Title: Impact of an Early Perinatal Depression Intervention on Longer-term Child Development Outcomes

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Abstract

Background: Perinatal depression has been linked with deleterious child development outcomes, yet there is limited evidence of maternal depression interventions having lasting impacts on child development, and no previous evidence from a developing country.

The Thinking Healthy Programme (THP) RCT was a perinatal depression intervention in Pakistan in 2006-2007; the THP was found to significantly reduce depression levels 12-months post-partum relative to the control arm.

We evaluated the THP intervention's impact on cognitive, socio-emotional, and physical development of children 7 years post-intervention.

Methods: Mother-child dyads who participated in the THP RCT were interviewed at mean child age 7.6 years. Additionally, a reference group of 300 mothers who were non-depressed prenatally, and not part of the intervention, was enrolled with their children at the same time.

The primary cognitive outcome was the Wechsler Preschool and Primary Scale of Intelligence-IV (WPPSI-IV); socio-emotional outcomes included the Strength and Difficulties Questionnaire (SDQ) and the Spence Children's Anxiety Scale (SCAS); physical outcomes were height,–weight and BMI z-scores. Generalized linear modelling with random effects to account for clustering was the main method of analysis.

Results: Of the 705 THP participating mother-child dyads interviewed at the end of the trial, 584 dyads were successfully re-enrolled (83% re-enrollment rate). Children in the treatment and control arms did not differ on overall cognitive, socio-emotional, or physical development outcomes. When compared with the reference group of children whose mothers were non-depressed prenatally, the THP trial children had higher (worse) SDQ Total Difficulty, beta=0·78 (95% CI 0·09, 1·47) and anxiety symptom

scores, beta=2·93 (95% CI 1·15-4·71); there were no differences in full scale IQ or height-weight-BMI z-scores.

Conclusions: Further exploration is needed to understand what kinds of complex interventions or approaches are needed for long term maternal and child well-being gains. Longer, more detailed and more frequent follow-up is warranted for all interventions.

Introduction

Depression during pregnancy and the postnatal period strongly predicts negative physical and mental health outcomes throughout childhood and into adulthood[1-6]. Given that 10-35% of children worldwide are exposed to perinatal depression in their first year of life, understanding the potential for interventions to help alleviate this risk is a global public health priority.[7, 8]

Interventions to improve outcomes among children of depressed mothers in high income countries have shown some promising results in the short term, typically within 1-18 months of the intervention.[9, 10] Among the few studies that have followed children for a longer period, such as five years post-intervention, the main finding is that the initial positive effects do not persist.[11, 12] A possibility raised in these studies is that longer term effects may be found in samples of children of lower socioeconomic status amongst whom cognitive or behavioral deficits are more common.[11, 12] We present the first evidence of long term effects from communities of low socio-economic status, from a 7-year follow-up of a population-level perinatal depression intervention in rural Pakistan. There appears to be no previous evidence from a developing country. The infant mortality rate in the Punjab region of Pakistan is 78/1000 live births.[13] Not only is the average family poor (per capita GDP USD1202) but, in addition, public inputs to child development delivered through health and educational systems are less well-resourced to buffer children against a bad start (public expenditure on health and education total 2.1% of GDP). This makes child development potentially more sensitive to the condition of the mother which could result in a successful perinatal depression intervention having greater impacts on indicators of child development that persist to the age of 7 or 8. Developmental differences present by this age are likely to translate to improved academic performance and potentially other longer term outcomes. Moreover, the above mentioned studies had small sample sizes with multiple arms, and were likely underpowered for longer term follow-up hypothesis testing. We use substantially larger samples and analyze a single treatment.

Our seven-year follow-up is of the Thinking Healthy Programme (THP). This was one of the first perinatal depression Cluster Randomized Controlled Trials (cRCT), delivered by community health workers in rural Pakistan, to demonstrate large improvements in depression, even when poverty related factors were carefully controlled.[14] The cRCT began in the third trimester in pregnancy and lasted through 10 months post-partum in 2005-2006. At 12 months post-partum, 73% of mothers in the treatment arm had recovered from their depressive disorder compared to 41% in the control arm. The women in the treatment arm also reported higher levels of social support and improved overall functioning. Although there were no differences in infant weight-for-age or height-for-age z scores at 12 months, infants in the treatment arm had fewer episodes of diarrhea and were more likely to have completed immunizations. Finally, both parents in the treatment arm reported spending more time every day on play-related activities.[14] Based on these initial findings, we hypothesized that children in the treatment arm would have better cognitive, socio-emotional and physical outcomes 7-8 years later than children from the control arm. We furthermore hypothesized that outcomes between children whose mothers were not depressed prenatally and those participating in the intervention would converge.

