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A pragmatic randomised controlled trial to compare antidepressants with a community-based psychosocial intervention for the treatment of women with postnatal depression: the RESPOND trial

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The research reported in this issue of the journal was commissioned by the HTA programme as project number 02/07/04. The contractual start date was in June 2004. The draft report began editorial review in August 2008 and was accepted for publication in October 2009. As the funder, by devising a commissioning brief, the HTA programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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Abstract

A pragmatic randomised controlled trial to compare antidepressants with a community-based psychosocial intervention for the treatment of women with postnatal depression: the RESPOND trial

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Objectives: To evaluate clinical effectiveness at 4 weeks of antidepressant therapy for mothers with postnatal depression (PND) compared with general supportive care; to compare outcome at 18 weeks of those randomised to antidepressant therapy with those randomised to listening visits as the first intervention (both groups were to be allowed to receive the alternative intervention after 4 weeks if the woman or her doctor so decided); and to assess acceptability of antidepressants and listening visits to users and health professionals.

Design: A pragmatic two-arm individually randomised controlled trial.

Setting: Participants were recruited from 77 general practices: 21 in Bristol, 21 in south London and 35 in Manchester.

Participants: A total of 254 women who fulfilled International Classification of Diseases version 10 criteria for major depression in the first 6 postnatal months were recruited and randomised.

Interventions: Women were randomised to receive either an antidepressant, usually a selective serotonin reuptake inhibitor prescribed by their general practitioner (GP), or non-directive counselling (listening visits) from a specially trained research health visitor (HV). The trial was designed to compare antidepressants with general supportive care for the first 4 weeks, after which women allocated to listening visits commenced their sessions. It allowed for women to receive the alternative intervention if they had not responded to their allocated intervention or wished to change to, or add in, the alternative intervention at any time after 4 weeks.

Main outcome measures: The duration of the trial was 18 weeks. Primary outcome, measured at 4 weeks and 18 weeks post randomisation, was the proportion of women improved on the Edinburgh Postnatal Depression Scale (EPDS), that is scoring < 13. Secondary outcomes were the EPDS measured as a continuous variable at 4 and 18 weeks, and scores on various other questionnaires.

Results: At 4 weeks, women were more than twice as likely to have improved if they had been randomised to antidepressants compared with listening visits, which started after the 4-week follow-up, i.e. after 4 weeks of general supportive care [primary intention-to-treat (ITT), 45% versus 20%; odds ratio (OR) 3.4, 95% confidence interval (CI) 1.8 to 6.5, $p < 0.001$]. Explanatory analyses emphasised these findings. At 18 weeks, ITT analysis revealed that the proportion of women improving was 11% greater in the antidepressant group, but logistic regression analysis showed no clear benefit for one group over the other [62% versus 51%, OR 1.5 (95% CI 0.8 to 2.6), $p = 0.19$]. Overall, there was a difference between the groups in favour of the antidepressant group of about 25 percentage points at 4 weeks, which reduced at 18 weeks. No statistical support existed for a benefit

of antidepressants at 18 weeks, but 95% CIs could not rule out a clinically important benefit. It was difficult for GPs not to prescribe antidepressants to women randomised to listening visits after the initial 4 weeks, so many women received both interventions in both groups by 18 weeks and consequently power was reduced. Qualitative interviews with women revealed a preference for listening visits but an acceptance that antidepressants might be necessary. They wished to be reassured that their GP and HV were offering continuity of care focusing on their particular set of circumstances. Interviews with GPs and HVs revealed lack of collaboration in managing care for women with PND; neither professional group was willing to assume responsibility.

Conclusions: At 4 weeks, antidepressants were significantly superior to general supportive care. Trial design meant that by 18 weeks many of the women initially randomised to listening visits were also receiving antidepressants, and more vice versa. The lack of evidence for differences at 18 weeks is likely to reflect a combination of reduced power and the considerable degree of switching across the two interventions. Qualitative study revealed that women found both antidepressants and listening visits effective depending on their circumstances and preferences. The trial indicates that early treatment with antidepressants leads to clinical benefit for women with PND.

Trial registration: Current Controlled Trials ISRCTN16479417.

Funding: The National Institute for Health Research Health Technology Assessment programme.

Contents

List of abbreviations

CACE	Complier-Average Causal Effect
CBT	cognitive behavioural therapy
CI	confidence interval
CIS-R	Clinical Interview Schedule (Revised)
CONSORT	Consolidated standards of reporting trials
DSM-III-R	Diagnostic and Statistical Manual of Mental Disorders, revised third edition
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, fourth edition
EPDS	Edinburgh Postnatal Depression Scale
EQ-5D	EuroQol self-report questionnaire
GHQ-12	General Health Questionnaire
GRIMS	Golumbok–Rust Inventory of Marital State
GP	general practitioner
GSC	general supportive care
HTA	Health Technology Assessment
HV	health visitor
ICD-10	World Health Organization International Classification of Diseases, version 10
ITT	intention-to-treat
MAMA	Maternal Adjustment and Maternal Attitudes Questionnaire
MREC	Multi-centre Research Ethics Committee
NICE	National Institute for Health and Clinical Excellence
PAPA	Paternal Adjustment and Paternal Attitudes Questionnaire
PCT	primary care trust
PHQ-9	Patient Health Questionnaire
PHV	practice health visitor
PND	postnatal depression
QALY	quality-adjusted life-years
QRA	qualitative research associate
RESPOND	Randomised evaluation of antidepressants and support for women with postnatal depression
RHV	research health visitor
SD	standard deviation
SF-12	Short Form Health Survey-12 items
SSRI	selective serotonin reuptake inhibitor
VAS	visual analogue scale

All abbreviations that have been used in this report are listed here unless the abbreviation is well-known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices, in which case the abbreviation is defined in the figure legend or in the notes at the end of the table.

Executive summary

Background

Postnatal depression (PND) is a substantial public-health problem, affecting up to one in seven newly delivered mothers and leading to long-term adverse consequences for maternal mood and infant development. Its high prevalence makes PND one of the most important adverse psychological outcomes of childbirth. Despite the large increase in the prescribing of antidepressants for depressive disorders in primary care there is very little evidence as to the risks and benefits for their use in PND. Many women are said to prefer psychological therapies for depression especially in the postnatal period if they are breastfeeding. The comparative effectiveness of antidepressants and listening visits from health visitors (HVs), the most commonly available psychological treatment available for this group of women, has not been previously studied.

Objectives

The aims of the RESPOND study were:

- to evaluate the clinical effectiveness at 4 weeks of antidepressant therapy for mothers with PND compared with general supportive care
- to compare the outcome at 18 weeks of those randomised to antidepressant therapy with those randomised to listening visits as the first intervention (both groups were to be allowed to receive the alternative intervention after 4 weeks if the woman or her doctor so decided)
- to assess the acceptability of antidepressants and listening visits to users and health professionals.

Design

A pragmatic two-arm individually randomised controlled trial was undertaken in women who fulfilled International Classification of Diseases version 10 (ICD-10) criteria for major depression in the first 6 postnatal months. A nested qualitative study explored the acceptability and satisfaction with listening visits and antidepressant therapy from the perspective of the women and the attitudes of general practitioners (GPs) and HVs to women with PND and their management in primary care.

Setting

Participants were recruited from 77 general practices: 21 in Bristol in south-west England, 21 in south London and 35 in Manchester in north-west England.

Participants

A total of 254 women were recruited and randomised.

Interventions

Women were randomised to receive either an antidepressant, usually a selective serotonin reuptake inhibitor (SSRI) prescribed by their GP or non-directive counselling (listening visits) from a specially trained research HV. The trial design compared antidepressants with general supportive care for the first 4 weeks after which time women allocated to listening visits commenced their sessions. The design allowed for women to receive the alternative intervention if they had not responded to their allocated intervention or wished to change to or add the alternative intervention at any time after 4 weeks.

Outcome measures

The duration of the trial was 18 weeks. The primary outcome, measured at 4 weeks and 18 weeks post randomisation, was the proportion of women improved on the Edinburgh Postnatal Depression Scale (EPDS), that is scoring < 13. Secondary outcomes were the EPDS measured as a continuous variable at 4 weeks and 18 weeks, and scores on the short form-12 health survey, the EuroQol self-report questionnaire, the Maternal Adjustment and Maternal Attitudes Questionnaire and the Golombuk–Rust Inventory of Marital State.

Results

Invitations to participate in the study were sent to 10,604 women between 5 and 6 weeks after the birth of their child. Valid replies were received from 4158 women who completed a screening EPDS and 15 women were referred by their GP or HV, all of whom indicated their willingness to continue in the study. The characteristics of responders and non-responders were very similar. Of these 4158 women, 989 scored ≥11 on the EPDS and were offered a home visit to assess their eligibility for the trial. Home visits were conducted with 628 women where, in addition to a further EPDS with a threshold score required of ≥13, a self-administered computerised structured psychiatric interview, the CIS-R, was used to determine ICD-10 depression status. Two hundred and sixty-nine women were eligible for entry into the trial, of whom 254 participated. The women who were randomised were less likely to be married or living with a partner and have less social support and fewer educational qualifications but more likely to have had previous treatment with antidepressants than those who were not randomised. One hundred and twenty-nine women were randomised to antidepressants and 125 women to listening visits. Follow-up rates at 4 weeks and 18 weeks were 86% and 81%, respectively.

At 4 weeks, women were more than twice as likely to have improved, (score < 13 on the EPDS), if they had been randomised to antidepressants, compared with women randomised to listening visits, which started after the 4-week follow-up, i.e. after receiving general supportive care for 4 weeks [primary intention-to-treat (ITT), 45% versus 20%; odds ratio (OR) 3.4 (95% CI 1.8 to 6.5), $p < 0.001$]. Explanatory analyses based on treatments received emphasised this result. At 18 weeks, the ITT analysis revealed that the proportion of women improving was 11% greater in the antidepressant group, but the logistic regression analysis showed no clear benefit for one group compared with the other [62% versus 51%, OR 1.5, (95% CI 0.8 to 2.6) $p = 0.19$]. As a result of the pragmatic nature of the trial, which allowed women to receive the alternative intervention instead of or as well as their randomised allocation after the 4-week assessment, the explanatory analyses at 18 weeks are more difficult to interpret. Overall, there is evidence of a difference between the groups in favour of the antidepressant group of about 25 percentage points at 4 weeks that is reduced at 18 weeks. There is no statistical support for a benefit of antidepressants at 18 weeks, but the confidence intervals cannot rule out a clinically important benefit. As the trial design allowed for women to switch groups or add the alternative intervention at any time after 4 weeks, by 18 weeks many women had received both interventions. It is therefore difficult to separate the contribution of the individual interventions to the assessment of effectiveness at 18 weeks. This was an intentional part of the design, to allow clinicians and patients to adopt the treatment they thought appropriate once the initial randomisation had occurred.

Considering the EPDS as a continuous outcome resulted in a two-point difference in means in favour of the antidepressant group at 4 weeks [OR −2.1 (95% CI −3.3 to −0.9) $p < 0.001$] but at 18 weeks this difference had reduced to less than one point with no evidence of a significant difference between the groups. With regard to the other secondary outcomes, the results were in the expected directions with scales measuring mental well-being showing some evidence of benefit in the antidepressant group at 4 weeks in the ITT analyses and less evidence at 18 weeks.

The interviews with women who participated in the trial revealed that the majority had wanted to be randomised to listening visits. This preference appeared to be related more to a concern about taking antidepressants than to a particular expectation of the visits. The concerns about antidepressants were mainly to do with stigma, side effects and dependency. However, many women who received listening visits to start with went on to take antidepressants because they felt that they had not improved sufficiently. This change of attitude towards antidepressants was facilitated by encouragement from the research HV and by concerns being allayed by their GP. Women who took antidepressants mainly benefited, describing a lifting of mood that enabled them to manage their lives more effectively. Women who received listening visits welcomed the opportunity to talk and found the advice and support from the research HV helpful.

The interviews with GPs highlighted the importance of taking a holistic approach to agreeing a diagnosis of PND in the setting of a long-term patient–practitioner relationship. However, practice HVs did not feel that it was their responsibility to make a diagnosis of PND and that while the label might be useful, referring back to the GP whose only management option was antidepressants which women might not want, prevented them from actively detecting depressive

symptoms. The GPs and HVs were aware of the change in the working relationship between the two professional groups, which had led to poorer communication and a sense that no one wanted to take responsibility for this group of women.

Conclusions

This study has shown that at 4 weeks, antidepressants were significantly superior to general supportive care. The data have also confirmed that there is a substantial number of women who suffer from depression in the 6-month postnatal period. The lack of evidence for differences at 18 weeks is likely to be the result of a combination of reduced power consequent on the original sample size not being achieved and a genuinely reducing effect over time, exacerbated by the considerable degree of switching across the two interventions by the later follow-up, especially for the explanatory analyses of listening visits, which such a large proportion had received by the later follow-up.

The results from the qualitative study confirm that that there is an urgent need for GPs and HVs to agree the care pathway for these women. It would appear that commencing women on antidepressants early in the course of the illness is likely to result in the greatest improvement in symptoms. This will require GPs and HVs to accept responsibility for making the diagnosis and agreeing management with individual women.

This morbidity justifies the need for services to be made available to support families through this illness. This need is made more urgent by the potential for the long-term adverse impact of depression not only for the mother but also the child. The responsibility for providing care must lie in primary care.

The issue of detection needs to be resolved. Research comparing the use of a screening instrument such as the EPDS and face-to-face questions (the 'Arroll' questions) which have a high predictive validity in routine primary care needs to be undertaken to give primary care practitioners a means of detecting those most at risk. Interviews with women have revealed a preference for listening visits. HVs must see this as their responsibility. Services need to be configured such that there are HVs available who can focus their attention on the mother's mental state rather than on the child's needs. Research evaluating the effectiveness and cost-effectiveness of different models of HV provision are needed. Women are willing to take antidepressants when they perceive their illness to require this approach. They need to be supported in reaching this decision by their HV and GP and offered regular follow-up while taking medication.

Trial registration

This trial is registered as ISRCTN16479417.

Chapter 1
Introduction

Epidemiology of postnatal depression

By the year 2020 it has been estimated that depression will be the second most common cause of disability worldwide.[1] In the UK it affects 5–10% of individuals and is the third most common reason for consultation in general practice.[2] Postnatal depression (PND) is a substantial public-health problem, affecting up to one in seven of newly delivered mothers[3,4] and leading to long-term adverse consequences for maternal mood and infant development. PND has been identified in the National Service Framework for Mental Health (in England) as one of the core diagnoses for which primary care teams must develop clinical guidelines.[5]

From a public-health perspective, its high prevalence makes PND one of the most important adverse psychological outcomes of childbirth. Longitudinal and epidemiological studies have yielded varying prevalence rates, ranging from 3% to more than 25% of women in the first year following delivery; these rates fluctuate because of sampling, timing of assessment, differing diagnostic criteria (major or minor depression), and whether the studies were retrospective (low rates) or prospective (6- to 10-fold higher). Frequently cited estimates range between 10% and 15%. Some of this variation is population dependent with countries having widely varying rates. A meta-analysis of 59 studies (including 12,810 women, mainly from developed countries) found an average prevalence of PND of 13% [95% confidence interval (CI) 12.3 to 13.4%].[6] This meta-analysis only included studies in which the diagnosis was made using validated psychiatric interviews and self-report questionnaires. The prevalence varied depending on the method of assessment, the differing inclusion criteria for the studies and the length of the follow-up. The incidence was highest in the first 3 months postpartum with the peak time of onset in the first 4–6 weeks. This depression may be the start of a chronic relapsing illness or a relatively short-lived episode never to be repeated. In either case the consequences for the woman herself, both at home and at work, for her partner and the quality of their relationship, and for her family and friends may be irrevocable.

Classification and aetiology of postnatal depression

Postnatal depression is defined as a non-psychotic depressive episode meeting standardised diagnostic criteria for a minor or major depressive disorder, beginning in or extending into the postnatal period.[7] In the two major classification systems, International Classification of Diseases version 10 (ICD-10) and the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV), ICD-10 categorises mental disorders that occur postpartum as 'puerperal', but only if they cannot otherwise be classified, whereas DSM-IV allows 'postpartum onset' to be specified for mood disorders starting within 4 weeks of delivery. The WHO Guide to Mental and Neurological Health in Primary Care (also known as ICD-10 PHC) does classify postnatal disorders separately (F53), and offers guidance concerning diagnosis and management to primary care health professionals in the UK.[8] There is some evidence for the specificity of the diagnostic concept – one study has found that women who experienced PND with no previous episodes of depression were at increased risk of further episodes of PND but not depressive episodes outside the perinatal time frame, whereas women who experienced PND as a recurrence of a depressive illness were at increased risk of repeated PND as well as the development of depression outside the perinatal time frame.[9]

The aetiology of postpartum depression remains unclear with little evidence to support a biological basis,[10,11] though a small experimental study reported that stimulating hormone changes after delivery led to a significant change in mood in five of eight women with a previous history of PND, compared with none of eight control women, suggesting differential sensitivity to hormone changes.[12] Premenstrual dysphoric disorder has also been reported as a risk factor for PND[13] and is suggestive of a risk of hormonal sensitivity in some women. However, despite considerable research, no single causative factor has been isolated and a multifactorial aetiology has been suggested.

Consistent findings suggest the importance of psychosocial variables.[11,14] In particular, stressful life events,[15,16] marital conflict,[15–18] a past history of depression, younger maternal age[19] and the lack of social support[10,15,17,20,21] have been found to significantly increase the risk of postpartum depression.

There are still unanswered questions as to whether there is an increased relative risk of depression within a given time after the birth of a child, what these time limits might be, whether there are any characteristic clinical features that distinguish PND from any other kind of depression, and whether aside from the coincidence with childbirth, there are any other pathognomonic aetiological factors associated with it. Women with PND characteristically exhibit symptoms of uneasiness, irritability, confusion and forgetfulness, anhedonia, fatigue, insomnia, anxiety, guilt, inability to cope and thoughts of suicide. Frequently exacerbating these symptoms are low self-esteem, lack of confidence and unrealistic expectations of motherhood. It can be seen to be very similar to depression occurring at other times in a woman's life. The most recent controversy surrounding PND concerns the timing of its onset and the question as to whether it is an extension of antenatal depression or a totally different entity.[22]

Although the range of mental-health problems occurring in the postnatal period is not dissimilar to those affecting all adults, the nature, treatment and impact are different in several ways. When considering the diagnosis and treatment of postnatal mental-health problems, there is more than one patient to consider. A severe depressive illness after the birth may place the infant as well as the mother at risk. Lengthy PND may have long-term adverse effects on the child's development and the marital relationship. Follow-up studies have found that approximately one-third of cases of PND become chronic or recurrent.[23] Women who have suffered from postpartum depression are twice as likely to experience future episodes of depression over a 5-year period.[9] The last Confidential Enquiry into Maternal and Child Health (CEMACH) report[24] identified one of the leading causes of maternal death as suicide, with more than half of the women who died having an underlying history of mental illness not all of which was depression. Many of these women had regular contact with health-care professionals. There is a tendency in the literature and in practice to use the term 'postnatal depression' in a generic sense for all postnatal mental illness. This is not entirely helpful because it leads to other types of mental illness being missed or treated inappropriately. The need to prevent, identify as early as possible and treat such potentially life-threatening conditions optimally is clear.

The impact of postnatal depression on the child

Postnatal depression can result in impaired mother–infant interactions[25] and negative perceptions of infant behaviour that have been linked to insecure attachment.[26,27] Infants of mothers who suffer PND have been shown to have poorer development as assessed by the Bayley scales,[27] cognitive developmental delay[26,28,29] with lower scores on the General Cognitive Index (GCI) of the McCarthy scales (possibly confined to male infants[30]) and social/interaction difficulties.[31,32] It has also been reported that children of depressed mothers are two to five times more likely to develop long-term behavioural problems,[33] raised rates of emotional and behavioural problems[30] and difficulties in adjustment to school.[32] Child neglect/abuse[34] and marital stress resulting in separation or divorce[35] are other reported outcomes.

These impairments are influenced by current maternal mental state,[36] the duration of the initial depression and other factors such as marital conflict, domestic violence[37] and paternal psychiatric disorder.[38] Whether these adverse child outcomes are ameliorated by treatment has been addressed by only one efficacy study, which reported that some but not all outcomes showed a benefit from treatment, findings that need to be examined in further research.[39]

Detection of postnatal depression

In line with other common mental disorders in primary care, a significant proportion of postnatal mental illness goes undetected. In the case of postnatal illness, there is often reluctance by mothers to disclose symptoms to reduce the possibility of statutory involvement in the care of the baby. Postnatally, women need sensitive care from health professionals with highly developed communication skills who will encourage women to talk openly and safely about their difficulties. Once a diagnosis has been made, involvement of the woman in her care plan is mandatory; including her partner or family where appropriate is also an important consideration.

The Edinburgh Postnatal Depression Scale (EPDS),[40] is a valid and reliable screening tool which is acceptable to women and their carers. However, the National Screening Committee decided that screening for PND using the EPDS did not meet their stringent criteria,[41] even though less than 50% of cases of PND are detected by primary health-care professionals in routine clinical practice.[42]

Boyd *et al*.[43] reviewed eight self-report scales including the EPDS and reported that while the EPDS had been most widely studied, its psychometric properties were relatively modest. This conclusion was in line with that of the National Screening Committee who suggested that despite its high sensitivity, the low specificity of the EPDS, and hence the poor positive predictive value, meant that it could not be recommended for routine use. It should be noted that the Patient Health Questionnaire (PHQ-9),[44] a scale currently used by many general practitioners (GPs) in the UK when measuring the severity of depression before management, was not included in this review.

The debate on screening has been reinvigorated with recent guidance from the National Institute for Health and Clinical Excellence (NICE)[45] advocating prediction of women at high risk and early detection of perinatal mental illness. There is now reasonable evidence, in terms of sensitivity and specificity, from general populations, for the use of a two-question screen which asks about recent low mood or recent loss of pleasure.[46] The addition of the third 'do you need help?' question[47] improves the specificity. Despite the lack of any research evidence in the perinatal period, these questions are now recommended for use by health professionals early in pregnancy and after the birth to facilitate the detection of depression.[45] Research into the detection of perinatal depression has focused on postnatal rather than antenatal depression but the NICE guidelines highlight the importance of detection antenatally as well as postnatally. The use of self-report questionnaires such as the EPDS or PHQ-9 can be used as a follow-up in those women who are positive on the two-question or three-question screen during pregnancy and/or postnatally. The Health Technology Assessment (HTA) programme has recently published a systematic review of methods of identification of PND that provides some answers as to the most useful instruments for use by health professionals.[48]

Treating postnatal depression

High-quality evidence is now available for the effectiveness of antidepressants and psychological interventions for depression in the general primary care population with consequent interest in the role of these interventions in particular subgroups such as women with PND. Hence, the principles of management are not too dissimilar to those observed for similar illnesses in a non-perinatal population. However, when considering the risk : benefit ratio of treatment, the needs of the infant must also be taken into account. Discussion about treatment preferences needs to be based on clear, up to date and comprehensible information, with written documents available in languages relevant to the local population. Sufficient time to make decisions about treatment, and reassurance that decisions are not irrevocable, i.e. that if one approach does not work, then another can be substituted or added, are important aspects of consultations.

Antidepressants

The prescribing of antidepressants in the UK over the last few years has increased considerably.[49] There is now good evidence regarding the efficacy of antidepressants compared with placebo for patients with major depression and/or dysthymia in primary care. Their efficacy in minor depression has been poorly studied and results are conflicting.[50] It does however appear that for acute-onset depression, the size of the antidepressant–placebo difference increases with severity of depression and that there is uncertainty about the clinical importance of any benefit in milder depression. The recent HTA-funded THREAD (THREshold for AntiDepressant response) trial[51] does provide some evidence in favour of selective serotonin reuptake inhibitors (SSRIs) when combined with supportive care over supportive care alone for mild to moderate depression although this study did not have a placebo so the estimate of benefit includes any placebo response.

The SSRIs have become the first-line choice of antidepressant[52] with strong evidence for continuing therapy for at least 6 months to prevent early relapse.[53] In trials comparing antidepressants with a variety of different psychological treatments or in combination with such treatments [e.g. cognitive behavioural therapy (CBT), interpersonal psychotherapy, problem solving[53]], it appears

that there is little difference in efficacy between antidepressants and psychological therapies in mild and moderate depression, with little extra benefit from a combination of the two except possibly in more severe depression.[52] The literature with regard to non-directive counselling shows modest benefit compared with the usual treatment provided by the GP.[53]

Although PND is in essence no different from depression at other times in respect of its phenomenology, and therefore in its likely response to antidepressants, there has so far only been one placebo-controlled trial of an SSRI for PND.[54] This found that fluoxetine was significantly more effective than placebo, and after an initial session of counselling, as effective as a full course of CBT. There have been two other trials in this area – one comparing nortriptyline and sertraline, which showed no differences between the tricyclic antidepressant and SSRI,[55] and a second comparing paroxetine and CBT.[56]

The only special issue to consider is that of breastfeeding. Mothers are often reluctant to take antidepressants because of concerns about transmission in breastmilk or potential side effects.[57] A recent review[58] concluded that 'with the exception of a few cases, no serious adverse events have been reported in infants exposed to antidepressant medications through breastmilk.' The available evidence suggests that antidepressants are relatively safe for breastfed infants. A pooled analysis of studies found that plasma levels of sertraline are usually undetectable in breastfed infants, with paroxetine levels somewhat higher, but citalopram and fluoxetine produced infant plasma levels above 10% of the maternal plasma level (in 22% and 17%, respectively).[59] There is therefore no prima facie case for excluding breastfeeding women from a treatment trial of SSRIs, even though the *British National Formulary*[60] advises caution in their use. However, fluoxetine should probably not be used in breastfeeding women because of its long half-life and citalopram should be used with caution.

Psychosocial interventions

Many patients, and perhaps especially women, state a preference for non-medical treatments or talking therapies for depression in primary care. A Cochrane review considering the effectiveness and cost-effectiveness of counselling in primary care including eight trials, concluded that counselling offers significantly greater improvement than usual care from a GP in the short term but not in the long term and might not be associated with increased costs.[61] There has been substantially more research on the effectiveness of psychological and psychosocial interventions for PND than the use of antidepressants. The role of psychosocial factors in the aetiology of PND has been clearly demonstrated, and research findings support the view that 'therapeutic listening' and extra support may be particularly helpful in depression occurring at this time. The treatments that have been evaluated include various types of psychotherapy including CBT and interpersonal psychotherapy, psychoeducational strategies, psychodynamic therapy, counselling and other less well-defined psychosocial interventions such as social support.[62] A variety of different counselling interventions has been studied. For instance, six, weekly 1-hour counselling visits from Child Health Care clinic nurses were found to be more effective in relieving PND than the usual primary care.[63] However, this was a very small trial with only 20 women randomised to receive counselling, commencing about 4 months postpartum and the outcome was measured 1 week after the final counselling session. A psychoeducational group intervention was more effective than routine primary care in reducing depressive symptoms but had no impact on psychosocial outcomes.[64] However, again, the sample size was small, 23 women randomised to the psychoeducational groups, and CBT only comprised one part of the intervention. A Cochrane review on caregiver support for PND included two trials (137 women) and concluded that professional and/or social support may help in the treatment of PND.[65] The provision of counselling by the voluntary sector may also be effective in alleviating symptoms of PND.[66]

Health visitors (HVs) are the health-care professionals best placed to offer psychological support for women with PND in the UK because they are in regular contact with women throughout the first postnatal year. Corney found that HVs can help alleviate depression by visiting clients frequently and encouraging the expression of feelings.[67] Hennessy,[68] however, reported that a HV had recognised only 27% of mothers she identified as depressed, and Briscoe and Williams observed that HVs should be given opportunities to develop their counselling skills.[69] The first controlled trial of counselling by HVs for women with PND in general practice took place in the early 1990s.[70] It is this non-directive counselling intervention that has been widely taken up by HVs as the model

most likely to be implementable in the service setting. However, with the recent reduction in the number of HVs, their associated increased workload, particularly in terms of child protection, and the reduced use of routine screening with EPDS for PND following the report from the National Screening Committee,[41] the availability of health visitor non-directive counselling is not as widespread as might be anticipated.

A recent Cochrane review on psychological and psychosocial interventions for treating PND[62] included four trials that evaluated non-directive counselling,[63,70,71,72] three in the UK and one in Sweden. The intervention in all four trials was provided by trained HVs/nurses. The earliest of these studies was the first to report the potential effectiveness of non-directive counselling for PND, although the trial was rather small, 26 women randomised to counselling, and the final outcome was measured very soon after the intervention ended.[70] Overall, these interventions were effective for the depressive symptomatology in postpartum women, suggesting that this treatment modality may be an important option for mothers with mild to moderate postpartum depression but the methodological quality of these trials was rather poor, particularly in terms of concealment of allocation to groups. These trials also demonstrated the feasibility of population-based screening and the application of home visiting using trained health professionals.

Non-directive client-centred counselling is a form of counselling that is based on Rogerian principles.[73] The understanding is that in many situations, people can resolve their own problems without being provided with a solution by the counsellor. In particular, the counsellor's role is to listen to people, be empathic with them, encouraging the person to express their feelings but not suggesting what decision the person should make. By listening and reflecting back what the person reveals to them, the counsellor helps them to explore and understand their feelings. With this understanding, the person is able to make the decision that is best for them. It is the listening quality that has resulted in the synonym 'listening visits' for non-directive counselling when offered by health professionals. A qualitative study of women who had undergone listening visits revealed that they felt positive about the intervention if they had a good prior relationship with their HV but were less positive if that relationship was poor. Women perceived the intervention as supportive rather than therapeutic and ascribed their recovery to other factors.[74]

Rationale for the trial

The brief literature review above outlines the research evidence for the use of antidepressants and HV non-directive counselling (listening visits) for women in the UK suffering from PND. The trial was designed in response to an HTA-commissioned call for research to assess the long-term cost-effectiveness of antidepressant drug therapy versus community-based psychosocial interventions for the treatment of PND (HTA commissioning brief: 02/07).

Objectives

The objectives of the Randomised Evaluation of antidepressants and Support for women with Postnatal Depression (RESPOND) study were to:

1. Evaluate the clinical effectiveness at 4 weeks of antidepressant therapy for mothers with PND compared with general supportive care.
2. Compare the outcome at 18 weeks of those randomised to antidepressant therapy versus those randomised to listening visits as the first intervention. (Both groups were to be allowed to receive the alternative intervention after 4 weeks if the woman or her doctor so decided.)
3. Assess the acceptability of antidepressants and listening visits to users and health professionals.

Chapter 2
Methods

Trial design, funding and approval

The RESPOND trial was designed to compare, on an essentially pragmatic basis, two interventions for the treatment of PND in the UK. Full details are given in the Interventions section of this chapter, but the two interventions were the prescription of antidepressant medication and a community-based psychosocial intervention, non-directive counselling (listening visits). The trial was a two-arm, multicentre individually randomised controlled trial.

The original HTA brief suggested using a factorial design, an approach that presupposes that the long-term treatment of PND is a question of either pharmacotherapy or psychological treatment. In practice, patients and doctors are more likely to adopt a stepped care approach in which treatments will be 'added' if the patient does not respond to the first-line therapy. Our research design allowed women to receive both the antidepressants and the psychological therapy if required, thereby mimicking real-world NHS practice while addressing some of the important research questions concerned with the treatment of PND. The main difference between the trial arms was the order in which the interventions were made available as first-line therapies. This design reflected current practice, should have improved the acceptability of the trial and allowed us to maintain randomisation over the follow-up period. We considered using a placebo arm for comparison with antidepressants but chose not to include a placebo because the real choice in clinical practice is between antidepressants and no medication. Furthermore, we believe that the drugs of choice in PND are the SSRIs and that the use of tricyclic antidepressants for PND in UK general practice is now rather uncommon.

We therefore randomly allocated newly delivered mothers who fulfilled our inclusion criteria to either antidepressants or listening visits. Women in the antidepressants group were asked to attend their GP and receive a prescription of an SSRI, whereas those in the listening visits group were placed on a 4-week waiting period (to mimic a clinical waiting list) before receiving listening visits between weeks 4 and 18 of the trial. During the 4-week waiting period the listening visits group received general supportive care (GSC) from the primary care team. During this 4-week period women could see their GP and their practice health visitor (PHV) as they wished. We asked PHVs not to undertake any listening visits and GPs not to prescribe antidepressants unless the clinical severity of the depression required this protocol deviation. The 4-week assessment therefore allowed a comparison between SSRIs and GSC. After the 4-week assessment, women in the antidepressants group could receive listening visits as well as or instead of their antidepressants. The protocol allowed for women in the listening visits group to receive antidepressants after the 18-week assessment. However, it became clear that it was not going to be possible to deny women access to antidepressants until after the 18-week follow-up and the trial became more pragmatic, allowing women in the listening visits group to commence an SSRI at any time after 4 weeks. The 18-week assessment therefore allowed comparison between SSRIs plus listening visits (if needed) versus listening visits plus antidepressants if needed.

The original protocol envisaged a 44-week follow-up when the child was about 12 months old. Women randomised to either group who required the alternative intervention as well as or instead of their original allocation had the opportunity to do so. We therefore expected similar clinical outcomes at this stage, and had originally proposed to focus on the cost-effectiveness of the two approaches at that stage. Unfortunately, because of difficulties in recruitment, the trial was curtailed by the HTA at the 18-week stage and the report does not include any later outcomes.

The main trial was supplemented with a qualitative study involving purposive samples of trial participants and health professionals (GPs and PHVs) designed to assess the acceptability of the trial interventions and attitudes towards the management of PND in primary care.

The trial was funded by the National Institute for Health Research Health Technology Assessment

Programme and commenced in June 2004. The trial was approved by the Scotland A Multi-centre Research Ethics Committee (MREC; reference number MREC/03/0/127) and site-specific approval was obtained from 10 relevant local ethics committees and 10 primary care trusts (PCTs). The Department of Health sponsored the trial. The trial is registered with the International Standard Randomised Controlled Trial Register (ISRCTN16479417) and the National Research Register (N0484135402).

Participants

Study population

All eligible women were recruited between January 2005 and August 2007, from 77 collaborating practices in the UK located in Bristol (21 practices), London (Croydon and Bromley) (21 practices) and Manchester (35 practices). These practices served a wide range of neighbourhoods including both affluent and socioeconomically deprived urban areas. All 18-week follow-ups were completed by March 2008.

Eligibility criteria for screening phase

Inclusion Recently-delivered women aged 18 years or over; who had a live birth; and were living with their baby.

Exclusion Women who had a stillbirth or neonatal death; whose baby was more than 26 weeks old, whose baby had been fostered or adopted; those with psychosis; alcohol or drug abuse; or those already receiving treatment for depression.

