**Task-Shared Psychological Interventions for Depression in Low- and Middle-Income countries**

A Systematic Review and Individual Patient Data Meta-analysis

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**Key Points**

**Question:** What arethe depression outcomes and moderators of task-shared psychological interventions in Low- and Middle-Income Countries (LMICs)?

**Findings:** This individual patient data meta-analysis showed thattask-shared psychological interventions were significantly better in reducing depression severity and enhancing response and remission rates compared to controls. These outcomes were associated with the presence of psychomotor symptoms, while no other significant associations were identified.

**Meaning:** The present findings underline the need for scaling up task-sharing to reduce the burden of depression in LMICs.

**IMPORTANCE** Task-sharing is a promising solution for the large treatment gap for depression in Low- and Middle-Income Countries (LMICs).

**OBJECTIVE** To examine the outcomes and moderators of task-shared psychological interventions related to depression severity, response, and remission to enable more efficient resource allocations.

**DATA SOURCES** We performed systematic literature searches in PubMed, Embase, PsycINFO and Cochrane Library (up to 1/1/2021)

**STUDY SELECTION** We included randomised trials on task-shared psychological interventions compared to controls for adults with depressive symptoms in LMICs. The protocol registration is available at <https://osf.io/h4kf3>

**DATA EXTRACTION AND SYNTHESIS** We conducted a systematic review and individual patient data meta-analysis (IPD-MA) to estimate the outcomes of task-shared psychological interventions across patient characteristics using mixed-effects models. The PRISMA guidelines were used for abstracting data and assessing data quality and validity.

**MAIN OUTCOMES AND MEASURES** Our primary outcome was the reduction in depression symptom severity measured by the Patient Health Questionnaire-9 (PHQ-9). We also estimated response and remission rates.

**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 controls. (g = 0.32; 95% CI -0.26 to -0.38) Also, participants in the intervention groups had a higher chance of responding (OR = 2.11, 95%CI 1.60 to 2.80) and remitting (OR = 1.87, 95%CI 1.20 to 1.99). Finally, the presence of psychomotor symptoms was significantly associated with the outcomes of task-shared psychological interventions. No other significant associations were identified.

**CONCLUSIONS AND RELEVANCE** These findings show potential for the use of task-sharing of psychological interventions across different groups of patients with depression. Further research would allow us to refine who are those people most likely to benefit and improve the chances of a successful scaling up of this strategy to address the huge burden of depression in LMICs.

Depression is a leading cause of the global burden of disease1. Although psychological interventions effectively promote remission and are recommended as first-line treatment for depression by World Health Organisation (WHO), most affected persons in low- and middle-income countries (LMICs) do not have access to them2,3. A major barrier to improving access to psychological interventions is the lack of skilled human resources4,5. Task-sharing to the frontline, i.e., delegating care tasks to community or primary care-based non-specialist workers, has been advocated to address this barrier6,7. Several studies have examined the effects of psychological interventions delivered by such workers8. Recent trials in this field have demonstrated a range of effects in treating depression9-12 from moderate or large 10,11,13 to no effect12,14. Given the mixed evidence, there is still reluctance in scaling up task-sharing 15.

Moreover, critical outcomes for clinical decision making, such as intervention response and remission, are underreported by Randomised Controlled Trials (RCTs). It also remains unclear whether patient-level factors may influence the responsiveness to task-sharing. Notable examples of such factors include clinical and socio-demographic characteristics. Identifying patients who are more or less likely to benefit from these interventions would inform improvement efforts to reach these individuals more efficiently and improve task sharing scalability.

The individual patient data meta-analytic approach (IPD-MA), which uses raw data from RCTs, has been increasingly used to synthesize evidence across trials, improve the precision of overall estimates, and maximize the power to identify patient characteristics that moderate intervention outcomes16. In the present study, we conducted an IPD-MA to examine the outcomes of task-shared psychological interventions (i.e., reducing symptom severity, improving response and remission rates) compared to controls in adults with depression in LMICs. We also aimed at evaluating participant- and study-level characteristics as moderators of treatment outcomes.

**Methods**

The study was registered with Open Science Framework (<https://osf.io/h4kf3>https://osf.io/h4kf3) and reported according to PRISMA IPD-MA guidelines17

**Eligibility criteria**

We included RCTs that were conducted in LMICs on (a) task-shared psychological interventions, (b) compared to controls like treatment as usual (TAU), (c) for adults ( ≥18 years old) with depression as established by either a diagnostic interview or cut-off scores on self-report measures (e.g., Patient Health Questionnaire 9-items – PHQ-918). We included psychological interventions that were delivered by non-specialists (e.g., lay counsellors, health workers, peers) who were not mental health experts (i.e., psychiatrists, psychologists, or psychiatric nurses).

We excluded studies on collaborative care defined as coordinated multidisciplinary teams with assigned roles and tasks working together to draw individualized plans for patients according to WHO definition19. Further, self-help and telephone-administered interventions were not eligible for inclusion as they constitute a different format. We also excluded prevention trials since we focused on treatment. Finally, trials focusing on comorbid depression with other mental health disorders (e.g., alcohol misuse) were not excluded by the present study.

**Identification of studies**

To identify eligible studies, we searched an existing generic meta-analytic database that includes all RCTs on psychotherapy for depression. This database has been developed based on comprehensive searches in PubMed, Embase, PsycINFO and Cochrane library from database inception to January 1st, 2021. The full search string for PubMed is provided in the supplement. In these searches, two reviewers (PC and EK) screened independently the titles and abstracts and the full texts of retrieved papers. In case of disagreement, consensus was reached through discussion. Detailed description of this database can be found elsewhere (<https://osf.io/825c6/>). This generic meta-analytic database was searched by two independent reviewers (EK and YA) using the eligibility criteria of the present study. Disagreements between the reviewers were resolved through discussion. In addition, we screened meta-analyses of psychological interventions in LMICs20-24 (“reference tracking”) and invited the primary authors of the identified RCTs to indicate any other relevant study, which they were aware of. Reference tracking and asking the primary authors did not result in any additional RCTs that have not been identified through our searches.

**Data extraction and acquisition**

We extracted a range of study-level data from the published reports of the trials including type of psychological interventions, type of controls, trial setting, target group, country where the study was conducted, World Bank classification of the country, and data related to the risk of bias assessment. We gathered and synthesized all available socio-demographic and clinical characteristics (see the list of moderators with respective definitions in eTable 1 in the Supplement). Individual patient-level variables were chosen based on their availability in the included studies25. To gather these variables, we contacted the corresponding author of each eligible study to ask access to the raw trial data. In case of no response after one month, the trial was excluded as unavailable. After checking each dataset (no issues identified), we merged the data into the IPD-MA dataset.

**Quality assessment**

To assess the risk of bias of the included studies, we used the Risk of bias (RoB) tool 2.0 of the Cochrane Collaboration26. This tool examines bias arising from (a) the randomisation process, (b) deviations from intended interventions, (c) missing outcome data, (d) measurement of the outcome and (e) selection of reported results. Since the present study is an IPD-MA, we did not evaluate criteria c and e of the RoB tool. Incomplete outcome data were addressed by the IPD-MA and selective reporting was not relevant for our study since we had access to the full datasets of the trials. The RoB was evaluated based on the information provided in the published reports of the papers. In case of unclear items, the authors of the trials were consulted. Thus, each item of the RoB assessment tool was evaluated as at low or high risk of bias. The risk of bias was performed by two reviewers independently (EK and CM).

