Effectiveness of the Thinking Healthy Programme for perinatal depression delivered through peers: pooled analysis of two randomized controlled trials in India and Pakistan

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ABSTRACT

Background: The Thinking Healthy Programme (THP) is recommended to treat perinatal depression in resource-limited settings, but scale-up is hampered by a paucity of community health workers. THP was adapted for peer-delivery (THPP) and evaluated in two randomized controlled trials in India and Pakistan. Our aim was to estimate the effectiveness of THPP on maternal outcomes across these two settings, and evaluate effect-modification by country and other pre-defined covariates.

Methods: Participants were pregnant women aged≥18 years with depression (Patient Health Questionnaire (PHQ-9) score≥10), randomized to THPP plus enhanced usual care (EUC) or EUC-only. Primary outcomes were symptom severity and remission (PHQ-9 score<5) 6 months post-childbirth. Secondary outcomes included further measures of depression, disability and social support at 3 and 6 months post-childbirth.

Results: Among 850 women (280 India; 570 Pakistan), 704 (83%) attended 6-month follow-up. Participants in the intervention arm had lower symptom severity (PHQ-9 score adjusted mean difference -0.78 (95% confidence interval -1.47,-0.09)) and higher odds of remission (adjusted odds ratio 1.35 (1.02,1.78)) versus EUC-only. There was a greater intervention effect on remission among women with short chronicity of depression, and those primiparous. There were beneficial intervention effects across multiple secondary outcomes.

Limitations: The trials were not powered to assess effect-modifications. 10-20% of participants were missing outcome data.

Conclusions: This pooled analysis demonstrates the effectiveness, acceptability and feasibility of THPP, which can be scaled-up within a stepped-care approach by engaging with the existing health care systems and the communities to address the treatment gap for perinatal depression in resource-limited settings.

Key words: Pregnancy; community health workers; depression; patient health questionnaire; Pakistan; India

Trial registrations: ClinicalTrials.gov: NCT02104232, NCT02111915

INTRODUCTION

Depression is the main cause of disability globally, and its prevalence is increasing (Friedrich, 2017). More than one in ten women experience a major depressive episode in the vulnerable perinatal period (pregnancy or the year following delivery) in high income countries (Fisher et al., 2012; Hendrick et al., 1998), with prevalences in low- and middle-income countries (LMIC) of up to 20% (Fisher et al., 2012; Woody et al., 2017). Perinatal depression is associated with adverse maternal outcomes including suicidal ideation (Gelaye et al., 2016), pregnancy and birth complications, and poorer mental, motor and emotional development of the infant (Field et al., 2006).

Psychological therapies like cognitive behavior therapy or behavioral activation are recommended for the treatment of mild and moderate perinatal depression (Guille et al., 2013). Due to the paucity of mental health professionals in LMIC (Kakuma et al., 2011), some of these interventions are modified, and provided as low-intensity psychological interventions delivered by trained para-professionals to depressed mothers in need (Rahman et al., 2013). One such low-intensity psychological intervention is the Thinking Healthy Programme (THP), developed by Rahman and colleagues (Rahman, 2007) and recommended by the World Health Organization (WHO) for the treatment of perinatal depression in LMIC (World Health Organization, 2015). THP is delivered by community healthcare workers (CHW) and has shown to be highly effective, halving the risk of perinatal depression and significantly improving infant health outcomes in a study in Pakistan (Rahman et al., 2008). However, the public health impact of THP has been hampered by the high occupational load of CHWs (Haq et al., 2008), therefore impairing the scale up of this programme (Jaskiewicz and Tulenko, 2012). To address this challenge, the National Institute of Mental Health (NIMH), through the Collaborative Hubs for International Research on Mental Health (CHIRMH) initiative, commissioned two studies in India and Pakistan to adapt the Thinking Healthy Programme for delivery by trained peers, namely local women with no prior experience of healthcare delivery (Atif et al., 2017; D. Singla et al., 2014). Randomized controlled trials were conducted in two distinct

settings, in urban/peri-urban Goa, India and rural Rawalpindi, Pakistan (Sikander et al., 2015), to evaluate the effectiveness and cost-effectiveness of the Thinking Healthy Programme Peer-delivered (THPP) compared to enhanced usual care (EUC). There were some differences in the trial designs (outlined below), but both trials found moderate effects of THPP on depression symptom severity and remission at 3 months post-childbirth (Fuhr et al., 2019; Sikander et al., 2019).

Our aim was to estimate the overall effectiveness of THPP on maternal outcomes, and evaluate effect modifications by country and other pre-defined covariates. The increased power from the pooled analysis enables us to look for consistency of results across the two settings, to assess the external validity of the intervention effect, and hence the ability to generalize findings regarding acceptability and feasibility of this peer-delivered intervention to other settings.