Methods

Original Thinking Healthy Program (THP) Intervention

The THP is a Cognitive Behavioral Therapy (CBT) based intervention; its development and trial results are described elsewhere[14]. Briefly, 40 Union Councils (UC), the smallest geo-political administrative unit of Pakistan, in Punjab province, were randomized to treatment or control arms (20 clusters each). Pregnant women residing in these clusters were identified by local community health workers as part of their routine work, and all women in their third trimester of pregnancy (married, ages 16-45, no significant illness) were diagnosed for depression in their homes; those who met Diagnostic and Statistical Manual of Mental Disorders, IV-TR (DSM-IV) diagnostic criteria for Major Depressive Episode (26% of the

sample) were invited to participate in the trial (n=903). The THP intervention was delivered by community health workers ("Lady Health Workers", LHWs) through 16 home visits.[14] The LHWs were trained to deliver the CBT intervention, beginning in the last month of pregnancy and ending 12 months postpartum. The intervention was based on a psychosocial model and not presented as a 'treatment' for a 'mental health problem' but rather as a way to improve positive and healthy thinking around the mother and the baby (see Online Appendix for more details).

Follow-up of the trial:

There has been no follow-up with the women who participated in the THP trial since 2007, after the trial ended, when their children were 12 months old. Our goal was to re-enroll the mother-child pairs beginning in 2013. The comparison of these dyads who were randomized to treatment and control arms would thus enable a causal estimate of any long-term impacts of the intervention on the children. We extracted contact information of the original sample of women, including women who were prenatally non-depressed at the time of screening for the trial (reference group). These reference mother-child dyads resided in the same UCs and villages as the depressed women. We were interested in the reference group for two reasons: Firstly, we hypothesized that, if the intervention improved child development trajectories, it could also meaningfully reduce the expected developmental gap between children of prenatally depressed vs. non-depressed mothers. Second, in order to interpret any differences observed between the trial arms, we needed to better understand the baseline population levels of key constructs of interest: cognitive, socio-emotional, physical development indicators in this age group.

Women were located with assistance from local LHWs as well as queries with neighbors or relatives, and local hospital record checks. We successfully re-enrolled 83% (n=584) mother-child dyads, corresponding to 85·5% (n=295) of control arm dyads and 80·3% (n=289) of treatment arm dyads (Figure

1). In addition we enrolled 300 reference group dyads. All fieldworkers were blind to the women's original depression or trial arm status; fieldwork lasted March 2013-January 2014.

Each dyad interview consisted of two parts: the first in the mother's home and the second either in the child's school or in the local LHW's house ("health house"). The purpose of the second contact was to administer cognitive tests to the child in a quiet and more standardized environment than the home. Data was checked for completeness and accuracy at the end of each interview. This study received ethical approval from the IRBs of the Human Development Research Foundation, Pakistan and the Duke University, USA. The original THP cRCT was registered as ISRCTN65316374.

Measures

Our main outcome of interest comprised of three dimensions of child development: cognitive development, socio-emotional development, and physical development. These were assessed as follows:

Cognitive development was assessed with the WPPSI-IV (Wechsler Preschool and Primary Scale of Intelligence-IV). The full battery was translated with minor adaptations after consulting with experts and community members. Piloting was conducted on 51 children and further refinements were made. The major composite scores consist of the Verbal Comprehension Index (VCI), Visual Spatial Index (VSI), and the Full Scale IQ (FSIQ). The VCI reflects abilities related to comprehension, reasoning and expression, while the VSI assesses non-verbal skills related to pattern discrimination and object manipulation.

Socio-emotional development included two main domains: behavioral/emotional problems, assessed with the Strengths and Difficulties Questionnaire (SDQ)[15, 16] and anxiety with the Spence Children's Anxiety Scale (SCAS).[17] The SDQ is parent administered and has been validated in Pakistan; 20 questions inquire about the child's difficulties in four areas: emotional, conduct problems, hyperactivity, peer

problems, and pro-social.[15, 16] The total difficulties score is generated by summing the problem scale scores, ranging from 0 to 40. The SCAS is also parent administered and comprises of six different subscales in addition to an overall anxiety score: panic and agoraphobia, separation anxiety, physical injury fears, social phobia, obsessive-compulsive problems, and generalized anxiety. The sum of items has a range of 0-114. These two instruments exhibited acceptable internal consistency with SDQ Cronbach's alpha=0·66 and SCAS=0·86.

Physical development was assessed with height (cm) and weight (kg) to calculate the height-for-age, weight-for-age, and BMI Z-scores according to WHO criteria.[18]

Maternal depression was assessed using the Structured Clinical Interview (SCID) for DSM-IV diagnosis, identical to the original trial.[19]

Information on multiple socio-demographic and potential confounder variables was also collected, including maternal age, maternal/paternal education, family/household structure, presence of grandmother in the household, father's migration for work, socio-economic status as rated by the LHW, number of living children; index child's age, gender, and current schooling status. To the extent possible, we aimed to keep the same format of questions as in the original THP study to enable continuity of measures. All measures were trans-adapted and administered in Urdu; many were already available in Urdu (e.g. SDQ, SCID), and had been used by members of our team.[15]

Analysis

Summary comparisons of key variables across treatment arms and between the trial and reference groups were conducted with t-tests for continuous variables and $\chi 2$ tests for categorical variables. The main exposure variable for the first hypothesis was an indicator variable for whether the mother was residing in a treatment cluster during the original RCT. The main exposure variable for the second

hypothesis was membership in the reference group cohort, defined by not being depressed in the third trimester of pregnancy. The main outcomes were summary measures of cognitive, socio-emotional, and physical development, all treated as continuous variables.