**Statistical analysis**

All analyses were conducted in STATA (version 16.0) and R (version 4.0.3) using the “meta” package27. Our primary outcome was reduction in depressive symptom severity on PHQ-918 at post-intervention because PHQ-9 was the most commonly used scale across the trials (8/11). Other depression scales were converted into PHQ-9 using conversion algorithms28,29. To test the impact of conversion on our outcomes, we performed a sensitivity analysis including only the studies that used the PHQ-9 scale. We also examined response rates (50% reduction of baseline depression symptoms) and remission (score < cut-off indicating mild depressive symptoms, e.g., PHQ-9 < 5) at post-intervention. Response and remission rates were calculated based on the original depression scales used by the trials.

To examine whether there is a difference between the effects of the studies that provided IPD and those that did not, we performed a conventional meta-analysis using data from the published reports of the papers. Regarding the IPD-MA, all analyses were conducted according to the intention-to-treat (ITT) principle. We used multiple imputation to handle incomplete outcome data at the post-intervention (missing-at-random assumption - 20 imputations). We conducted a sensitivity analysis using complete cases to test the robustness of our findings. To calculate the outcomes of task shared psychological interventions, we merged the IPD from all available studies using the one-stage IPD-MA with participants nested within trials while adjusting for baseline depression symptom severity30,31. Under the random effects model, we performed a mixed effect linear/ logistic regression (depending on whether the outcome was continuous or dichotomous) using the xtmixed/ meqrlogit functions in STATA, respectively.. Symptom severity, response, and remission were the dependent variables, while the treatment group was the independent variable. The resulting outcome of the mixed effect linear/ logistic regression is a β coefficient, which shows how many standard deviations (SD) the dependent variable changes per each SD change in the independent variable. The higher the β value is, the greater the effect. To test the robustness of the findings of the one-stage IPD-MA, we replicated all outcomes using a two-stage IPD-MA in which the outcomes per each trial are calculated separately and then are pooled together using the random effects model16. We also calculated the Hedges’ g32 for continuous outcomes and the Number Needed to Treat (NNT)33 and Odds Ratios (OR) for binary outcomes to allow a better understanding of the current findings in comparison with previous literature. Finally, we converted the main β coefficient to Hedges’ g based on the procedures described by Lipsey and Mark (2002)34.

We tested whether sociodemographic and clinical variables moderate intervention outcomes at the post-intervention. To examine potential moderators, we added the interaction term between each moderator variable and depression severity, response, and remission rates into the mixed-effects linear/ logistic regression model. Each potential moderator variable was added into separate bivariate models. To adjust for multiple testing, we performed the Bonferroni correction35, and the new p-value was 0.0026 (p=0.05/19 maximum number of moderator analyses = 0.0026). To examine study-level variables, we ran a series of subgroup analyses including type of psychological interventions, type of control condition, target group, type of outcome measure, depression diagnosis, income of country, and region.

We measured heterogeneity across the included studies using the *I2* statistic with values of 0% indicating no observed heterogeneity and values of 25%, 50%**,** and 75% indicating low, moderate, and high heterogeneity, respectively. Using the non-central chi-squared-based approach36, we calculated the 95% Confidence Intervals (CI) around *I2* to give the full magnitude of heterogeneity. We also calculated 95% Prediction intervals (PIs) around the pooled effect sizes, showing the range within which the effect of a future study would fall37. We examined possible publication bias by inspecting the funnel plot on primary outcome measures (also known as a test for small study effects38). If asymmetry due to publication bias was suspected, we tested whether the observed asymmetry was significant by performing Egger’s test39 and adjusted the effect for possible publication bias using the Duval and Tweedie’s trim and fill procedure40.

To evaluate the certainty of our main results, we performed the GRADE methodology (eTable 6 in the Supplement).

**Ethical Review of the study**

This study was exempted by the Harvard Longwood Campus Institutional Review Board (IRB) from an IRB application.

**Results**

**Studies selection**

The systematic literature search resulted in 13 eligible RCTs9-14,41-47 of the 3238 papers screened on full text. We obtained IPD from most of the eligible trials (11/13) and were able to synthesise approximately 94% of all existing IPD (4145/ 4419). Two datasets9,47 were not available because of data loss9 and no response47 (Figure 1).

**Studies characteristics**

Table 1 shows the characteristics of the included studies. Most of the included studies (10/11) recruited participants through clinical samples, while one trial12 recruited participants through community. Six studies included participants based on elevated depressive symptoms on a self-report measure10-12,14,41,42 and five used a diagnostic interview13,43-46. Most of the included studies examined mainly the effects of Cognitive Behavioral Therapy (CBT)-based interventions 10,12,14,41-43 against enhanced TAU 10-12,14,41,42,44 in three target groups, i.e., adults with depression in general10,42-44, women with perinatal depression11-14, and people living with HIV and depression41,45,46 (In the Supplement, the eTable 2 shows the interventions’ content). The interventions were delivered by lay counsellors10,41,42,45,46, non-specialist health workers14,43,44, or peers11-13. The studies were conducted in four low-income countries41, one lower-middle income country10,11,42, and two upper-middle income countries14,44,46.

**Participant characteristics**

Of the 4145 participants, the mean (SD) age was 33 (9.8) years, 2180 (52%) were male, 1750 completed primary education, 3546 were in a relationship (85.5%), and 1669 were unemployed (46.8%). Across the included studies, there was 11.5% (479/ 4145) of missing values at post-test, indicating a small study dropout rate (13% in the intervention and 10% in the controls). The mean (SD) score on PHQ-9 was 14.3 (6.5) at baseline and 5.3 (6.2) at the primary endpoint (mean = 3.7 months; SD = 1.8; range 2-6 months). Overall, at the primary endpoint, 67% (2453/ 3661) of participants showed response and 61.6% (2254/ 3661) remission. Response rates were 75.4% (1361/ 1806) for the intervention and 59% (1092/ 1855) for the control groups whereas remission rates were 69% (1246/ 1806) for the intervention and 54.3% (1008/ 1855) for the controls.

**Risk of bias**

Overall, all included studies were at low risk of bias across most domains, except for bias in measurement of the outcome. All trials were at low risk of bias arising from the randomisation process, and deviation from the intended intervention (see description of training and supervision of non-specialists in eTable3). Missing data were handled by the present IPD-MA using multiple imputation, while the percentage of missing values was small across the studies (up to 20.7%) and acceptably balanced between the intervention and control conditions. Most of the studies used measures administered by a blind assessor, while two did not perform blinding (see eTable 3 in the Supplement).

**Results of conventional meta-analysis**

The conventional meta-analysis of the 13 eligible trials showed that task-shared psychological interventions resulted in significantly larger reduction in depressive symptom severity compared to controls at post-test (g = 0.48, 95% CI 0.26 to 0.68; p < 0.001). Heterogeneity was high I2 = 86% (78% to 91%). We found no evidence of a difference between studies providing IPD and those that did not (between subgroups p = 0.52).