METHODS

Trial settings, designs, and participants

Data were pooled from the Goa, India trial (hereafter, THPP-India) and the Rawalpindi, Pakistan trial (hereafter, THPP-Pakistan). The trial settings are diverse, with higher rates of poverty (60% versus 4%), lower proportions of women educated (65% versus 84%), higher fertility rates (3.8 versus 1.8) and larger households (6.2 versus 4.2 persons per household) in rural Rawalpindi compared to urban Goa (D. Singla et al., 2014). The trial designs were similar (Table 1): both trials enrolled pregnant women aged ≥18 years with moderate to severe depression defined by scoring ≥10 on the nine-item Patient Health Questionnaire (PHQ-9). THPP-India was run through healthcare facilities with women individually-randomized, while THPP-Pakistan was conducted in a community setting with woman randomized in village clusters to avoid contamination. The trials have been described in full elsewhere (Fuhr et al., 2019; Sikander et al., 2019, 2015).

Trial interventions

Participants were randomized to THPP plus EUC or EUC-only. THPP consisted of 6-14 sessions over the prenatal period to six months post-childbirth, covering behavioral activation, active listening, collaboration with the family, guided discovery and homework. In India, THPP was delivered as 6-14 individual sessions, and in Pakistan, THPP was delivered as ten individual and four group sessions. Peers received classroom and field training, and received regular supervisions by the trainers. Emphasis was on behavior activation strategies to enable the delivery by peers with no previous experience of delivering healthcare. Further details of THPP have been published previously (Atif et al., 2017) and manuals are available from the authors on request.

Trial outcomes

In both trials, the primary outcomes were symptom severity (PHQ-9 score) and remission (PHQ-9 score <5) at 6 months post-childbirth. In this analysis, we included the primary and secondary maternal outcomes.

Statistical methods

Baseline characteristics of the two trial populations were described, and a multivariable logistic regression model was used to assess factors independently associated with country. Process indicators were summarized by country, including peer characteristics and attendance to therapy sessions among women in the intervention arm.

Outcome data were analyzed using logistic and linear regression models to estimate odds ratios and mean differences, respectively (with 95% confidence intervals). Generalized estimating equations (GEEs) with an exchangeable correlation structure were used to account for the village-level clustering in THPP-Pakistan (Sikander et al., 2019), with individuals in THPP-India acting as their own clusters. Models were adjusted for all variables included in the main trials' analyses, because they were: pre-specified in the analysis plan, stratification factors in the randomization, unbalanced between groups at baseline, or associated with missing outcome data at 6 months. We also included

country. The following baseline variables were adjusted for as fixed effects: country, recruitment site, residence (rural/urban), union council, symptom severity, treatment expectations, education, chronicity of depression, and time between screening and birth. Participants with missing values were omitted from the models.

For the primary outcomes, the following variables were assessed as a priori effect modifiers, by fitting interactions between the intervention and the covariate: country, age, chronicity of depression, baseline symptom severity, treatment expectations, and parity. We also assessed effect modification by country for the secondary outcomes. Repeated measures analyses were performed, combining the 3 and 6 months results, with assessment of group by time interactions. All models were adjusted for the covariates listed above.

Sensitivity analyses were performed for the primary outcomes, using GEEs with individuals grouped as one cluster, and mixed effects models. No adjustments were made for multiple testing; results were interpreted based on the strength of evidence of effect size and consistency of results across outcomes. Analyses were conducted in Stata (StataCorp, 2015), following intention-to-treat principles. Data are available on request (Fiona Vanobberghen et al., 2018; F Vanobberghen et al., 2018).

Ethical considerations

Ethical approval for the THPP-India trial was obtained from the Institutional Review Boards (IRBs) at the London School of Hygiene and Tropical Medicine (LSHTM), Sangath (the trial-implementing institution in India), and the Indian Council of Medical Research. Ethical approval for the THPP-Pakistan trial was obtained from the IRBs at the University of Liverpool, LSHTM, and the Human Development Research Foundation (the trial-implementing institution in Pakistan). Participants in both trials provided written informed consent (or witnessed informed consent/audio-recordings for illiterate participants).

RESULTS

Overall, 280 women were enrolled in THPP-India and 570 in THPP-Pakistan (Table 2). After adjusting for confounders (Appendix Table A1), THPP-Pakistan participants were less likely than those in THPP-India to work (6% versus 15%, with these low rates reflecting the national populations where the majority of women are housewives) (WHO Country Office Pakistan, 2013; World Bank, 2013), had received more education, had higher expectations of the usefulness of counseling, had higher baseline symptom severity, had lower social support scores, were more likely to have had a previous miscarriage or stillbirth, and were less likely to report domestic violence. Data on chronicity of depression at baseline were missing for 30% of THPP-Pakistan and no THPP-India participants. There were some differences between the women who did and did not have chronicity data in THPP-Pakistan: those with missing data were somewhat less likely to work, had higher treatment expectations, had lower symptom severity, were more likely to be multiparous, were more likely to have had a previous non-live birth, and were less likely to report domestic violence. Data were missing on the time between screening and birth of the child for 15% of THPP-Pakistan and 4% of THPP-India participants, due to women being lost to follow-up after screening. Depression was more chronic among THPP-Pakistan than THPP-India participants and time between screening and the birth of the child was shorter.

