studies. Studies which do not fulfil the PICOS criteria (see online supplementary appendix 4) will be excluded. Overall reasons for exclusion at full-text screening will be documented and reported in a PRISMA flow chart in the results manuscript. A detailed overview of reasons for inclusion/exclusion of studies at the PICOS item level will be presented in a table in the results manuscript. Disagreements between reviewers will be resolved by discussion or, if needed, by consulting a third review author.

Data extraction

Two reviewers will independently extract data from included studies following a standardised data extraction form (see online supplementary appendix 5), developed in accordance with CRD guidelines.⁴⁹ In case of disagreement, a third review author will be consulted. Intervention components of included studies will be reported following the Template for Intervention Description and Replication checklist.⁸² In addition to extraction of standard study information (ie, study identification features, research ethics, study characteristics, outcome measurements, statistical techniques, participant flow, risk of bias, and results) the following information will be extracted.

Participant characteristics

Informal caregiver: inclusion criteria, average age, per cent adult children, per cent female, per cent ethnic minority, per cent non-white, average education level, per cent employed, average household income, primary and secondary outcomes at baseline, only participants screened for elevated depressive symptoms prior to enrolment included (yes/no), average amount of care provided, average length of time as a caregiver and per cent coresiding with the care recipient.

Care recipient: inclusion criteria, health condition, average severity of health condition, average number of health comorbidities, per cent receiving care from several informal caregivers, average age, per cent female, per cent ethnic minority and average education level.

Intervention and control group components

Theory informing intervention (eg, CBT, IPT), individual or dyadic intervention, method of delivery (face to face, group, internet administered or mixed), multicomponent

intervention (yes/no), tailored (yes/no), intensity, type of support (eg, unsupported self-help, supported self-help or guided support), length of follow-up, number of sessions, length of sessions, adherence and provider (eg, lay worker, psychologist).

Risk of bias in individual studies

Each study will be evaluated by two reviewers independently for risk of bias following Cochrane Collaboration's Risk of Bias tool 2.0.³² Specifically, studies will be rated on the following domains: (1) sequence generation (selection bias), (2) allocation concealment (selection bias), (3) blinding of outcome assessment (detection bias), (4) completeness of outcome data (attrition bias), (5) selective outcome reporting (reporting bias) and (6) baseline imbalance. Ratings in each domain will be categorised as being of low (=0), unclear (=1) or high (=2) risk of bias. Overall risk of bias in each study will be categorised as

- Low if all domains are rated as low.
- Moderate if one domain is rated as unclear.
- High if one domain is rated as high or if two or more domains are rated as unclear.

If possible, reporting bias will be examined by comparing outcomes reported in the study protocol with outcomes reported in study paper.

Data synthesis

Meta-analysis

If data allow, a meta-analysis will be performed to examine the effectiveness of psychological interventions for depression among informal caregivers of older adults by calculating post-treatment between-group standardised mean effect sizes for the primary outcome (ie, self-report, clinician or proxy administered standardised measurements of depression) using Hedges' *g*. Similarly, effectiveness of psychological interventions will be examined for secondary outcomes commonly comorbid with depression among informal caregivers (ie, depression recovery, anxiety, stress, caregiver burden, psychological distress, quality of life, well-being and self-efficacy). The longest follow-up period ≤ 6 months post-treatment will be used as primary time-point to reduce the potential risk of bias due to examining short-term post-treatment effects which may inflate effect sizes.^{31 83 84}

For studies with multiple treatment groups, such as different types of psychological interventions, bias caused by multiple statistical comparisons with one control group will be avoided by analysing comparisons separately and splitting the control group sample size in half. Similarly, comparisons will be analysed separately with the sample size in the treatment condition halved for studies in which two control conditions are compared with one treatment condition.⁸⁵ In the event that all studies are assessed as high risk of bias in terms of sequence generation and allocation concealment according to the Cochrane Collaboration's Risk of Bias tool 2.0³² or studies do not provide enough data a meta-analysis will not be performed and

a narrative synthesis will be undertaken to summarise findings.