**Results of the IPD-MA**

Table 2 presents the findings of the one-stage IPD-MA on depressive symptom severity. Task-shared psychological interventions were significantly associated with greater reduction in depressive symptom severity compared to controls (β = -2.11, SE = .51; g = 0.32; 95% CI 0.26 to 0.38; p < .001). Complete case and sensitivity analyses including only the studies that originally used PHQ-9 showed similar outcomes. Of the individual participant-level factors, only the presence of psychomotor symptoms at baseline (n = 2628 participants experienced either agitation or retardation) was associated with intervention outcome (β = -1.21, SE = 0.39; p = .002), suggesting that the outcomes of intervention are much more pronounced when individuals experience psychomotor symptoms at baseline. This association was confirmed in both complete case analysis and sensitivity analysis including only the studies that originally used PHQ-9. No other significant associations were identified.

The two-stage IPD-MA resulted in g = 0.32 (95% CI 0.18 to 0.46; p = < 0.001) in favour of task-shared psychological interventions. The PIs ranged from g = −0.12 to 0.76. Heterogeneity was 74% (95% CI 53% to 86%) and there was no indication of publication bias. Similar outcomes were observed in complete case and sensitivity analyses. Subgroup analyses showed no evidence of a difference between target patient groups, studies that originally used PHQ-9 and those that did not, types of interventions, control conditions, income of country, and region (p > 0.05). Results of the two-stage IPD-MA are presented in Figure 2 and in eTable 4 & eFigure 1 in the Supplement.

Table 3 presents the findings of the one-stage IPD-MA on response and remission. Overall, the likelihood of response and remission was significantly higher in the intervention compared to control groups (Response: β = 0.75, SE = 0.14; OR = 2.11, 1.60 to 2.80 & Remission: β = 0.63, SE = 0.15; OR = 1.87, 95%CI 1.20 to 1.99; p < 0.001) with broad PIs (see eFigures 2-5 in the Supplement). Complete case analyses resulted in comparable outcomes. Moderator analysis showed that the chance of remission and response after task-shared psychological interventions was significantly higher among individuals with psychomotor symptoms. Moreover, the two-stage IPD-MA resulted in identical findings with the one-stage IPD-MA for both response and remission. Similar results were observed in complete case and sensitivity analyses. No evidence of a difference was observed between the examined subgroups. Finally, we found no evidence of publication bias (eTable 5, eFigures 2-5 in the Supplement).

The GRADE assessment of main outcomes showed moderate strength of the resulting evidence (see eTable 6 in the Supplement).

**Discussion**

In this study, we utilized individual patient data from 11 RCTs to study the depression outcomes of task-shared psychological interventions for adults with depression in LMICs, and to identify moderators of these outcomes. Task-shared psychological interventions were associated with a larger reduction in depressive symptom severity and a greater chance of response and remission than controls (moderate strength of evidence). We also found that the presence of psychomotor symptoms is associated with more pronounced effects of task-shared psychological interventions. None of the other participant- or study-level factors were associated with the intervention outcomes.

The present findings are in line with previous reviews on interventions delivered by non-specialist providers for common mental disorders in LMICs7,8,23,24. However, our novel methodological approach provides more robust estimates of task-shared psychological interventions diverse outcomes related to depression, including response, remission, NNTs, participant- and study-level moderators, which have not been reported earlier. We found that seven individuals need to be treated to expect one individual with a 50% reduction of the baseline depressive symptoms, while the NNT for remission was eight. Although these NNTs are relatively large, their magnitude should be interpreted considering that the delivery model of these interventions is through the lowest-cost human resource in the community and controls often received an enhanced TAU. Such NNTs are still promising since task-shared psychological interventions may have a significant impact when scaled up and delivered to large populations. Notably, the NNTs found by the present IPD-MA are comparable to those of two of the most common antidepressants, based on previous research mainly conducted in high-income countries, i.e., paroxetine [NNT = 5.6 based on Standardised Mean Difference (SMD) = -0.32] and fluoxetine (NNT = 7.7 based on SMD = -0.23), when compared to pill placebo48.

To our knowledge, the association of psychomotor symptoms with intervention outcomes has not been identified by previous literature on task-sharing for depression. However, previous research has suggested that psychomotor retardation is associated with functional impairment, depression severity and treatment prognosis25,49. The higher response in patients with psychomotor symptoms may be partly related to the type of intervention. Most of the included studies evaluated a CBT-based intervention that involved behavioural activation, a skill that may be particularly relevant to patients with psychomotor symptoms. Nevertheless, future studies are needed to replicate this finding to draw robust conclusions on the association of psychomotor symptoms with the response to task-shared psychological interventions.

The present findings should be interpreted considering several limitations. First, the included studies were conducted across seven LMICs, suggesting that our findings cannot be generalised to all LMICs. Second, although we could test the association of a wide range of participant characteristic with the intervention outcomes, our analysis was limited to variables examined by the included studies. Thus, we could not investigate the role of some clinically important variables associated with depression prognosis50 (e.g., number of previous episodes, the existence of other psychiatric conditions such as anxiety, substance use disorders, neurocognitive impairments, etc.). Third, some of the examined moderators (e.g., domestic violence) were available only in a small number of trials, limiting our conclusions for the respective associations. Nevertheless, the number of participants was large in all moderator analyses (n > 1300), suggesting that the statistical power was adequate. Fourth, similar to previous meta-analyses on studies in LMICs21, we found moderate to large heterogeneity and broad prediction intervals across most of our analyses, which might be related to various reasons, including the differences between the examined settings (i.e., primary care, antenatal clinics, HIV clinics, and community), comorbidities, type of providers and the quality of their training, and contextual determinants. However, we did not confirm such differences in subgroup analyses (e.g., target group). Thus, the present findings should be interpreted cautiously due to the unexplained heterogeneity.

Fifth, although we made every effort to include purely psychological interventions, it is possible that the included studies used other components, such as referrals as part of research safety protocols in case of high suicidal ideation. However, this is a typical procedure in trials to ensure the safety of participants. Sixth, most of the examined interventions involved CBT techniques. Still, in some of the included studies, these techniques had to be simplified and adapted for use in settings where participants and providers have limited general/ health literacy or training. Nevertheless, this is a commonly done practice in these and other settings51, as adaptation to local contexts is an essential step in the design of intervention studies. Seventh, we observed high response and remission rates among participants in the control groups. Such rates are possibly related to the active control groups used by most of the included trials (i.e., enhanced usual care and HIV counselling). It is, therefore, possible that participants in the controls received more substantial care than one would typically receive in these low resourced settings. However, this is a hypothesis that needs further investigation in future research. Further, although we excluded collaborative care studies, collaborative care can involve a wide range of different options, making it more difficult to disentangle its components across studies. Some of the enhanced TAU controls may have consisted of such collaborative care components. Thus, in some studies, it is possible that collaborative enhanced usual care was compared to the active arm (i.e., the psychological intervention), something that could have attenuated any differences across arms, which may partly explain the high response rates in the controls. Also, the possibility that there might be a synergistic effect in which lay counsellors could have enhanced further the usual care in the active arm cannot be dismissed either, as counsellors do not act in a vacuum but within a healthcare system Finally, in this work, we focused only on depression, however, patients in these settings may (co-) experience other common mental health problems like anxiety and/ or post-traumatic stress. Thus, future research should examine the effects of task-shared psychological interventions in patients with common mental disorders in LMICs.