Overall, 26 and 66 peers were trained and delivered at least one session in THPP-India and THPP-Pakistan, respectively, with corresponding mean ages of 38 and 30 years and mean years of education completed 12 years in both trials (Table 3). No peers were lost during the THPP-India trial, whereas 23 (35%) were lost during the THPP-Pakistan trial. Attendance to supervisions was 67% and 88% in THPP-India and THPP-Pakistan, respectively. Quality was assessed differently in the two trials. In THPP-India, 18 items were assessed on the Therapy Quality scale of 0-2 (higher better) (D. R. Singla et al., 2014); the overall score across 72 sessions rated by independent raters was 1.49 (standard deviation 0.33). In THPP-Pakistan, assessments were done by independent raters for each peer in

three sessions at each of three time-points using an 18-item competency checklist; the overall average was 84%. These results indicate average to good therapy quality.

The mean number of sessions attended by participants in the intervention arm was slightly higher in THPP-Pakistan compared to THPP-India (10.9 versus 9.8); this was driven by higher attendance in the postnatal period (Table 3). In THPP-India, treatment completion was defined as attending at least six sessions with at least one session in each of four phases (prenatal, and 1-2, 3-4 and 5-6 months postnatal); 99/138 (72%) women completed treatment. In THPP-Pakistan, treatment completion was defined as attending at least ten sessions; 201/258 (78%) women completed treatment.

Average symptom severity decreased considerably over time in both groups (Appendix Figure A1). There was evidence of a beneficial effect of the intervention on both primary outcomes at 6 months, with participants in the intervention group having lower symptom severity (adjusted mean difference -0.78, 95% confidence interval -1.47,-0.09) and higher odds of remission (adjusted odds ratio 1.35, 95% confidence interval 1.02,1.78) compared with those in the control group (Table 4, Figures 1A and 1B). There was a trend towards stronger intervention effects in THPP-India compared to THPP-Pakistan for remission, but the difference was not statistically significant (p=0.18, with p=0.77 for symptom severity). Results were robust to sensitivity analyses (Appendix Table A2).

After adjusting for confounders including country, there was evidence of a greater intervention effect on remission at 6 months among women with shorter chronicity of depression at baseline, and those primiparous (p=0.03 for both interactions, Figure 1B and Appendix Table A3). Similar trends were observed for symptom severity with chronicity and parity, although the p values were large (p=0.49 and 0.30, respectively; Figure 1A and Appendix Table A4). For both outcomes, there were non-significant trends towards greater intervention effects among younger women (p=0.14 and 0.27 for remission and symptom severity, respectively). There was no consistent evidence of effect-modification by baseline symptom severity or treatment expectations.

After adjusting for confounders including intervention group, the following factors were associated with higher symptom severity and lower odds of remission at six months: country, higher baseline symptom severity, and lower level of education (Appendix Table A5).

There was consistently strong evidence of beneficial intervention effects across a number of secondary outcomes (Table 4). For symptom severity and WHO-DAS score, there were slightly stronger intervention effects at 3 months than at 6 months. For remission and MSPSS score, results were broadly similar at 3 and 6 months. For the composite outcomes of recovery and response at both 3 and 6 months, there was consistent and strong evidence of a benefit of the intervention. There was no evidence of an intervention effect on number of days unable to work in the last month. There was no evidence of effect modification by country for any of the secondary outcomes.

There was no statistical evidence of group by time interactions, and assuming a constant intervention effect at 3 and 6 months (Appendix Table A6), there were strong evidence of intervention effects on symptom severity, remission, WHO-DAS score and MSPSS score (3 and 6 months combined), in line with the results of the individual trials (Fuhr et al., 2019; Sikander et al., 2019). There was no evidence of an intervention effect on number of days unable to work in the last month.

DISCUSSION

We present results of a pooled analysis of two of the largest trials evaluating a psychological intervention for perinatal depression in LMIC delivered by peers. With the increased power from this pooled analysis, we found small (Rahman et al., 2013) but important benefits of THPP across a range of maternal depression, disability and social support outcomes, with 35% higher odds of remission at 6 months post-childbirth compared to EUC-only. These findings open the possibilities of peer-delivered THPP to be implemented in other settings where there are limited numbers of mental health professionals to tackle the treatment gap for perinatal depression.

Historically, intervention studies of depression in LMIC have generally had small sample sizes, with different recruitment mechanisms of study participants and using varying methodological designs and outcome measures (Chowdhary et al., 2014; Rahman et al., 2013). Our studies represent a new generation of complementary trials of psychological therapies nested in the community using innovative delivery mechanisms based on lay care providers and peer supervisors. THPP-India was conducted in a peri-urban setting in Goa while THPP-Pakistan was embedded in rural communities of Rawalpindi. These contextual and socio-economic differences were reflected in the trial populations and delivery agents (peers), with the THPP-Pakistan participants having more severe and more chronic depression at baseline compared to those in the THPP-India trial. THPP-Pakistan participants reported on average more years of education than those in THPP-India, contrary to expected (D. Singla et al., 2014) and compared to lower nationwide literacy rates of 45-50% (Population Census Organization, 1998; World Bank, 2013). There may have been over-reporting of education among the participants in Pakistan due to social desirability. Participants in THPP-Pakistan also had poorer depression outcomes at 6 months compared to those in THPP-India, after adjustment for confounders including baseline severity and chronicity. Slightly different models of incentivization were used across the two trials: peers in urban Goa received financial incentives since this was identified as an important motivator, while peers in rural Rawalpindi were volunteers, devoting their time to THPP for altruistic motives (Fuhr et al., 2019; Sikander et al., 2019; D. Singla et al., 2014). This may have been one reason for a greater turnover of peers during the trial in Pakistan (35% compared to none in India), though attendance to supervision was excellent (88%, compared to 67% in India). Furthermore, most peers in Pakistan who left were able to identify their own replacements, indicating that there was a pool of women interested in this work. The health systems in which peers were trained to operate THPP were also distinct. Peers in Rawalpindi worked alongside government lady health workers delivering care in the community, while peers in Goa worked more independently and within a tiered public healthcare system (D. Singla et al., 2014). There were some differences in the design of the intervention between the two trials (Sikander et al., 2015), although