Assessment of heterogeneity

Between-study heterogeneity will be measured with Cochrane's test of heterogeneity (Q) and reported using I^2 statistics, alongside CIs.^{86 87} A random-effects model will be adopted in each analysis, assuming heterogeneity among studies due to variations in methodological and participant characteristics.⁸⁸ However, if the Q and I^2 analysis suggest no heterogeneity, a fixed-model approach will be adopted. Sources of heterogeneity will be explored by conducting moderator- and sensitivity analyses.

Moderator analyses

If data permit, sources of heterogeneity will be explored by conducting subgroup analyses and meta-regression analyses. Moderating effects of the following categorical factors on effectiveness will be examined using subgroup analyses:

- ▶ Care recipient's health condition.
- ▶ Theory informing intervention (eg, CBT, IPT).
- ▶ Individual or dyadic intervention.
- ▶ Method of delivery (face to face, group, internet administered or mixed).
- ▶ Multicomponent intervention (yes/no).
- ▶ Type of support (eg, unsupported self-help, supported self-help or guided support).³¹
- ▶ Length of follow-up (≤ 2 months, 3–6 months, 7–11 months or > 12 months post-treatment).
- ▶ Type of control condition (eg, no-treatment control, wait-list control, treatment as usual, non-specific factors component control, specific factors component control and active comparator).³³
- ▶ Recruitment setting (clinical, community, mixed).

Moderating effects of the following continuous factors on effectiveness will be examined using meta-regression analyses:

- ▶ Per cent adult children.
- ▶ Per cent female.
- ▶ Care recipient's health condition severity.
- ▶ Severity of depression at baseline.

Moderators will be examined by calculating post-treatment between-group standardised mean effect sizes for the primary outcome using Hedges' g . With

heterogeneity being anticipated, subgroup analyses and meta-regression analyses will be conducted using random-effects models, as is generally preferred,^{50 89} with Q and I^2 reported as measures of heterogeneity.

Sensitivity analyses

Sensitivity analyses will be conducted to examine the overall effect size of the primary outcome measurement while temporarily removing: (1) each study individually from the meta-analysis, (2) studies with sample sizes ≤ 20 across conditions, (3) studies with attrition rates $\geq 30\%$ in at least one trial arm, and (4) studies in each rating category of overall risk of bias (ie, high- moderate- respectively low risk of bias).

Dealing with missing data

Study authors will be contacted in the event of missing data. Intention-to-treat data will be used when available.⁹⁰

Funnel asymmetry

If ≥ 10 studies are included, the Egger's test of the Intercept will be used to examine funnel plot asymmetry for sources of biases such as publication bias, language bias, poor methodological quality in small studies and heterogeneity.⁹¹ Effect sizes for each outcome will be calculated taking potential publication bias into account by using the trim-and-fill procedure.⁹²

Confidence in cumulative evidence

Confidence in evidence for the primary outcome (depression) across studies will be assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) tool.^{93 94} The GRADE classification of confidence in evidence ratings can be seen in [table 1](#), alongside how each rating should be interpreted. As only randomised controlled trials will be included in this review, evidence will begin with high ratings, but may be modified downward for each of the following domains: risk of bias, imprecision of effect estimates, inconsistency of results, indirectness of evidence and likelihood of publication bias.

Patient and public involvement

Patients and members of the public were not involved in the development of this protocol due to funding and time constraints.

Table 1 The GRADE classification of confidence in evidence ratings and its interpretation

Confidence in evidence	Interpretation
High	Further research is very unlikely to change our confidence in the estimate of the effect.
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low	We are very uncertain about the estimate.

GRADE, Grading of Recommendations Assessment, Development and Evaluation.

ETHICS AND DISSEMINATION

There are ethical considerations to take into account when conducting systematic reviews, specifically in regard to lack of informed consent from participants in the original studies and the risk of including unethical studies.⁹⁵ Thus, data on funding source and ethical considerations of included studies will be extracted and reported in the results manuscript. However, given the current study will not collect data at the individual participant level there is no need for ethical approval from the National Ethical Review Board in Sweden.

Results will inform the development of a psychological intervention targeting depression among adult-child caregivers of older parents. Further, results will be disseminated through publication in peer-reviewed journals, as well as presentations at conferences, meetings and for various lay audiences. Dissemination targets will include organisations and authorities within the fields of informal caregiving, mental health and geriatric care.

