Delivering the Thinking Healthy Programme for perinatal depression through peers: an individually-randomised controlled trial in India

Authors: Daniela C Fuhr[1], Benedict Weobong[2,3], Anisha Lazarus[4], Fiona Vanobberghen[5], Helen A Weiss[5], Daisy Radha Singla[6], Hanani Tabana[7], Ejma Afonso[4], Aveena De Sa[4], Ethel D'Souza[4], Akankasha Joshi[4], Priya Korgaonkar[4], Revathi Krishna[4], LeShawndra N Price[8], Atif Rahman[9,V], Vikram Patel[4,10,V]

[1]Faculty of Public Health and Policy, Department of Health Services Research and Policy, London School of Hygiene and Tropical Medicine, UK (Dr DC Fuhr, DrPH)

[2]Faculty of Epidemiology and Population Health, Department of Population Health, London School of Hygiene and Tropical Medicine, UK (Dr B Weobong, PhD)

[3]College of Health Sciences, School of Public Health, Department of Social and Behavioural Sciences, University of Ghana (Dr B Weobong, PhD)

[4]Sangath Centre, Socorro Village, Bardez- Goa, Goa, India (Dr B Weobong, PhD; Ms Anisha Lazarus, Mphil; Ms Ethel D'Souza, M.Com.; Ms Ejma Afonso, MA; Ms Aveena De Sa, MA, MSc; Ms Akankasha Joshi, MA; Ms Priya Korgaonkar, MA; Ms Revathi Krishna, MSc; Prof V Patel, PhD)

[5]MRC Tropical Epidemiology Group, Faculty of Epidemiology and Population Health, Department of Infectious Disease Epidemiology, London School of Hygiene & Tropical Medicine, London, UK (Dr F Vanobberghen, PhD; Prof HA Weiss, PhD)

[6] Department of Psychiatry, Sinai Health System and University of Toronto, Toronto, Canada (Dr DR Singla, PhD)

[7]School of Public Health, Faculty of Community and Health, University of the Western Cape, Cape Town, South Africa (Dr H Tabana, PhD)

[8]National Institute of Mental Health, National Institutes of Health, USA (Dr LN Price*)

[9] Institute of Psychology, Health and Society, University of Liverpool, Liverpool, UK (Prof A Rahman, PhD)

[10] Department of Global Health and Social Medicine, Harvard Medical School, Boston, USA (Prof V Patel, PhD)

[V] Contributed equally

* Currently working at the National Heart, Lung, and Blood Institute, National Institutes of Health

Correspondence to Prof V. Patel, Harvard Medical School, Department of Global Health and Social Medicine, Boston, USA, e-mail: vikram_patel@hms.harvard.edu

SUMMARY

Background: The Thinking Healthy Programme (THP) is a psychological intervention recommended for the treatment of perinatal depression. We assessed the effectiveness and cost-effectiveness of THP delivered by peers (THPP) in Goa, India.

Methods: In this single-blind, individually-randomised controlled trial, we recruited pregnant women aged ≥18 years attending antenatal clinics, who scored ≥10 on the Patient Health Questionnaire (PHQ-9). Participants were randomly allocated (1:1) to THPP plus enhanced usual care (EUC), or to EUC alone in randomly-sized blocks, stratified by area of residence. Allocation was concealed using sequentially-numbered opaque envelopes. Primary outcomes were severity of depressive symptoms (PHQ-9 score) and remission (PHQ-9 score <5) 6 months post-birth assessed by researchers masked to the treatment allocation. Analyses were by intention to treat, adjusting for covariates defined *a priori* or that showed imbalance at baseline. The trial is registered with ClinicalTrials.gov (NCT02104232).

Findings: 280 women were enrolled between 24th October 2014 and 22nd June 2016 (140 per group). At 6 months, 122 (87%) and 129 (92%) women in the THPP plus EUC, and EUC alone groups, respectively, contributed primary outcome data. There was evidence of higher prevalence of remission at 6 months in the THPP plus EUC versus EUC alone group (n=89 (73%) versus n=77 (60%), respectively; prevalence ratio (PR)=1·21; 95% confidence interval (CI) 1·01 to 1·45, p=0·04), but weaker evidence for lower symptom severity (mean 3·47, standard deviation (SD) 4·49 versus 4·48 (SD=5·11), respectively; standardised mean difference (SMD)=-0·18; 95% CI -0·43 to 0·07, p=0·16).Repeated measures analyses over the duration of the trial (measured at 3 and 6 months post-birth) showed beneficial effects on symptom severity (SMD -0·37, 95% CI -0·88 to -0·24, p=0·01), remission (PR=1·21, 95% CI 1·01 to 1·41, p=0·02), WHO-Disability Assessment Schedule (WHO-DAS) scores (SMD=-0·32, 95% CI -0·76 to -0·21, p=0·02) and Multidimensional Scale of Perceived Social Support (MSPSS) scores (SMD=0·51, 95% CI 0·43 to 1·20, p=0·02). . The incremental societal cost per unit improvement on PHQ-9 was –US$ 29·64 (95% CI-32·88 to -26·41) at 3 months, and –US$93·53 (95% CI -180·21 to -6·84) for the whole duration of the trial, with a 87% likelihood of being cost-saving in the study setting. The mean cost of providing THPP was US$ 1·36 per beneficiary (95% CI 1·32 to 1·39). There was no evidence of differences in serious adverse events by group, except stigmatisation was more often reported in the EUC alone (9%) versus the THPP plus EUC group (4%; p=0·08).

Interpretation: THPP had a moderate effect on symptom severity and remission from perinatal depression over the 6 month post-natal period. THPP is relatively cheap to deliver and pays for itself through reduced health care, time and productivity costs.

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INTRODUCTION

Depression, the leading cause of disability worldwide,[1] is a major contributor to the overall global burden of disease in women. Perinatal depression, defined as depression occurring during pregnancy or within the first year postpartum,[2] affects between 5-25% of women.[3] Perinatal depression has been associated with an array of negative child outcomes ranging from impaired physical health to poor neurodevelopmental and behavioural outcomes.[4]

In many low-resource settings, perinatal depression is largely undiagnosed and untreated, due to human resource constraints and ill-equipped health systems, leaving over 90% of those in need untreated.[5] Psychological interventions for perinatal depression in low and middle-income countries have shown to be effective when delivered by non-specialist providers.[6] The Thinking Healthy Programme (THP) is such a programme for perinatal depression and is the first "low-intensity" psychological intervention recently adopted by the World Health Organization (WHO).[7] The active ingredient of THP is based on cognitive behavior therapy (CBT) and includes strategies incorporating behavioural activation, active listening, collaboration with the family, guided discovery and homework. THP - delivered by female community health workers (CHWs) - more than halved the prevalence of perinatal depression among women in a large community-based randomised controlled trial in Pakistan.[8] Despite the effectiveness shown, competing demands of CHWs have greatly limited their role in scaling up the THP.[9]

The aim of the THP delivered by peers (THPP) programme was to modify THP for delivery by trained peer counsellors (referred to as 'Sakhis' in the Indian study setting) and to evaluate its effectiveness and cost-effectiveness compared to enhanced usual care (EUC).[10] By using Sakhis we intend to improve scalability of this intervention by demonstrating the feasibility and effectiveness of task-sharing to a wider range of non-specialist providers. We adapted the intervention for implementation in two diverse rural and peri-urban contexts in South Asia (India and Pakistan).[11] In this paper, we describe the findings of the trial in India where THPP was delivered through individual sessions. The results of the Pakistan trial, which delivered THPP through both individual and group sessions, are reported in the companion paper.[12]

METHODS

Setting

The study was conducted in the north district of the state of Goa. Its population of 1.46 million makes Goa one of India's smallest states, with 62.2% of the population living in urban areas.[13] Goa has a high literacy rate (male 92.6%, female 84.2%), an even gender ratio (50.7% male, 49.3% female)[13] and a fertility rate of 1.8 per woman.[14] The most widely spoken language is Konkani, followed by Marathi, Hindi and English. Public healthcare is provided through a network of healthcare providers working in urban primary health centres, sub-centres, community health centres and a district hospital.[15] Antenatal care coverage is high in India with 89% of women attending at least four antenatal care visits (urban areas 91%; rural areas 86%).[16]