the mean number of sessions attended by intervention recipients was similar. Despite these contextual differences, the impact of THPP by country was very similar, demonstrating the external validity of the intervention. In both countries, peers were trained to competently deliver THPP, with high proportions of women in the intervention arms completing their treatment. This indicates that delivery by peers was not seen as stigmatizing, and demonstrates a high degree of acceptability of a psychological therapy delivered by peers in community settings to mothers with depression in both contexts. Further, the intervention was shown to offer an appreciable improvement in health at low cost in THPP-Pakistan (incremental cost-effectiveness ratio US$ 15.50 over the whole trial period) and even cost saving in THPP-India (–US$ 93·53) (Fuhr et al., 2019; Sikander et al., 2019), despite monetary incentivisation for the peers contributing to 12% of the cost in the latter trial (D. Singla et al., 2014).

While the benefits of THPP were consistent for remission across three and six months post-childbirth, we observed stronger intervention effects at three compared to six months for symptom severity (PHQ-9 score) and disability (WHO-DAS). Similar effects were found in the individual trials (Fuhr et al., 2019; Sikander et al., 2019). This may be explained by the intervention design which puts emphasis on the first three months after child-birth by front-loading sessions antenatally and soon after childbirth, and/or by the natural remission rates of untreated depression over time (Austin et al., 2008; Posternak and Miller, 2001; Rojas et al., 2007; Tandon et al., 2018; Whiteford et al., 2013). The benefits at three months remain important to reduce the duration of the depression episode at such a critical time-point in childcare. Considering effect modification of the intervention, we observed greater benefits of THPP among women with shorter chronicity of depression at baseline and those primiparous. THPP may be best adopted as a first-step psychological intervention to be used in a stepped care system for maternal depression in LMIC, most suitable for lower-risk groups. The need for a stepped collaborative care model is highlighted by the fact that nearly half of women in the intervention arm across both countries did not achieve remission by 6 months. Future research should explore if peers are able to sign-post higher risk women, and refer them to primary or

specialist care where they may receive additional interventions. However, we did not observe a difference in the benefits of THPP by baseline severity, in contrast to previous studies of THP (Patel et al., 2017).

There are some limitations of this study. The control group received enhanced usual care in a well-resourced setting, thus the intervention effects might be greater in a health system where no such care is provided (Fuhr et al., 2019). The individual trials were not powered for assessing effect modifications; while the pooling of the data from the two trials provides more power we cannot rule out having missed some effect modifications, including those by country. Some baseline covariates were missing, most notably chronicity of depression in 30% of THPP-Pakistan participants. Outcome data were missing for approximately 10% of THPP-India participants, and 20% of THPP-Pakistan participants, although we adjusted for factors associated with missingness which yielded similar results to multiple imputation analyses in the individuals trials (Fuhr et al., 2019; Sikander et al., 2019).

THPP-India and THPP-Pakistan were pragmatic trials with high internal validity delivered in community settings to mothers recruited from routine healthcare settings. By aligning THPP with routine clinical practice and working alongside CHWs and clinicians, we were able to evaluate real-life treatment effects in two diverse South Asian contexts. This pooled analysis demonstrates the effectiveness, acceptability and feasibility of the THP intervention delivered by peers. This is important because although the theoretical model was the same in the two settings, there were contextual differences in implementation. The fact that the intervention effects were similar in the two trials demonstrates the external validity of the intervention, and hence potential for generalizability to other settings and populations.

THP uses cognitive behaviour therapy techniques and was designed to be delivered by lady health workers (Atif et al., 2017). THPP represents a further adaptation, with focus on behaviour activation

strategies to enable successful delivery by peers (Atif et al., 2017; Singla et al., 2019). Other interventions for perinatal depression include educational sessions led by healthcare professionals, or interpersonal therapy with problem-solving methods through group activities (Rahman et al., 2013) but to our knowledge none have been adapted for delivery by non-healthcare professionals. Although the benefits of THPP were relatively small (Rahman et al., 2013), it has proven to be cost-effective (Fuhr et al., 2019; Sikander et al., 2019). These results therefore open avenues for collaborative care, where peers can be the "missing" community agent or case manager to increase awareness and provide first-line interventions, and work alongside specialists in primary, secondary and tertiary care. Further, the delivery through peers provides opportunities for women in the community to develop skills and improve their chances of employability. To make this happen, there is a need in global mental health to advocate for accreditation of evidence-based and cost-effective low-intensity psychological interventions like THPP. We conclude that THPP is suitable for implementation as part of a stepped-care approach by engaging with the existing healthcare systems and the communities to treat perinatal depression in other contexts.

