Depression module – evidence profile DEP3: Brief, structured psychological treatment for adults with depressive episode/disorder

WHO mhGAP guideline update: Mental Health Gap Action Programme (mhGAP) guideline for mental, neurological and substance use disorders

2023

World Health Organization

Contents

Mental Health Gap Action Programme (mhGAP) guideline for mental, neurological and substance use disorders, available at: https://www.who.int/publications/i/item/9789240084278

1. Background

Depression is a highly prevalent and recurrent mental disorder (Kessler, R. C., & Bromet, 2013). It has a great negative impact on the quality of life and functioning of the individuals, and it is associated with high societal and economic costs (Bloom et al., 2011; Ferrari et al., 2010; World Health Organization [WHO], 2008). By 2030, depression is predicted to be one of the leading causes of disability and premature mortality worldwide (Mathers & Loncar, 2006). Reducing the burden of depression by developing evidence-based interventions is now a major global priority (World Bank Group & WHO, 2016). Different types of psychological interventions are effective in the treatment of depression over the short and the long term (Cuijpers et al., 2021), and psychotherapy is recommended as one of the first-line treatments of depression (Nathan & Gorman, 2015; Fletcher, Leaman, McSloy, & Leng, 2020).

An increasing number of trials assessing the effectiveness of psychotherapies are published every year, and recent meta-analyses using more precise techniques (e.g., network analyses) are providing updated evidence that should be considered in clinical guidelines. In the current report, we aimed to present the results of a systematic review of meta-analyses covering the efficacy and safety of psychotherapies for depression. Bearing in mind the feasibility and available resources, it is important to investigate the effectiveness of scalable interventions such as those that can be delivered by non-specialists or in self-help/digital formats. Therefore, focusing on brief, structured, and scalable psychotherapies, we reviewed whether psychological treatments are more effective and as safe as treatment as usual (TAU) in adults with depressive disorders or elevated symptoms of depression. We reviewed the effects in a wide range of outcomes, including symptom reduction, suicide-related outcomes, adverse effects, and improvements in quality of life and functioning.

2. Methodology

Evidence was summarized from recent meta-analyses covering the effectiveness and safety of brief, structured and scalable psychotherapies compared to treatment as usual for adults with depressive episode or disorders.

2.1.   PICO question

DEP3. Is brief, structured psychological treatment better (more effective than/as safe as) than treatment as usual in people with depressive episode/disorder?

Population (P): Adults with depressive episode/disorder and/or elevated depressive symptoms
Intervention (I): Brief psychological treatment in non-specialist health care settings (e.g. Interpersonal therapy, cognitive behavioural therapy and problem-solving treatment, ACT, meta-cognitive therapy, supportive counselling)
Comparator (C): Treatment as usual
Outcomes (O):

> **List critical outcomes:**
> - **Critical outcome 1:** Reduction of symptoms
> - **Critical outcome 2** Improvement in quality of life and functioning
> - **Critical outcome 3:** Relapse
>
> **List important outcomes:**
> None specified

2.2.   Search strategy

Existing systematic reviews were identified by conducting searches in the following bibliographic databases:
- PubMed
- PsycINFO
- Embase

- Cochrane reviews
- Global Index Medicus

The search strings were designed in collaboration with a Medical Information Specialist at Vrije Universiteit Amsterdam. We designed the search strings by combining blocks with free and index terms indicative for 1) Depression (*Type of Participants*), 2) Psychotherapies (*Types of interventions*), and 3) terms related to systematic reviews and meta-analyses (*Type of studies*). The search strings for PubMed can be accessed in Appendix I. In line with the WHO guideline methodology, indicating that evidence obtained for the development of guidelines should be as recent as possible (World Health Organization, 2014), the period of the searches covered from 1 January 2019 until 31 January 2022. No restrictions were applied for language.

2.3. Data collection and analysis

As the first stage in selecting relevant studies, records retrieved from the bibliographic databases were assessed for eligibility by examining their titles and abstracts, based on the inclusion and exclusion criteria developed a priori. Studies were included if they were (i) Systematic reviews of randomized controlled trials (RCTs). (ii) Had adult participants (>18 years) with a primary diagnosis of depression as established by a diagnostic interview or elevated symptoms of depression according to cut off scores on self-report scales. (iii) Evaluated the effectiveness or safety of brief or scalable psychological treatments compared to treatment as usual (iv) Reported outcomes regarding mental health symptoms, adverse effects, quality of life and functioning and relapse. We excluded studies that had participants with secondary depression (due to medical conditions/illness, trauma, etc), bipolar disorder, psychotic depression, and treatment resistant depression. The full text of articles found to be potentially relevant based on their titles and abstracts were retrieved and examined, considering the same inclusion criteria in the second stage of study selection. Data from eligible studies were extracted into pre-defined templates that include the general characteristics of the study, population, intervention, comparator, and outcomes. When there was an overlap between studies (i.e. they evaluated the same antidepressant medications, in similar target populations, and reported the same outcomes), we selected the meta-analysis based on the following criteria and in the following order: (i) Recency (more recent publication covering a more recent search period) (ii) number of included RCTs, (iii) broadness of the review (covering multiple psychotherapies compared to treatment as usual, with a wide range of outcomes) (iv) AMSTAR ratings.

Two reviewers (AA and MC/CM) independently assessed the eligibility of the studies identified and extracted data from study reports. Discrepancies between the reviewers were resolved through discussions. The search strategy and results reporting the databases searched, the strategy used to search each database, the total number of citations retrieved from each database, and the reasons for excluding some publications after reviewing the full text have been carefully documented. The flow of articles throughout the search and up to the final cohort of included studies is shown in Figure 1, which includes the number of excluded articles and the reasons for any exclusions at the full-text screening stage.

2.4. Selection and coding of identified records

Rayyan and Endnote were used for the management of references. Rayyan was used during the first two stages of the project, involving the selection of studies based on titles, abstracts, and full texts. Endnote was used to store the references and pdfs of the included studies for the remaining stages of the project. Data extraction was conducted in excel files with a predefined format which was designed by the involved reviewers. A wide range of study level data regarding date of searches, target population characteristics, type of intervention and control, average length of interventions, total number of participants, mean age, proportion of women and risk of bias were extracted. All data was collected by two independent reviewers and discrepancies were resolved through discussions.

2.5. Quality assessment

The quality of the included systematic reviewers was assessed with the **AMSTAR quality appraisal tool 2**. Two independent researchers (AA and MC/CM) applied the AMSTAR-2 checklist to the included studies, and any disagreements were discussed with a third researcher.

The certainty of the evidence was assessed using **GRADE** (Grading of Recommendations, Assessment, Development and Evaluations). When available, we extracted the GRADE assessments from the meta-analysis. When the GRADE assessment was not available, we assessed it ourselves examining the following criteria:

- **Risk of bias (RoB):** We extracted the RoB ratings from the individual studies included in the meta-analyses (when available). We calculated the percentage of trials rated at low, high, and unclear risk of bias. Based on this information, and to take consistent decisions across the available evidence, we rated the RoB GRADE item using a decision tree. This decision tree can be accessed in Appendix II.
- **Inconsistency:** We judged inconsistency by examining heterogeneity statistics: I^2, which indicates the percentage of heterogeneity between effect sizes, and its 95% confidence interval (95% CI). When the 95% CI of the I^2 is not reported, we computed it and used it in our judgements. We judged inconsistency as serious when I^2 was over 75% and its 95% CI substantially overlaps with the category of considerable heterogeneity (above 75%). Substantial overlap was estimated with the median of the 95% CI. If the 95% CI was not available or could not be calculated, we rated it as serious if heterogeneity was larger than 50% (category of substantial heterogeneity). If I^2 was not reported and could not be calculated, we rated it as serious.
- **Indirectness**: Direct evidence was derived from research that directly compares the interventions which we are interested in, delivered to the participants in which we are interested, and that measures the outcomes important to patients. We rated for each comparison how indirect the reviewed evidence was in terms of population, intervention, and outcomes.
- **Imprecision**: We rated this item based on a standard power calculation (α 0.05 and β 0.20) for detecting an effect size of 0.2, which requires a sample size of 400 participants in total. We judged as serious for all analyses that included less than 400 participants. Analyses including less than 100 participants was rated as very serious. A rating of serious was given when the number of participants included in the analyses was not available.
- **Other considerations**: For this item we explored publication bias. We rated it as serious if there was evidence for publication bias in the meta-analyses, based on statistical tests. However, we did not downgrade the evidence if a meta-analysis did not investigate it.

2.6. Analysis of subgroups or subsets

Since we reviewed existing systematic reviews, we considered the subgroups or subsets that were available in the included meta-analyses. The subgroups of interest were:

- Types of interventions: e.g., different subtypes of psychotherapies, different types of delivery formats (e.g., task-shifted, e-health)

3. Results

3.1. Systematic reviews and/or studies identified by the search process

Figure 1: PRISMA 2020 flow diagram for systematic review of reviews which includes searches of databases and registers only
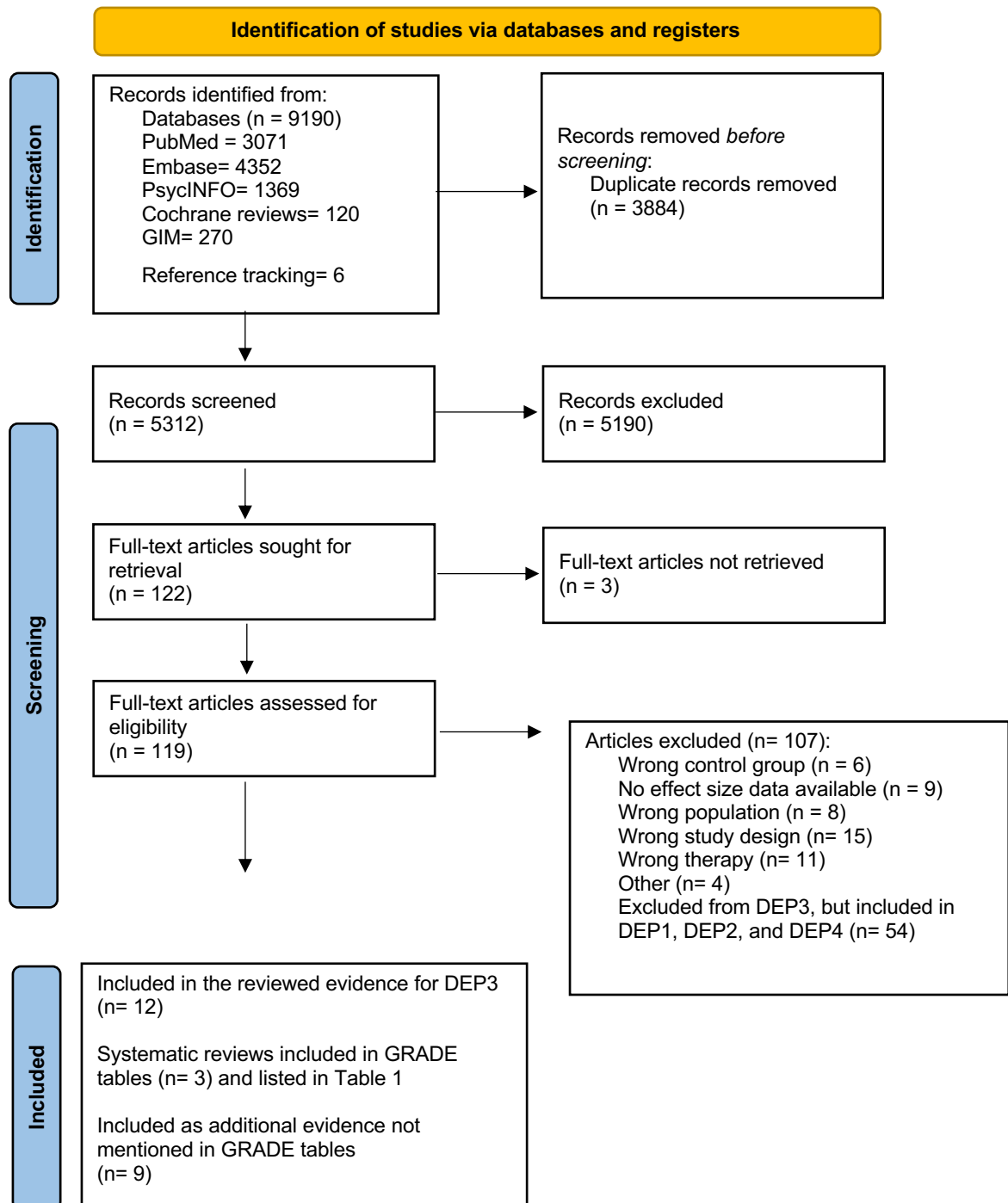
GIM: Global Index Medicus

3.2. Included In GRADE tables/footnotes

CUIJPERS, P., QUERO, S., NOMA, H., CIHAROVA, M., MIGUEL, C., KARYOTAKI, E., CIPRIANI, A., CRISTEA, I. A. & FURUKAWA, T. A. 2021. Psychotherapies for depression: a network meta-analysis covering efficacy, acceptability and long-term outcomes of all main treatment types. *World Psychiatry,* 20**,** 283-293.

