

Research Article

Cite this article: Fuhr DC, Sikander S, Vanobberghen F, Weobong B, Rahman A, Weiss HA (2023). Predictors of spontaneous remission and recovery among women with untreated perinatal depression in India and Pakistan. *Cambridge Prisms: Global Mental Health*, 10, e34, 1–8
<https://doi.org/10.1017/gmh.2023.26>

Received: 05 January 2023

Revised: 23 April 2023

Accepted: 08 June 2023

Keywords:

perinatal depression; remission; untreated depression; India; Pakistan

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Predictors of spontaneous remission and recovery among women with untreated perinatal depression in India and Pakistan

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Abstract

Background: Mothers with perinatal depression can show different symptom trajectories and may spontaneously remit from depression, however, the latter is poorly understood. This is the first study which sought to investigate predictors of spontaneous remission and longer-term recovery among untreated women with perinatal depression.

Methods: We analysed data from two randomised controlled trials in women with perinatal depression in India and Pakistan. Analyses were restricted to women in the control groups who did not receive active treatment. Generalised estimating equations and logistic regressions were used to estimate odds ratios (ORs) and 95% confidence intervals (CIs), adjusting for within-person correlation.

Results: In multivariable analyses, remission was associated with a husband who is not working (adjusted OR, aOR = 2.04, 95% CI 1.02–4.11), lower Patient Health Questionnaire-9 score at baseline (aOR = 0.43, 95% CI 0.20–0.90 for score of ≥ 20 vs. 10–14) and better social support at baseline (aOR = 2.37, 95% CI 1.32–4.27 for high vs. low social support).

Conclusions: Women with low baseline severity may remit from perinatal depression with adequate social support from family and friends. These factors are important contributors to the management of perinatal depression and the prevention of clinical worsening, and should be considered when designing low-threshold psychological interventions.

Impact statement

Perinatal depression is a disabling mental condition that can significantly affect mothers after child birth and within the first year postpartum. The majority of women who develop depression after birth may show mild or moderate symptoms only, that have the potential to resolve over time without providing treatment. However, there is paucity of evidence of what may trigger spontaneous remission of perinatal depression and which factors are associated with this. With this study, we shed light on factors that may determine remission and recovery of symptoms. We do this by analysing data of mothers with depression who did not receive active treatment for their symptoms and followed them up over 6 months' time.

Introduction

Perinatal depression is a disabling mental condition that has its onset during pregnancy or within the first year after delivery, and can significantly impair psycho-social functioning (DSM-V, 2013; Woody et al., 2017). In a recent systematic review and meta-analysis, the estimated prevalence of perinatal depression globally was higher among women in low- and middle-income countries (18.7% postnatally and 19.2% prenatally) than among women in high income countries (9.5% postnatally and 9.2% prenatally) (Woody et al., 2017). Mild and moderate symptoms of depression are most common (Hegel et al., 2006), however, for perinatal depression specifically, heterogeneity of symptoms has been reported (Santos et al., 2017). Low, medium and chronic symptom trajectories for perinatal depression have been established (Santos et al., 2017) but these may not necessarily follow expected patterns and may be transient (Baron et al., 2017). It is speculated that symptom trajectories may be influenced by specific biological, social and

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psychological risk factors. These include prior history of psychopathology, high parity, low social support, lack of education and exposure to negative life events (Yim *et al.*, 2015; Ahmed *et al.*, 2019). However, we currently lack knowledge about modifiable risk factors and these still need to be established (Baron *et al.*, 2017). The heterogeneity of symptoms of perinatal depression led to a call to personalise treatment to improve the response to treatment and facilitate recovery (Johansen *et al.*, 2019). Our previous research on the effectiveness of brief psychological interventions for women with perinatal depression supports this tailored approach to treatment and suggests that a low-intensity psychological intervention for perinatal depression delivered by peers may be most suitable for women whose depression is mild and acute rather than chronic and severe (Fuhr *et al.*, 2019; Sikander *et al.*, 2019; Singla *et al.*, 2021).