The main method of analysis was a random-effects generalized linear model (PROC GLIMMIX, SAS, Cary, NC), with random effects for UC to account for clustering. Analyses were intention-to-treat. For the main hypothesis, the effect estimates were interpreted as the adjusted mean difference in outcome scores between children whose mothers were in the treatment vs. control arm. These models include covariates for child gender, maternal age, baseline maternal education, baseline family SES, and current maternal depression status. To control for interviewer influences, we also included a control for each assessor. Baseline variables were extracted from the original THP intake interview.

For the secondary hypothesis, regression coefficients were interpreted as the adjusted mean difference in outcomes comparing the trial participants with the prenatally non-depressed reference group. These models included the same covariates as above with the exception that maternal education and family SES were used from the current interview since no baseline data was available for the reference group, although the question format was identical. Since these models are no longer based on randomization and more susceptible to potential bias, we added controls for the number of children the mother has, the presence of a grandmother in the household and whether the father travels away for work. Normality assumptions were checked by examining model residuals; when there was evidence of non-normality alternative model specifications were fitted.

Results

Of the 705 (360 treatment and 345 control) mother-child dyads who were included in the original 12-month post-partum trial analysis, we were able to interview 584 dyads (289 from treatment arm and 295 from control arm), a follow-up rate of 82·84%. Of the dyads not assessed, 106 women moved and

could not be relocated, four women died, seven children died, two children were disabled, one dyad was broken and one woman had psychosis (figure 1). Comparing women who were lost-to-follow-up to those who were re-enrolled revealed no differences in treatment arm allocation, maternal age, maternal education, number of children already born to the woman, or initial depression severity rating.

The mean age of the index child in our sample was 7·57 (SD=0·1), 49·3% of the children were female and 98% were enrolled in some type of school. Each child had an average of 3 siblings and 45·6% co-resided with a grandmother. As seen in Table 1, there were some small variations in socio-demographic variables across treatment arms and between the THP intervention and reference cohorts. For example, mothers in the treatment arm were slightly younger than their control arm counterparts (34·1 vs. 35·4 years old, p=0·03). When comparing the two cohorts of dyads, children of prenatally non-depressed women were more likely to come from families with higher SES and maternal education (mean years 5·54 (SD=4·5) vs. 4·01 (SD=3·9), p-value for difference <0·001), and fewer siblings (mean children 4·0 (SD=1·4) vs. 4·3 (SD=1·5) p-value=0·003) compared to children whose mothers participated in the THP trial. This is consistent with research correlating depression with lower socioeconomic status.[20]

We first tested our main hypothesis that treatment arm allocation would result in improved child outcomes. We found no significant differences in cognitive development between the children of women in the treatment and control arms (Table 2): The mean FSIQ of children in the treatment arm was 82.53 (SD=11·3) and of control arm children, 82·13 (SD=11·4)(adjusted mean difference 0.01, 95% CI -2·09- 2·07, p-value=0·99). For the socio-emotional outcomes, the mean difference in SDQ Total Difficulties score was 0·51 (95%CI -0·45 -1·47, p-value=0·29). For anxiety, children in the treatment arm had a 1·83 higher overall SCAS anxiety score compared with children in the control arm (95% CI -0·37-

4·04), although this difference did not reach statistical significance (p-value=0·10). Finally, there were no differences in height-for-age, weight-for-age and BMI-for-age z-scores.

A comparison of cognitive and socio-emotional component subscales revealed differences in two of the SCAS anxiety subscales: the panic/agoraphobia subscale (0·52 point difference, 95% CI 0·02-1·03, p-value=0·04) and the obsessive-compulsive subscale (0·57 point difference, 95% CI 0·18-0·95, p-value<0·001). Overall, even though only two of the component subscales reached statistical significance, in general mean values favored the control arm children.

We next explored the 1·83 point association (p-value=0·10) between treatment arm assignment and anxiety (SCAS): Using the overall score, we found an association between treatment arm and SCAS score that suggests that it may be driven by children of mothers who relapsed. Among this subset (n=66: 44 treatment and 22 control), there is a 13·61 point difference in SCAS score between the treatment and control arm children (95% CI 5·80-21·42). This same association was not observed among children of mothers who never recovered (n=93, 26 in treatment and 67 in control arm; beta= -2·52, 95% CI -11·36-6·32). However, given the small cell sizes and exploratory nature of this comparison, the results should be interpreted with caution.

The inclusion or exclusion of model covariates, including current depression status, had no discernable impacts on the effect estimates or standard errors. There was some evidence heteroskedacity in error residuals for the SCAS models; alternate modelling functions that improved residual distributions, such as a count of symptoms (Poisson) or as an ordinal variable (e.g. tertiles) produced results consistent with the main model.

