



Integrated care for older people (ICOPE)
Guidelines on community-level interventions
to manage declines in intrinsic capacity

Evidence profile: depressive symptoms

Scoping question:

Does psychological intervention (behavioural activation, cognitive behavioural therapy, psychoeducational therapy, interpersonal therapy, problem-solving therapy, stepped-care protocol therapy, or life-review therapy) produce any benefit or harm for older people with depressive symptoms?

The full ICOPE guidelines and complete set of evidence profiles are available at:
who.int/publications/i/item/9789241550109

Painting: "Wet in Wet" by Gusta van der Meer. At 75 years of age, Gusta has an artistic style that is fresh, distinctive and vibrant. A long-time lover of art, she finds that dementia is no barrier to her artistic expression. Appreciated not just for her art but also for the support and encouragement she gives to other artists with dementia, Gusta participates in a weekly art class. Copyright by Gusta van der Meer. All rights reserved

Contents

Background	1
Interaction with WHO mhGAP intervention guide.....	1
Part 1: Evidence review	6
Scoping question in PICO format (population, intervention, comparison, outcome)	6
Search strategy.....	7
List of systematic reviews identified by the search	7
PICO table	8
Narrative description of the studies that went into the analysis	9
GRADE table 1: Behavioural activation treatment compared with usual care for depression in older people	11
GRADE table 2: Psychological interventions compared with usual care for depressive symptoms in older people (not meeting the diagnostic criteria for depressive episode)	12
Part 2: From evidence to recommendations	14
Summary-of-evidence table	14
Evidence-to-recommendations table.....	15
Guideline development group recommendations and remarks	18
References	19
Annex 1: PRISMA flow diagram for systematic review of the reviews – sub-threshold depression	21

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Background

Although 10–16% of people aged 65 years and over are likely to experience significant depressive symptoms, the condition is largely under-diagnosed and often inadequately treated in primary care. The determinants of later-life depression include chronic illness and limitations in functional ability, cognitive impairment, and social isolation. In most older people, late-life depressive symptoms are strongly associated with reduced functional ability and linked to poor quality of life. Therefore, there is a pressing need to scale up evidence-based public health interventions for prevention, early detection and management of depression. At present, management of depression is over-reliant on antidepressants, placing older people at risk of polypharmacy and falls. Additional concerns include the uncertain efficacy of antidepressants for older people with comorbid cognitive impairment and dementia, and problems with adherence.

Psychological interventions may be considered for older people with depressive symptoms, but the limited evidence on the efficacy of such interventions and the unavailability of trained health-care professionals constitute major barriers. Psychological interventions may be delivered in different ways (to groups or to individuals, by professionals or paraprofessionals, and guided and unguided, i.e. self-help involving use of the Internet or books), which may help to promote coverage and access. Recently, there has been increasing interest in research and implementation to explore the potential for these interventions to reduce the incidence of depressive episodes among older people at risk. Since the aim, within the World Health Organization (WHO) guideline on integrated care for older people (ICOPE), is to address symptoms of depression in older community-dwelling people, it is important to review therapeutic

options for sub-threshold depression and for depressive symptoms when a clinical diagnosis is not a specific inclusion or exclusion criterion. Non-specialist community health workers should be able to identify clinically relevant symptoms associated with distress and indicators of marked severity requiring referral, but may not be expected routinely to distinguish the clinical diagnoses of moderate and severe depressive episode.

Interaction with WHO mhGAP intervention guide

The evidence for the effectiveness of pharmacological and psychological interventions for mild, moderate and severe depression was reviewed in 2012 as part of the Mental Health Gap Action Programme intervention guide (mhGAP-IG) development (1), resulting in some specific evidence-based recommendations regarding therapeutic options for older people. The evidence for effectiveness of these interventions specifically among older adults was not, however, documented in detail. This evidence is therefore briefly described here, as essential background to the ICOPE guideline for the management of low mood.

Treatment with antidepressants

The current mhGAP recommendations are as follow.

- Antidepressants should not be considered for the initial treatment of adults with mild depressive episode.
Strength of recommendation: conditional.

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- Tricyclic antidepressants or fluoxetine should be considered in adults with moderate to severe depressive episode/disorder.
Strength of recommendation: conditional.
- If drug treatment is required in older people, tricyclic antidepressants should be avoided if possible.
Strength of recommendation: conditional.