Despite these limitations, our results showed that task-shared psychological interventions are associated with promising depression outcomes and may be particularly well-suited to patients with psychomotor symptoms. Moreover, these outcomes are not associated with several other patient- and study-level factors, which are assessed in the examined trials, suggesting the generalizability of the findings to diverse populations. Considering the limited availability of mental health professionals in all countries of the world, and particularly so in LMICs7,8, our study shows that it is possible and beneficial to use non-specialist providers in the delivery of psychological interventions for most patients with depression. Scaling up of this delivery model is probably a unique, low-cost, and widely accessible approach to reducing the burden of depression in LMICs.

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The Netherlands Organization for Health Research and Development (NW) had no role in design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication."

**Non-Author Contributions**

None

**Access to Data and Data Analysis**

Dr Eirini Karyotaki had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis

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| **Table 1** Characteristics of included studies | | | | | | | | | | |
| **Study** | **Inclusion criteria\*\*** | **Target group** | **Setting** | **PT** | **N** | **Control** | **N** | **Country** | **Region** | **Income\*** |
| Abas et al. 201841 | PHQ-9 ≥ 5 | Adults with HIV | HIV clinics | PST | 14 | eTAU | 18 | Zimbabwe | Sub-Sah. Africa | Low |
| Chowdhary et al. 201642 | PHQ-9 > 14 | Adults in general | Primary care | BA&PST | 24 | eTAU | 31 | India | South Asia | Lower-middle |
| Fuhr et al. 201911 | PHQ-9 > 9 | Perinatal depress. | Antenatal clinics | BA&PST | 140 | eTAU | 140 | India | South Asia | Lower-middle |
| Jordans et al. 201943 | Depression diagnosis\*\*\* | Adults in general | Primary care | BA | 60 | TAU | 60 | Nepal | South Asia | Low |
| Lund et al. 201914 | EPDS > 12 | Perinatal depress. | Antenatal clinics | BA&PST | 216 | eTAU | 209 | South Africa | Sub-Sah. Africa | Upper-middle |
| Matsuzaka et al. 201744 | MDD/ dysthymia (MINI) | Adults in general | Primary care | IPT | 43 | eTAU | 43 | Brazil | Latin America | Upper-middle |
| Nakimul-Mpungu et al. 202045 | Depression (MINI) | Adults with HIV | HIV clinics | SUP | 578 | HIV-c | 562 | Uganda | Sub-Sah. Africa | Low |
| Patel et al. 201710 | PHQ-9 > 14 | Adults in general | Primary care | BA&PST | 245 | eTAU | 248 | India | South Asia | Lower-middle |
| Petersen et al. 201446 | MDD (SCID)a | Adults with HIV | HIV clinics | IPT | 41 | HIV-c | 35 | South Africa | Sub-Sah. Africa | Upper-middle |
| Rahman et al. 200813 | MDD (SCID)b | Perinatal depress. | Primary care | CBT | 463 | TAU | 440 | Pakistan | South Asia | Low |
| Sikander et al. 201912 | PHQ-9 > 9 | Perinatal depress. | Villages | BA&PST | 283 | eTAU | 287 | Pakistan | South Asia | Low |
| *BA: Behavioural Activation; CBT: Cognitive Behavioural Therapy; Ctr: controls; EPDS: Edinburgh Postnatal Depression Scale; depress: depression; eTAU: enhanced Treatment as Usual; HIV: Human Immunodeficiency Virus; HIV-c: HIV counselling; IPT: Interpersonal Psychotherapy; MDD: Major Depressive Disorder; MINI: The Mini-International Neuropsychiatric Interview; N: number of participants; PHQ-9: Patient Health Questionnaire – 9 items; PST: Problem Solving Therapy; PT: psychotherapy; SCID: The Structural Clinical Interview; Sub-Sah: Sub-Saharan; SUP: Supportive Psychotherapy; TAU: Treatment as Usual*  *\*Income-level of the country by the time of the study publication based on the World Bank Classification*  *\*\* This is based on the eligibility criteria of the studies and does not include all depressive measures assessed by these studies (e.g., three studies used PHQ-9 to measure depressive symptoms but did not use it as an inclusion criterion)*  *\*\*\*Inclusion was determined by health worker diagnosis using the mental-health GAP guidelines of the World Health Organization for assessment and clinical decision making.*  *aThe SCID was conducted by a clinical psychologist*  *bThe SCID was conducted by a psychiatrist* | | | | | | | | | | |

