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/ageing/publications/guidelines-icope

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
Evidence profile: depressive symptoms

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 ........................................................................................................................................................................................................................................... 6
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

© World Health Organization 2017

Some rights reserved. This work is available under the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 IGO licence (CC BY-NC-SA 3.0 IGO; http://creativecommons.org/licenses/by-nc-sa/3.0/igo)
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.*

(continued next page)
• 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

(continued next page)
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-52) 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

---

1 Available at http://www.who.int/classifications/icd
2 Available at http://www.psychiatry.org/psychiatrists/practice/dsm

(continued next page)
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, 

*(continued next page)*
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)
Search strategy

The search for systematic reviews was performed (in October 2015) using MEDLINE, EMBASE, the Cochrane Database of Systematic Reviews and the Cochrane Central Register of Controlled Clinical Trials. The following search terms were used to identify relevant studies:

("depression" [MeSH] OR "depressive disorder" [MeSH]) OR ("subthreshold depression" OR "minor depression" OR "mild depression" OR "subsyndromal depression" OR "non-major depression") AND ("cognitive therapy" [MeSH] OR "psychotherapy"

[MeSH]) OR ("depression/drug therapy" [MeSH]) OR (depressive disorder [MeSH]) OR (antidepressants [MeSH]) OR (antidepressive agents [MeSH]) AND (aged [MeSH]) OR (adult, frail elderly [MeSH]) OR (oldest old [MeSH]) OR ("older people" OR "older adults" OR "elderly").

An additional search for systematic reviews in the Cochrane Library was performed using the following search terms:

(depress*) AND "older" AND (treatment OR therap*).

List of systematic reviews identified by the search

Included in GRADE3 tables


Excluded from GRADE tables


### PICO table

<table>
<thead>
<tr>
<th>Population</th>
<th>Intervention/comparison</th>
<th>Outcome</th>
<th>Systematic reviews used for GRADE</th>
<th>Explanation</th>
</tr>
</thead>
</table>
Narrative description of the studies that went into the analysis

GRADE table 1: Behavioural activation versus controls or antidepressant medicine for depressive disorder

A systematic review of randomized controlled trials (RCTs) assessed the effectiveness of behavioural activation for depression versus control or antidepressant medicine (11). Twenty-six RCTs including 1524 participants were included in the meta-analysis. A random-effects meta-analysis of symptom-level post treatment showed behavioural activation to be superior to control (SMD: -0.74, 95% CI: -0.91 to -0.56, k = 25, n = 1088) and medication (SMD: -0.42, 95% CI: -0.83 to -0.00, k = 4, N = 283). Meta-regression indicated no effect of mode of delivery, therapist level, dose or content of the intervention. However, study quality was generally low, and follow-up time periods were short. Four trials had been deemed to have been conducted on older participants (n = 55 in the intervention arms and n = 71 in the control arms). These RCTs were all conducted in the United States of America, using specialist therapists and providing 6–16 intervention sessions. Follow-up periods were 6–10 weeks. The subgroup analysis also indicated evidence of effectiveness (SMD: -0.68, 95% CI: -1.02 to -0.34, I² = 0.0%). However, one of the trials included in this subgroup analysis (Lovett et al.) targeted caregivers of frail dependent older people who were not exclusively elderly (41% were caring for a parent), and 51% did not have minor or major depression at baseline, hence the study did not meet inclusion criteria for the original review and should probably have been excluded. The authors concluded, overall, that the results of the meta-analysis support and strengthen the evidence base indicating that behavioural activation is an effective treatment for depression.

However, they also drew attention to the need for further high-quality research with longer-term follow-up to strengthen the evidence base.

GRADE table 2: Psychological interventions for depressive symptoms (not meeting the diagnostic criteria for depressive episode)