Three relevant Cochrane reviews summarize the evidence for the efficacy of antidepressants in the older population, their relative efficacy and their potential to prevent relapse. For the review of efficacy of antidepressants in the treatment of depression, the authors included 17 randomized controlled trials (RCTs) based on 245 patients treated with tricyclic antidepressants (TCAs; 223 with placebo), 365 receiving selective serotonin reuptake inhibitors (SSRIs; 372 with placebo) and 58 patients receiving monoamine oxidase inhibitors (MAOIs; 63 with placebo) (2). Fixed-effect meta-analysis showed that TCAs (odds ratio [OR] favouring antidepressants: 0.32; 95% CI: 0.21 to 0.47), SSRIs (OR favouring antidepressants: 0.51, 95% CI: 0.36 to 0.72) and MAOIs (OR favouring antidepressants: 0.17, 95% CI: 0.07 to 0.39) are effective in the treatment of depression in older adults. The second review (updated to include publications in 2008) compared the efficacy of different antidepressant classes and withdrawal rates associated with each class (3). The authors analysed 32 studies including participants aged over 55 years. There was no significant difference in efficacy between TCAs and SSRIs (relative risk [RR]: 1.07, 95% CI: 0.94 to 1.22), but TCAs compared less favourably in terms of numbers of discontinuations irrespective of reason (RR: 1.23, 95% CI: 1.05 to 1.43) and withdrawal due to side-effects (RR: 1.36, 95% CI: 1.09 to 1.70). The third review examined the efficacy of antidepressants in preventing the relapse and recurrence of depression in older people (4) since higher rates of relapse have

been identified in older people (5). Six RCTs comparing medication with placebo only showed long-term benefits of continuing antidepressant medication for 12 months (including 3 trials $n = 247$, RR: 0.67, 95% CI: 0.55 to 0.82). However, no significant benefit for antidepressants was observed at follow-up at 6, 24 or 36 months. Authors concluded that the long-term benefits of continuation and maintenance of pharmacological treatments for depression in older people are unclear with marked heterogeneity between the studies.

During the preparation of the evidence base to support the mhGAP-IG, a systematic review and meta-analysis of double-blind RCTs (6) was conducted to assess the evidence of efficacy and acceptability of antidepressant and benzodiazepine treatment for adults with minor depression. Six RCTs involving 234 patients treated with antidepressants and 234 with placebo showed no significant difference in terms of failure to respond (RR: 0.94, 95% CI: 0.81 to 1.08). Although the review did not focus on older people, the two RCTs on older adults with minor depression (7, 8) showed similar results (RR: 0.88, 95% CI: 0.47 to 1.63; and RR: 1.03, 95% CI: 0.79 to 1.35, respectively). The authors concluded that there is unlikely to be a clinical advantage for antidepressants over placebo in the treatment of minor depression.

Thus, evidence from RCTs conducted among older people is consistent with current mhGAP recommendations.

Psychological treatments

The current mhGAP recommendations are as follow.

- Interpersonal therapy, cognitive behavioural therapy and problem-solving treatment should be considered as

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psychological treatment of depressive episode/disorder in non-specialized health-care settings if there are sufficient human resources (e.g. supervised community health workers).

Strength of recommendation: conditional.

- Behavioural activation should be considered as treatment of adults with depressive episode/disorder. In moderate and severe depression, this intervention should be considered as adjunct to antidepressants.

Strength of recommendation: conditional.

A fourth Cochrane review assessed the efficacy of psychotherapeutic treatments for depression in older people (9). This included RCTs among older adults with any diagnosis of depression (including minor depression) according to International Classification of Diseases and Related Health Problems 10th Revision (ICD-10¹) or *Diagnostic and Statistical Manual of Mental Disorders (DSM-5)*² criteria. All types of psychotherapeutic interventions were included: cognitive behavioural therapy (CBT; including cognitive therapy, cognitive bibliotherapy and problem-solving therapy), psychodynamic therapy, interpersonal therapies and supportive/counselling therapies. Comparison arms included waiting list controls and placebo control interventions, such as bibliotherapy with non-therapeutic material, reminiscence, educational therapy or visual imagery. Primary outcomes were the reduction in severity of depression (usually clinician-rated). Five RCTs compared CBT versus waiting list controls using the Hamilton Depression Rating Scale, with 73 participants in the treatment groups and 80 in the control groups, in community, outpatient, nursing home or primary care settings. Patients with

cognitive impairment or other psychiatric disorders were excluded, but none of the trials excluded participants with physical illnesses. Fixed-effect meta-analysis on the main outcome favoured CBT intervention (weighted mean difference [WMD] -9.85 points, 95% CI: -11.97 to -7.73). No significant difference in treatment effect between CBT and psychodynamic therapy was found. The authors advised caution when generalizing the evidence, mainly due to the small number of trials included.