Recruitment procedures

Initial postal screening

General practices receive two notifications when a baby is born to a woman registered at the practice: from the hospital where the baby was born and from the local PCT. During the recruitment phase of the study, these notifications were collated by a clerical assistant at each collaborating practice, and reviewed by the PHV to exclude women who did not fulfil the eligibility criteria.

Eligible women were then sent an invitation to participate in RESPOND when their baby was 5–6 weeks old. This invitation pack was prepared by the research team but completed and sent from the general practice by practice staff, and included information about the RESPOND study (see Appendix 2), a consent form (see Appendix 3), a screening EPDS[75] questionnaire, and a prepaid envelope for return to the study team.

Women were sent a reminder letter and further screening EPDS if they had not replied after 2 weeks. If a woman returned a signed consent form and scored 11 or more on this first EPDS, her GP was asked to review the exclusion criteria and exclude her if she was not eligible to participate further. All eligible, consenting women who had scored 11 or more on the screening EPDS were invited to participate in a home visit to further assess their eligibility for the trial. If a woman was ineligible, her GP and PHV were informed of her initial EPDS score. Trial recruitment procedures are summarised in *Figure 1*.

Self-harm risk at the screening stage

If a woman reported thoughts of self-harm (see Measures) at the screening stage, as requested by the MREC, she was telephoned by the research team and asked if her GP could be informed of her distress, regardless of whether she was eligible to continue to the home visit stage (see Appendix 4). With consent, the GP was contacted and, if she was otherwise eligible, her GP was asked if these thoughts precluded her from participating further in the RESPOND study. The information on self-harm risk was also shared with PHVs because they were often in a better position to advise GPs on the appropriateness of eligibility for the trial. This was to ensure that women who were seriously unwell were not randomised to receive listening visits when it may have been more appropriate for them to receive antidepressants. Women who were excluded by their GP were not offered a home visit.

Other recruitment methods: referral by health professionals

Although postal screening was intended as the primary route for entry into the study, collaborating GPs and PHVs were also able to refer women who became depressed between 6 and 26 weeks postnatally. Women who agreed to be referred were invited to participate in a home visit with the research associate.

Home visit (baseline)

Once a potentially eligible woman was identified, a research associate would arrange a visit, usually in the woman's home. This visit was usually conducted at about 8 weeks postpartum

(2 weeks after the screening EPDS had been completed); however, women could receive a home visit up to 26 weeks postpartum. Women were given further information about the study (see Appendix 5), given the opportunity to ask questions, and completed a second written consent form (see Appendix 6). To confirm eligibility, women completed a baseline EPDS and the revised computerised Clinical Interview Schedule (CIS-R).[76] However, at the start of the trial, women who scored below 13 on the EPDS were not always asked to complete the CIS-R so these data are not available for all women who received a home visit.

Women were eligible for entry to the intervention phase of the trial if they met the inclusion criteria (see Participants) and:

- scored ≥ 13 on the baseline EPDS
- received an ICD-10 primary diagnosis of depression on the CIS-R
- were proficient in English at a level to complete all research assessments (two women whose first language was not English had some language assistance in completing the assessments and/or listening visit intervention)
- their recently delivered baby was less than 26 weeks old.

Women were excluded if they met any of the exclusion criteria or:

- were already taking psychoactive medication or receiving psychological therapy
- were actively suicidal.

Demographic data and psychiatric history were collected by self-report questionnaire. This included age, employment and income, ethnicity, marital status, parity, baby's age and method of feeding the baby, and history of depression and its treatment. The questionnaire also included three adapted items on social support[77] (see Appendix 7). If the woman had a partner, she was asked to provide details of his employment, income and ethnicity. These data were collected for descriptive purposes because these factors may contribute to the depressive episode and affect outcomes.

Women who were eligible for randomisation were asked to complete further questionnaires to assess quality of life [Short Form Health Survey (SF-12[78]), EuroQol Self-report Questionnaire (EQ-5D[79])], Maternal Adjustment and Maternal Attitudes Questionnaire (MAMA[80]) and the quality of their relationship with their partner if applicable [Golombuk–Rust Inventory of Marital State (GRIMS[81])]. For details of these instruments, see Measures. Furthermore, if an eligible woman had a partner, she was asked if a short battery of questionnaires comprising the General Health Questionnaire (GHQ-12),[82] SF-12, PAPA[83] (the paternal version of the MAMA; i.e. Paternal Adjustment and Paternal Attitudes Questionnaire) and GRIMS, and prepaid envelope, could be left for her partner to complete and return to the study centre. Trial follow-up procedures are summarised in *Figure 2*.

If a woman was ineligible, her GP and PHV were informed of her EPDS score and CIS-R diagnosis. Eligible women were randomised to receive either antidepressants or listening visits using the procedure outlined below.

Self-harm risk at the home visit

If a woman expressed thoughts of self-harm at the home visit, and her GP had not previously been informed, she was asked if her GP could be contacted (see Appendix 4). As before, for eligible women, the GP was also asked to judge whether they viewed it appropriate for the woman to participate further in RESPOND. Randomisation was delayed until the GP had provided approval for the woman to participate.

Randomisation

Before the baseline home visit, the woman's trial identification number, date of birth and trial centre were entered into a web-based randomisation program. After eligibility had been determined and consent had been obtained at the home visit, the researcher telephoned the remote computerised randomisation service and responded to a series of questions by keying numbers (e.g. patient identification number, baseline EPDS score) on the telephone keypad. The researcher then immediately informed the woman of her treatment allocation and provided her with further information about the allocated treatment (see Appendix 8).

Randomisation was stratified according to the baseline EPDS score (13–15, or > 15) and trial centre. The randomisation sequence was generated using a computer program with block sizes of six, eight and ten, varied randomly. The methods of sequence generation were concealed from the researchers involved in enrolling and randomising the women into the trial. Participants, researchers and those delivering the interventions were not blinded to the treatment allocation.

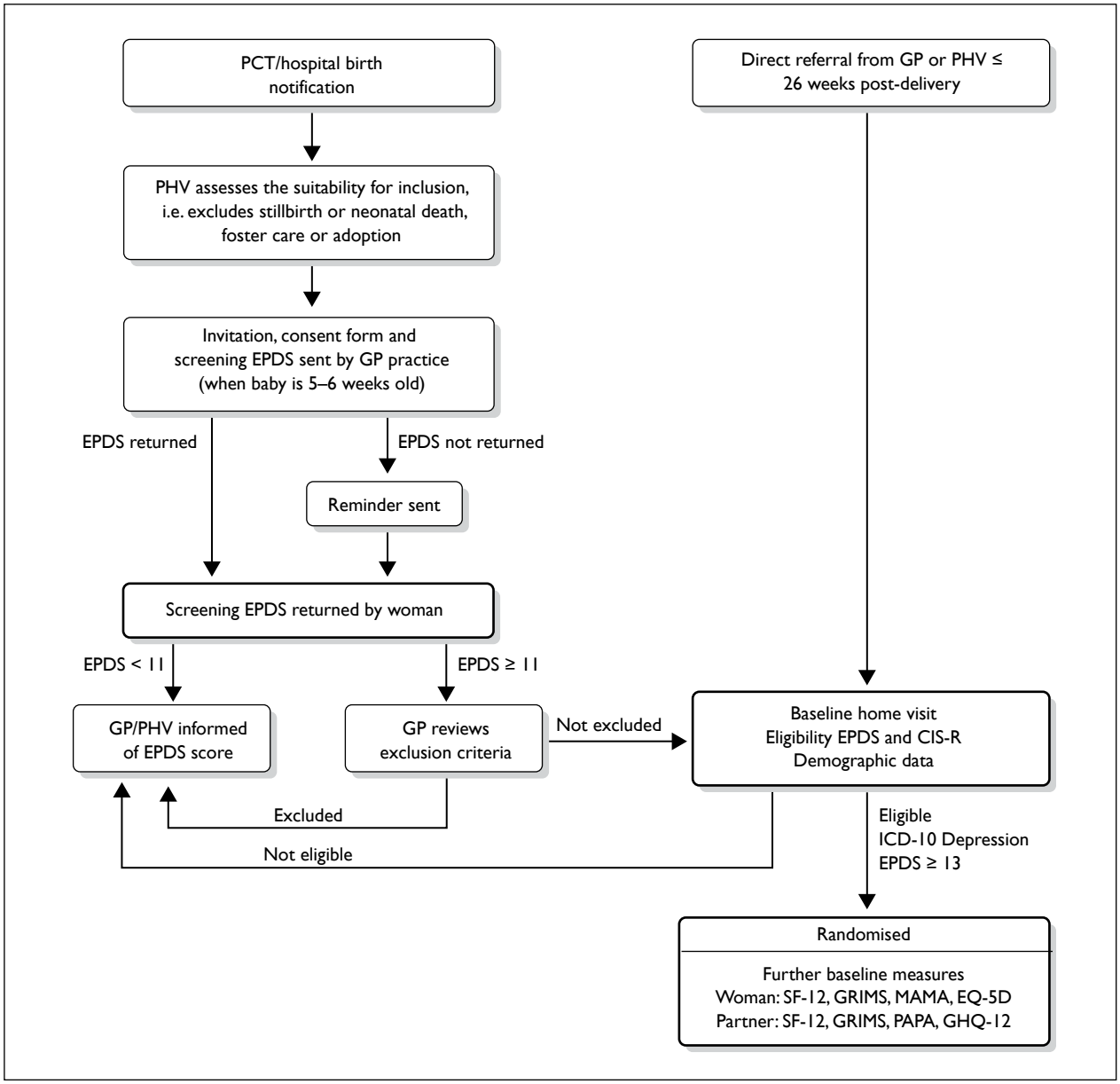

FIGURE 1 *Summary of RESPOND recruitment procedures. Note: If suicide ideation was reported at any stage in this process the self-harm protocol was implemented (see Appendix 4).*

Follow-up schedule

Follow-ups were scheduled at 4 weeks, 18 weeks and 44 weeks for randomised women. (It should be noted that in the original RESPOND protocol, a 44-week follow-up was planned; however, funding to extend the trial only provided for data collection up to 18 weeks.) At these three time points, postal questionnaires and prepaid envelopes were sent to collect outcome measurements (EPDS, SF-12, MAMA, GRIMS, EQ-5D, adherence with antidepressant medication if applicable) and to obtain information on employment and income. Women who had agreed for their partners to receive a questionnaire at baseline were provided with a further short battery of questionnaires (GHQ-12, SF-12, PAPA and GRIMS) for their partner to complete at each follow-up. If the woman reported thoughts of self-harm at a follow-up assessment, and her GP had not previously been notified of this, the research associate asked the woman for permission to contact her GP (see Appendix 4).

The target time frame for follow-up was 3–6 weeks for the 4-week follow-up; 16–20 weeks for the 18-week follow-up; and 42–48 weeks for the 44-week follow-up. Women who had not returned their questionnaire after 1 week were contacted by

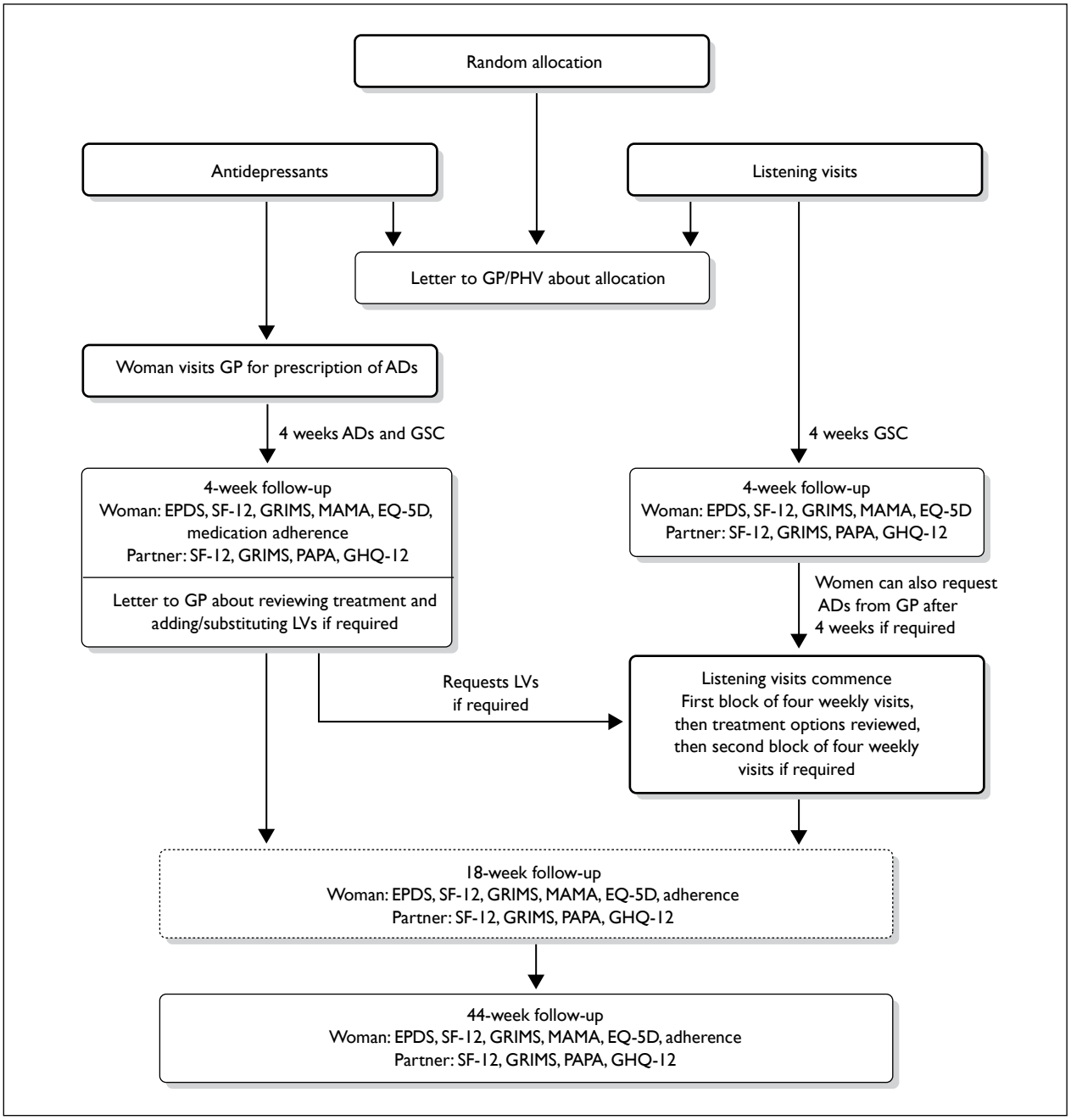

FIGURE 2 *Summary of intervention and follow-up procedures. Note: If suicide ideation was reported at any stage in this process the self-harm protocol was implemented (see Appendix 4).*

phone or post and reminder questionnaires and prepaid envelopes were posted when necessary. If the woman had not replied after these reminders, the research associate attempted to telephone her to collect the EPDS outcome measure over the telephone.

Over the course of the trial, it became evident that follow-up rates were lower than anticipated. To obtain more complete data and reduce attrition, women were offered home visits by the research associate at 4 weeks and 18 weeks to collect the questionnaire data. The questionnaires were completed by the woman but the research associate was able to answer any queries if required. Research health visitors (RHVs) were also able to help with collection of outcome questionnaires at 4 and 18 weeks for women receiving listening visits by requesting women to complete their self-report questionnaires before commencing or continuing with the listening visits.

Strategies to monitor and improve recruitment rates

To monitor recruitment rates, practice staff were asked to record the number of women aged 18 years and over who had given birth, the number excluded by their GP or PHV, and the number of invitations sent out, on a monthly basis. To corroborate these figures, the relevant PCTs were also approached periodically and asked to provide statistics for the number of women aged 18 years and over who had given birth in each collaborating practice.

To improve the trial profile and recruitment rates, members of the research team and local Mental Health Research Network hub clinical studies officers visited collaborating GPs and PHVs to promote the trial and address any concerns or queries. In addition, the protocol was amended to include a number of additional strategies. Research associates and RHVs visited antenatal and postnatal clinics to publicise the trial and to distribute EPDS screening questionnaires to postnatal women. Posters advertising the RESPOND trial were distributed to collaborating practices and HV clinics. Three newsletters were sent to GPs and PHVs, locally adapted for each centre, to promote the trial and keep health professionals informed of trial progress. PHVs offered to remind women to complete the screening EPDS, and were provided with RESPOND leaflets and screening invitation packs to distribute to women at postnatal home visits and clinics. In addition, the patient invitation and information sheets were condensed and adapted at each centre to make them more accessible and reduce the burden on newly delivered mothers. Finally, women who had previously completed an EPDS screening questionnaire and had been ineligible to participate had the opportunity to be referred back to the trial by their GP or PHV if they were thought to be depressed; and the time frame for all health professionals' referrals was increased from 3 months to 6 months after the birth.

Interventions

Antidepressant medication

Women randomised to antidepressants were asked to make an appointment with their own GP as soon as possible, to discuss the prescription of an appropriate antidepressant. Women were contacted approximately 1 week after randomisation by the research associate to ascertain what progress they had made with this.

The woman's GP and PHV were informed of the antidepressant group allocation by fax. The PHV was asked not to start any form of counselling or other psychological intervention specifically aimed at alleviating the symptoms of depression. The GP was told to expect the woman to make an appointment at the practice, and was asked to prescribe an antidepressant according to a simple clinical practice guideline developed by the research team (see Appendix 9) based on the North of England Guidelines[84] and the British Association for Psychopharmacology 2000 Guidelines.[85] Although an SSRI was recommended as a first-line treatment, a pragmatic approach was employed whereby the GP and the patient agreed which antidepressant medication should be prescribed. The guidelines recommended the prescription of fluoxetine (20 mg) if not breastfeeding, sertraline (50 mg), paroxetine (20 mg), citalopram (20 mg) or escitalopram (10 mg) as first-line treatments. (It should be noted that since the study was designed it has been reported that citalopram treatment results in significant infant plasma levels.[52]) Lofepramine (70 mg twice daily) or reboxetine (4 mg) were recommended as second-line treatments. However, it was noted that there is a lack of safety data on the use of escitalopram and reboxetine by breastfeeding mothers. The guidelines also advised noting the past response to an SSRI, previous adverse effects of any SSRIs, any concurrent medication and potential interactions, and the profile of the preferred SSRI regarding breastfeeding. The guidelines suggested that women be monitored after 2 weeks to assess side effects, and at 4 weeks to review treatment efficacy, and then every 4 weeks until 28 weeks. GPs were also guided on increasing the dose, changing the antidepressant medication or stopping pharmacotherapy altogether.

Information on the antidepressant prescribed and treatment adherence was obtained through women's self-report at all follow-up points, and by recording prescribing information from women's medical notes.

Health visitor non-directive counselling (listening visits)

Listening visits are a psychotherapeutic intervention that uses a form of non-directive counselling, often referred to as 'active listening' when delivered by HVs to women with PND, and originates from client-centred psychotherapy.[70] Non-directive counselling employs a person-centred approach and focuses on the feelings of

the client, and as such the content of listening visits is determined by the client themselves. Using listening visits, HVs aim to facilitate the expression of the woman's feelings without interfering, in a way that is respectful, empathic and reflective. HV-delivered non-directive counselling is referred to throughout this report as 'listening visits'. During the visits, HVs discourage discussion of the practicalities of baby care and encourage expression of the mother's feelings.

If a woman was randomised to listening visits, her GP and PHV were notified that this allocation had been made and that visits would commence after a 4-week waiting period. The protocol specified the 4-week waiting period to (1) test the effectiveness of antidepressants against usual care and (2) replicate the likely wait a woman might have for referral to a counsellor.

To avoid contamination between treatment groups, GPs were asked to provide GSC to these women, and not to prescribe antidepressants or any extra psychological care unless absolutely necessary. Furthermore, PHVs were asked not to provide any psychological intervention aimed to alleviate the women's symptoms of depression. Although certain PCTs offer training in non-directive counselling to HVs to use with women with PND, we worked closely with HV leads in the participating PCTs to ensure that this was not the case for the practices recruited to this trial.

Location, duration and structure of listening visits

After the 4-week waiting period, listening visits were delivered in a series of up to eight sessions by trained RHVs, one in each centre. The RHVs contacted women 2 weeks after randomisation to make the first appointment, which reminded women about the care they were to receive and allayed the fears of PHVs that women with known PND were not receiving active treatment during the 4-week wait. The visits took place in the woman's home whenever possible, and were scheduled at the woman's convenience.

Women were initially offered a series of four listening visits over 4–6 weeks. At the fourth visit, the RHV and woman reviewed progress and decided whether to end treatment, to refer on (to the GP for antidepressants or to alternative services), and/or to undertake a second set of four listening visits to take place over a further 4–6 weeks. The first visit took up to 90 minutes. This visit set the scene for what would and would not be discussed and the guarantee of confidentiality, except in circumstances where the woman or child could be deemed to be at risk of harm. This was important not only in winning the woman's trust, but also in ensuring that the RHV could seek outside assistance if necessary. Subsequent visits were no more than 1 hour long, of which at least 30 minutes was active listening. A typical visit began with 10 minutes of orientation (settling in and discussing aims, goals and expectations of the visits), 30 minutes of listening to how the woman had been and talking through the issues she wanted to discuss, 5 minutes to summarise the issues raised and 5 minutes to close the discussion and agree what should happen next regarding subsequent visits or further referral.

The role of the RHV was solely to provide the listening visit intervention that focused on the woman's depression and as such, the RHV was not involved in the woman's usual care. The woman could maintain access to her own PHV with whom the RHV liaised, therefore the family-health visiting role continued to be provided by the PHV. The RHV informed the woman's PHV before the listening visits commenced, and the GP and PHV at the end of the sessions.

Each trial centre employed an experienced RHV to deliver the intervention. These three RHVs attended formal training at Keele University organised by a consultant clinical psychologist, one of the coinvestigators for RESPOND who cofounded the HV non-directive counselling approach, using a previously developed and evaluated training package.[86] Training comprised two full-day sessions and covered the detection, treatment and prevention of PND, and the value and practice of non-directive counselling. Participants received a training manual, engaged in group discussion, viewed a video of 'active listening' and took part in role play. Subsequently, each RHV received regular peer supervision (every 2–4 weeks) from an experienced mental-health professional. In addition, the HV non-directive counselling trainer met with the RHVs on several further occasions to offer ongoing guidance. The RHVs also met with each other several times to discuss the content of listening visits and were in regular e-mail and telephone contact to ensure consistency in their approach. A protocol was developed by the consultant clinical psychologist and the RHVs to standardise the provision of listening visits across the three centres. Formal taping of sessions to assess adherence to the model was not undertaken because of concerns that

women with PND might find these intrusive and decline to participate.

Over the period of the trial there were four RHVs in post. The Manchester and London centres employed the same RHVs throughout the study. However, there were two staff changes in Bristol. The first Bristol RHV left the study in December 2006 due to ill health. An experienced and qualified counsellor from a women's mental-health organisation, who was not a HV, was employed for 4 months and conducted visits with seven women to ensure that counselling commenced as soon as possible after the scheduled 4-week waiting period for women randomised to listening visits. A second RHV with counselling training and experience of providing listening visits joined the Bristol team in May 2007 and completed visits with 20 women. These two therapists had not completed the 2-day non-directive counselling training detailed above, but were both qualified and experienced counsellors. One woman received non-directive counselling from two of the Bristol therapists.

Change to alternative intervention

Women allocated listening visits were able to visit their GP at any time during the study period as part of their GSC. Although GPs could prescribe antidepressants for these women at any time during the study period, they were asked not to offer a prescription before 4 weeks unless absolutely necessary. RHVs also discussed the use of antidepressants with women during listening visits if this was thought to be necessary. This discussion most commonly occurred at the fourth visit as part of a review of treatment progress, but the use of antidepressants may have been suggested earlier if the woman was particularly unwell.

When the 4-week follow-up assessment had been completed, women allocated antidepressants were reminded by the research associate that they could also receive listening visits. In addition, a letter was sent to the GPs of women allocated antidepressants 4 weeks after randomisation (see Appendix 10) to remind them of the treatment options available to women allocated antidepressants. This included offering listening visits instead of, or in addition to, antidepressants. Women who requested these were then offered a series of up to eight listening visits with the RHV which were scheduled to commence as soon as possible after the crossover was requested.

Measures

Data were collected using the self-report questionnaires detailed below.

Diagnosis of depression

The EPDS,[75] a 10-item self-report questionnaire, was used to screen for PND. Several validation studies have been carried out in English-speaking samples as well as in other languages.[75,87] The case definition for probable depression is a score of ≥ 13[88] and this threshold was used to determine eligibility to the trial. At the screening stage to reduce the chance of missing false negatives we used a threshold of ≥ 11. The EPDS was completed at the screening stage, the baseline home visit and at all follow-ups.

The self-administered computerised version of the CIS-R was used at baseline to obtain a more accurate measure of the woman's clinical state, to confirm a diagnosis of depression and to ensure eligibility. Questions were presented to the woman on the computer screen and she responded independently using the keyboard. The CIS-R is a fully structured psychiatric assessment for 14 common symptoms of depression and anxiety in the week before interview.[76] It has been used widely, including in the UK Psychiatric Morbidity Surveys.[89] The questions in the CIS-R enable the ICD-10 criteria for depressive episode, generalised anxiety disorder, phobias, panic disorder and obsessive compulsive disorder to be defined. The CIS-R also generates a total score that ranges from 0 to 57. There is excellent agreement between the interview-administered version and the self-administered computerised version.[90] In particular, there is no evidence of any consistent bias between the two methods of administration. The original CIS was used in the first trial of listening visits for PND,[70] and the CIS-R was used in a more recent trial comparing an SSRI with CBT.[54]

Self-harm risk

Thoughts of self-harm in the past 7 days were assessed using a question on the EPDS at all time points and with appropriate questions from the CIS-R at baseline. Risk of self-harm was defined as:

- an answer of 'Sometimes' or 'Yes, quite often' to question 10 of the EPDS 'The thought of harming myself has occurred to me'

- reporting that 'life isn't worth living', suicidal thoughts or suicidal plans on the CIS-R.

Primary outcomes

The primary outcome was depression assessed using the EPDS at 4 and 18 weeks after randomisation to address research objectives 1 and 2, respectively. The EPDS was selected as the primary outcome (rather than a longer, more thorough assessment of psychopathology such as the CIS-R[76]) because the EPDS is shorter, has been used in previous studies more often than any other measure, allowing comparability with previous research, and is easier to complete, hence facilitating more successful follow-up rates. The primary outcome was the binary variable of whether or not the woman had 'improved' her EPDS score such that she no longer satisfied the entry criterion of an EPDS ≥ 13. The comparisons between the randomisation groups at the two follow-up time points therefore compared the proportions of women whose scores were < 13 as opposed to ≥ 13.

Secondary outcomes

All secondary outcomes were collected at baseline and at both follow-ups. The main secondary outcome was the continuous score on the EPDS at 4 and 18 weeks, analysed both separately and together.

Quality of life was measured using the standard SF-12 version 2 questionnaire. This 12-item measure is a widely used and well validated[78,91] generic measure of functional quality of life. The questionnaire was modified (see Appendix 7) to include three additional items from the SF-36[92] to incorporate the five-item Mental Health Index (5-MHI), a measure gaining in popularity as a short self-report questionnaire for emotional well-being,[93] but not used in our analysis. Mental and physical component scores were calculated using standard algorithms, with higher scores indicating better health. If a woman returned an incomplete SF-12 questionnaire, it was not scored and was regarded as missing.

Health-related quality of life was measured using the EQ-5D[79] questionnaire, with the intention of using the data to estimate Quality Adjusted Life-Years (QALYs). This widely used instrument includes questions about mobility, self-care, usual activities, pain/discomfort and anxiety/depression to describe health status. Utility scores for each health state have been determined using valuations from the general population.[94] We also recorded personal health state valuation using the EQ-5D visual analogue scale (VAS), a 'thermometer' ranging from 0 to 100, where 100 represents the best state imaginable and 0 represents the worst state. Total scores were not calculated for women with incomplete responses to this scale, and were regarded as missing.

Maternal attitudes were measured using the relevant 12-item subscale (attitudes towards pregnancy and the baby) of the MAMA questionnaire (postpartum version).[80] This questionnaire included 12 items (see Appendix 7) and is acceptable to women.[80] Higher scores on this measure indicate a more positive attitude. Incomplete responses to this scale were not scored and were regarded as missing.

The quality of the marital relationship was assessed using the short form of the GRIMS.[81] This questionnaire (see Appendix 7) has been used in previous studies with acceptable validity (Golombok, personal communication 2008). This measure could only be completed by women in a current relationship. Total scores were calculated with higher scores indicating a poorer relationship. Incomplete responses to this scale were not scored and were regarded as missing.

The woman's partner was invited to complete a small number of questionnaires. These included the GHQ-12[82] to assess mental health, their role as a parent using the PAPA,[83] the GRIMS[81] and the modified SF-12 as detailed above. The data obtained from partners will be presented in a separate publication.

Process measures

Attendance for listening visits was as recorded by the RHV. Adherence with antidepressant medication was assessed at 4 and 18 weeks using a modified version of the Morisky Adherence Scale[95] and four items adapted from a scale reported by Schroeder *et al*. (see Appendix 7).[96] Provided the woman had given consent, GP medical notes were also examined to extract information on consultations and medication prescribed for depression (date prescribed, drug name, strength, dose, amount issued), during the period between randomisation and the 18-week follow-up.

Resource use

As requested in the HTA commissioning brief, the original protocol described a full cost-effectiveness analysis at 44 weeks, i.e. around the time of the child's first birthday. However, when the recruitment extension request was curtailed to allow data collection only as far as the 18-week assessment, this part of the work plan ceased.

Sample size

Original sample size justification

In the original protocol, the primary outcome was the binary EPDS score at 4 weeks, comparing women randomised to antidepressants with those receiving GSC, and repeated at 18 weeks to compare randomisation to antidepressants plus or minus listening visits with listening visits alone. A positive outcome was defined as an EPDS that had 'improved' to the extent that the woman no longer satisfied the entry criterion for EPDS – namely, an EPDS < 13. For the original sample size calculation, it was anticipated that about 40% would improve by 4 weeks among women receiving GSC compared with 55% receiving antidepressants, and that in the same group of women this would rise to 50% at 18 weeks given the addition of listening visits compared with 65% in those receiving antidepressants. A difference of 15 percentage points in the proportions scoring < 13 on the EPDS was considered by clinical judgement to be substantial and worth detecting at each follow-up time point.

For a two-sided 5% significance level, 211 women were required in each group to have an 85% power of detecting a difference of 40% versus 55%, requiring a total of 468 women to be recruited to allow for 10% attrition at the 4-week follow-up. Assuming an 85% follow-up rate at 18 weeks, this sample size would yield 83% power to detect a difference of 50% versus 65% as significant with a two-sided 5% significance level. Attrition would have to exceed 22% for either power to fall below 80% for these specifications, and any sample size such as that derived here would be expected to have considerably higher power to detect clinically important differences in mean EPDS when the outcome is considered as a continuous score.

Assuming a prevalence of PND of 10% and an acceptance rate of 50%, recruiting 468 women was calculated to require a total of 9360 births to be covered by the recruitment period for the participating practices. Assuming that a practice with a list size of 10,000 has about 100 births per year, then 63 practices over an 18-month period was thought sufficient for the trial. It was intended that each centre would therefore recruit 21 practices for the trial.

Revised sample size calculation

Due to the difficulties in recruiting sufficient numbers of participants, and a higher than anticipated attrition rate, a revised sample size calculation was derived in late 2006/early 2007, in conjunction with the Data Monitoring Committee. For these calculations, an attrition rate of between 10% and 20% was assumed for the primary end point of 4 weeks, and (conservatively) up to 30% for the 18-week follow-up. Moreover, a total sample size of 250 women was projected, which would therefore yield 100–112 women available for analysis in each group at 4 weeks, and (for a range of 20–30%) 88–100 at 18 weeks. For the original target difference of 15 percentage points (40% versus 55%), power was very low, at between 45% and 56% for the two follow-up times depending on the attrition observed (again all with a two-sided 5% significance level). As indicated in *Table 1*, however, power was just over 80% for a target difference of about 20 percentage points across the same range of assumed attrition rates. In the event, with 254 women randomised and attrition rates of about 15% and 20% observed at 4 and 18 weeks respectively, the study had 80% power to detect a difference of 20–20.5 percentage points at the two follow-up points.

Although it was still felt preferable to base the sample size calculation (conservatively) on the binary version of the EPDS score at follow-up, this approach is in general highly conservative. As an indication of this, with a two-sided 5% significance level a sample size of 250 would yield 80–90% power to detect differences on the continuous EPDS scale of 0.4–0.5 standard deviations (SDs). Assuming an SD of about 5 (as observed at initial screening and at baseline in this trial) we would have adequate power to detect differences of 2.0–2.5 points, all of which are smaller than differences that would be considered clinically significant.[97]

Statistical methods

Data handling and software

All data were entered into Microsoft® ACCESS 2000 databases at all three study centres and then merged onto the central databases (currently in

TABLE 1 *Power (given a two-sided 5% significance level) to detect target differences in the binary version of the primary outcome for various levels of attrition from an initial total sample size of 250 women randomised*

Proportion EPDS < 13 in 'comparator group'	Proportion EPDS < 13 in 'intervention group'	Difference in proportions (% points)	Assumed attrition at follow-up (*n* per group for analysis)	Power
40%	60%	20	10%	80%
40%	60.5%	20.5	15%	81%
40%	61%	21	20%	81%
40%	62.5%	22.5	30%	81%

ACCESS 2003). Data validation was conducted in both Microsoft® ACCESS 2003 and STATA version 9.2, including checks for missing and inconsistent values, plus logic and range checks. The original paper questionnaires were checked where necessary and values were amended in the database. Statistical analysis was conducted according to a predefined analysis plan, using STATA version 9.2.

Preliminary analyses

Descriptive statistics were obtained to compare: the number of births recorded and screening invitations sent out and returned; characteristics of women who screened positive and negative at the initial screening; and characteristics of women randomised to the two treatment groups. The purposes of these analyses were to assess the epidemiology of PND, consider the generalisability of the group of women randomised, and to assess the baseline comparability of the two randomised groups.

Primary comparative analyses

The primary outcomes of the trial were the EPDS scores (as a binary variable, 'improved' < 13 versus 'not improved' ≥ 13) at the 4-week and 18-week follow-up time points. At 4 weeks and 18 weeks the primary analysis was an intention-to-treat (ITT) logistic regression of the EPDS score at follow-up, adjusting for baseline EPDS as a continuous variable and centre as the other stratification variable.

Secondary analyses

Using ordinary linear regression models at each follow-up point separately, the ITT analysis was then applied to all the secondary outcomes: the continuous version of the EPDS score; SF-12 (mental and physical components); EQ-5D (five-item utility score and VAS valuation); MAMA and GRIMS. All the following remaining secondary analyses were conducted on the full set of primary and secondary outcomes.

