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 of older adults 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. PROSPERO registration number CRD42020157763.

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 2019.3 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 healthcare systems.3 This, in combination with...
reductions in residential care provision for older adults, 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). However, informal caregiving is associated with a number of negative impacts for the caregiver such as chronic stress, physical and emotional burden, sleep difficulties, role strain, loneliness and financial problems. 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, multimorbid (ie, suffering from more than one health condition), and/or neglected in terms of public support provision.

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. However, the prevalence of depression among informal caregivers may vary depending on the health condition of the care recipient and its trajectory. For example, 25% 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. Other studies have found 30%–33% of informal caregivers of stroke survivors and 43% of informal caregivers of cancer patients experience depression. Not only is depression detrimental to informal caregivers’ overall health, such as leading to a higher risk of mortality, but may also lead to lower quality of care provided. Further, informal caregiving may lead to reductions in paid employment and engagement in social and recreational activities. 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, and particularly dementia. 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. 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 findings 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).

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 according to the Cochrane Collaboration’s Risk of Bias tool 2.0, (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 comparators and (4) including studies conducted since the previous review was performed in 2002.

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, stress, caregiver burden, low quality of life, low well-being and low self-efficacy. 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) 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, such as dementia or severe forms of stroke and cancer. 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, role strain, role reversal in terms of responsibility, overall stress and lower quality of life). 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. 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, intervention type (e.g., CBT, IPT), individual versus dyadic intervention, method of delivery (face to face, group, internet administered or mixed), multicomponent intervention or not, and length of follow-up. Other potential moderating factors of interest are type of support (e.g., unsupported self-help, supported self-help or guided support), 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 (e.g., 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). A systematic review will be performed to identify eligible studies following the Centre for Reviews and Dissemination (CRD) guidance on undertaking systematic reviews. If data permit, meta-analysis, moderator analyses and sensitivity analyses will be performed in accordance with guidelines provided by Cochrane, and reported in accordance with the PRISMA statement.

**Inclusion and exclusion criteria**

Inclusion and exclusion criteria are categorised by population, interventions, comparators, outcomes and study design (PICO:S). 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. Because we anticipate that many older adults who receive informal care have age-related diseases, 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. Such diseases may include, but are not limited to, cardiovascular diseases, cerebrovascular diseases, chronic respiratory diseases, neoplasms, neurodegenerative disorders and sense organ disorders. 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 (e.g., post-traumatic stress disorder and psychosis) or with mood disorders other than depression (e.g., 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 (i.e., CBT, SUP, BA, DYN, PST, TWCBT, IPT and LRT), alongside the use of measurement of depression as a primary outcome, will be included. Interventions with more than one primary target (e.g., mixed depression and anxiety) will be excluded. However, interventions are anticipated to additionally target secondary outcomes related to psychological well-being (e.g., 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 psychoeducation, support groups and brief interventions.
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 control (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), the Beck Depression Inventory (BDI-II), the Depression Anxiety Stress Scale (DASS-D), the Centre for Epidemiological Depression Scale (CES-D), the Montgomery–Åsberg Depression Rating Scale (MADRS) or the Clinical Global Impression Improvement Scale.

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 Disorders or Mini-International Neuropsychiatric Interview and/or (2) scoring below a clinical cut-off score on the PHQ-9, BDI-II, DASS-D, CES-D, MADRS and Hospital Anxiety and Depression Scale.

Other secondary outcomes of interest are self-report, clinician or proxy administered standardised measurements of anxiety (eg, Beck Anxiety Inventory), stress (eg, the perceived stress scale, the Trier inventory for chronic stress), caregiver burden (eg, the Burden Interview, the Caregiver Strain Index), psychological distress (eg, Kessler 6, the psychological distress manifestations measurement scale), quality of life (eg, the Quality of Life scale), well-being (eg, the satisfaction with life scale), self-efficacy (eg, the generalised self-efficacy scale).

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 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 to minimise the risk of including low quality studies which may inflate effect sizes.

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. 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, 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 guidelines (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. 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. 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. 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 coexisting 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. 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.

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. 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 2.0 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 using Cochrane’s test of heterogeneity (Q) and reported using I² statistics, alongside CIs. A random-effects model will be adopted in each analysis, assuming heterogeneity among studies due to variations in methodological and participant characteristics. However, if the Q and I² 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).
- 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).
- 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, with Q and I² 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 ≥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.

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. Effect sizes for each outcome will be calculated taking potential publication bias into account by using the trim-and-fill procedure.

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. 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

| 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. 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, LDeV 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.

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