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| **Table 2** *Mixed effects RELM model outcomes on depressive symptoms severity, 1-stage IPDMA a* | | | | | | |
|  | **Full sample** | | | **Complete cases analysis b** | | |
|  | **Nobs** | **β coefficient (SE)** | **P Value** | **Nobs** | **β coefficient (SE)** | **p-value** |
|  | **(Ns)** |  |  | **(Ns)** |  |  |
| **Main effects – depression severity** |  |  |  |  |  |  |
| Baseline severity | 4118 | 0.13 (0.02) | 0.000 | 3660 | 0.13 (0.02) | 0.000 |
| Group | (11) | -2.11 (0.51) | 0.000 | (11) | -2.37 (0.53) | 0.000 |
| Sensitivity analysis – only PHQ-9 studies |  |  |  |  |  |  |
| Baseline severity |  | 0.35 (0.05) | 0.000 | 1469 | 0.34 (0.04) | 0.000 |
| Group |  | -2.29 (0.65) | 0.000 | (8) | -2.54 (0.65) | 0.000 |
| **Moderators** |  |  |  |  |  |  |
| *Age* |  |  |  |  |  |  |
| Baseline severity | 4118 | 0.13 (0.02) | 0.000 | 3660 | 0.13 (0.02) |  |
| Group | (11) | -1.64 (0.84) | 0.005 | (11) | -2.14 (0.83) | 0.01 |
| Age (continuous) |  | 0.03 (0.01) | 0.03 |  | 0.02 (0.01) | 0.07 |
| Age\*group |  | -0.01 (0.02) | 0.50 |  | -0.01 (0.02) | 0.72 |
| *Gender* |  |  |  |  |  |  |
| Baseline severity | 4118 | 0.13 (0.02) | 0.000 | 3660 | 0.13 (0.02) | 0.000 |
| Group | (11) | -2.06 (0.55) | 0.000 | (11) | -2.31 (0.56) | 0.000 |
| Male gender |  | 0.25 (0.37) | 0.49 |  | 0.07 (0.35) | 0.84 |
| Gender\*Treatment group |  | -0.13 (0.51) | 0.80 |  | -0.17 (0.49) | 0.72 |
| *Educational level (ref. illiterate)* |  |  |  |  |  |  |
| Baseline severity | 4118 | 0.13 (0.02) | 0.000 | 3660 | 0.13 (0.02) | 0.000 |
| Group | (11) | -2.33 (0.66) | 0.000 | (11) | -2.54 (0.68) | 0.000 |
| Primary |  | -0.65 (0.36) | 0.07 |  | -0.75 (0.34) | 0.03 |
| Secondary |  | -0.87 (0.40) | 0.03 |  | -0.90 (0.37) | 0.01 |
| Tertiary |  | -1.54 (0.76) | 0.04 |  | -1.51 (0.70) | 0.03 |
| Other |  | 0.47 (1.27) | 0.71 |  | 1.02 (1.22) | 0.41 |
| Primary\*group |  | 0.74 (0.49) | 0.13 |  | 0.83 (0.48) | 0.08 |
| Secondary\*group |  | -0.06 (0.54) | 0.92 |  | -0.20 (0.52) | 0.70 |
| Tertiary\*group |  | -0.27 (1.05) | 0.79 |  | -0.65 (1.03) | 0.53 |
| Other\*group |  | -1.16 (1.81) | 0.52 |  | -1.73 (1.75) | 0.32 |
| p-value of educational level\*group |  |  | 0.43 |  |  | 0.19 |
| *Relationship status* |  |  |  |  |  |  |
| Baseline severity | 4118 | 0.13 (0.02) | 0.000 | 3660 | 0.13 (0.02) | 0.000 |
| Group | (11) | -2.42 (0.67) | 0.000 | (11) | -2.64 (0.67) | 0.000 |
| In a relationship |  | 0.067 (0.37) | 0.859 |  | 0.02 (0.37) | 0.96 |
| Relationship\*group |  | 0.38 (0.54) | 0.48 |  | 0.33 (0.52) | 0.53 |
| *Employment status (ref. unemployed)* |  |  |  |  |  |  |
| Baseline severity | 3537 | 0.12 (0.02) | 0.000 | 3194 | 0.12 (0.02) | 0.000 |
| Group | (10) | -2.35 (0.65) | 0.000 | (10) | -2.56 (0.67) | 0.000 |
| Employed |  | 0.09 (0.42) | 0.82 |  | 0.20 (0.39) | 0.62 |
| Student |  | -0.76 (0.97) | 0.44 |  | -0.75 (0.93) | 0.42 |
| Other |  | 0.65 (0.40) | 0.10 |  | 0.77 (0.38) | 0.04 |
| Employed\*group |  | 0.39 (0.58) | 0.50 |  | 0.32 (0.57) | 0.57 |
| Student\*group |  | 0.95 (1.47) | 0.52 |  | 0.81 (1.38) | 0.56 |
| Other\*group |  | -0.57 (0.55) | 0.30 |  | -0.70 (0.53) | 0.18 |
| p-value of employment status\*group |  |  | 0.28 |  |  | 0.17 |
| *Baseline severity of depression* |  |  |  |  |  |  |
| Baseline severity | 4118 | 0.16 (0.03) | 0.000 | 3660 | 0.16 (0.02) | 0.000 |
| Group | (11) | -1.35 (0.73) | 0.06 | (11) | -1.52 (0.73) | 0.04 |
| Baseline severity\*group |  | -0.05 (0.04) | 0.15 |  | -0.06 (0.03) | 0.10 |
| *Depression duration* |  |  |  |  |  |  |
| Baseline severity | 1645 | 0.29 (0.04) | 0.000 | 1405 | 0.31 (0.04) | 0.000 |
| Group | (4) | -2.02 (0.86) | 0.02 | (4) | -2.47 (0.90) | 0.01 |
| Duration in months |  | 0.003 (0.003) | 0.346 |  | 0.003 (0.003) | 0.328 |
| Duration\* group |  | 0.001 (0.01) | 0.72 |  | 0.002 (0.005) | 0.66 |
| *Loss of interest in daily activities* |  |  |  |  |  |  |
| Baseline severity | 4113 | 0.13 (0.02) | 0.000 | 3655 | 0.13 (0.02) | 0.000 |
| Group | (11) | -2.16 (0.73) | 0.003 | (11) | -2.40 (0.72) | 0.001 |
| Loss of interest (yes) | 0 | 0.07 (0.41) | 0.87 |  | 0.08 (0.39) | 0.84 |
| Loss of interest \*group |  | 0.06 (0.59) | 0.92 |  | 0.03 (0.55) | 0.92 |