Contributors

DCF, BW, AL, HAW, AR and VP designed the THPP-India trial. EA, ADS, AJ, PK, and RK were responsible for intervention implementation and data gathering instruments in the THPP-India trial. BW, AL, and VP were responsible for THPP-India trial conduct. ED'S designed and managed the database for the THPP-India trial. SS, IA, DCF, HAW, VP and AR designed the THPP-Pakistan trial. IA, NA, AB, TB, SB, RL, MS and SZ were responsible for intervention implementation and data gathering instruments in the THPP-Pakistan trial. SS, AZ, and AR were responsible for THPP-Pakistan trial conduct. AZ designed and managed the database for the THPP-Pakistan trial. FV and HAW performed the statistical analyses. VP and AR provided oversight. FV and HAW drafted the manuscript. All authors read and approved the manuscript.

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Declaration of interest

Declarations of interest: none.

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FIGURE LEGENDS

Figure 1. A) Remission (PHQ-9 score <5) and B) symptom severity (PHQ-9 score) at 6 months by potential effect modifiers.

PHQ=Patient Health Questionnaire. Results are from linear or logistic generalized estimating equation models, adjusted for country, recruitment site, residence, union council, baseline symptom severity, treatment expectations, education, chronicity of depression, and time between screening and birth. The sizes of the squares indicating the point estimates are proportional to the number of participants in each category. These results are described further in Table 4 and Appendix Tables A3 and A4.