The primary analyses were repeated after additional adjustment for the precise time that had elapsed between randomisation and the date of completion of the relevant follow-up questionnaire. This was conducted by first adjusting for this time as an additional covariate in the primary (logistic) regression models and second by restricting the analysis to those who completed the questionnaire between 3 and 6 weeks and 16 and 20 weeks for the 4-week and 18-week follow-ups, respectively. The next secondary analysis adjusted for any variables that exhibited potentially influential imbalance at baseline from the 23 variables considered.

The next set of secondary analyses comprised explanatory investigations of the effects of the interventions, comparing women based on treatment(s) received. Although the crude (biased) treatment(s) received analyses are noted for comparative purposes where it is deemed helpful, the tabulated results derive from Complier-Average Causal Effect (CACE) analyses employing instrumental variables regression to estimate unbiased treatment effects.[98,99] These were performed for all primary and secondary outcomes at each follow-up, using ordinary linear regression models for continuous outcomes. In the absence of well-established methods of this kind for logistic models, the following approach was adopted for the (primary) binary outcome: ordinary instrumental variables regression for outcome percentages, plus probit models as sensitivity analyses to check that model assumptions were not seriously violated. In all cases the probit models gave very similar p-values to those from the ordinary regression models, and hence only the latter are presented here given their advantages in terms of interpretability of the regression coefficients (as differences in percentages).

All CACE analyses included the same women available for the corresponding ITT analysis. At 4 weeks these analyses compared those who had received antidepressants with those who had received GSC, with the CACE method accounting for selection effects operating after randomisation. At 18 weeks, some women in both randomisation groups had received all four possible combinations of the two interventions, that is: neither (GSC only); antidepressants only; listening visits only; both interventions. Whereas at 4 weeks a conventional instrumental variables regression is possible, at 18 weeks there is a larger number of observed combinations than randomisation groups and a combined instrumental variables regression is not possible. At 18 weeks, therefore, each intervention was considered separately in two parallel CACE analyses.

In respect of the listening visits, the explanatory analyses always used the RHV records. For antidepressants, two sets of data were used: first, the self-report data from the follow-up questionnaires and second the prescription data from the primary care records (specifically, whether or not there was evidence of a prescription for antidepressants by the relevant time point). Before the regression analyses, the levels of agreement between the two sources of antidepressant data were compared at the two time points using cross-tabulations and kappa statistics. At 18 weeks it is emphasised that this comparison has a number of limitations. First, the self-report data at 18 weeks only refer to the previous 4 weeks. Second, the prescribing data were only collected up to the target time of the 18-week follow-up rather than when this follow-up actually took place – hence the time period for the '18-week' record-based analyses was up to the actual 18-week follow-up or 18 weeks after randomisation, whichever was the shortest. For both these reasons a certain degree of discrepancy between the sources at 18 weeks would be expected. It remains that at 4 weeks the timing of the two sources was identical – namely, the date at which the 4-week EPDS was completed.

The remaining secondary analyses involved various sensitivity analyses to reduce the impact of missing data. First, a repeated measures (logistic) regression model was fitted to the 4-week and 18-week (binary) primary outcome data combined, using generalised estimating equations. This analysis initially investigated the interaction between intervention group and time (to assess whether there was evidence of a change in magnitude of effect between the two follow-up times), and then the main effect of intervention, in both cases adjusted for baseline EPDS and centre. Not only does interpretation of the latter effect depend on the presence or absence of an interaction with time, but in this study particular care is needed in the emphasis to be placed on the results of this analysis given that the interventions being compared changed considerably between the two follow-up times. The repeated measures analysis was also conducted for the continuous EPDS score, again adjusting for baseline EPDS and centre.

The second (missing data) sensitivity analysis involved the application of multiple imputation by chained equation (MICE) methods[100] in STATA (*ice* procedure: 25 April 2008 version 1.4.6). A total of 25 data sets were generated by this procedure and 10 switching procedures were undertaken. The imputation model included any potential confounders where there was any suggestion of a relationship with missing EPDS scores at either 4 or 18 weeks (ascertained by simple cross-tabulations between relevant factors and inclusion or attrition by 4 weeks and 18 weeks, separately). Initially it was the continuous EPDS scores that were imputed, from which imputed binary outcome variables of < 13 versus ≥ 13 were calculated. The primary ITT analyses were then repeated for four EPDS outcomes (the binary and continuous versions at each of the 4-week and 18-week follow-ups), with in each case the results compared with the original complete-case primary analyses.

Subgroup analyses

The preplanned subgroup analyses were all performed for the primary ITT regression models, adjusting for centre. The primary subgroup analysis investigated the interaction between the CIS-R score at baseline and randomisation group in regression models for the (binary) 4-week and 18-week EPDS outcomes. Further (more pragmatic) subgroup analyses repeated these analyses replacing the CIS-R with the continuous baseline EPDS and its binary version in the form of the stratification groups (baseline EPDS < 16 and ≥ 16). To potentially increase the power for these essentially exploratory analyses, the subgroup analyses were repeated for the continuous version of the EPDS score.

Economic evaluation

An economic evaluation was designed to estimate the cost-effectiveness of each treatment strategy

over the 44-week period by relating the costs of each strategy to the number of cases of depression resolved and to QALYs gained. We also planned a cost–consequences analysis relating the costs of each strategy to all primary and secondary outcomes measured at that follow-up.

Data on resource use by mother and baby were collected using a participant self-report questionnaire administered within the main trial questionnaire at 4 weeks and 18 weeks. We also collected data on the use of primary care and prescribed medication from GP records. The questionnaire was designed to be comparative across the two arms rather than fully descriptive of continuous resource use over the period and the intention was to validate the data obtained in this way using those from the GP records. Hence, we restricted the questions to information about resource use over the immediate 4-week period. At the 18-week follow-up half of all respondents were asked about resource use over the previous 8 weeks, with the intention of comparing their responses with the data from GP records and investigating the reliability of different recall periods.

The costs identified as being of relevance, and included in the questionnaire were: face-to-face and telephone consultations with, and home visits by: GP, practice nurse, and HVs; contacts with other health-care professionals such as counsellors and community psychologists; use of other primary care resources such as NHS Direct and walk-in centres; outpatients appointments, inpatient stays, visits to Accident and Emergency departments; and use of community and social services such as nurseries and mother and baby units.

Prescribed medication was also identified as relevant though data on this were collected only via GP records. We have used the questionnaire data to compare resource use by women and babies in each arm of the trial at 4 and 18 weeks. We have also estimated QALYs, by allocation over the 18-week period using data from the EQ-5D administered at baseline, 4 weeks and 18 weeks.

Qualitative study

The qualitative study, nested within the RESPOND trial, aimed to explore two main issues:

- acceptability and satisfaction with listening visits and antidepressant therapy from the perspective of the women
- attitudes of members of the primary care teams (GPs and PHVs) to women with PND, the management of PND in primary care and the role of HV-delivered listening visits.

The study consisted of conducting semi-structured interviews with women who had completed the trial or had declined to take part, and with GPs and HVs working in practices collaborating with RESPOND. (In a deviation from the original trial protocol, women were sampled on the basis of having completed the trial, not on the basis of having completed treatment.) As with all qualitative research, attention was given to issues of understanding, meaning and process.[101]

Approval was secured from MREC for the qualitative study with health professionals as part of the main ethics application submitted for the trial. Separate approval had to be sought for the study of women's attitudes and experiences. This was secured at a later stage from the MREC committee that had approved the main trial. Relevant PCT Research and Development approval was also obtained.

Recruitment and sampling of women and health professionals

In order to contact women who had completed the trial, i.e. had their final outcome measures for the trial taken, the research associates posted a letter explaining that interviews were being held with trial participants to all women taking part. The research associates then telephoned women to ask if they would be willing to be interviewed and, if they were, whether or not they could pass their contact details on to the qualitative research associate (RA) responsible for conducting the interviews. If the woman agreed to this, the research associate completed a 'release of personal details form' and gave this to the RA, along with information about which trial site the woman had been recruited in and to which intervention arm she had been randomised.

To contact individuals who had declined to take part in the trial, either before or at the stage of randomisation, at the time that the individual declined, the research associate present informed the individual about the qualitative study. The research associate then asked the individual if her contact details could be passed to the RA and followed the same procedure as described above.

Using the information provided by the research associates, a purposive sampling approach was used to ensure that interviews were held with both 'completers' and 'decliners' and in the case of the former, with women who had been randomised to different treatment arms and recruited in different centres. Within this sampling approach, maximum variation was sought in relation to age, socioeconomic background, ethnicity and women who had and had not complied with their allocated treatment.

Thirty-seven women were sampled and contacted by telephone to discuss the study further and, if they were still willing to be interviewed, to arrange an interview time and place. On being contacted, 28 women (27 completers and one decliner) agreed to be interviewed. Before interview, they were posted a letter confirming the interview time and an information sheet with details about the qualitative study. Two versions of the information sheet were available: one for completers and one for decliners. Written consent to take part was secured at the time of interview.

Sampling was also purposive for the health professionals' interviews. Maximum variation was achieved in relation to GPs' age, sex, length of time in general practice, practice size, and level of deprivation in the area. An attempt was made to interview GPs who had and who had not referred patients to the trial. For the HVs, variation was attained in relation to time since completion of training, length of service in that area and level of engagement with the trial. At the start of the trial, most HVs were practice-based, but corporate working was introduced to all areas during the first year of RESPOND. An attempt was made to interview HVs who were still practice-based, as well as those who had been moved to a corporate way of working.

Thirty-seven GPs were approached by letter and telephone and 19 agreed to be interviewed. Twenty HVs employed within participating PCTs were invited to participate and 14 agreed to be interviewed. For both sets of interviews, data collection and analysis proceeded in parallel, and recruitment ended when data saturation had been reached.

Interviews

The interviews with the women and with the health professionals were semi-structured in nature. Flexible interview guides were used to ensure that key areas were covered, while allowing participants to raise issues that were salient to them. The interview guide used with the women who had completed the trial (see Appendix 11) explored a number of topics: experiences of PND; treatment preference at the time of randomisation; expectations and experiences of antidepressants, listening visits and GSC; and views of the trial. The guide used with women who had declined to take part (see Appendix 12) also focused on their experiences of PND and expectations of the treatments delivered in the trial, as well as asking about their reasons for not taking part. The interview guides for health professionals (see Appendices 13 and 14) covered the following areas: understanding of PND; diagnosis and management of PND; and the patient–professional relationship, professional–professional relationships, and experience of the RESPOND study, in particular, views on the interventions.

Interviews with trial participants were held between November 2006 and June 2007. Two of the 28 women interviewed were interviewed over the telephone. The remaining women were interviewed face-to-face in their own homes. The interviews lasted between 40 minutes and 2 hours. The interviews with the health professionals were conducted between January 2006 and February 2007. Participants were interviewed at their place of work, and interviews lasted between 25 and 67 minutes. With participant consent, all the interviews were audio-recorded and transcribed verbatim.

Analysis of the interview data

For both the women's and the health professionals' interviews, analysis proceeded in parallel with data collection, allowing for modification of the interview guides in the light of emerging themes and for thematic categories identified in the initial interviews to be tested or explored in subsequent interviews where disconfirmatory evidence was sought.[102] For both data sets, analysis was inductive and a thematic approach was taken.[103] Hence, each transcript was read and re-read to gain an overall understanding of the participants' views and experiences. Emerging themes were then noted and coding frames (one for the women's data and one for the health professionals' data) developed. Transcripts were read and discussed by researchers from different professional backgrounds (primary care and psychology), so that the analysis and the coding frames could be debated and refined through discussion.

To allow electronic coding and retrieval of data, transcripts from the women's interviews were imported into the software package QSR NVIVO (version 2). Several transcripts were independently coded by K.M.T. and the RA, who then met to discuss areas of consensus and discrepancy. This led to further codes being developed and to existing codes being defined more clearly. Once all the transcripts had been electronically coded, data were analysed using a framework approach.[104] Using this method, K.M.T. summarised in tables what participants had said in relation to specific issues (e.g. concerns about medication, effect of antidepressants), and then made comparisons both within and across interviews to identify thematic patterns and deviant cases. As a result of the pragmatic nature of the trial, with women being able to have both treatments (either simultaneously or sequentially) at some point, the comparisons made were between participants who varied in terms of treatment preference and use, rather than their treatment allocation.

The health professional transcripts were independently coded as data were collected by C.A.C-G. and a research associate (E.C.), supported by a medical student (L.C.) and another research associate (C.R.). This led to further codes being developed and to existing codes being defined more clearly as data collection progressed. Regular meetings were held at all stages to discuss discrepancy and to achieve consensus. Once all the data had been collected and transcripts had been coded, data were analysed using a framework approach. C.A.C-G. and E.C. summarised in tables the themes agreed and made comparisons across transcripts, both within and across the two groups (i.e. GP and HV).

Trial monitoring

Supervision of trial

The trial was independently supervised by a Trial Steering Committee, which comprised an independent academic GP as chair, statistician/trialist, psychiatrist, representative from the Community Practitioners and Health Visitors Association, a consumer representative, the lead investigators and the trial co-ordinator. The trial was also supervised by a Data Monitoring and Ethics Committee, which comprised an academic health services researcher (chair), statistician and psychiatrist. Members of these committees are named in the Acknowledgements.

Other protocol amendments

Most of the protocol amendments were introduced to improve recruitment and retention rates within the trial, and these changes have been documented in the previous sections. Additional changes were made to the screening process, the CIS-R inclusion criteria and the procedure for crossing over from antidepressants to the listening visit arm at 4 weeks. These changes are detailed below.

In routine clinical use, where the EPDS is used to screen for PND, further clinical assessment is recommended at a score of ≥ 13. The original trial protocol used this criterion at the screening stage. However, to reduce the possibility of missing false negatives, this threshold was reduced to ≥ 11 for initial screening. Furthermore, the original protocol included a second interim EPDS, to be conducted by telephone 1 week after the initial postal screening questionnaire was completed. The purpose of this additional screen was to exclude women who might have had a more transient disorder (EPDS score < 8) at this point, to avoid unnecessary home visit assessments. As a consequence, the home visit only took place for women who scored ≥ 8 at telephone interim screening. However, after 272 women had completed this measure, of whom 55 (20%) scored < 8 and were considered improved, interim screening was abandoned because it proved an inefficient filter for home visit assessments.

The original protocol also specified a criterion of > 11 on the CIS-R for inclusion in the trial. However, this was not implemented because the inclusion criterion we were primarily interested in was an ICD-10 diagnosis of depression, rather than the total CIS-R score. A high score on the CIS-R can reflect other diagnoses such as generalised anxiety and panic disorders.

In response to the MREC's concerns about including women with more severe depression, women who scored ≥ 13 on the CIS-R were initially referred to the GP to make a final decision about their eligibility for the trial. However, as the trial progressed it became apparent that question 10 of the EPDS, and the response to CIS-R questions about self-harm were more reliable measures of emotional distress than the CIS-R total score, mainly because the CIS-R measures all emotional symptoms and not just depression. The protocol was amended so that women were only referred to the GP if they indicated suicidal ideation.

The final protocol change relates to the crossover of women from antidepressants to listening visits after their 4-week follow-up. We initially planned to offer listening visits to these women if they had failed to show an adequate improvement on their antidepressant. However, it became clear that within a pragmatic trial, we could not reasonably withhold treatment from trial participants that was generally available from PHVs. Therefore women in the antidepressant arm were able to access listening visits delivered by the RHV at any time after the 4-week follow-up, regardless of their 4-week EPDS score.

Chapter 3

Results: main trial results

Recruitment

Practices

Figures obtained from the practice monitoring visits and the PCTs are shown in *Table 2*, and relate to the 21 practices from each of Bristol and London, and 35 in Manchester. This table shows that the total number of invitations sent to women by practices was less than the number of births recorded by the practices, even after the exclusions by GPs were considered. Moreover, the PCTs in each centre reported more births than the practices recorded although some of the PCT figures were estimated. The PCTs were requested to provide monthly figures. However, because of other priorities, some PCTs were only able to provide annual totals for each practice and as practices were recruited at different times and for different periods, annual figures were calculated pro rata where necessary, for practices that had been active for only part of the year.

Patients

Practices sent a total of 10,666 invitations to recently delivered women and 4409 replies were received, including 15 who were referred to the study directly by the GP or HV. However, 62 of the invitations had been sent to women who had given birth twice during the recruitment period and had responded to the invitation to participate on both occasions. These second responses were therefore discarded giving a total of 4347 responses. After scrutinising the data, it was found that a further 19 replies were from women who had responded to both the initial invitation and to a reminder sent shortly afterwards and these duplicate responses were also removed leaving a total of 4328 responses. The overall response rate was therefore 41%. The numbers of responses/referrals from each centre were 2251 from Bristol, 951 from Manchester, and 1126 from London, with response rates of 44%, 29% and 53%, respectively. Of the 15 women referred directly by practitioners, two declined a home visit, four did not have an ICD-10 diagnosis of depression, four were randomised to antidepressants and five to listening visits.

The 'screening' Consolidated Standards of Reporting Trials (CONSORT) diagram (*Figure 3*) shows the outcome of the 10,604 (10,666 minus 62 second births) invitations to participate in the RESPOND study across the three centres. Of the 4328 replies received (after the removal of the 19 duplicate responses described above), 155 (3.6%) women did not complete the initial ('screening') EPDS questionnaire. A further 113 women who returned the questionnaire scoring < 11 (and hence included in the 3184 within *Figure 3*) indicated on the consent form that they

TABLE 2 *Number of births estimated from figures provided by the relevant PCTs (January 2005 to August 2007), together with the number of births recorded by the practices (% of those provided by the PCT), the number (%) of exclusions and the number (%) of invitations sent by practices*

	Bristol	Manchester	London	Total
PCT data				
Number of births	6135	4293	2782	13,210
Practice data				
Number of births	5355 (87%)	3491[a] (81%)	2437 (88%)	11,283 (85%)
Number of exclusions	242 (5%)	28 (<1%)	103 (4%)	373 (3%)
Invitations sent	5138 (96%)	3417 (98%)	2111 (87%)	10,666[b] (95%)

a Practice monitoring data are not available for one Manchester practice.
b This figure includes a small number of second births to women in the study period (which have been excluded from the CONSORT diagrams).

wished no further contact with the study, and 181 women who scored ≥ 11 on the EPDS questionnaire also refused further participation or could not be contacted after returning the initial questionnaire and consent form. Therefore, the total number of women to refuse the invitation to participate at the initial screening stage was 449 (10.4%). Women who declined to participate were entered onto the database with all identifiable information removed including the woman's date of birth even if this was available.

The total number of women who returned a completed screening EPDS ($n = 4158$) or who were referred to the study by their GP/HV ($n = 15$) was therefore 4173 (termed from now on as the 'questionnaire responders'). Of these 4173 responders, 3184 (76%) women scored 10 or less on the initial EPDS questionnaire and a total of 989 (24%) women scored ≥ 11, or were referred directly by their GP/HV (*Table 3*). These 989 (23%) women were offered a home visit assessment to assess eligibility for the trial. A diagnosis of PND was confirmed if the women scored ≥ 13 on a further EPDS at the home visit and had a diagnosis of depression according to ICD-10 criteria as assessed by the CIS-R.

The mean (SD) age and EPDS score of the 4173 responders were 31.4 (5.5) years and 7.3 (5.5), respectively. The mean (SD) age of their babies was 7.5 (3.0) weeks. Corresponding figures for each centre are shown in *Table 4*, which also shows distributions of these characteristics and the proportion of women answering 2 or 3 on the self-harm item on the EPDS questionnaire – that is, 'the thought of harming myself has occurred to me' either 'Sometimes' or 'Quite often'. Women from Manchester tended to be younger, have slightly older babies, have higher EPDS scores and be more likely to admit to thoughts of self-harm.

A comparison of age and EPDS data is shown in *Table 5* for those women with an EPDS score < 11 and for those with an EPDS score ≥ 11 or referred. Women who had high EPDS scores early in the postnatal period tended to be younger and were much more likely to admit to thoughts of harming themselves (15.2% compared with 0.2%).

Eligibility screen

The purpose of the eligibility screen was to ascertain whether women ($n = 989$) who scored ≥ 11 on the initial screening EPDS ($n = 974$), or who were referred ($n = 15$), met the criteria for a diagnosis of PND. For the purposes of *Figure 3*, the following hierarchy of exclusions was applied:

- refused/did not reply
- already receiving treatment
- excluded by GP/HV
- improved (interim telephone EPDS < 8 or home visit EPDS < 13)
- no ICD-10 diagnosis of depression
- other exclusion criteria.

The screening CONSORT diagram (*Figure 3*) shows the outcome for each of the 989 women who were invited to an eligibility home visit. A total of 361 women who scored ≥ 11 on the screening EPDS did not proceed to the home visit for the reasons given in the (screening) CONSORT diagram (*Figure 3*). One hundred and eighty-one women declined or did not reply. Their reasons for declining the home visit interview included 'feeling better/not wanting to take antidepressants' and 'lack of time'. However, this information was not systematically obtained or recorded. A further 180 women were found to meet one or more exclusion criteria before the interview took place, including 88 women who were already receiving treatment for depression and the 55 women who scored < 8 on the interim telephone EPDS (see Chapter 2, Trial monitoring). Reasons for exclusions either by GPs/HVs or researchers were not always given but reasons that were recorded are as follows: poor English ($n = 8$); infant older than 6 months ($n = 3$); infant-related reasons such as foster care/died/child protection ($n = 4$); GP concern ($n = 4$).

TABLE 3 *Number (%) of women from each centre scoring 0–10, and the number (%) scoring 11–30 on the initial EPDS questionnaire or who were referred by their GP/HV*

EPDS-2 score	Bristol	Manchester	London	Total
< 11	1720 (80%)	652 (70%)	812 (75%)	3184 (76%)
≥ 11 or referred	442 (20%)	280 (30%)	267 (25%)	989 (24%)
Total	2162	932	1079	4173

TABLE 4 *Comparison of age of women, age of babies and EPDS score at each centre at the time of completion of the screening EPDS; the number (%) of women indicating thoughts of self-harm and the distribution of the EPDS scores are also shown*

	Bristol	Manchester	London	Total
Age of women				
Mean (SD) years	31.6 (5.4)	30.2 (5.9)	32.0 (5.5)	31.4 (5.6)
< 18 years	–	5 (0.6%)	1 (0.1%)	6 (0.2%)
18 to 30 years	788 (37.2%)	399 (45.6%)	335 (32.2%)	1522 (37.7%)
> 30 to 40 years	1228 (58.0%)	434 (49.5%)	639 (61.4%)	2301 (57.0%)
> 40 years	103 (4.9%)	38 (4.3%)	66 (6.3%)	207 (5.1%)
Unknown	132 (5.9%)	75 (7.9%)	85 (7.6%)	292 (6.8%)
Age of babies				
Mean (SD) weeks	7.3 (2.7)	8.3 (3.9)	7.3 (2.4)	7.5 (3.0)
0 to 5 weeks	130 (6.0%)	87 (9.4%)	50 (4.6%)	267 (6.4%)
> 5 to 12 weeks	1916 (88.6%)	719 (77.4%)	987 (91.6%)	3622 (86.9%)
> 12 to 16 weeks	74 (3.4%)	66 (7.1%)	29 (2.7%)	169 (4.1%)
> 16 to 26 weeks	37 (1.7%)	51 (5.5%)	11 (1.0%)	99 (2.4%)
> 26 weeks	5 (0.2%)	6 (0.7%)	1 (0.1%)	12 (0.3%)
Unknown	89 (4.0%)	22 (2.3%)	48 (4.3%)	159 (3.7%)
EPDS				
Mean (SD)	7.0 (5.0)	8.2 (6.4)	7.2 (5.3)	7.3 (5.5)
< 11	1720 (79.6%)	652 (70.0%)	812 (75.3%)	3184 (76.6%)
≥ 11	440 (20.4%)	274 (29.0%)	260 (24.2%)	964 (23.4%)
Unknown (direct GP referral)	2 (0.1%)	6 (0.6%)	7 (0.7%)	15 (0.4%)
Positive answer to self-harm question	60 (2.8%)	54 (5.9%)	41 (3.9%)	155 (3.7%)

A total of 628 home visit assessments were conducted during which a further six women were found to be receiving treatment for depression. Of the remaining 622 women, 298 women scored < 13 on the EPDS so were ineligible and 54 scored ≥ 13 on the EPDS but did not have an ICD-10 diagnosis of depression and so were also ineligible as was one woman whose baby was more than 26 weeks old. Of the 269 eligible women (those who scored above 12 on the home visit EPDS and had a diagnosis of depression according to the CIS-R), seven were excluded by their GP or HV after the home visit had taken place and eight declined randomisation. Therefore, including the 94 (88 of the 989 and six of the 628) women who were already being treated for PND, the overall prevalence of PND in the 4173 questionnaire responders was 8.7% (95% CI 7.9 to 9.6%).

Table 6 (and *Figures 6–8* in Appendix 15) shows the breakdown of these exclusions by centre. This table incorporates the initial screening and the eligibility assessment. At the time of the eligibility EPDS, women in Bristol and London were almost twice as likely as those in Manchester to have 'improved' – that is, to have an EPDS score below the cut-off point and/or fail to get a diagnosis of depression as assessed by the CIS-R. As well as being more likely to be eligible for the study, women in Manchester were also more likely to have already been diagnosed with depression and be receiving treatment. In addition 73 (45%) of the women in Manchester were in the more severe stratum (EPDS at home visit ≥ 16) compared with 74 (25%) in London and 52 (31%) in Bristol.

Comparison of randomised and not randomised women

Table 7 shows the sociodemographic characteristics of the women who were eventually randomised compared with all other women who completed the home visit interview. Although all sociodemographic variables were collected by the

TABLE 5 *Comparison of high and low scorers on the EPDS at 7–8 weeks after the birth*

	n	EPDS < 11 (*n* = 3184)	*n*	EPDS ≥ 11 or referred (*n* = 989)
Age of women				
Mean (SD) age (years)	3078	31.7 (5.4)	958	30.2 (5.9)
< 18 years		6 (0.2%)		–
18 to 30 years		1072 (34.8%)		450 (47.0%)
> 30 to 40 years		1834 (59.6%)		467 (48.8%)
> 40 years		166 (5.4%)		41 (4.3%)
Unknown		106 (3.3%)		31 (3.1%)
Age of babies				
Mean (SD) age (weeks)	3181	7.4 (2.9)	987	8.2 (4.5)
> 0 to 5 weeks		196 (6.2%)		71 (7.2%)
> 5 to 12 weeks		2817 (88.6%)		804 (81.5%)
> 12 to 16 weeks		106 (3.3%)		63 (6.4%)
> 16 to 26 weeks		56 (1.8%)		43 (4.4%)
> 26 weeks		6 (0.2%)		6 (0.6%)
Unknown		3 (0.1%)		2 (0.2%)
EPDS				
Mean (SD)	3184	4.9 (2.9)	974	15.4 (3.9)
Median		5		14.5
Interquartile range		3–7		12–18
Positive answer to self-harm		8 (0.3%)		147 (15.2%)

researcher at the time of the home visit interview for all randomised women, this was not initially the case for women who were found to be ineligible. After the study had been recruiting for several months, it was decided that these variables were necessary for epidemiological purposes and so these data were then collected retrospectively by telephone by researchers at each centre.

Women who were randomised were less likely to be married or living with a partner and tended to have less social support. They were also more likely to report previous antidepressant treatment, to have fewer qualifications, and to be in routine occupations.

Intervention phase

Randomisation

A total of 254 eligible women were randomised and allocated to either the antidepressant arm ($n = 129$) or to the listening visits arm ($n = 125$). A further eight women were randomised incorrectly: four with no ICD-10 diagnosis of depression, one who scored < 13 on the home visit EPDS, one who was later found to be receiving counselling; and two who had a second birth during the recruitment period and were randomised on both occasions. Data for these women have been removed from the analysis of the randomised controlled trial, and in *Figure 3* they appear in their 'correct' boxes, albeit on a post hoc basis.

The sociodemographic variables collected at the eligibility home visit were compared for the two treatment groups and are shown in *Table 8*. These variables were collected using a self-report questionnaire and as a result data were incomplete, particularly for questions relating to partner data.

Table 8 indicates a good balance between the two randomisation groups, although there are some differences that may need to be adjusted for in secondary analyses – in particular, diagnosis, number of children, previous antidepressant treatment, breastfeeding and employment status. The small imbalance in respect of the GRIMS is of less general concern because this will reflect their current partner status (i.e. can only be completed if there is a current partner). Hence this baseline variable was only adjusted for in analyses involving the GRIMS outcome itself.

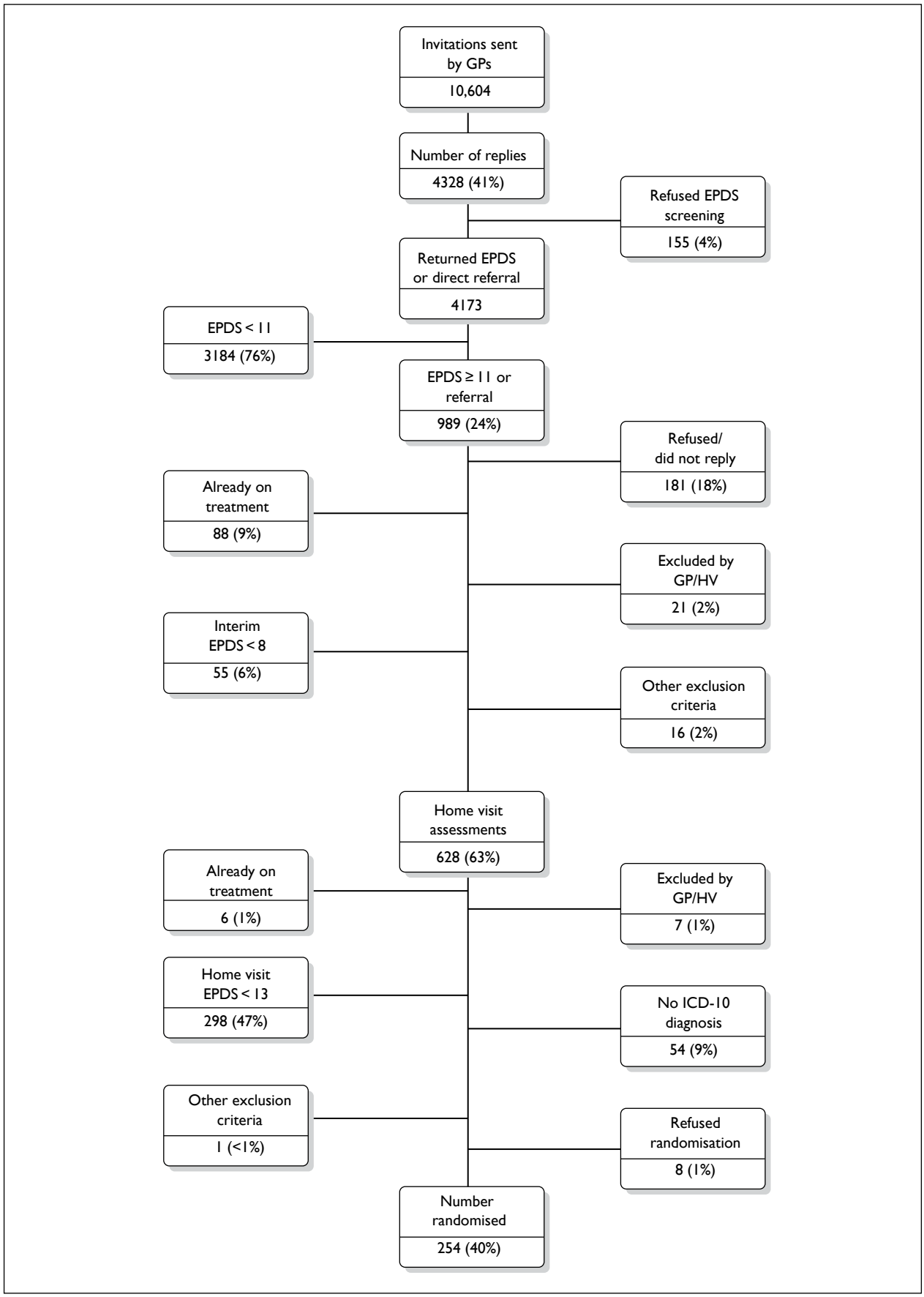

FIGURE 3 *Screening CONSORT diagram for all sites.*

TABLE 6 *Outcome of women who screened positive for PND on the initial EPDS (or who were referred directly) by centre*

	Bristol (*n* = 442)	Manchester (*n* = 280)	London (*n* = 267)	Total (*n* = 989)
Refused or unable to contact	81[a] (18.3%)	58 (20.7%)	50 (18.7%)	189 (19.1)
Already on treatment (antidepressants or counselling)	34 (7.7%)	42 (15.0%)	18 (6.7%)	94 (9.5%)
Excluded by GP/HV	16 (3.6%)	3 (1.1%)	9 (3.4%)	28 (2.8%)
Improved[b]	179 (40.5%)	68 (24.3%)	106 (39.3%)	353 (35.7%)
No ICD-10 diagnosis of depression	33 (7.5%)	10 (3.6%)	11 (4.1%)	54 (5.5%)
Other exclusion criteria	5 (1.1%)	9 (3.2%)	3 (1.1%)	17 (1.7%)
Randomised	94 (21.3%)	90 (32.1%)	70 (26.6%)	254 (25.8%)

a Includes eight women who met the criteria for PND but refused randomisation.
b Either scoring < 8 on the interim telephone EPDS or < 13 at the home visit assessment.