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Contributors EM and JW conceptualised the study. EM drafted the proposal. EM and JW designed the study. All authors (EM, OB, DP, RS, LVE and JW) assisted with manuscript writing and critical revision of the study design and manuscript. All authors read and approved the final manuscript. JW is the guarantor of the review.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

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REFERENCES

- Chatterji S, Byles J, Cutler D, *et al.* Health, functioning and disability in older adults – current status and future implications. *Lancet* 2016;385:563–75.
- United Nations Department of Economic and Social Affairs Population Division. World population prospects, 2019. Available: <https://population.un.org/wpp/Publications/>
- Broese van Groenou MI, De Boer A. Providing informal care in a changing society. *Eur J Ageing* 2016;13:271–9.
- Ullman P, Szebehely M. From the state to the family or to the market? consequences of reduced residential eldercare in Sweden. *Int J Soc Welf* 2015;24:81–92.
- Pinquart M, Sörensen S. Associations of stressors and uplifts of caregiving with caregiver burden and depressive mood: a meta-analysis. *J Gerontol B Psychol Sci Soc Sci* 2003;58:P112–28.
- Pinquart M, Sörensen S. Correlates of physical health of informal caregivers: a meta-analysis. *J Gerontol B Psychol Sci Soc Sci* 2007;62:P126–37.
- Schulz R, Beach SR. Caregiving as a risk factor for mortality. *JAMA* 1999;282:2215.
- Koyanagi A, DeVolder JE, Stubbs B, *et al.* Depression, sleep problems, and perceived stress among informal caregivers in 58 low-, middle-, and high-income countries: a cross-sectional analysis of community-based surveys. *J Psychiatr Res* 2018;96:115–23.
- Barnett AE. Adult child caregiver health trajectories and the impact of multiple roles over time. *Res Aging* 2015;37:227–52.
- Stephens MA, Townsend AL, Martire LM, *et al.* Balancing parent care with other roles: interrole conflict of adult daughter caregivers. *J Gerontol B Psychol Sci Soc Sci* 2001;56:24–34 <http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L32047339>
- Vasileiou K, Barnett J, Barreto M, *et al.* Experiences of loneliness associated with being an informal caregiver: a qualitative investigation. *Front Psychol* 2017;8:1–11.
- Grenade L, Boldy D. Social isolation and loneliness among older people: issues and future challenges in community and residential settings. *Aust Health Rev* 2008;32:468–78.
- Nordin AA, Hairi FM, Choo WY, *et al.* Care recipient multimorbidity and health impacts on informal caregivers: a systematic review. *Gerontologist* 2018;1–18.
- Courtin E, Jemai N, Mossialos E. Mapping support policies for informal carers across the European Union. *Health Policy* 2014;118:84–94.
- Pinquart M, Sörensen S. Differences between caregivers and noncaregivers in psychological health and physical health: a meta-analysis. *Psychol Aging* 2003;18:250–67.
- Givens JL, Mezzacappa C, Heeren T, *et al.* Depressive symptoms among dementia caregivers: role of mediating factors. *Am J Geriatr Psychiatry* 2014;22:481–8.
- Berg A, Palomäki H, Lönnqvist J, *et al.* Depression among caregivers of stroke survivors. *Stroke* 2005;36:639–43.
- Geng H-M, Chuang D-M, Yang F, *et al.* Prevalence and determinants of depression in caregivers of cancer patients: a systematic review and meta-analysis. *Medicine* 2018;97:e11863.
- Bauer JM, Sousa-Poza A. Impacts of informal caregiving on caregiver employment, health, and family. *J Popul Ageing* 2015;8:113–45.
- Cooper C, Selwood A, Blanchard M, *et al.* The determinants of family carers' abusive behaviour to people with dementia: results of the card study. *J Affect Disord* 2010;121:136–42.
- Wilson MR, Van Houtven CH, Stearns SC, *et al.* Depression and missed work among informal caregivers of older individuals with dementia. *J Fam Econ Issues* 2007;28:684–98.
- Dunn NJ, Strain LA. Caregivers at risk?: changes in leisure participation. *J Leis Res* 2001;33:32–55.
- Cheng HY, Chair SY, Chau JP-C. The effectiveness of psychosocial interventions for stroke family caregivers and stroke survivors: a systematic review and meta-analysis. *Patient Educ Couns* 2014;95:30–44.
- Legg LA, Quinn TJ, Mahmood F, *et al.* Non-Pharmacological interventions for caregivers of stroke survivors. *Cochrane Database Syst Rev*. 2011:CD008179.
- Lins S, Hayder-Beichel D, Rücker G, *et al.* Efficacy and experiences of telephone counselling for informal carers of people with dementia (review). *Cochrane database Syst Rev* 2014;9:1–96.
- Weinbrecht A, Rieckmann N, Renneberg B. Acceptance and efficacy of interventions for family caregivers of elderly persons with a mental disorder: a meta-analysis. *Int Psychogeriatr* 2016;28:1615–29.
- Jütten LH, Mark RE, Wicherts JM, *et al.* The effectiveness of psychosocial and behavioral interventions for informal dementia caregivers: meta-analyses and meta-regressions. *J Alzheimers Dis* 2018;66:149–72.
- Sörensen S, Pinquart M, Duberstein P. How effective are interventions with caregivers? an updated meta-analysis. *Gerontologist* 2002;42:356–72.
- Cuijpers P, Karyotaki E, de Wit L, *et al.* The effects of fifteen evidence-supported therapies for adult depression: a meta-analytic review. *Psychother Res* 2020;30:279–93.
- Farrand P, Woodford J. Effectiveness of cognitive behavioural self-help for the treatment of depression and anxiety in people