Study design and participants

THPP in India was a single-blind, individually-randomised controlled trial. Participants were women in their second or third trimester of pregnancy aged ≥18 years, recruited from two antenatal clinics and two primary health centres. Participants who did not speak Konkani, Hindi or Marathi, or who were in need of immediate medical or psychiatric inpatient care were not eligible. Potentially eligible participants were screened for depression with a locally-validated version of the Patient Health

Questionnaire 9 (PHQ-9) after providing written informed consent for screening (or witnessed informed consent/audio-recordings for illiterate participants). Women who screened positive (PHQ-9 score ≥10) were eligible for enrolment. The PHQ-9 cut-off score of ≥ 10 has shown a positive predictive value of 55[17] , and has previously been used in the study context.[18] Ethical approval was obtained from the Institutional Review Boards (IRBs) at the London School of Hygiene and Tropical Medicine, Sangath (the implementing institution in India), and the Indian Council of Medical Research. The study protocol has been published previously.[10]

Randomisation and masking

Eligible, consenting participants were randomised to either THPP plus EUC or EUC alone using a 1:1 allocation ratio. The randomisation list, in randomly-sized blocks of four or six stratified by area of residence (urban/rural), was generated by an independent statistician. The randomisation code was concealed and allocated using sequentially-numbered opaque sealed envelopes,[19] an allocation concealment scheme which has been used successfully in previous trials in this setting.[18] Research assistants opened the envelopes immediately after consent for enrolment and the baseline questionnaire had been completed, and assigned participants to the THPP plus EUC or EUC alone groups. Daily cross-checks were done by the data manager to check that allocations were consistent with the allocation code. Independent outcome assessors and the gynaecologists providing care to participants in both arms were masked to treatment allocation of the participant. Outcome assessors had no interaction with the study team. All members of the Trial Steering Committee (TSC), except the data manager (ED), remained masked to the allocation status until the data were unmasked after interpretation of the results at a TSC meeting on 23 October 2017.

Procedures

After enrolment and before randomisation, a baseline socio-demographic questionnaire was administered to participants to collect data on potential moderators of treatment effects (including age, participant's treatment expectations, chronicity and severity of depression)[20].

Treatment as usual was enhanced as usual care for perinatal depression in India is no care at all. Participants in the EUC alone group received standard care from the gynaecologist plus enhanced treatment: (1) patients and gynaecologists were informed that the participant screened positive for depression; (2) gynaecologists were given the adapted mental health Gap Action Programme (mhGAP) treatment guidelines for perinatal depression which included information on how to refer severe cases and patients with suicide risk to specialist mental health care; and (3) participants were provided with an information sheet including details on where to seek appropriate health care during pregnancy and beyond.

Participants in the intervention group received THPP in addition to EUC. THPP was developed during a two-year formative research phase.[11,15] Two major adaptations, related to the content and delivery mechanism, were made to the original THP intervention to make it deliverable by peers. Firstly, we shifted the focus from CBT (the active ingredient of the original THP intervention) to behavioural activation, because formative research indicated that CBT is more difficult for lay providers such as peers to learn.[11] Secondly, we reduced the number of sessions. THPP was delivered over 6-14 individual sessions in four phases over 7-12 months depending on the eligible trimester of recruitment, with sessions lasting between 30 and 45 minutes each. The four phases were: 1) prenatal phase focusing on the second or third trimester of pregnancy in which one to six sessions were delivered; 2) early infancy (first two months after childbirth; one to four sessions); 3) middle infancy

(three to four months post-childbirth; two sessions); and 4) late infancy (five to six months post-childbirth; two sessions). Treatment completion was defined as receiving a minimum of six sessions with at least one session within each of the four phases.

The peers who delivered THPP were lay women (i.e. without any mental health training) who have shown an interest or desire to help and support other women within their community). They were middle-aged with children, and showed a similar socio-demographic background as participants and had good communication skills; they were referred to as "Sakhi" which translates to "friend" in Hindi. Additional criteria of Sakhis are published elsewhere.[15] Sakhis were recruited from the local community through word-of-mouth, particularly through key informants in women's self-help groups and CHWs responsible for the well-being and nutrition of mothers and their new-borns.
In total, 26 Sakhis entered the trial and each received 25-40 hours of classroom-based training focusing on intervention content and relationship-building skills. This included sessions on dealing with difficult situations, recognition of symptom worsening, and serious adverse events (SAEs). Training was primarily interactive and comprised discussion and role-plays. A clinical internship period of two months followed the training, during which Sakhis delivered two to four sessions of THPP to at least two mothers. At the end of their training and internship period, Sakhis were assessed on their competence using standardized role plays. Only Sakhis who passed pre-defined competence levels were selected for THPP delivery. Sakhis and trial participants were matched by location, i.e. a Sakhi delivered THPP to participants living closest to them. THPP sessions were delivered at the participant's home, unless the participant chose a different venue for intervention delivery. If a Sakhi's caseload exceeded four women, the next closest-living Sakhi was chosen. Sakhis were instructed to schedule their first sessions with the participants within three days of recruitment.

During the trial, Sakhis continued to receive fortnightly group supervision sessions (with four to five Sakhis per group), once a month with a supervisor present and once a month without a supervisor being present. A peer group leader was chosen on a rotation basis at each session to lead the discussion; when the supervisor was present the peer group leader and supervisor co-facilitated the session together. An audio-recorded THPP session delivered by a Sakhi was played at each session, and successes and difficulties were discussed. The audio-recordings were rated on the Therapy Quality Scale (TQS)[21], and feedback was exchanged in the group.

In addition, audio-recordings of a random sample of 5% of sessions stratified by phase were rated on the TQS[21] by independent raters experienced in CBT. The mean score across 18 items (0-2) was used to monitor quality of intervention delivery. Other fidelity measures included the number and duration of sessions delivered, number of participants who completed treatment, and number of participants who were treatment failures (and were referred to specialist mental health care).

Outcomes

Primary outcomes were symptom severity (PHQ-9 score) and remission (PHQ-9 score <5) assessed at 6 months post-childbirth. Remission was originally defined as PHQ-9 score <10 in the published trial protocol[10]; however, this was amended to PHQ-9 score <5 as a more robust and clinically meaningful measure of remission[17] after discussion with the TSC and prior to finalisation of the analysis plan. We confirmed that we would have adequate power for this outcome in October 2016, using data from the 6 months outcome data in the initial 136 participants, pooled across the arms. Approval for this change was obtained from the Data Safety Monitoring Board (DSMB) of the National Institute of Mental Health (NIMH) and the IRBs before unblinding.

Secondary outcomes were symptom severity and remission at 3 months and recovery (PHQ-9 score <5 at both 3 and 6 months). Further secondary outcomes at 3 and 6 months were disability (WHO Disability Assessment Schedule, WHO-DAS score), number of days unable to work in the last month, maternal support (Multidimensional Scale of Perceived Social Support, MSPSS score), exclusive breastfeeding (WHO definition, namely feeding breastmilk exclusively in the previous 24 hours), and infant weight- and height-for-age assessed with z-scores. Minimal clinically important difference (MCID) was assessed by asking participants how much of their tension had changed since entering the study. We also collected information on SAEs (death of the participant due to any cause, loss of child, suicide attempt, hospitalisation, victimisation, infant abuse/neglect, stigmatization and reported violence towards others).