KARYOTAKI, E., EFTHIMIOU, O., MIGUEL, C., BERMPOHL, F. M. G., FURUKAWA, T. A., CUIJPERS, P., RIPER, H., PATEL, V., MIRA, A., GEMMIL, A. W., YEUNG, A. S., LANGE, A., WILLIAMS, A. D., MACKINNON, A., GERAEDTS, A., VAN STRATEN, A., MEYER, B., BJÖRKELUND, C., KNAEVELSRUD, C., BEEVERS, C. G., BOTELLA, C., STRUNK, D. R., MOHR, D. C., EBERT, D. D., KESSLER, D., RICHARDS, D., LITTLEWOOD, E., FORSELL, E., FENG, F., WANG, F., ANDERSSON, G., HADJISTAVROPOULOS, H., CHRISTENSEN, H., EZAWA, I. D., CHOI, I., ROSSO, I. M., KLEIN, J. P., SHUMAKE, J., GARCIA-CAMPAYO, J., MILGROM, J., SMITH, J., MONTERO-MARIN, J., NEWBY, J. M., BRETÓN-LÓPEZ, J., SCHNEIDER, J., VERNMARK, K., BÜCKER, L., SHEEBER, L. B., WARMERDAM, L., FARRER, L., HEINRICH, M., HUIBERS, M. J. H., KIVI, M., KRAEPELIEN, M., FORAND, N. R., PUGH, N., LINDEFORS, N., LINTVEDT, O., ZAGORSCAK, P., CARLBRING, P., PHILLIPS, R., JOHANSSON, R., KESSLER, R. C., BRABYN, S., PERINI, S., RAUCH, S. L., GILBODY, S., MORITZ, S., BERGER, T., POP, V., KALDO, V., SPEK, V. & FORSELL, Y. 2021. Internet-Based Cognitive Behavioral Therapy for Depression: A Systematic Review and Individual Patient Data Network Meta-analysis. *JAMA Psychiatry,* 78**,** 361-371.

KARYOTAKI, E., ARAYA, R., KESSLER, R. C., WAQAS, A., BHANA, A., RAHMAN, A., MATSUZAKA, C. T., MIGUEL, C., LUND, C., GARMAN, E. C., NAKIMULI-MPUNGU, E., PETERSEN, I., NASLUND, J. A., SCHNEIDER, M., SIKANDER, S., JORDANS, M. J. D., ABAS, M., SLADE, P., WALTERS, S., BRUGHA, T. S., FURUKAWA, T. A., AMANVERMEZ, Y., MELLO, M. F., WAINBERG, M. L., CUIJPERS, P. & PATEL, V. 2022. Association of Task-Shared Psychological Interventions With Depression Outcomes in Low- and Middle-Income Countries: A Systematic Review and Individual Patient Data Meta-analysis. *JAMA Psychiatry*.

3.3. Excluded from GRADE tables/footnotes

CIHAROVA, M., FURUKAWA, T. A., EFTHIMIOU, O., KARYOTAKI, E., MIGUEL, C., NOMA, H., CIPRIANI, A., RIPER, H. & CUIJPERS, P. 2021. Cognitive restructuring, behavioral activation and cognitive-behavioral therapy in the treatment of adult depression: A network meta-analysis. *J Consult Clin Psychol,* 89**,** 563-574.

CORPAS, J., MORIANA, J. A., VENCESLÁ, J. F. & GÁLVEZ-LARA, M. 2021. Brief psychological treatments for emotional disorders in Primary and Specialized Care: A randomized controlled trial. *Int J Clin Health Psychol,* 21**,** 100203.

CUIJPERS, P., KARYOTAKI, E., CIHAROVA, M., MIGUEL, C., NOMA, H. & FURUKAWA, T. A. 2021. The effects of psychotherapies for depression on response, remission, reliable change, and deterioration: A meta-analysis. *Acta Psychiatr Scand,* 144**,** 288-299.

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HOWARTH, A., SMITH, J. G., PERKINS-PORRAS, L. & USSHER, M. 2019. Effects of brief mindfulness-based interventions on health-related outcomes: A systematic review. *Mindfulness,* 10**,** 1957-1968.

LO, H. H.-M., ZHANG, J. & CHOI, C.-W. 2020. Short-term psychological interventions on economically disadvantaged families: A systematic review and meta-analysis. Research on Social Work Practice, 30, 330-343.

SIMMONDS-BUCKLEY, M., BENNION, M. R., KELLETT, S., MILLINGS, A., HARDY, G. E. & MOORE, R. K. 2020. Acceptability and Effectiveness of NHS-Recommended e-Therapies for Depression, Anxiety, and Stress: Meta-Analysis. *J Med Internet Res,* 22**,** e17049.

SIMMONDS-BUCKLEY, M., BENNION, M. R., KELLETT, S., MILLINGS, A., HARDY, G. E. & MOORE, R. K. 2020. Acceptability and Effectiveness of NHS-Recommended e-Therapies for Depression, Anxiety, and Stress: Meta-Analysis. *J Med Internet Res,* 22**,** e17049.

ZHANG, A., FRANKLIN, C., JING, S., BORNHEIMER, L. A., HAI, A. H., HIMLE, J. A., KONG, D. & JI, Q. 2019. The effectiveness of four empirically supported psychotherapies for primary care depression and anxiety: A systematic review and meta-analysis. J Affect Disord, 245, 1168-1186.

Table 1: PICO Table

Serial Number	Intervention/ Comparison	Outcomes	Systematic reviews (Name, Year)	Justification/Explanation for systematic review
1	**Psychotherapy (CBT) compared to treatment as usual in adults with depressive disorders**	Reduction in mental health symptoms	Cuijpers et al., 2021	Most recent high-quality meta-analysis available on the effectiveness of CBT compared to TAU on depressive symptoms in adults with elevated symptoms and/or diagnosis of depression
		Adverse effects	Cuijpers et al., 2021	Most recent high-quality meta-analysis available on the adverse effects of CBT compared to TAU on depressive symptoms in adults with elevated symptoms and/or diagnosis of depression
		Improvement in quality of life and functioning	-	No available recent meta-analytic evidence on this outcome (N/A)
		Relapse	-	(N/A)
2	**Psychotherapy (BAT) compared to treatment as usual in adults with depressive disorders**	Reduction in mental health symptoms	Cuijpers et al., 2021	Most recent high-quality meta-analysis available on the effectiveness of BAT compared to TAU on depressive symptoms in adults with elevated symptoms and/or diagnosis of depression
		Adverse effects	Cuijpers et al., 2021	Most recent high-quality meta-analysis available on the adverse effects of BAT compared to TAU on depressive symptoms in adults with elevated symptoms and/or diagnosis of depression
		Improvement in quality of life and functioning	-	(N/A)
		Relapse	-	(N/A)
3	**Psychotherapy (PST) compared to treatment as usual in**	Reduction in mental health symptoms	Cuijpers et al., 2021	Most recent high-quality meta-analysis available on the effectiveness of PST compared to TAU on depressive symptoms in adults with elevated symptoms and/or diagnosis of depression

Serial Number	Intervention/ Comparison	Outcomes	Systematic reviews (Name, Year)	Justification/Explanation for systematic review
	adults with depressive disorders	Adverse effects	Cuijpers et al., 2021	Most recent high-quality meta-analysis available on the adverse effects of PST compared to TAU on depressive symptoms in adults with elevated symptoms and/or diagnosis of depression
		Improvement in quality of life and functioning	-	(N/A)
		Relapse	-	(N/A)
4	**Psychotherapy (3WV) compared to treatment as usual in adults with depressive disorders**	Reduction in mental health symptoms	Cuijpers et al., 2021	Most recent high-quality meta-analysis available on the effectiveness of 3WV compared to TAU on depressive symptoms in adults with elevated symptoms and/or diagnosis of depression
		Adverse effects	Cuijpers et al., 2021	Most recent high-quality meta-analysis available on the adverse effects of 3WV compared to TAU on depressive symptoms in adults with elevated symptoms and/or diagnosis of depression
		Improvement in quality of life and functioning	-	(N/A)
		Relapse	-	(N/A)
5	**Psychotherapy (IPT) compared to treatment as usual in adults with depressive disorders**	Reduction in mental health symptoms	Cuijpers et al., 2021	Most recent high-quality meta-analysis available on the effectiveness of IPT compared to TAU on depressive symptoms in adults with elevated symptoms and/or diagnosis of depression
		Adverse effects	Cuijpers et al., 2021	Most recent high-quality meta-analysis available on the adverse effects of IPT compared to TAU on depressive symptoms in adults with elevated symptoms and/or diagnosis of depression
		Improvement in quality of life and functioning	-	(N/A)
		Relapse	-	(N/A)

Serial Number	Intervention/ Comparison	Outcomes	Systematic reviews (Name, Year)	Justification/Explanation for systematic review
6	**Psychotherapy (DYN) compared to treatment as usual in adults with depressive disorders**	Reduction in mental health symptoms	Cuijpers et al., 2021	Most recent high-quality meta-analysis available on the effectiveness of DYN compared to TAU on depressive symptoms in adults with elevated symptoms and/or diagnosis of depression
		Adverse effects	Cuijpers et al., 2021	Most recent high-quality meta-analysis available on the adverse effects of DYN compared to TAU on depressive symptoms in adults with elevated symptoms and/or diagnosis of depression
		Improvement in quality of life and functioning	-	(N/A)
		Relapse	-	(N/A)
7	**Psychotherapy (SUP) compared to treatment as usual in adults with depressive disorders**	Reduction in mental health symptoms	Cuijpers et al., 2021	Most recent high-quality meta-analysis available on the effectiveness of SUP compared to TAU on depressive symptoms in adults with elevated symptoms and/or diagnosis of depression
		Adverse effects	Cuijpers et al., 2021	Most recent high-quality meta-analysis available on the adverse effects of SUP compared to TAU on depressive symptoms in adults with elevated symptoms and/or diagnosis of depression
		Improvement in quality of life and functioning	-	(N/A)
		Relapse	-	(N/A)
8	**Psychotherapy (LRT) compared to treatment as usual in adults with depressive disorders**	Reduction in mental health symptoms	Cuijpers et al., 2021	Most recent high-quality meta-analysis available on the effectiveness of LRT compared to TAU on depressive symptoms in adults with elevated symptoms and/or diagnosis of depression
		Adverse effects	Cuijpers et al., 2021	Most recent high-quality meta-analysis available on the adverse effects of LRT compared to TAU on

Serial Number	Intervention/ Comparison	Outcomes	Systematic reviews (Name, Year)	Justification/Explanation for systematic review
				depressive symptoms in adults with elevated symptoms and/or diagnosis of depression
		Improvement in quality of life and functioning	-	(N/A)
		Relapse	-	(N/A)
9	**Psychotherapy (Guided iCBT) compared to treatment as usual in adults with depressive disorders**	Reduction in mental health symptoms	Karyotaki et al., 2021	Most recent high-quality meta-analysis available on the effectiveness of guided iCBT compared to TAU on depressive symptoms in adults with elevated symptoms and/or diagnosis of depression
		Adverse effects	-	(N/A)
		Improvement in quality of life and functioning	-	(N/A)
		Relapse	-	(N/A)
10	**Psychotherapy (Unguided iCBT) compared to treatment as usual in adults with depressive disorders**	Reduction in mental health symptoms	Karyotaki et al., 2021	Most recent high-quality meta-analysis available on the effectiveness of unguided iCBT compared to TAU on depressive symptoms in adults with elevated symptoms and/or diagnosis of depression
		Adverse effects	-	(N/A)
		Improvement in quality of life and functioning	-	(N/A)
		Relapse	-	(N/A)
10	**Psychotherapy (Task shared psychotherapies) compared to treatment as usual in adults with depressive disorders**	Reduction in mental health symptoms	Karyotaki et al., 2022	Most recent high-quality meta-analysis available on the effectiveness of task shared psychotherapies compared to TAU on depressive symptoms in adults with elevated symptoms and/or diagnosis of depression
		Adverse effects	-	(N/A)
		Improvement in quality of life and functioning	-	(N/A)

Serial Number	Intervention/ Comparison	Outcomes	Systematic reviews (Name, Year)	Justification/Explanation for systematic review
		Relapse	-	(N/A)

CBT: Cognitive behavioural therapy; iCBT: Internet-based cognitive behavioural therapy; TAU: Treatment as usual; BAT: Behavioural activation therapy; PST: Problem-solving therapy; 3WV: Third wave therapies; IPT: Interpersonal psychotherapy; DYN: Brief psychodynamic therapy; SUP: Non-directive support counseling; LRT: Life review therapy; iCBT: internet based cognitive behavioural therapy

3.4. Narrative description of studies that contributed to GRADE analysis[1]

Cuijpers et al., 2021: The effects of psychotherapies for depression have been examined in several hundreds of randomized trials, but no recent network meta-analysis (NMA) has integrated the results of these studies. We conducted an NMA of trials comparing cognitive behavioural, interpersonal, psychodynamic, problem-solving, behavioural activation, life-review and "third wave" therapies and non-directive supportive counseling with each other and with care-as-usual, waiting list and pill placebo control conditions. Response (50% reduction in symptoms) was the primary outcome, but we also assessed remission, standardized mean difference, and acceptability (all-cause dropout rate). Random-effects pairwise and network meta-analyses were conducted on 331 randomized trials with 34,285 patients. All therapies were more efficacious than care-as-usual and waiting list control conditions, and all therapies - except non-directive supportive counseling and psychodynamic therapy - were more efficacious than pill placebo. Standardized mean differences compared with care-as-usual ranged from -0.81 for life-review therapy to -0.32 for non-directive supportive counseling. Individual psychotherapies did not differ significantly from each other, with the only exception of non-directive supportive counseling, which was less efficacious than all other therapies. The results were similar when only studies with low risk of bias were included. Most therapies still had significant effects at 12-month follow-up compared to care-as-usual, and problem-solving therapy was found to have a somewhat higher long-term efficacy than some other therapies. No consistent differences in acceptability were found. Our conclusion is that the most important types of psychotherapy are efficacious and acceptable in the acute treatment of adult depression, with few significant differences between them. Patient preference and availability of each treatment type may play a larger role in the choice between types of psychotherapy, although it is possible that a more detailed characterization of patients with a diagnosis of depression may lead to a more precise matching between individual patients and individual psychotherapies.