Research also reports spontaneous remission for perinatal depression (Yazici *et al.*, 2015; Maselko *et al.*, 2020). Spontaneous remission is attained when sub-clinical levels of symptoms of depression are achieved without treatment, determined for example by a below-threshold score on a standardised symptom severity measure (Whiteford *et al.*, 2013). It has been more extensively studied for major depressive disorder, and a systematic review found that among people with untreated depression, 53% had spontaneous remission within 1 year (Whiteford *et al.*, 2013). Spontaneous remission may be associated with the presence of other mental health problems, the duration of the overall episode and severity of symptoms, individual genetic vulnerabilities, personality traits as well as environmental supports and stressors (Paykel, 1998; Rush *et al.*, 2006). It is especially common among people who show mild or moderate symptoms of depression only (Posternak and Miller, 2001; Hegel *et al.*, 2006), and this has been confirmed for pregnant and post-partum women as well (Yazici *et al.*, 2015; Santos *et al.*, 2017; Maselko *et al.*, 2020). Although there is evidence that women with perinatal depression may show spontaneous remission, and improve symptoms over time, the predictors for spontaneous remission and recovery (defined as remission at both 3 and 6 months) still need to be investigated further. This will strengthen the evidence base for the prevention and treatment of perinatal depression, and increase our understanding of the contribution of active treatment to remission and recovery.

In this study, we conducted secondary analyses of data from two completed randomised controlled trials (RCTs) in India and Pakistan which demonstrated the effectiveness of a peer-delivered psychological intervention on symptoms of perinatal depression (Fuhr *et al.*, 2019; Sikander *et al.*, 2019). We analysed data from women with perinatal depression in the control groups of the two trials who did not receive active treatment. The objectives of this study were a) to understand factors associated with remission among women with untreated perinatal depression in India and Pakistan; b) to explore factors associated with longer-term recovery; and c) to investigate if these factors differ by country.

Methods

We pooled data from two RCTs which sought to investigate the effect of a task-shifted psychological intervention (The Thinking Healthy Programme-Peer delivered [THPP]) on the severity of symptoms for perinatal depression and remission (Vanobberghen *et al.*, 2020). The results from the trials (an individually randomised trial in urban Goa, India; and a cluster RCT in rural sub-districts of Rawalpindi, Pakistan) have been published previously (Fuhr *et al.*, 2019; Sikander *et al.*, 2019). Data from these trials were collected

during 2014–2016. Participants were recruited from antenatal centres and primary health care in Goa, and from community-based households in Rawalpindi. In both countries, participants were aged ≥ 18 years, in their second or third trimester of pregnancy at enrolment, and scored ≥ 10 on the Patient Health Questionnaire-9 (PHQ-9). The intervention was delivered by peers who were women from the local community who had children themselves and had gone through the experience of pregnancy, childbirth and raising a family.

Women in the control group received enhanced usual care. This included the following: First, women and their antenatal health care providers (antenatal health care providers were gynaecologists in Goa, and local government employed community health workers in Rawalpindi) were informed about the PHQ-9 score and depression status of participants. We also provided referral information to the gynaecologist (in Goa) and to the primary care physician (in Pakistan) who received training on the mental health gap intervention guide and referrals. Second, participants were provided with an information leaflet containing information about self-care during pregnancy and local self-referral pathways to mental health care. In addition to enhanced usual care, women in the intervention group received the THPP, a task-shifted psychological intervention based on behavioural activation which was delivered in 6–14 sessions over 6 months.

The primary trial outcome was remission, defined as the absence of depressive symptoms (PHQ-9 < 5) at 3 months post birth. The PHQ-9 was translated and validated in the local languages. Secondary outcomes included remission at 6 months, and recovery (PHQ-9 < 5 at both 3 and 6 months post birth).