A systematic review of RCTs (18) assessed evidence for the effectiveness of psychological treatments in reducing symptoms in sub-threshold depression. A meta-analysis was conducted on 18 selected RCTs (excluding those focusing on children or adolescents) with 1913 participants with depressive symptoms but no full diagnosis of major depressive disorder. Participants were mainly recruited from the community, outpatient clinics or primary health care settings. Several of the included studies presented unclear risk of bias, mainly due to uncertainties relating to randomization, blinding and selective reporting of results. The majority of the trials used cognitive behavioural therapy (CBT) although other therapies, such as problem-solving therapy or stepped-care, were also included. Care-as-usual was used as the control condition for the majority of the trials. The comparison of the pooled effect sizes (Hedges’ g) was calculated from a total of 14 studies and results indicated that psychological treatments for subclinical depression have a significant effect compared with the control (g = 0.35, 95% CI: 0.23 to 0.47, NNT [number needed to treat to prevent one new case of depressive disorder] = 5.1). The authors conducted a subgroup analysis targeting older adults only (aged 50 years and over). Six RCTs were included, with 400 older people in the intervention arms (three received CBT [19–21], one problem-solving therapy [8], one interpersonal therapy [22] and one life review therapy [23]) versus 426 in care-as-usual control groups. The intervention was administered to groups in five of the trials and individually in one. Participants were recruited on the basis of

(continued next page)
Evidence profile: depressive symptoms

Various cut-off points on the Geriatric Depression Scale (GDS), or the Centre for Epidemiological Studies Depression Scale (CES-D), or symptoms of major depression, or on the basis of self-reported depression symptoms, and the absence of major depressive disorder. Three studies were conducted in the community, one in primary care, one with “medically ill elderly” recruited from medical centres and one in a nursing home. In GRADE table 2, only trials included in the subgroup analysis for older adults are presented. Similar to overall findings, these results replicated the moderate effectiveness of psychotherapy on sub-threshold depression in older adults ($g = 0.30$, 95% CI: 0.14 to 0.46, NNT = 6). The authors suggested caution when interpreting the results as they found that positive results were only observed when based on self-report measures (in contrast to clinician-rated outcomes), which could mean that therapeutic effects could be affected by detection bias. The small-to-moderate (yet significant) psychotherapeutic effects on subclinical depression might be considered consistent with expectations, given the limited possibilities for symptomatic improvement in this sub-threshold group.

A further recent review considered the effects of psychological interventions on reducing the incidence of depressive disorder (24). Overall, 32 trials with 6214 participants were included. The overall pooled relative risk (RR) of developing a depressive disorder was 0.79 (95% CI: 0.69 to 0.91), with low heterogeneity among studies ($I^2 = 24\%$, NNT = 20). The review included four RCTs conducted among older adults, only one of which had featured in the first review of the effect of psychological interventions on depression symptoms. One of these studies was conducted through primary health care, one in a nursing home, one on older caregivers of people with dementia, and one on older outpatients with macular degeneration. Follow-up periods ranged from 6 to 24 months. Where multiple end-points were reported, the authors “calculated the mean [relative risk] by combining the IRRs at different follow-up times into a single estimate”. However, the method used to do this was not described (further information was requested from the authors), and, without this none of the effect size estimates contained in the review could be replicated from the original sources. The IRR from one of the source studies seemed to have been miscalculated when first reported (25), and was corrected in a later publication (26). The pooled meta-analysed effect for older people is reported as RR: 0.55 (95% CI: 0.36 to 0.85) with no heterogeneity among studies (NNT = 11). We have therefore conducted a fresh meta-analysis summarizing outcomes at two months (1 RCT), six months (2 RCTs), 12 months (2 RCTs) and 6–12 months (4 RCTs). One trial indicated a reduced incidence of depressive disorder at two months (26), and one at 12 months (27). However, the pooled meta-analysed effects at 6 months, 12 months, and 6–12 months did not show any statistically significant effect of the intervention. There was, however, marked heterogeneity of the effects among studies at 12 months ($I^2 = 85.8\%$) and 6–12 months ($I^2 = 66.2\%$)
## Evidence profile: depressive symptoms

### ICOPE guidelines – World Health Organization

### GRADE table 1: Behavioural activation treatment compared with usual care for depression in older people

<table>
<thead>
<tr>
<th>Author:</th>
<th>WHO systematic review team</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date:</td>
<td>11 November 2015</td>
</tr>
<tr>
<td>Question:</td>
<td>What is the effectiveness of behavioural activation compared with usual care for depression in older people?</td>
</tr>
<tr>
<td>Settings:</td>
<td>Primary care, community or hospital</td>
</tr>
</tbody>
</table>