TABLE 7 *Age of mothers and babies, EPDS and CIS-R scores, and sociodemographic variables at home visit assessment of the 254 randomised women compared with the 374 women who received a home visit but were not randomised (mostly because they were not eligible for randomisation)*

	Randomised (*n*)		Not randomised (*n*)	
Mean (SD) age of women (years)	254	29.3 (6.3)	374	30.9 (5.7)
Mean (SD) age of babies (weeks)	254	11.5 (4.5)	366	11.1 (5.8)
EPDS score (home visit)	254		374	
Mean (SD)		17.5 (3.4)		9.7 (4.7)
Median		17		10
Interquartile range		15–20		7–12
Thoughts of self-harm	254		372	
Yes (sometimes/often)		46 (18.1%)		19 (5.1%)
No (never/hardly ever)		208 (81.9%)		353 (94.9%)
CIS-R score	254		140	
Mean (SD)		26.0 (7.6)		14.4 (10.0)
Median		26.0		12
Interquartile range		20–31		6.5–19
Number of children	254		352	
1		96 (37.8%)		167 (47.4%)
2 or 3		138 (54.3%)		162 (46.0%)
≥ 4		20 (7.9%)		23 (6.5%)
Marital status	237		317	
Married		105 (44.3%)		191 (60.3%)
Not married		132 (55.7%)		126 (39.8%)
Living with partner	253		349	
Yes		184 (72.7%)		295 (84.5%)
No		69 (27.3%)		54 (15.5%)

TABLE 7 *Age of mothers and babies, EPDS and CIS-R scores, and sociodemographic variables at home visit assessment of the 254 randomised women compared with the 374 women who received a home visit but were not randomised (mostly because they were not eligible for randomisation) (continued)*

	Randomised (*n*)		**Not randomised (*n*)**	
Social support[a] (range 0–6)	253		344	
Mean (SD)		4.5 (1.8)		5.2 (1.3)
Median		5		6
Previous antidepressant treatment	250		344	
Yes		121 (48.4%)		106 (30.8%)
No		129 (51.6%)		238 (69.2%)
Breastfeeding	252		349	
Yes		108 (42.9%)		186 (53.3%)
No		144 (57.1%)		163 (46.7%)
Women:				
Ethnic group	252		337	
White		196 (77.8%)		273 (81.0%)
Black		29 (11.5%)		28 (8.3%)
Asian		13 (5.2%)		22 (6.5%)
Other		14 (5.6%)		14 (4.2%)
Current paid employment/maternity leave	250		92	
Yes		133 (53.2%)		51 (55.4%)
No		117 (46.8%)		41 (44.6%)
Job classification	171		67	
Higher managerial		41 (24.0%)		19 (28.4%)
Lower managerial		28 (16.4%)		20 (29.9%)
Intermediate		38 (22.2%)		12 (17.9%)
Self-employed		5 (2.9%)		0
Lower supervisory		2 (1.2%)		3 (4.5%)
Semi-routine		41 (24.0%)		10 (14.9%)
Routine		16 (9.4%)		3 (4.5%)
Highest qualification	244		341	
None		36 (14.8%)		25 (7.3%)
GCSE		67 (27.5%)		62 (18.2%)
A-level		32 (13.1%)		46 (13.5%)
NVQ		48 (19.7%)		81 (23.8%)
Degree		61 (25.0%)		127 (37.2%)
Partner:				
Ethnic group	238		308	
White		178 (74.8%)		243 (78.9%)
Black		29 (12.2%)		28 (9.1%)
Asian		14 (5.9%)		22 (7.1%)
Other		17 (7.1%)		15 (4.9%)

continued

TABLE 7 *Age of mothers and babies, EPDS and CIS-R scores, and sociodemographic variables at home visit assessment of the 254 randomised women compared with the 374 women who received a home visit but were not randomised (mostly because they were not eligible for randomisation) (continued)*

	Randomised (*n*)	Not randomised (*n*)
Employed	201	79
Yes	170 (84.6%)	63 (79.7%)
No	31 (15.4%)	16 (20.3%)
Job classification	192	73
Higher managerial	44 (22.9%)	23 (31.5%)
Lower managerial	26 (13.5%)	16 (21.9%)
Intermediate	25 (13.0%)	3 (4.1%)
Self-employed	15 (7.8%)	3 (4.1%)
Lower supervisory	30 (15.6%)	12 (16.4%)
Semi-routine	21 (10.9%)	5 (6.9%)
Routine	31 (16.2%)	11 (15.1%)

a See Appendix 7 for details.

TABLE 8 *Comparison of baseline characteristics of women randomised to each treatment group*

	Antidepressants (*n* = 129)	Listening visits (*n* = 125)
Age of women		
Mean (SD) years	29.6 (6.2)	29.1 (6.4)
Range	18.9–44.0	18.0–44.1
Age of babies		
Mean (SD) weeks	11.3 (4.5)	11.8 (4.4)
Range	3.3–26.6	6.1–25.1
EPDS (home visit)		
Mean (SD)	17.3 (3.3)	17.7 (3.5)
Median	17	17
Interquartile range	15–19	15–20
Stratum		
EPDS < 16	45 (34.9%)	41 (32.5%)
EPDS ≥ 16	84 (65.1%)	85 (67.5%)
CIS-R		
Mean (SD)	25.9 (7.3)	26.0 (7.9)
Median	26	25
Interquartile range	20–30	20–31
Diagnosis		
Mild depression	29 (22.5%)	21 (16.8%)
Moderate depression	71 (55.0%)	78 (62.4%)
Severe depression	29 (22.5%)	26 (20.8%)

TABLE 8 *Comparison of baseline characteristics of women randomised to each treatment group (continued)*

	Antidepressants (*n* = 129)	**Listening visits (*n* = 125)**
Suicide ideation		
Self-harm (EPDS)		
No (never/hardly ever)	107 (83.0%)	101 (80.8%)
Yes (sometimes/often)	22 (17.1%)	24 (19.2%)
Suicide ideation (CIS-R)		
No	94 (72.9%)	88 (70.4%)
Yes (felt worthless)	35 (27.1%)	37 (29.6%)
SF-12 – mental component		
n	121	118
Mean (SD)	–1.48 (0.68)	–1.59 (0.79)
Median	–1.47	–1.62
Interquartile range	–1.95 to –0.99	–2.18 to –1.07
SF-12 – physical component		
n	121	118
Mean (SD)	0.29 (0.89)	0.27 (0.99)
Median	0.51	0.55
Interquartile range	–0.32 to 0.95	–0.23 to 0.97
EQ-5D (utility score)		
n	126	119
Mean (SD)	0.68 (0.24)	0.69 (0.23)
Median	0.73	0.81
Interquartile range	0.69–0.85	0.69–0.85
EQ-5D (VAS valuation)		
n	127	123
Mean (SD)	54.6 (22.2)	51.5 (23.4)
Median	55	50
Interquartile range	40–70	40–70
MAMA		
n	122	118
Mean (SD)	33.0 (5.6)	32.1 (5.1)
Median	33	32
Interquartile range	29–38	29–37
GRIMS		
n	104	109
Mean (SD)	13.6 (5.8)	15.5 (6.1)
Median	13	15
Interquartile range	10–17	11–20

continued

TABLE 8 *Comparison of baseline characteristics of women randomised to each treatment group (continued)*

	Antidepressants (*n* = 129)	Listening visits (*n* = 125)
Number of children		
1	53 (41.1%)	43 (34.4%)
2 or 3	69 (53.5%)	69 (55.2%)
≥ 4	7 (5.4%)	13 (10.4%)
Marital status		
Married	49 (42.2%)	56 (46.3%)
Not married	67 (57.8%)	65 (53.7%)
Living with partner		
Yes	93 (72.1%)	91 (73.4%)
No	36 (27.9%)	33 (26.6%)
Social support (range 0–6)		
Mean (SD)	4.6 (1.8)	4.4 (1.8)
Median	5	5
Previous antidepressant treatment		
Yes	64 (50.8%)	57 (46.0%)
No	62 (49.2%)	67 (54.0%)
Breastfeeding		
Yes	59 (46.5%)	49 (39.2%)
No	68 (53.5%)	76 (60.8%)
Women:		
Ethnic group		
White	102 (79.7%)	94 (75.8%)
Black	14 (10.9%)	15 (12.1%)
Asian	4 (3.1%)	9 (7.3%)
Other	8 (6.3%)	6 (4.8%)
Current paid employment/maternity leave		
Yes	73 (57.5%)	60 (48.8%)
No	54 (42.5%)	63 (51.2%)
Job classification		
Higher managerial	21 (22.6%)	20 (25.5%)
Lower managerial	12 (12.9%)	16 (20.5%)
Intermediate	22 (23.7%)	16 (20.5%)
Self-employed	4 (4.3%)	1 (1.3%)
Lower supervisory	2 (2.2%)	0
Semi-routine	23 (24.7%)	18 (23.1%)
Routine	9 (9.7%)	7 (9.0%)
Highest qualification		
None	19 (15.6%)	17 (13.9%)
GCSE	32 (26.2%)	35 (28.7%)
A-level	17 (13.9%)	15 (12.3%)
NVQ	21 (17.2%)	27 (22.1%)
Degree	33 (27.1%)	28 (23.0%)

TABLE 8 *Comparison of baseline characteristics of women randomised to each treatment group (continued)*

	Antidepressants (*n* = 129)	Listening visits (*n* = 125)
Partner:		
Ethnic group		
White	92 (78.0%)	86 (71.7%)
Black	15 (12.7%)	14 (11.7%)
Asian	4 (3.4%)	10 (8.3%)
Other	7 (5.9%)	10 (8.3%)
Employed		
Yes	86 (85.2%)	84 (84.0%)
No	15 (14.9%)	16 (16.0%)
Job classification		
Higher managerial	20 (21.3%)	24 (24.5%)
Lower managerial	16 (17.0%)	10 (10.2%)
Intermediate	11 (11.7%)	14 (14.3%)
Self-employed	8 (8.5%)	7 (7.1%)
Lower supervisory	15 (16.0%)	15 (15.3%)
Semi-routine	13 (13.8%)	8 (8.2%)
Routine	11 (11.7%)	20 (20.4%)

Follow-up

The 'intervention' CONSORT diagram (*Figure 4*) shows the progress of the randomised women up to the 18-week follow-up. Individual CONSORT diagrams for each centre appear in Appendix 16 (*Figures 9–11*). Outcome measures were scheduled to be collected at 4 and 18 weeks after randomisation within a target time frame of, for example, 1 week before to 2 weeks after the due 4-week follow-up date. These time frames were not always achieved and some women withdrew or were lost to follow-up. *Table 9* shows the actual time of questionnaire completion at the 4-week and 18-week follow-ups.

TABLE 9 *Timing of questionnaire completion at the 4-week and 18-week follow ups*

	Period	Number (%)
4-week follow-up	<3 weeks	2 (0.9%)
	3–6 weeks[a]	160 (73.4%)
	>6–8 weeks	35 (16.1%)
	>8–12 weeks	17 (7.8%)
	>12 weeks	4 (1.8%)
	Missing	36 (14.2%)
18-week follow-up	<16 weeks	1 (0.5%)
	16–20 weeks[a]	134 (65.1%)
	>20–24 weeks	45 (21.8%)
	>24–30 weeks	13 (6.3%)
	>30 weeks	13 (6.3%)
	Missing	48 (18.6%)

a Target time frame for the respective follow-up.

The numbers of questionnaires returned at 4 and 18 weeks were 218 and 206, respectively. The overall follow-up rate was therefore 86% at 4 weeks (Bristol 90%, Manchester 88%, London 77%) and 81% at 18 weeks (Bristol 84%, Manchester 87%, London 70%). More women in the antidepressant group withdrew or were lost to follow-up [4 weeks: antidepressants 23 (18%), listening visits 13 (10%) $p = 0.090$; 18 weeks: antidepressants 32 (25%), listening visits 16 (13%) $p = 0.015$].

In terms of the interventions actually received by those who were lost to follow-up, of the 36 women not followed up at 4 weeks, none received listening visits as part of the study. In addition, information on prescribing was available from the primary care records for all but three of these women. From this source, eight (24%) of 33 received a prescription for antidepressants; the remainder apparently received GSC only. Of the 48 women not followed up at 18 weeks, information about treatment actually received was known from RHV and primary care records for all but seven women. Of

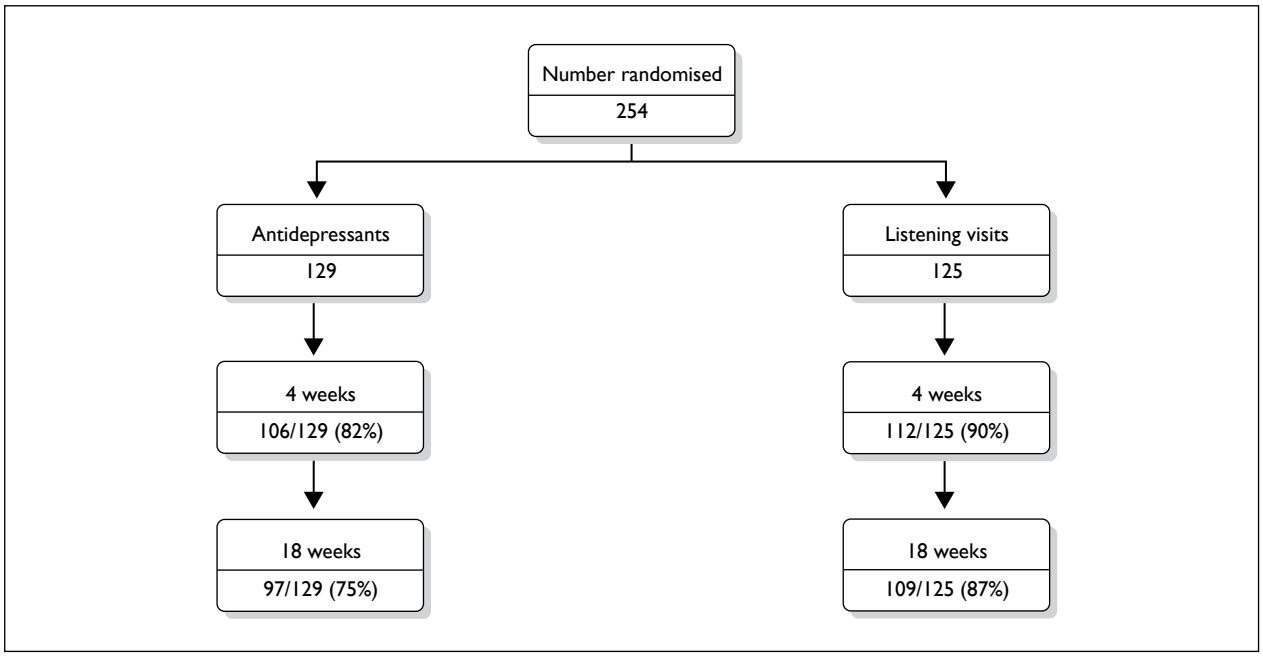

FIGURE 4 *Intervention CONSORT diagram for all sites.*

the remaining 41 women: 11 (27%) received GSC only; 13 (32%) received antidepressants, nine (22%) received listening visits and eight (20%) received both interventions. At both time points, the women who were lost to follow-up received substantially less in the way of intervention than those who were included.

Table 10 and *Table 11* present the relationships with attrition at 4 and 18 weeks for a selection of variables. This selection was driven by the requirements of the multiple imputation analyses (see Chapter 2, Statistical methods) so as to identify the potential confounding variables to be included in the (imputation) models for missing EPDS outcome data. From these results it was considered sufficient to include the following variables in the imputation models for (missing) EPDS at follow-up: intervention group; centre; EPDS itself at all time points including baseline; diagnosis; previous antidepressants; mother's age; number of children; living with partner and employment status. Overall, the primary EPDS outcomes were known for 218 and 204 women at the 4-week and 18-week follow-up points, respectively. Moreover, this outcome was only missing at both time points for 22 women, since 14 of the 36 scores missing at 4 weeks had known values at 18 weeks, and 26 of the 48 missing at 18 weeks were known at 4 weeks.

The mean (SD) time interval between randomisation and completion of the questionnaires was 5.4 (2.1) weeks at the 4-week time point and 160 (73%) were completed between 3 and 6 weeks after randomisation (*Table 9*). At 18 weeks, the mean (SD) time interval was 20.9 (5.0) weeks and 134 (65%) were completed between 16 and 20 weeks.

Adherence to protocol

A total of 129 women were randomised to receive antidepressants and 125 to receive listening visits. Inevitably, not all adhered to the protocol. Furthermore, the protocol stated that women randomised to the listening visits arm and who did not respond (EPDS score $\geq$ 13 at the 18-week follow-up) should be offered antidepressant treatment *after* the 18-week follow-up. However, practically and ethically it was not possible to prevent women accessing treatment options recommended by NICE. Consequently after the 4-week follow-up, both randomised groups had access to both treatments and so by 18 weeks some women had received either antidepressants or listening visits, some both, while others had refused both treatment options and opted for GSC from their PHV and/or GP. The diversity of treatment received by 18 weeks in each treatment arm is shown in *Table 12*.

A total of 125 women were randomised to listening visits, which commenced approximately 4 weeks after randomisation, and 117 women had at least one visit. In addition, 68 women in the antidepressant arm requested listening visits after

TABLE 10 *Comparison of various characteristics of those followed up and not followed up at 4 weeks*

	Lost to follow-up (*n*)		**Followed up (*n*)**	
Centre	36		218	
Bristol		9 (25%)		85 (39%)
Manchester		11 (31%)		79 (36%)
London		16 (44%)		54 (25%)
EPDS score (baseline)	36		218	
Mean (SD)		19.3 (4.4)		17.3 (3.7)
Median		19.5		17
Interquartile range		16–22.5		14–20
EPDS score (18 weeks)	14		192	
Mean (SD)		15.8 (5.0)		11.8 (5.6)
Median		17		11
Interquartile range		12–20		8–5
Stratum	36		218	
EPDS < 16		12 (33%)		73 (33%)
EPDS 16+		24 (67%)		145 (67%)
Diagnosis	36		218	
Mild depression		4 (11%)		46 (21%)
Moderate depression		21 (58%)		128 (59%)
Severe depression		11 (31%)		44 (20%)
CIS-R score	36		218	
Mean (SD)		26.6 (7.0)		25.9 (7.7)
Median		26.0		25
Interquartile range		21–31		20–31
Previous antidepressant treatment	35		215	
Yes		13 (37%)		108 (50%)
No		22 (63%)		107 (50%)
Mean (SD) age of women (years)[a]	36	26.8 (6.0)	218	29.8 (6.3)
18–30 years		26 (72%)		114 (52%)
30–40 years		10 (28%)		94 (43%)
40–48 years		0		10 (5%)
Mean (SD) age of babies (weeks)[a]	36	11.3 (4.2)	218	11.6 (4.6)
> 0 to 5 weeks		0		2 (1%)
> 5 to 12 weeks		26 (72%)		146 (67%)
> 12 to 16 weeks		5 (14%)		36 (17%)
> 16 to 26 weeks		5 (14%)		33 (15%)
> 26 weeks		0		1 (<1%)

continued

TABLE 10 *Comparison of various characteristics of those followed up and not followed up at 4 weeks (continued)*

	Lost to follow-up (*n*)		Followed up (*n*)	
Number of children	36		218	
1		17 (47%)		79 (38%)
2 or 3		14 (39%)		124 (57%)
≥ 4		5 (14%)		15 (7%)
Marital status	34		203	
Married		13 (38%)		92 (45%)
Not married		21 (62%)		111 (56%)
Living with partner	36		217	
Yes		22 (61%)		162 (75%)
No		14 (39%)		55 (25%)
Social support (range 0–6)	36		217	
Mean (SD)		4.7 (1.5)		4.4 (1.8)
Median		5		5
Current paid employment/maternity leave	35		215	
Yes		15 (43%)		118 (55%)
No		20 (57%)		97 (45%)

a Ages are those at randomisation.

TABLE 11 *Comparison of various characteristics of those followed up and not followed up at 18 weeks*

	Lost to follow-up (*n*)		Followed up (*n*)	
Centre	48		206	
Bristol		15 (31%)		79 (38%)
Manchester		12 (25%)		78 (38%)
London		21 (44%)		49 (24%)
EPDS score (baseline)	48		206	
Mean (SD)		18.3 (4.0)		17.3 (3.2)
Median		18		17
Interquartile range		14.5–21		15–19
EPDS score (4 weeks)	26		206	
Mean (SD)		13.8 (6.0)		15.5 (5.2)
Median		13.5		16
Interquartile range		10–17		12–19
Stratum	48		206	
EPDS < 16		17 (35%)		68 (33%)
EPDS 16+		31 (65%)		138 (67%)

TABLE 11 *Comparison of various characteristics of those followed up and not followed up at 18 weeks (continued)*

	Lost to follow-up (*n*)		Followed up (*n*)	
Diagnosis	48		206	
Mild depression		10 (21%)		40 (19%)
Moderate depression		25 (52%)		124 (60%)
Severe depression		13 (27%)		42 (20%)
CIS-R score	48		206	
Mean (SD)		26.3 (7.7)		25.9 (7.6)
Median		26		25
Interquartile range		21–31		20–31
Previous antidepressant treatment	46		204	
Yes		21 (46%)		100 (49%)
No		25 (54%)		104 (51%)
Mean (SD) age of women (years)[a]	48	28.6 (6.5)	206	29.5 (6.2)
18–30 years		28 (58%)		112 (54%)
30–40 years		19 (40%)		85 (41%)
40 – 48 years		1 (2%)		9 (4%)
Mean (SD) age of babies (weeks)[a]	48	12.2 (4.6)	206	11.4 (4.5)
>0 to 5 weeks		0		2 (1%)
>5 to 12 weeks		32 (67%)		140 (68%)
>12 to 26 weeks		5 (10%)		36 (17%)
>16 to 26 weeks		11 (23%)		27 (13%)
>26 weeks		0		1 (<1%)
Number of children	48		206	
1		18 (37%)		78 (38%)
2 or 3		24 (50%)		114 (55%)
≥4		6 (13%)		14 (7%)
Marital status	43		194	
Married		18(41%)		87 (45%)
Not married		25 (58%)		107 (55%)
Living with partner	48		205	
Yes		30 (63%)		154 (75%)
No		18 (37%)		51 (25%)
Social support (range 0–6)	36		217	
Mean (SD)		4.7 (1.5)		4.4 (1.8)
Median		5		5
Current paid employment/maternity leave	47		215	
Yes		24 (51%)		109 (53%)
No		23 (49%)		94 (46%)

a Ages are those at randomisation.

TABLE 12 *Actual treatment received according to self-report and research health visitor records for women who returned the 18-week questionnaire by randomisation group*

	Antidepressants (*n* = 97)	Listening visits (*n* = 109)
GSC only	16 (16%)	3 (3%)
ADs	24 (25%)	1 (< 1%)
LVs	19 (20%)	69 (63%)
ADs and LVs	38 (39%)	36 (33%)

ADs, antidepressants; GSC, general supportive care; LVs, listening visits.

the 4-week follow-up. Of these, 64 had at least one visit. During the course of the study, a total of 181 women therefore received some listening visits (*Table 13*). Among the 206 women providing primary outcome data at 18 weeks, from *Table 12* a total of 162 (79%) received some listening visits according to RHV records, 57 (59% of the 97 followed up) and 105 (96% of 109 followed up) in the antidepressants and listening visits groups, respectively.

Adherence to medication was ascertained by self-report at 4 and 18 weeks with the intention of verifying these reports with prescription data collected from women's medical records. At the 4- and 18-week follow-ups, women were asked to complete an adherence questionnaire relating to the previous 4 weeks if they had been prescribed antidepressants. Results are shown in *Table 14*. At 4 weeks only 59 (56%) of the 106 women followed up among those randomised to the antidepressants and who completed the questionnaire reported taking any antidepressants. In the listening visits group seven (6%) of the 112 women followed up

TABLE 13 *Number of listening visits received according to randomisation group*

Number of visits	Antidepressants	Listening visits
0	4 (5.9%)	8 (6.4%)
1	2 (2.9%)	8 (6.4%)
2	4 (5.9%)	7 (5.6%)
3	0	3 (2.4%)
4	10 (14.7%)	14 (11.2%)
5	1 (1.5%)	6 (4.8%)
6	4 (5.9%)	4 (3.2%)
7	3 (4.4%)	4 (3.2%)
8	40 (58.8%)	71 (56.8%)

TABLE 14 *Adherence to medication by randomisation group among those who took any antidepressants*

	Antidepressants	Listening visits
4 weeks		
Every day – same time	15 (25.4%)	3 (42.9%)
Every day – different times	19 (32.2%)	2 (28.6%)
Missed one dose	7 (11.9%)	2 (28.6%)
Missed many doses	18 (30.5%)	0
18 weeks		
Every day – same time	12 (22.6%)	10 (27.8%)
Every day – different times	10 (18.9%)	6 (16.7%)
Missed one dose	12 (22.6%)	11 (30.6%)
Missed many doses	19 (35.9%)	9 (25.0%)

also reported taking antidepressants. This makes a total of 66 (30% of 218) women who reported taking antidepressants at 4 weeks, all of whom responded to the adherence questionnaire depicted in *Table 14*. At the 18-week time point, the numbers in each group who reported taking antidepressants during the previous 4 weeks were 62 (64% of the 97 followed up) and 37 (34% of 109 followed up) in the antidepressants and listening visits groups, respectively. This makes a total of 99 (48% of 206) women who reported taking antidepressants at the 18-week follow-up, of whom all but 10 provided data for *Table 14* (nine and one missing from the two groups, respectively).

The antidepressant prescriptions data collected directly from practices were not available for 20 women: 12 who had refused consent and eight who had signed a version of the consent form that was not acceptable to practices for this purpose. Prescribing data were available for 201 of the 218 women followed up at 4 weeks; of the 97 and 104 in the antidepressant and listening visits groups, respectively, the numbers (percentages) being treated as intended were according to the notes, 52 (54%) and 99 (95%). These are very similar to the corresponding figures of 56% and 94% according to the self-report data, and agreement between these two sources was reasonably high. In particular, among the 97 in the antidepressant

group, crude agreement was 78% with a kappa of 0.56. Of the 55 women who self-reported taking an antidepressant, 43 (78%) had been prescribed such a drug; conversely, of the 42 who claimed not to have taken an antidepressant, 9 (21%) had such a prescription noted in their primary care records. Overall, by 4 weeks, 57 women had according to their records been prescribed antidepressants (52 in the antidepressant group, five in the listening visits group); 144 women had not (45 and 99, respectively).

At 18 weeks, prescribing data were available for 193 of the 206 women followed up (90 and 103 in the antidepressant and listening visits groups, respectively). According to the notes the number (percentage) being treated with antidepressants in the antidepressants group was 58 (64%); likewise, in the listening visits group the number (percentage) receiving at least one visit was 95 (92%). These are nearly identical to the corresponding figures of 64% and 90% according to the self-report data, and agreement between these two sources was very high. In particular, among the 90 in the antidepressant group, crude agreement was 84% with a kappa of 0.66. Of the 58 women who self-reported taking an antidepressant, 51 (88%) had been prescribed such a drug; conversely, of the 32 who claimed not to have taken an antidepressant, seven (22%) had such a prescription noted in their primary care records. Overall, by 18 weeks 92 women had according to their records been prescribed antidepressants (58 in the antidepressant group, 34 in the listening visits group); 101 had not (32 and 69, respectively).

Primary outcome

Descriptive statistics

Of the 106 women allocated to receive antidepressants with EPDS ≥ 13 at 4 weeks, 48 (45%) had improved as defined by having an EPDS score < 13 at follow-up. This compares with 22 (20%) out of 112 women allocated to receive listening visits. At 18 weeks the corresponding figures were 60/97 (62%) and 56/109 (51%), respectively.

Proportion improved at 4 weeks

Differences in proportions improved (that is, EPDS < 13) at 4 weeks between those randomised to antidepressants and those randomised to listening visits were analysed using a logistic regression model adjusting for baseline EPDS score and centre and analysed on an ITT basis. Results are shown in *Table 15*, row a. Women in the antidepressant group were more than twice as likely to have improved 4 weeks after randomisation as those randomised to the listening visit group.

As there was considerable variation in the elapsed time of follow-up, the effect of this was examined first by adding the elapsed time to the regression model and then by restricting the analysis to those women who completed the questionnaire within the target time frame (3–6 weeks). The inclusion of the elapsed time in the model had no effect either on the adjusted odds ratio or its confidence interval (*Table 15*, row b). Only 161 women (73 antidepressants, 87 listening visits) completed the questionnaire in the target time frame. Restricting the analysis to these women barely altered the results (*Table 15*, row c).

The model was then adjusted for the baseline imbalances apparent in *Table 8* (diagnosis, number of children, breastfeeding, previous antidepressant treatment, employment status). This had very little effect, if anything increasing the odds ratio slightly (*Table 15*, row d).

The efficacy of drug therapy during the first 4 weeks of the trial was explored using explanatory analyses to derive CACE estimates: first involving self-report data and second prescription data. Both analyses gave very similar results.

As detailed in *Table 14*, during the first 4 weeks of the trial, 66 (59 antidepressant, seven listening visits) of the women who returned the questionnaire reported taking antidepressants whereas 152 (47 antidepressants, 105 listening visits) were receiving only GSC. In this case, the difference in the percentages improving by the 4-week follow-up was reduced (41% and 28% for the antidepressant and listening visits groups, respectively), but from the corresponding instrumental variables regression model there was still strong evidence in favour of antidepressants – namely, an adjusted difference in percentages of 48% albeit with a wide 95% CI of 23 to 73% (*Table 15*, row e). This difference is much larger than that from both a corresponding (ITT) difference according to allocated group (24%; 95% CI 12 to 36%) and a crude, biased comparison of the 66 women who reported taking antidepressants versus the 152 who did not (15%; 95% CI 2 to 28%). The latter comparison is based on the two observed proportions (*Table 15*, row e), albeit after adjustment for baseline EPDS and

TABLE 15 *Comparisons between groups of the proportion improved at the 4-week follow-up (with higher percentages reflecting better mental health)*

	Antidepressants		Listening visits			
	n	**% improved**	***n***	**% improved**	**Odds ratio (95% CI)**	***p*-value**
Primary ITT analysis						
(a)	106	45	112	20	3.4 (1.8 to 6.5)[a]	<0.001
Secondary analyses						
(b)	106	45	112	20	3.4 (1.8 to 6.5)[b]	<0.001
(c)	73	45	87	21	3.3 (1.6 to 6.8)[c]	0.002
(d)	100	46	110	20	3.7 (1.9 to 7.2)[d]	<0.001
	Antidepressants		***GSC***		***Difference[g] (95% CI)***	***p-value***
(e)	66	41	152	28	48% (23 to 73%)[e]	<0.001
(f)	57	37	144	28	47% (21 to 73%)[f]	0.001

a ITT analysis adjusting for baseline EPDS score and centre.
b ITT analysis adjusting for baseline EPDS score, centre and elapsed time.
c ITT analysis adjusting for baseline EPDS score, centre but restricting to those who completed questionnaire between 3 and 6 weeks after randomisation.
d ITT analysis adjusting for baseline EPDS score, centre and baseline imbalances (diagnosis, number of children, breastfeeding, previous antidepressant treatment, employment status).
e CACE analysis (self-report) adjusting for baseline EPDS score and centre.
f CACE analysis (practice prescribing data) adjusting for baseline EPDS score and centre.
g Comparatively favourable outcomes for the antidepressant group are denoted by odds ratios greater than 1 and differences in percentages greater than 0.

centre; the CACE estimates, on the other hand, are very different from the crude difference, reflecting the considerable selection effects operating after randomisation. Very similar results were obtained comparing the 57 women followed up who were prescribed an antidepressant according to practice data compared with the 144 who were not (*Table 15*, row f).

Proportion improved at 18 weeks

The above analyses were repeated to examine the differences in proportions improved 18 weeks after randomisation (*Table 16*).

In the ITT analysis, the likelihood of improvement was 10 percentage points higher in the antidepressant group than in the listening visits group, although from the logistic regression analysis there was no clear evidence of benefit for one group compared with the other (*Table 16*, row a). Adjustment for timing of questionnaire completion and baseline imbalance had very little impact on these results (*Table 16*, rows b to d).

Self-report and practice data were again used to examine treatment effects for antidepressants in CACE analyses (*Table 16*, rows e and f), and RHV records for listening visits (*Table 16*, row g). For both interventions the observed differences were small [up to 6 percentage points with a standard error of 7–8 percentage points in crude treatment(s) received analyses]. The differences from the CACE analyses were larger (in one direction or the other) than the crude differences, and were plausible in light of the selection effects apparent from the ITT and crude treatment(s) received results. In addition to reservations about the assumption of independent effects of the two interventions in these (separate) CACE analyses, all the estimates in these models had wide confidence intervals and were within chance variation (*Table 16*).

The lack of evidence for differences at 18 weeks is likely to be the result of a combination of reduced power consequent on the original sample size not being achieved and a genuinely reducing effect over time, exacerbated by the considerable degree of switching across the two interventions by the later follow-up. Indeed, the precision of the CACE analyses will very likely be reduced by the latter, especially for listening visits which such a large proportion had received by the later follow-up.

TABLE 16 *Comparisons between groups of the proportion improved at the 18-week follow-up (with higher percentages reflecting better mental health)*

	Antidepressants		Listening visits			
Row	***n***	**% improved**	***n***	**% improved**	**Odds ratio[h] (95% CI)**	***p*-value**
Primary ITT analysis						
(a)	97	62	109	51	1.5 (0.8 to 2.6)[a]	0.19
Secondary analyses						
(b)	97	62	109	51	1.5 (0.8 to 2.6)[b]	0.19
(c)	61	62	73	53	1.4 (0.7 to 2.7)[c]	0.40
(d)	92	63	107	51	1.6 (0.8 to 2.9)[d]	0.16
(e)	99	54	107	59	29% (–18 to 77%)[e]	0.22
(f)	92	55	101	55	34% (–12 to 80%)[f]	0.15
	Listening visits		***No listening visits***			
(g)	162	55	44	61	–24% (–61 to 13%)[g]	0.20

a ITT analysis adjusting for baseline EPDS score and centre.
b ITT analysis adjusting for baseline EPDS score, centre and elapsed time.
c ITT analysis adjusting for baseline EPDS score, centre but restricting to those who completed questionnaire between 3 and 6 weeks after randomisation.
d ITT analysis adjusting for baseline EPDS score, centre and baseline imbalances (diagnosis, number of children, breastfeeding, previous antidepressant treatment, employment status).
e CACE analysis (self-report) adjusting for baseline EPDS score and centre.
f CACE analysis (practice prescribing data) adjusting for baseline EPDS score and centre.
g CACE analysis (RHV records) adjusting for baseline EPDS score and centre.
h Comparatively favourable outcomes for the antidepressant group are denoted by odds ratios greater than 1, and for each intervention in the CACE analyses by differences in percentages greater than 0.

A repeated measures logistic regression analysis was also performed to compare the improvement in the EPDS over time in both randomisation groups, adjusted for baseline score and centre. An interaction test led to evidence of a reduction in the odds ratio between the randomisation groups between 4 and 18 weeks ($p = 0.032$); ignoring this differential effect led to an overall odds ratio between the groups of 2.0 (95% CI 1.3 to 3.0), $p = 0.001$.

Secondary outcomes

EPDS score as a continuous variable–descriptive statistics

The mean (SD) EPDS scores of both randomisation groups from the initial screen to the 18-week follow-up are shown in *Table 17* and *Figure 5*. Both groups had similar mean scores at the initial EPDS screen and at the home visit eligibility assessment but the improvement was greater for the antidepressant group at the 4-week follow-up. However, by 18 weeks there appeared to be convergence. The distribution of EPDS was investigated by considering the histograms of the change in score from baseline to the 4-week follow-up within each intervention group separately for various candidate transformations (using the *gladder* command in STATA). In no case was there any indication that the distributional assumption of the regression models would be improved by transforming the data, and in any case the sample sizes are generally large enough for such methods to be robust. These investigations were repeated for all the other secondary outcomes, with the same conclusion drawn in each case.