Data were collected on the following baseline characteristics of the mother: Age in years; level of education (no formal education, up to primary education, up to secondary education, beyond secondary education); employment status (employed or not being currently employed); total number of children; previous miscarriage or still birth (none, one or more); sex of the current baby (girl or boy); family structure (nuclear or extended, i.e., living on their own with family or extended families living together); financial empowerment (yes/no), that is, asking if mother is able to put aside money for their own personal use or not; debt (yes/no), that is, asking if anyone in household is currently in debt or not; and if the mother has experienced any domestic violence in the past 3 months (yes/no). Perceived social support of the mother was measured with the Multidimensional Scale of Perceived Social Support. We also asked the mother about her expectation and how she would find the THPP intervention prior to starting it (not/little useful, somewhat useful, moderately useful, very useful). We collected data on her husband, namely, his level of education (no formal education, up to primary education, up to secondary education, beyond secondary education), employment status (employed or not being currently employed) and the number of months the husband had been away from home in the past 6 months (less than 1 month, 1 month or more).

For this paper, analyses were restricted to participants randomised to the control group of the trials. Data analysis was conducted using Stata version 17.0 (Stata, 2022). We used generalised estimating equations (GEEs) to adjust for within person correlation, and estimated odds ratios (ORs) and 95% confidence intervals (CIs) using logistic regression. Factors associated with remission were estimated by conducting a repeat measures analysis using data from both 3- and 6-month visits for each woman. We adjusted for country and month of visit (*a priori*), and factors associated with missing outcome data ('minimally adjusted

model'). We performed complete case analyses, that is, visits were included if remission data were available for that visit. We conducted sensitivity analyses using multiple imputation as an alternative strategy to account for missing outcome data. This imputed missing outcome data with 25 imputations. The final multivariable model included variables independently associated with the outcome, determined by starting with a full model of variables associated with the outcome with $p < 0.1$ in the minimally adjusted model, and retaining them if they were independently associated with the outcome in the multivariable model ($p < 0.05$). Country was an a priori effect-modifier, and effect-modification by country was assessed for the final models by fitting an interaction term of country and each exposure variable.

The study was performed in accordance with the ethical standards as laid down in the Declaration of Helsinki and its later amendments. Ethical approval was obtained from the Institutional Review Boards at the London School of Hygiene and Tropical Medicine, Sangath (the implementing institution in India), the Indian Council of Medical Research, the University of Liverpool and the Human Development Research Foundation (the implementing organisation in Pakistan). All study participants provided their informed consent prior to their inclusion in the study.

Results

In India, 118,260 women were assessed for eligibility over a 2-year period, of whom 6,369 were screened using the PHQ-9, and 333 were eligible. Of these, 280 (84.1%) women were enrolled into the trial (140 randomly allocated per group). Over the same period, 1,910 pregnant women in Pakistan from 40 village clusters were assessed. Of these, 1,731 were screened using the PHQ-9, and 572 were eligible. Of these 570 (99%) were enrolled into the trial (283 in the intervention group and 287 in the control group).

Baseline characteristics of the 427 participants randomised to the control groups are shown in Table 1. Participants in India were slightly younger than those in Pakistan (mean 25.3 and 27.3 years, respectively) and had less education overall (55.7% of those in India had no formal education or primary education only, compared with 26.9% in Pakistan). The majority of participants in both countries did not work, however, participants in India were less likely to be in debt and reported being more financially empowered than those in Pakistan (78.6% vs. 54.7%). A higher proportion of participants in India had fewer than two children, and reported fewer miscarriages or stillbirths than participants in Pakistan. Participants in India tended to have less severe depression than those in Pakistan (71.4% with moderate depression in India vs. 58.2% in Pakistan), and to have had depression for a shorter period (35.7% with chronicity ≥ 12 weeks at baseline assessment vs. 80.3% in Pakistan). Participants in India reported higher perceived social support but had lower expectations of the usefulness of psychological counselling.