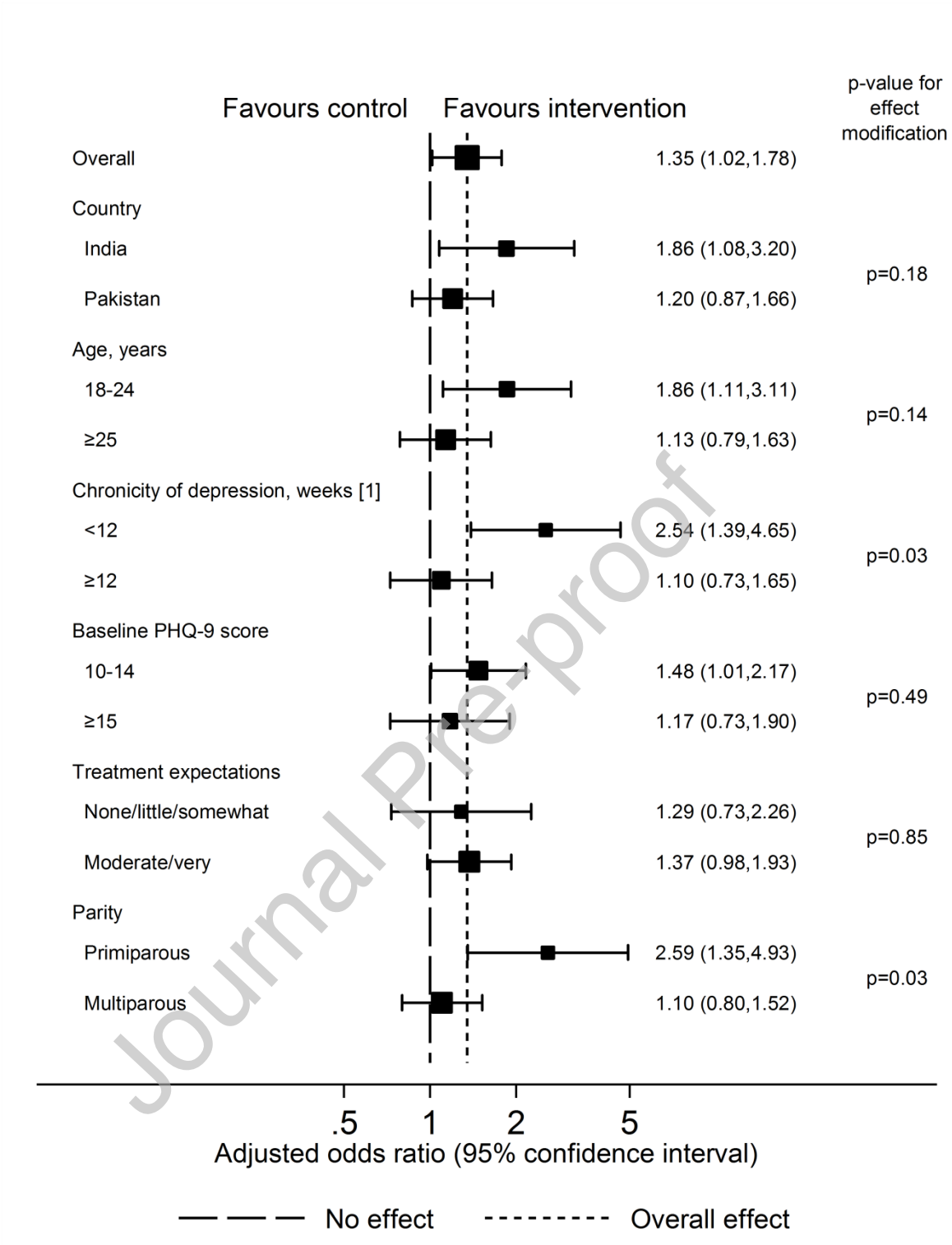

Fig-1A

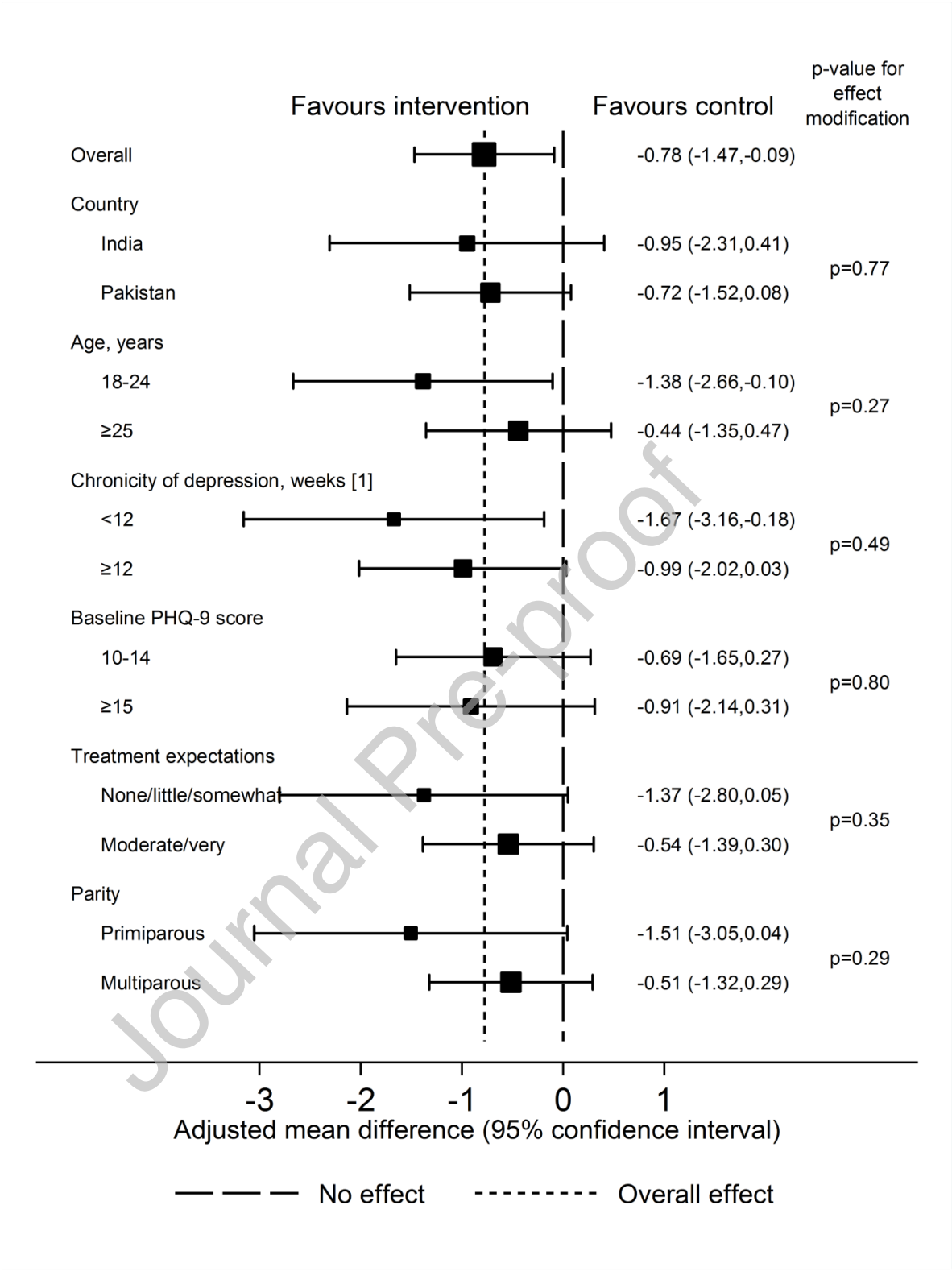

Fig-1B

TABLES

Table 1. Summary of the trial designs.