A tailored version of the Client Service Receipt Inventory (CSRI) (a copy can be made available from the corresponding author) was used as an interviewer-administered measure to collect self-reported information on health service use, including the intervention, at 3- and 6-months post-childbirth for the purpose of estimating costs and cost-effectiveness of the intervention. [22]Evaluation of costs and effects was based on both a health system and a broader societal perspective. Health system costs were derived from in-patient and out-patient costs, costs of laboratory tests and investigations, medications, and intervention delivery costs (that is, time taken by Sakhis to deliver each THPP session, including training and supervision, plus travel time and transportation costs for home visits including 'no-shows'). Societal costs encompassed these health system costs and also time and productivity costs of mother's time out of usual activities because of their health, as well as time costs for mothers (and accompanying family members) related to the use of health services. Care-giver and mother's time-costs were valued using the human capital approach making use of different daily wage rates recommended in 2015 by the Indian Office of the Labour Commissioner (see appendix O for a summary of unit costs of these wage group classifications). Unit costs for doctor contacts and inpatient stays were inflated (using International Monetary Fund consumer price index) to 2015 prices using unit costs that had previously been used for an economic evaluation in Goa.[23] Unit costs of counselling sessions by peers and other health care services were calculated on the basis of local facility records using simplified costing templates (see appendix O for a summary of unit costs used in this analysis). Costs were evaluated and reported for three periods of time: 1) the 6-month period of service use covering the third trimester and the first 3 months post-childbirth; 2) the 3-month period of service use since the 3-month post-childbirth assessment; and 3) the 9-month period of service use covering the third trimester and the first 6 months post-childbirth (that is, the total period of the trial).

Statistical analysis

As per our trial protocol, assuming an intra-cluster correlation (within-peer counsellor clustering) of 0.05 in the intervention group, 25-30 peers, and loss to follow up of 15%, 280 participants would provide 84% power to detect a difference for the primary outcome of remission of 78% in the THPP plus EUC group compared to 60% in the EUC alone group; and 84% power to detect a standardised mean difference (SMD) of 0·4 for the primary outcome of PHQ-9 score/symptom severity.[10] The original sample size calculations were based on remission (defined as PHQ-9>10) in the THP trial in Pakistan[8] and conditional power was estimated based on blinded preliminary data from 134 participants (prevalence of 67% across the two arms); for symptom severity it was also based on the THP trial in Pakistan[8] (using the THP Hamilton Depression Rating Scale at 6 months: THP group mean 4·5, SD 6·0; control group mean 8·7, SD 7·4). We assumed a more conservative effect size to allow for the possibility of contamination between arms and a diluted effect due to the delivery of the intervention by Sakhis.

Outcomes were analysed on an intention-to-treat basis, among complete cases and adjusted for recruitment centre (with the primary health centres combined due to low frequencies), baseline PHQ-9 score, and residence (urban/rural) *a priori*, plus those showing imbalance at baseline (treatment expectations, education and chronicity). For continuous outcomes, we used linear regression models, with results reported as standardised mean differences (SMD). The SMDs were calculated as the mean difference from the adjusted regression model divided by the pooled standard deviation. For categorical outcomes, we used logistic regression models, with results reported as prevalence ratios (PR), estimated using the marginal standardisation technique, with 95% CIs estimated using the delta method.[24] For each primary outcome, we assessed effect-modification of treatment effect with *a priori*-defined potential moderators and we performed repeated measures analyses (pooling the 3 and 6 months results) using generalised estimating equations to account for within-person correlations. We estimated MCID as a patient-centered metric that captures both the magnitude of improvement and the value the patient places on that improvement, using an anchor-based approach[25] via a receiver operating characteristic (ROC) curve. That is, we examined the cut points for relative reduction in PHQ-9 at 6 months versus baseline for sensitivity and specificity against the "gold standard" of the mother's subjective sense of improvement, classified as better if answered "a lot better" or "a little better".[26]Windows of -1 to +2 months were permitted for the follow-up visits; in sensitivity analyses these were restricted to -0.5 to +1 months. Sensitivity analyses included multiple imputation for missing outcome data, adjustment for clustering by Sakhi using generalised estimating equations, and fitting alternative models for PHQ-9 score, which had a positively skewed distribution (Poisson with robust standard errors, and negative binomial, respectively).

Cost and cost-effectiveness was evaluated at 3 and 6 months post-childbirth, and for the period of the trial as a whole, both from the health system (health system costs) and societal perspective (health system costs plus impacts on the productivity of patients and their families). We used ordinary least squares regression models with margins in order to generate predicted means. All analyses were adjusted for the same baseline covariates as in the effectiveness analysis. Incremental cost-effectiveness ratios (ICERs) and their respective confidence intervals were derived using a non-parametric Monte-Carlo bootstrapping technique (with 1000 replications), involving random resampling of effectiveness outcomes and costs for intervention and control group.[27] A distribution plot of mean incremental costs and effects was generated on a cost-effectiveness plane in order to examine the probability of the intervention being cost-effective.

Statistical analyses were conducted using Excel 2016 and Stata 15 for the cost-effectiveness analyses, and all other analyses were conducted in Stata 14. The DSMB of the NIMH oversaw the study. The trial is registered with ClinicalTrials.gov, number NCT02104232.

Data sharing

Data from our trial has been made available at the LSHTM data repository available at http://datacompass.lshtm.ac.uk/ (doi:10.17037/DATA.00000793).

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report, except for LNP who was a Scientific Collaborator, under the cooperative agreement that funded the research. DCF, VP, FV, HAW, BW and ES had full access to trial data. DCF and VP had final responsibility for the decision to submit for publication.

RESULTS

Between 24th October 2014 and 22nd June 2016, 118,260 women were assessed for eligibility and 6369 (5%) were screened using the PHQ-9, of whom 333 (5%) screened positive (PHQ-9 score ≥10; Figure 1). A total of 280 (84%) women consented, and were enrolled, with 140 randomly allocated to each group. Baseline characteristics were broadly similar by treatment group (Table 1). The median PHQ-9 score was 13 in the THPP plus EUC group and 12 in the EUC group, the mean age was 25 years, all participants but one were married, the majority (85%) were not working and most (87%) did not have schooling beyond secondary school. There was no evidence of a difference in baseline characteristics between participants and those who declined (appendix A).

Overall, 122 (87%) women in the THPP plus EUC group contributed primary outcome data at 6 months, compared to 129 (92%) in the EUC group (p=0.17; Figure 1). There was no evidence of a difference in baseline characteristics by having 6-month outcome data or not (appendix B), nor by having the visit in the protocol-defined window (appendix C). The final 6-month visit was completed on 9th June 2017.

We observed a modest effect of the intervention on the prevalence of remission at 6 months (89 (73%) versus 77 (60%); PR=1·21; 95%CI 1·01 to 1·45; p=0.04; Table 2). There was weak evidence of an intervention effect on symptom severity at 6 months (mean PHQ-9 score 3·47 (standard deviation (SD) 4·49) versus 4·48 (SD 5·11); SMD=-0·18, 95% CI -0·43 to 0·07; p=0.16). We found some evidence of effect modification of remission by chronicity of depression (p=0.04) with women showing shorter duration of chronicity being more likely to respond; no other effect moderation was observed (appendices D and E). Primary outcome results were robust to sensitivity analyses restricting the analysis window (appendix F), adjustment for clustering by therapist, alternative model specifications, and imputation for missing values (appendices G and H respectively).

Figure 2 shows the intervention effect on remission and recovery by group over 6 months. There was evidence of intervention effects on depression symptom severity at 3 months (SMD=-0·34, 95%CI -0·59 to -0·09, p=0·01), on disability scores (SMD=-0·34, 95%CI -0·59 to -0·10, p=0·009) and social support scores (SMD=0·32, 95%CI 0·06 to 0·57, p=0·02) at 3 months, and on social support scores at 6 months (SMD=0·27, 95%CI 0·02 to 0·52, p=0·04). There was evidence of intervention effects on recovery (PR=1·35, 95%CI 1·03 to 1·78, p=0·03), and weaker evidence of an intervention effect on remission at 3 months, , and WHO-DAS score at 6 months (p=0·08, 0·16, and 0·16, respectively). Secondary outcomes presented as adjusted mean differences and odds ratios are presented in appendix I. MCID analyses are included in appendix J.

There was no evidence of an intervention effect at either 3 or 6 months on other secondary outcomes (i.e. the number of days unable to work in the last month (p=0·98 and 0·70, respectively), breastfeeding (p=0·41 and 0·65) or infant weight (p=0·42 and 0·84) and height (p=0·58 and 0·89)).

In repeated measures analyses, we found no evidence of group-by-time interactions and therefore assumed a constant intervention effect at 3 and 6 months (Appendix K). This showed evidence of a beneficial intervention effect on symptom severity (SMD -0·37, 95% CI -0·88 to -0·24, p=0·01), prevalence of remission (PR=1·21, 95% CI 1·01 to 1·41, p=0·02), WHO-DAS score (SMD=-0·32, 95% CI -0·76 to -0·21, p=0·02), and MSPSS score (SMD=0·51, 95% CI 0·43 to 1·20, p=0·02) but no evidence of an effect on number of days unable to work in the last month (p=0·77) (see table 3).