### Behavioural activation treatment compared with usual care for depression in older people

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Study design</th>
<th>Quality assessment</th>
<th>Number of patients</th>
<th>Effect</th>
<th>Quality</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression symptoms (follow-up 6–10 weeks; assessed with self-reported and structured clinical interview)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>randomized trials</td>
<td>very serious</td>
<td>50</td>
<td>SMD 0.81 lower (1.22 lower to 0.40 lower)</td>
<td>VERY LOW</td>
<td>CRITICAL</td>
</tr>
<tr>
<td></td>
<td>trials a</td>
<td>not serious</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>serious c</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>serious d</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>none</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Control</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Psychological treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Relative (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Absolute (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Relative (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Absolute (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CI: confidence interval; SMD: standardized mean difference

a Trials presented constitute subgroup analysis for older adults only. One of the trials included in the published review (Lovett et al.) was excluded from this meta-analysis, since, on inspection of the original source article, the caregivers of frail dependent older people were not exclusively elderly (41% were caring for a parent), and 51% did not have minor or major depression at baseline, hence this trial did not meet inclusion criteria for the original review.
b Risk of bias: Downgraded twice as only one of the three trials accounted adequately for missing data and in none of the three trials was the randomization sequence generated adequately, allocation concealed or outcome assessor masked to allocation.
c Indirectness: Downgraded once as heterogeneity in terms of treatment format was observed.
d Imprecision: Downgraded once as sample size was small (less than 200).

Additional trial not included in the GRADE table: A small RCT (28) studied the effect of behaviour therapy – pleasant events (BT-PE) and problem solving (BT-PS) in older people with probable dementia and major or minor depression. Authors reported that both patients (F(3,66) = 4.73, P < 0.01) benefited significantly from behaviour treatment as clinically significant improvement was observed in 50% (BT-PE) and 68% (BT-PS) versus 20% in the two control groups.

Authors reported that both patients (F(3,71) 4.52, P < 0.001) and their caregivers
GRADE table 2: Psychological interventions compared with usual care for depressive symptoms in older people (not meeting the diagnostic criteria for depressive episode)

**Author:** WHO systematic review team  
**Date:** 11 November 2015  
**Question:** What is the effectiveness of psychological treatment compared with usual care or waiting list control group for depressive symptoms in older people?  
**Settings:** Primary care, community or hospital  

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Study design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>Number of patients</th>
<th>Effect</th>
<th>Quality</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression symptoms (follow-up 3–6 months; assessed with the Geriatric Depression Scale (GDS), Center for Epidemiological Studies Depression Scale [CES-D] or self-reported depression symptom)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 randomized trials a</td>
<td>serious b</td>
<td>not serious</td>
<td>serious c</td>
<td>not serious</td>
<td>none</td>
<td>400</td>
<td>426</td>
<td>–</td>
<td>SMD 0.3 lower (0.46 lower to 0.14 lower)</td>
<td>LOW</td>
</tr>
<tr>
<td>Incidence of depressive disorder (follow-up 2 months; assessed with diagnostic instruments)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 randomized trials a</td>
<td>not serious</td>
<td>not serious</td>
<td>serious c</td>
<td>serious *</td>
<td>none</td>
<td>11/94</td>
<td>23/99</td>
<td>RR 0.50 (0.28 to 0.97)</td>
<td>116 fewer per 1000 (from 172 fewer to 7 fewer)</td>
<td>LOW</td>
</tr>
</tbody>
</table>

(continued next page)
## Evidence profile: depressive symptoms

### ICOPE guidelines

#### Quality assessment

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Study design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>Psychological treatment</th>
<th>Usual care</th>
<th>Effect</th>
<th>Quality</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Incidence of depressive disorder</strong> (follow-up 6 months; assessed with diagnostic instruments)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>randomized trials ✴</td>
<td>serious b</td>
<td>not serious</td>
<td>serious c</td>
<td>serious *</td>
<td>none</td>
<td>20/110</td>
<td>28/96</td>
<td>RR 0.74 (0.45 to 1.22)</td>
<td>66 fewer per 1000 (from 146 fewer to 14 more)</td>
<td>●●● ●●● VERY LOW</td>
</tr>
<tr>
<td><strong>Incidence of depressive disorder</strong> (follow-up 12 months; assessed with diagnostic instruments)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>randomized trials ✴</td>
<td>serious b</td>
<td>serious d</td>
<td>serious c</td>
<td>serious *</td>
<td>none</td>
<td>37/145</td>
<td>38/141</td>
<td>RR 1.00 (0.66 to 1.51)</td>
<td>29 fewer per 1000 (from 111 fewer to 55 more)</td>
<td>●●● ●●● VERY LOW</td>
</tr>
<tr>
<td><strong>Incidence of depressive disorder</strong> (follow-up 12 months; assessed with diagnostic instruments)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>randomized trials ✴</td>
<td>serious b</td>
<td>not serious</td>
<td>serious c</td>
<td>not serious</td>
<td>none</td>
<td>57/255</td>
<td>66/235</td>
<td>RR 0.88 (0.64 to 1.21)</td>
<td>48 fewer per 1000 (from 105 fewer to 9 more)</td>
<td>●●● ●●● LOW</td>
</tr>
</tbody>
</table>