Karyotaki et al., 2021: IMPORTANCE: Personalized treatment choices would increase the effectiveness of internet-based cognitive behavioral therapy (iCBT) for depression to the extent that patients differ in interventions that better suit them. OBJECTIVE: To provide personalized estimates of short-term and long-term relative efficacy of guided and unguided iCBT for depression using patient-level information. DATA SOURCES: We searched PubMed, Embase, PsycInfo, and Cochrane Library to identify randomized clinical trials (RCTs) published up to January 1, 2019. STUDY SELECTION: Eligible RCTs were those comparing guided or unguided iCBT against each other or against any control intervention in individuals with depression. Available individual patient data (IPD) was collected from all eligible studies. Depression symptom severity was assessed after treatment, 6 months, and 12 months after randomization. DATA EXTRACTION AND SYNTHESIS: We conducted a systematic review and IPD network meta-analysis and estimated relative treatment effect sizes across different patient characteristics through IPD network meta-regression. MAIN OUTCOMES AND MEASURES: Patient Health Questionnaire-9 (PHQ-9) scores. RESULTS: Of 42 eligible RCTs, 39 studies comprising 9751 participants with depression contributed IPD to the IPD network meta-analysis, of which 8107 IPD were synthesized. Overall, both guided and unguided iCBT were associated with more effectiveness as measured by PHQ-9 scores than control treatments over the short term and the long term. Guided iCBT was associated with more effectiveness than unguided iCBT (mean difference [MD] in posttreatment PHQ-9 scores, -0.8; 95% CI, -1.4 to -0.2), but we found no evidence of a difference at 6 or 12 months following randomization. Baseline depression was found to be the most important modifier of the relative association for efficacy of guided vs unguided iCBT. Differences between unguided and

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[1]Please note that this section includes the abstracts as taken directly from the publications.

guided iCBT in people with baseline symptoms of subthreshold depression (PHQ-9 scores 5-9) were small, while guided iCBT was associated with overall better outcomes in patients with baseline PHQ-9 greater than 9. CONCLUSIONS AND RELEVANCE: In this network meta-analysis with IPD, guided iCBT was associated with more effectiveness than unguided iCBT for individuals with depression, benefits were more substantial in individuals with moderate to severe depression. Unguided iCBT was associated with similar effectiveness among individuals with symptoms of mild/subthreshold depression. Personalized treatment selection is entirely possible and necessary to ensure the best allocation of treatment resources for depression.

Karyotaki et al., 2022: IMPORTANCE: Task sharing, the training of nonspecialist workers with no formal experience in counseling, is a promising strategy for addressing the large gap in treatment for depression in low- and middle-income countries (LMICs). OBJECTIVE: To examine the outcomes and moderators of task-shared psychological interventions associated with depression severity, response, and remission. DATA SOURCES : Systematic literature searches in PubMed, Embase, PsycINFO, and Cochrane Library up to January 1, 2021. STUDY SELECTION: Randomized clinical trials (RCTs) of task-shared psychological interventions compared with control conditions for adults with depressive symptoms in LMICs were included. DATA EXTRACTION AND SYNTHESIS: Two researchers independently reviewed the titles, abstracts, and full text of articles from an existing generic meta-analytic database that includes all RCTs on psychotherapy for depression. A systematic review and individual patient data (IPD) meta-analysis was used to estimate the outcomes of task-shared psychological interventions across patient characteristics using mixed-effects models. Procedures for abstracting data and assessing data quality and validity followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses reporting guideline. MAIN OUTCOMES AND MEASURES: Primary outcome was reduction in depression symptom severity measured by the 9-item Patient Health Questionnaire (PHQ-9). Response and remission rates were also estimated. RESULTS: Of 13 eligible trials, 11 (4145 participants) contributed IPD. Task-shared psychological interventions were associated with a greater decrease in depressive symptom severity than control conditions (Hedges g, 0.32; 95% CI, –0.26 to –0.38). Participants in the intervention groups had a higher chance of responding (odds ratio, 2.11; 95% CI, 1.60 to 2.80) and remitting (odds ratio, 1.87; 95% CI, 1.20 to 1.99). The presence of psychomotor symptoms was significantly associated with the outcomes of task-shared psychological interventions (β [SE], –1.21 [0.39]; P = .002). No other significant associations were identified. Heterogeneity among the trials with IPD was 74% (95% CI, 53%-86%). CONCLUSIONS AND RELEVANCE: In this meta-analysis of IPD, task-shared psychological interventions were associated with a larger reduction in depressive symptom severity and a greater chance of response and remission than control conditions. These findings show potential for the use of task-sharing of psychological interventions across different groups of patients with depression. Further research would help identify which people are most likely to benefit and strengthen larger-scale implementation of this strategy to address the burden of depression in LMIC.

3.5. Grading the Evidence

GRADE Table 1: Psychotherapy (Cognitive Behavioural Therapy) compared to treatment as usual in adults with depressive disorders

Author(s): Arpana Amarnath, Marketa Ciharova, Clara Miguel
Question: Psychotherapy (CBT) compared to treatment as usual (TAU) in adults with depression [a]
Population: General adult[b]
Reference List: Cuijpers et al., 2021

№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	№ of patients	Absolute (95% CI)	Certainty	Importance
Certainty assessment								Effect		
Reduction in mental health symptoms – Reduction in depressive symptoms – Cuijpers, 2021										
75	RCT	not serious [c]	serious [d]	not serious	not serious	none	8040	SMD **-0.67** [CI -0.79 to -0.56]	⊕⊕⊕◯ MODERATE	CRITICAL
Reduction in mental health symptoms – Treatment response – Cuijpers, 2021										
75	RCT	not serious [c]	serious [d]	not serious	not serious	none	8513	OR **0.43** [CI 0.37 to 0.50]	⊕⊕⊕◯ MODERATE	CRITICAL
Reduction in mental health symptoms – Remission – Cuijpers, 2021										
40	RCT	not serious [c]	serious [d]	not serious	not serious	none	4926	OR **0.35** [CI 0.29 to 0.43]	⊕⊕⊕◯ MODERATE	IMPORTANT
Adverse effects – All cause drop out – Cuijpers, 2021										

Certainty assessment								Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	№ of patients	Absolute (95% CI)		
85	RCT	not serious c	serious d	not serious	not serious	none	4926	OR **0.89** [CI 0.77 to 1.03]	⊕⊕⊕◯ MODERATE	CRITICAL
Improvement in QOL and Functioning – Not available										
-	-	-	-	-	-	-	-	-	-	CRITICAL
Relapse – Not available										
-	-	-	-	-	-	-	-	-	-	CRITICAL

CI: Confidence interval; **OR:** Odds Ratio; **RCTs**: Randomized Controlled Trials; **SMD:** Standard Mean Difference; **QOL:** Quality of life

Interpretation of outcomes:
Change in depressive symptoms - Below 0 favors treatment; above 0 favors TAU
Response (efficacy) – Below 1 favors treatment; above 1 favors TAU
Remission - Below 1 favors treatment; above 1 favors TAU
All cause drop-out - Above 1 favors treatment; below 1 favors TAU

Explanations:
a.   Adults with elevated symptoms and/or diagnosis of depression
b.   Adults (> 18 years) with elevated symptoms and/or diagnosis of depression. The baseline severity of depression was not reported, 54.1% was diagnosed with a mood disorder and 45.9% scored above a cut-off
       on a self-report or a clinician-rated measure.
c.   The risk of bias was aggregated for the entire meta-analysis. It has been rated as not serious because the number of high-risk studies was below 25%
d.   The I^2 was not reported and could not be calculated.

GRADE Table 2: Psychotherapy (Behavioural Activation Therapy) compared to treatment as usual in adults with depressive disorders

Author(s): Arpana Amarnath, Marketa Ciharova, Clara Miguel
Question: Psychotherapy (BAT) compared to treatment as usual (TAU) in adults with depression [a]
Population: General adult[b]
Reference List: Cuijpers et al., 2021

Certainty assessment								Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	№ of patients	Absolute (95% CI)		
Reduction in mental health symptoms – Reduction in depressive symptoms – Cuijpers, 2021										
14	RCT	not serious [c]	serious [d]	not serious	not serious	none	1257	SMD **-0.73** [CI -0.95 to -0.52]	⊕⊕⊕◯ MODERATE	CRITICAL
Reduction in mental health symptoms – Treatment response – Cuijpers, 2021										
12	RCT	not serious [c]	serious [d]	not serious	not serious	none	832	OR **0.36** [CI 0.26 to 0.48]	⊕⊕⊕◯ MODERATE	CRITICAL
Reduction in mental health symptoms – Remission – Cuijpers, 2021										
15	RCT	not serious [c]	serious [d]	not serious	not serious	none	NR	OR **0.31** [CI 0.21 to 0.45]	⊕⊕⊕◯ MODERATE	IMPORTANT
Adverse effects – All cause drop out – Cuijpers, 2021										

№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	№ of patients	Absolute (95% CI)	Certainty	Importance
								Effect		
13	RCT	not serious [c]	serious [d]	not serious	not serious	none	1348	OR **0.83** [CI 0.61 to 1.13]	⊕⊕⊕◯ MODERATE	CRITICAL
Improvement in QOL and Functioning – Not available										
-	-	-	-	-	-	-	-	-	-	CRITICAL
Relapse – Not available										
-	-	-	-	-	-	-	-	-	-	CRITICAL

CI: Confidence interval; **OR:** Odds Ratio; **RCTs**: Randomized Controlled Trials; **SMD:** Standard Mean Difference; **QOL:** Quality of life

Interpretation of outcomes:
Change in depressive symptoms - Below 0 favors treatment; above 0 favors TAU
Response (efficacy) – Below 1 favors treatment; above 1 favors TAU
Remission - Below 1 favors treatment; above 1 favors TAU
All cause drop-out - Above 1 favors treatment; below 1 favors TAU

Explanations:
a. Adults with elevated symptoms and/or diagnosis of depression
b. Adults (> 18 years) with elevated symptoms and/or diagnosis of depression. The baseline severity of depression was not reported, 54.1% was diagnosed with a mood disorder and 45.9% scored above a cut-off on a self-report or a clinician-rated measure.
c. The risk of bias was aggregated for the entire meta-analysis. It has been rated as not serious because the number of high-risk studies was below 25%
d. The I^2 was not reported and could not be calculated.

GRADE Table 3: Psychotherapy (Problem Solving Therapy) compared to treatment as usual in adults with depressive disorders

Author(s): Arpana Amarnath, Marketa Ciharova, Clara Miguel
Question: Psychotherapy (PST) compared to treatment as usual (TAU) in adults with depression [a]
Population: General adult[b]
Reference List: Cuijpers et al., 2021

Certainty assessment								Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	№ of patients	Absolute (95% CI)		
Reduction in mental health symptoms – Reduction in depressive symptoms – Cuijpers, 2021										
9	RCT	not serious [c]	serious [d]	not serious	not serious	none	1024	SMD **-0.64** [CI -0.88 to -0.40]	⊕⊕⊕◯ MODERATE	CRITICAL
Reduction in mental health symptoms – Treatment response – Cuijpers, 2021										
10	RCT	not serious [c]	serious [d]	not serious	not serious	none	1250	OR **0.43** [CI 0.33 to 0.57]	⊕⊕⊕◯ MODERATE	CRITICAL
Reduction in mental health symptoms – Remission – Cuijpers, 2021										
5	RCT	not serious [c]	serious [d]	not serious	not serious	none	596	OR **0.32** [CI 0.22 to 0.46]	⊕⊕⊕◯ MODERATE	IMPORTANT
Adverse effects – All cause drop out – Cuijpers, 2021										

Certainty assessment								Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	№ of patients	Absolute (95% CI)		
11	RCT	not serious [c]	serious [d]	not serious	not serious	none	1286	OR **0.84** [CI 0.63 to 1.13]	⊕⊕⊕◯ MODERATE	CRITICAL
Improvement in QOL and Functioning – Not available										
-	-	-	-	-	-	-	-	-	-	CRITICAL
Relapse – Not available										
-	-	-	-	-	-	-	-	-	-	CRITICAL

CI: Confidence interval; **OR:** Odds Ratio; **RCTs**: Randomized Controlled Trials; **SMD:** Standard Mean Difference; **QOL:** Quality of life

Interpretation of outcomes:
Change in depressive symptoms - Below 0 favors treatment; above 0 favors TAU
Response (efficacy) – Below 1 favors treatment; above 1 favors TAU
Remission - Below 1 favors treatment; above 1 favors TAU
All cause drop-out - Above 1 favors treatment; below 1 favors TAU

Explanations:
a. Adults with elevated symptoms and/or diagnosis of depression
b. Adults (> 18 years) with elevated symptoms and/or diagnosis of depression. The baseline severity of depression was not reported, 54.1% was diagnosed with a mood disorder and 45.9% scored above a cut-off on a self-report or a clinician-rated measure.
c. The risk of bias was aggregated for the entire meta-analysis. It has been rated as not serious because the number of high-risk studies was below 25%
d. The I^2 was not reported and could not be calculated.