Overall, 51 (18%) participants had at least one SAE, with the most common being hospitalisations, victimisation and stigmatisation (appendix L). There was no evidence of any differences between the groups, except stigmatisation was somewhat more often reported in the EUC alone (9%) than the THPP plus EUC group (4%; p=0·08).

The overall mean number of sessions attended by participants in the intervention group was 9·8 (95% CI 9·1 to 10·6), with a mean duration of 38 minutes. The mean number of sessions attended in phase one was 4·5 out of a possible six sessions (95% CI 4·2 to 4·8), in phase two out of four sessions, 2·5 (95% CI 2·2 to 2·8), in phase three out of two sessions, 1·4 (95% CI 1·3 to 1·6), and in phase four out of two sessions, 1·4 (95% CI 1·3 to 1·6). 99/138 (72%) participants met the criteria for treatment completion and 14/122 (11%) were treatment failures (participants in the intervention group needing referral to specialist mental health care at the end of treatment at 6 months either because of clinical deterioration or lack of improvement). The mean therapy quality score as determined by independent raters was 1·51 (95% CI 1·40 to 1·62) (n=42) indicating average to good therapy quality.

The mean cost of providing THPP was US$ 1·36 per beneficiary (95% CI 1·32 to 1·39) and 12% of this cost was attributed to incentives alone (appendix M). When other health care costs (health system perspective) and time and productivity costs were added (societal perspective), costs were appreciably (but not statistically significantly) lower in the THPP plus EUC group at 3 and 6 months post-childbirth (table 4). The adjusted mean difference in societal cost was -US$ 53·98 (95% CI -109·64 to 1·68) and -US$17·69 (95%CI -45·94 to 10·54) at 3 and 6 months post-childbirth, respectively. Combining these cost findings with the primary outcome measure of symptom relief gave rise to dominant and, in some cases, also statistically significant ICERs; at 3 months post-childbirth, the incremental societal cost per unit improvement on PHQ-9 was –US$ -29·64 (-32·88 to -26·41) and for the whole period of the trial it was –US$ 93·53 (95%CI -180·21 to -6·84), indicating that THPP is a cost-saving intervention strategy (table 4). At 6 months post-childbirth, though THPP plus EUC was not cost-saving in the sense of better outcome and lower cost, it was still cost-effective, with cost-effectiveness planes revealing that THPP plus EUC has an 87% chance of being both more effective and less costly than EUC alone when a societal perspective is adopted (Figure 3B) and a 72% chance under a health system perspective (Figure 3A). ICERs for remission and recovery also demonstrated that THPP plus EUC was cost-saving; for example, the incremental cost per additional recovered case is –US$ 151·07 (health system perspective) and –US$ 736 (societal perspective). Costs per beneficiary (appendix M), and service use patterns (table 1) and the costs of health care as well as foregone time and productivity (table 2) are detailed in appendix N for the intervention and control group at 3 and 6 month post-childbirth, respectively.

DISCUSSION

THPP, a psychological intervention for the treatment of moderate to severe perinatal depression, delivered by peers (Sakhis) in community settings in Goa, India, produced better outcomes than EUC

alone, and led to moderate effects on clinical, social and functional outcomes over six months post-natal. THPP was effective in reducing symptom severity of depression. THPP was of greater benefit to women with shorter duration of chronicity. THPP enhanced remission at 6 months following childbirth and promoted recovery from depression over the post-natal period. THPP significantly improved perceived social support and reduced disability in the post-natal period, in particular over the early post-natal period, but had no effect on the other pre-specified outcomes of the number of days unable to work in the last month, breastfeeding practices, and infant weight and height. Another important finding is that it costs only a little over a dollar (US) per beneficiary mother to provide THPP (12% of this cost is attributed to incentives), and when this is done, THPP not only leads to an improvement in depression severity and recovery but also pays for itself through reduced health care, time and productivity costs.

First, we conclude that lay women in the community can be trained and empowered to deliver first line psychological care to depressed mothers in this urban setting of a relatively low resource country. This finding is of public health relevance as this may give rise to a new cadre of health care workers able to tackle the treatment gap of maternal depression in India. We found that incentives for lay health care workers and contextual differences between the more urban Indian and predominately rural Pakistan setting need to be taken into account when designing intervention delivery. Incentives for women living in urban Goa were financial rewards compared to rural Rawalpindi where altruistic motives were of greater importance.[15] Evidence shows that the type of remuneration is indeed context-specific and has implications for the acceptability and sustainability of the intervention, and its scaling up.[28] Second, we observed that the reduction in symptom severity was greatest within the first 3 months post-childbirth. This may be explained by the intervention architecture which involved front-loading of sessions provided antenatally and soon after childbirth—during which period participants received 80% of the total dose of the intervention. In addition to the dose, the content of the intervention was also front-loaded. THPP focussed on three main content areas (personal health of mothers, her relationship with her baby, and her relationship with others around her) which were delivered over four phases. While all three content areas were addressed in the first three phases, the purpose of phase four, delivered after three months post-natal, was to review the previous phases, and discuss relapse prevention; therefore, new content was not included during the last phase of the intervention. Third, we observed that a high proportion (60%) of participants in the control group showed remission at 6 months which also accounted for waning intervention effects at 6 months compared with 3 months, as observed in other perinatal depression trials.[29,30] The most likely explanation for this remission is the natural history of the condition, in particular for mild and moderate cases.[31] In addition it may be plausible that some non-specific elements, for example the participation in the research interviews or the enhancement of usual care, may have mediated symptom improvement. Fouth, although there was an effect on mother's severity of depression, no significant difference on baby's weight and height for age was observed. Similar results were found in the original THP study[8] and in other trials[32] and we assume that there may be other potent determinants of these outcomes, notably poverty,[6] which our intervention did not address. Additionally, there were no differences in the proportion of mothers exclusively breastfeeding in the previous 24 hours. We found that the internal validity of the study was high; the trial conduct and analyses were done in accordance with the protocol, and there was a high participation rate, high adherence to the intervention with good fidelity of the intervention delivery, and low attrition.

There are some limitations of our study. First, we did not employ diagnostic interviews to ascertain depression. Instead, we have used the PHQ-9, a validated screening tool that is simple to administer and has been used successfully in other depression trials in India.[18] It has been validated in perinatal depression populations in other LMIC such as in Ghana[33] or Pakistan[34] and shows acceptable criterion-

related validity and reliability for screening for depressive symptoms among women in the antenatal and postnatal period. Second, our study was conducted in a state with relatively high literacy levels. Generalizability and acceptability of peer-delivered psychological treatments, including training and supervision procedures may therefore differ when conducted among populations living in poorer socio-demographic circumstances, and in different health systems contexts. Third, we note that our control arm was well resourced and thus the effects of the intervention might be even larger in less resourced settings, for e.g. where obstetric care is not provided by gynaecologists. Fourth, we assumed a constant intervention effect of THPP during the study duration as we did not find evidence of group-by-time interactions; however, this may be due to lack of power to detect interaction. Finally, a true intention-to-treat analysis was not possible due to missing outcome data for about 10% of participants, but the results using complete case analysis adjusted for factors associated with missingness (primary analysis) and multiple imputation analysis (Appendices G and H) were similar.