A more recent, more up-to-date and more comprehensive review included trials focusing on older people with sub-threshold depression as well as those with a diagnosis of depressive episode or disorder (10). Specific types of psychotherapies that were found to be effective included CBT (14 RCTs, $g = 0.45$, 95% CI: 0.29 to 0.60), life review therapy (7 RCTs, $g = 0.59$, 95% CI: 0.36 to 0.82) and problem-solving therapy (5 RCTs, $g = 0.46$, 95% CI: 0.18 to 0.74). Trials of treatment compared with placebo control groups were associated with larger effect sizes than waiting list and care-as-usual control comparators. Lower-quality trials reported larger effect sizes than high-quality studies. Direct comparisons between different types of psychotherapy suggested that CBT and problem-solving therapy may be more effective than non-directive counselling. Too few data were available to judge the relative benefits of other structured psychological treatments. Since the publication of these reviews, the evidence base for behavioural activation has been extended, with the publication of an expanded systematic review including stratified analyses by dose, duration, therapist and age group of recipient (11), which was not previously considered during the development of the mhGAP-IG.

Thus, evidence from RCTs conducted among older people is consistent with current mhGAP recommendations. However, it

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¹ Available at <http://www.who.int/classifications/icd>

² Available at <http://www.psychiatry.org/psychiatrists/practice/dsm>

should be noted that the quality of the evidence with respect to CBT for older people is low (as opposed to moderate for adults in general), and that there is currently very limited evidence regarding the effectiveness of interpersonal therapy for older adults. We have now formulated a new scoping question regarding the effectiveness of behavioural activation, given the recently expanded evidence base.

Physical activity

The current mhGAP recommendation is as follows.

- Advice on physical activity should be encouraged as part of treatment for adults with depressive episode/disorder with inactive lifestyles. In moderate and severe depression, this intervention should be considered as adjunct to antidepressants or brief structured psychological treatments.

Strength of recommendation: conditional.

A Cochrane systematic review (12) was conducted to examine the effectiveness of exercise in the treatment of depression in adults of all ages. Thirty-five RCTs were identified (including 1356 participants) that compared physical activity with no treatment or a control intervention (including placebo treatment, pharmacological treatment, psychological treatment or any other active treatment). The meta-analysis indicated a moderate clinical effect in favour of exercise (standardized mean difference [SMD]: -0.62, 95% CI: -0.81 to -0.42), with moderate heterogeneity ($I^2 = 63\%$). Eight trials (377 participants) that provided long-term follow-up data showed a smaller beneficial effect for exercise (SMD: -0.33, 95% CI: -0.63 to -0.03). Authors also explored the influence of the type of exercise (aerobic, mixed or resistance), finding a moderate clinical effect for aerobic exercise (SMD: -0.55, 95% CI: -0.77

to -0.34) and larger size effects for both mixed and resistance exercise (SMD -0.85, 95% CI: -1.85 to 0.15; and SMD: -1.03, 95% CI: -1.52 to -0.53, respectively). They did not find a significant difference when compared with psychological or pharmacological treatments. However, the latter are based on small trials and further research is required.