Comparison with reference group

Because the intervention failed to improve child developmental outcomes, we could not test our second hypothesis about the treatment reducing the gap between children of prenatally depressed and non-depressed mothers. However, we were able to describe the overall association between prenatal depression status and current child outcomes, independent of current maternal depression levels. In order to accomplish this, we compared the reference children of the prenatally non-depressed mothers with those of all of the mothers who were depressed and participated in the trial (merging the treatment and control groups) (Table 3). The two groups of children were fairly equivalent in terms of cognitive development: The main FSIQ scores of children in the reference and trial participant children differed by only 0·73 points (95% CI -0·80-2·27, p-value=0·35). In contrast, prenatal depression did predict socio-emotional outcomes: reference group children had 0·78 lower total SDQ TD score (95% CI 0·09- 1·47, p-value=0·03) as well as lower SCAS anxiety scores (mean difference 2·93, 95% CI 1·15- 4·71, p-value<0·01). These differences were also evident in these measures' subscales. Prenatal depression status was not correlated with current physical development indicators.

Discussion

In the present study we examined the impact of a perinatal depression intervention on children 7 years post-intervention: We found that even though the intervention initially reduced depressive symptoms among mothers, there were no meaningful differences between children in treatment or control arms in cognitive, socio-emotional, or physical developmental outcomes. The correlational comparison of children of mothers in the prenatal depression study with a reference group of children whose mothers were not depressed prenatally revealed that the reference children had fewer socio-emotional problems, but were equivalent cognitively and physically. In the original trial, 12months postnatally, in addition to improved symptom levels, women in the treatment arm were more likely to breastfeed, and they and their husbands reported spending more time playing with their infants[14]. Our findings show

that these improvements in the first year of life were relatively short-term and children of perinatally depressed mothers remained at a disadvantage in terms of socio-emotional outcomes.

Several recent studies, including a meta-analysis of maternal depression interventions, suggest that a single depression intervention may not suffice in significantly altering child psychological and cognitive developmental trajectories.[21, 22] Our results extend this conclusion to lower resource settings in a South Asian context. Research linking maternal depression to child developmental outcomes is robust, but the unique contribution of *perinatal* depression, independent of factors such as the chronicity of depression in the child's first years of life, is less well understood.[2-6, 23] The strongest correlations are often with current depressive symptoms (although not the focus of our analysis, we also observed a concurrent association between maternal symptoms and the child outcomes). Our finding that prenatal depression in the third trimester of pregnancy was correlated with the SDQ Total Difficulties score and the SCAS anxiety score independent of the mother's current depressive symptoms suggests that depression in the perinatal period may make a unique contribution to a child's socio-emotional development.

Advances in the understanding of child brain development may assist in the interpretation of the null intervention effect findings. The child's first years of life beginning prenatally comprise of multiple sensitive periods for the development of various cognitive and socio-emotional functions.[24] The external environment provides crucial inputs leading to the activation of specific epigenetic pathways and ultimately a unique set of risk and resilience factors.[25] Perinatal depression is thought to shape this developmental trajectory through, for instance, lower maternal sensitivity, insecure attachment, and less stimulation.[2, 26] It's therefore possible that the intervention may have had greater impact if it started earlier in pregnancy and/or continued for longer after birth. However, the early years are not the sole sensitive period and evidence of later plasticity can be seen in adoption studies as well as interventions

among older children.[27, 28] In our context, it is possible that early positive changes were offset by multiple later risks which in effect "updated" the child's developmental trajectory; as mentioned above, the treatment arm was associated with worse anxiety scores among children of relapsed mothers, but not among the children of the never recovered. One explanation of this is that children of women who were successfully treated for depression but then relapsed experienced an inconsistent child rearing environment.[29] This is one area for future study as we were not able to fully explore the differential impact of chronic versus recurrent depression episodes on child outcomes with our data. Multiple other factors such as interpersonal violence or financial hardship have been linked with increased risk of depression relapse as well as negative child outcomes.[20, 30, 31] Small cell sizes did not permit us to fully explore the extent to which these factors explained our findings. The limited data available suggests that these risk factors were balanced across treatment/control arms at the 7 year follow-up but more information is needed about changes in risk factors in the intervening years. For example, if women in the treatment arm experienced even a short term increase in the risk of interpersonal violence relative to the control arm, this might lead to both higher likelihood of relapse and socio-emotional problems in the child.

Interactions between different risk factors in early childhood are evident in findings of an independent association between maternal depression and poor growth in low income settings.[32] There is also growing evidence that inputs such as nutrition and stimulation interact in the production of child developmental outcomes[33] and previous trials in which depression treatment is combined with nutritional and parenting components are among the most successful.[33] It is hence possible that, in environments with multiple adversities (e.g. malnutrition, low social support, overall poor health), treating maternal depression alone may not be sufficient to address children's cumulative risk.[21, 22, 34]

Another possibility is that the intervention we analyze does in fact have a positive impact on child development but that this is latent at age seven, becoming discernible at a later stage in life. One mechanism by which this may occur is that an initially small difference in capabilities between children in the treated and control arms is magnified by "dynamic complementarities"[35] which refers to the tendency for inputs to child development in the early years to complement one another: Cognitive skills may be reinforced by non-cognitive skills. Evidence of such a process has been observed in pre-school interventions such as the Project STAR in which differences in test scores were visible until kindergarten, then faded away but re-emerged as earnings differences in adulthood.[36] In response to their children's health in the early years, parents may reinforce rather than compensate and, if the opportunities arise, raise their investments in the children over time.[37] These factors will tend to lead to continuously diverging trajectories, making it plausible that initially small differences between children will grow larger as they age and, at some stage, become empirically significant.