EPDS score at 4 weeks as a continuous variable

Differences in EPDS scores from baseline to 4 weeks between those randomised to antidepressants and those randomised to listening visits were analysed using multiple linear regression models for the 4-week EPDS score adjusting for baseline EPDS and centre on an ITT basis. The mean EPDS score was about 2 points lower in the antidepressant group than in the listening visit group, with a margin of error of about 1 point

TABLE 17 *Descriptive statistics of the EPDS scores for the 254 women randomised to antidepressants or listening visits, from initial screening to the 18-week follow-up (with lower scores reflecting better mental health)*

	Antidepressants	Listening visits
EPDS (screening)[a]	n = ***122***	n = ***119***
Mean (SD)	17.4 (4.0)	17.7 (3.8)
Median	17	17
Interquartile range	14–20	15–20
EPDS (home visit)	n = ***129***	n = ***125***
Mean (SD)	17.3 (3.3)	17.7 (3.5)
Median	17	17
Interquartile range	15–19	15–20
EPDS (4 weeks)	n = ***106***	n = ***112***
Mean (SD)	13.9 (5.4)	16.4 (4.9)
Median	13	*17*
Interquartile range	10–18	14–20
EPDS (18 weeks)	n = ***97***	n = ***109***
Mean (SD)	11.6 (5.6)	12.6 (5.7)
Median	11	12
Interquartile range	7–15	8–17

a Excluding the 13 randomised women who were referred directly by their GP or HV (two of the original 15 women referred directly into the trial were not randomised).

(*Table 18*, row a). The point estimate corresponds to a standardised difference of about 0.4 SDs. Neither adjustments for time elapsed to follow-up, nor baseline imbalance made any substantial difference to these results (*Table 18*, rows b to d).

From the CACE analyses, an instrumental variables regression for the continuous EPDS score at 4 weeks (adjusting for baseline EPDS and centre) led to an estimated difference in means between those who reported taking an antidepressant and those reporting not doing so of –4.2 (95% CI –6.8 to –1.6), $p = 0.002$ (*Table 18*, row e). This difference is larger than that from both the corresponding ITT analysis (*Table 18*, row a) and a crude (biased) comparison of the 66 women who reported taking antidepressants versus the 152 who did not (–1.1, 95% CI –2.4 to 0.3). The latter comparison is based on the two observed means (*Table 18*, row e), albeit after adjustment for baseline EPDS and centre; the CACE estimates, on the other hand, are very different from the crude difference, reflecting the considerable selection effects operating after randomisation. Very similar results were obtained comparing the 57 women followed up who were prescribed an antidepressant according to practice data compared with the 144 who were not (*Table 18*, row f).

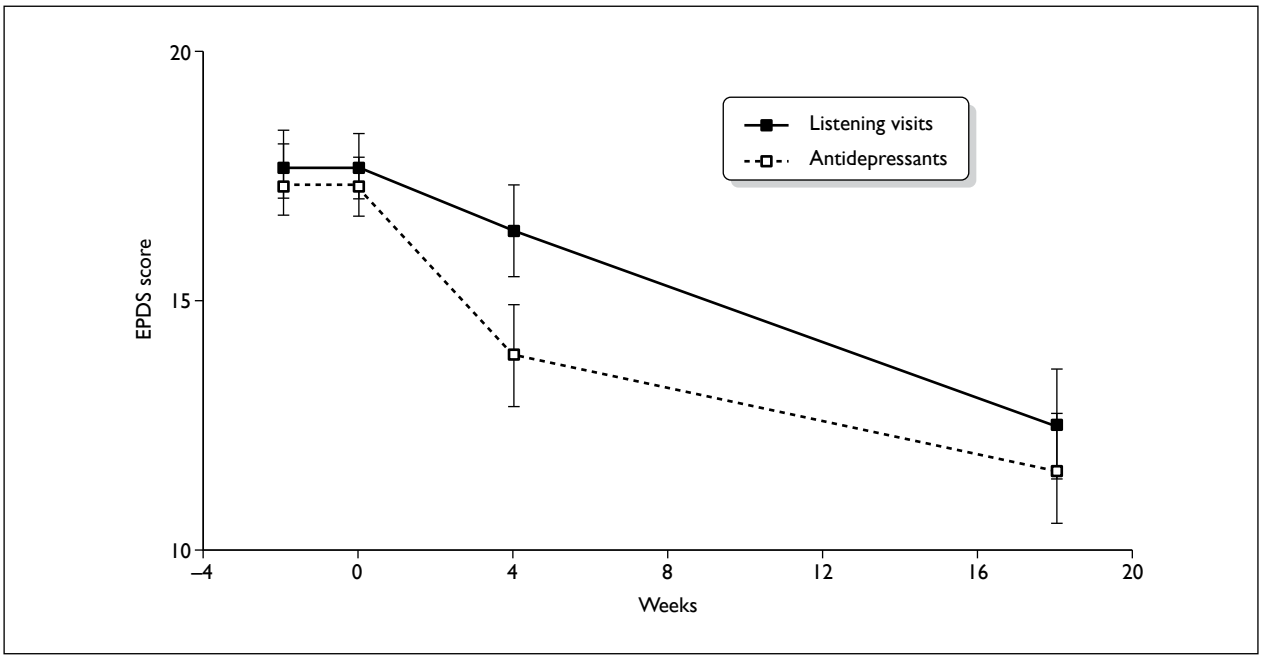

FIGURE 5 *Comparison of the mean (± 2SE) EPDS scores for the women randomised to antidepressants or listening visits, from initial screening to the 18-week follow-up (with lower scores reflecting better mental health).*

TABLE 18 *Comparisons between groups of the EPDS score at the 4-week follow-up (with lower scores reflecting better mental health)*

	Antidepressants		Listening visits			
	n	**Mean (SD)**	***n***	**Mean (SD)**	**Adjusted difference[g] (95% CI)**	***p*-value**
Primary ITT analysis						
(a)	106	13.9 (5.4)	112	16.4 (4.9)	−2.1 (−3.3 to −0.9)[a]	0.001
Secondary analyses						
(b)	106	13.9 (5.4)	112	16.4 (4.9)	−2.1 (−3.4 to −0.9) [b]	0.001
(c)	73	14.2 (5.1)	87	16.3 (4.8)	−1.8 (−3.2 to −0.4) [c]	0.012
(d)	100	13.9 (5.4)	110	16.3 (4.9)	−2.0 (−3.3 to −0.7)[d]	0.002
	Antidepressants		***GSC***		***Adjusted difference***	
(e)	66	14.8 (5.4)	152	15.3 (5.2)	−4.2 (−6.8 to −1.6)[e]	0.002
(f)	57	15.1 (5.4)	144	15.6 (5.1)	−4.1 (−6.8 to −1.4)[f]	0.003

a ITT analysis adjusting for baseline EPDS score and centre.
b ITT analysis adjusting for baseline EPDS score, centre and elapsed time.
c ITT analysis adjusting for baseline EPDS score, centre but restricting to those who completed questionnaire between 3 and 6 weeks after randomisation.
d ITT analysis adjusting for baseline EPDS score, centre and baseline imbalances (diagnosis, number of children, breastfeeding, previous antidepressant treatment, employment status).
e CACE analysis (self-report) adjusting for baseline EPDS score and centre.
f CACE analysis (practice prescribing data) adjusting for baseline EPDS score and centre.
g Comparatively favourable outcomes for the antidepressant group are denoted by differences in means less than 0.

EPDS score at 18 weeks as a continuous variable

The number of questionnaires returned at the 18-week follow-up point was 206 (97 antidepressants, 109 listening visits). The analyses for the 18-week EPDS scores are shown in *Table 19*. Although the mean EPDS score at 18 weeks was still lower for those in the antidepressant group than the listening visits group in all analyses performed, the difference between the groups had reduced considerably and the scores for both groups appeared to be converging (*Figure 5*). For the primary ITT comparison and the initial secondary analyses (*Table 19*, rows a to d), the differences between the means of the randomisation groups reduced to less than 1 point (about 0.2 SD) by 18 weeks. Moreover, the *p*-values all indicate lack of evidence of differences beyond chance and the 95% confidence intervals spanned zero.

Self-report and practice data were again used to examine treatment effects for antidepressants in CACE analyses (*Table 19*, rows e and f), and RHV records for listening visits (*Table 19*, row g). As with the primary outcome, for all CACE analyses the differences were larger (in one direction or the other) than the crude differences, and were plausible in light of the selection effects apparent from the ITT and crude treatment(s) received results. In addition to reservations about the assumption of independent effects of the two interventions in these (separate) CACE analyses, again all the estimates in these models had wide confidence intervals and were within chance variation (*Table 19*).

As with the primary outcome, the lack of evidence for differences at 18 weeks is likely to be the result of a combination of reduced power and the considerable degree of switching across the two interventions by the later follow-up, especially for the CACE analyses.

A repeated measures analysis was also performed to compare the improvement in the EPDS score over time in both randomisation groups depicted in *Figure 5*. The outcome EPDS scores at 4 and 18 weeks were again adjusted for baseline score and centre. An interaction test led to marginal evidence of a reduction in the difference between the randomisation groups between 4 and 18 weeks ($p = 0.070$); ignoring this possible differential effect led to an overall difference between the groups of −1.4 (95% CI −2.4 to −0.3), $p = 0.013$.

TABLE 19 *Comparisons between groups of the EPDS score at the 18-week follow-up (with lower scores reflecting better mental health)*

	Antidepressants		Listening visits			
Row	***n***	**Mean (SD)**	***n***	**Mean (SD)**	**Adjusted difference[h] (95% CI)**	***p*-value**
Primary ITT analysis						
(a)	97	11.6 (5.6)	109	12.6 (5.7)	−0.7 (−2.1 to 0.8)[a]	0.37
Secondary analyses						
(b)	97	11.6 (5.6)	109	12.6 (5.7)	−0.7 (−2.1 to 0.8)[b]	0.37
(c)	61	11.5 (5.5)	73	12.5 (6.0)	−0.6 (−2.5 to 1.3)[c]	0.56
(d)	92	11.4 (5.5)	107	12.5 (5.7)	−0.7 (−2.1 to 0.8)[d]	0.36
	Antidepressants		***No antidepressants***			
(e)	99	12.8 (6.0)	107	11.4 (5.3)	−2.2 (−7.3 to 2.9)[e]	0.39
(f)	92	12.9 (6.4)	101	11.6 (5.1)	−2.6 (−7.7 to 2.4)[f]	0.30
	Listening visits		***No listening visits***			
(g)	162	12.3 (5.8)	44	11.3 (5.3)	1.8 (−2.2 to 5.8)[g]	0.37

a ITT analysis adjusting for baseline EPDS score and centre.
b ITT analysis adjusting for baseline EPDS score, centre and elapsed time.
c ITT analysis adjusting for baseline EPDS score, centre but restricting to those who completed questionnaire between 16 and 20 weeks after randomisation.
d ITT analysis adjusting for baseline EPDS score, centre and baseline imbalances (diagnosis, number of children, breastfeeding, previous antidepressant treatment, employment status).
e CACE analysis (self-report) adjusting for baseline EPDS score and centre.
f CACE analysis (practice prescribing data) adjusting for baseline EPDS score and centre.
g CACE analysis (RHV records) adjusting for baseline EPDS score and centre.
h Comparatively favourable outcomes for the antidepressant group are denoted by differences less than 0; likewise for each intervention in the CACE analyses.

Other secondary outcomes

There were no adverse events or serious side effects of treatment in the trial. For the continuous secondary outcomes, results for the mental and physical component *z*-scores for the SF-12, the EQ-5D score and thermometer, the MAMA and GRIMS scores are presented in *Tables 20–31*.

From these tables (in which the sample sizes vary because of missing scores; see Chapter 2), the results for the SF-12 mental component score (*Tables 20, 21*) are very similar to those for the EPDS score, especially in its continuous version (*Tables 18, 19*). Specifically: the comparative benefit in scores for the antidepressants group at 4 weeks is apparent for the primary ITT analysis and all of the initial secondary analyses; likewise for the CACE analyses at 4 weeks: at 18 weeks the differences were reduced and not beyond chance variation albeit with wide confidence intervals especially for the CACE analyses. There was no evidence in any of the analyses for differences between the various groups in terms of the SF-12 physical component score (*Tables 22, 23*).

For the EQ-5D utility score (*Tables 24, 25*) all analyses indicated marginal evidence in favour of the antidepressant group at 4 weeks, with no differences at 18 weeks. For the EQ-5D VAS valuation (*Tables 26, 27*) the pattern was similar to the score although in this case the evidence was even weaker for the 4-week analyses.

For the MAMA attitude to baby subscale (*Tables 28, 29*) there was weak evidence of benefit to the antidepressant group at 4 weeks from the ITT analyses, and secondary analyses including the CACE models. At 18 weeks there were mostly similar differences but the evidence was even weaker.

For the GRIMS relationship scale (*Tables 30, 31*) there was no evidence of differences at 4 weeks in any of the analyses, and while the differences were slightly greater at 18 weeks, there remained no convincing evidence of any differences.

Sporadic low *p*-values among these secondary outcomes should be interpreted with caution given the number of such outcomes considered.

TABLE 20 *Comparisons between groups of the SF-12 mental component z-score at the 4-week follow-up (with higher scores reflecting better mental health)*

	Antidepressants		Listening visits			
Row	***n***	**Mean (SD)**	***n***	**Mean (SD)**	**Adjusted difference[g] (95% CI)**	***p*-value**
Primary ITT analysis						
(a)	79	−0.91 (0.85)	96	−1.36 (0.78)	0.36 (0.14 to 0.57)[a]	0.001
Secondary analyses						
(b)	79	−0.91 (0.85)	96	−1.36 (0.78)	0.34 (0.12 to 0.55)[b]	0.002
(c)	54	−0.93 (0.83)	75	−1.33 (0.81)	0.35 (0.11 to 0.60)[c]	0.005
(d)	75	−0.90 (0.86)	94	−1.36 (0.78)	0.39 (0.17 to 0.62)[d]	0.001
	Antidepressants		***GSC***		***Adjusted difference***	
(e)	47	−1.19 (0.85)	128	−1.14 (0.84)	0.79 (0.25 to 1.33)[e]	0.004
(f)	40	−1.15 (0.75)	118	−1.20 (0.86)	0.66 (0.13 to 1.19)[f]	0.015

a ITT analysis adjusting for baseline score, EPDS stratum and centre.
b ITT analysis adjusting for baseline score, EPDS stratum, centre and elapsed time.
c ITT analysis adjusting for baseline score, EPDS stratum and centre but restricting to those who completed questionnaire between 3 and 6 weeks after randomisation.
d ITT analysis adjusting for baseline score, EPDS stratum, centre and baseline imbalances (diagnosis, number of children, breastfeeding, previous antidepressant treatment, employment status).
e CACE analysis (self-report) adjusting for baseline score, EPDS stratum and centre.
f CACE analysis (practice prescribing data) adjusting for baseline score, EPDS stratum and centre.
g Comparatively favourable outcomes for the antidepressant group are denoted by differences in means greater than 0.

TABLE 21 *Comparisons between groups of the SF-12 mental component z-score at the 18-week follow-up (with higher scores reflecting better mental health)*

	Antidepressants		Listening visits			
Row	***n***	**Mean (SD)**	***n***	**Mean (SD)**	**Adjusted difference[h] (95% CI)**	***p*-value**
Primary ITT analysis						
(a)	77	−0.64 (0.88)	92	−0.77 (0.98)	0.09 (−0.19 to 0.37)[a]	0.53
Secondary analyses						
(b)	77	−0.64 (0.88)	92	−0.77 (0.98)	0.09 (−0.19 to 0.37)[b]	0.53
(c)	49	−0.66 (0.88)	62	−0.76 (0.99)	0.12 (−0.23 to 0.47)[c]	0.51
(d)	74	−0.59 (0.86)	92	−0.77 (0.98)	0.09 (−0.19 to 0.38)[d]	0.51
	Antidepressants		***No antidepressants***			
(e)	77	−0.94 (0.96)	92	−0.52 (0.87)	0.33 (−0.75 to 1.42)[e]	0.54
(f)	71	−0.89 (0.95)	86	−0.57 (0.94)	0.31 (−0.84 to 1.46)[f]	0.60
	Listening visits		***No listening visits***			
(g)	135	−0.76 (0.98)	34	−0.51 (0.73)	−0.27 (−1.13 to 0.58)[g]	0.53

a ITT analysis adjusting for baseline score, EPDS stratum and centre.
b ITT analysis adjusting for baseline score, EPDS stratum, centre and elapsed time.
c ITT analysis adjusting for baseline score, EPDS stratum and centre but restricting to those who completed questionnaire between 3 and 6 weeks after randomisation.
d ITT analysis adjusting for baseline score, EPDS stratum, centre and baseline imbalances (diagnosis, number of children, breastfeeding, previous antidepressant treatment, employment status).
e CACE analysis (self-report) adjusting for baseline score, EPDS stratum and centre.
f CACE analysis (practice prescribing data) adjusting for baseline score, EPDS stratum and centre.
g CACE analysis (RHV records) adjusting for baseline score, EPDS stratum and centre.
h Comparatively favourable outcomes for the antidepressant group are denoted by differences in means greater than 0; likewise for each intervention in the CACE analyses.

TABLE 22 *Comparisons between groups of the SF-12 physical component z-score at the 4-week follow-up (with higher scores reflecting better physical health)*

	Antidepressants		Listening visits			
Row	***n***	**Mean (SD)**	***n***	**Mean (SD)**	**Adjusted difference[g] (95% CI)**	***p*-value**
Primary ITT analysis						
(a)	79	0.12 (0.90)	96	0.09 (1.00)	−0.002 (−0.24 to 0.23)[a]	0.98
Secondary analyses						
(b)	79	0.12 (0.90)	96	0.09 (1.00)	0.02 (−0.23 to 0.26)[b]	0.90
(c)	54	0.05 (0.98)	75	0.14 (0.99)	−0.09 (−0.38 to 0.20)[c]	0.54
(d)	75	0.11 (0.92)	94	0.09 (1.02)	0.03 (−0.22 to 0.27)[d]	0.84
	Antidepressants		***GSC***		***Adjusted difference***	
(e)	47	0.14 (0.89)	128	0.09 (0.99)	−0.005 (−0.54 to 0.53)[e]	0.98
(f)	40	−0.01 (1.00)	118	0.07 (0.98)	0.02 (−0.53 to 0.58)[f]	0.94

a ITT analysis adjusting for baseline score, EPDS stratum and centre.
b ITT analysis adjusting for baseline score, EPDS stratum, centre and elapsed time.
c ITT analysis adjusting for baseline score, EPDS stratum and centre but restricting to those who completed questionnaire between 3 and 6 weeks after randomisation.
d ITT analysis adjusting for baseline score, EPDS stratum, centre and baseline imbalances (diagnosis, number of children, breastfeeding, previous antidepressant treatment, employment status).
e CACE analysis (self-report) adjusting for baseline score, EPDS stratum and centre.
f CACE analysis (practice prescribing data) adjusting for baseline score, EPDS stratum and centre.
g Comparatively favourable outcomes for the antidepressant group are denoted by differences in means greater than 0.

TABLE 23 *Comparisons between groups of the SF-12 physical component z-score at the 18-week follow-up (with higher scores reflecting better physical health)*

	Antidepressants		Listening visits			
Row	***n***	**Mean (SD)**	***n***	**Mean (SD)**	**Adjusted difference[h] (95% CI)**	***p*-value**
Primary ITT analysis						
(a)	77	0.20 (0.87)	92	0.01 (0.97)	0.12 (−0.12 to 0.36)[a]	0.34
Secondary analyses						
(b)	77	0.20 (0.87)	92	0.01 (0.97)	0.12 (−0.12 to 0.36)[b]	0.33
(c)	49	0.19 (0.81)	62	0.02 (0.99)	0.09 (−0.22 to 0.39)[c]	0.58
(d)	74	0.20 (0.86)	92	0.01 (0.97)	0.13 (−0.12 to 0.38)[d]	0.29
	Antidepressants		***No antidepressants***			
(e)	77	0.08 (1.00)	92	0.11 (0.87)	0.45 (−0.51 to 1.41)[e]	0.36
(f)	71	−0.01 (1.01)	86	0.12 (0.86)	0.54 (−0.49 to 1.58)[f]	0.30
	Listening visits		***No listening visits***			
(g)	135	0.10 (0.94)	34	0.07 (0.87)	−0.35 (−1.09 to 0.38)[g]	0.34

a ITT analysis adjusting for baseline score, EPDS stratum and centre.
b ITT analysis adjusting for baseline score, EPDS stratum, centre and elapsed time.
c ITT analysis adjusting for baseline score, EPDS stratum and centre but restricting to those who completed questionnaire between 3 and 6 weeks after randomisation.
d ITT analysis adjusting for baseline score, EPDS stratum, centre and baseline imbalances (diagnosis, number of children, breastfeeding, previous antidepressant treatment, employment status).
e CACE analysis (self-report) adjusting for baseline score, EPDS stratum and centre.
f CACE analysis (practice prescribing data) adjusting for baseline score, EPDS stratum and centre.
g CACE analysis (RHV records) adjusting for baseline score, EPDS stratum and centre.
h Comparatively favourable outcomes for the antidepressant group are denoted by differences in means greater than 0; likewise for each intervention in the CACE analyses.

TABLE 24 *Comparisons between groups of the EQ-5D utility score at the 4-week follow-up (with higher scores reflecting better general health)*

	Antidepressants		Listening visits			
Row	***n***	**Mean (SD)**	***n***	**Mean (SD)**	**Adjusted difference[g] (95% CI)**	***p*-value**
Primary ITT analysis						
(a)	98	0.75 (0.20)	100	0.70 (0.25)	0.05 (−0.002 to 0.11)[a]	0.059
Secondary analyses						
(b)	98	0.75 (0.20)	100	0.70 (0.25)	0.05 (−0.003 to 0.11)[b]	0.063
(c)	70	0.75 (0.20)	78	0.69 (0.26)	0.06 (0.001 to 0.13)[c]	0.048
(d)	93	0.75 (0.21)	99	0.70 (0.26)	0.05 (−0.004 to 0.11)[d]	0.066
	Antidepressants		***GSC***		***Adjusted difference***	
(e)	61	0.73 (0.22)	137	0.72 (0.24)	0.11 (−0.007 to 0.22)[e]	0.066
(f)	51	0.69 (0.24)	132	0.73 (0.23)	0.10 (−0.02 to 0.23)[f]	0.093

a ITT analysis adjusting for baseline score, EPDS stratum and centre.
b ITT analysis adjusting for baseline score, EPDS stratum, centre and elapsed time.
c ITT analysis adjusting for baseline score, EPDS stratum and centre but restricting to those who completed questionnaire between 3 and 6 weeks after randomisation.
d ITT analysis adjusting for baseline score, EPDS stratum, centre and baseline imbalances (diagnosis, number of children, breastfeeding, previous antidepressant treatment, employment status).
e CACE analysis (self-report) adjusting for baseline score, EPDS stratum and centre.
f CACE analysis (practice prescribing data) adjusting for baseline score, EPDS stratum and centre.
g Comparatively favourable outcomes for the antidepressant group are denoted by differences in means greater than 0.

TABLE 25 *Comparisons between groups of the EQ-5D utility score at the 18-week follow-up (with higher scores reflecting better general health)*

	Antidepressants		Listening visits			
Row	***n***	**Mean (SD)**	***n***	**Mean (SD)**	**Adjusted difference[h] (95% CI)**	***p*-value**
Primary ITT analysis						
(a)	93	0.76 (0.24)	101	0.77 (0.24)	−0.01 (−0.08 to 0.05)[a]	0.68
Secondary analyses						
(b)	93	0.76 (0.24)	101	0.77 (0.24)	−0.01 (−0.08 to 0.05)[b]	0.71
(c)	59	0.77 (0.21)	67	0.78 (0.24)	−0.004 (−0.08 to 0.07)[c]	0.91
(d)	89	0.77 (0.24)	100	0.77 (0.24)	−0.01 (−0.08 to 0.05)[d]	0.69
	Antidepressants		***No antidepressants***			
(e)	96	0.73 (0.26)	98	0.80 (0.21)	−0.05 (−0.27 to 0.17)[e]	0.68
(f)	89	0.74 (0.25)	94	0.78 (0.22)	0.006 (−0.21 to 0.22)[f]	0.95
	Listening visits		***No listening visits***			
(g)	152	0.76 (0.23)	42	0.79 (0.27)	0.04 (−0.14 to 0.21)[g]	0.68

a ITT analysis adjusting for baseline score, EPDS stratum and centre.
b ITT analysis adjusting for baseline score, EPDS stratum, centre and elapsed time.
c ITT analysis adjusting for baseline score, EPDS stratum and centre but restricting to those who completed questionnaire between 3 and 6 weeks after randomisation.
d ITT analysis adjusting for baseline score, EPDS stratum, centre and baseline imbalances (diagnosis, number of children, breastfeeding, previous antidepressant treatment, employment status).
e CACE analysis (self-report) adjusting for baseline score, EPDS stratum and centre.
f CACE analysis (practice prescribing data) adjusting for baseline score, EPDS stratum and centre.
g CACE analysis (RHV records) adjusting for baseline score, EPDS stratum and centre.
h Comparatively favourable outcomes for the antidepressant group are denoted by differences in means greater than 0; likewise for each intervention in the CACE analyses.

TABLE 26 *Comparisons between groups of the EQ-5D VAS valuation score at the 4-week follow-up (with higher scores reflecting better general health)*

	Antidepressants		Listening visits			
Row	***n***	**Mean (SD)**	***n***	**Mean (SD)**	**Adjusted difference (95% CI)**	***p*-value**
Primary ITT analysis						
(a)	97	58.6 (24.7)	107	53.5 (24.3)	3.5 (–1.8 to 8.8)[a]	0.20
Secondary analyses						
(b)	97	58.6 (24.7)	107	53.5 (24.3)	3.6 (–1.8 to 8.9)[b]	0.19
(c)	67	60.0 (24.8)	82	53.5 (25.7)	4.6 (–1.9 to 11.1)[c]	0.16
(d)	92	58.4 (25.3)	105	53.6 (24.4)	3.3 (–2.2 to 8.9)[d]	0.24
	Antidepressants		**GSC**		**Adjusted difference**	
(e)	61	55.2 (25.2)	143	56.2 (24.4)	7.0 (–3.7 to 17.6)[e]	0.20
(f)	52	52.7 (24.5)	135	55.2 (24.9)	4.7 (–6.9 to 16.2)[f]	0.43

a ITT analysis adjusting for baseline score, EPDS stratum and centre.
b ITT analysis adjusting for baseline score, EPDS stratum, centre and elapsed time.
c ITT analysis adjusting for baseline score, EPDS stratum and centre but restricting to those who completed questionnaire between 3 and 6 weeks after randomisation.
d ITT analysis adjusting for baseline score, EPDS stratum, centre and baseline imbalances (diagnosis, number of children, breastfeeding, previous antidepressant treatment, employment status).
e CACE analysis (self-report) adjusting for baseline score, EPDS stratum and centre.
f CACE analysis (practice prescribing data) adjusting for baseline score, EPDS stratum and centre.
g Comparatively favourable outcomes for the antidepressant group are denoted by differences in means greater than 0.

TABLE 27 *Comparisons between groups of the EQ-5D VAS valuation score at the 18-week follow-up (with higher scores reflecting better general health)*

	Antidepressants		Listening visits			
Row	***n***	**Mean (SD)**	***n***	**Mean (SD)**	**Adjusted difference[h] (95% CI)**	***p*-value**
Primary ITT analysis						
(a)	92	56.8 (29.9)	102	57.6 (28.8)	–1.6 (–8.1 to 4.9)[a]	0.63
Secondary analyses						
(b)	92	56.8 (29.9)	102	57.6 (28.8)	–1.5 (–8.1 to 5.0)[b]	0.64
(c)	59	59.5 (27.1)	69	60.7 (28.6)	–3.5 (–11.3 to 4.2)[c]	0.37
(d)	88	57.9 (29.6)	100	57.3 (28.9)	–0.2 (–6.8 to 6.5)[d]	0.96
		Antidepressants		***No antidepressants***		
(e)	95	49.7 (29.9)	99	64.4 (26.8)	–5.3 (–27.0 to 16.4)[e]	0.63
(f)	88	51.9 (30.3)	94	60.2 (28.4)	–3.0 (–23.9 to 17.9)[f]	0.78
		Listening visits		***No listening visits***		
(g)	151	56.3 (29.2)	43	60.5 (29.5)	3.8 (–12.2 to 19.9)[g]	0.64

a ITT analysis adjusting for baseline score, EPDS stratum and centre.
b ITT analysis adjusting for baseline score, EPDS stratum, centre and elapsed time.
c ITT analysis adjusting for baseline score, EPDS stratum and centre but restricting to those who completed questionnaire between 3 and 6 weeks after randomisation.
d ITT analysis adjusting for baseline score, EPDS stratum, centre and baseline imbalances (diagnosis, number of children, breastfeeding, previous antidepressant treatment, employment status).
e CACE analysis (self-report) adjusting for baseline score, EPDS stratum and centre.
f CACE analysis (practice prescribing data) adjusting for baseline score, EPDS stratum and centre CACE analysis (RHV records) adjusting for baseline score, EPDS stratum and centre.
g Comparatively favourable outcomes for the antidepressant group are denoted by differences in means greater than 0; likewise for each intervention in the CACE analyses.

TABLE 28 *Comparisons between groups of the attitude to baby subscale on the MAMA at the 4-week follow-up (with higher scores reflecting a more positive attitude)*

	Antidepressants		Listening visits			
Row	***n***	**Mean (SD)**	***n***	**Mean (SD)**	**Adjusted difference[g] (95% CI)**	***p*-value**
Primary ITT analysis						
(a)	92	35.3 (6.1)	100	33.5 (5.3)	1.1 (−0.02 to 2.2)[a]	0.05
Secondary analyses						
(b)	92	35.3 (6.1)	100	33.5 (5.3)	0.9 (−0.2 to 2.0)[b]	0.09
(c)	65	34.8 (5.9)	77	33.9 (5.2)	0.7 (−0.6 to 1.9)[c]	0.29
(d)	87	35.1 (6.1)	98	33.4 (5.3)	1.1 (−0.01 to 2.2)[d]	0.05
		Antidepressants		***GSC***		
(e)	59	35.0 (6.6)	133	34.1 (5.3)	2.0 (−0.09 to 4.0)[e]	0.06
(f)	50	34.8 (6.3)	128	34.0 (5.5)	1.9 (−0.4 to 4.2)[f]	0.1

a ITT analysis adjusting for baseline score, EPDS stratum and centre.
b ITT analysis adjusting for baseline score, EPDS stratum, centre and elapsed time.
c ITT analysis adjusting for baseline score, EPDS stratum and centre but restricting to those who completed questionnaire between 3 and 6 weeks after randomisation.
d ITT analysis adjusting for baseline score, EPDS stratum, centre and baseline imbalances (diagnosis, number of children, breastfeeding, previous antidepressant treatment, employment status).
e CACE analysis (self-report) adjusting for baseline score, EPDS stratum and centre.
f CACE analysis (practice prescribing data) adjusting for baseline score, EPDS stratum and centre.
g Comparatively favourable outcomes for the antidepressant group are denoted by differences in means greater than 0.

TABLE 29 *Comparisons between groups of the attitude to baby subscale on the MAMA at the 18-week follow-up (with higher scores reflecting a more positive attitude)*

	Antidepressants		Listening visits			
Row	***n***	**Mean (SD)**	***n***	**Mean (SD)**	**Adjusted difference[h] (95% CI)**	***p*-value**
Primary ITT analysis						
(a)	89	37.1 (5.2)	94	36.1 (4.8)	1.0 (−0.3 to 2.2)[a]	0.14
Secondary analyses						
(b)	89	37.1 (5.2)	94	36.1 (4.8)	0.9 (−0.3 to 2.2)[b]	0.15
(c)	56	36.9 (4.7)	66	36.0 (4.8)	1.1 (−0.5 to 2.6)[c]	0.17
(d)	86	37.2 (5.1)	92	36.1 (4.8)	1.1 (−0.2 to 2.4)[d]	0.10
		Antidepressants		***No antidepressants***		
(e)	86	36.5 (5.6)	97	36.7 (4.4)	3.1 (−1.3 to 7.4)[e]	0.17
(f)	81	35.9 (5.6)	90	37.0 (4.5)	2.9 (−1.5 to 7.2)[f]	0.19
		Listening visits		***No listening visits***		
(g)	141	36.2 (5.2)	42	37.8 (3.9)	−2.5 (−5.8 to 0.8)[g]	0.14

a ITT analysis adjusting for baseline score, EPDS stratum and centre.
b ITT analysis adjusting for baseline score, EPDS stratum, centre and elapsed time.
c ITT analysis adjusting for baseline score, EPDS stratum and centre but restricting to those who completed questionnaire between 3 and 6 weeks after randomisation.
d ITT analysis adjusting for baseline score, EPDS stratum, centre and baseline imbalances (diagnosis, number of children, breastfeeding, previous antidepressant treatment, employment status).
e CACE analysis (self-report) adjusting for baseline score, EPDS stratum and centre.
f CACE analysis (practice prescribing data) adjusting for baseline score, EPDS stratum and centre.
g CACE analysis (RHV records) adjusting for baseline score, EPDS stratum and centre.
h Comparatively favourable outcomes for the antidepressant group are denoted by differences in means greater than 0; likewise for each intervention in the CACE analyses.

TABLE 30 *Comparisons between groups of the GRIMS relationship scale at the 4-week follow-up (with a lower scores reflecting a better relationship)*

	Antidepressants		Listening visits			
Row	***n***	**Mean (SD)**	***n***	**Mean (SD)**	**Adjusted difference (95% CI)**	***p*-value**
Primary ITT analysis						
(a)	75	12.7 (6.1)	92	14.6 (6.1)	−0.6 (−1.9 to 0.7)[a]	0.39
Secondary analyses						
(b)	75	12.7 (6.1)	92	14.6 (6.1)	−0.5 (−1.8 to 0.8)[b]	0.44
(c)	55	13.1 (5.9)	69	15.3 (6.0)	−0.7 (−2.1 to 0.8)[c]	0.35
(d)	72	12.8 (6.2)	91	14.6 (6.1)	−0.5 (−1.8 to 0.9)[d]	0.52
	Antidepressants		***GSC***		***Adjusted difference***	
(e)	50	13.2 (5.6)	117	13.9 (6.3)	−1.0 (−3.4 to 1.4)[e]	0.39
(f)	43	13.1 (6.1)	110	14.1 (6.2)	−0.4 (−2.9 to 2.2)[f]	0.78

a ITT analysis adjusting for baseline score, EPDS stratum and centre.
b ITT analysis adjusting for baseline score, EPDS stratum, centre and elapsed time.
c ITT analysis adjusting for baseline score, EPDS stratum and centre but restricting to those who completed questionnaire between 3 and 6 weeks after randomisation.
d ITT analysis adjusting for baseline score, EPDS stratum, centre and baseline imbalances (diagnosis, number of children, breastfeeding, previous antidepressant treatment, employment status).
e CACE analysis (self-report) adjusting for baseline score, EPDS stratum and centre.
f CACE analysis (practice prescribing data) adjusting for baseline score, EPDS stratum and centre.
g Comparatively favourable outcomes for the antidepressant group are denoted by differences in means less than 0.