| *Depressed mood* |  |  |  |  |  |  |
| Baseline severity | 4113 | 0.13 (0.02) | 0.000 | 3655 | 0.13 (0.02) | 0.000 |
| Group | (11) | -1.78 (0.76) | 0.02 | (11) | -1.93 (0.76) | 0.01 |
| Depressed mood (yes) |  | 0.17 (0.44) | 0.70 |  | 0.22 (0.43) | 0.60 |
| Depressed mood\*group |  | -0.35 (0.62) | 0.56 |  | -0.48 (0.61) | 0.43 |
| *Sleep problems* |  |  |  |  |  |  |
| Baseline severity | 4111 | 0.13 (0.02) | 0.000 | 3653 | 0.13 (0.02) | 0.000 |
| Group | (11) | -1.61 (0.63) | 0.01 | (11) | -1.66 (0.64) | 0.009 |
| Sleep problems (yes) |  | 0.64 (0.32) | 0.05 |  | 0.79 (0.31) | 0.01 |
| Sleep problems\*group |  | -0.61 (0.45) | 0.17 |  | -0.86 (0.43) | 0.05 |
| *Tiredness* |  |  |  |  |  |  |
| Baseline severity | 4026 | 0.11 (0.02) | 0.000 | 3652 | 0.11 (0.02) | 0.000 |
| Group | (11) | -1.53 (0.62) | 0.01 | (11) | -1.65 (0.62) | 0.008 |
| Tiredness (yes) |  | 1.60 (0.32) | 0.000 |  | 1.75 (0.31) | 0.000 |
| Tiredness\*group |  | -0.71 (0.44) | 0.11 |  | -0.83 (0.43) | 0.05 |
| *Concentration problems* |  |  |  |  |  |  |
| Baseline severity | 4112 | 0.13 (0.02) | 0.000 | 3654 | 0.13 (0.02) | 0.000 |
| Group | (11) | -1.87 (0.63) | 0.003 | (11) | -2.13 (0.64) | 0.001 |
| Concentration (yes) |  | 0.50 (0.34) | 0.14 |  | 0.54 (0.32) | 0.09 |
| Concentration\*group |  | -0.29 (0.47) | 0.54 |  | -0.31 (0.46) | 0.51 |
| *Appetite change* |  |  |  |  |  |  |
| Baseline severity | 4113 | 0.13 (0.02) | 0.000 | 3655 | 0.13 (0.02) | 0.000 |
| Group | (11) | -2.31 (0.61) | 0.000 | (11) | -2.57 (0.62) | 0.000 |
| Appetite change (yes) |  | 0.19 (0.31) | 0.54 |  | 0.19 (0.29) | 0.53 |
| Appetite change\*group |  | -0.26 (0.43) | 0.61 |  | 0.25 (0.41) | 0.54 |
| *Sense of worthlessness/ guilt* |  |  |  |  |  |  |
| Baseline severity | 4112 | 0.13 (0.02) | 0.000 | 3654 | 0.13 (0.02) | 0.000 |
| Group | (11) | -1.68 (0.60) | 0.005 | (11) | -1.91 (0.62) | 0.002 |
| Sense of worthlessness/ guilt (yes) |  | 0.18 (0.31) | 0.56 |  | 0.24 (0.29) | 0.41 |
| Sense of worthlessness/ guilt\*group |  | -0.57 (0.42) | 0.16 |  | -0.64 (0.40) | 0.11 |
| *Psychomotor symptoms* |  |  |  |  |  |  |
| Baseline severity | 4111 | 0.13 (0.02) | 0.000 | 3653 | 0.14 (0.02) | 0.000 |
| Group | (11) | -1.36 (0.54) | 0.001 | (11) | -1.49 (0.55) | 0.007 |
| Psychomotor symptoms (yes) |  | 0.56 (0.28) | 0.05 |  | 0.68 (0.26) | 0.01 |
| Psychomotor\*group |  | -1.21 (0.39) | 0.002\*\* |  | -1.45 (0.37) | 0.000\*\* |
| *Suicidal ideation* |  |  |  |  |  |  |
| Baseline severity | 4111 | 0.12 (0.02) | 0.000 | 3653 | 0.11 (0.02) | 0.000 |
| Group | (11) | -1.85 (0.53) | 0.000 | (11) | -2.12 (0.26) | 0.001 |
| Suicidal ideation (yes) |  | 0.83 (0.28) | 0.003 |  | 0.89 (0.26) | 0.001 |
| Suicidal ideation\*group |  | -0.63 (0.37) | 0.09 |  | -0.63 (0.36) | 0.08 |
| *Domestic violence* |  |  |  |  |  |  |
| Baseline severity | 1560 | 0.04 (0.02) | 0.06 | 1401 | 0.03 (0.02) | 0.04 |
| Group | (2) | -0.48 (0.29) | 0.09 | (2) | -0.67 (0.24) | 0.005 |
| Domestic violence (yes) |  | 0.79 (0.27) | 0.004 |  | 0.90 (0.26) | 0.001 |
| Domestic violence\*group |  | -0.16 (0.47) | 0.73 |  | -0.07 (0.41) | 0.86 |
| *Problematic alcohol drinking* |  |  |  |  |  |  |
| Baseline severity | 2509 | 0.08 (0.02) | 0.000 | 2278 | 0.07 (0.02) | 0.000 |
| Group | (8) | -1.69 (0.55) | 0.002 | (8) | -1.89 (0.55) | 0.001 |
| Problematic alcohol drinking (yes) |  | 0.64 (0.40) | 0.107 |  | 0.76 (0.37) | 0.04 |
| alcohol\*group |  | -0.09 (0.58) | 0.88 |  | -0.25 (0.53) | 0.64 |
| *Comorbid physical disorder* |  |  |  |  |  |  |
| Baseline severity | 1327 | 0.01 (0.01) | 0.45 | 1259 | 0.01 (0.01) | 0.27 |
| Group | (5) | -1.64 (1.34) | 0.22 | (5) | -1.45 (1.26) | 0.25 |
| Comorbid physical disorder (yes) |  | 0.11 (0.92) | 0.91 |  | 0.38 (0.79) | 0.63 |
| Comorbid physical disorder\*group |  | -1.11 (1.38) | 0.42 |  | -1.65 (1.19) | 0.16 |
| *Nobs: Number of observations; Ns: Number of studies; REML: Restricted Maximum Likelihood; ref.: reference category; SE: Standard error*  *a Parameters are standardized beta weights of the composite of PHQ-9 scores - Two tailed P values are presented*  *b This a sensitivity analysis that was conducted including only participants who completed post-treatment depression questionnaire*  *\*\*Significant association* | | | | | | |