Some methodological limitations may also be relevant. It is possible that there was some geographic diffusion of THP components over time between the lady health workers, once the trial ended. Hence women in the control arm may have become exposed to some components of THP and thus become similar to the treatment arm women. It is difficult to determine if such a process occurred and ideally data would have been available from time points between the end of the intervention trial at 12 months post-partum and this 7 year follow-up. Potential loss of randomization through loss-to-follow-up, common with all longitudinal studies, cannot be ruled out, although there was little evidence of differential attrition between study arms.

Reporting bias may have occurred since the child socio-emotional outcomes were mother reported, and it is possible that THP intervened women had become more emotionally literate thus more likely to notice specific symptoms in their children. Similarly, current depressive symptoms may have influenced

maternal report, although all models adjusted for current depression. Factors such as the child's gender may further influence how the mother responds to questions, in addition to influencing multiple other factors of interest.

Utilizing measurement tools created in a different cultural context from the one they are being used in raises assessment validity issue. This was especially important with the anxiety measure, the SCAS, which, to our knowledge, has not been previously used in South Asia. We conducted extensive testing, consultations with child psychiatrists, and piloting, but were not able to conduct a formal measure validation. In Asia, the SCAS has been validated in China among 8-15 year olds, and found to have good convergent and divergent validity with satisfactory reliability.[38] With regard to modelling associations of interest, heteroskedastic error terms remained with various SCAS specifications; while not expected to bias our estimate, this might lead to the variance being estimated with error. The reliability coefficient for the SDQ TD was also lower than coefficients previously reported in other non-Western settings, suggesting that additional validation studies may be needed in South Asia[15, 39-42] The comparisons of the reference group of prenatally non depressed women with trial participants is based on observational data (vs. the randomized RCT comparison) and hence are more subject to bias by unmeasured confounders. We included multiple statistical controls in the models, including for current depression, but the possibility of additional bias cannot be ruled out.

Finally, there remain several unexplored cultural factors that might influence child development and may be correlated with the treatment. For example, there is evidence that the presence of grandmothers may be protective against maternal depression.[43] In the context of more communal child rearing in extended families, it is possible that a resident grandmother took on more early child rearing responsibilities in the control arm where the mother was more likely to remain depressed around the

time of the intervention. The child would thus be less exposed to maternal depression, potentially making children between treatment and control arms more similar.

Conclusions

Maternal depression influences child development, hence efforts to ameliorate its effects should be an integral part of maternal and child health programs. However, further exploration is needed to understand the types of interventions that are needed for long term developmental trajectory improvements. It is possible that the most successful interventions are integrated and multi-component, combining a perinatal depression program with nutrition and early stimulation[44]. More understanding is also needed of how remission of depressive symptoms impacts child development, through mechanisms such as lack of maternal warmth or sensitivity, as well as the cultural factors that promote resilience and promote health child development.[21, 45] Longer, more detailed and more frequent follow-up is thus warranted for all interventions.

Research in Context

Evidence before this study

Before we undertook this study, we conducted a literature review on existing evidence on the effect of treating perinatal depression on longer term child outcomes, with a focus on lower and middle income settings. Our focus was on randomized trials since causal relationships are difficult to establish from observational studies, given the many environmental factors that increase both risk of maternal depression and negative child outcomes. Evidence from RCTs showed that treating perinatal depression can improve some developmental outcomes among children, especially in the short term.[9-11, 22, 46] However two meta-analyses found overall support mixed for evidence of improved child outcomes with improvements in depression symptoms and called for more rigorous research in this area[21, 47]. We did

not find experimental evidence of the impact of treating perinatal depression on longer term child outcomes in a lower and middle income setting. Furthermore, we found a paucity of research on maternal depression and child development from South Asia.[23, 48, 49]

Added value of this study

This study provides the first evidence from South Asia of a perinatal depression RCT on school aged child outcomes. We found that the intervention was not able to reduce deficits in socio-emotional functioning that exist between children of perinatally depressed and non-depressed mothers, even after accounting for current depressive symptoms.

Implications

The policy and practice implications of this finding are that initial evidence of positive impact of an intervention may not translate to longer term change. More evidence is needed on the types of interventions that are most likely to have longer term impact on improving child developmental trajectories. Longer, more detailed and more frequent follow-up is thus warranted for all interventions.