Overall, 56 (13.1%) of participants were not seen at both 3 and 6 months (i.e., lost to follow-up). Of these, 9 participants were in India (6.4% loss to follow-up), and 47 were in Pakistan (16.5% loss to follow-up). Factors independently associated with loss to follow-up were country ($p = 0.003$), and whether the woman worked outside the home ($p = 0.01$). These were adjusted for in subsequent analyses.

The prevalence of remission at 3 months and 6 months, respectively, were each lower among participants in Pakistan than those in India (44.1% vs. 50.8% at 3 months; 44.7% vs. 59.7% at 6 months; Appendix 1 of the Supplementary Material). This difference was

Table 1. Baseline characteristics of participants with untreated perinatal depression

	India (N = 140)	Pakistan (N = 287)
Age, years of mother (mean (SD; range))	25.3 (4.74) (18–39)	27.3 (4.97) (18–45)
Sex of current baby (n (%))		
Girl	63 (48.1%)	114 (47.3%)
Boy	68 (51.2%)	127 (52.7%)
Missing	9	46
Level of education (mother) (n (%))		
No formal education	13 (9.3%)	55 (19.2%)
Up to primary	65 (46.4%)	22 (7.7%)
Up to secondary	46 (32.9%)	162 (56.5%)
Beyond secondary	16 (11.4%)	48 (16.7%)
Occupation (mother) (n (%))		
Not employed	118 (84.3%)	270 (94.1%)
Employed	22 (15.7%)	17 (5.9%)
Level of education (husband) (n (%))		
No formal education/up to primary	66 (47.1%)	26 (9.1%)
Up to secondary	52 (37.1%)	222 (77.4%)
Beyond secondary	22 (15.7%)	39 (13.6%)
Occupation (husband) (n (%))		
Employed	138 (98.6%)	258 (89.9%)
Not employed	2 (1.4%)	29 (10.1%)
Husband away from home during past 6 months (n (%))		
<1 month	127 (90.7%)	200 (77.5%)
≥ 1 month	13 (9.3%)	58 (22.5%)
Total number of children (n (%))		
0	65 (46.4%)	54 (20.2%)
1	52 (37.1%)	82 (30.7%)
≥ 2	23 (16.4%)	131 (49.1%)
Family structure (n (%))		
Nuclear family	63 (45.0%)	71 (24.7%)
Extended families living together	77 (55.0%)	216 (75.5%)
Debt of household (n (%))		
No	83 (59.3%)	118 (41.1%)
Yes	57 (40.7%)	169 (58.9%)
Financial empowerment of mother (n (%))		
No	30 (21.4%)	130 (45.3%)
Yes	110 (78.6%)	157 (54.7%)
PHQ-9 score (median (IQR))	12 (11–15)	14 (12–17)
PHQ-9 category (n (%))		
Moderate (score 10–14)	100 (71.4%)	167 (58.2%)
Moderately severe (15–19)	35 (25.0%)	88 (30.7%)
Severe (20–27)	5 (3.6%)	32 (11.2%)

(Continued)

Table 1. (Continued)

	India (N = 140)	Pakistan (N = 287)
Chronicity of depression, weeks (n (%))		
<12 weeks	90 (64.3%)	38 (19.7%)
≥12 weeks	50 (35.7%)	155 (80.3%)
Missing	0	94
MSPSS score (mean (SD))	5.40 (1.10)	3.95 (1.33)
Participant's expectation of usefulness of counselling (n (%))		
Not/a little useful	30 (21.4%)	15 (5.2%)
Somewhat useful	32 (22.9%)	60 (21.0%)
Moderately useful	28 (20.0%)	124 (43.4%)
Very useful	50 (35.7%)	87 (30.4%)
Parity (n (%))		
Primiparous	58 (41.4%)	50 (17.4%)
Multiparous	82 (58.6%)	237 (82.6%)
Previous miscarriage or still birth (n (%))		
None	130 (92.9%)	185 (64.5%)
One/more	10 (7.1%)	102 (35.5%)
Any domestic violence in last 3 months (n (%))		
No	119 (85.0%)	241 (85.5%)
Yes	21 (15.0%)	41 (14.6%)

Abbreviation: MSPSS, Multidimensional Scale of Perceived Social Support.

statistically significant (minimally adjusted OR [aOR] = 1.55; 95% CI 1.08–2.22; $p = 0.02$; for the two endpoints combined; Table 2).