- with long-term physical health conditions: a systematic review and meta-analysis of randomised controlled trials. *Ann Behav Med* 2015;49:579–93.
- 31 Farrand P, Woodford J. Impact of support on the effectiveness of written cognitive behavioural self-help: a systematic review and meta-analysis of randomised controlled trials. *Clin Psychol Rev* 2013;33:182–95.
 - 32 Sterne JAC, Savović J, Page MJ, et al. Rob 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*;2:14898.
 - 33 Mohr DC, Ho J, Hart TL, et al. Control condition design and implementation features in controlled trials: a meta-analysis of trials evaluating psychotherapy for depression. *Transl Behav Med* 2014;4:407–23.
 - 34 Dura JR, Stukenberg KW, Kiecolt-Glaser JK. Anxiety and depressive disorders in adult children caring for demented parents. *Psychol Aging* 1991;6:467–73.
 - 35 Adelman RD, Tmanova LL, Delgado D, et al. Caregiver burden: a clinical review. *JAMA* 2014;311:1052–9.
 - 36 Thomas P, Lalloué F, Preux P-M, et al. Dementia patients caregivers quality of life: the PIXEL study. *Int J Geriatr Psychiatry* 2006;21:50–6.
 - 37 Pettersson A, Boström KB, Gustavsson P, et al. Which instruments to support diagnosis of depression have sufficient accuracy? A systematic review. *Nord J Psychiatry* 2015;69:497–508.
 - 38 Given B, Wyatt G, Given C, et al. Burden and depression among caregivers of patients with cancer at the end of life. *Oncol Nurs Forum* 2004;31:1105–17.
 - 39 Bei E, Rotem-Mindali O, Vilchinsky N. Providing care from afar: a growing yet understudied phenomenon in the caregiving field. *Front Psychol* 2020;11:110–12.
 - 40 Miller KI, Shoemaker MM, Willyard J, et al. Providing care for elderly parents: a structural approach to family caregiver identity. *J Fam Commun* 2008;8:19–43.
 - 41 Rubin RM, White-Means SI. Informal caregiving: dilemmas of sandwiched caregivers. *J Fam Econ Issues* 2009;30:252–67.
 - 42 Rigby T, Ashwill RT, Galvin JE, et al. P2-559: differences in the experience of caregiving between spouse and adult child caregivers in dementia with Lewy bodies. *Alzheimer's & Dementia* 2018;14:P951.
 - 43 Pinquart M, Sörensen S. Gender differences in caregiver stressors, social resources, and health: an updated meta-analysis. *J Gerontol B Psychol Sci Soc Sci* 2006;61:33–45.
 - 44 Brodaty H, Green A, Koschera A. Meta-Analysis of psychosocial interventions for caregivers of people with dementia. *J Am Geriatr Soc* 2003;51:657–64.
 - 45 Pinquart M, Sörensen S. Helping caregivers of persons with dementia: which interventions work and how large are their effects? *Int Psychogeriatr* 2006;18:577–95.
 - 46 Laver K, Milte R, Dyer S, et al. A systematic review and meta-analysis comparing carer focused and dyadic multicomponent interventions for carers of people with dementia. *J Aging Health* 2017;29:1308–49.
 - 47 Gitlin N, Belle S, Burzio L. Effect of multicomponent interventions on caregiver burden and depression. *Psychol Aging* 2003;18:361–74.
 - 48 Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015;4:1.
 - 49 Centre for Reviews and Dissemination (Organization/Institution). *Systematic reviews: CRD's guidance for undertaking reviews in health care*. 3rd edn. New York: University of York, 2009.
 - 50 Higgins J, Green S. *Cochrane Handbook for Systematic Reviews of Interventions*. Version 5.1.0 [updated March 2011]. Cochrane Collab, 2011. Available: www.handbook.cochrane.org
 - 51 Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009;6.
 - 52 Huang X, Lin J, Demner-fushman D. *Evaluation of PICO as a knowledge representation for clinical questions*. Washington D.C: Annual Symposium of the American Medical Informatics Association (AMIA 2006), 2006: 359–63.
 - 53 OECD. Elderly population (indicator) 2019.
 - 54 Chang AY, Skirbekk VF, Tyrovolas S, et al. Measuring population ageing: an analysis of the global burden of disease study 2017. *Lancet Public Health* 2019;4:e159–67.
 - 55 Cuijpers P, van Straten A, Andersson G, et al. Psychotherapy for depression in adults: a meta-analysis of comparative outcome studies. *J Consult Clin Psychol* 2008;76:909–22.
 - 56 Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001;16:606–13.
 - 57 Beck A, Steer R, Brown G. *Beck depression inventory*. 2nd ed. San Antonio, TX: Psychological Corporation, 1996.
 - 58 Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry* 1960;23:56–62.