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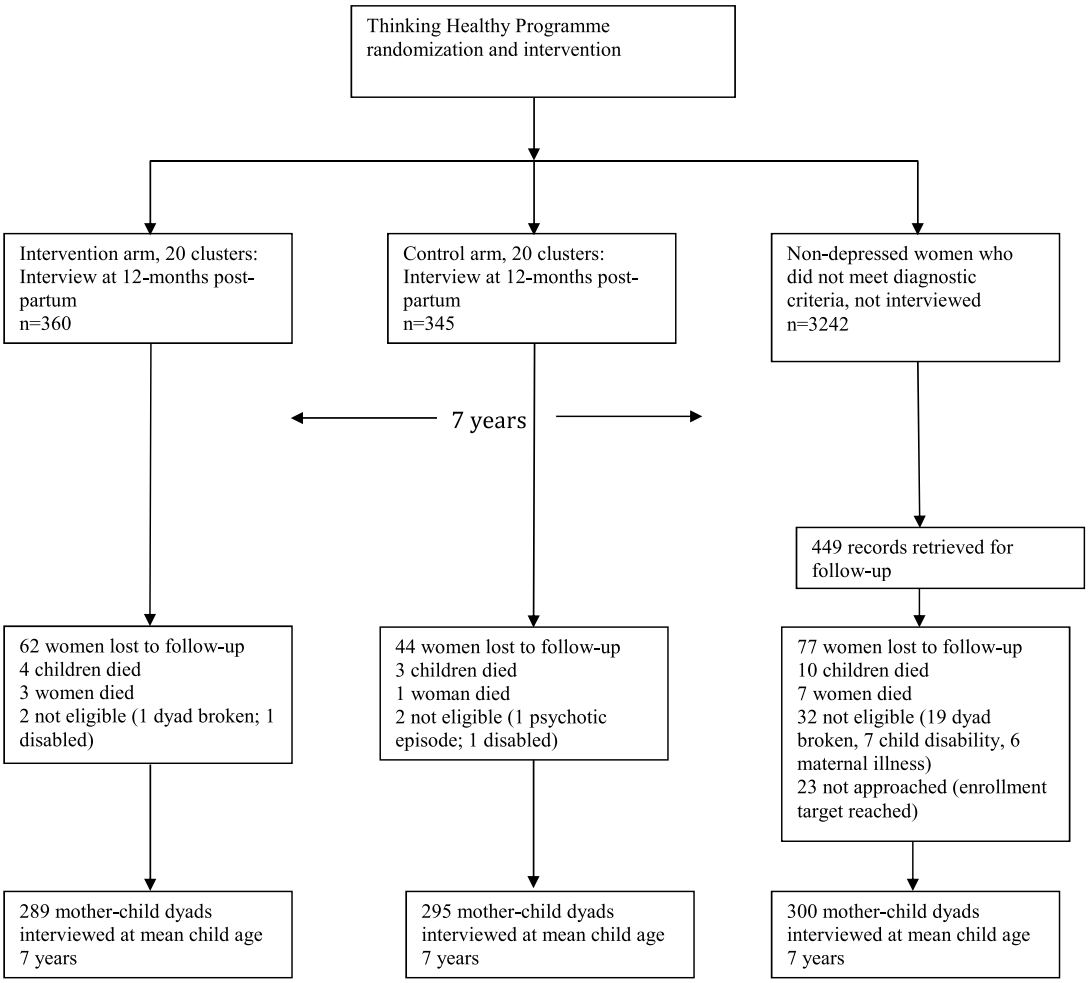
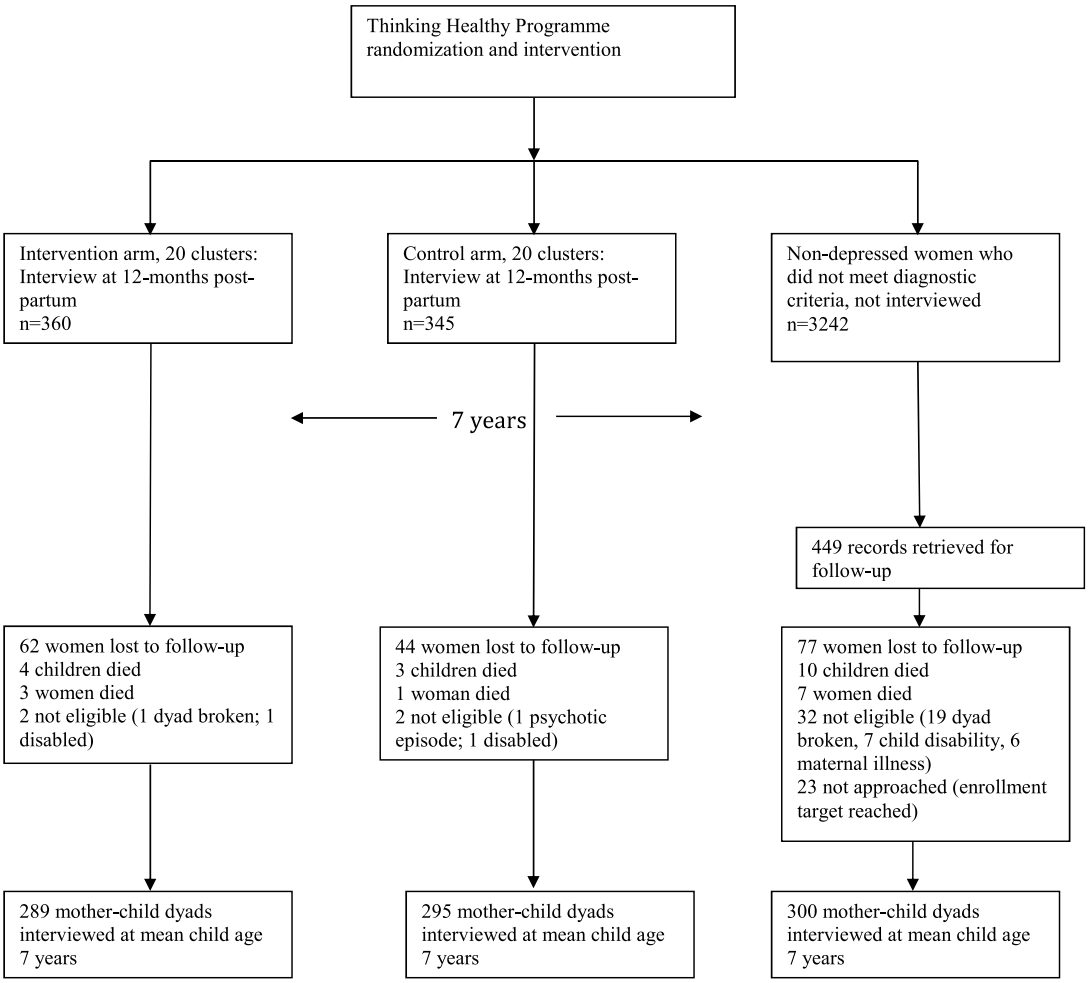
Figure