GRADE Table 4: Psychotherapy (Third Wave Therapies) compared to treatment as usual in adults with depressive disorders

Author(s): Arpana Amarnath, Marketa Ciharova, Clara Miguel
Question: Psychotherapy (3rd wave) compared to treatment as usual (TAU) in adults with depression [a]
Population: General adult[b]
Reference List: Cuijpers et al., 2021

Certainty assessment								Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	№ of patients	Absolute (95% CI)		
Reduction in mental health symptoms – Reduction in depressive symptoms – Cuijpers, 2021										
7	RCT	not serious [c]	serious [d]	not serious	not serious	none	482	SMD **-0.69** [CI -0.93 to -0.45]	⊕⊕⊕◯ MODERATE	CRITICAL
Reduction in mental health symptoms – Treatment response – Cuijpers, 2021										
7	RCT	not serious [c]	serious [d]	not serious	not serious	none	496	OR **0.42** [CI 0.31 to 0.58]	⊕⊕⊕◯ MODERATE	CRITICAL
Reduction in mental health symptoms – Remission – Cuijpers, 2021										
3	RCT	not serious [c]	serious [d]	not serious	serious [e]	none	137	OR **0.34** [CI 0.22 to 0.53]	⊕⊕◯◯ LOW	IMPORTANT
Adverse effects – All cause drop out – Cuijpers, 2021										

№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	№ of patients	Absolute (95% CI)	Certainty	Importance
5	RCT	not serious [c]	serious [d]	not serious	not serious	none	466	OR **0.89** [CI 0.62 to 1.30]	⊕⊕⊕◯ MODERATE	CRITICAL
Improvement in QOL and Functioning – Not available										
-	-	-	-	-	-	-	-	-	-	CRITICAL
Relapse – Not available										
-	-	-	-	-	-	-	-	-	-	CRITICAL

The header spans: **Certainty assessment** (№ of studies, Study design, Risk of bias, Inconsistency, Indirectness, Imprecision, Other considerations, № of patients), **Effect** (Absolute (95% CI)), **Certainty**, **Importance**

CI: Confidence interval; **OR:** Odds Ratio; **RCTs**: Randomized Controlled Trials; **SMD:** Standard Mean Difference; **QOL:** Quality of life

Interpretation of outcomes:
Change in depressive symptoms - Below 0 favors treatment; above 0 favors TAU
Response (efficacy) – Below 1 favors treatment; above 1 favors TAU
Remission - Below 1 favors treatment; above 1 favors TAU
All cause drop-out - Above 1 favors treatment; below 1 favors TAU

Explanations:
a.   Adults with elevated symptoms and/or diagnosis of depression
b.   Adults (> 18 years) with elevated symptoms and/or diagnosis of depression. The baseline severity of depression was not reported, 54.1% was diagnosed with a mood disorder and 45.9% scored above a cut-off on a self-report or a clinician-rated measure.
c.   The risk of bias was aggregated for the entire meta-analysis. It has been rated as not serious because the number of high-risk studies was below 25%
d.   The I^2 was not reported and could not be calculated.
e.   This has been rated as serious because the number of participants is below 400

GRADE Table 5: Psychotherapy (Interpersonal Psychotherapy) compared to treatment as usual in adults with depressive disorders

Author(s): Arpana Amarnath, Marketa Ciharova, Clara Miguel
Question: Psychotherapy (IPT) compared to treatment as usual (TAU) in adults with depression [a]
Population: General adult[b]
Reference List: Cuijpers et al., 2021

Certainty assessment								Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	№ of patients	Absolute (95% CI)		
Reduction in mental health symptoms – Reduction in depressive symptoms – Cuijpers, 2021										
15	RCT	very serious [c]	serious [d]	not serious	not serious	none	1215	SMD **-0.54** [CI -0.76 to -0.32]	⊕⊕⊕◯ MODERATE	CRITICAL
Reduction in mental health symptoms – Treatment response – Cuijpers, 2021										
17	RCT	very serious [c]	serious [d]	not serious	not serious	none	1590	OR **0.43** [CI 0.33 to 0.56]	⊕⊕⊕◯ MODERATE	CRITICAL
Reduction in mental health symptoms – Remission – Cuijpers, 2021										
11	RCT	very serious [c]	serious [d]	not serious	not serious	none	1190	OR **0.40** [CI 0.29 to 0.55]	⊕⊕⊕◯ MODERATE	IMPORTANT
Adverse effects – All cause drop out – Cuijpers, 2021										

Certainty assessment								Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	№ of patients	Absolute (95% CI)		
17	RCT	very serious [c]	serious [d]	not serious	not serious	none	1671	OR **0.97** [CI 0.73 to 1.28]	⊕⊕⊕◯ MODERATE	CRITICAL
Improvement in QOL and Functioning – Not available										
-	-	-	-	-	-	-	-	-	-	CRITICAL
Relapse – Not available										
-	-	-	-	-	-	-	-	-	-	CRITICAL

CI: Confidence interval; **OR:** Odds Ratio; **RCTs**: Randomized Controlled Trials; **SMD:** Standard Mean Difference; **QOL:** Quality of life

Interpretation of outcomes:
Change in depressive symptoms - Below 0 favors treatment; above 0 favors TAU
Response (efficacy) – Below 1 favors treatment; above 1 favors TAU
Remission - Below 1 favors treatment; above 1 favors TAU
All cause drop-out - Above 1 favors treatment; below 1 favors TAU

Explanations:
a. Adults with elevated symptoms and/or diagnosis of depression
b. Adults (> 18 years) with elevated symptoms and/or diagnosis of depression. The baseline severity of depression was not reported, 54.1% was diagnosed with a mood disorder and 45.9% scored above a cut-off on a self-report or a clinician-rated measure.
c. The risk of bias was aggregated for the entire meta-analysis. It has been rated as not serious because the number of high-risk studies was below 25%
d. The I^2 was not reported and could not be calculated.

GRADE Table 6: Psychotherapy (Brief Psychodynamic Psychotherapy) compared to treatment as usual in adults with depressive disorders

Author(s): Arpana Amarnath, Marketa Ciharova, Clara Miguel
Question: Psychotherapy (DYN) compared to treatment as usual (TAU) in adults with depression [a]
Population: General adult [b]
Reference List: Cuijpers et al., 2021

Certainty assessment								Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	№ of patients	Absolute (95% CI)		
Reduction in mental health symptoms – Reduction in depressive symptoms – Cuijpers, 2021										
6	RCT	not serious [c]	serious [d]	not serious	not serious	none	1170	SMD **-0.50** [CI -0.81 to -0.20]	⊕⊕⊕◯ MODERATE	CRITICAL
Reduction in mental health symptoms – Treatment response – Cuijpers, 2021										
5	RCT	not serious [c]	serious [d]	not serious	not serious	none	971	OR **0.48** [CI 0.33 to 0.69]	⊕⊕⊕◯ MODERATE	CRITICAL
Reduction in mental health symptoms – Remission – Cuijpers, 2021										
8	RCT	not serious [c]	serious [d]	not serious	not serious	none	1289	OR **0.47** [CI 0.33 to 0.68]	⊕⊕⊕◯ MODERATE	IMPORTANT
Adverse effects – All cause drop out – Cuijpers, 2021										

Certainty assessment								Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	№ of patients	Absolute (95% CI)		
7	RCT	not serious [c]	serious [d]	not serious	not serious	none	1230	OR **0.64** [CI 0.46 to 0.90]	⊕⊕⊕◯ MODERATE	CRITICAL
Improvement in QOL and Functioning – Not available										
-	-	-	-	-	-	-	-	-	-	CRITICAL
Relapse – Not available										
-	-	-	-	-	-	-	-	-	-	CRITICAL

CI: Confidence interval; **OR:** Odds Ratio; **RCTs**: Randomized Controlled Trials; **SMD:** Standard Mean Difference; **QOL:** Quality of life

Interpretation of outcomes:
Change in depressive symptoms - Below 0 favors treatment; above 0 favors TAU
Response (efficacy) – Below 1 favors treatment; above 1 favors TAU
Remission - Below 1 favors treatment; above 1 favors TAU
All cause drop-out - Above 1 favors treatment; below 1 favors TAU

Explanations:
a.   Adults with elevated symptoms and/or diagnosis of depression
b.   Adults (> 18 years) with elevated symptoms and/or diagnosis of depression. The baseline severity of depression was not reported, 54.1% was diagnosed with a mood disorder and 45.9% scored above a cut-off on a self-report or a clinician-rated measure.
c.   The risk of bias was aggregated for the entire meta-analysis. It has been rated as not serious because the number of high-risk studies was below 25%
d.   The I^2 was not reported and could not be calculated.

GRADE Table 7: Psychotherapy (Non-directive Supportive Counseling) compared to treatment as usual in adults with depressive disorders

Author(s): Arpana Amarnath, Marketa Ciharova, Clara Miguel
Question: Psychotherapy (SUP) compared to treatment as usual (TAU) in adults with depression [a]
Population: General adult[a]
Reference List: Cuijpers et al., 2021

Certainty assessment								Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	№ of patients	Absolute (95% CI)		
Reduction in mental health symptoms – Reduction in depressive symptoms – Cuijpers, 2021										
8	RCT	not serious [c]	serious [d]	not serious	not serious	none	952	SMD **-0.32** [CI -0.53 to -0.11]	⊕⊕⊕◯ MODERATE	CRITICAL
Reduction in mental health symptoms – Treatment response – Cuijpers, 2021										
8	RCT	not serious [c]	serious [d]	not serious	not serious	none	1041	OR **0.73** [CI 0.56 to 0.96]	⊕⊕⊕◯ MODERATE	CRITICAL
Reduction in mental health symptoms – Remission – Cuijpers, 2021										
6	RCT	not serious [c]	serious [d]	not serious	serious [e]	none	397	OR **0.60** [CI 0.42 to 0.82]	⊕⊕◯◯ LOW	IMPORTANT
Adverse effects – All cause drop out – Cuijpers, 2021										

Certainty assessment								Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	№ of patients	Absolute (95% CI)		
10	RCT	not serious [c]	serious [d]	not serious	not serious	none	1182	OR **0.85** [CI 0.62 to 1.17]	⊕⊕⊕◯ MODERATE	CRITICAL
Improvement in QOL and Functioning – Not available										
-	-	-	-	-	-	-	-	-	-	CRITICAL
Relapse – Not available										
-	-	-	-	-	-	-	-	-	-	CRITICAL

CI: Confidence interval; **OR:** Odds Ratio; **RCTs**: Randomized Controlled Trials; **SMD:** Standard Mean Difference; **QOL:** Quality of life

Interpretation of outcomes:
Change in depressive symptoms - Below 0 favors treatment; above 0 favors TAU
Response (efficacy) – Below 1 favors treatment; above 1 favors TAU
Remission - Below 1 favors treatment; above 1 favors TAU
All cause drop-out - Above 1 favors treatment; below 1 favors TAU

Explanations:
a.   Adults with elevated symptoms and/or diagnosis of depression
b.   Adults (> 18 years) with elevated symptoms and/or diagnosis of depression. The baseline severity of depression was not reported, 54.1% was diagnosed with a mood disorder and 45.9% scored above a cut-off on a self-report or a clinician-rated measure.
c.   The risk of bias was aggregated for the entire meta-analysis. It has been rated as not serious because the number of high-risk studies was below 25%
d.   The I^2 was not reported and could not be calculated.
e.   This has been rated as serious because the number of participants is below 400

GRADE Table 8: Psychotherapy (Life Review Therapy) compared to treatment as usual in adults with depressive disorders

Author(s): Arpana Amarnath, Marketa Ciharova, Clara Miguel
Question: Psychotherapy (LRT) compared to treatment as usual (TAU) in adults with depression [a]
Population: General adult[b]
Reference List: Cuijpers et al., 2021

№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	№ of patients	Absolute (95% CI)	Certainty	Importance
Certainty assessment								Effect	Certainty	Importance
Reduction in mental health symptoms – Reduction in depressive symptoms – Cuijpers, 2021										
6	RCT	not serious [c]	serious [d]	not serious	serious [e]	none	271	SMD **-0.81** [CI -1.15 to -0.46]	⊕⊕◯◯ LOW	CRITICAL
Reduction in mental health symptoms – Treatment response – Cuijpers, 2021										
6	RCT	not serious [c]	serious [d]	not serious	serious [e]	none	278	OR **0.29** [CI 0.17 to 0.49]	⊕⊕◯◯ LOW	CRITICAL
Reduction in mental health symptoms – Remission – Cuijpers, 2021										
1	RCT	not serious [c]	serious [d]	not serious	very serious [f]	none	26	OR **0.49** [CI 0.23 to 1.07]	⊕◯◯◯ VERY LOW	IMPORTANT
Adverse effects – All cause drop out – Cuijpers, 2021										