	THPP-India	THPP-Pakistan
Location	Goa	Rawalpindi
Study setting	Antenatal clinics in two hospitals and three primary health centers	Community setting in rural sub-district
Participants	Pregnant women aged ≥18 years with moderate to severe depression as defined by PHQ-9 score ≥10	
Intervention	THPP delivered as 6-14 individual sessions, each lasting 30-45 minutes, in four phases (prenatal, up to two months post childbirth, 3-4 months after childbirth, and 5-6 months after childbirth), plus enhanced usual care	THPP delivered as ten individual and four group sessions, each lasting 30-45 minutes, from the third trimester of pregnancy to six months after childbirth, plus enhanced usual care
Control	Enhanced usual care: Standard care from the gynecologist plus (1) patients and gynecologists were informed of participants screening results; (2) gynecologists were given the adapted mental health Gap Action Programme (mhGAP) treatment guidelines for perinatal depression; (3) participants were provided with an information sheet on healthcare during pregnancy and beyond	Enhanced usual care: Standard care from LHWs plus (1) all participants and LHWs were informed of participants screening results; (2) doctors and midwives at the primary healthcare centers were given the adapted mental health Gap Action Programme (mhGAP) treatment guidelines for perinatal depression; (3) participants were provided with an information sheet on healthcare during pregnancy and beyond
Peers	Women with children, a similar socio-demographic background as participants, and good communication skills. Recruited from the local community through word-of-mouth, particularly through key informants in women's self-help groups and CHWs. Financial incentives were paid based on sessions delivered, up to a maximum of Rs. 5900 (approximately US$80) per trial participant, plus a monthly honorarium of Rs. 100 (approximately US$1) to cover phone call costs	Women with children, a similar socio-demographic background as participants, and good communication skills. Identified through LHWs and elders, with recruitment and placement through primary healthcare centers. Peers received a travel allowance for supervision meetings and a phone card/top-up to be able to stay in touch with their respective supervisors in case of support needed. No remunerations were paid for delivering sessions
Randomization	Individually-randomized (1:1 allocation ratio), stratified by place of residence (rural/urban)	Cluster-randomized (1:1 allocation ratio; 40 village clusters), stratified by 11 union councils
Blinding	Outcome assessors were blinded to participants' treatment allocation	
Primary outcomes	Symptom severity (PHQ-9 score) and remission (PHQ-9 <5) at 6 months post-childbirth	
Secondary outcomes[a]	Symptom severity (PHQ-9 score) at 3 months post-childbirth Remission (PHQ-9 score <5) at 3 months post-childbirth Recovery (PHQ-9 score <5 at both 3 and 6 months post-childbirth) Response I (PHQ-9 score <10 at both 3 and 6 months post-childbirth) Response II (≥50% reduction from baseline PHQ-9 score at both 3 and 6 months post-childbirth) WHO-DAS score, at 3 and 6 months post-childbirth Number of days unable to work in the last month, at 3 and 6 months post-childbirth MSPSS score, at 3 and 6 months post-childbirth	
Recruitment period and follow up	October 2014-June 2017	October 2014-March 2017
Number of participants	280	570

The trial designs have been described previously in detail (Sikander et al., 2015). CHW=community health workers. LHW= Lady Health Worker. THPP=Thinking Healthy Programme Peer-delivered. PHQ=Patient Health Questionnaire. MSPSS=Multidimensional Scale of Perceived Social Support. WHO-DAS=World Health Organization Disability Assessment Schedule. [a]Maternal secondary outcomes only.

Table 2. Baseline characteristics by trial.

	THPP-India	THPP-Pakistan	Total
Number enrolled	280	570	850
Age, years (mean (SD; range))	25 (4.6; 18-41)	27 (4.8; 18-45)	26 (4.8; 18-45)
Level of education (n (%))			
No formal education	34 (12%)	107 (19%)	141 (17%)
Up to primary	120 (43%)	39 (7%)	159 (19%)
Up to secondary	90 (32%)	333 (58%)	423 (50%)
Beyond secondary	36 (13%)	91 (16%)	127 (15%)
Occupation (n (%))			
Does not work	237 (85%)	533 (94%)	770 (91%)
Works	43 (15%)	37 (6%)	80 (9%)
Chronicity of depression, weeks (n (%))[a]			
<12	173 (62%)	73 (18%)	246 (36%)
≥12	107 (38%)	326 (82%)	433 (64%)
Symptom severity (PHQ-9 score) (median (IQR))	12 (11,15)	14 (12,17)	14 (11,17)
Symptom severity category (n (%))			
Moderate (PHQ-9 score 10-14)	197 (70%)	312 (55%)	509 (60%)
Moderately severe (15-19)	67 (24%)	187 (33%)	254 (30%)
Severe (20-27)	16 (6%)	71 (12%)	87 (10%)
MSPSS score (mean (SD))	5 (1.1)	4 (1.4)	4 (1.4)
Participant's expectation of usefulness of counseling (n (%))[b]			
Not useful	1 (0%)	4 (1%)	5 (1%)
A little	55 (20%)	26 (5%)	81 (10%)
somewhat useful	54 (19%)	114 (20%)	168 (20%)
Moderately useful	58 (21%)	246 (43%)	304 (36%)
Very useful	112 (40%)	178 (31%)	290 (34%)
Parity (n (%))			
Primiparous	119 (43%)	102 (18%)	221 (26%)
Multiparous	161 (57%)	468 (82%)	629 (74%)
Previous miscarriage or still birth (n (%))			
None	261 (93%)	377 (66%)	638 (75%)
One/more	19 (7%)	193 (34%)	212 (25%)
Any domestic violence in last three months (n (%))[c]			
No	243 (87%)	486 (87%)	729 (87%)
Yes	37 (13%)	71 (13%)	108 (13%)
Time between screening and birth of child, months (mean (SD))[d]	4 (1.6)	3 (1.2)	3 (1.5)

Percentages are of non-missing values. PHQ=Patient Health Questionnaire. MSPSS=Multidimensional Scale of Perceived Social Support. SD=standard deviation. [a]Missing for 171 THPP-Pakistan participants. [b]Missing for 2 THPP-Pakistan participants. [c]Missing for 13 THPP-Pakistan participants. [d]Missing for 11 THPP-India and 85 THPP-Pakistan participants.