Figure 1. Sample size flow from original Thinking Healthy Programme (THP) intervention to current follow-up study.



Figure

Figure 1. Sample size flow from original Thinking Healthy Programme (THP) intervention to current follow-up study.



Table

Table 1: Sample characteristics of the THP depression intervention follow-up study.

	Treatment arm n=289		Control arm n=295		Prenatally Non-depressed n=300	
	n or mean	% or SD	n or mean	% or SD	n or mean	% or SD
Maternal						
Maternal age (mean)	34.06	5.8	35.41	6.1	34.08	5.2
20-24	6	2%	2	0.7%	1	0.3%
25-29	47	16.3%	38	12.9%	46	15.3%
30-34	98	33.9%	86	29.2%	117	39.0%
35-39	85	29.4%	86	29.2%	83	27.7%
40-44	25	8.7%	57	19.3%	35	11.7%
45+	28	9.7%	26	8.8%	18	6.0%
Schooling	4.34	4.0	3.67	3.8	5.54	4.5
0	109	37.7%	123	41.7%	91	30.3%
1-6 (primary)	91	31.5%	105	35.6%	83	27.7%
7-10 (secondary)	82	28.4%	59	20.0%	94	31.3%
>10	7	2.4%	8	2.7%	32	10.7%
Family/household						
Structure						
Nuclear	127	43.9%	155	52.5%	121	40.3%
Joint/extended	126	43.6%	108	36.6%	153	51.0%
Multiple households	36	12.5%	32	10.9%	26	8.7%
Number of children (mean)	4.23	1.46	4.40	1.5	4.00	1.4
1	2	0.7%	5	1.7%	1	0.3%
2 to 3	100	34.6%	77	26.1%	121	40.4%
4 to 5	132	45.7%	152	51.5%	140	46.7%
More than 5	55	19%	61	20.7%	38	12.6%
SES rating by LHW (mean)	3.42	0.7	3.55	0.8	3.34	0.8
Rich	17	5.9%	13	4.4%	31	10.3%
Moderate	156	54.0%	142	48.1%	155	51.7%
Poor	93	32.2%	105	35.6%	93	31.0%

Poorest	23	8.0%	35	11.9%	21	7.0%
Mean husband schooling	6.96	3.9	6.96	3.8	8.01	3.6
Index Child						
Age (mean)	7.57	0.14	7.56	0.12	7.57	0.09
Child gender						
Male	133	46.0%	155	52.5%	160	53.3%
Female	156	54.0%	140	47.5%	140	46.7%
Current education status						
Not in school	6	2.1%	4	1.40%	2	0.6%
Preschool/prep./nursery	18	6.2%	16	5.4%	26	8.7%
1st grade	67	23.2%	64	21.7%	53	17.7%
2nd grade	137	47.4%	132	44.7%	121	40.3%
3rd grade	61	21.1%	79	26.8%	98	32.7%

Table 2. Child developmental outcomes in the treatment and control arms among THP trial participants.