We have shown that a psychological intervention based on behavioural activation delivered by peers is effective in reducing the severity of symptoms of perinatal depression and promoting recovery from depression after childbirth, is relatively cheap to deliver and pays for itself, and leads to improved functional outcomes and social support. Women with postpartum depression represent a heterogenous group of clinical subtypes who need diverse interventions to improve long-term treatment outcomes.[35] Therefore, our intervention may be conceputualized as the front-line, first step, intervention, in a stepped care system for maternal depression. We argue that mothers who show no response after the first three months of THPP should be offered a higher frequency of sessions during the final three months of treatment and/or should be stepped-up to a more intensive intervention delivered by a specialist provider. Further research should explore if early response predicts long-term outcomes, which might pave the way for more personalized allocation of treatment options, which could start with provision of THPP to all women with perinatal depression, discontinuation of early responders after a few sessions, and more intensive interventions for non-responders after the first three months of treatment. Such a programme would allow the recovery of as many mothers as possible through the stepped allocation of treatments of different intensities and would be tailored to individual need and response. Replications of THPP are essential to further the evidence on the use of THPP in different contexts, and this will need to include adaptations to ensure context-specific determinants of perinatal depression are addressed during implementation (e.g. addressing domestic violence). Finally, we note the high concordance of results between the two trials implemented concurrently in two distinct settings in India (urban/peri-urban) and Pakistan (predominantly rural)[12], providing evidence of the external validity of our results. We conclude that THPP is low cost and widely accessible, so that even despite the modest effects we have observed, its scale up can have significant public health impact. Our results also support the WHO's recommendation for the use of THP, and offer evidence of the potential to scale-up its delivery using widely available and low-cost community resources such as peers.

CONTRIBUTORS

DCF drafted the report and all authors reviewed and approved it. VP, AR, DCF, AL, HAW and BW were responsible for the design of the trial. RK, AJ, PK, EA were responsible for intervention content and data gathering instruments. BW, AL and VP were responsible for trial conduct. ES was responsible for database design and management. HAW, FV, BW, HT were responsible for analyses.

DECLARATION OF INTERESTS

Authors declare no competing interests.

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RESEARCH IN CONTEXT

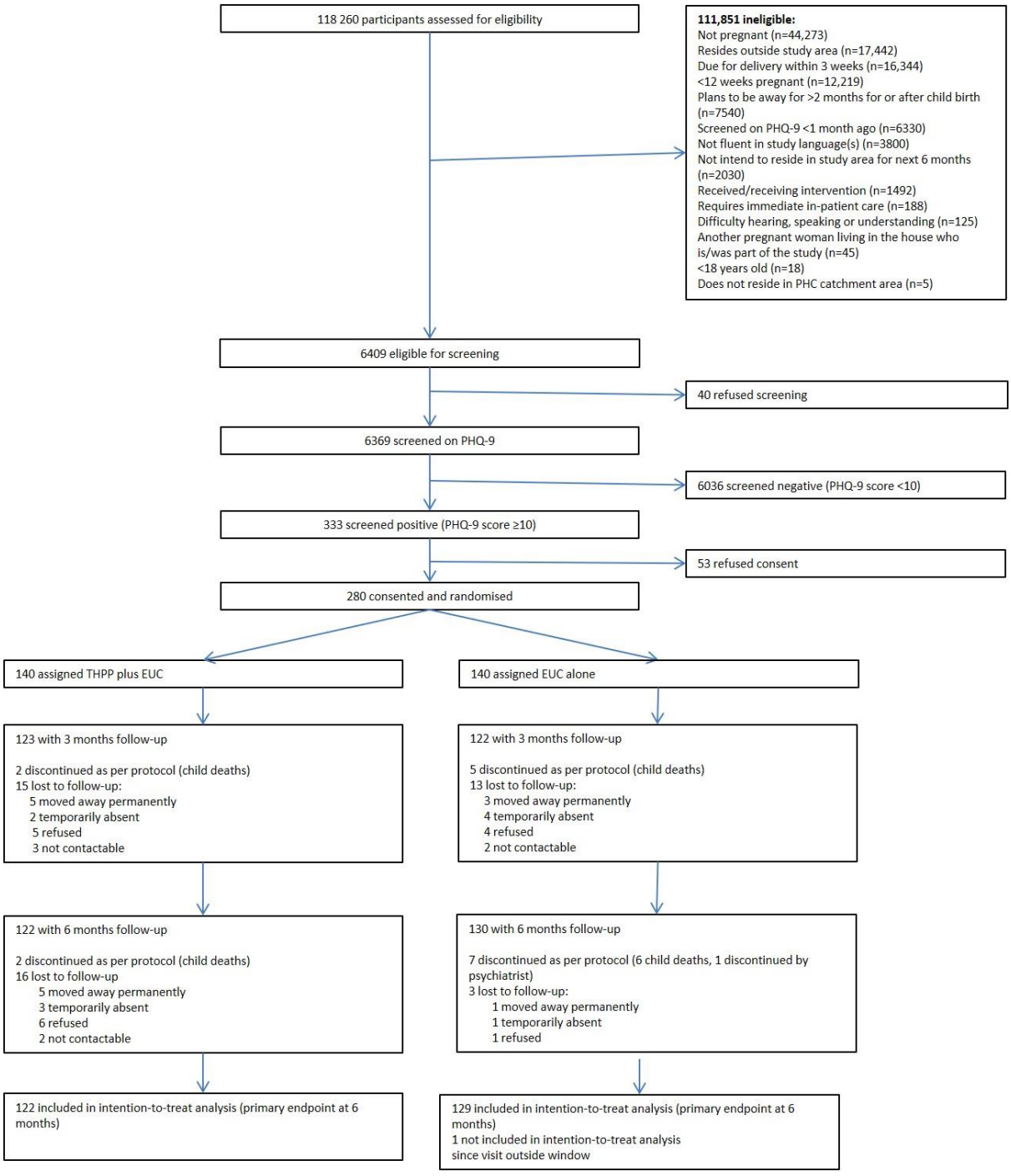
Evidence before this study Systematic reviews provide robust evidence that perinatal depression can be effectively managed with psychological treatments, and there is increasing evidence that non-specialist health workers can effectively deliver such interventions. We conducted a systematic review to update earlier evidence on the topic to assess the effect of (non-pharmacological) psychological interventions on common perinatal mental disorders in LMIC. Seven electronic bibliographic databases including MEDLINE, EMBASE, CINAHL, PsycINFO, the British Nursing Index, the Allied and Complementary Medicine database and the Cochrane Central Register were searched from 1 January 2012 – 1 January 2018 combining search terms for depression and controlled evaluations. The search was restricted to English articles and studies conducted in LMIC. 17 trials on perinatal depression were retrieved. The pooled effect size was -0.695, 95% CI= -0.92 to -0.47 for maternal depressive symptoms. The studies employed a range of delivery agents, including CHWs; however, none of the studies employed peers as delivery agents for the intervention. The largest reported effects have been achieved by the Thinking Healthy Program (THP), delivered by community health workers (CHWs) to depressed mothers in rural Pakistan. The intervention based on cognitive behaviour therapy more than halved the rate of depression compared with usual care and led to significant improvements in women's functioning and disability. Efforts to integrate the intervention in the CHW's daily routine at scale was however compromised by multiple health care responsibilities of CHWs. Feasibility and delivery of this intervention by lay health care providers such as peers remained unclear.

Added value of this study We adapted the Thinking Healthy Programme for delivery by peers (THPP). This study showed that the adapted intervention, whose focus was primarily on behavioural activation, was acceptable to participants and feasible to deliver by lay women in the community who had no previous health background. The intervention produced better outcomes than enhanced usual care and led to moderate effects on clinical, social and functional outcomes. THPP was highly cost-effective in this setting.

Implications of all the available evidence Psychological interventions like THPP may be considered for scaling up through peer workers as the first stage of care in a collaborative stepped care model for perinatal depression.

Figures and Tables

Figure 1: Trial profile



THPP= Thinking Healthy Programme delivered by peers. EUC=enhanced usual care. PHQ-9=Patient Health Questionnaire 9. Child deaths indicated at month 6 include those reported at month 3. Of those reported moved away permanently at month 3, 3 women in each of the groups returned at month 6. One woman in the EUC group attended her 6 month visit at 8.1 months (therefore excluded from the primary endpoint analysis).