Table 3. Process indicators.

	THPP-India	THPP-Pakistan
Peers		
Peers trained and delivered at least one session (number)	26	66
Age of peers, years (mean, SD)	38 (7.5)	30 (5.5)
Years of education completed by peers (mean, SD)	12 (2.7)	12 (2.5)
Peers lost during the trial (number, %)	0	23 (35%)
Attendance to supervisions (%)	67%	88%
Participants in the intervention arm		
Number[a]	138	258
Sessions attended (mean, SD)[b]	9.8 (4.3)	10.9 (3.9)
Prenatal sessions attended (mean, SD)[c]	4.5 (1.9)	3.7 (1.7)
Postnatal sessions attended (mean, SD)[d]	5.4 (2.9)	7.3 (2.7)
Attended at least 6 sessions	113 (82%)	230 (89%)
Attended at least 10 sessions	87 (63%)	201 (78%)
Completed treatment[e]	99 (72%)	201 (78%)

SD=standard deviation. [a]Excluding 2 women in THPP-India and 25 in THPP-Pakistan who were discontinued as per protocol before month 3 due to child death, still birth or abortion. [b]Of possible 14 sessions in each trial. [c]Of possible 6 sessions in THPP-India and 5 in THPP-Pakistan. [d]Of possible 8 sessions in THPP-India and 9 in THPP-Pakistan. [e]Defined in THPP-India as attended at least 6 sessions, with at least 1 session in each of four phases (prenatal, and 1-2, 3-4 and 5-6 months postnatal); defined in THPP-Pakistan as attended at least 10 sessions.

Table 4. Primary and secondary outcomes.

	Number of participants[a]		Mean (SE) or number (%)[a]		Intervention effect (adjusted mean difference or odds ratio; 95% CI)[b]	P value
	Control	Interven-tion	Control	Interven-tion		
Primary outcomes						
Symptom severity (PHQ-9 score) at 6 months						
Overall	355	349	6.0 (0.3)	5.1 (0.3)	-0.78 (-1.47,-0.09)	0.03
India	129	122	4.5 (0.4)	3.5 (0.4)	-0.95 (-2.31,0.41)	
Pakistan	226	227	6.8 (0.4)	6.0 (0.4)	-0.72 (-1.52,0.08)	
Remission (PHQ-9 score <5) at 6 months						
Overall	355	349	178 (50%)	201 (58%)	1.35 (1.02,1.78)	0.04
India	129	122	77 (60%)	89 (73%)	1.86 (1.08,3.20)	
Pakistan	226	227	101 (45%)	112 (49%)	1.20 (0.87,1.66)	
Secondary outcomes						
Continuous variables						
Symptom severity (PHQ-9 score) at 3 months	333	346	7.1 (0.4)	5.5 (0.3)	-1.84 (-2.43,-1.25)	<0.001
WHO-DAS score						
3 months	332	346	17.0 (1.0)	14.2 (0.9)	-3.17 (-5.73,-0.61)[c]	0.02[c]
6 months	354	349	16.0 (1.0)	13.6 (0.9)	-2.11 (-4.77,0.55)	0.12
Number of days unable to work in last month						
3 months	332	346	1.7 (0.3)	1.6 (0.3)	-0.24 (-0.86,0.39)	0.46
6 months	354	349	1.6 (0.2)	1.6 (0.3)	0.02 (-0.51,0.55)	0.95
MSPSS score						
3 months	333	345	4.7 (0.1)	4.9 (0.1)	0.17 (0.03,0.31)	0.01
6 months	354	349	4.7 (0.1)	5.0 (0.1)	0.27 (0.11,0.43)	0.001
Categorical variables						
Remission (PHQ-9<5) at 3 months	333	346	155 (47%)	186 (54%)	1.34 (1.13,1.60)	0.001
Recovery (PHQ-9<5 at both 3 and 6 months)	317	325	100 (32%)	135 (42%)	1.60 (1.21,2.10)	0.001
Response I (PHQ-9<10 at both 3 and 6 months)	317	325	188 (59%)	224 (69%)	1.57 (1.16,2.10)	0.003
Response II (≥50% reduction from baseline PHQ-9 at both 3 and 6 months)	317	325	144 (45%)	190 (58%)	1.69 (1.27,2.24)	<0.001

PHQ=Patient Health Questionnaire. MSPSS=Multidimensional Scale of Perceived Social Support. WHO-DAS=World Health Organization Disability Assessment Schedule. SE=standard error. CI=confidence interval. [a]India and Pakistan trials combined for the secondary outcomes. [b]Linear or logistic GEE models, adjusted for country, recruitment site, residence, union council, baseline symptom severity, treatment expectations, education, chronicity of depression, and time between screening and birth (see methods). Baseline treatment expectations missing for one woman in Pakistan control group, therefore models are based on one fewer woman than the numbers indicated. Country-level intervention effects are based on models with interaction between group and country. [c]Using independent correlation matrix due to convergence problems when using exchangeable correlation structure.