CI: confidence interval; RR: relative risk; SMD: standardized mean difference

- Trials presented constitute subgroup analysis for older adults only.
- Risk of bias: Downgraded once as three trials had unclear randomization generation and allocation concealment procedures. Only one trial had adequate masking of outcome assessment, two trials did not carry out intention to treat, and outcome reporting was uncertain for four trials.
- Indirectness: Downgraded once as interventions were conducted in high-income countries and therefore may not generalize to resource-poor settings.
- Inconsistency: Rated as “serious”: high heterogeneity ($I^2 = 85.8\%$). No subgroup analysis was performed and we were not able to explain the heterogeneity.
- Imprecision: Downgraded once as sample size was small.
### Part 2: From evidence to recommendations

#### Summary-of-evidence table

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Outcome</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Behavioural activation</strong></td>
<td>Reduction of depressive symptoms in older adults with depression</td>
<td>SMD 0.81 lower (1.22 lower to 0.40 lower)</td>
</tr>
<tr>
<td><strong>GRADE table 1</strong></td>
<td></td>
<td>VERY LOW</td>
</tr>
<tr>
<td><strong>Psychological interventions</strong></td>
<td>Reduction of depressive symptoms in older adults with sub-threshold depression</td>
<td>SMD 0.3 higher (0.46 lower to 0.14 lower)</td>
</tr>
<tr>
<td><strong>GRADE table 2</strong></td>
<td></td>
<td>LOW</td>
</tr>
<tr>
<td></td>
<td>Incidence of depression (2 months follow-up)</td>
<td>RR 0.50 (0.26 to 0.97)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LOW</td>
</tr>
<tr>
<td></td>
<td>Incidence of depression (6 months follow-up)</td>
<td>RR 0.74 (0.45 to 1.22)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>VERY LOW</td>
</tr>
<tr>
<td></td>
<td>Incidence of depression (12 months follow-up)</td>
<td>RR 1.00 (0.66 to 1.51)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>VERY LOW</td>
</tr>
<tr>
<td></td>
<td>Incidence of depression (6–12 months follow-up)</td>
<td>RR 0.88 (0.64 to 1.21)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LOW</td>
</tr>
</tbody>
</table>

RR: relative risk; SMD: standardized mean difference
## Evidence-to-recommendations table

<table>
<thead>
<tr>
<th>Problem</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is the problem a priority?</td>
<td>Sub-threshold depression, conventionally defined as distressing or disabling symptoms, not meeting diagnostic criteria for depressive episode (according to the ICD) or major depressive disorder (according to the DSM), is a common condition in older people. Prevalence of sub-threshold depression is two to three times higher than that of major depression, particularly in primary healthcare and long-term care settings; and, every year, approximately 8–10% of older adults with this condition develop depressive episodes or disorders (29). Minor depression is associated with psychological suffering, functional impairment and a significant adverse impact on quality of life (30). Therefore, it is important to review therapeutic options for this condition both for the amelioration of sub-threshold depression symptoms, and with the aim of preventing the onset of new episodes of clinically significant depression. Since pharmacological interventions may be ineffective, psychological therapies should be evaluated as possible treatments for sub-threshold depression in older people.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Benefits and harms</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do the desirable effects outweigh the undesirable effects?</td>
<td>Consistent with mhGAP recommendations, psychological interventions (cognitive behavioural therapy [CBT], problem-solving and behavioural activation) have been shown to be effective in older people with clinically significant depression. There is consistent evidence of modest clinical benefit of psychological interventions in managing depressive symptoms in older people. There is limited low-quality evidence suggesting that the use of CBT, problem-solving therapy, interpersonal counselling and life review therapy techniques may reduce depression symptoms in older adults. Effect sizes were significant in trials using different psychological interventions. Evidence on their potential to prevent future depressive episodes is more equivocal. There is limited very low-quality evidence suggesting that behavioural activation interventions are effective in older adults with depression. This technique may also be effective in relieving depressive</td>
</tr>
</tbody>
</table>

(continued next page)
symptomatology among individuals with dementia and depression, where antidepressants have been shown to be ineffective. The evidence of the potential to prevent the onset of depressive episodes among at-risk groups is less clear. Adverse effects and dropouts have not been systematically recorded, but the potential for harm is likely to be modest. Many sub-threshold episodes remit spontaneously with “watchful waiting”. Hence, the balance of benefits versus harms will be optimized by focusing on those most likely to progress, using a targeted and stepped-care approach.