Table 1: Baseline characteristics

	THPP plus EUC (N=140)	**EUC alone (N=140)**
Recruitment site (n [%])		
GMC hospital	70 (50%)	71 (51%)
Asilo hospital	63 (45%)	62 (44%)
Bicholim PHC	6 (4%)	7 (5%)
Sanquelim PHC	1 (1%)	0
Residence (n [%])		
Rural	103 (74%)	103 (74%)
Urban	37 (26%)	37 (26%)
Age, years (mean [SD])	25·04 (4.42)	25·31 (4·74)
Marital status (n [%])		
Married	139 (99%)	140 (100%)
Divorced/separated	1 (1%)	0
Occupation (n [%])		
Does not work	119 (85%)	118 (84%)
Manual worker	15 (11%)	15 (11%)
Non-manual worker	6 (4%)	7 (5%)
Education status (n [%])		
No formal education	21 (15%)	13 (9%)
Completed primary	55 (39%)	65 (46%)
Completed secondary	44 (31%)	46 (33%)
Completed higher secondary	13 (9%)	12 (9%)
Graduate/above	7 (5%)	4 (3%)
Patient's expectation of usefulness of counselling (n [%])		
Not useful	1 (1%)	0
A little useful	25 (18%)	30 (21%)
Somewhat useful	22 (16%)	32 (23%)
Moderately useful	30 (21%)	28 (20%)
Very useful	62 (44%)	50 (36%)
Chronicity of depression category (n [%])	83 (59%)	90 (64%)
<12 weeks	57 (41%)	50 (36%)
≥12 weeks		
PHQ-9 score		
Median [IQR]	13 [11 to 15]	12 [11 to 15]
PHQ-9 score category (n [%])		
10-14 (moderate)	97 (69%)	100 (71%)
15-19 (moderately severe)	32 (23%)	35 (25%)
20-27 (severe)	11 (8%)	5 (4%)
PHQ question 10 (n [%])[1]		
Not difficult at all	22 (16%)	21 (15%)
Somewhat difficult	82 (59%)	83 (59%)
Very difficult	15 (11%)	12 (9%)
Extremely difficult	21 (15%)	24 (17%)

	THPP plus EUC (N=140)	**EUC alone (N=140)**
MSPSS score (mean [SD])	5·31 [1·11]	5·27 [1·11]
Parity (n [%]) Primiparous Multiparous	 61 (44%) 79 (56%)	 58 (41%) 82 (59%)
Previous non-live birth (n [%]) None One/more	 131 (94%) 9 (6%)	 130 (93%) 10 (7%)
Any domestic violence in last three months (n [%]) No Yes	 124 (89%) 16 (11%)	 119 (85%) 21 (15%)
Time between screening and birth of child, months (mean [SD]) [2] Missing	 3·87 [1·66] 8 (6%)	 3·93 [1·64] 3 (2%)

[1] Question: If you checked off any problems (PHQ questions 1-9), how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people? [2] Women who did not attend any follow up visits have missing information relating to the date of birth of the child. MSPSS=Multidimensional Scale of Perceived Social Support. THPP= Thinking Healthy Programme delivered by peers. EUC=enhanced usual care. PHQ-9=Patient Health Questionnaire 9. SD=Standard Deviation. IQR=Interquartile range. GMC=Goa Medical College. PHC=Primary health care.

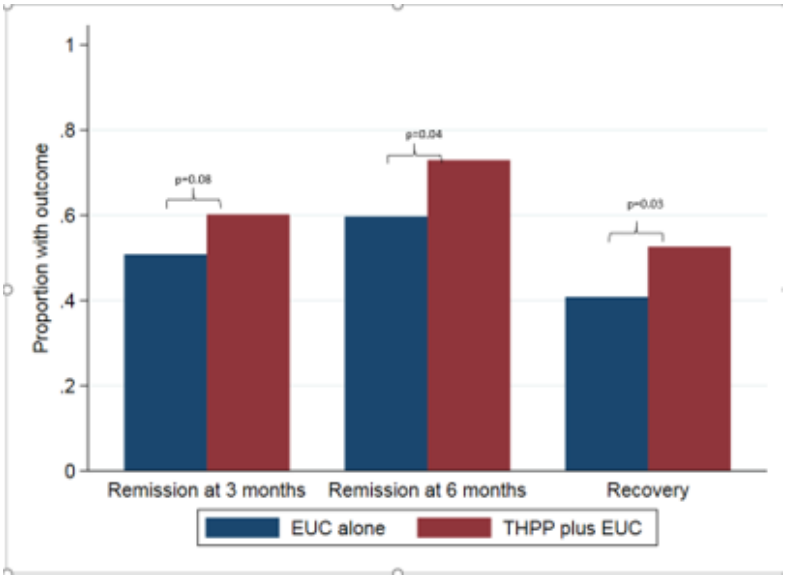
Table 2: Primary and secondary outcomes

	THPP plus EUC [1] (n=122)*	**EUC alone [1] (n=129)***	**Standardised mean difference (SMD) or prevalence ratio (PR) (95% CI) for THPP plus EUC versus EUC alone [2]**	**p-value**
Primary outcomes				
PHQ-9 score at 6 months	3.47 (4.49)	4.48 (5.11)	SMD=-0·18 (-0·43 to 0·07)	0·16
Remission (PHQ-9 score <5) at 6 months	89 (73%)	77 (60%)	PR=1·21 (1·01 to 1·45)	0·04
Secondary outcomes				
PHQ-9 score at 3 months [3]	4.26 (4.23)	5.81 (5.74)	SMD=-0·34 (-0·59 to -0·09)	0·01
Remission (PHQ-9 score <5) at 3 months	74/123 (60%)	62/122 (51%)	PR=1·22 (0·97 to 1·52)	0·08
Recovery (PHQ-9 score <5 at both 3 and 6 months)	61/116 (53%)	49/120 (41%)	PR=1·35 (1·03 to 1·78)	0·03
WHO-DAS score				
3 months [3]	11.86 (13.29)	16.17 (15.48)	SMD=-0·34 (-0·59 to -0·10)	0·009
6 months [4]	9.47 (11.91)	12.11 (13.65)	SMD=-0·18 (-0·43 to 0·07)	0·16
Number of days unable to work in last month				
3 months [3]	2.10 (5.20)	2.07 (4.88)	SMD=0·00 (-0·25 to 0·25)	0·98
6 months [4]	2.47 (5.61)	2.72 (5.53) [4]	SMD=-0·05 (-0·30 to 0·20)	0·70
MSPSS score				
3 months [5]	5.65 (1.07)	5.30 (1.12) [5]	SMD=0·32 (0·06 to 0·57)	0·02
6 months [4]	5.59 (1.12)	5.27 (1.20) [4]	SMD=0·27 (0·02 to 0·52)	0·04
Exclusive breastfeeding in last 24 hours				
3 months	86/121 (71%)	82/122 (67%)	PR=1·07 (0·91 to 1·27)	0·41
6 months	9/121 (7%)	10/128 (8%)	PR=0·82 (0·35 to 1·92)	0·65
Infant weight for age z score				
3 months [6]	-1.21 (0.95)	-1.30 (1.05)	SMD=0·11 (-0·15 to 0·37)	0·42
6 months [7]	-1.03 (0.88)	-1.05 (1.03)	SMD=0·03 (-0·23 to 0·29)	0·84
Infant height for age z score				
3 months [6]	-0.38 (1.23)	-0.30 (1.10)	SMD=-0·08 (-0·34 to 0·18)	0·58

6 months [7]	-0.43 (1.12)	-0.42 (1.13)	SMD=-0·02 (-0·28 to 0·24)	0·89

[1] Results are mean (standard deviation) or number (%). [2] By linear or logistic regression, adjusted for recruitment centre, baseline PHQ-9 score, residence, treatment expectations, education and chronicity (see Methods). [3] N=123 and 122 in the THPP plus EUC and EUC alone groups, respectively. [4] N=122 and 128 in the THPP plus EUC and EUC alone groups, respectively. [5] N=122 and 122 in the THPP plus EUC and EUC alone groups, respectively. [6] N=110 and 115 in the THPP plus EUC and EUC alone groups, respectively. [7] N=106 and 122 in the THPP plus EUC and EUC alone groups, respectively. MSPSS=Multidimensional Scale of Perceived Social Support. THPP= Thinking Healthy Programme delivered by peers. EUC=enhanced usual care. PHQ-9=Patient Health Questionnaire 9. WHO-DAS=WHO -Disability Assessment Schedule. *Among those with observed outcome data at 6 months. Secondary outcomes as adjusted mean differences and odds ratios are presented in appendix I.