The association between other factors and remission are presented in Table 2.

In the multivariable model (Table 3), remission was more likely among participants with a husband who was not working (aOR = 2.04, 95% CI 1.02–4.11 for not working vs. working), lower PHQ-9 score at baseline (aOR = 0.43, 95% CI 0.20–0.90 for score of ≥20 vs. 10–14) and better social support at baseline (aOR = 2.41, 95% CI 1.35–4.31 for high vs. low social support). There was no evidence of a difference in remission by country after adjusting for these factors ($p = 0.28$). The results from multiple imputation gave similar results (Table 3). There was strong evidence of a greater effect of high social support versus low/moderate support on remission in India than in Pakistan ($p = 0.003$), and strong evidence of a trend with greater social support in India ($p = 0.003$) (Appendix 2 of the Supplementary Material).

Overall, 317 participants had data at both 3- and 6-month time points, and of these 100 (31.6%) had recovery. In multivariable analyses, improved recovery was associated with country (aOR = 1.81, 95% CI 1.02–3.19, $p = 0.04$ for India vs. Pakistan), and to a lesser extent with better social support (aOR = 2.03, 95% CI 0.84–4.89 for high vs. low social support; p -value for trend = 0.08), higher husband's education (aOR = 2.22, 95% CI 0.98–5.03; p -value for trend = 0.05) and lower PHQ-9 score (aOR = 0.36, 95% CI 0.10–1.29, p -value for trend = 0.09). Power was relatively lower for this analysis. With 317 participants with data on recovery, we had 80% power to detect a difference in proportions of 25% vs. 40% for variables where 50% of the study population are exposed. Data

on recovery are presented in Appendix 3 of the Supplementary Material.

Discussion

To the best of our knowledge, this is the first study which assesses predictors of spontaneous remission and recovery in women with untreated perinatal depression. Almost half the women who did not receive active treatment for perinatal depression had spontaneous remission at 3 or 6 months post birth. Baseline factors associated with remission were lower baseline severity, strong social support from family and friends, and a husband who was not working. Recovery was lower than remission with around a third of women showing spontaneous remission at both 3 and 6 months post birth. Power was lower to detect associations with recovery but there were indications of similar factors as for remission. Remission and recovery were more common in India than in Pakistan in univariable analyses, with evidence of improved remission with greater social support in India.

The finding that participants with lower baseline symptom severity are more likely to remit is similar to research on major depressive disorder (Keller et al., 1992; Paykel, 1998; Posternak and Miller, 2001; Rush et al., 2006). Social support, in the form of instrumental and emotional help has also been identified as an important factor influencing spontaneous remission for depression (Hegel et al., 2006; Fuller-Thomson et al., 2014). Qualitative research further substantiates this finding and confirms that women with depression need a reliable social support system to facilitate the process of natural recovery (Naeem et al., 2004). A mother with a husband who is not working was also associated with remission in our analyses. One could speculate that this might infer social support being provided, however, unemployment of the husband may also strain the financial situation of the household and may lead to stress and insecurities in the household. This may aggravate mental health symptoms as seen in other studies (Patel et al., 2002). Therefore, this finding should be interpreted with caution and unpacked further in future studies. Strengths of our study include the size and strong internal validity of the trial procedures (such as no differential drop out, use of adequate control groups, and adherence to research protocols) but our study has also some limitations. First, we were reliant on the baseline variables of the trials and did not have measures of some factors for spontaneous remission and recovery which have been identified for major depressive disorder (Rush et al., 2006; Fuller-Thomson et al., 2014). These include the presence of other mental health problems, personality disorders or physical health problems. Whilst we screened for serious mental health problems such as psychosis, and excluded women who needed acute medical help, we did not screen for personality disorders. Personality traits might hinder spontaneous remission, and there is evidence suggesting a negative association between passive dependent personality traits and remission (Paykel, 1998). The type of coping and how to generally deal with life problems may also be important. Problem-focused coping has been shown to promote spontaneous remission, whereas the use of avoidant coping mechanisms may leave people feeling stuck in a specific situation, not allowing them to experience reinforcing activities (Hegel et al., 2006).