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| **Table 3** *Mixed effects ML model outcomes on response and remission, 1-stage IPDMA a* | | | | | | | | | | | | |
|  | **Response**  **Full sample** | | | **Response**  **Complete cases analysis b** | | | **Remission**  **Full sample** | | | **Remission**  **Complete cases analysis b** | | |
|  | **Nobs** | **β coefficient (SE)** | **P Value** | **Nobs** | **β (SE)** | **p-value** | **Nobs** | **β (SE)** | **P Value** | **Nobs** | **β (SE)** | **p-value** |
|  | **(Ns)** |  |  | **(Ns)** |  |  | **(Ns)** |  |  | **(Ns)** |  |  |
| **Main effects** | 4118 |  |  | 3661 |  |  | 4118 |  |  | 3661 |  |  |
| Group | (11) | 0.75 (0.14) | 0.000 | (11) | 0.89 (0.16) | 0.000 | (11) | 0.63 (0.15) | 0.000 | (11) | 0.79 (0.17) | 0.000 |
| **Moderators** |  |  |  |  |  |  |  |  |  |  |  |  |
| *Age* |  |  |  |  |  |  |  |  |  |  |  |  |
| Group | 4118 | -0.02 (.001) | 0.01 |  | -0.01 (0.01) | 0.01 | 4118 | 0.31 (0.34) | 0.37 | 3661 | 0.53 (0.36) | 0.14 |
| Age | (11) | 0.44 (0.32) | 0.17 | 3661 | 0.71(0.35) | 0.04 | (11) | -0.02 (0.01) | 0.003 |  | -0.02 (0.01) | 0.001 |
| Age\*group |  | 0.01 (0.01) | 0.28 | (11) | 0.01 (0.01) | 0.55 |  | 0.01 (0.01) | 0.30 | (11) | 0.01 (0.01) | 0.42 |
| *Sex* |  |  |  |  |  |  |  |  |  |  |  |  |
| Group | 4118 | 0 .66 (0.17) | 0.000 | 3661 | 0.79 (0.19) | 0.000 | 4118 | 0.58 (0.18) | 0.001 | 3661 | 0.74 (0.20) | 0.000 |
| Male gender | (11) | -0.18 (0.18) | 0.31 | (11) | -0.10 (0.18) | 0.56 | (11) | -0.13 (0.22) | 0.54 | (11) | 0.05 (0.23) | 0.81 |
| Sex\*group |  | 0.19 (0.24) | 0.42 |  | 0.24 (0.25) | 0.34 |  | 0.11 (0.25) | 0.66 |  | 0.15 (0.28) | 0.60 |
| *Educational level (ref. illiterate)* |  |  |  |  |  |  |  |  |  |  |  |  |
| Group | 4118 | 0.84 (0.23) | 0.000 | 3661 | 0.97 (0.25) | 0.000 | 4118 | 0.65 (0.24) | 0.006 | 3661 | 0.77 (0.27) | 0.004 |
| Primary | (11) | 0.17 (0.15) | 0.26 | (11) | 0.24 (0.15) | 0.13 | (11) | 0.16 (0.17) | 0.33 | (11) | 0.22 (0.17) | 0.20 |
| Secondary |  | 0.16 (0.16) | 0.30 |  | 0.21 (0.16) | 0.21 |  | 0.21 (0.17) | 0.20 |  | 0.24 (0.17) | 0.16 |
| Tertiary |  | 0.30 (0.28) | 0.29 |  | 0.31 (0.30) | 0.30 |  | 0.25 (0.29) | 0.40 |  | 0.18 (0.31) | 0.55 |
| Other |  | -0.07 (0.50) | 0.88 |  | -0.13 (0.51) | 0.78 |  | 0.10 (0.49) | 0.83 |  | 0.10 (0.51) | 0.85 |
| Primary\*group |  | -0.28 (0.22) | 0.20 |  | -0.33 (0.23) | 0.15 |  | -0.23 (0.23) | 0.32 |  | -0.25 (0.24) | 0.29 |
| Secondary\*group |  | -0.001 (0.23) | 0.99 |  | 0.07 (0.24) | 0.77 |  | 0.17 (0.23) | 0.45 |  | 0.31 (0.25) | 0.20 |
| Tertiary\*group |  | 0.37 (0 .47) | 0.42 |  | 0.63 (0.49) | 0.20 |  | 0.50 (0.43) | 0.25 |  | 0.80 (0.47) | 0.09 |
| Other\*group |  | 0.21 (0.74) | 0.77 |  | 0.28 (0.75) | 0.71 |  | -0.62 (0.71) | 0.38 |  | -0.62 (0.74) | 0.40 |
| p-value of educational level\*group |  |  | 0.48 |  |  | 0.24 |  |  |  |  |  |  |
| *Relationship status* |  |  |  |  |  |  |  |  |  |  |  |  |
| Group | 4118 | 0.97 (0.27) | 0.000 | 3661 | 1.12 (0.29) | 0.000 | 4118 | 0.73 (0.29) | 0.01 | 3661 | 0.87 (0.31) | 0.006 |
| In a relationship | (11) | 0.01 (0.18) | 0.05 | (11) | 0.04 (0.18) | 0.20 | (11) | -0.01 (0.22) | 0.94 | (11) | -0.01 (0.23) | 0.95 |
| Relationship\*group |  | -0.27(0.27) | 0.27 |  | -0.27 (-0.95) | 0.34 |  | -0.12 (0.30) | 0.68 |  | -0.09 (0.31) | 0.79 |
| *Employment status (ref. unemployed)* |  |  |  |  |  |  |  |  |  |  |  |  |
| Group | 3537 | 0.90 (0.18) | 0.000 | 3195 | 1.03 (0.20) | 0.000 | 3537 | 0.82 (0.20) | 0.000 | 3195 | 0.95 (0.21) | 0.00 |
| Employed | (10) | 0.08 (0.18) | 0.64 | (10) | 0.08 (0.18) | 0.68 | (10) | -0.14 (0.19) | 0.46 | (10) | -0.24 (0.20) | 0.24 |
| Student |  | 0.38 (0.37) | 0.30 |  | 0.44 (0.38) | 0.26 |  | 0.46 (0.38) | 0.22 |  | 0.55 (0.38) | 0.15 |
| Other |  | -0.13 (0.20) | 0.51 |  | -0.22 (0.21) | 0.30 |  | -0.22 (0.23) | 0.34 |  | -0.41 (0.25) | 0.11 |
| Employed\*group |  | -0.19 (0.26) | 0.47 |  | -0.18 (0.27) | 0.51 |  | -0.15 (0.26) | 0.56 |  | -0.09 (0.28) | 0.74 |
| Student\*group |  | -.058 (0.54) | 0.28 |  | -0.66 (0.57) | 0.25 |  | -1.06 (0.54) | 0.05 |  | -1.17 (0.57) | 0.04 |
| Other\*group |  | 0.07 (0.27) | 0.78 |  | 0.17 (0.29) | 0.55 |  | -0.03 (0.29) | 0.92 |  | -0.09 (0.32) | 0.76 |
| p-value of employment status\*group |  |  | 0.85 |  |  | 0.50 |  |  | 0.28 |  |  | 0.08 |
| *Baseline severity of depression* |  |  |  |  |  |  |  |  |  |  |  |  |
| Group | 4118 | 0.57 (0.29) | 0.05 | 3661 | 0.65 (0.32) | 0.04 | 4118 | 0.62 (0.31) | 0.05 | 3661 | 0.79 (0.35) | 0.02 |
| Baseline severity | (11) | 0.03 (0.01) | 0.00 | (11) | 0.03 (0.01) | 0.01 | (11) | -0.07 (0.01) | 0.000 | (11) | -0.08 (0.01) | 0.000 |
| Baseline severity\*group |  | 0.01 (0.02) | 0.55 |  | 0.01 (0.02) | 0.42 |  | 0.004 (0.02) | 0.83 |  | 0.005 (0.20) | 0.81 |
| *Depression duration* |  |  |  |  |  |  |  |  |  |  |  |  |
| Group | 1645 | 0.79 (0.20) | 0.00 | 1405 | 0.98 (0.20) | 0.00 | 1645 | 0.58 (0.24) | 0.01 | 1405 | 0.69 (0.25) | 0.006 |
| Duration in months | (4) | -0.001 (0.001) | 0.64 | (4) | -0.001 (0.001) | 0.56 | (4) | -0.001 (0.001) | 0.43 | (4) | -0.001 (0.001) | 0.48 |
| Duration\* group |  | -0.002 (0.002) | 0.35 |  | -0.002 (0.002) | 0.26 |  | 0.001 (0.002) | 0.66 |  | 0.001 (0.002) | 0.67 |
| *Loss of interest* |  |  |  |  |  |  |  |  |  |  |  |  |