Figure 2: Intervention effect on remission and recovery by group over 6 months



. EUC=Enhanced Usual Care. THPP=Thinking Healthy Programme Peer-Delivered. Remission defined as PHQ-9 score <5; recovery defined as PHQ-9 score <5 at both 3 and 6 months; P-values are from logistic regression models, adjusted for recruitment hospital, residence, baseline PHQ-9 score, treatment expectations, education, and chronicity of depression (see methods for more details).

Table 3: Intervention effect for depression, disability and social support outcomes analysed as repeated measures

	P value for group by time interaction	Overall adjusted SMD or PR (95% CI) for THPP plus EUC versus EUC alone[1]	P value for overall effect
Primary			
PHQ-9 score	0·32	-0·37 (-0·88, to 0·24)	0·01
Remission (PHQ-9<5)	0·56	1·21 (1·01 to 1·41)	0·02
Secondary			
WHO DAS score	0·44	-0·32 (-0·76 to -0·21)	0·02
Number of days unable to work	0·72	-0·03 (-0·30 to 0·20)	0·77
MSPSS score	0·98	0·51 (0·43 to 1·20)	0·02

[1] Adjusted for recruitment centre, baseline PHQ-9 score, residence, treatment expectations, education and chronicity (see Methods), and in addition visit, using generalised estimating equations to account for within-person correlations.. Standarised mean differences calculated using the mean difference from the adjusted GEE models divided by the standard deviation estimated from adjusted random effects model, with confidence intervals estimated using bootstrap with 1000 replicates and percentile estimation. CI=confidence interval, PHQ=Patient Health Questionnaire, MSPSS= Multidimensional Scale of Perceived Social Support, WHO DAS=WHO Disability Assessment Schedule, AMD=Adjusted mean difference.

Table 4: Cost-effectiveness analysis from health system and societal perspectives at 3 months, 6 months, and over the trial period.

	Adjusted mean difference between THPP plus EUC and EUC alone at 3 months post-childbirth [1] *(Mean, 95% CI)*	Adjusted mean difference between THPP plus EUC and EUC alone at 6 months post-childbirth [2] *(Mean, 95% CI)*	Adjusted mean difference between THPP plus EUC and EUC alone over total period of trial [3] *(Mean, 95% CI)*
COSTS			
a) **Total health system costs (incl. intervention)**	*US$* -11·03 (-41·94 to 19·87)	*US$* -2·49 (-8·12 to 3·14)	*US$* -14·86 (-46·91 to 17·19)
b) **Total Societal Costs (health system and productivity costs)**	*US$* -53·98 (-109·64 to 1·68)	*US$* -17·69 (-45·94 to 10·54)	*US$* -72·41 (-141·84 to -2·98)
CLINICAL OUTCOMES			
1) PHQ-9 summary score[4]	1·86 (0·53 to 3·18)	-1·04 (-2·36 to 0·28)	0·73 (-0·57 to 2·02)
2) Additional number of mothers remitted in THPP (%):PHQ-9 score < 5 at 3 or 6 months[5]	12 (8·8%)	11 (6·6%)	NA
3) Additional number of patients recovered in THPP (%): PHQ-9 score < 5 at 3 and 6 months	12 (11%)		
	ICER *(US$, 95% CI)*	ICER *(US$, 95% CI)*	ICER *(US$, 95% CI)*
COST-EFFECTIVENESS			
A. Total health system costs (incl. intervention)			
· Cost per unit improvement in PHQ-9 score	-6·14 (-7·15 to -5·12)	2·44 (0·24 to 4·65)	-19·09 (-49·45 to 11·25)
· [6]Cost per additional case remitted	-112·1	-27·6	NA
· [7]Cost per additional case recovered (over total trial duration)	-151·07		

B. Total societal costs (health system and productivity costs)			
· Cost per unit improvement in PHQ-9 score	-29·64 (-32·88 to -26·41)	16·95 (5·56 to 28·35)	-93·53 (-180·21 to -6·84)
· [6]Cost per additional case remitted	-548·8	-196·2	NA
· [7]Cost per additional case recovered (over total trial duration	-736		

[1] Cost and outcome estimates relate to the 6-month period covering the third trimester and the first 3 months post-childbirth

[2] Cost and outcome estimates relate to the 3-month period since the 3-month post-childbirth assessment

[3] Cost and outcome estimates relate to the 9-month period covering the third trimester and the first 6 months post-childbirth

[4] Reduction in PHQ-9 scores converted to a positive change score to aid interpretation of cost-effectiveness results.

[5] Out of total remitted in both arms

[6] Estimated as: (cost difference*total number of mothers in THPP)/additional number of patients remitted in THPP arm.

[7] Estimated as: (cost difference*total number of mothers in THPP)/additional number of patients recovered in THPP arm.

Figure 3. Cost-effectiveness planes: THPP plus EUC compared to EUC per unit improvement in depression severity score over total period of trial.

Figure 3A: Health System Perspective

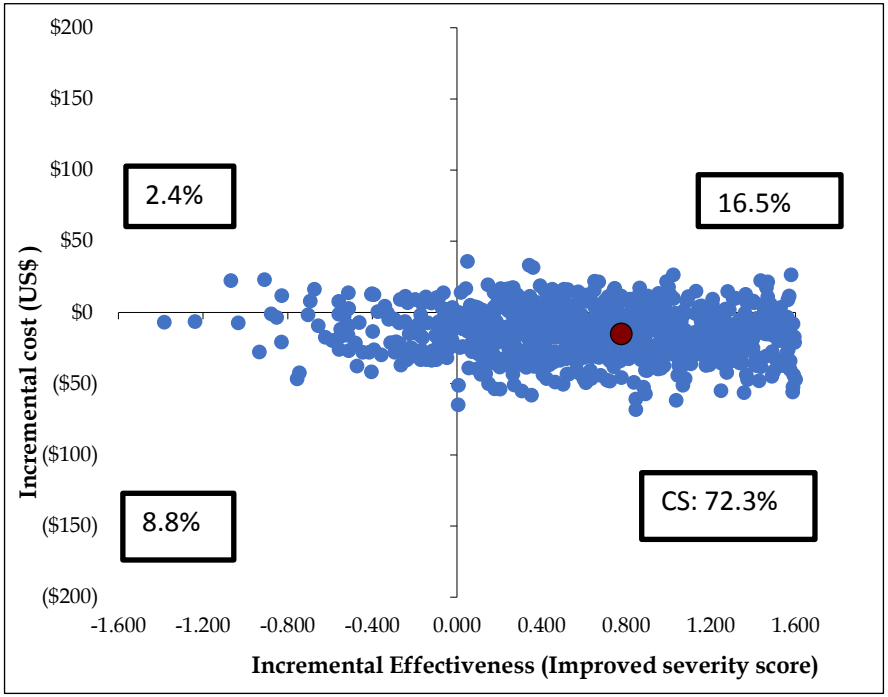
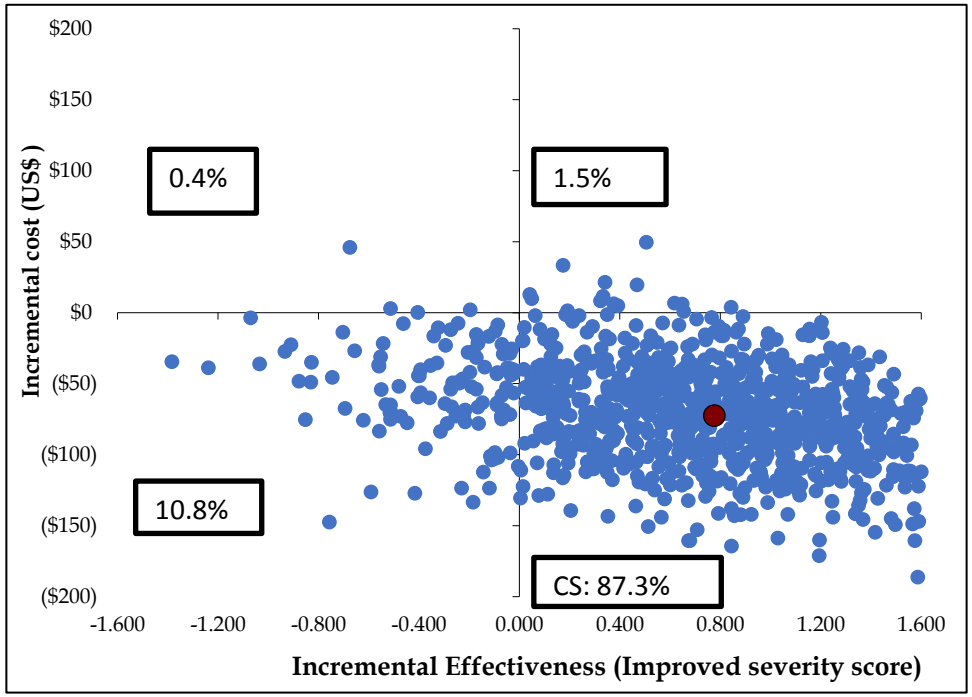