TABLE 31 *Comparisons between groups of the GRIMS relationship scale at the 18-week follow-up (with lower scores reflecting a better relationship)*

	Antidepressants		Listening visits			
	n	**Mean (SD)**	***n***	**Mean (SD)**	**Adjusted difference[h] (95% CI)**	***p*-value**
Primary ITT analysis						
(a)	64	11.5 (5.1)	89	13.8 (6.8)	−1.2 (−2.8 to 0.4)[a]	0.14
Secondary analyses						
(b)	64	11.5 (5.1)	89	13.8 (6.8)	−1.2 (−2.8 to 0.4)[b]	0.14
(c)	42	11.6 (4.5)	59	13.2 (6.6)	−1.6 (−3.6 to 0.4)[c]	0.13
(d)	63	11.5 (5.2)	88	13.9 (6.9)	−1.5 (−3.2 to 0.2)[d]	0.09
	Antidepressants		***No antidepressants***			
(e)	70	12.7 (5.9)	83	12.9 (6.6)	−3.6 (−8.8 to 1.5)[e]	0.16
(f)	65	12.7 (6.2)	77	13.0 (6.5)	−3.3 (−8.4 to 1.7)[f]	0.19
	Listening visits		***No listening visits***			
(g)	124	13.6 (6.3)	29	9.7 (5.0)	3.8 (−1.2 to 8.7)[g]	0.13

a ITT analysis adjusting for baseline score, EPDS stratum and centre.
b ITT analysis adjusting for baseline score, EPDS stratum, centre and elapsed time.
c ITT analysis adjusting for baseline score, EPDS stratum and centre but restricting to those who completed questionnaire between 3 and 6 weeks after randomisation.
d ITT analysis adjusting for baseline score, EPDS stratum, centre and baseline imbalances (diagnosis, number of children, breastfeeding, previous antidepressant treatment, employment status).
e CACE analysis (self-report) adjusting for baseline score, EPDS stratum and centre.
f CACE analysis (practice prescribing data) adjusting for baseline score, EPDS stratum and centre.
g CACE analysis (RHV records) adjusting for baseline score, EPDS stratum and centre.
h Comparatively favourable outcomes for the antidepressant group are denoted by differences in means less than 0; likewise for each intervention in the CACE analyses.

Nonetheless, overall the results for the secondary outcomes support an effect specific to mental-health benefits of antidepressants at the 4-week follow-up, with equivocal findings at the 18-week follow-up (albeit in the context of the above-stated caveats about power at 18 weeks).

Other secondary analyses

The results of the regression models for the primary (binary EPDS) outcome at 4 and 18 weeks including the imputed missing data are given in *Table 32*, and for comparison these are given alongside the corresponding primary (complete-case) ITT analyses already presented. Likewise comparative results for the secondary outcome of the continuous EPDS scores are given in *Table 33*. In no situation does the imputation of missing data have any material effect on the results.

Subgroup analyses

The primary subgroup analyses investigated the interaction between the CIS-R score at baseline and randomisation group in regression models for the 4-week and 18-week EPDS binary outcomes, with further analyses replacing the CIS-R with the continuous baseline EPDS and its binary version in the form of the stratification groups (baseline EPDS < 16 and ≥ 16), and then repeating all of these analyses for the continuous EPDS outcomes. All analyses were adjusted for centre.

The *p*-values for the subgroup analyses by CIS-R score, and by baseline EPDS score as a continuous and a binary variable were, respectively, 0.25, 0.19 and 0.040 at 4 weeks, and 0.97, 0.065 and 0.40 at 18 weeks. Repeating these subgroup analyses for the (secondary) continuous EPDS outcome led to similar results (although if anything the *p*-values were generally numerically higher). Overall, there was little evidence of differential effects according to baseline severity, especially in the primary subgroup analysis according to baseline CIS-R score. However, it is acknowledged that the power of these tests is low, and it is worth noting that in general the pattern of differential effects (especially those by baseline EPDS) suggests that the increased proportion improving in the antidepressant group is if anything exaggerated among those with

TABLE 32 *Sensitivity analyses comparing results of complete-case analyses with those including imputed (missing) data – primary outcome (binary EPDS) at 4- and 18-week follow-up*

	Complete case (*n* = 218 for 4 weeks, *n* = 206 for 18 weeks) [a]		Including missing data imputed using mice (*n* = 254) [a]	
Outcome	**OR (95% CI)[b]**	***p*-value**	**OR (95% CI)[b]**	***p*-value**
EPDS < 13 at 4 weeks	3.4 (1.8 to 6.5)	< 0.001	3.2 (1.7 to 6.1)	< 0.001
EPDS < 13 at 18 weeks	1.5 (0.8 to 2.6)	0.19	1.4 (0.8 to 2.4)	0.30

a Adjusted for baseline EPDS score and centre.
b Comparatively favourable outcomes for the antidepressant group compared with the listening visits group are denoted by odds ratios (ORs) greater than 1.

TABLE 33 *Sensitivity analyses comparing results of complete-case analyses with those including imputed (missing) data – secondary outcome of continuous EPDS score at 4-week and 18-week follow-up*

	Complete case (*n* = 218 for 4 weeks, *n* = 206 for 18 weeks) [a]		Including missing data imputed using mice (*n* = 254) [a]	
Outcome	**Difference in means (95% CI)[b]**	***p*-value**	**Difference in means (95% CI)[b]**	***p*-value**
EPDS score at 4 weeks	−2.1 (−3.3 to −0.9)	0.001	−2.1 (−3.4 to −0.8)	0.001
EPDS score at 18 weeks	−0.7 (−2.1 to 0.8)	0.37	−0.6 (−2.1 to 0.9)	0.42

a Adjusted for baseline EPDS score and centre.
b Comparatively favourable outcomes for the antidepressant group compared with the listening visits group are denoted by differences in means less than 0.

more severe depression at baseline. For example, among the 73 women scoring < 16 on the EPDS at baseline, 23/37 (62%) of those in the antidepressant group scored < 13 at the 4-week follow-up compared with 17/36 (47%) of those in the listening visits group, a difference of about 15 percentage points. The corresponding values among the 145 women scoring ≥ 16 at baseline were 25/69 (36%), 5/76 (7%) and a difference of 30 percentage points (interaction *p*-value 0.040).

Economic analysis

The economic evaluation was designed to be carried out at 44 weeks. Here we present a limited set of results of resource use at 4 weeks and 18 weeks. *Tables 34* and *35* show descriptive results for resource use by mothers and babies separately at 4 weeks and 18 weeks. Data on primary care resource use were available for about 70% of women and babies at 4 weeks and for 75% at 18 weeks; and on secondary-care resource use for about 50%, though the level of completeness varies across categories. It is likely that many of the missing observations, particularly the secondary-care items, reflect no resource use because respondents may have completed only the sections of the questionnaire that were applicable, leaving others blank rather than entering 'none'. Nevertheless we have treated these as missing in the analysis, which does not affect the frequencies (except the zeros) although the means may be an underestimate.

At the 4-week follow-up, two-thirds of women reported having had some contact with a GP or practice nurse since entering the study. More women in the antidepressant group consulted than in the listening visit group, although there is no evidence of a difference in the mean number of visits. At 18 weeks fewer women (54%) had consulted their GP or practice nurse in the preceding 4 weeks; 63% of those in the listening visits group had done so compared with 43% of those in the antidepressants group. The comparison of means suggests there is a difference between the two groups at this follow-up with women in the listening visits group seeing a GP or practice nurse more than those in the antidepressants group. Similarly, contact with HVs followed the same pattern. More women in the antidepressants group had had contact with a HV at the 4-week stage than had those in the listening visits group (30% versus 20%) but at 18 weeks the reverse applied with 16% of women in the listening visits group and 6% of women in the antidepressants group having had HV contact during the previous 4 weeks. Again, the comparison of mean number of contacts suggests a difference.

Women reported having used a number of other different primary, community and social care services including: NHS Direct, counsellor, mental-health worker, social worker, family-care worker, physiotherapist, acupuncturist, walk-in centre, psychologist, occupational health and victim support. Use of these services was similar at 4 weeks and 18 weeks, and between the two groups of women.

Few women used secondary-care services during the follow up period and there was no difference in amount between the two groups. Outpatient appointments were the most likely means of accessing secondary care and a wide range of reasons for these was reported. A few were clearly related to mental health e.g. 'repeat prescription for Prozac', 'psychology department – was attending prior to birth on PND watch', 'psychologist clinic at Southmead Hospital' though most were more general or gynaecological, e.g. 'physiotherapist torn abdominals', 'blood test', 'scan – fibroid'.

Table 35 gives the results for babies. At 4 weeks most babies (73%) had been seen by a GP or practice nurse and 52% by a HV. The contact with HVs was maintained at 18 weeks, although by this time only half of babies had been seen by a GP or practice nurse in the previous 4 weeks. There was no evidence of a difference in use of these services between the two groups. Few other primary, community and social-care services were used at either time point. Those mentioned include: dietitian, eczema nurse, and walk-in centre. Babies in the listening visits group were consistently higher users of Accident and Emergency and outpatient services than were those in the antidepressants group, though the numbers are too small to detect a difference. Nine mothers gave their reason for visiting Accident and Emergency; four were for an unexplained rash with or without other symptoms such as vomiting and fever. Reasons for outpatients' appointments were varied; several were general developmental, e.g. 'hearing' or 'weight', four were for 'gastric reflux' but many were unspecified, e.g. 'check-up'.

TABLE 34 *Comparisons between groups of the frequency of resource use by mothers at the 4-week and 18-week follow-up: number of contacts during the previous 4 weeks[a]; values are frequency (%)*

Number of contacts	4 weeks		18 weeks	
	Antidepressants	**Listening visits**	**Antidepressants**	**Listening visits**
Comparisons between groups of the frequency of resource use by mothers at the 4-week and 18-week follow-up (a) GP or Practice Nurse, including surgery and telephone consultations, home visits and out-of-hours contacts				
0	19 (22)	45 (48)	51 (57)	38 (37)
1	25 (29)	23 (25)	19 (21)	36 (35)
2	35 (40)	11 (12)	10 (11)	12 (12)
3+	8 (9)	14 (15)	9 (10)	17 (17)
Total	87 (100)	93 (100)	89	100
Mean (SD)	1.5 (1.1)	1.12 (1.5)	0.8 (1.2)	1.2 (1.4)
			0.7 (1.0)[a]	1.0 (1.2)[a]
Mean difference (95% CI)	0.37 (−0.01 to 0.76)		−0.44 (−0.81 to −0.06)	
			−0.36 (−0.67 to −0.04)[a]	
Comparisons between groups of the frequency of resource use by mothers at the 4-week and 18-week follow-up (b) HV, including surgery consultations and home visits, and out-of-hours contacts				
0	60 (70)	74 (80)	84 (94)	86 (84)
1	14 (16)	10 (11)	3 (3)	7 (7)
2+	12 (14)	9 (10)	2 (2)	10 (10)
Total	86 (100)	93 (100)	89 (100)	103 (100)
Mean (SD)	0.6 (1.1)	0.4 (1.0)	0.1 (0.4)	0.4 (1.0)
			0.04 (0.2)[a]	0.23(0.6)[a]
Mean difference (95% CI)	0.16 (−0.15 to 0.48)		−0.28 (−0.50 to −0.06)	
			−0.19 (−0.32 to −0.06)[a]	
Comparisons between groups of the frequency of resource use by mothers at the 4-week and 18-week follow-up (c) Other primary-, community- and social-care professionals				
0	51(91)	52 (80)	80 (90)	88 (85)
1	5 (9)	12 (20)	4 (4)	9 (9)
2+	0 (0)	0 (0)	5 (6)	6 (6)
Total	56 (100)	65 (100)	89 (100)	103 (100)
Mean (SD)	0.1 (0.3)	0.4 (0.8)	0.2 (1.0)	0.2(0.7)
			0.2 (1.0)[a]	0.2 (0.6)[a]
Mean difference (95% CI)	−0.28 (−0.51 to 0.12)		−0.01 (−0.25 to 0.23)	
			0.00 (−0.23 to 0.23)[a]	
Comparisons between groups of the frequency of resource use by mothers at the 4-week and 18-week follow-up (d) Visits to Accident and Emergency Department				
0	60 (98)	60 (94)	52 (95)	64 (94)
1+	1 (2)	4 (6)	3 (5)	4 (6)
Total	61 (100)	64 (100)	55 (100)	68 (100)
Mean (SD)	0.02 (0.13)	0.17 (1.02)	0.1 (0.3)	0.1 (0.4)
Mean difference (95% CI)	−0.16 (−0.42 to 0.10)		−0.02 (−0.15 to 0.12)	

continued

TABLE 34 *Comparisons between groups of the frequency of resource use by mothers at the 4-week and 18-week follow-up: number of contacts during the previous 4 weeks[a]; values are frequency (%) (continued)*

Number of contacts	4 weeks		18 weeks	
	Antidepressants	**Listening visits**	**Antidepressants**	**Listening visits**
Comparisons between groups of the frequency of resource use by mothers at the 4-week and 18-week follow-up (e) Outpatient appointments				
0	53 (83)	57 (92)	51 (91)	58 (81)
1+	11 (17)	5 (8)	5 (9)	14 (19)
Total	64 (100)	62 (100)	56 (100)	72 (100)
Mean (SD)	0.2 (0.5)	0.1 (0.5)	0.1 (0.5)	0.3 (0.7)
Mean difference (95% CI)	0.09 (−0.09 to 0.27)		−0.15 (−0.36 to 0.06)	
Comparisons between groups of the frequency of resource use by mothers at the 4-week and 18-week follow-up (f) Inpatient stays				
0	53(0)	56 (97)	49 (96)	61 (98)
1+	0 (0)	2 (3)	2 (4)	1 (2)
Total	53 (100)	58 (100)	51 (100)	62 (100)
Mean (SD)	0 (0)	0.1 (0.4)	0.04 (0.2)	0.02 (0.1)
Mean difference (95% CI)	−0.07 (−0.18 to 0.04)		0.02 (−0.04 to 0.08)	

a At 18 weeks half of the respondents were asked about resource use over the previous 8 weeks rather than 4 weeks. The adjusted mean number of contacts reflects this and has been estimated by scaling down the 8-week responses by a factor estimated from the overall means for each category. This adjustment has not been applied to secondary-care resource use, where missing data and small number of observations make this adjustment less meaningful.

TABLE 35 *Comparisons between groups of the frequency of resource use by babies at the 4-week and 18-week follow-up: number of contacts during the previous 4 weeks[a]; values are frequency (%)*

Number of contacts	4 weeks		18 weeks	
	Antidepressants	**Listening visits**	**Antidepressants**	**Listening visits**
Comparisons between groups of the frequency of resource use by babies at the 4-week and 18-week follow-up (a) GP or Practice Nurse, including surgery and telephone consultations, home visits and out-of-hours contacts				
0	25 (29)	24 (26)	48 (54)	46 (45)
1	30 (34)	31 (34)	26 (29)	27 (26)
2	20 (23)	16 (17)	5 (6)	13 (13)
3+	12 (14)	21 (23)	10 (11)	17 (17)
Total	87 (100)	92 (100)	89 (100)	103 (100)
Mean (SD)	1.4 (1.3)	1.6 (1.7)	0.8 (1.5)	1.2 (1.7)
			0.8 (1.4)[a]	1.1 (1.6)[a]
Mean difference (95% CI)	−0.25 (−0.70 to 0.20)		−0.38 (−0.83 to 0.07)	
			−0.35 (−0.78 to 0.08)[a]	
Comparisons between groups of the frequency of resource use by babies at the 4-week and 18-week follow-up (b) HV, including surgery consultations and home visits, and out-of-hours contacts				
0	44 (51)	42 (45)	51 (57)	52 (50)
1	25 (29)	27 (29)	23 (26)	32 (31)
2+	9 (10)	13 (14)	15 (17)	19 (18)
Total	86 (100)	93 (100)	89 (100)	103 (100)

TABLE 35 *Comparisons between groups of the frequency of resource use by babies at the 4-week and 18-week follow-up: number of contacts during the previous 4 weeks[a]; values are frequency (%)*

Number of contacts	4 weeks		18 weeks	
	Antidepressants	**Listening visits**	**Antidepressants**	**Listening visits**
Mean (SD)	0.9 (1.3)	1.1 (1.6)	0.7 (1.0)	0.9 (1.3)
			0.6 (0.9)[a]	0.8 (1.2)[a]
Mean difference (95% CI)	−0.26 (−0.69 to 0.18)		−0.16 (−0.49 to 0.18)	
			−0.18 (−0.48 to 0.13)[a]	
Comparisons between groups of the frequency of resource use by babies at the 4-week and 18-week follow-up (c) Other primary-, community- and social-care professionals				
0	51 (89)	53 (83)	80 (90)	87 (84)
1	4 (7)	10 (16)	7 (8)	11 (11)
2+	2 (4)	1 (2)	2 (2)	5 (5)
Total	57 (100)	64 (100)	89 (100)	103 (100)
Mean (SD)	0.2 (0.6)	0.2 (0.4)	0.1 (0.4)	0.2 (0.6)
			0.6 (0.9)[a]	0.2 (0.5)[a]
Mean difference (95% CI)	−0.01 (−0.20 to 0.18)		−0.10 (−0.25 to 0.05)	
			−0.07 (−0.19 to 0.04)[a]	
Comparisons between groups of the frequency of resource use by babies at the 4-week and 18-week follow-up (d) Visits to Accident and Emergency Department				
0	59 (92)	52 (80)	49 (89)	60 (86)
1+	5 (8)	13 (20)	6 (11)	10 (14)
Total	64 (100)	65 (100)	55 (100)	7 (10)
Mean (SD)	0.1 (0.3)	0.3 (1.0)	0.2 (0.5)	0.2 (0.6)
Mean difference (95% CI)	−0.23 (−0.50 to 0.04)		−0.04 (−0.23 to 0.16)	
Comparisons between groups of the frequency of resource use by babies at the 4-week and 18-week follow-up (e) Outpatient appointments				
0	52 (81)	50 (78)	52 (91)	58 (79)
1+	12 (19)	14 (22)	5 (9)	15 (21)
Total	64 (100)	64 (100)	57 (100)	73 (100)
Mean (SD)	0.3 (0.6)	0.3 (0.7)	0.1 (0.4)	0.4 (1.0)
Mean difference (95% CI)	−0.06 (−0.30 to 0.17)		−0.26 (−0.54 to 0.01)	
Comparisons between groups of the frequency of resource use by babies at the 4-week and 18-week follow-up (f) Inpatient stays				
0	51 (98)	55 (100)	50 (98)	62 (97)
1+	1 (2)	0 (0)	1 (2)	2 (3)
Total	52 (100)	55 (100)	51 (100)	64 (100)
Mean (SD)	0.04 (0.28)	0 (0)	0.02 (0.14)	0.06 (0.35)
Mean difference (95% CI)	0.04 (−0.04 to 0.11)		−0.04 (−0.15 to 0.06)	

a At 18 weeks half of the respondents were asked about resource use over the previous 8 weeks rather than 4 weeks. The adjusted mean number of contacts reflects this and has been estimated by scaling down the 8-week responses by a factor estimated from the overall means for each category. This adjustment has not been applied to secondary-care resource use, where missing data and small number of observations make this adjustment less meaningful.

Quality-adjusted life-years

We estimated QALYs using data from the EQ-5D administered at baseline, 4 weeks and 18 weeks. We had complete data for 192 (76%) women. Those in the antidepressants group achieved 0.263 QALYs over the 18 weeks, an annual equivalent of 0.76, and those in the listening visits group achieved 0.253 (annual equivalent 0.73). These results provide no evidence of a difference between the two groups.

Chapter 4

Results: qualitative study with women

The women interviewed

Twenty-eight women were interviewed in total. Twenty-seven of them were individuals who had completed the trial, i.e. had their final outcome measures taken. The characteristics of these women are detailed in *Table 36*.

The remaining individual was someone who had declined to take part in the trial. The data from this interview have not been included in the findings presented below, as the focus of this interview was slightly different from the others. It was apparent this individual had declined to take part in the trial for a number of reasons. She reported the main reason had been that she was concerned about being allocated to antidepressants, having taken them in the past and felt that they had made her 'hyperactive' and less rational. Other reasons included not wanting listening visits because she did not want to 'wallow' in her PND, something she associated with counselling approaches; wanting to deny that she had PND because of the stigma that surrounds this condition; feeling that she was not 'really depressed' because she was able to function; and finally, feeling that she could cope with her depression without professional help. This last point might relate to the fact that she had actively sought and received emotional and practical support from family and friends.

TABLE 36 *Characteristics of women interviewed having completed the trial (n = 27)*

Age range	19–45 years old
Study site	
Bristol	11
Manchester	9
London	7
Ethnicity	
White	21
Pakistani	1
Indian	1
Black Caribbean/African/Other	4
Highest qualification achieved	
Degree	11
A-level	3
GCSE	10
NVQ	2
None	1
Job classification	
Higher managerial	7
Lower managerial	4
Intermediate	2
Self-employed	1
Lower supervisory	0
Semi-routine	5
Routine	1
Not currently in paid employment	7

This chapter details which treatment women were randomised to and then received during the trial. It then reports their treatment expectations and preference, before describing their treatment experiences. The text is presented under headings and subheadings that relate to these areas and reflect analytic codes used during the analysis. Quotations reproduced in this chapter have been labelled with the participant's interview number and with details of the treatment she received during the trial.

Treatment allocation and treatment received

Seventeen of the women interviewed having completed the trial had been randomised to listening visits and 10 to antidepressants (*Table 37*). All but one individual allocated to the visits had gone on to receive this treatment. The exception was someone who had received no treatment during the trial because by the time the visits had started she felt she was better and so had declined treatment. Over half (10/16) of the women who had received listening visits having been randomised to this intervention, had also taken antidepressants either during or after the visits.

Six out of the ten women randomised to antidepressants had gone on to receive this

TABLE 37 *Women's treatment allocation and treatment received*

	Treatment allocation		
Treatment received	**Listening visits**	**Antidepressants**	**Total**
Antidepressants	0	3	3
Listening visits	6	3	9
Both treatments	10	3	13
Neither treatment	1	1	2
Total	17	10	27

treatment, and three of these women had also had listening visits. Three of the remaining four women allocated to antidepressants had refused medication and started listening visits by 4 weeks post randomisation. The remaining individual randomised to antidepressants had received no treatment during the trial, as she felt better by the time she had made an appointment to see her GP.

To understand why women had refused treatment or had gone on to have a treatment they had not been allocated to, attention needed to be given to their treatment preference at the time of randomisation and to their treatment experiences.

Treatment expectations and preference at time of randomisation

Only four women stated that they had wanted to be randomised to antidepressants. The majority of the women (16) had hoped for listening visits. The remaining seven women said they did not mind which treatment they received. However, as four of these seven women detailed reasons why they did not want to take antidepressants, for the purpose of the analysis, they were viewed as having a preference for listening visits.

Three of the four women who had a preference for antidepressants were individuals who had been randomised to this treatment and had only received antidepressants during the trial (*Table 38*). The remaining woman had been randomised to listening visits. She accepted the visits, but only because she knew this would not prevent her from also having medication:

> 'I just thought I'll do [the visits], as long as I get the medication.' (Participant 15, listening visits then antidepressants)

The women who had stated a preference for antidepressants described how they felt they had needed an emotional 'lift' and thought antidepressants would provide this. They described not being worried about taking medication. Three of them had taken antidepressants before and all of them said they had a good relationship with their GP and felt able to go and ask for antidepressants. These women also described how they had felt no need to talk to a counsellor, as they had friends or relatives they could talk to and/or because they had received counselling in the past, which they had either not found helpful or felt was not necessary on this occasion:

> 'I wanted to try the antidepressants primarily because I'd actually had counselling when I had depression as a teenager…used to find it very difficult to open up and talk…and also I had a couple of very close friends that I'd met when I was pregnant with [child's name] who I'm still in touch with.…So I sort of had them as a listening ear for me so I felt I didn't need the counselling necessarily because I sort of had friends I could talk to.' (Participant 12, antidepressants only)

Most of the women (14/20) who had wanted listening visits were randomised to this treatment. Four of the six women who were not allocated to their treatment of choice refused medication and waited for the visits (although one of these women went on to take antidepressants once the visits had ended), one individual received no treatment during the trial and another individual accepted the allocation and went to her GP. It was apparent that knowing she could go on to have the visits, and her GP's reaction to her allocation, had encouraged her to consider taking medication:

> Interviewer: 'You were allocated antidepressants and at that point how did you feel?'

TABLE 38 *Women's treatment preference and allocation, and treatment received during the trial*

Preference	*n*	Allocation	*n*	Received	*n*
Antidepressants	4	Antidepressants	3	Antidepressants only	3
		Listening visits	1	Both treatments	1
Listening visits	20	Antidepressants	6	Listening visits only	3
				Both treatments	2
				No treatment received	1
		Listening visits	14	Listening visits only	6
				Both treatments	8
No preference	3	Antidepressants	1	Both treatments	1
		Listening visits	2	Both treatments	1
				No treatment received	1

> Participant: 'I was a bit surprised and then I thought, because she said you could change after four weeks and I thought, well no harm, is it. When I went to the doctors I thought that was going to be quite hard and then the doctor who's really, really nice just said "I'm surprised I haven't seen you already." And "I'm really pleased you've been put in to that group." And that really shocked me…'
>
> Interviewer: 'Mm, and did you ask her why?'
>
> Participant: 'Yes.'
>
> Interviewer: 'And she said?'
>
> Participant: 'And she said that she thought I would need something to help lift my mood. And that this would.' (Participant 26, antidepressants then listening visits)

In contrast to the women who had wanted to be allocated to antidepressants, the women who had wanted listening visits described how they had needed to talk issues through and to understand with the help of another, why they were feeling depressed. They may have felt this need because they had little social support. Individuals explained that they did not have friends and family they could confide in, and a few of the women said that they did not feel comfortable talking to their GP or HV:

> 'I didn't want to take antidepressants. The main reason was I didn't feel I could talk to the GP about it. I didn't really want to go and talk to the GP.' (Participant 14, listening visits only)

Other reasons given by women for not wanting to visit their GP were a fear of being prescribed antidepressants without being listened to; being prescribed antidepressants, not because this was what they needed but because this was what was available; and being judged as a 'poor' mother. Ability to access help, and to see the same practitioner, had also influenced women's willingness to consider taking antidepressants:

> 'The problem is as well, is the GP, it's basically two weeks before you get an appointment, so it's not really helping if you can't see your GP straight away.' (Participant 14, listening visits only)
>
> 'I don't want to take tablets. I want to cope with it myself and then I don't have to go to the doctors every few minutes…I can't be doing with that…whenever I go, I don't ever see the same doctor, so every time I go I have to explain it all and it's just stupid.' (Participant 2, listening visits only)

Women who had hoped for the listening visits also described how they thought the visits would be the more effective treatment and that antidepressants simply masked the symptoms of PND and so delayed recovery:

> 'I think it [antidepressants] just masks it…if you can talk it out and work it out that way, I think that's probably better.' (Participant 8, listening visits only)
>
> 'The tablets just block it out…it's better but it's still there because you haven't talked about it. All you've done is took a tablet to block it

> out, which is a waste of time.' (Participant 23, listening visits then antidepressants)

As the accounts of participants indicating a preference for listening visits included large numbers of negative views about antidepressants, it appeared that, in most cases, it was more a case of the participant not wanting to take medication than particularly wanting listening visits.

Women described how they felt that there was a stigma attached to taking antidepressants. They thought being on medication would imply to themselves and others that they were mentally unstable and had been unable to cope without intervention. The appropriateness of using pills to address a mental-health problem was also questioned:

> '[there is] a sort of stigma attached to taking pills to get you through something like this.' (Participant 16, listening visits only)

Concerns were also expressed in relation to becoming physically dependent on antidepressants, experiencing side effects, taking medication when breastfeeding, and antidepressants changing the individual's personality or affecting her ability to parent by making her drowsy. Women also detailed how they were concerned about taking medication when breastfeeding, and it was apparent that even when reassured by health professionals that antidepressants would not have a negative impact on breastfeeding, concerns had remained:

> Participant: 'I wanted counselling and I knew that if it had been the medication route I probably would have said no.'
>
> Interviewer: 'But why, what was it about the medication?'
>
> Participant: 'The main reason was that I was breast feeding…although, you know, I vaguely remember people reassuring me, I think perhaps I'd talked to my doctor about it and I'd talked to [HV's name] and they'd said, "no, it won't affect your breast feeding", I just didn't want to be on tablets while I was breast feeding.' (Participant 16, listening visits only)

In addition, seven of the participants who had a preference for listening visits had taken antidepressants before. Five of them had not found them helpful and two of them had experienced side effects: this was another reason why they had wanted listening visits.

To summarise, most of the women interviewed reported that they had had clear ideas about which treatment they had wanted to be randomised to, and it was apparent that in some cases their treatment preference had determined which treatment they had received, e.g. women allocated to antidepressants had refused this treatment and waited for listening visits, and one individual had started listening visits but gone on to take medication, which was her treatment of choice. Most (20) of the women had wanted listening visits and in many cases this preference appeared to have been linked more to a concern about taking medication than to a particular expectation of the visits. Yet, half of these women had gone on to take medication during the trial (*Table 38*). Some of these women commented that their views about antidepressants had changed during the study and mentioned several factors that had led to this, including their experiences of the listening visits.

The women's experiences of the listening visits

Twenty of the 22 women who had received listening visits during the trial had only had this treatment or had started listening visits then gone on to take antidepressants (*Table 39*). Thus, most individuals who had experienced listening visits had needed to wait four weeks before starting treatment.

The 4-week wait

Some women described how they had found the 4-week wait difficult but bearable because they knew they would be receiving help and the treatment they wanted. Most of the women, however, detailed how they had been desperate to start. One individual had even worried about harming her child:

> 'I felt at first when she said you had a wait a month or whatever, anything could happen in that month, you know, what if I lost my temper, lost my rag with this baby?' (Participant 20, listening visits then antidepressants)

Another individual (participant 10, listening visits only) recalled wondering why she was not receiving treatment when she had just been told that she needed it.

Although women detailed how they had been desperate to start the visits, only two of them mentioned receiving any support during this period: one individual had been visited by her own

TABLE 39 *Women's treatment allocation and order of treatments received*

	Treatment allocation		
Treatment received	**Listening visits**	**Antidepressants**	**Total**
Antidepressants	0	3	3
Listening visits	6	3	9
Listening visits then antidepressants	10	1	11
Antidepressants then listening visits	0	2	2
Neither treatment	1	1	2
Total	17	10	27

PHV and another participant by her aunt. The only evidence of women proactively seeking help during the 4-week wait came from one woman who had called the RESPOND research associate, asking if the visits could start early.

The listening visits

Only one individual, who had listening visits, had received just four visits. All the other women who had received this treatment had the maximum number of visits available in the trial, i.e. eight. All the women who had received listening visits reported that they had found the visits helpful. Women appeared to have benefited because the visits gave them an opportunity to talk, because they had found the process of talking therapeutic, and because they had found the support and advice given by RHVs helpful.

An opportunity to talk

A few women said they had been nervous about the visits or had taken a while to open up because they were unsure of what to expect or did not find it easy to discuss their feelings. It was also apparent that individuals could be concerned from the start that only eight visits would be available:

> 'I was always very aware of the time, not necessarily the time of day but like how many sessions there were and when they were going to end…before I even started, I felt at most it's going to be eight weeks, and what if it's not, everything's not hunky-dory by then, what happens next? Where do I go from there?… in the past, I've had counselling for like six months, so eight weeks is a drop in the ocean really isn't it, just on its own. That's probably why I felt so anxious about it.' (Participant 20, listening visits then antidepressants)

Most of the women, however, described how they had felt comfortable and able to talk to their RHV. There appeared to have been a number of factors that had led to this. Some of the women had wanted listening visits because they felt they had needed to talk and mentioned that, having waited 4 weeks, they had been keen to discuss their situations and feelings. As a few of the women described how they had told very few people about their PND it was also apparent that, for some women, the visits were one of the few contexts in which they could discuss their situation. In addition, women described the visits as 'their time' and as having a specific focus on them and their PND and this, in turn, appeared to have encouraged them to focus on themselves:

> 'It was very clear that my health visitor was there for me and for [baby] equally, whereas [RHV] was really there for me…specifically for the postnatal depression bit. And, I mean, I suppose I could have asked her advice on, you know, bottle feeding him or something, but I never felt that…that wasn't the purpose of those visits, it was quite clear that they had one specific purpose.' (Participant 10, listening visits only)

The RHV's personality and approach was another factor that had encouraged women to talk. All of the women commented that they had felt comfortable with the RHV they saw, and the RHVs were described as kind, non-judgemental, understanding and knowledgeable about PND. They were also described as listening carefully, giving praise and encouragement, and not criticising or judging what the individual had said or done. In addition, a few of the women mentioned that the RHV had allowed them to set the boundaries of the discussion, and explained

that this had made them feel safe and in control of what was discussed. The fact that the RHV was a 'stranger' had also encouraged women to discuss their thoughts:

> 'I always find that much better [to talk to a stranger], really open up and to really get all your weird things out, like to my friends, I couldn't have sat there and gone 'I hate that child.…' I couldn't have said that because they would have been horrified. My parents would have looked horrified, you know, but, when it's a complete stranger that doesn't know you and that doesn't have a personal attachment to you, that doesn't, you don't have to impress or not offend, you know what I mean, that you don't have to really care about their feelings and I don't mean that in a nasty way…because they're not going to go home at night and start worrying about you, because it's their job…, you know, it's hopefully, when you do a job like that, you develop some sort of skill at leaving your job at the door…that made me feel better in terms of sort of knowing she wasn't going to sit worrying about it and whereas with my family I couldn't talk openly and frankly about it because they would…I'd just know they would be worrying.' (Participant 20, listening visits then antidepressants)

The quotation reproduced above shows how this individual had viewed the RHV as someone who was there to listen to her; that was her job and she had the skills and experience to deal with being in that position. This was probably another factor that had encouraged women to talk during the visits.