Second, there may be effects of being enrolled in a trial which may have led to the improvement of symptoms and to spontaneous remission of perinatal depression in our study. Evidence shows that follow-up assessments (Posternak and Zimmerman,

Table 2. Factors associated with remission (PHQ < 5 at 3 or 6 months)

	N (3 m)	Remission at 3 m n (%)	N (6 m)	Remission at 6 m n (%)	OR for remission* (95% CI)	p-Value*
Country						
Pakistan	211	93 (44.1%)	226	101 (44.7%)	1	0.02
India	122	62 (50.8%)	129	77 (59.7%)	1.55 (1.08–2.23)	
Age group, years						
≤24	126	59 (46.8%)	135	74 (54.8%)	1	0.82
25–29	105	48 (45.7%)	111	49 (44.1%)	0.92 (0.60–1.40)	
≥30	102	48 (47.1%)	109	55 (50.5%)	1.05 (0.69–1.61)	
Sex of current baby						
Male	156	72 (46.2%)	168	82 (48.8%)	1	0.66
Female	177	83 (46.9%)	186	96 (51.6%)	1.08 (0.77–1.52)	
Level of education (mother)						
No formal education	46	14 (30.4%)	56	28 (50.0%)	1	0.67
Up to primary	75	34 (45.3%)	80	46 (57.5%)	1.16 (0.63–2.13)	
Up to secondary	166	84 (50.6%)	172	80 (46.5%)	1.30 (0.78–2.15)	
Beyond secondary	46	23 (50.0%)	47	24 (51.1%)	1.43 (0.75–2.72)	
Occupation (mother)						
Employed	28	14 (50.0%)	29	13 (44.8%)	1	0.58
Not employed	305	141 (46.2%)	326	165 (50.6%)	1.20 (0.64–2.25)	
Level of education (husband)						
No formal education/up to primary	73	27 (37.0%)	81	43 (53.1%)	1	0.06
Up to secondary	209	98 (46.9%)	221	106 (48.0%)	1.55 (0.95–2.51)	
Beyond secondary	51	30 (58.8%)	53	29 (54.7%)	2.05 (1.12–3.75)	
Occupation (husband)						
Employed	310	143 (46.1%)	330	162 (49.1%)	1	0.06
Not employed	23	12 (52.2%)	25	16 (64.0%)	1.93(0.97–3.84)	
Months husband away from home in last 6 months						
0	257	117 (45.5%)	274	140 (51.1%)	1	0.76
≥1 month	54	26 (48.1%)	57	22 (38.6%)	0.93 (0.58–1.50)	
Total number of children						
0	94	45 (47.9%)	100	54 (54.0%)	1	0.87
1	106	48 (45.3%)	117	58 (49.6%)	0.93 (0.60–1.45)	
≥2	120	55 (45.8%)	125	61 (48.8%)	1.04 (0.66–1.65)	
Family structure						
Nuclear	104	47 (45.2%)	106	54 (50.9%)	1	0.51
Extended	229	108 (47.2%)	249	124 (49.8%)	1.14 (0.78–1.68)	
Debt						
Yes	168	69 (41.1%)	192	91 (47.4%)	1	0.13
No	165	86 (52.1%)	163	87 (53.4%)	1.30 (0.92–1.85)	
Financial empowerment						
No	118	46 (39.0%)	128	55 (43.0%)	1	0.03
Yes	215	109 (50.7%)	227	123 (54.2%)	1.48 (1.03–2.14)	
Chronicity of depression, weeks						
<12	108	51 (47.2%)	105	55 (52.4%)	1	0.60
≥12	151	63 (41.8%)	172	79 (45.9%)	1.13 (0.72–1.77)	