| Group | 4113 | 0.72 (0.30) | 0.02 | 3656 | 0.80 (0.31) | 0.01 | 4113 | 0.55 (0.30) | 0.06 | 3656 | 0.70 (0.33) | 0.032 |
| Loss of interest (yes) | (11) | 0.02 (0.20) | 0.92 | (11) | 0.001 (0.20) | 0.99 | (11) | -0.35 (0.21) | 0.10 | (11) | -0.42 (0.22) | 0.059 |
| Loss of interest \*group |  | 0.03 (0.29) | 0.92 |  | 0.10 (0.29) | 0.73 |  | 0.08 (0.28) | 0.78 |  | 0.10 (0.31) | 0.755 |
| *Depressed mood* |  |  |  |  |  |  |  |  |  |  |  |  |
| Group | 4113 | 0.52 (0.30) | 0.08 | 3656 | 0.64 (0.31) | 0.04 | 4113 | 0.70 (0.30) | 0.02 | 3656 | 0.90 (0.33) | 0.006 |
| Depressed mood (yes) | (11) | -0.09 (0.20) | 0.66 | (11) | -0.14 (0.20) | 0.50 | (11) | -0.29 (0.20) | 0.14 | (11) | -0.36 (0.21) | 0.092 |
| Depressed mood\*group |  | 0.25 (0.29) | 0.40 |  | 0.28 (0.30) | 0.34 |  | -0.078 (0.29) | 0.788 |  | -0.12 (0.30) | 0.699 |
| *Sleep problems* |  |  |  |  |  |  |  |  |  |  |  |  |
| Group | 4111 | 0.57 (0.21) | 0.008 | 3654 | 0.64 (0.23) | 0.005 | 4111 | 0.69 (0.22) | 0.002 | 3654 | 0.81 (0.24) | 0.001 |
| Sleep problems (yes) | (11) | -0.01 (0.13) | 0.94 | (11) | -0.07 (0.13) | 0.60 | (11) | -0.31 (0.14) | 0.03 | (11) | -0.40 (0.14) | 0.004 |
| Sleep problems \*group |  | 0.22 (0.19) | 0.26 |  | 0.31 (0.19) | 0.12 |  | -0.07 (0.20) | 0.74 |  | -0.01 (0.20) | 0.963 |
| *Tiredness* |  |  |  |  |  |  |  |  |  |  |  |  |
| Group | 4026 | 0.59 (0.22) | 0.01 | 3653 | 0.67 (0.24) | 0.005 | 4026 | 0.50 (0.22) | 0.03 | 3653 | 0.61 (0.24) | 0.011 |
| Tiredness (yes) | (11) | -0.56 (0.14) | 0.00 | (11) | -0.65 (0.15) | 0.00 | (11) | -0.76 (0.14) | 0.000 | (11) | -0.86 (0.15) | 0.000 |
| Tiredness\*group |  | 0.20 (0.21) | 0.35 |  | 0.26 (0.21) | 0.22 |  | 0.17 (0.20) | 0.39 |  | 0.22 (0.21) | 0.292 |
| *Concentration problems* |  |  |  |  |  |  |  |  |  |  |  |  |
| Group | 4112 | 0.88 (0.24) | 0.00 | 3655 | 1.11 (0.25) | 0.00 | 4112 | 0.59 (0.25) | 0.02 | 3655 | 0.72 (0.26) | 0.007 |
| Concentration (yes) | (11) | 0.18 (0.15) | 0.24 | (11) | 0.20 (0.15) | 0.20 | (11) | -0.38 (0.16) | 0.02 | (11) | -0.46 (0.16) | 0.005 |
| Concentration\*group |  | -0.17(0.24) | 0.47 |  | -0.27 (0.24) | 0.26 |  | 0.05 (0.23) | 0.81 |  | 0.10 (0.24) | 0.678 |
| *Appetite change* |  |  |  |  |  |  |  |  |  |  |  |  |
| Group | 4113 | 0.99 (0.21) | 0.00 | 3656 | 1.15 (0.23) | 0.000 | 4113 | 0.80 (0.22) | 0.000 | 3656 | 1.00 (0.23) | 0.000 |
| Appetite change (yes) | (11) | 0.13 (0.13) | 0.29 | (11) | 0.13 (0.13) | 0.31 | (11) | -0.05 (0.13) | 0.73 | (11) | -0.03 (0.14) | 0.838 |
| Appetite change\*group |  | -0.31 (0.19) | 0.11 |  | -0.33 (0.20) | 0.10 |  | -0.21 (0.19) | 0.26 |  | -0.26 (0.20) | 0.187 |
| *Sense of worthlessness/ guilt* |  |  |  |  |  |  |  |  |  |  |  |  |
| Group | 4112 | 0.67 (0.20) | 0.001 | 3655 | 0.80 (0.22) | 0.000 | 4112 | 0.47 (0.21) | 2.23 | 0.026 | 0.57 (0.23) | 0.012 |
| worthlessness/ guilt (yes) | (11) | 0.17 (0.13) | 0.18 | (11) | 0.17 (0.13) | 0.18 | (11) | -0.26 (0.13) | -1.94 | 0.053 | -0.34 (0.14) | 0.014 |
| worthlessness/ guilt \*group |  | 0.11 (0.19) | 0.57 |  | 0.14 (0.19) | 0.46 |  | 0.22 (0.19) | 1.15 | 0.251 | 0.30 (0.20) | 0.124 |
| *Psychomotor symptoms* |  |  |  |  |  |  |  |  |  |  |  |  |
| Group | 4111 | 0.41 (0.16) | 0.01 | 3654 | 0.46 (0.18) | 0.01 | 4111 | 0.31 (0.17) | 0.07 | 3654 | 0.36 (0.18) | 0.053 |
| Psychomotor symptoms (yes) | (11) | -0.20 (0.11) | 0.09 | (11) | -0.28 (0.12) | 0.01 | (11) | -0.39 (0.12) | 0.002 | (11) | -0.51 (0.12) | 0.000 |
| Psychomotor\*group |  | 0.56 (0.16) | 0.001\*\* |  | 0.72 (0.17) | 0.000\*\* |  | 0.55 (0.17) | 0.002\*\* |  | 0.74 (0.17) | 0.000\*\* |
| *Suicidal ideation* |  |  |  |  |  |  |  |  |  |  |  |  |
| Group | 4111 | 0.69 (0.16) | 0.000 | 3654 | 0.84 (0.18) | 0.000 | 4111 | 0.62 (0.16) | 0.000 | 3654 | 0.77 (0.19) | 0.000 |
| Suicidal ideation (yes) | (11) | -0.04 (0.11) | 0.70 | (11) | -0.07 (0.12) | 0.57 | (11) | -0.32 (0.12) | 0.008 | (11) | -0.40 (0.13) | 0.002 |
| Suicidal ideation\*group |  | 0.12 (0.17) | 0.45 |  | 0.1 (0.17) | 0.49 |  | 0.07 (0.17) | 0.66 |  | 0.10 (0.17) | 0.56 |
| *Domestic violence* |  |  |  |  |  |  |  |  |  |  |  |  |
| Group | 1560 | 0.47 (0.32) | 0.14 | 1401 | 0.90 (0.51) | 0.08 | 1560 | 0.11 (0.19) | 0.56 | 1401 | 0.20 (0.20) | 0.31 |
| Domestic violence (yes) | (2) | 0.002 (0.29) | 0.99 | (2) | 0.05 (0.30) | 0.86 | (2) | -0.23 (0.31) | 0.46 | (2) | -0.31 (0.36) | 0.39 |
| Domestic violence\*group |  | -0.12 (0.48) | 0.81 |  | -0.44 (0.48) | 0.36 |  | -0.004 (0.47) | 0.99 |  | 0.01 (0.53) | 0.98 |
| *Problematic alcohol drinking* |  |  |  |  |  |  |  |  |  |  |  |  |
| Group | 2509 | 0.75 (0.18) | 0.000 | 2279 | 0.92 (0.21) | 0.000 | 2509 | 0.64 (0.17) | 0.000 | 2279 | 0.80 (0.19) | 0.000 |
| Problematic alcohol drinking (yes) | (8) | -0.35 (0.22) | 0.11 | (8) | -0.45 (0.23) | 0.04 | (8) | -0.38 (0.26) | 0.14 | (8) | -0.62 (0.27) | 0.02 |
| alcohol\*group |  | .014 (0.37) | 0.97 |  | -0.03 (0.38) | 0.94 |  | -0.17 (0.36) | 0.63 |  | 0.02 (0.41) | 0.95 |
| *ML: Maximum Likelihood; Nobs: Number of observations; Ns: Number of studies; ref.: reference category; SE: Standard error*  *a Parameters are standardized beta weights of the composite of PHQ-9 scores - Two tailed P values are presented*  *b This a sensitivity analysis that was conducted including only participants who completed post-treatment depression questionnaire*  *\*\*Significant association* | | | | | | | | | | | | |