Just three of these trials focused on older people (13–15), all conducted on community volunteers, with a total of 73 participants in the intervention arms and 54 in the control arms. The results from this older adult subgroup also indicated that exercise has a significant effect on depressive disorders (SMD: -1.02, 95% CI: -1.97 to -0.08 [13]; SMD: -0.65, 95% CI: -1.29 to -0.02 [14]; and SMD: -1.00, 95% CI: -1.69 to -0.31 [15]). The pooled effect for studies conducted in older adults was SMD -0.85 (95% CI: -1.27 to -0.43, $I^2 = 0.0\%$). Thus, treatment effect sizes were, if anything, slightly greater for older people, with less heterogeneity of effect among studies. Nevertheless, the evidence base must be considered to be limited, and of low quality, given the prominent risk of bias in all three studies (randomization, allocation concealment, blinding of outcome assessment and complete reporting of outcomes). The low study quality may be an important limitation since, when the authors of the original review meta-analysed only the six trials (464 participants, none of them conducted with older adults) with adequate allocation concealment, intention-to-treat analysis and blinded outcome assessment, the pooled SMD for the main depression outcome was much attenuated and not statistically significant (SMD: -0.18, 95% CI: -0.47 to 0.11). Also of note is that in one of the three trials involving older adults (13) adverse events were reported in detail (visits to a health-care professional, minor illness, muscular pain,

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chest pain, injuries requiring training adjustment, falls, deaths and hospital days) with no significant difference between the groups.

Thus, evidence from RCTs conducted among older people is consistent with current mhGAP recommendations, but with a very limited evidence base, and very low- to low-quality evidence.

Relaxation training

The current mhGAP recommendation is as follows.

- Relaxation training may be considered as treatment of adults with depressive episode/disorder. In moderate and severe depression, this intervention should be considered as adjunct to antidepressants or structured brief psychological treatments.

Strength of recommendation: conditional.

The review carried out for mhGAP focused on evidence previously synthesized and meta-analysed for a Cochrane review published in 2008, on the effectiveness of relaxation training (RT) as a treatment for depression of clinical significance. This provided low-quality evidence favouring RT over treatment as usual in reducing depression symptoms post-treatment (5 RCTs, $n = 136$, SMD: -0.59, 95% CI: -0.94 to -0.24) and in treatment response (2 RCTs, $n = 52$, RR [nonresponse]: 0.28, 95% CI: 0.14 to 0.54). There was limited/very low-quality evidence favouring RT over treatment as usual in reducing depression symptoms six months post-treatment (1 RCT, $n = 22$, SMD: -0.39, 95% CI: -1.24 to -0.45). This review reported tentative evidence to the effect that (a) RT was less effective than other psychological

treatments and (b) RT plus medication was more effective than medication alone. None of these trials were conducted in older adult populations, and hence this evidence base may not generalize to this group. However, trials of RT excluded from this Cochrane review were carried out on older people, but with anxiety symptoms as the primary inclusion criteria. Anxiety symptoms are highly comorbid with depression at diagnostic and sub-threshold level (16), and reduction in depression symptoms was a secondary outcome on most of the trials. This literature has recently also been subject to systematic review and meta-analysis (17). Three RCTs of RT, and four trials of CBT plus RT (CBT+RT) were identified. All used active control conditions matched for therapist time. All were conducted in high-income countries. Results of the meta-analysis suggest moderate effectiveness of RT (SMD: -0.90, 95% CI: -1.44 to -0.44) and CBT plus RT (SMD: -0.33, 95% CI: -0.74 to 0.07) for anxiety outcome measures. However, there was no evidence for effectiveness for depression outcome measures either for RT (SMD: -0.23, 95% CI: -0.76 to 0.29) or CBT+RT (SMD: -0.12, 95% CI: -0.52 to 0.29). The trials were of very low quality (bias, imprecision and indirectness, both because of the anxiety disorder selection criteria and due to the use of specialist therapists in high-income countries).

The available evidence from trials conducted specifically among older people is very limited and indirect. There is no specific evidence to support the use of relaxation training as an intervention for depression in older people, but equally there is no evidence that the current mhGAP intervention guide, based on trials among working age adults, may not generalize to older people.

Part 1: Evidence review

Scoping question in PICO format (population, intervention, comparison, outcome)

Population

- Older people 60 years of age and over (both male and female) with depressive symptoms with or without diagnostic status (depressive episode or disorder)

Interventions

- Behavioural activation, cognitive behavioural therapy (CBT), psychoeducational therapy, interpersonal therapy, problem-solving therapy, stepped-care protocol or life review therapy

Comparison

- Usual care, or waiting list

Outcomes

- *Critical:* depressive symptoms, incidence of clinically significant depression (depressive episode or major depressive episode)

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https://www.yunbaogao.cn/report/index/report?reportId=5_26665