(Continued)

Table 2. (Continued)

	<i>N</i> (3 m)	Remission at 3 m <i>n</i> (%)	<i>N</i> (6 m)	Remission at 6 m <i>n</i> (%)	OR for remission* (95% CI)	<i>p</i> -Value*
PHQ-9 category						
10–14	209	100 (47.9%)	223	124 (55.6%)	1	0.02
15–19	99	50 (50.5%)	105	45 (42.9%)	0.83 (0.57–1.21)	
≥20	25	5 (20.0%)	27	9 (33.3%)	0.37 (0.18–0.76)	
MSPSS category						
Low	51	17 (33.3%)	58	19 (32.8%)	1	0.006
Moderate	164	70 (42.7%)	176	89 (50.6%)	1.72 (1.03–2.88)	
High	118	68 (57.6%)	121	70 (57.9%)	2.53 (1.42–4.50)	
Participant's expectation of usefulness of counselling						
Not/a little useful	39	17 (43.6%)	38	19 (50.0%)	1	0.88
Somewhat useful	70	33 (47.1%)	76	39 (51.3%)	1.23 (0.65–2.33)	
Moderately useful	116	55 (47.4%)	123	58 (47.2%)	1.26 (0.69–2.33)	
Very useful	108	50 (46.3%)	118	62 (52.5%)	1.28 (0.70–2.33)	
Parity						
Primiparous	84	42 (50.0%)	91	52 (57.1%)	1	0.36
Multiparous	249	113 (45.4%)	264	126 (47.7%)	1.21 (0.81–1.81)	
Previous miscarriage or still birth						
None	244	118 (48.4%)	263	137 (52.1%)	1	0.48
One or more	89	37 (41.6%)	92	41 (44.6%)	0.86 (0.57–1.30)	
Domestic violence						
No	284	137 (48.2%)	297	155 (52.2%)	1	0.07
Yes	45	18 (40.0%)	53	21 (39.6%)	0.64 (0.39–1.04)	

Abbreviation: MSPSS, Multidimensional Scale of Perceived Social Support.

*Using both 3- and 6-month data, assuming a constant association of exposure at these two time points, and adjusted for month of visit and factors associated with loss to follow-up (namely, country and women's occupation).

2007), and informing the patient about their clinical status and illness (Maselko *et al.*, 2020) may lead to the improvement of outcomes. This may be explained by the installation of hope, the positive expectation from receiving guidance or therapeutic assessments (Posternak and Miller, 2001). Other authors (Hengartner, 2020) substantiate this and explain symptom reduction in depression trials by the Hawthorne effect resulting from receiving any care or additional support such as enhanced usual care. Regression to the mean is another plausible explanation of spontaneous remission and recovery for depression (Hengartner, 2020) which might have contributed to the high prevalence of remission in our study. Furthermore, we did not conduct clinical interviews with women, but measured symptom severity with the PHQ-9 scale. Symptom scales have been shown to overestimate the prevalence of depression (Thombs *et al.*, 2018), and may have facilitated the inclusion of women with low baseline severity. For perinatal depression specifically, there have been calls to suggest that the assessment of symptoms lasting 2 weeks may not be sufficient to exclude spontaneous remission without treatment (Scott, 1997). Inclusion of a high proportion of moderate cases of perinatal depression (overestimated by the screening tool) may have led in turn to the overestimation of remission rates in our study, given that cases with mild or moderate symptoms are more likely to remit (Whiteford *et al.*, 2013). Third, our definition of

spontaneous remission and recovery did not include an assessment of psycho-social functioning and physiological factors (Whiteford *et al.*, 2013) which at times is also considered in the definition of remission and recovery; this may have led to apparent higher remission and recovery rates in our sample.