<table>
<thead>
<tr>
<th>Values and preferences/acceptability</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is there important uncertainty or variability about how much people value the options?</td>
<td>The interventions trialled are highly heterogeneous and the demands on the participants varied greatly. The willingness to participate in structured programmes may depend upon the severity and impact of depression symptoms and on the dose and duration of the therapeutic intervention. Acceptability to key stakeholders is likely to be variable, given the relatively resource-intensive commitment for a potentially large number of sub-threshold cases, and the limited evidence on cost-effectiveness of the approach. Acceptability would be boosted by clear demonstration of effectiveness and cost-effectiveness of low-intensity, task-shifted interventions.</td>
</tr>
</tbody>
</table>

(continued next page)
**Feasibility/resource use**

<table>
<thead>
<tr>
<th>Question</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>How large are the resource requirements?</td>
<td>Several of the interventions, as trialled, are quite resource-intensive, with up to 12 sessions. CBT is likely to be more resource intensive than problem-solving and behavioural activation, which lend themselves more to task shifting. Resource utilization can be limited through administration to groups, but this may be less feasible for frail or dependent older people.</td>
</tr>
<tr>
<td>Is the option feasible to implement?</td>
<td>The administration of behavioural activation is a relatively unsophisticated procedure that can be quickly learnt compared with most other evidence-based psychological treatments. However, the intervention has been studied mostly as a multiple-session intervention performed by specialists (or student specialists), which may not generalize to non-specialized health care. Nonetheless, the intervention can be modified into a brief intervention as adjunct treatment or as part of a first step in a stepped-care approach in non-specialized care.</td>
</tr>
</tbody>
</table>

**Equity**

<table>
<thead>
<tr>
<th>Question</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Would the option improve equity in health?</td>
<td>The guideline development group strongly believes that the recommendation will increase equity in health.</td>
</tr>
</tbody>
</table>

**ICOPE guidelines – World Health Organization**
### Guideline development group recommendations and remarks

#### Recommendation

**Older adults who are experiencing depressive symptoms can be offered brief, structured psychological interventions, in accordance with WHO mhGAP intervention guidelines, delivered by health care professionals with a good understanding of mental health care for older adults.**

*Quality of the evidence: very low*

*Strength of the recommendation: conditional*

#### Remarks

- The recommendation is applicable to older people without major depressive disorder.
- The duration of the psychological intervention administered in the included trials ranged from 3 to 12 months. Trials of behavioural activation administered the intervention for a minimum of between 6 weeks and 10 weeks.
- All of the primary studies available were carried out in high-income countries and few available trials focused specifically on older people with sub-threshold depression.
- The mhGAP intervention guideline recommendations should be implemented for those older people who meet the criteria for the clinical diagnosis of major depressive disorder set out by the *International Classification of Diseases*, 10th revision (*ICD-10*).
- In line with the mhGAP guidelines:
  - Antidepressants should not be considered for the initial treatment of older adults with mild depressive episodes or depressive symptoms.
  - Fluoxetine could be prescribed for older adults with moderate to severe depressive episodes/disorder but without dementia.
  - Physical activity should be encouraged as part of the treatment for older adults with inactive lifestyles and depressive symptoms.
- In cases of moderate-to-severe depression, psychological intervention should be considered as an adjunct to antidepressants.
References


16. Prina AM, Ferri CP, Guerra M, Brayne C, Prince M. Co-occurrence of anxiety and depression amongst older adults (continued next page)


Annex 1: PRISMA flow diagram for systematic review of the reviews – sub-threshold depression

Records identified through database searching (n = 627) → Records after duplicates removed (n = 586) → Records screened (title and abstract) (n = 586) → Records excluded (n = 579)

Records after duplicates removed (n = 586) → Full-text articles assessed for eligibility (n = 7) → Studies included in narrative synthesis (n = 4) → Studies (systematic reviews) included in GRADE table (n = 3)

4 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). For more information: http://www.prisma-statement.org