Figure 3B: Societal Perspective



CS: Cost-saving

References

1. Friedrich MJ. Depression is the leading cause of disability around the world *JAMA* 2017; **317**(15): 1517.
2. Woody CA, Ferrari AJ, Siskind DJ, Whiteford HA, Harris MG. A systematic review and meta-regression of the prevalence and incidence of perinatal depression. *J Affect Disord* 2017; **219**: 86-92.
3. Fisher J, Cabral de Mello M, Patel V, et al. Prevalence and determinants of common perinatal mental disorders in women in low- and lower-middle-income countries: a systematic review. *Bull World Health Organ* 2012; **90**(2): 139g-49g.
4. Parsons CE, Young KS, Rochat TJ, Kringelbach ML, Stein A. Postnatal depression and its effects on child development: a review of evidence from low- and middle-income countries. *Br Med Bull* 2012; **101**: 57-79.
5. Eaton J, McCay L, Semrau M, et al. Scale up of services for mental health in low-income and middle-income countries. *Lancet* 2011; **378**(9802): 1592-603.
6. Rahman A, Fisher J, Bower P, et al. Interventions for common perinatal mental disorders in women in low- and middle-income countries: a systematic review and meta-analysis. *Bull World Health Organ* 2013; **91**(8): 593-601i.
7. Thinking Healthy Programme. Am manual for psychological management for perinatal depression. . Geneva: WHO; 2015.
8. Rahman A, Malik A, Sikander S, Roberts C, Creed F. Cognitive behaviour therapy-based intervention by community health workers for mothers with depression and their infants in rural Pakistan: a cluster-randomised controlled trial. *Lancet* 2008; **372**(9642): 902-9.
9. Rahman A. Challenges and opportunities in developing a psychological intervention for perinatal depression in rural Pakistan--a multi-method study. *Arch Womens Ment Health* 2007; **10**(5): 211-9.
10. Sikander S, Lazarus A, Bangash O, et al. The effectiveness and cost-effectiveness of the peer-delivered Thinking Healthy Programme for perinatal depression in Pakistan and India: the SHARE study protocol for randomised controlled trials. *Trials* 2015; **16**: 534.
11. Atif N, Krishna RN, Sikander S, et al. Mother-to-mother therapy in India and Pakistan: adaptation and feasibility evaluation of the peer-delivered Thinking Healthy Programme

BMC Psychiatry 2017; **17**(1): 79.
12. Sikander S, Ahmad I, Atif N, et al. Delivering the Thinking Healthy Programme for perinatal depression through volunteer peers: a cluster randomised controlled trial in Pakistan *Lancet Psychiatry* 2018.
13. Goa Population Census Data. 2011. https://www.census2011.co.in/ (accessed 19.04. 2018).
14. National Family Health Survey (NFHS-3). IIPS,Goa/Mumbai,India: International Institute for Population Sciences (IIPS) and Macro International; 2009.
15. Singla D, Lazarus A, Atif N, et al. "Someone like us": delivering maternal mental health through peers in two South Asian contexts. *J Affect Disord* 2014; **168**: 452-8.
16. National Family Health Survey-4 (2015-2016). http://rchiips.org/nfhs/pdf/NFHS4/India.pdf (accessed 22.8. 2018).
17. Kroenke K, Spitzer RL. The PHQ-9: A new depression diagnostic and severity measure. *Psychiatric Annals* 2002; **32**(9): 1-7.
18. Patel V, Weobong B, Weiss HA, et al. The Healthy Activity Program (HAP), a lay counsellor-delivered brief psychological treatment for severe depression, in primary care in India: a randomised controlled trial. *Lancet* 2017; **389**(10065): 176-85.
19. Schulz KF, Grimes DA. Allocation concealment in randomised trials: defending against deciphering. *Lancet* 2002; **359**(9306): 614-8.

20. Driessen E, Hollon SD. Cognitive behavioral therapy for mood disorders: efficacy, moderators and mediators. *Psychiatr Clin North Am* 2010; **33**(3): 537-55.
21. Singla DR, Weobong B, Nadkarni A, et al. Improving the scalability of psychological treatments in developing countries: an evaluation of peer-led therapy quality assessment in Goa, India. *Behav Res Ther* 2014; **60**: 53-9.
22. Chisholm D, Conroy S, Glangeaud-Freudenthal N, et al. Health services research into postnatal depression: results from a preliminary cross-cultural study. *Br J Psychiatry Suppl* 2004; **46**: s45-52.
23. Buttorff C, Hock RS, Weiss HA, et al. Economic evaluation of a task-shifting intervention for common mental disorders in India. *Bull World Health Organ* 2012; **90**(11): 813-21.
24. Localio AR, Margolis DJ, Berlin JA. Relative risks and confidence intervals were easily computed indirectly from multivariable logistic regression. *J Clin Epidemiol* 2007; **60**(9): 874-82.
25. McGlothlin AE, Lewis RJ. Minimal clinically important difference: defining what really matters to patients. *JAMA* 2014; **312**(13): 1342-3.
26. Button KS, Kounali D, Thomas L, et al. Minimal clinically important difference on the Beck Depression Inventory--II according to the patient's perspective. *Psychol Med* 2015; **45**(15): 3269-79.
27. Sonnenberg F, Beck R. Markov Models in medical decision making: a practical guide. *Med Decis Making* 1993; **13**: 322-38.
28. Singh D, Negin J, Otim M, Orach CG, Cumming R. The effect of payment and incentives on motivation and focus of community health workers: five case studies from low- and middle-income countries. *Hum Resour Health* 2015; **13**: 58.
29. Rojas G, Fritsch R, Solis J, et al. Treatment of postnatal depression in low-income mothers in primary-care clinics in Santiago, Chile: a randomised controlled trial. *Lancet* 2007; **370**(9599): 1629-37.
30. Tandon SD, Ward EA, Hamil JL, Jimenez C, Carter M. Perinatal depression prevention through home visitation: a cluster randomized trial of mothers and babies 1-on-1. *J Behav Med* 2018.
31. Whiteford HA, Harris MG, McKeon G, et al. Estimating remission from untreated major depression: a systematic review and meta-analysis. *Psychol Med* 2013; **43**(8): 1569-85.
32. Stein A, Netsi E, Lawrence PJ, et al. Mitigating the effect of persistent postnatal depression on child outcomes through an intervention to treat depression and improve parenting: a randomised controlled trial. *Lancet Psychiatry* 2018; **5**(2): 134-44. doi: 10.1016/S2215-0366(18)30006-3.
33. Weobong B, Akpalu B, Doku V, et al. The comparative validity of screening scales for postnatal common mental disorder in Kintampo, Ghana. *J Affect Disord* 2009; **113**(1-2): 109-17. doi: 10.1016/j.jad.2008.05.009. Epub Jul 9.
34. Gallis JA, Maselko J, O'Donnell K, et al. Criterion-related validity and reliability of the Urdu version of the patient health questionnaire in a sample of community-based pregnant women in Pakistan. *PeerJ* 2018; **6:e5185.**(doi): 10.7717/peerj.5185. eCollection 2018.
35. Putnam KT, Wilcox M, Robertson-Blackmore E, et al. Clinical phenotypes of perinatal depression and time of symptom onset: analysis of data from an international consortium. *Lancet Psychiatry* 2017; **4**(6): 477-85.