Conclusion

Women with perinatal depression represent a diverse sub-group, and it is important to identify modifiable factors which may offset symptom trajectories and facilitate the way to recovery. Our study has confirmed that spontaneous remission from depression is a common outcome among mothers. For the first time, we now know that factors such as less severe depression at baseline, and more social support from friends and family are predictive of spontaneous remission. For the purposes of management of depression and the prevention of clinical worsening, these factors can be screened at baseline to help assess treatment prognosis. We were unable to assess relapse of depressive symptoms and if recovery remained stable over the long term. This would have to be investigated in further research, alongside the assessment of relevance of these factors with regards to the specific symptom trajectory women might find themselves in. Future research should also explore the

Table 3. Factors independently associated with remission from depression

	AOR for remission (95% CI) ¹	p-value	AOR for remission (95%CI) ² , using MI ³	p-value
Country				
Pakistan	1	0.28	1	0.35
India	1.25 (0.84–1.86)		1.21 (0.81–1.80)	
Occupation (participant)				
Employed	1	0.51	1	0.62
Not employed	1.24 (0.65–2.35)		1.17 (0.63–2.17)	
Occupation (husband)				
Employed	1	0.04	1	0.08
Not employed	2.04 (1.02–4.11)		1.91 (0.94–3.91)	
PHQ-9 category				
10–14	1	0.04**	1	0.03**
15–19	0.87 (0.59–1.28)		0.84 (0.58–1.23)	
≥20	0.43 (0.20–0.90)		0.47 (0.24–0.92)	
MSPSS category				
Low	1	0.003**	1	0.003**
Moderate	1.58 (0.93–2.67)		1.59 (0.98–2.59)	
High	2.37 (1.32–4.27)		2.41 (1.35–4.29)	

Abbreviation: MSPSS, Multidimensional Scale of Perceived Social Support.

¹Adjusted for other variables in the table (country and women's occupation are included as they are associated with LTFU; month of visit is also adjusted for; other variables are included since $p < 0.05$ in the multivariable model).

²MI, multiple imputation for missing outcome data (imputed data at 166/854 data points).

³** P -value for trend.

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Open peer review. To view the open peer review materials for this article, please visit <http://doi.org/10.1017/gmh.2023.26>.

Supplementary material. The supplementary material for this article can be found at <https://doi.org/10.1017/gmh.2023.26>.

Data availability statement. Data from our trials have been made available at the LSHTM data repository available at <http://datacompass.lshtm.ac.uk/> (doi: 10.17037/DATA.00000793).

Author contribution. All authors contributed to the study conception and design. D.C.F. conceived the study and H.A.W. and F.V. analysed the data. The first draft of the manuscript was written by D.C.F. and all authors commented on previous versions of the manuscript. All authors read and approved the final version.

Financial support. The research reported in this publication was supported by the National Institute of Mental Health of the National Institutes of Health under award number 1U19MH095687. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute of Mental Health, the National Institutes of Health, or the U.S. Department of Health and Human Services. F.V. and H.A.W. were funded by the UK Medical Research Council (MRC) and the UK Department for International Development (DFID) under the MRC/DFID Concordat agreement which is part of the EDCTP2 programme supported by the European Union (Grant No. MR/R010161/1).

Competing interest. The authors declare that they have no competing interest.

Ethics standard. The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki. Ethical approval was obtained from the institutional review boards at the London School of Hygiene and Tropical Medicine, Sangath (the implementing institution in India), the Indian Council of Medical Research, the University of Liverpool and the Human Development Research Foundation (the implementing organisation in Pakistan).

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