Certainty assessment								Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	№ of patients	Absolute (95% CI)		
6	RCT	not serious [c]	serious [d]	not serious	serious [e]	none	278	OR **1.08** [CI 0.64 to 1.83]	⊕⊕◯◯ LOW	CRITICAL
Improvement in QOL and Functioning – Not available										
-	-	-	-	-	-	-	-	-	-	CRITICAL
Relapse – Not available										
-	-	-	-	-	-	-	-	-	-	CRITICAL

CI: Confidence interval; **OR:** Odds Ratio; **RCTs**: Randomized Controlled Trials; **SMD:** Standard Mean Difference; **QOL:** Quality of life

Interpretation of outcomes:
Change in depressive symptoms - Below 0 favors treatment; above 0 favors TAU
Response (efficacy) – Below 1 favors treatment; above 1 favors TAU
Remission - Below 1 favors treatment; above 1 favors TAU
All cause drop-out - Above 1 favors treatment; below 1 favors TAU

Explanations:
a.   Adults with elevated symptoms and/or diagnosis of depression
b.   Adults (> 18 years) with elevated symptoms and/or diagnosis of depression. The baseline severity of depression was not reported, 54.1% was diagnosed with a mood disorder and 45.9% scored above a cut-off on a self-report or a clinician-rated measure.
c.   The risk of bias was aggregated for the entire meta-analysis. It has been rated as not serious because the number of high-risk studies was below 25%
d.   The I^2 was not reported and could not be calculated.
e.   This has been rated as serious because the number of participants is below 400
f.   This has been rated as very serious because the number of participants is below 100

GRADE Table 9: Psychotherapy (Guided Internet based Cognitive Behaviour Therapy) compared to treatment as usual in adults with depressive disorders

Author(s): Arpana Amarnath, Marketa Ciharova, Clara Miguel
Question: Psychotherapy (Guided iCBT) compared to treatment as usual (TAU) in adults with depression
Population: General adult [a]
Reference List: Karyotaki et al., 2021

Certainty assessment [b]								Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	№ of patients	Absolute (95% CI)		
Reduction in mental health symptoms – Efficacy – Karyotaki, 2021										
36	RCT	serious	not serious	not serious	not serious	none	1914	SMD **-0.4** [CI -0.6 to -0.3]	⊕⊕⊕◯ MODERATE	CRITICAL
Reduction in mental health symptoms – Efficacy (mean difference in PHQ-9) – Karyotaki, 2021										
36	RCT	serious	not serious	not serious	not serious	none	1914	MD **-1.7** (PHQ-9) [CI -2.5 to -0.9]	⊕⊕⊕◯ MODERATE	CRITICAL
Adverse effects – Not available										
-	-	-	-	-	-	-	-	-	-	CRITICAL
Improvement in QOL and Functioning – Not available										
-	-	-	-	-	-	-	-	-	-	CRITICAL
Relapse – Not available										

Certainty assessment [b]								Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	№ of patients	Absolute (95% CI)		
-	-	-	-	-	-	-	-	-	-	CRITICAL

CI: Confidence interval; **OR:** Odds Ratio; **RCTs**: Randomized Controlled Trials; **SMD:** Standard Mean Difference; **QOL:** Quality of life

Interpretation of outcomes:
Efficacy - Below 0 favors treatment; above 0 favors TAU

Explanations:
a.   Adults (> 18 years) with elevated symptoms and/or diagnosis of depression. The participants had moderate to moderately severe depression with a mean baseline PHQ-9 scores of 13.7 (SD 4.3) for the treatment group and 15.2 (SD 5.3) for the control - treatment as usual group. The mean age of the participants was 40.76 years and 68% were women.
b.   The certainty assessment is based on the CINeMA approach conducted by the study

GRADE Table 10: Psychotherapy (Unguided Internet based Cognitive Behaviour Therapy) compared to treatment as usual in adults with depressive disorders

Author(s): Arpana Amarnath, Marketa Ciharova, Clara Miguel

Question: Psychotherapy (Unguided iCBT) compared to treatment as usual (TAU) in adults with depression

Population: General adult [a]

Reference List: Karyotaki et al., 2021

№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	№ of patients	Absolute (95% CI)	Certainty	Importance
Certainty assessment [b]								Effect	Certainty	Importance
Reduction in mental health symptoms – Efficacy – Karyotaki, 2021										
36	RCT	serious	not serious	not serious	not serious	none	3783	SMD **-0.2** [CI -0.4 to -0.1]	⊕⊕⊕◯ MODERATE	CRITICAL
Reduction in mental health symptoms – Efficacy (mean difference in PHQ-9) – Karyotaki, 2021										
36	RCT	serious	not serious	not serious	not serious	none	3783	MD **-0.9** (PHQ-9) [CI -1.5 to -0.2]	⊕⊕⊕◯ MODERATE	CRITICAL
Adverse effects – Not available										
-	-	-	-	-	-	-	-	-	-	CRITICAL
Improvement in QOL and Functioning – Not available										
-	-	-	-	-	-	-	-	-	-	CRITICAL
Relapse – Not available										

Certainty assessment [b]								Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	№ of patients	Absolute (95% CI)		
-	-	-	-	-	-	-	-	-	-	CRITICAL

CI: Confidence interval; **OR:** Odds Ratio; **RCTs**: Randomized Controlled Trials; **SMD:** Standard Mean Difference; **QOL:** Quality of life

Interpretation of outcomes:
Efficacy - Below 0 favors treatment; above 0 favors TAU

Explanations:
a. Adults (> 18 years) with elevated symptoms and/or diagnosis of depression. The participants had moderate to moderately severe depression with a mean baseline PHQ-9 scores of 14.2 (SD 4.9) for the treatment group and 15.2 (SD 5.3) for the control - treatment as usual group. The mean age of the participants was 40.76 years and 68% were women.
b. The certainty assessment is based on the CINeMA approach conducted by the study

GRADE Table 11: Psychotherapy (Task Shared Psychotherapies) compared to control in adults with depressive disorders

Author(s): Arpana Amarnath, Marketa Ciharova, Clara Miguel

Question: Psychotherapy (Task shared psychotherapies) compared to control conditions [a] in adults with depression [b]

Population: General adults in low- and middle-income countries

Reference List: Karyotaki et al., 2022

№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	№ of patients	Absolute (95% CI)	Certainty	Importance
			Certainty assessment					Effect	Certainty	Importance
Reduction in mental health symptoms – Reduction in depressive symptoms – Karyotaki, 2022										
11	RCT	not serious	not serious	not serious	not serious	none	4118	SMD **0.32** [CI 0.18 to 0.46]	⊕⊕⊕⊕ HIGH	CRITICAL
Reduction in mental health symptoms – Treatment response – Karyotaki, 2022										
11	RCT	not serious	not serious	not serious	not serious	none	4118	OR **2.11** [CI 1.58 to 2.82]	⊕⊕⊕⊕ HIGH	CRITICAL
Reduction in mental health symptoms – Remission – Karyotaki, 2022										
11	RCT	not serious	not serious	not serious	not serious	none	4118	OR **1.87** [CI 1.34 to 2.61]	⊕⊕⊕⊕ HIGH	CRITICAL
Adverse effects – Not available										
-	-	-	-	-	-	-	-	-	-	CRITICAL
Improvement in QOL and Functioning – Not available										

Certainty assessment								Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	№ of patients	Absolute (95% CI)		
-	-	-	-	-	-	-	-	-	-	CRITICAL
Relapse – Not available										

CI: Confidence interval; **OR:** Odds Ratio; **RCTs**: Randomized Controlled Trials; **SMD:** Standard Mean Difference; **QOL:** Quality of life

Interpretation of outcomes:
Reduction in depressive symptoms - Above 0 favors treatment; below 0 favors control
Response (efficacy) – Above 1 favors treatment; below 1 favors control
Remission - Above 1 favors treatment; below 1 favors control

Explanations:
a. Control conditions include treatment as usual, enhanced treatment as usual and HIV counseling
b. Adults (> 18 years) with elevated symptoms and/or diagnosis of depression. The participants had moderate depression with a mean PHQ-9 scores of 14.3 (SD 6.5) at baseline. The mean age of the participants was 33 years and 48% were women.

3.6. Additional evidence not mentioned in GRADE tables

Ciharova et al., 2021: OBJECTIVE: To examine if cognitive restructuring (CR), behavioral activation (BA), and cognitive-behavioral therapy (CBT) result in differential effects in the treatment of adult depression. METHOD: We extracted randomized controlled trials (RCTs) from a database updated yearly from PubMed, PsycINFO, Embase, and Cochrane Library. Network and pairwise meta-analyses were conducted to investigate the effects of CR, BA, and CBT delivered in a face-to-face individual format, compared with waiting list (WL) and care-as-usual (CAU), on adult depression. The primary outcome was a standardized mean difference (SMD) in posttreatment depression severity. Tolerability of treatments and depression severity at follow-up were also assessed. RESULTS: A total of 45 studies with 3,382 participants were included. There was no evidence of a difference in effectiveness between CR, BA, and CBT. All three interventions were superior to CAU; SMD 0.57, 95% confidence interval [CI 0.08-1.07]; 0.52 [0.34-0.71]; 0.44 [0.28-0.60], respectively and WL 1.20 [0.69-1.70]; 1.15 [0.90-1.40]; 1.07 [0.87-1.26]. No difference in tolerability was found (risk ratio [RR] vs. CAU: 1.01 [0.04-22.81], 0.84 [0.63-1.11], and 0.96 [0.76-1.21], respectively). Metaregression and sensitivity analyses did not produce material differences. CONCLUSIONS: Results suggest that CR or BA alone and their combination (CBT) may be effective interventions in comparison to WL and CAU in the treatment of adult depression. There was no evidence suggesting differences in effectiveness among the three treatments. More research is needed to derive conclusions about the performance of CR.

Corpas et al., 2021: Brief psychological therapies might be a solution for the treatment of emotional disorders in primary care. We aim to determine the effectiveness of these therapies compared with medication. Studies were selected from the Medline, Embase, and PsycInfo databases. Eligibility criteria included adults with emotional disorders treated with 2–10 psychotherapeutic sessions provided in primary care. We analyzed 33 trials involving 3,868 patients following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). A moderate effect size (d = 0.37, 95% confidence interval, CI [0.21, 0.52]) favorable to brief therapies was found at posttreatment, but this was not maintained at follow-up. Heterogeneity among the studies was the main limitation. We conclude that brief therapies could be superior to pharmacological interventions for the treatment of emotional disorders in primary care.

Cuijpers et al., 2021: OBJECTIVE: Meta-analyses of psychotherapies usually report effects sizes, while clinicians and patients need to know the proportion of patients who benefit from therapy. We conducted a meta-analysis of therapies for depression reporting the rates of response (50% symptom reduction), remission (HAM-D <7), clinically significant deterioration for psychotherapy, and control conditions (CAU, waitlist, and pill placebo), as well as the relative risk of these outcomes and the numbers-needed-to-be-treated (NNTs). METHODS: We searched bibliographic databases and included 228 randomized trials comparing psychotherapy for depression against control conditions (75 with low risk of bias). Only therapies with at least 10 trials were included. We extracted outcomes from the studies, and for those studies not reporting the outcomes, we used a validated method to estimate the rates. RESULTS: The overall response rate in psychotherapies at 2 (±1) months after baseline was 41% (95% CI: 38~43), 17% (15~20) for usual care (CAU), and 16% (95% CI: 14~18) for waitlist. No significant differences between types of therapy were found. The NNT for therapy versus CAU was 5.3 and versus waitlist 3.9. About one third of patients remitted after therapy compared with 7%-13% in control conditions. The rates of deterioration were 5% versus 12%-13%, respectively. Most sensitivity analyses supported the general findings. CONCLUSION: Psychotherapies for depression may be effective compared with control conditions, but more than half of patients receiving therapy do not respond and only one

third remitted. More effective treatments and treatment strategies such as sequencing and combining treatments are clearly needed.

Cuijpers at al., 2020: Objective: In the past decades, many different types of psychotherapy for adult depression have been developed. Method: In this meta-analysis we examined the effects of 15 different types of psychotherapy using 385 comparisons between a therapy and a control condition: Acceptance and commitment therapy, mindfulness-based cognitive behavior therapy (CBT), guided self-help using a self-help book from David Burns, Beck's CBT, the "Coping with Depression" course, two subtypes of behavioral activation, extended and brief problem-solving therapy, self-examination therapy, brief psychodynamic therapy, non-directive counseling, full and brief interpersonal psychotherapy, and life review therapy. Results: The effect sizes ranged from g = 0.38 for the "Coping with Depression" course to g = 1.10 for life review therapy. There was significant publication bias for most therapies. In 70% of the trials there was at least some risk of bias. After adjusting studies with low risk of bias for publication bias, only two types of therapy remained significant (the "Coping with Depression" course, and self-examination therapy). Conclusions: We conclude that the 15 types of psychotherapy may be effective in the treatment of depression. However, the evidence is not conclusive because of high levels of heterogeneity, publication bias, and the risk of bias in the majority of studies.