A few of the women also mentioned that they felt comfortable confiding in the RHV because she was not attached to their GP surgery. In their view, this meant their GP and PHV would not be informed about what had been discussed, none of the information they gave would go on to their medical notes, and/or that they were less likely to see the RHV when going to their general practice. It was also felt that information was less likely to get back to people they knew:

> Interviewer: 'You don't think you'd have talked to your own health visitor about it in the same way or about those things.'
>
> Participant: 'No.'
>
> Interviewer: 'Why do you think that is?'
>
> Participant: 'I mean my health visitor, she's lovely and I really, really like her but so many people have her as a health visitor…I know she wouldn't say anything but you know it could just come out and I didn't really want that I suppose, it's too close to home.' (Participant 7, antidepressants then listening visits)

Many of the women compared their relationship with their RHV to the relationship they had with their own PHV. Although a few of the women mentioned that the listening visits would have worked with their PHV, most of the women felt this was not the case. A few of the women said they did not have a good relationship with their PHV having found her critical of the way the individual was parenting, having a rather brisk, factual approach, or simply because they had not seen her very often. Women also commented that their PHV was always rushing and so did not have time to listen, or rarely visited the individual at home and therefore was only available at the clinic where there were other people around. The PHV was also viewed as someone for the child, rather than someone for the mother, which was considered the case with the RHV:

> 'I think it's more you just go there and discuss baby, you don't have time for your…to talk about yourself or…you just, even if you do want to say anything to the health visitor, you just feel a bit rushed and they haven't got much time for you. (sure) So, I mean, like I said, when like [RHV] came to see me, it was nice because it was like my time and our time and we could talk and stuff.' (Participant 13, antidepressants and listening visits)

In addition, women talked about being more careful about what they said to their PHV, explaining that they felt she would be more likely to judge their ability to mother:

> 'With [RHV] I feel like I could have just said what I wanted, how I wanted, if you see what I mean and I could cry with [RHV] but with my health visitor, I try not to let too much out because then she won't think I'm a bad mum, if you see what I mean, so I tend not to let too much out with the health visitor.' (Participant 2, listening visits only)

However, there were also women who commented that they had also been careful about what they said to their RHV, acknowledging that she also had a responsibility to ensure the child's well-being.

The benefits of talking

Women described that, having talked, they felt they had 'offloaded', 'unlocked' issues and unburdened or shared their concerns, and felt better having done so. A few of the women also mentioned that talking had given them a different perspective on issues they had been worrying about. It was also apparent that, having talked, a woman could feel more confident about telling people that she had PND:

> Interviewer: 'Do you think the visits helped you to get to that point?'
>
> Participant: 'Definitely did help because it sort of like made me realise you know talking about it isn't going to do anything bad.'
>
> Interviewer: 'Had you worried about it beforehand, had that been one of your concerns?'
>
> Participant: 'I just thought everyone is going to judge me, I'm going to be a bad person you know, I shouldn't feel like this I should be okay…[the visits] made it realise you know you can talk about it, it isn't going to go wrong, nothing bad is going to happen about you talking about it. If anything better is going to come from it and I did end up speaking to my mum and my sister about it afterwards.' (Participant 7, antidepressants then listening visits)

The areas discussed and the support received

Women described that during the visits they had discussed how they were feeling, how they felt towards their children, their relationships with their partners and relatives, financial concerns, expectations of self, and their experiences of motherhood, both positive and negative. Some women, and particularly those who did not see their PHV very often, also asked what they termed 'health visitor' questions, e.g. questions about their child's sleeping and feeding.

Women's accounts of how the RHV had responded indicated that the RHVs had listened and reflected back to the individual what she had said, allowing them to clarify and reconsider their thoughts; had asked questions to encourage the individual to explain exactly what was happening; had explained that what the individual was experiencing was a symptom of PND and feelings that other women had experienced having had a child; provided reassurance by saying that they thought the individual would feel better with time and that they had seen women recover from PND; and had made suggestions, e.g. put less pressure on self, and discussed strategies that they thought the individual might find helpful, e.g. ways to approach sensitive subjects with their partner. Women detailed how such responses had given them a different perspective on issues that had concerned them, had given them hope that they would recover, had made them aware of some of the reasons why they were feeling depressed, and had given them some ideas about how they could manage the situation and help themselves get better. In addition, one individual described how she had gained a better understanding of what was happening and so had felt less scared:

> 'I had quite a lot of anxiety about things that to me were really, seemed mad. Which was where the listening visits really helped.…when I was talking to [RHV] about them…and I'd like think they were barking and that was a sign of madness and she would be quite reassuring… she gave me understanding. I think I was very scared because I didn't understand why I was doing things and thinking things and feeling things and she put things in to words… she basically told me that is part of it [PND] whereas to me that wasn't being depressed that was going mad…she asked the right questions so that I then was actually able to think, I was able to describe it…I started being more aware of what was happening to me and then it made it a bit less scary.' (Participant 26, antidepressants then listening visits)

Based on the women's accounts it was also apparent that the RHVs had given practical help and support. One individual described how the RHV had referred her to a parenting class and to anger management, and another woman discussed how her RHV had helped her to write a letter to work, explaining why she was not ready to go back. The RHVs were also reported to have discussed antidepressants with women who were not getting better. This had clearly influenced women's views of this treatment and was a reason why some women had gone on to take medication having had the listening visits:

> Interviewer: 'Do you think if you hadn't had the listening visits you wouldn't have taken the antidepressants?'

> Participant: 'No, probably not because it was, you know, talking to her [RHV], you know, she was saying, "you know, about how antidepressants…you know, there's nothing wrong with taking them, they do sometimes for some people offer some relief and do make them see things in a better light." So, you know, talking to her made me realise that she wasn't knocking antidepressants or saying they were bad or you don't want to do that…made me realise that perhaps that was an alternative if I felt that, you know, counselling wasn't enough. And as I said, it wasn't the fact that maybe I didn't want to change, I just couldn't because I didn't know how to.' (Participant 1, listening visits then antidepressants)

Women nervous about going to see their GPs mentioned that the RHV had written to their GPs, so that they would know why the women had made an appointment. They felt that this had made it easier for them to go and see their GP.

It was apparent that women had benefited from talking, and from having emotional and practical support from a health professional. Yet, a few of the women talked about how they would only feel better for a few days following a visit and several women talked about the listening visits not being enough to improve their mood. This became another reason why women had gone on to take antidepressants, either during or following the visits, despite the fact they had held negative views towards medication at the time of randomisation:

> Participant: 'So I started the antidepressants…'
>
> Interviewer: 'And how did you feel about that then, because you'd been quite opposed to that earlier?'
>
> Participant: 'I thought, well I've tried counselling…but me as a person wasn't changing…My relationship was still really poor and it just came to a head one night when we were shouting at each other, I just realised how bad I was…I did need help. So I went to the GP and I started on a very low dose.' (Participant 1, listening visits then antidepressants)

A couple of women explained that they had felt the visits could not solve the causes of their depression, so had either decided to make changes that they thought would help, i.e. change their job, or had pretended to the RHV that they were feeling better.

A few of the women also mentioned that an hour did not feel long enough for each visit and nearly all of the women described how they felt eight visits had not been enough to address their PND.

Ending the visits

Fourteen out of the 22 women who had received listening visits stated that they felt eight visits had not been enough. Having completed the visits, 10 of these women went on to see their GP. Six of them were then prescribed antidepressants, two of them received counselling and the remaining two women were referred to a psychiatrist. The other four women had gone on to see a private counsellor, had stayed on medication having started antidepressants before the visits, or had not sought further help because they were nervous about going to their GP or talking to their PHV.

Most of the women who had visited their GP reported that their concerns about antidepressants had been addressed, indicating that the GP consultation could be a factor in changing women's views of antidepressants. GPs had discussed women's fears and explained how antidepressants might help. In addition, they had prescribed antidepressants in a way that had been reassuring:

> 'She [GP] said, "Well just try it and see how you get on…I'll give you something very light… it's not that addictive…this is a low dosage one." And I think that probably helped as well…You're thinking, okay, I can cope with that.' (Participant 19, listening visits then antidepressants)

However, a few of the women described how, despite talking to their GP, their concerns about taking medication had remained and it was apparent that they had gone on to take medication because of a lack of treatment choice. Antidepressants had been used to tide women over while they waited for counselling arranged through their general practice, or were turned to when the individual was unhappy with the counsellor available through her practice. It was also apparent that the responsibilities of parenthood, and the symptoms of depression, could mean that visiting a counsellor was not feasible:

> 'I did say was there any counselling that was available that I could access, and they said "not really…[and] they don't come for you at home…" It was very difficult because I have two children to look after, in my present state

> of mind as well, like just driving a car and catching a bus is something that would be a nightmare for me. And they said the other option is antidepressants, and they started me on antidepressants.' (Participant 22, listening visits then antidepressants)

When comparing the accounts of women who commented that they felt eight visits had not been sufficient with those of women who reported that they had received enough visits, it appeared that women who had wanted further support were individuals whose PND did not relate primarily to their experiences of motherhood or to their circumstances during the postnatal period, which appeared mainly to be the case for the other women. Women who had wanted more listening visits described how they had felt depressed before their pregnancy or detailed how they had struggled with depression for years, or mentioned that the birth of their child had raised memories of past negative events, e.g. terminating a pregnancy, death of a father. Some of these women also described how they had overdosed in the past, had suicidal thoughts and/or self harmed. In contrast, the women who felt that four or eight visits had been sufficient, related their PND to a hormonal imbalance, needing to adjust to parenthood, having a particularly difficult time following the birth of their child, or to problems that had now been resolved, e.g. relationship difficulties, unrealistic expectations of self. It was also apparent that most of these women, while receiving the visits, had put other sources of support in place, e.g. they had started Sure Start, made new friends, attended parenting classes, started taking antidepressants which they felt were now working.

During the interviews held with women who had felt a need for further treatment, women talked about how they had felt angry that the visits had ended, and individuals described how they felt that they had been 'left hanging' and 'completely exposed'. In addition, it was pointed out that that if no further support had been available through the GP, the individual would have felt that the listening visits had been pointless:

> 'Just me thinking about it [the idea of no treatment after the visits] now makes me feel quite panicky. I am feeling like, oh my god, oh that's awful…what would have been the point of ripping off the plaster and starting to abrade the wound, only to then just say, oh well.' (Participant 10, listening visits only)

The women's experiences of antidepressants

Despite the fact that many of the women had expressed concerns about taking medication, 16 of the 26 women interviewed had received antidepressants during the trial. Four participants reported that the antidepressants had had little effect and one individual described feeling 'angry' and 'manic' as a result of her medication. However, most (11/16) of the women who had taken antidepressants reported benefits. A couple of these women had experienced side effects, i.e. nausea and tiredness, but viewed these as manageable.

Women reported slight but sustained improvements in mood. They had felt calmer and less tearful, and this had enabled them to think more clearly and put other forms of support in place:

> 'I didn't ever get this "I feel wonderful"… it wasn't a real massive change, it was just enough to shift my mood so that I'd actually do things, like go for a walk and things that I knew would make me feel better.' (Participant 3, antidepressants only)

Many women described the antidepressants as helping them to function and to deal with the demands of daily life. It was also apparent that women who had taken antidepressants while receiving listening visits felt medication had been necessary to stabilise their mood and had helped them to focus on the visits:

> 'The antidepressants put me on that keel for me to be able to sort my own mind out…that even keel where I could get through the day; I wasn't feeling, you know, I wasn't crying every five seconds, so then I could sit there and think "right, I can sort my head out now, I can talk, I can get things un-jumbled and I can work on that," so I think with me, it was definitely better to have the both of them [listening visits and antidepressants] together.' (Participant 25, listening visits then antidepressants)

Yet despite taking medication and in some cases experiencing benefits, some women had remained uncomfortable with the idea of taking antidepressants. Women described how their worries about dependency had led them to take a lower dose than prescribed or to only accept medication when prescribed a low dose. Women also talked about wanting to be monitored to

check that antidepressants remained necessary. In addition, among the women who had received both treatments, it was also argued that although the individual had taken antidepressants, the listening visits had been necessary for her to get better:

> 'It would have just gone pear shaped [if she had only received antidepressants]…I bottled a lot of things, it wasn't just the whole postnatal depression thing you know, I bottled loads and loads and loads of things and I think it all needed to come out, for anything to get better.' (Participant 7, antidepressants then listening visits)

Coming off antidepressants

At the time of interview, seven women were still on antidepressants. In some cases this appeared to be because of a fear of stopping:

> Interviewer: 'You persevered with them [antidepressants]?'
>
> Participant: 'I still am (laughs)…I'm too scared to come off them.' (Participant 26, antidepressants then listening visits)
>
> 'I sometimes feel what's the point in taking these but I know they're in my system, so I'd like to just keep it like that.' (Participant 22, listening visits then antidepressants)

Women who had stopped taking their antidepressants had done so because they had felt better. In some cases, individuals had stopped without consulting their GP.

While 11 out of the 21 women whose first treatment was listening visits had gone on to take antidepressants, only two of the five women whose first treatment was medication went on to have listening visits. Although one individual could not remember why she had started the visits, the other individual explained that she had always intended to have them as this had been her treatment preference at the time of randomisation. The reason so few women taking antidepressants went on to receive listening visits might have been because three of the five women who started on antidepressants as their first treatment, were individuals who had wanted this treatment and had found antidepressants sufficient for them to cope with their PND.

Strengths and limitations of the study

Interviewing women 1 year after the birth of their child meant that participants had to remember past views and events, making their accounts open to recall bias. These women were also individuals who had remained in the trial and therefore might have held a particularly positive view of RESPOND or the treatment they had received. However, interviewing 1 year after the birth of the study child did allow us to assess what the women's treatment experiences had been during this time period, and to identify processes or situations that had influenced their views about treatment. Also it was apparent that women had felt able to criticise the study during their interview.

As women with PND may refuse to take part in trials because of their concerns about antidepressants,[54] and within our study we had evidence of this, we might have sampled from a biased group of women. The design of the RESPOND trial might have reduced this problem, as each individual recruited knew she could request listening visits during the study. Certainly it was apparent that women were aware that they could refuse antidepressants and 'crossover' to listening visits. The purposeful nature of the sampling strategy used will also have limited the extent to which findings can be generalised. However, this approach did ensure that we interviewed women randomised to both arms of the trial, and women of varying age and from different socioeconomic backgrounds.

It was disappointing that we managed to interview only one individual who had declined to take part in the trial. Although the reasons she gave related to her views of antidepressants, and so were in keeping with the literature regarding difficulties in recruiting to trials in which antidepressants are given,[54] the difficulties we experienced in recruiting 'decliners' suggests that there was a general unwillingness among these women to take part in research.

Summary of main findings

The majority of the women interviewed had wanted to be randomised to listening visits. In most cases this treatment preference appeared to be linked more to a concern about taking antidepressants, than to a particular expectation of the visits.

Women's concerns about taking antidepressants were linked to issues associated with being on medication, e.g. stigma, side effects and dependency; to worries about accessing and obtaining treatment; to concerns about taking medication when breastfeeding; and to a fear of antidepressants affecting their ability to care for their child. Yet women who had expressed concerns about taking medication, and had received listening visits at the start of the trial, had gone on to take antidepressants. A number of factors had led to this: the visits had not been sufficient to improve the individual's mood; the woman's RHV had encouraged her to consider taking medication; a woman's concerns about taking medication had been addressed by her GP; antidepressants were the only treatment option available to the individual having completed the visits.

In contrast to the number of women who had expressed negative views about antidepressants, none of the women voiced any major concerns about having listening visits. Women who reported a preference for antidepressants were not against listening visits, they had simply felt no need to talk and thought medication would be the most effective treatment for them.

Most of the women who had received antidepressants during the trial reported benefits. Women described a lifting and stabilisation of mood, which had enabled them to function and to undertake activities which, in themselves, could be therapeutic. Some women, however, had remained concerned about taking medication and it was apparent that individuals had stopped taking their antidepressants without consulting their GP.

Women who had received listening visits during the trial reported benefits. They had welcomed the opportunity to talk, found the process of talking therapeutic, and had found the support and advice provided by their RHV helpful. However, in most cases, listening visits alone had not been sufficient to improve the individual's mood and further treatment had been sought. It did appear that women who went on to receive further treatment were individuals whose PND did not relate to their experiences of motherhood, but to events that existed before the pregnancy and to a personal susceptibility to mental ill health.

Chapter 5

Results: qualitative study with health professionals

Respondents

Thirty-seven GPs in participating practices were approached by letter and telephone and 19 agreed to be interviewed (see *Tables 40, 41*). Twenty HVs employed within participating PCTs were invited to participate and 14 agreed to be interviewed (see *Tables 40, 42*). Recruitment was continued until category saturation was achieved.

TABLE 40 *Number of GPs and HVs interviewed from each centre*

	Bristol	Manchester	London	Total
GP	6	11	2	19
HV	6	5	5	14

Recruitment of GPs was particularly difficult in London, partly because the field researchers for the qualitative study were based in Manchester and Bristol, and had no personal contact with the participating practices which seemed vital to secure participation.

Summary of main themes

The analysis presented in this report illustrates the following themes: making and negotiating the diagnosis of PND, how labelling affects management, enabling disclosure, the importance of an established relationship with the woman, perceptions of each others' roles and how imposed organisational changes impact on patient care with no one taking overall responsibility for the care of

TABLE 41 *Characteristics of GP respondents*

GP identifier	Age range (years)	Gender	Time in general practice (years)	Practice size (number of registered patients)	Practice demography (self-defined)[a]
B1	25–34	M	2	9600	U
B2	35–44	F	8	12,000	IC/U
B3	35–44	M	12	2800	IC
B4	35–44	M	8	7500	S
B5	55–64	M	28	5400	S/U
B6	25–34	F	3	7800	S/U
M1	45–54	M	20	8400	IC
M2	45–54	M	24	230	IC
M3	25–34	F	6	12,000	IC
M4	45–54	F	23	12,000	IC
M5	35–44	M	18	10,500	IC/U
M6	35–44	F	12	5600	U
M7	35–44	M	14	3200	U/SU
M8	45–54	F	20	5400	U
M9	45–54	F	18	4800	U/IC
M10	25–34	F	3	12,000	IC
M11	35–44	F	16	5800	U
L1	55–64	M	26	7000	U
L2	45–54	F	18	12,000	SU

a IC, inner city; S, suburban; U urban.

TABLE 42 *Characteristics of HV respondents*

HV identifier	Time since completion of HV training (years)	Length of service in area (years)	Corporate working?
B1	3	2	No
B2	12	10	No
B3	6	6	Yes
B4	12	3	Yes
M1	9	2	Moved to corporate working 6 months before
M2	30	23	Yes
M3	16	8	No (but in process of change)
M4	26	12	Moved to corporate working 12 months before
M5	4	2	Moved to corporate working 3 months before
L1	21	6	No
L2	14	4	Moving towards corporate working
L3	18	15	Yes
L4	15	12	Yes
L5	12	7	Yes

women with PND. Initial analysis of interview data about acceptability of the RESPOND intervention from the health professional viewpoint is also presented.

In reporting the final analysis, data are presented to illustrate the range and commonality of meaning of each category of analysis from the perspectives of GPs and HVs. In presenting the data, similarities and differences between GP and HV accounts are noted.

Illustrative data are presented within each theme. When reproducing data, a unique identifier has been given to indicate the respondent's profession, location and interview number (a prefix of M indicates Manchester; B indicates Bristol; and L indicates London).

The diagnosis of postnatal depression

Making the diagnosis

All respondents attributed a psychosocial aetiology to PND and demonstrated ambivalence about the separate status of PND as a condition:

> 'I call it emotional turmoil rather than depression…psychological disturbance, at various stages after the birth, and I don't think of them as adjustment disorders, and often they are what I would think of as existential crises.' (GP, M1)

> 'I can certainly give you a list of things that would put women at risk, but, you know, clearly doesn't always result in PND. So a previous history of mental-health problems or depression, unfulfilled expectation, difficult birth, wrong sex, partner unsupportive…but, I think there's quite a large proportion where there appears to be no risk factors.' (HV, B2)

None of the GPs interviewed used schedules such as the EPDS in making the diagnosis of PND; they instead described relying on instinct or clinical intuition:

> 'So I'm not saying I actively look for it, but I am hoping my antennae would tell me if there was a problem.' (GP, M5)

Other GPs described how they would attempt to explore mood in postnatal checks, but again, led by instinct:

> 'I generally ask about how they're coping and then gradually, if I was getting an instinct that there was something not quite right, then I would go into more depth and ask about sleep, appetite, how they felt about themselves, feelings of unworthiness, that sort of thing.' (GP, M2)

Health visitors similarly described the use of clinical intuition in assessing women:

> 'I think any kind of flatness…it's a difficult thing to explain, isn't it?…You can just tell by having a conversation.…just chatting to them.' (HV, B1)

In addition, however, HVs emphasised that it was not their role to make a diagnosis:

> 'I'm reluctant to say postnatal depression because I'm not in a position to actually diagnose PND.' (HV, M2)

This may indicate that the HVs felt that their own professional position was subordinate to that of GPs, rather than having an equal role in the division of work in primary care:

> '…it's not actually postnatal depression unless it's been diagnosed by the GP. That is 'cos, we have total care, which is, you know, a computer input system and we only input people where there are concerns, and one of them might be postnatal depression, but you only input them as being postnatally depressed if it's been diagnosed.' (HV, L5)

A few GPs did state that a more objective means should be used to assist in making the diagnosis:

> 'I've thought for a long time that the Edinburgh Postnatal Depression score would be a good way of identifying women rather than just going on the doctor's gut feeling as to who might be depressed and who might not.' (GP, M11)

So GPs and HVs appeared reluctant to make a diagnosis of PND in biomedical terms although possibly for different reasons, and respondents did not use the EPDS routinely in their clinical care of postnatal women.

Labelling affects management

The GPs described a variety of strategies for managing women in the postnatal period, and how the label they used for the woman's problems determined what management strategies they employed:

> 'I think we regard depression as an object, as a thing that exists, which is a completely unsophisticated way of looking at the way people work…It's about normalising how they think…I don't always offer anything…I very rarely prescribe on the first visit…so I think many depressions are like PND actually, they exist in the context of somebody's life and it has a meaning for them which you have to attend to…I hate these things where they say if you've got five tick-boxes then you have six months of fluoxetine, that's gross.' (GP, M1)

> 'I don't want to medicalise it too much really I think it needs to be a sort of informal sort of network because I do think most of the time people do recover from it if they are just given some support rather than medication.' (GP, M8)

A few GPs described a reluctance to use the term 'postnatal depression' because of a lack of resources to which they could refer women:

> 'If I call it depression, I need to do something. There's no one to refer to, so I would rather call it something else and manage her myself.' (GP, M10)

The importance of an established doctor–patient relationship was emphasised by GPs who described how their knowledge of the woman would impact on the label given to the patient's presentation:

> 'But some patients, as I say, its more of an adjustment disorder rather than postnatal depression. But I think some of these things, they are, they are based in some science with the scores and everything else, but some of it is based on your knowledge of the patient before and it's a judgement, it's a clinical judgement.' (GP, M11)

Such views were in contrast with those of HVs who, although reluctant themselves to make a diagnosis of PND, suggested that using a label of depression could be beneficial for the woman:

> 'I mean some would probably like to have a label put on it if they're feeling unwell, at least it's a recognised sort of thing isn't it, that they can say "well I've got this".' (HV, M4)

This may also reflect that HVs might be more comfortable with managing a woman whose symptoms have been given a name. Some HVs, however, suggested that by using the label 'depression' the woman would then have to see her GP, and that women assume that seeing a GP means the prescription of antidepressants:

> 'Because I think they think that seeing a GP means having medication and they don't want to have medication because, addiction, and a lot of women don't want to get addicted to it, and I think also probably don't like the stigma of being, er, having postnatal depression and having medication.' (HV, B3)

Negotiating the diagnosis

The GPs described difficulties in using the label for PND with women, particularly referring to the stigma that they perceived women felt, and the effect of this on the consultation:

> 'I mean, if they deny that they have got a problem but are still in tears, it becomes very difficult, because you can't treat somebody if they don't accept that there's something to treat.' (GP, B1)

> 'By the time they're getting round to any sort of formal label or naming it, you've explored quite a bit, and the woman herself has realised that, yes, there is a problem.' (GP, B5)

Other GPs, however, described consultations where the woman was happy to accept the label:

> '…and equally others will just come in and say "my husband said I've got to get this sorted out, and I need a tablet to calm me down" or whatever. You get the whole spectrum, really.' (GP, M2)

Health visitors did not describe such dilemmas within their consultations with women, although they recognised the reluctance that women might feel to accept the label of depression and the anticipated treatment:

> 'But yes, I've found there are many clients who don't want to take medication, because they do think there is a stigma attached.' (HV, L5)

Is an established relationship important?

Some HVs recognised that having an established relationship with a woman was important in whether PND was detected and managed by the health professional or disclosed by the woman, but there was ambivalence:

> 'I think that is, I think that is quite important, but I don't think it's the be all and end all, I really don't, I do, I think some health visitors get a bit precious about, you know, "my client", and all that.' (HV, L5)

All HVs referred to how recent changes in their way of working, moving to corporate working, had removed the potential for relationships to be ongoing, which had a direct impact on the detection of PND:

> '…but I think they used to get to know us, and we used to get to know them and obviously if they know someone they're more likely to sort of be forthcoming with any problems aren't they? Whereas now they, they probably don't get that input so they're probably less likely to come forward with things.' (HV, M4)

Most GPs, however, assumed that continuity of care was something HVs still provided, and that this relational continuity meant that the HVs were best positioned to detect and manage PND:

> 'She [the HV] and the GP are the ones who provide continuity and the woman will generally, unless she is about to move, would be expected to see her fairly regularly throughout the next few years. A good health visitor is excellent. The other good thing with a health visitor is, there is no stigma to see a health visitor, everyone sees a health visitor, more or less. Whereas seeing a counsellor or psychiatrist, well that gives you a label of mental illness. But you can see a health visitor who provides the same sort of counselling and there is no stigma involved at all.' (GP, M8)

The GPs were more likely to suggest that knowing the patient was important in making the diagnosis and determining management:

> 'I mean if I have known them since childhood…probably have for most of them round here…I know exactly what their past history, their family history, everything…' (GP, L1)

Although disadvantages of an ongoing relationship were also cited:

> '…but by the same token, I mean, I think sometimes that can be a disadvantage if it's something very personal…' (GP, L1)

These accounts again illustrate a reluctance on the part of GPs to medicalise PND and links with the lay discourses used and apparent reluctance to offer biomedical interventions.

Disclosure

Some GPs described strategies used to facilitate disclosure and offer women ongoing support:

> 'Once you kind of know they're in distress you don't just give them one session, you ask them to come back always…you get them to come back 2 weeks later to see how they're doing.' (GP, L1)

In addition, a minority of HVs described exploring depressive symptoms as a routine part of their interactions with women:

> '…but I think most people have actually heard about it now and don't find it unusual that you ask them about their mood and how they are feeling.' (HV, B2)

Both GPs and HVs, however, described the current systems of care as hindering disclosure of symptoms of PND:

> 'You know, we're not user-friendly in the health services…say someone is de-motivated because of low mood, then they ring for an appointment and they can't get through and then we ask patients "do you really need to be seen today?"…they have to jump through hurdles.' (GP, B6)

> 'They know it's a hurried environment, and they know it's hardly the environment for them to give you clues or confide in you that they're depressed.' (HV, M5)

Health visitors, however, suggested that there was limited value in identifying women with PND as all they could do was to refer a woman to the GP and they viewed the GP's role as limited to the prescribing of antidepressants:

> 'So, there's almost an ethical dilemma of, well, is there any point in identifying them if you can't do anything with them other than send them to the GP for antidepressants, which isn't good, you know.' (HV, M5)

This view pervaded the HV transcripts and was suggested to be a major reason why HVs did not encourage women to disclose their feelings.

Team work

Perceptions of others' roles

Some GPs emphasised the important role that HVs could play in the management of PND and their assumptions about how the HVs worked such as offering practical help to women:

> 'I think it depends very much on the skills and the experience of the health visitor but I think very much about helping the women to, providing some sort of support I guess someone to talk to and listen to but also perhaps about, one hopes that you are giving people some structure and some practical things to do in order to um maybe to cope with crying babies and you know poor sleep and perhaps lack of support in the house. Well there is what I think and what I hope they do…They are there within the community, they are not seen as distant as a doctor is or quite on a different level as GPs are often so hopefully they are a bit more approachable… They have got the resources and the access and the knowledge about what is available in the community that might help support them, like baby massage you know parenting groups, whatever their problem is. So hopefully they would be a source of referral or just even just general advice about where people go for help and support and so on.' (GP, M10)

Other GPs reported observing unwillingness on the part of HVs to manage women with PND:

> '…because I think they seem very constrained on what they are prepared to do really. I think that they seem just to play not a very non-interventionist role and see themselves as being preventative which I think is quite tragic because there is lots of, if you don't integrate sort of preventative curative resources it's not a great service really.' (GP, M6)

A few HVs saw themselves as offering an alternative approach to the GP, assuming that GPs adopted a biomedical approach (antidepressants):

> 'I find quite often though they say they don't want to come and see the doctor and they don't want to have medication…and then I would end up going and seeing them at home, regularly for a little bit, just offering support, just being there for listening.' (HV, B3)

Many HVs expressed negative attitudes to, and experiences of working with, GPs, and made assumptions about the limited role the GP could play in the management of a woman with PND:

> 'The GPs, and I think they're even worse than we are because they, from experience of women

I've visited, they just write a prescription, put them on antidepressants.' (HV, M2)

'Not with all the GPs, no, as I say, you know, sometimes the GPs are, they don't have a very sympathetic attitude to postnatal depression, let's say. And so I would imagine it puts the mothers off going to see them actually. And then hopefully they'll come and see us, but I'm sure there's some who don't, you know.' (HV, L5)

Ways of working

Recent reorganisation and the introduction of corporate working had affected HVs' perceptions of their relationships with both GPs and women:

'The [patient] notes go back into the pot and if anything arises in the future it's whoever's around to deal with it, whoever gets allocated. That's what they call corporate working.' (HV, B4)

'For the vast majority of them we don't see them again, we're not able to offer even a routine follow up visit, even if it's their first baby. We explain the situation to them in terms of staff and resource, and we encourage them to come to clinic or to phone us and we explain that we do visit some families at home and offer them extra support…however, in terms of listing the priorities I would say the postnatal depressed ones aren't high up on the agenda. When we've got much more prioritised.' (HV, M5)

Other HVs commented on the effect of physical isolation that had accompanied the move to corporate working:

'I don't, I personally don't think health visitors know their families like they, like you used to know them, you know, you'd perhaps, er, you'd have a geographical patch and knew everybody…we'd meet on the street and, I think, you know, especially since we've been moved right out of the areas.' (HV, L4)

GPs were aware of these changes in the organisation of HV services and described an impact on their day to day relationships with HVs, and confusion over the expected roles and responsibilities of the HV:

'I would say that of all the practitioners here they are the least integrated and they are the least, erm, we get least communication with them…there's nothing wrong with them, they're perfectly nice and friendly, but there's just not that clinical sort of connectiveness really.' (GP, B3)

'Yeah, I think, yeah, I mean I think it's really in terms of you used to have a health visitor, used to be attached to the practice. The powers that be decided they don't need new health visitors, cutting down, we share a health visitor or we share a group of health visitors. I frankly don't have a faintest idea who this woman is or whether she's coming here or not, used to have a very strong ongoing relationship with the health visitor, that's all stopped…In the old days I would have said, you know, there's an ongoing relationship with the health visitor, would have said 'fine', you know, they can monitor her, they can keep an eye on her that's what she used to do, you know, keep in close contact.' (GP, L1)

This GP describes vividly the change that he has experienced with the move to HV corporate working, from a time when a HV was attached to the primary care team and would visit women before and after delivery, offer support and practical advice as well as 'a listening ear', and how this has changed.

Whose responsibility is postnatal depression?

Although a few GPs talked about the pivotal role they perceived HVs to play in the detection and management of women with PND, most alluded to the recent reorganisation and change in role with a perception that women with PND go undetected. Other GPs describe how HVs have actively declined to support women with what was dismissed as a 'mental-health problem', although agreed that HV teams still had a role in offering practical support to women with PND:

'Well, our health visitors tend to say that it's a mental-health problem 'nothing really to do with me', which is disappointing really. They do go in and offer support but it's very vague what that support is. They cover some practical things around sort of nursery services for the children, stuff like that and it depends which health visitor team it is because not all will take an interest.' (GP, M7)

Many HVs suggested that there was little point in identifying women with PND, as they felt they had nothing to offer women themselves and no resources to refer women to:

> 'In an ideal world we'd want to pick them up and then offer them more support, but we can't do that. So there's almost this ethical dilemma of well is there any point in identifying them if you can't do anything with them other than send them to the GP for antidepressants, which isn't good, you know?' (HV, M5)

The HV view that there is limited value of referring a woman back to the GP is seen again in these data. Other HVs, however, were quite clear that it was the GP who was the responsible clinician. HVs agreed that they no longer saw the detection and management of women with PND as a priority for them:

> '…erm, at the moment we're short-staffed, so we're really on priority cases at the moment.' (HV, M1)

And a few HVs described negative aspects of providing support to women with PND with a risk of dependence on them:

> 'You cannot emotionally and mentally prop somebody up for years and years, it's got to end…sounds awful, doesn't it?' (HV, B4)

So both GPs and HVs reported that the current systems within which they work constrain the care that can be provided to women at risk of PND and HVs no longer see the management of women with PND as an integral part of their work.