 - 59 Brown TA, Chorpita BF, Korotitsch W, et al. Psychometric properties of the depression anxiety stress scales (DASS) in clinical samples. *Behav Res Ther* 1997;35:79–89.
 - 60 Radloff L. The CES-D scale: a self-report depression scale for research in the general population. *Appl Psychol Meas* 1977;1:385–401.
 - 61 Bondolfi G, Jermann F, Rouget BW, et al. Self- and clinician-rated Montgomery-Asberg depression rating scale: evaluation in clinical practice. *J Affect Disord* 2010;121:268–72.
 - 62 Busner J, Targum SD. The clinical global impressions scale: applying a research tool in clinical practice. *Psychiatry* 2007;4:28–37.
 - 63 First MB, Spitzer RL, Miriam G, et al. Structured clinical interview for DSM-5 (SCID-5 for DSM-5, research version; SCID-5-RV). *Am Psychiatr Assoc*.
 - 64 Sheehan DV, Lecrubier Y, Sheehan KH, et al. The Mini-International neuropsychiatric interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry* 1998;59 Suppl 20:22–33.
 - 65 Bjelland I, Dahl AA, Haug TT, et al. The validity of the hospital anxiety and depression scale. An updated literature review. *J Psychosom Res* 2002;52:69–77.
 - 66 de Lima Osório F, Crippa JAS, Loureiro SR. Further psychometric study of the Beck anxiety inventory including factorial analysis and social anxiety disorder screening. *Int J Psychiatry Clin Pract* 2011;15:255–62.
 - 67 Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. *J Health Soc Behav* 1983;24:385–96.
 - 68 Petrowski K, Kliem S, Sadler M, et al. Factor structure and psychometric properties of the English version of the trier inventory for chronic stress (TICS-E). *BMC Med Res Methodol* 2018;18:1–8.
 - 69 Zarit SH, Reever KE, Bach-Peterson J. Relatives of the impaired elderly: correlates of feelings of burden. *Gerontologist* 1980;20:649–55.
 - 70 Robinson BC. Validation of a caregiver strain index. *J Gerontol* 1983;38:344–8.
 - 71 Kessler RC, Barker PR, Colpe LJ, et al. Screening for serious mental illness in the general population. *Arch Gen Psychiatry* 2019;60:184–9.
 - 72 Massé R. Qualitative and quantitative analyses of psychological distress: methodological complementarity and ontological incommensurability. *Qual Health Res* 2000;10:411–23.
 - 73 Burckhardt CS, Anderson KL. The quality of life scale (QOLS): reliability, validity, and utilization. *Health Qual Life Outcomes* 2003;1:1–7.
 - 74 Diener E, Emmons RA, Larsen RJ, et al. The satisfaction with life scale. *J Pers Assess* 1985;49:71–5.
 - 75 Schwarzer R, Jerusalem M, Scale GS-E. Measures in health psychology: A user's portfolio. In: Weinman J, Wright S, Johnston M, eds. *Causal and control beliefs*. Windsor, UK: NFER-Nelson, 1995: 35–7.
 - 76 Woodford J, Farrand P, Richards D, et al. Psychological treatments for common mental health problems experienced by informal carers of adults with chronic physical health conditions (protocol). *Syst Rev* 2013;2:9.
 - 77 Gellatly J, Bower P, Hennessy S, et al. What makes self-help interventions effective in the management of depressive symptoms? meta-analysis and meta-regression. *Psychol Med* 2007;37:1217–28.
 - 78 Cuijpers P, van Straten A, Bohlmeijer E, et al. The effects of psychotherapy for adult depression are overestimated: a meta-analysis of study quality and effect size. *Psychol Med* 2010;40:211–23.
 - 79 Robinson KA, Whitlock EP, Oneil ME, et al. Integration of existing systematic reviews into new reviews: identification of guidance needs. *Syst Rev* 2014;3:1–17.
 - 80 McGowan J, Sampson M, Salzweid DM, et al. PRESS peer review of electronic search strategies: 2015 guideline explanation and elaboration (PRESS E & E) 2016.
 - 81 Ouzzani M, Hammady H, Fedorowicz Z, et al. Rayyan—a web and mobile APP for systematic reviews. *Syst Rev* 2016;5:1–10.
 - 82 Hoffmann TC, Glasziou PP, Boutron I, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ* 2014;348:1–12.
 - 83 Ekers D, Webster L, Van Straten A, et al. Behavioural activation for depression; an update of meta-analysis of effectiveness and subgroup analysis. *PLoS One* 2014;9:e100100.
 - 84 Flückiger C, Del Re AC, Munder T, et al. Enduring effects of evidence-based psychotherapies in acute depression and anxiety disorders versus treatment as usual at follow-up—a longitudinal meta-analysis. *Clin Psychol Rev* 2014;34:367–75.
 - 85 Simblett S, Birch J, Matcham F, et al. A systematic review and meta-analysis of e-mental health interventions to treat symptoms of posttraumatic stress. *JMIR Ment Health* 2017;4:e14.