Howarth et al., 2019: Objectives: Traditional mindfulness-based interventions (MBIs) have been applied successfully across many populations. The time commitment for these programs is often a barrier, and while brief MBIs have become popular, the impact of these on health-related outcomes is unclear as they have not yet been reviewed. Methods: A search of databases, including Medline, Embase, and PsycINFO, was conducted with qualitative and case studies being excluded. Findings were summarized using a narrative approach for all studies that met the inclusion criteria. Results: With one exception, all 85 studies that were included were randomized controlled trials and were relatively robust methodologically. Seventy-nine reported significant positive effects on at least one health-related outcome and over a quarter targeted a clinical population. The majority of studies focused on psychological outcomes, such as anxiety and depression, as well as emotion regulation, stress, and cognitive outcomes. Conclusions: Despite heterogeneity of outcomes across studies, there is evidence that brief MBIs can impact numerous health-related outcomes, after only one session and with interventions as brief as 5 min. These interventions have the potential to be the initial steps leading to sustainable and positive health outcomes

Lo et al., 2019: Purpose: To examine the effects of short-term psychological interventions on reducing family stress of economically disadvantaged families. Method: Systematic review and meta-analytic procedures were used to synthesize the results of randomized controlled studies published between 1980 and 2018. Results: The search yielded 8 studies that included results for 1,538 families in total. The risk of bias varied across studies. The meta-analysis results suggest a small positive effect (g = .38, p < .001) on child behavioral problems. Heterogeneity was relatively high and significant. We also found small to moderate effects on parenting stress, parental depression, and parenting quality (g ranging from .30 to .51). Discussion: The findings of this review suggest that short-term psychological interventions may reduce the family stress of economically disadvantaged families, with effect sizes that are comparable to those of interventions delivered to ordinary families. Implications for further research and practice are discussed.

Simmonds-Buckley et al., 2020: Background: There is a disconnect between the ability to swiftly develop e-therapies for the treatment of depression, anxiety, and stress, and the scrupulous evaluation of their clinical utility. This creates a risk that the e-therapies routinely provided within publicly funded psychological health care have evaded appropriate rigorous evaluation in their

development. Objective: This study aims to conduct a meta-analytic review of the gold standard evidence of the acceptability and clinical effectiveness of e-therapies recommended for use in the National Health Service (NHS) in the United Kingdom. Methods: Systematic searches identified appropriate randomized controlled trials (RCTs). Depression, anxiety, and stress outcomes at the end of treatment and follow-up were synthesized using a random-effects meta-analysis. The grading of recommendations assessment, development, and evaluation approach was used to assess the quality of each meta-analytic comparison. Moderators of treatment effect were examined using subgroup and meta-regression analysis. Dropout rates for e-therapies (as a proxy for acceptability) were compared against controls. Results: A total of 24 studies evaluating 7 of 48 NHS-recommended e-therapies were qualitatively and quantitatively synthesized. Depression, anxiety, and stress outcomes for e-therapies were superior to controls (depression: standardized mean difference [SMD] 0.38, 95% CI 0.24 to 0.52, N=7075; anxiety and stress: SMD 0.43, 95% CI 0.24 to 0.63, n=4863), and these small effects were maintained at follow-up. Average dropout rates for e-therapies (31%, SD 17.35) were significantly higher than those of controls (17%, SD 13.31). Limited moderators of the treatment effect were found. Conclusions: Many NHS-recommended e-therapies have not been through an RCT-style evaluation. The e-therapies that have been appropriately evaluated generate small but significant, durable, beneficial treatment effects. Trial Registration: International Prospective Register of Systematic Reviews (PROSPERO) registration CRD42019130184;
https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=130184

Simmonds-Buckley et al., 2019: The evidence base for behavioral activation (BA) as a front-line treatment for depression is grounded in individual delivery. No valid previous meta-analytic reviews of BA delivered in groups have been conducted. This study therefore examined the efficacy and acceptability of group BA drawn from clinical trial evidence. Randomized controlled trials of group BA were identified using a comprehensive literature search. Depression outcomes at posttreatment/follow-up, recovery and dropout rates were extracted and analyzed using a random-effects meta-analysis. Treatment moderators were analyzed using meta-regression and subgroup analyses. Nineteen trials were quantitatively synthesized. Depression outcomes post group BA treatment were superior to controls (SMD 0.72, CI 0.34 to 1.10, k=13, N=461) and were equivalent to other active therapies (SMD 0.14, CI -0.18 to 0.46, k=15, N=526). Outcomes were maintained at follow-up for group BA and moderators of treatment outcome were limited. The dropout rate for group BA (14%) was no different from other active treatments for depression (17%). Further research is required to refine the conditions for optimum delivery of group BA and define robust moderators and mediators of outcome. However, BA delivered in groups produces a moderate to large effect on depressive symptoms and should be considered an appropriate front-line treatment option.

Zhang et al., 2019: BACKGROUND: Depressive and anxiety disorders are highly prevalent and detrimental in primary care settings. However, there are gaps in the literature concerning effectiveness and generalizability of empirically supported interventions and treatment of both depression and anxiety in primary care settings. The aim of this review is to systematically assess and meta-analyze the effectiveness of brief empirically supported psychotherapies for treating depression and/or anxiety in primary care. METHODS: Seven electronic databases, five professional websites and manual search of reference lists were searched through April 2017 for randomized controlled trials (RCTs) of four psychotherapies treating primary care depression and anxiety: cognitive-behavior therapy (CBT), problem-solving therapy (PST), motivational interviewing (MI), and solution-focused brief therapy (SFBT). RESULTS: From an initial pool of 1140 articles, 179 articles were eligible for full-text review and 65 articles were included for final analysis. Sixty-five articles containing 198 effect sizes reported an overall treatment effect size of d = 0.462, p < 0.001. Single-predictor meta-regression indicated that marital status, treatment

modality (individual versus group), and treatment composition were significant moderators. Multiple-predictor meta-regression discovered treatment setting (inside versus outside primary care) significantly moderated treatment effect, b = -0.863, p = 0.039 after controlling for other intervention characteristics. CONCLUSION: Treatment effects were found for CBT and PST, both for depressive and anxiety disorders. Interventions delivered outside primary care settings were more effective than those within, individual treatment had greater treatment effects compared to group treatment, and both technology-assisted and in-person treatments were found to be effective.

4. From Evidence to Recommendations

4.1. Summary of findings

Table 3: Summary of findings table

GRADE table	Source	Outcome	Specific outcome	RCTs	Effects	Certainty of the evidence
GRADE Table 1: Psychotherapy (Cognitive Behavioural Therapy) compared to treatment as usual in adults with depressive disorders	Cuijpers et al., 2021	Reduction in mental health symptoms	Reduction in depressive symptoms	75	SMD **-0.67** [CI -0.79 to -0.56]	⊕⊕⊕◯ MODERATE
			Treatment response	75	OR **0.43** [CI 0.37 to 0.50]	⊕⊕⊕◯ MODERATE
			Remission	40	OR **0.35** [CI 0.29 to 0.43]	⊕⊕⊕◯ MODERATE
		Adverse effects	All cause drop out	85	OR **0.89** [CI 0.77 to 1.03]	⊕⊕⊕◯ MODERATE
		Improvement in quality of life and functioning	-	-	-	N/A
		Relapse	-	-	-	N/A
GRADE Table 2: Psychotherapy (Behavioural Activation Therapy) compared to treatment as usual in adults with depressive disorders	Cuijpers et al., 2021	Reduction in mental health symptoms	Reduction in depressive symptoms	14	SMD **-0.73** [CI -0.95 to -0.52]	⊕⊕⊕◯ MODERATE
			Treatment response	12	OR **0.36** [CI 0.26 to 0.48]	⊕⊕⊕◯ MODERATE
			Remission	15	OR **0.31** [CI 0.21 to 0.45]	⊕⊕⊕◯ MODERATE

GRADE table	Source	Outcome	Specific outcome	RCTs	Effects	Certainty of the evidence
		Adverse effects	All cause drop out	13	OR **0.83** [CI 0.61 to 1.13]	⊕⊕⊕◯ MODERATE
		Improvement in quality of life and functioning	-	-	-	N/A
		Relapse	-	-	-	N/A
GRADE Table 3: Psychotherapy (Problem Solving Therapy) compared to treatment as usual in adults with depressive disorders	Cuijpers et al., 2021	Reduction in mental health symptoms	Reduction in depressive symptoms	9	SMD **-0.64** [CI -0.88 to -0.40]	⊕⊕⊕◯ MODERATE
			Treatment response	10	OR **0.43** [CI 0.33 to 0.57]	⊕⊕⊕◯ MODERATE
			Remission	5	OR **0.32** [CI 0.22 to 0.46]	⊕⊕⊕◯ MODERATE
		Adverse effects	All cause drop out	11	OR **0.84** [CI 0.63 to 1.13]	⊕⊕⊕◯ MODERATE
		Improvement in quality of life and functioning	-	-	-	N/A
		Relapse	-	-	-	N/A
GRADE Table 4: Psychotherapy (Third Wave Therapies) compared to treatment as usual in adults with depressive disorders	Cuijpers et al., 2021	Reduction in mental health symptoms	Reduction in depressive symptoms	7	SMD **-0.69** [CI -0.93 to -0.45]	⊕⊕⊕◯ MODERATE
			Treatment response	7	OR **0.42** [CI 0.31 to 0.58]	⊕⊕⊕◯ MODERATE
			Remission	3	OR **0.34** [CI 0.22 to 0.53]	⊕⊕◯◯ LOW

GRADE table	Source	Outcome	Specific outcome	RCTs	Effects	Certainty of the evidence
		Adverse effects	All cause drop out	5	OR **0.89** [CI 0.62 to 1.30]	⊕⊕⊕◯ MODERATE
		Improvement in quality of life and functioning	-	-	-	N/A
		Relapse	-	-	-	N/A
GRADE Table 5: Psychotherapy (Interpersonal Psychotherapy) compared to treatment as usual in adults with depressive disorders	Cuijpers et al., 2021	Reduction in mental health symptoms	Reduction in depressive symptoms	15	SMD **-0.54** [CI -0.76 to -0.32]	⊕⊕⊕◯ MODERATE
			Treatment response	17	OR **0.43** [CI 0.33 to 0.56]	⊕⊕⊕◯ MODERATE
			Remission	11	OR **0.40** [CI 0.29 to 0.55]	⊕⊕⊕◯ MODERATE
		Adverse effects	All cause drop out	17	OR **0.97** [CI 0.73 to 1.28]	⊕⊕⊕◯ MODERATE
		Improvement in quality of life and functioning	-	-	-	N/A
		Relapse	-	-	-	N/A
GRADE Table 6: Psychotherapy (Brief Psychodynamic Psychotherapy) compared to treatment as usual in adults with depressive disorders	Cuijpers et al., 2021	Reduction in mental health symptoms	Reduction in depressive symptoms	6	SMD **-0.50** [CI -0.81 to -0.20]	⊕⊕⊕◯ MODERATE
			Treatment response	5	OR **0.48** [CI 0.33 to 0.69]	⊕⊕⊕◯ MODERATE
			Remission	8	OR **0.47** [CI 0.33 to 0.68]	⊕⊕⊕◯ MODERATE

GRADE table	Source	Outcome	Specific outcome	RCTs	Effects	Certainty of the evidence
		Adverse effects	All cause drop out	7	OR **0.64** [CI 0.46 to 0.90]	⊕⊕⊕◯ MODERATE
		Improvement in quality of life and functioning	-	-	-	N/A
		Relapse	-	-	-	N/A
GRADE Table 7: Psychotherapy (Non-directive Supportive Counseling) compared to treatment as usual in adults with depressive disorders	Cuijpers et al., 2021	Reduction in mental health symptoms	Reduction in depressive symptoms	8	SMD **-0.32** [CI -0.53 to -0.11]	⊕⊕⊕◯ MODERATE
			Treatment response	8	OR **0.73** [CI 0.56 to 0.96]	⊕⊕⊕◯ MODERATE
			Remission	6	OR **0.60** [CI 0.42 to 0.82]	⊕⊕◯◯ LOW
		Adverse effects	All cause drop out	10	OR **0.85** [CI 0.62 to 1.17]	⊕⊕⊕◯ MODERATE
		Improvement in quality of life and functioning	-	-	-	N/A
		Relapse	-	-	-	N/A
GRADE Table 8: Psychotherapy (Life Review Therapy) compared to treatment as usual in adults with depressive disorders	Cuijpers et al., 2021	Reduction in mental health symptoms	Reduction in depressive symptoms	6	SMD **-0.81** [CI -1.15 to -0.46]	⊕⊕◯◯ LOW
			Treatment response	6	OR **0.29** [CI 0.17 to 0.49]	⊕⊕◯◯ LOW
			Remission	1	OR **0.49** [CI 0.23 to 1.07]	⊕◯◯◯ VERY LOW

GRADE table	Source	Outcome	Specific outcome	RCTs	Effects	Certainty of the evidence
		Adverse effects	All cause drop out	6	OR **1.08** [CI 0.64 to 1.83]	⊕⊕◯◯ LOW
		Improvement in quality of life and functioning	-	-	-	N/A
		Relapse	-	-	-	N/A
GRADE Table 9: Psychotherapy (Guided Internet based Cognitive Behaviour Therapy) compared to treatment as usual in adults with depressive disorders		Reduction in mental health symptoms	Efficacy	36	SMD **-0.4** [CI -0.6 to -0.3]	⊕⊕⊕◯ MODERATE
			Efficacy (mean difference in PHQ-9)	36	MD **-1.7** (PHQ-9) [CI -2.5 to -0.9]	⊕⊕⊕◯ MODERATE
		Adverse effects	-	-	-	N/A
		Improvement in quality of life and functioning	-	-	-	N/A
		Relapse	-	-	-	N/A
GRADE Table 10: Psychotherapy (Unguided Internet based Cognitive Behaviour Therapy) compared to treatment as usual in adults with depressive disorders		Reduction in mental health symptoms	Efficacy	36	SMD **-0.2** [CI -0.4 to -0.1]	⊕⊕⊕◯ MODERATE
			Efficacy (mean difference in PHQ-9)	36	MD **-0.9** (PHQ-9) [CI -1.5 to -0.2]	⊕⊕⊕◯ MODERATE
		Adverse effects	-	-	-	N/A
		Improvement in quality of life and functioning	-	-	-	N/A
		Relapse	-	-	-	N/A

GRADE table	Source	Outcome	Specific outcome	RCTs	Effects	Certainty of the evidence
GRADE Table 11: Psychotherapy (Task Shared Psychotherapies) compared to control in adults with depressive disorders		Reduction in mental health symptoms	Reduction in depressive symptoms	11	SMD **0.32** [CI 0.18 to 0.46]	⊕⊕⊕⊕ HIGH
			Treatment response	11	OR **2.11** [CI 1.58 to 2.82]	⊕⊕⊕⊕ HIGH
			Remission	11	OR **1.87** [CI 1.34 to 2.61]	⊕⊕⊕⊕ HIGH
		Adverse effects	-	-	-	N/A
		Improvement in quality of life and functioning	-	-	-	N/A
		Relapse	-	-	-	N/A

CI: Confidence interval; **MD**: Mean Difference; **OR:** Odds Ratio; **SMD:** Standard Mean Difference

4.2. Evidence to decision

Table 4: Evidence to decision table
Please note * indicates evidence from overarching qualitative review by Gronholm et al, 2023.