	Thinking Healthy Programme RCT group (Prenatally Depressed) n=584						
	Treatment n=289		Control n=295		Adjusted mean difference (treatment-control)		
	Mean	SD	Mean	SD	beta	(95% CI)	p-value
Primary Outcomes							
Cognitive Outcomes							
WPPSI FSIQ	82.53	11.30	82.13	11.40	-0.01	(-2.09,2.07)	0.99
Socio-emotional Outcomes							
SDQ Total Difficulties	11.55	5.3	11.12	5.2	0.51	(-0.45,1.47)	0.29
SCAS anxiety	22.31	14.1	20.37	13.4	1.83	(-0.37,4.04)	0.10
Physical Growth Outcomes							
Height-for-age z score	-0.88	1.0	-0.80	1.1	-0.06	(-0.25,0.14)	0.56
Weight-for-age z score	-1.18	1.2	-1.12	1.1	-0.13	(-0.32,0.07)	0.20
BMI-for-age z score	-1.06	1.2	-0.97	1.2	0.01	(-0.21,0.22)	0.95
Secondary Outcomes (component sub-scales of primary outcomes)							
WPPSI Components							
Verbal comprehension (vci)	86.26	14.15	85.24	13.60	0.32	(-2.52,3.17)	0.82
Visual spatial (vsi)	87.92	14.15	87.54	15.04	-1.56	(-3.83,0.72)	0.18
SDQ Components							
Emotional	2.49	2.1	2.35	2.1	0.15	(-0.22,0.51)	0.43
Conduct problems	3.29	2.1	3.32	2.0	0.04	(-0.28,0.37)	0.79
Hyperactivity	3.72	2.5	3.52	2.6	0.27	(-0.19,0.74)	0.25
Peer problems	2.04	1.6	1.94	1.6	0.03	(-0.23,0.30)	0.82
Pro-social	7.69	2.5	7.49	2.5	0.04	(-0.37,0.44)	0.86
SCAS Anxiety components							

Panic/agoraphobia	2.01	3.4	1.48	2.7	0.52	(0.02,1.03)	0.04
Separation	6.30	4.3	5.92	4.0	0.45	(-0.21,1.11)	0.18
Injury fear	6.21	3.7	6.01	3.7	0.06	(-0.52,0.64)	0.85
Social phobia	2.35	2.9	2.40	2.9	-0.08	(-0.59,0.42)	0.75
Obsessive compulsive	1.61	2.5	1.19	1.9	0.57	(0.18,0.95)	0.00
General anxiety	3.83	3.3	3.37	3.3	0.34	(-0.25,0.92)	0.26

Table 3. Child developmental outcomes by prenatal depression status

	Thinking Healthy Programme RCT group (Prenatally Depressed) n=584		Reference Group (Prenatally Non Depressed) n=300		Adjusted mean difference (RCT group - reference group)		
	Mean	SD	Mean	SD	beta	(95% CI)	p-value
Primary Outcomes							
Cognitive Outcomes							
WPPSI FSIQ	82.32	11.4	83.64	12.9	0.73	(-0.80,2.27)	0.35
Socio-emotional Outcomes							
SDQ Total Difficulties	11.34	5.3	10.35	5.0	0.78	(0.09, 1.47)	0.03
SCAS anxiety	21.33	13.8	17.57	11.2	2.93	(1.15, 4.71)	0.00
Physical Growth Outcomes							
Height-for-age z score	-0.80	1.1	-0.88	1.1	0.12	(-0.04,0.28)	0.15
Weight-for-age z score	-1.10	1.1	-1.21	1.1	0.13	(-0.03,0.30)	0.10
BMI-for-age z score	-0.97	1.3	-0.99	1.1	0.05	(-0.13,0.22)	0.60
Secondary Outcomes (component sub-scales of primary outcomes)							
WPPSI Components							
Verbal comprehension (vci)	85.75	13.9	87.69	15.7	0.52	(-1.26,2.30)	0.57
Visual spatial (vsi)	86.73	14.2	87.33	15.4	0.98	(-1.03,2.99)	0.34
SDQ Components							
Emotional	2.42	2.1	1.76	1.7	0.53	(0.26, 0.80)	0.00
Conduct problems	3.30	2.1	3.23	2.0	0.08	(-0.20, 0.36)	0.60
Hyperactivity	3.62	2.5	3.42	2.6	0.11	(-0.24, 0.45)	0.55
Peer problems	1.99	1.6	1.94	1.5	0.07	(-0.14, 0.28)	0.50
Pro-social	7.59	2.5	7.61	2.5	0.06	(-0.26, 0.38)	0.71

SCAS Anxiety components							
Panic/agoraphobia	1.75	3.0	1.05	2.0	0.48	(0.10, 0.86)	0.01
Separation	6.10	4.2	5.08	3.9	0.75	(0.19,1.31)	0.01
Injury fear	6.12	3.7	5.48	3.7	0.37	(-0.13,0.86)	0.15
Social phobia	2.38	2.9	1.70	2.3	0.61	(0.23,0.99)	0.00
Obsessive compulsive	1.40	2.3	1.19	1.9	0.26	(-0.03,0.54)	0.08
General anxiety	3.59	3.3	3.08	2.7	0.45	(0.04,0.87)	0.03