- 86 Higgins JPT, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med* 2002;21:1539–58.
- 87 Higgins JPT, Thompson SG, Deeks JJ, *et al.* Measuring inconsistency in meta-analyses. *BMJ* 2003;327:557–60.
- 88 Schmidt FL, Oh I-S, Hayes TL. Fixed- versus random-effects models in meta-analysis: model properties and an empirical comparison of differences in results. *Br J Math Stat Psychol* 2009;62:97–128.
- 89 Higgins JPT, Thompson SG. Controlling the risk of spurious findings from meta-regression. *Stat Med* 2004;23:1663–82.
- 90 Gupta SK. Intention-To-Treat concept: a review. *Perspect Clin Res* 2011;2:109.
- 91 Egger M, Smith GD, Schneider M, *et al.* Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1998;316:469
- 92 Duval S, Tweedie R. Trim and fill: a simple funnel-plot-based method. *Biometrics* 2000;56:455–63.
- 93 Ryan R, Hill S. How to grade the quality of the evidence. *Cochrane Consum. Commun. Gr* 2016:1–25.
- 94 Guyatt GH, Oxman AD, Vist GE, *et al.* Grade: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;336:924–6.
- 95 Vergnes J-N, Marchal-Sixou C, Nabet C, *et al.* Ethics in systematic reviews. *J Med Ethics* 2010;36:771–4.