CRITERIA, QUESTIONS		JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
	Is the problem a priority? The more serious a problem is, the more likely it is that an option that addresses the problem should be a priority (e.g., diseases that are fatal or disabling are likely to be a higher priority than diseases that only cause minor distress). The more people who are affected, the more likely it is that an option that addresses the problem should be a priority.			
Priority of the problem	• Are the consequences of the problem serious (that is, severe or important in terms of the potential benefits or savings)? • Is the problem urgent? • Is it a recognised priority (such as based on a political or policy decision)? [Not relevant when an individual patient perspective is taken]	☐ No ☐ Probably no ☐ Probably yes ☒ **Yes** ☐ Varies ☐ Don't know	• By 2030, depression is predicted to be one of the leading causes of disability and premature mortality worldwide. • Reducing the burden of depression by developing evidence-based interventions is now a major global priority. • Bearing in mind the feasibility and available resources, it is important to investigate the effectiveness of scalable interventions such as those that can be delivered by non-specialists or in self-help/digital formats.	

CRITERIA, QUESTIONS	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
How substantial are the desirable anticipated effects? The larger the benefit, the more likely it is that an option should be recommended.			
Desirable Effects • Judgments for each outcome for which there is a desirable effect • How substantial (large) are the desirable anticipated effects (including health and other benefits) of the option (taking into account the severity or importance of the desirable consequences and the number of people affected)?	☐ Trivial ☐ Small ☒ **Moderate** ☐ Large ☐ Varies ☐ Don't know	• All psychotherapies (CBT, BAT, PST, 3WV, IPT, DYN, SUP, LRT) including guided/unguided iCBT and task shared psychotherapies were significantly better than treatment as usual in reducing depressive symptoms. • For those with severe depressive symptoms, guided iCBT was more effective than unguided iCBT. • There were no significant differences between age and gender in the effectiveness of guided iCBT, unguided iCBT and task shared therapies. • In the meta-regression of CBT vs TAU, there was no significant moderating effect of a diagnosis of depression (mood disorder vs elevated symptoms) and mean age in the effectiveness of treatment.	

CRITERIA, QUESTIONS		JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Undesirable Effects	How substantial are the undesirable anticipated effects? The greater the harm, the less likely it is that an option should be recommended.			
	• Judgments for each outcome for which there is an undesirable effect • How substantial (large) are the undesirable anticipated effects (including harms to health and other harms) of the option (taking into account the severity or importance of the adverse effects and the number of people affected)?	☐ Large ☐ Moderate ☐ Small ☒ **Trivial** ☐ Varies ☐ Don't know	• While there was no available data on adverse effects for guided/unguided iCBT and task shared psychotherapies, there were no significant differences between CBT, BAT, PST, 3WV, IPT, SUP, LRT and treatment as usual in acceptability of treatment (all cause drop out). DYN interventions had a significantly higher drop-out rate than TAU.	
Certainty of evidence	What is the overall certainty of the evidence of effects? The less certain the evidence is for critical outcomes (those that are driving a recommendation), the less likely that an option should be recommended (or the more important it is likely to be to conduct a pilot study or impact evaluation, if it is recommended).			
	• What is the overall certainty of this evidence of effects, across all of the outcomes that are critical to making a decision? • See GRADE guidance regarding detailed judgments about the quality of evidence or certainty in estimates of effects	☐ Very low ☐ Low ☒ **Moderate** ☐ High ☐ No included studies	• The certainty of evidence was moderate for reduction in depressive symptoms, treatment response, remission and all cause dropout for CBT, BAT, PST, IPT and DYN. • The certainty of evidence was moderate for reduction in depressive symptoms, treatment response and all cause dropout,	

CRITERIA, QUESTIONS	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
		and low for remission, for 3WV and SUP. • For LRT, the certainty of evidence was low for reduction in depressive symptoms, treatment response and all cause dropout, and very low for remission. • For both guided and unguided internet-based CBT, the certainty of evidence was moderate for reduction in mental health symptoms. • The certainty of evidence was high for reduction in depressive symptoms, treatment response and remission for task-shared psychotherapies.	
Values	Is there important uncertainty about or variability in how much people value the main outcomes? The more likely it is that differences in values would lead to different decisions, the less likely it is that there will be a consensus that an option is a priority (or the more important it is likely to be to obtain evidence of the values of those affected by the option). Values in this context refer to the relative importance of the outcomes of interest (how much people value each of those outcomes). These values are sometimes called 'utility values'.		
	• Is there important uncertainty about how much people value each of the main outcomes? • Is there important variability in how much people value each of the main outcomes?	☐ Important uncertainty or variability ☐ Possibly important	• There was no direct evidence to evaluate values and preferences of people. • *Overall, the studies highlighted importance and recognition of importance of mental health	

CRITERIA, QUESTIONS	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
	uncertainty or variability ☒ **Probably no important uncertainty or variability** ☐ No important uncertainty or variability	interventions and the outcomes of those interventions on people's mental health and wellbeing. • The utility value could be limited by certain factors and barriers present in the health systems. For instance, low awareness, poor funding and poor political buy-in, or other social barriers (Badu *et al.* 2018; Padmanathan & De Silva 2013; Sarkar *et al.* 2021; Verhey *et al.* 2020). • Social networks or raising awareness can facilitate adoption and recognition of mental health issues and the perceived value of the interventions (Amaral *et al.* 2018; Brooke-Sumner *et al.* 2015; Dickson & Bangpan 2018; Verhey *et al.* 2020).	

CRITERIA, QUESTIONS		JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
	Does the balance between desirable and undesirable effects favor the intervention or the comparison? The larger the desirable effects in relation to the undesirable effects, taking into account the values of those affected (i.e. the relative value they attach to the desirable and undesirable outcomes) the more likely it is that an option should be recommended.			
Balance of effects	• Judgments regarding each of the four preceding criteria • To what extent do the following considerations influence the balance between the desirable and undesirable effects: - How much less people value outcomes that are in the future compared to outcomes that occur now (their discount rates)? - People's attitudes towards undesirable effects (how risk averse they are)? - People's attitudes towards desirable effects (how risk seeking they are)?	☐ Favors the comparison ☐ Probably favors the comparison ☐ Does not favor either the intervention or the comparison ☒ **Probably favors the intervention** ☐ Favors the intervention ☐ Varies ☐ Don't know	• All psychotherapies (CBT, BAT, PST, 3WV, IPT, DYN, SUP, LRT) including guided/unguided iCBT and task shared psychotherapies were significantly better than treatment as usual in reducing depressive symptoms. • There were no significant differences between CBT, BAT, PST, 3WV, IPT, DYN, SUP, LRT and treatment as usual in acceptability of treatment (all cause drop out). • There were no available data on adverse effects for guided/unguided iCBT and task shared psychotherapies.	*A potential undesirable effect of MNS interventions was stigma associated with mental health service use (Badu et al. 2018; Brooke-Sumner et al. 2015; Dickson & Bangpan 2018; Mutahi et al. 2022; Sarkar et al. 2021; Verhey et al. 2020), e.g. fear of stigma was found to be a disincentive to participation (Brooke-Sumner et al. 2015).

CRITERIA, QUESTIONS	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
How large are the resource requirements (costs)? The greater the cost, the less likely it is that an option should be a priority. Conversely, the greater the savings, the more likely it is that an option should be a priority.			
Resources required • How large is the difference in each item of resource use for which <u>fewer</u> resources are required? • How large is the difference in each item of resource use for which <u>more</u> resources are required? • How large an investment of resources would the option require or save?	☐ Large costs ☐ Moderate costs ☐ Negligible costs and savings ☐ Moderate savings ☐ Large savings ☐ Varies ☒ **Don't know**	There was no direct evidence to evaluate resource requirements. However, the current evidence suggests the effectiveness of guided and unguided internet-based CBT, as well as task shared psychotherapies, which aim to decrease resource requirements.	*There were some indications of task-shifting interventions reducing costs: two examples using trained and supervised lay health workers (non-medical personnel instead of health workers) reduced the implementation cost of psychoeducation programmes, which made their implementation more feasible (Brooke-Sumner et al. 2015; Verhey et al. 2020).

CRITERIA, QUESTIONS	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Certainty of evidence of required resources — What is the certainty of the evidence of resource requirements (costs)?			
• Have all-important items of resource use that may differ between the options being considered been identified? • How certain is the evidence of differences in resource use between the options being considered (see GRADE guidance regarding detailed judgments about the quality of evidence or certainty in estimates)? • How certain is the cost of the items of resource use that differ between the options being considered? • Is there important variability in the cost of the items of resource use that differ between the options being considered?	☐ Very low ☐ Low ☐ Moderate ☐ High ☒ **No included studies**	There was no direct evidence to evaluate resource requirements. However, the current evidence suggests the effectiveness of guided and unguided internet-based CBT, as well as task shared psychotherapies, which aim to decrease resource requirements.	

CRITERIA, QUESTIONS		JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Cost effectiveness	Does the cost-effectiveness of the intervention favor the intervention or the comparison? The greater the cost per unit of benefit, the less likely it is that an option should be a priority.			
	• Judgments regarding each of the six preceding criteria • Is the cost effectiveness ratio sensitive to one-way sensitivity analyses? • Is the cost effectiveness ratio sensitive to multivariable sensitivity analysis? • Is the economic evaluation on which the cost effectiveness estimate is based reliable? • Is the economic evaluation on which the cost effectiveness estimate is based applicable to the setting(s) of interest?	☐ Favors the comparison ☐ Probably favors the comparison ☐ Does not favor either the intervention or the comparison ☐ Probably favors the intervention ☐ Favors the intervention ☐ Varies ☒ **No included studies**	No reviews examining cost effectiveness identified. However, the current evidence suggests the effectiveness of guided and unguided internet-based CBT, as well as task shared psychotherapies, which aim to increase cost-effectiveness. Individualized CBT is likely to be cost-effective both in combination with medication compared with medication alone and as standalone therapy compared with usual care, community referral, or bibliotherapy (Brettschneider et al, 2015; Wong and Knapp 2020). Group CBT being cost-effective compared with SSRIs, TCAs, usual care, and bibliotherapy.	

CRITERIA, QUESTIONS	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
What would be the impact on health equity, equality and non-discrimination? (WHO INTEGRATE) Health equity and equality reflect a concerted and sustained effort to improve health for individuals across all populations, and to reduce avoidable systematic differences in how health and its determinants are distributed. Equality is linked to the legal principle of non-discrimination, which is designed to ensure that individuals or population groups do not experience discrimination on the basis of their sex, age, ethnicity, culture or language, sexual orientation or gender identity, disability status, education, socioeconomic status, place of residence or any other characteristics. All recommendations should be in accordance with universal human rights standards and principles. The greater the likelihood that the intervention increases health equity and/or equality and that it reduces discrimination against any particular group, the greater the likelihood of a general recommendation in favor of this intervention.			
• How are the condition and its determinants distributed across different population groups? Is the intervention likely to reduce or increase existing health inequalities and/or health inequities? Does the intervention prioritise and/or aid those furthest behind? • How are the benefits and harms of the intervention distributed across the population? Who carries the burden (e.g. all), who benefits (e.g. a very small sub-group)? • How affordable is the intervention for individuals, workplaces or communities? • How accessible - in terms of physical as well as informational access - is the intervention across different population groups? • Is there any suitable alternative to addressing the condition, does the intervention represent the only	☐ Reduced ☐ Probably reduced ☐ Probably no impact ☒ **Probably increased** ☐ Increased ☐ Varies ☐ Don't know	There was no direct evidence to evaluate health equity, equality and non-discrimination. However, the current evidence suggests the effectiveness of guided and unguided internet-based CBT, as well as task shared psychotherapies, which aim to increase accessibility of mental health care, thus potentially increasing health equity and equality. *The review noted considerations for ensuring MNS interventions are equitable, equally available and non-discriminatory: • Accessibility, physical/practical considerations • time & travel constraints. • Accessibility, informational barriers • Affordability - medication and treatment costs	The current evidence suggests the effectiveness of guided and unguided internet-based CBT, as well as task shared psychotherapies, which aim to increase accessibility of mental health care, thus potentially increasing health equity and equality.

Health equity, equality and non-discrimination

CRITERIA, QUESTIONS	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
available option? Is this option proportionate to the need, and will it be subject to periodic review?		These factors may be exacerbated for certain groups: • People with low education/literacy - e.g. written instructions, psychoeducation materials • Women - travel restrictions, stronger stigma/shame, caregiving responsibilities Low resource settings - affordability/cost considerations exacerbated	
Feasibility — Is the intervention feasible to implement? The less feasible (capable of being accomplished or brought about) an option is, the less likely it is that it should be recommended (i.e. the more barriers there are that would be difficult to overcome).			
• Can the option be accomplished or brought about? • Is the intervention or option sustainable? • Are there important barriers that are likely to limit the feasibility of implementing the intervention (option) or require consideration when implementing it?	☐ No ☐ Probably no ☐ Probably yes ☐ Yes ☒ **Varies** ☐ Don't know	• There was no direct evidence to evaluate feasibility. • However, the current evidence suggests the effectiveness of guided and unguided internet-based CBT, as well as task shared psychotherapies, which aim to decrease the feasibility of implementation. *Included reviews considered feasibility, and how this can be enhanced	

CRITERIA, QUESTIONS	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
		- Acceptability of interventions for stakeholders - requires increased engagement with specialist staff, increased visibility of the task-sharing workforce within health facilities, perception of usefulness by providers and service users (e.g. via positive feedback), context-specific interventions, standardised implementation steps for simpler decision-making and delivery - Health worker workload, competency- requires training, refreshers, supervision; networking with others in same role. - Availability of a task-sharing workforce - Availability of caregivers - Participant education and literacy requires verbal explanations/tasks. - Logistical issues such as e.g. mobile populations, affordability of travel to receive care, lack of private space. - Limited resources/mental health budget	

CRITERIA, QUESTIONS	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
		Sustainability considerations: • Training and supervision • Integrating into routine clinical practice Provider type (e.g. formally employed lay health workers vs. volunteers)	
Human rights and sociocultural acceptability	Is the intervention aligned with human rights principles and socio-culturally acceptable? (WHO INTEGRATE)		
	This criterion encompasses two distinct constructs: The first refers to an intervention's compliance with universal human rights standards and other considerations laid out in international human rights law beyond the right to health (as the right to health provides the basis of other criteria and sub-criteria in this framework). The second, sociocultural acceptability, is highly time-specific and context-specific and reflects the extent to which those implementing or benefiting from an intervention as well as other relevant stakeholder groups consider it to be appropriate, based on anticipated or experienced cognitive and emotional responses to the intervention. The greater the sociocultural acceptability of an intervention to all or most relevant stakeholders, the greater the likelihood of a general recommendation in favor of this intervention.		
	• Is the intervention in accordance with universal human rights standards and principles? • Is the intervention socio-culturally acceptable to patients/beneficiaries as well as to those implementing it? To which extent do patients/beneficiaries value different non-health outcomes? • Is the intervention socio-culturally acceptable to the public and other relevant stakeholder groups? Is the intervention sensitive to sex, age, ethnicity, culture or language, sexual orientation or gender identity, disability status, education, socio-	☐ No ☐ Probably no ☒ **Probably yes** ☐ Yes ☐ Varies ☐ Don't know	There was no direct evidence to evaluate alignment with human rights principle and socio-cultural acceptability. *The review noted a number of considerations which would impact the right to health and access to healthcare. E.g. stigma and discrimination and lack of confidentiality could affect the help-seeking among service users. • The importance of socio-cultural acceptability of MNS interventions was clearly	

CRITERIA, QUESTIONS	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
economic status, place of residence or any other relevant characteristics? • How does the intervention affect an individual's, population group's or organization's autonomy, i.e. their ability to make a competent, informed and voluntary decision? • How intrusive is the intervention, ranging from low intrusiveness (e.g. providing information) to intermediate intrusiveness (e.g. guiding choices) to high intrusiveness (e.g. restricting or eliminating choices)? Where applicable, are high intrusiveness and/or impacts on the privacy and dignity of concerned stakeholders justified?		expressed. Pre-intervention considerations that take into account cultural and social aspects improve the acceptability of implemented interventions. • When interventions were perceived as appropriate for the culture and target group, the content and medium of the intervention received more positive feedback from service users and caregivers Also, considerations of age, sex and language have been highlighted as important to acceptability and accessibility. Mitigating steps to improve sociocultural acceptability include: • To train health workers in non-judgemental care • Integrate preventative mental health awareness messages to reduce the stigma • Train acceptable counsellors for the local settings and target groups Facilitate the use of indigenous/ local phrases and terms to increase acceptability, accessibility and fidelity.	

4.3. Summary of judgements

Table 5: Summary of judgements

This provides a snapshot of the evidence to decision table.

Priority of the problem	- Don't know	- Varies		- No	- Probably No	- Probably Yes	✔ **Yes**
Desirable effects	- Don't know	- Varies		- Trivial	- Small	✔ **Moderate**	- Large
Undesirable effects	- Don't know	- Varies		- Large	- Moderate	- Small	✔ **Trivial**
Certainty of the evidence	- No included studies			- Very low	- Low	✔ **Moderate**	- High
Values				- Important uncertainty or variability	- Possibly important uncertainty or variability	✔ **Probably no important uncertainty or variability**	- No important uncertainty or variability
Balance of effects	- Don't know	- Varies	- Favors comparison	- Probably favors comparison	- Does not favor either	✔ **Probably favors intervention**	- Favors intervention
Resources required	✔ **Don't know**	- Varies	- Large costs	- Moderate costs	- Negligible costs or savings	- Moderate savings	- Large savings
Certainty of the evidence on required resources	✔ **No included studies**			- Very low	- Low	- Moderate	- High
Cost–effectiveness	✔ **No included studies**	- Varies	- Favors comparison	- Probably favors comparison	- Does not favor either	- Probably favors intervention	- Favors intervention
Equity, equality and non-discrimination	✔ **Don't know**	- Varies	- Reduced	- Probably reduced	- Probably no impact	- Probably increased	- Increased
Feasibility	✔ **Don't know**	- Varies		- No	- Probably No	- Probably Yes	- Yes
Human rights and socio-cultural acceptability	✔ **Don't know**	- Varies		- No	- Probably No	- Probably Yes	- Yes

✔ Indicates category selected, - Indicates category not selected

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Appendix I: Search terms used to identify systematic reviews
PubMed

1# Depression
"Depression"[Mesh] OR "Depressive Disorder"[Mesh] OR "depress*"[tiab] OR "dysthymi*"[tiab] OR "mood disorder*"[tiab] OR "affective disorder*"[tiab] OR "dysphoric disorder*"[tiab]

2# Psychotherapies
"Psychotherapy"[Mesh] OR "Counseling"[Mesh] OR psychotherap*[Tiab] OR cbt[Tiab] OR counselling[Tiab] OR counseling[Tiab] OR "Eye Movement Desensitization Reprocessing"[tiab] OR "Eye Movement Desensitization and Reprocessing"[tiab] OR "Eye Movement Desensitisation Reprocessing"[tiab] OR "Eye Movement Desensitisation and Reprocessing"[tiab] OR EMDR[tiab] OR "Bibliotherap*"[tiab] OR mindfulness[Tiab] OR "Autogenic Training"[tiab] OR Logotherap*[tiab] OR "cognitive restructuring"[Tiab] OR "self-control training*"[Tiab] OR "assertiveness training"[Tiab] OR (("therapy"[SubHeading] OR therap*[Tiab] OR "Therapeutics"[Mesh] OR treatment*[Tiab] OR intervention*[tiab]) AND ("brief psychodynamic"[Tiab] OR "short psychodynamic"[tiab] OR "problem-solving"[Tiab] OR "compassion-focused"[Tiab] OR "compassion-focussed"[Tiab] OR "compassion-based"[tiab] OR constructivist*[Tiab] OR metacognitive[tiab] OR "meta-cognitive"[Tiab] OR "solution-focused"[Tiab] OR "solution-focussed"[Tiab] OR "self-control"[Tiab] OR psychosocial[tiab] OR "peer support"[tiab] OR "task-shifted"[tiab] OR Relaxation[tiab] OR "dialectical behavior"[tiab] OR "emotion-focused"[tiab] OR narrative[tiab] OR "person-centred"[tiab] OR "person-centered"[tiab] OR "Narrative"[tiab] OR "meaning-centered"[tiab] OR "humanistic"[tiab] OR "client-centered"[tiab] OR "meaning-centred"[tiab] OR "client-centred"[tiab] OR "Rogerian"[tiab] OR "Nondirective"[tiab] OR "Non-directive"[tiab] OR "Supportive"[tiab] OR "Life review"[tiab] OR "acceptance and commitment"[Tiab] OR ("schema"[tiab] AND brief[tiab]) OR ("gestalt"[tiab] AND brief[tiab]))) OR "behavior therap*"[Tiab] OR "behaviors therap*"[Tiab] OR "behavioral therap*"[Tiab] OR "behaviour therap*"[Tiab] OR "behaviours therap*"[Tiab] OR "behavioural therap*"[Tiab] OR "cognition therap*"[Tiab] OR "cognitive therap*"[tiab] OR "behavior treatment*"[Tiab] OR "behaviors treatment*"[Tiab] OR "behavioral treatment*"[Tiab] OR "behaviour treatment*"[Tiab] OR "behaviours treatment*"[Tiab] OR "behavioural treatment*"[Tiab] OR "cognition treatment*"[Tiab] OR "cognitive treatment*"[tiab] OR "behavior intervention*"[Tiab] OR "behaviors intervention*"[Tiab] OR "behavioral intervention*"[Tiab] OR "behaviour intervention*"[Tiab] OR "behaviours intervention*"[Tiab] OR "behavioural intervention*"[Tiab] OR "cognition intervention*"[Tiab] OR "cognitive intervention*"[tiab] OR "behavior activation*"[Tiab] OR "behaviors activation*"[Tiab] OR "behavioral activation*"[Tiab] OR "behaviour activation*"[Tiab] OR "behaviours activation*"[Tiab] OR "behavioural activation*"[Tiab] OR exposure[tiab]

3# SR + MA filter

("Meta-Analysis" [Publication Type] OR "Meta-Analysis as Topic"[Mesh] OR metaanaly*[tiab] OR meta-analy*[tiab] or metanaly*[tiab] OR "Systematic Review" [Publication Type] OR systematic[sb] OR meta-analysis[Filter] OR systematicreview[Filter] OR "Cochrane Database Syst Rev"[Journal] or prisma[tiab] OR "preferred reporting items"[tiab] OR prospero[tiab] OR ((systemati*[ti] OR umbrella[ti] OR "structured literature"[ti]) AND (review[ti] OR overview[ti])) OR "systematic review"[tiab] OR "umbrella review"[tiab] OR "structured literature review"[tiab] OR "systematic qualitative review"[tiab] OR "systematic quantitative review"[tiab] OR "systematic search and review"[tiab] OR "systematized review"[tiab] OR "systematised review"[tiab] OR "systemic review"[tiab] OR "systematic literature review"[tiab] OR "systematic integrative literature review"[tiab] OR "systematically review"[tiab] OR "scoping literature review"[tiab] OR "scoping review"[tiab] OR "systematic critical review"[tiab] OR "systematic integrative review"[tiab] OR "systematic evidence review"[tiab] OR "systematic integrative literature review"[tiab] OR "systematic mixed studies review"[tiab] OR "systematized literature review"[tiab] OR "systematic overview"[tiab] OR "Systematic narrative review"[tiab] OR "narrative review"[tiab] OR metasynthes*[tiab] OR meta-synthes*[tiab]) NOT ("Comment" [Publication Type] OR "Letter" [Publication Type] OR "Editorial" [Publication Type] OR (("Animals"[Mesh] OR "Models, Animal"[Mesh]) NOT "Humans"[Mesh]))

 # Timeframe
2019-2022

Appendix II: Decision Tree used to evaluate ROB GRADE item

- No data available for risk of bias → serious

- When vast majority (>60%) of trials are <u>low risk</u> → not serious
- When low risk is between 50-60%:
    - High risk <25% → not serious
    - High risk >25% → serious

- When vast majority (>60%) is <u>high risk</u> → very serious
- When high risk is between 50-60%:
    - Low risk <25% → very serious
    - Low risk >25% → serious

- When vast majority is <u>unclear risk</u> (>60%) → serious
- When unclear risk is between 50-60%:
    - High risk <25% → not serious
    - High risk >25% → serious

- If unclear/high/low risk are all < 50%:
    - High risk <25% → not serious
    - High risk >25% → serious

Figure 2: Developed tree for the assessment of the risk of bias item in GRADE