Views on the RESPOND trial

Despite exploration with all respondents about their experiences with the RESPOND trial and the interventions that women in their practice or HV team had experienced, few GPs or HVs were able to discuss experiences or outcomes of women. There were few data in the interviews with GPs about the HV-delivered intervention in RESPOND, but they did talk positively about the trial itself:

> 'Well, I'm not quite sure what's going on now. I realise I should know because I was there at the meetings, and I know [receptionist's name] has a pile of those things that she sends out to people when she sends the postnatal thing and I presume they fill them in. I don't, actually, I've forgotten what happens after that.' (GP, M1)

They were particularly positive about the organisation of trial and information given about prescribing:

> 'I've been enormously impressed, the communication side is excellent, the information that you supply, that a patient has been randomised to antidepressant treatment and they'll be coming in, and an appointment's arranged and the information sheet about antidepressants and advice about breastfeeding is there…so it was all good to see.' (GP, M2)

> 'It highlighted a few patients who we saw earlier and who we treated, which we probably wouldn't have otherwise. I think that it was worth doing just for that if nothing else.' (GP, L1)

Some GPs suggested that the intervention being delivered by a separate HV might be beneficial:

> 'I think the benefit [of being involved in RESPOND] is the patients always feel that there's someone else interested in them, so they have benefited in that respect, otherwise no.' (GP, B2)

On the whole, the GPs valued the trial as providing a service for women who might otherwise not receive one:

> 'I think probably the two women diagnosed [within RESPOND] were not by our GPs, I think we feel confident that people are being looked after with their postnatal depression.' (GP, B5)

This view resonated with some HV accounts, where respondents were unaware of the intervention delivered by the RHV, possibly because they had insufficient women in the trial:

> 'I'm afraid on my caseload there's only one that has sort of completed the process, so I feel unable to comment on the value to individuals.' (HV, B2)

Others described how having women in the trial provided support to their own service:

> 'I think postnatal depression is very important, I think it's an unmet need so I carry a big guilt complex there, and this [being involved in RESPOND] will ease the guilt complex very, very slightly.' (HV, M5)

Health visitors suggested reasons why the trial might be useful for women, in particular, that it gave women permission to disclose how they felt:

> 'I think sometimes they don't like to disclose it because it's seen as, they think they're seen as not coping, you know, that's why I think this study has been useful because it's specifically for them, you know, they've done it in their own time, had it at home, read it through and decided that they do want help.' (HV, M1)

> '…I think with the study [RESPOND] somebody new goes in and says "it's all about you, I'm here to talk about you." Whereas they probably do get a bit of conflict thinking you're looking at the children all the time.' (HV, M1)

There were, however, some negative comments from HVs who felt the trial had encroached on their role:

> 'I'm finding it quite difficult, really, taking a back seat, I had a kind of rhythm going and that's been stopped.' (HV, M3)

> '…going back to the RESPOND trial, I mean, it's sort of taken away some of what we're doing if you see what I mean, but then we haven't got time to do it.' (HV, L3)

And some HVs expressed concerns about the EPDS being sent to women at home:

> 'It's not brilliant, unfortunately, and I'm sure they don't fill them in.' (HV, L5)

In summary, the interviews yielded insufficient data to allow a full exploration of the acceptability of the trial intervention by the primary care professionals, who had only experienced one or two of their patients being part of the trial. Although having mostly positive views of being involved in the study, they did not express any views on the HV-delivered intervention.

Strengths and limitations of the study

Strengths

This chapter reports a qualitative study embedded in a randomised controlled trial. The use of qualitative methods allows practitioners to raise issues that are of concern to them, and an inductive approach ensures that findings are related to the views articulated. The data were gathered from GPs and patients drawn from a large geographical area (nine PCTs). Using researchers from different professional and academic backgrounds is a recognised technique for increasing the trustworthiness of the analysis.[105]

Limitations

Only HVs and GPs who were already involved with the RESPOND trial were interviewed and it seemed difficult to engage with London GPs even though they were signed up to the main trial. PCTs were invited to participate in RESPOND if they did not have a well-established pathway of care for PND within the PCT, and so participating PCTs may have poorer provision of services and attitudes of the health professionals working in these areas will reflect this. For this reason, the findings may not be representative of (even neighbouring) PCTs who may have developed a PND strategy and services for this group of patients. As respondents had limited experience of their women being in the trial, it proved difficult to fully explore acceptability of the RHV-delivered intervention from GP and HV perspectives.

Summary of main findings

The importance of knowing the patient and taking a biopsychosocial approach in making and negotiating the diagnosis of PND is seen in the GP narratives, which also highlight the importance of a long-term relationship with the woman. HVs did not feel that it was their responsibility to make a diagnosis of PND. Although some HVs felt that the label of PND might be useful, giving a certainty and legitimacy to the symptoms, many HVs felt that if this diagnosis meant referring the patient back to their GP, then the only management on offer would be antidepressants, which they felt would not be wanted by women. Each group of health professionals (GPs and HVs) described perceptions of each others' roles, observing that

the move to corporate working had affected their relationships with each other, reduced home visiting by HVs and reduced continuity. In addition, HVs described prioritising 'vulnerable families' – but did not identify families in which the mother has PND as vulnerable. There was agreement between GPs and HVs that the clinical diagnosis of PND should be made by the GP, but both parties seemed to fail to take responsibility for detection of symptoms of PND, with GPs assuming that HVs are responsible, and HVs recognising and justifying a reduced responsibility because of their changed way of working.

Our data suggest that HVs and GPs make conscious decisions in their everyday work not to facilitate the disclosure of symptoms and the reasons that they give for not doing so are not the anticipated 'no time' but rather a lack of resources, personal resources to manage the women themselves, and NHS services to refer women to, and perhaps being unaware of third-sector provision. In addition, HVs lay the blame at the door of the new way of working – that of working corporately with no personal list of women, no relational continuity and no responsibility for individual women.

The GPs do see PND as a primary care problem but make assumptions about the role played by the HV in the management of these women. Some HVs, however, see PND as a mental-health problem and describe referring women with PND to the (primary care) mental-health team or back to the GP, rather than feeling comfortable to manage women themselves.

Respondents described how national policy and local organisational changes were impacting on patient care with no one individual taking overall responsibility for the care of women with PND.

Chapter 6

Results: comparing views of health professionals and women

Introduction

This chapter presents a comparison of some of the views of health professionals and women interviewed.

Summary of main themes

The themes presented reflect those particularly illustrated in chapter 5 and comprise: understanding PND, making the diagnosis, and hindering and facilitating disclosure of symptoms. Illustrative data are presented within each theme and unique identifiers are used to indicate respondent.

Understanding postnatal depression

Women attributed a psychosocial aetiology to their symptoms in relation to the stresses of parenthood, such as changed relationships, reality not meeting expectations, and the birth of the child triggering memories of past events:

> 'And then there was a whole set of issues about my relationship with my partner and how he was supporting me and these issues were all thrown up when my little girl was born and then when my little boy was born, it happened exactly the same. It was a real repeat, you know, and I'd done so much to try and prevent it going down the same route, but I just felt like we were going down the same groove.' (B, ID28)

Some women described their feelings as a response to physical changes around childbirth, but suggested that they were susceptible to depression in some way:

> 'I personally feel it…well, probably two factors…but I think perhaps it is some sort of chemical hormone or imbalance, you know, everything sort of all shifts it about and…and secondly, just the type of character that I am, and putting that pressure on myself the whole time.' (L, ID16)

Women described insights into and awareness of their symptoms, often because they had suffered from depression in the past, although they suggested that the cause of PND might be different to the cause of previous episodes:

> 'I'd had slight depression before, but this was quite different, I kind of knew why, whereas before it was kind of all suffering and something had triggered lots of other things, and here it was lack of sleep, and although I knew the reasons why I was feeling like I was feeling, but I couldn't stop it.' (B, ID3)

Health professionals also attributed a psychosocial aetiology to PND and demonstrated ambivalence about the status of PND as a separate condition as compared with depressive illness at other times in a woman's life:

> 'I can certainly give you a list of things that would put women at risk, but, you know, clearly doesn't always result in postnatal depression. So a previous history of mental-health problems or depression, unfulfilled expectation, difficult birth, wrong sex, partner unsupportive…but, I think there's quite a large proportion where there appears to be no risk factors.' (B, HV2)

Thus, both women and health professionals viewed the cause of PND as multifactorial and often a social response to birth.

Making the diagnosis

As discussed in the previous chapter, GPs and HVs described a reliance on instinct or clinical intuition, which would alert them to the possibility of PND, rather than using formal screening instruments or actively seeking out symptoms of depression:

> 'I think any kind of flatness…it's a difficult thing to explain, isn't it?…You can just tell by having a conversation…just chatting to them.' (B, HV1)

The GPs described difficulties in using the label for PND with women, particularly referring to the stigma that they perceived was felt by women, and the effect of this on the consultation:

> 'I mean, if they deny that they have got a problem but are still in tears, it becomes very difficult, because you can't treat somebody if they don't accept that there's something to treat.' (B, GP1)

Other GPs, however, described consultations where the woman was happy to accept the label:

> '…and equally others will just come in and say "my husband said I've got to get this sorted out, and I need a tablet to calm me down" or whatever. You get the whole spectrum, really.' (M, GP2)

Health visitors did not describe such dilemmas within their consultations with women, although they recognised the reluctance women might feel to accept the label of depression and the anticipated treatment:

> 'But yes, I've found there are many clients who don't want to take medication, because they do think there is a stigma attached.' (L, HV5)

Some GPs described a reluctance to use the term 'postnatal depression' because they felt that symptoms would recover without formal interventions, because of a lack of services or referral options, and the feeling that antidepressants were the only treatment option available:

> 'I don't want to medicalise it too much really. I think it needs to be a sort of informal sort of network because I do think most of the time people do recover from it if they are just given some support rather than medication.' (M, GP8)

> 'I mean, it's best if it's a multiple approach rather than just drugs. Unfortunately that's all we can offer.' (L, GP1)

Health professionals described a variety of difficulties making the diagnosis of PND; HVs because diagnosis was not felt to be within their remit, and GPs because of the perception that they had limited management options to use if they used the label of PND.

Disclosure and hindering disclosure

Women described making a conscious decision about whether or not to disclose their feelings to their GP or HV. Some women cited their own personal barriers to being able to talk to their GP:

> 'Again, GPs, I don't think, er, well I personally couldn't talk to my GP.' (M, ID16)

Other women mentioned characteristics of GPs which inhibited their ability to disclose, such as the GP being perceived as not willing to listen:

> '…he [GP] could have listened. Again, I think they could have done that at least, they could have listened…' (M, ID22)

Other women described system factors which made them reluctant to attempt to approach their GP to discuss how they were feeling:

> '…wouldn't go to the doctors because you can never get an appointment and it's crap. They always treat you like there's something else wrong and why are you wasting his time…I wouldn't have gone [to the doctors] even if I'd been dragged kicking and screaming.' (M, ID24)

Many women described a fear of disclosure because of how they would be perceived by their HVs, such as being a bad mother, and others described fear of having their children being referred to social services:

> '…with my health visitor, I, I try not to, try not to let too much out because then she won't think I am a bad mum, if you see what I mean, so I tend not to let too much out with the health visitor.' (B, ID2)

Women also questioned the role of the HV and who she was there for:

> '…what **is** the health visitor there for? Is she there for the welfare of the child, or is she there for the welfare of the mother, or both?' (M, ID24)

> 'No, I don't think I discussed that with the health visitor. I was more concerned with her [baby] at the time. So I just assumed health visitors were for looking after her [baby] needs, so if she had a rash or was throwing up, or whatever, things that I wouldn't necessarily know what to do about. Whereas your own needs you don't tend to think about them in the same way. So there's known and unknown, and she [the HV] was definitely an unknown' (L, ID12)

Other women described a fear of consulting their GP as they anticipated that the only treatment that would be offered would be antidepressants, which they did not feel was an acceptable treatment option:

> 'That's all they have, GPs, and I just didn't want to go onto antidepressants, because obviously I've heard people get addicted to them and then you're stuck on them and you have a vicious circle.' (M, ID24)

> 'My concern is that I will just get addicted and it will change my personality.' (B, ID1)

This view might be reinforced by the women's HVs because the HVs who were interviewed described GPs' role in the management of PND as being limited to the prescribing of antidepressants:

> 'The GPs…and I think they're even worse than we are because they…from experience of women I've visited, they just write a prescription, put them on antidepressants…' (HV, M2)

> '…sometimes the GPs are, they don't have a very sympathetic attitude to postnatal depression, let's say. And so I would imagine it puts the mothers off going to see them actually.' (HV, L5)

A few women did talk about why they felt able to discuss their symptoms with the GP and cited factors such as having been to their GP with depression or PND in the past and recognising the symptoms. Women who had previous experience of antidepressants were more accepting of this treatment being offered to them again:

> 'I thought, well, I'll try them and you know, it did help a bit last time, not, you know, it wasn't fantastic, but it did help a bit so I thought well, okay, I'll try them again.' (B, ID6)

Most importantly, those women who did feel comfortable seeking help from their GP described having a good relationship with him/her, making discussion of depression possible:

> 'I don't go to the doctor that often but, well [names child] was with [names doctor] so I've been quite a few times with having colds and stuff so I knew him quite well, so it was quite easy to go and say "look, I'm just, I'm not feeling right at the moment".' (M, ID25)

Some GPs described strategies used to facilitate disclosure and offer women ongoing support:

> 'Once you kind of know they're in distress you don't just give them one session, you ask them to come back always…you get them to come back two weeks later to see how they're doing.' (L, GP1)

In addition, a few of the HVs described exploring depressive symptoms as a routine part of their interactions with women:

> '…but I think most people have actually heard about it now and don't find it unusual that you ask them about their mood and how they are feeling.' (B, HV2)

Most HVs, however, suggested that there was limited value in identifying women with PND because all they could do was to refer a woman to the GP and they viewed the GP's role as limited to the prescribing of antidepressants:

> 'So, there's almost an ethical dilemma of, well, is there any point in identifying them if you can't do anything with them other than send them to the GP for antidepressants, which isn't good, you know.' (M, HV5)

This view pervaded the HV transcripts and was reported by the HVs to be a major reason why they did not encourage women to disclose their feelings to their GP.

How the system of care hinders disclosure

Both GPs and HVs described the current systems of care as hindering disclosure of symptoms of PND:

> 'You know, we're not user-friendly in the health services…say someone is de-motivated because of low mood, then they ring for an

> appointment and they can't get through and then we ask patients "do you really need to be seen today?"…they have to jump through hurdles.' (B, GP6)
>
> 'They know it's a hurried environment, and they know it's hardly the environment for them to give you clues or confide in you that they're depressed.' (M, HV5)

Some health professionals described consciously inhibiting disclosure so as not to be placed in this position citing lack of continuity of care as the reason:

> 'Easier not to ask, if I'm not going to see her again.' (L, GP1)
>
> 'For the vast majority of them we don't (see them again), we're not able to offer even a routine follow-up visit, even if it's their first baby. We explain the situation to them in terms of staff and resources, and we encourage them to come to clinic or to phone us, and we explain that we do visit some families at home and offer them extra support…however, in terms of listing the priorities I would say the postnatal depressed ones aren't high up on the agenda. When we've got much more prioritised.' (M, HV5)
>
> '…but I think they used to get to know us, and we used to get to know them and obviously if they know someone they're more likely to sort of be forthcoming with any problems aren't they? Whereas now they, they probably don't get that input so they're probably less likely to come forward with things.' (M, HV4)

A few of the HVs described a resistance to being involved in providing care for women with PND, and this reluctance was made easier by the move to corporate working:

> 'Working corporately, we all work between the GPs and as work comes in we allocate families…I mean the families aren't becoming reliant on you, that's the good thing.' (M, HV1)
>
> 'You cannot emotionally and mentally prop somebody up for years and years…sounds awful, doesn't it?' (B, HV4)

Some women suggested that neither their GP nor their HV could do very much, which resonates with the views of HVs on the GP role:

> 'There is nothing else available. No GP, no health visitor; they're there but not in a helpful sense, sort of like.' (M, ID22)
>
> '…because I was very struck by the health visiting that I'd had so far. I hadn't felt like my needs had been met at all.' (M, ID27)
>
> 'The doctors are like, always helpful, but I think they're limited as to what they can do, which is what I thought, you know…that they can't actually do that much…' (B, ID6)

Both GPs and HVs described organisational factors which precluded the facilitation of the disclosure of depressive symptoms in their postnatal women patients. Difficulties providing continuity of care were frequently cited. Women talked less about system factors, but rather suggested that neither the GP nor HV had much to offer. The development of long-term relationships which may facilitate disclosure may be impeded by the systems within which health professionals currently work.

Summary of main findings

Comparison of data from interviews with health professionals and women suggests that both groups conceptualise PND in similar ways citing psychosocial factors (including reality not meeting expectation, adjustment to new role, motherhood stirring up things from the past) as the main cause of their symptoms, and feeling that management of PND needs to address these factors. Our findings suggest that many women decide not to seek help with their symptoms and distress if they predict that medication will be the only treatment offered to them. The GPs and HVs do not use the label 'postnatal depression' if they feel they personally have nothing to offer the woman, or no services to refer women on to. Some HVs view GP management as limited to the prescribing of antidepressants. HVs and GPs make conscious decisions in their everyday work about whether or not to facilitate women's disclosure of symptoms of PND. In addition, HVs blame a new way of working (corporate working–with no personal lists of women, no relational continuity and no responsibility for individual women) as hindering the disclosure of symptoms of PND. GPs were aware of this change and reflected that this had made the management of PND more difficult.

Chapter 7
Discussion

Summary of main findings

Primary outcome

Two hundred and fifty-four women with PND were randomised to receive either antidepressants or listening visits from a HV. At 4 weeks, women with PND were more than twice as likely to have improved, i.e. EPDS < 13, if they had been randomised to antidepressants compared with women randomised to listening visits, which started after 4 weeks follow-up, i.e. after receiving GSC for 4 weeks (primary ITT, 45% versus 20%; odds ratio 3.4, 95% CI 1.8 to 6.5, $p < 0.001$). At 18 weeks, the proportion who improved was 11 percentage points higher in the antidepressant group than in the listening visits group (62% versus 51%), although from the logistic regression analysis there was no statistical evidence of benefit for one group compared with the other (primary ITT, odds ratio 1.5, 95% CI 0.8 to 2.6, $p = 0.19$). The trial has therefore provided answers to the two main questions posed. Antidepressants offer significantly greater improvement compared with GSC at 4 weeks, and at 18 weeks women randomised to antidepressants still seem to have an increased chance of improvement compared with those randomised to listening visits although this difference is no longer significant.

At 4 weeks, the secondary analyses of the primary outcome made virtually no difference to the size of the difference between the two groups. The increased magnitude of the differences in the CACE models is the result of patient choice entering after randomisation, where those who start to improve spontaneously or improve early on the allocated treatment may make a choice to wait and see whereas those not improving tend to add treatments. Using a 4-week end point is by current standards very early in treatment and if randomised allocation had continued unaltered to 8 or 12 weeks there may have been a further increase in difference – but this was not possible in a pragmatic trial that included an arm with no active treatment in the first instance. However, GPs can be reassured that prescribing antidepressants about 10 weeks postnatal gives a much better chance of improvement over the next 4 weeks than GSC.

It is not possible from these separate analyses to address directly the issue of the evidence for a change through time in the differences between the groups, but the interaction test from the repeated measures logistic regression analysis does indicate weak evidence that this reduction in the odds ratio is greater than would be expected by chance ($p = 0.032$) This supports the finding that the benefit of taking antidepressants was larger at 4 weeks than at 18 weeks when the comparison was between antidepressants and listening visits (if needed) versus listening visits. Unlike many trials, the comparison has changed between the two follow-up points. Overall, there is evidence of a difference between the groups in favour of the antidepressant group of about 25 percentage points at 4 weeks which is reduced at 18 weeks. There is no statistical support for a benefit of antidepressants at 18 weeks, but the confidence intervals cannot rule out a clinically important benefit.

Secondary outcomes

When the EPDS was considered as a continuous score, the difference in EPDS from baseline to 4 weeks between those randomised to antidepressants and those randomised to listening visits was about 2 points lower in the antidepressant group than in the listening visit group, with a margin of error of about 1 point. The point estimate corresponds to a standardised difference of about 0.4 SD which is very similar to differences found between antidepressants and placebo. Although the mean EPDS score at 18 weeks was still lower for those in the antidepressant group in all analyses performed, the difference between the groups had reduced considerably and the scores for both groups appeared to be converging. For both the primary ITT comparison and the secondary analyses, the differences between the means of the randomisation groups reduced to less than 1 point by 18 weeks, the p-values all indicated lack of evidence of differences beyond chance and the 95% CI spanned zero. The interaction test from the repeated measures regression analysis led to only marginal evidence of a change in the difference between the groups over the two follow-up times ($p = 0.070$). The average effect over the follow-ups

of –1.4 (95% CI –2.4 to –0.3, $p = 0.013$) should also be treated with caution for similar reasons to those given above for the primary ITT analysis.

For the other (continuous) secondary outcomes, the results for the SF-12 mental component score were very similar to those for the EPDS score, especially in its continuous version. In particular, the benefit in scores for the antidepressants group was observed at 4 weeks for the ITT and all secondary analyses, whereas no such differences were apparent at 18 weeks. The lack of any corresponding differences between groups for the SF-12 physical component score and the EQ-5D (which only includes one question about psychological symptoms) suggests that any effects are specific to mental-health quality of life.

For the MAMA attitudes to the baby subscale and the GRIMS partner relationship scale there was very little difference apparent between the various groups, although the suggestion that those who received both interventions by 18 weeks have the worst outcome is consistent with the other outcomes and presumably reflects strong selection effects by those who are not improving on their initial clinical management.

Other secondary analyses

Although there was a reasonably small amount of attrition overall in the context of this study (approximately 15% by 4 weeks and 20% by 18 weeks) there was evidence of differential attrition rates across the randomisation groups, with fewer lost to follow-up in the listening visits group ($p = 0.090$ and $p = 0.015$ at 4 weeks and 18 weeks, respectively). The sensitivity analyses involving multiple imputation, however, indicated that this had no appreciable effect on the results. Only 22 women had missing EPDS scores at both follow-up times and the differences between the groups were similar in direction (if not magnitude) at both time points. Furthermore, baseline EPDS was strongly associated with outcome and used as a covariate in the ITT analysis. It would appear that there was little impact of attrition on the observed results.

Reflecting their low power, overall the prespecified subgroup analyses gave only weak evidence of differential effects according to baseline severity of depression. The suggestion of greater effects for those more severe at baseline is both generally plausible and consistent with the pattern of findings for the binary and continuous version of the primary outcome.

Economic evaluation

Whereas the economic evaluation suffered from having originally been set up to report at 44 weeks and from a significant amount of missing data (particularly that relating to secondary care resource use) there is no clear evidence for differential resource use between intervention groups for either mothers or babies at 4 or 18 weeks. There are one or two findings that deserve consideration but all must be treated with caution because of the small sample size as well as the analysis using the original randomised groups with no adjustment for switching groups or adherence. By 4 weeks more women in the AD group had seen their GP than those in the listening visits group – possibly to receive their prescription but it might have been anticipated that women receiving GSC only, in those 4 weeks, might have visited their GP at least as often. By 18 weeks more women in the listening visits group had consulted so although most of these would have been receiving visits from the RHV, some will have been seeing the GP for a prescription for antidepressants. There were remarkably few consultations with the PHV for women but more surprising was that only about 50% of babies were seen by PHVs in either of the 4-week periods. There were no obvious differential patterns of use of either other primary/community-care or secondary-care facilities with on average no more than 20% of either women or babies attending outpatients or Accident and Emergency departments. The greatest resource utilisation by postnatal women is clearly in the primary care setting.

Statistical considerations

It is useful to compare the observed percentage improvement with those assumed in advance as worth detecting in the sample size considerations. At 4 weeks the difference of 25% exceeded that specified in the original power calculations of 15%, and was similar to that accepted for the revised calculations (20–22.5 percentage points). However, the power calculations assumed that 40% would improve in the listening visit (GSC) group at 4 weeks, and in the antidepressant group, 55% in the original and 60–62.5% in the revised calculations. The initial assumptions were therefore reasonably close for the antidepressant group but (quite considerably) overestimated the improvement in the listening visit (GSC) group. A meta-analysis of psychotherapy studies that randomised to a waiting list control group, not dissimilar to our GSC arm, found a similar

percentage, 20%, improved in the short term.[106] At 18 weeks, the original assumption of 50% improvement in the listening visits group was very close to that observed; at this follow-up, therefore, the lack of clear evidence of differences reflects the smaller difference observed (11 percentage points) than that either specified as clinically worth detecting in the original power calculations (15 percentage points) or that for which there was in the event adequate power (just over 20 percentage points; see Chapter 2, Sample size). However the confidence intervals are quite broad at 18 weeks and so an important difference cannot be excluded.

In a trial of this nature, the definition of a 'plausible, clinically important difference' is always debatable and (as can be seen above) cannot be determined, at present, with any confidence. It is also sometimes argued that small differences become more important for common conditions, and depression including PND is very common and leads to a substantial public-health burden. In RESPOND, the attained sample size was smaller than planned, so the detectable differences clearly increased. However, for what was considered at the outset to be an acceptable power (at least 80%), the attained sample size was adequate to detect a 20 percentage point difference, which is itself clearly clinically important. Moreover, on a number of grounds the sample size calculations could be argued to be conservative. First, although in the analysis the formal primary outcome was the binary version of improvement to an EPDS score of < 13, the continuous EPDS score was a secondary outcome and should have greater statistical power. Second, evidence from the literature reveals that we might have been overly conservative in our original assumptions for the binary version. We had assumed about 55% would have 'improved' on antidepressants at 4 weeks compared with 20% receiving no active treatment, whereas data from waiting list control groups similar to our supportive care only resulted in 20% having improved.[106] Moreover, the entry criteria to our study were fairly stringent and in line with NICE guidelines, meaning that randomised participants were more likely to benefit from an intervention, which in turn increases the magnitude of plausible differences.

Qualitative findings

Interviews with health professionals

The qualitative study with GPs and practice HVs elucidated views on the management of women with PND in primary care and the findings have implications for clinical practice. For GPs, the importance of knowing a woman and taking a holistic approach in negotiating a diagnosis of PND was evident, and was facilitated by a long-term relationship with the woman. HVs did not feel that it was their responsibility to make a diagnosis of PND. Some HVs felt that the label of PND might be useful but many felt that if this diagnosis meant referring the patient back to their GP, the likely management would be antidepressants, which they felt would not be acceptable to many women. This ambivalence might reduce the detection of PND by HVs. GPs and HVs described perceptions of each others' roles, observing that the move to corporate working had affected their relationship, reduced home visiting by HVs and reduced continuity. In addition HVs described prioritising 'vulnerable families'–which did not include families in which the mother had PND. There was agreement between GPs and HVs that the clinical diagnosis of PND should be made by the GP, but both parties seemed to fail to take responsibility for the detection of symptoms of PND, with GPs assuming that HVs are responsible, and HVs recognising and justifying a reduced responsibility because of their changed way of working.

Our data suggest that HVs and GPs make conscious decisions not to facilitate the disclosure of depressive symptoms as the result of a lack of personal resources to manage the women themselves, and of NHS services to refer women to; perhaps they are also unaware of third-sector provision. GPs see PND as a primary care problem but make assumptions about the role that the HV plays in the management of these women. Some HVs, however, see PND as a mental-health problem and describe referring women with PND to the (primary care) mental-health team or back to the GP, rather than feeling comfortable to manage women themselves. In addition, HVs blame a new way of working, (corporate working) with no personal lists of women, no relational continuity and no responsibility for individual women, as hindering the disclosure of symptoms of PND. GPs were aware of this change and reflected that this had made the management of PND more difficult.

Interviews with women

When comparing two treatments that are so very different, their acceptability to women is of importance when considering the implementation of the trial findings.[107] The literature tells us that women with PND are generally reluctant to take antidepressants.[54,108,109] The interviews with women revealed that most of them wanted to receive listening visits at the time of randomisation. This

preference appeared to be linked more to concerns about antidepressants than to a particular wish for the listening visits and has been found in previous studies.[74] However, there were many women who said they had had a preference for listening visits and had this treatment, but had then gone on to take medication. We identified various reasons for this. Most of the women who had listening visits found them helpful but felt that eight visits had not been enough and suggested that the listening visits had made them more receptive to trying antidepressants. Women who took antidepressants in the qualitative study had generally found them helpful. Only five women were interviewed who started with antidepressants, so we do not have much insight into what happened to women during this 4-week period when women randomised to the listening visit arm were receiving supportive care only. Only 66 out of 106 women randomised to antidepressants and followed up at 4 weeks actually took the treatment. The difference found at 4 weeks might be because contact with the GPs might have been beneficial even if they did not actually take antidepressants, but might also reflect that the women who chose to take antidepressants were those likely to benefit. It is also possible that having a diagnosis agreed with a known health-care professional, rather than by a research team, was helpful and may have encouraged women to be more open with others about how they were feeling and therefore receive more support. Women found that antidepressants worked – they described improvement in their mood and a feeling that the antidepressants helped them to function. Women who had listening visits, described how they had told few people about their PND and had no one to talk to. Those assigned to listening visits found the 4-week wait difficult – they did not see their GP, ask others for help, described feeling desperate and felt frustrated that they were not receiving treatment when they had been told they were ill and needed it. Being told they were ill, then not receiving treatment straight away, therefore might actually have made them feel worse.

Generalisability

The study centres were chosen to include three large urban areas of England – with some diversity in terms of deprivation and ethnicity. The population from which the trial sample was obtained is likely to have been representative of childbearing women generally in the UK. Among the 628 women who received a home visit, about 20% of women were from ethnic minority groups.

The overall valid response rate from women to the initial invitation was 41%. This is low by many standards for trials in primary care[110] but not wholly unexpected for this group of women. In the protocol, we assumed a response rate of 50%. In the end we achieved 41% overall with quite sizeable centre differences – 29% in Manchester, 44% in Bristol and 53% in London. There were also some centre differences in terms of the number of high scorers on the screening EPDS – 30% in Manchester, 25% in London and 20% in Bristol. Therefore Manchester, although having the lowest response rate, had the largest proportion of women with high scores on the screening EPDS. Manchester also tended to recruit women who were younger, had slightly higher mean screening EPDS scores and whose babies were a little older. PCTs in the three centres were chosen where routine use of EPDS and HV-delivered non-directive counselling (listening visits) for women with PND were not undertaken. Detailed discussions with PCT HV professional leads allowed us to target practices where this training had not been made routinely available to PHVs and also to avoid recruiting practices in areas where initiatives such as Sure Start[111] were working.

We were aware when we designed the trial that the inclusion of an antidepressant arm was likely to reduce participation[54,108,109] and one of the main reasons for including the qualitative component of the study was to further investigate this issue. In a trial of this nature where information sent to patients states very clearly that the trial is about, and for, women with PND, it is likely that a large number of well women who did not perceive it as being of interest or use to them personally decided not to reply to the initial invitation. In addition, the admission of PND to health professionals will be off-putting for some women who believe that this could lead to the involvement of social services with the family and the possibility of a baby being taken into care.

Methodological issues

The practices in each centre were approached with regard to participating in the study on the basis of having a sufficient number of births (about 100) each year, to result in about 21 practices being recruited in each centre. This approach worked well in Bristol and London but in Manchester, practices tended to be smaller, including some single-handed practices, resulting in 35 practices being recruited to ensure a sufficient number of births. This made monitoring of practice activity

by the Manchester research associate much more difficult because of both the wider geographical area covered and the number of practices. In each practice, a member of the administrative staff (clerical assistant) was identified as the main liaison with the centre research associate, who would be responsible for collating the practice birth data and on a regular basis, usually weekly, sending information packs out to women who were between 5 and 6 weeks postnatally. The research associate, on the basis of responses received, was then able to ask the clerical assistant to send reminders to the non-responders.

The requirement by ethics committees for patients to be contacted by the clinical team rather than the research team does require the development of a positive relationship between the two teams so that the research team can be sure that letters are being sent out on their behalf as requested. Although NHS support costs are provided to practices to undertake these roles, not all practices recognise the vital and responsible role they are playing in the research process and as the pressure of providing the front-line service for the NHS becomes inexorably greater, research activities are sometimes forgotten. This is demonstrated by the discrepancies between the numbers of invitations sent out by practices and the total births recorded (*Table 2*). In addition, the timing of sending out the invitations varied depending on how often the clerical assistant found time to undertake this task and this impacted on exactly how long after the birth women received their invitation. This also varied depending on how quickly hospital and PCT notifications of births were sent to practices. However, overall, 95% of women who had been recorded as being eligible for the study by practices received an invitation. This varied between 98% in Manchester and 89% in London. These differences may be explained by the list sizes in Manchester being systematically smaller than those in London and Bristol; also, in London the population mobility is very high, which may have resulted in women moving from their registered address soon after the birth. At PCT level, where the requirement was to provide researchers with regular birth data for each practice, some found this difficult to do on a monthly basis which meant that in some instances the denominator for total births per practice is not secure (*Table 2*).

During the course of the study, a number of PCTs moved from a system of practice-based HVs to corporate working, which does not provide for the same degree of either practice-linked or even family-linked working by HVs. As time went on, this made it harder to engage PHVs with the study in terms of both encouraging practices and women to participate. PHVs and GPs were vital to the running of the study. In particular, they were responsible for ensuring that the exclusion criteria for the study were adhered to. On the whole the notification system worked well but there were instances where women were not excluded who should have been (for example the two women whose English language skills should probably have made them ineligible). PHVs were also key in disseminating information about the study to pregnant and postnatal women. They gave out leaflets in antenatal classes and carried information packs with them on their postnatal home visits. GPs were less involved on a day-to-day basis and the study was designed so as to cause minimal extra work for primary care professionals. One of their major roles was to assess the real risk to women of entering the study who had revealed some degree of suicidal ideation – an answer of 'Sometimes' or 'Yes, quite often' to question 10 of the EPDS 'The thought of harming myself has occurred to me'. The MREC had made it a condition that women who expressed these thoughts had their suitability for the trial reviewed by their GP, mainly to ensure that severely ill women did not receive listening visits when antidepressants might have been the appropriate treatment. This process worked well and in the event very few women were excluded by GPs on the grounds that they were at a substantial risk. GPs and PHVs were also responsible for helping to ensure adherence to protocol. Hence, in the first 4 weeks we asked GPs not to prescribe antidepressants to women in the listening visits group unless necessary and we asked PHVs not to offer formal listening visits to women in either group. In the end GPs seemed to respond by excluding women who they thought might not benefit sufficiently if they were randomised to listening visits and PHVs were able to continue to provide their usual care with referral to the GP if they believed a more formal assessment was needed. It is worth noting that by the time the home visit to assess eligibility took place 94 women were already having some form of treatment for PND.

Recruitment

The consent process for the study was in two parts. This gave women the option to participate in the first screening phase with the use of their data on an anonymous basis but to opt out of the second eligibility (for the trial) phase which involved a

home visit and the potential to be randomised to antidepressants. As the consent form specifically stated that women could withdraw from the study at any time without giving a reason, it is not possible to define the reasons for declining further involvement. Hence, 155 (3.6%) did not complete the initial EPDS, and 113/3184 (3.5%) of those scoring < 11 and 181/989 (18.3%) of those scoring ≥ 11 declined to participate further. It is therefore possible that we lost a disproportionate number of women who were likely to fulfil diagnostic criteria for PND at the eligibility phase of the study (see above). Centre differences were again notable among the 969 women who were high scorers on the initial EPDS, ≥ 11, with women from Manchester less likely to have dropped their EPDS score to < 13, more likely to already be on treatment from their GP or HV and have had treatment for depression in the past.

At the time of requesting a home visit, 55 women were known to have improved such that an interim EPDS score was < 8. This method of reducing false positives before the eligibility home visit did not prove to be efficient and was dropped after the first 272 women. On the other hand, 88 women were already on treatment and therefore not eligible for the trial. We tried to encourage GPs and HVs in participating practices to desist from offering treatment to women who had screened positive on the EPDS but despite being able to offer a very tight timetable for randomisation, we lost these 88 women (9%). Home visits were therefore undertaken with 628 women of whom: 298 (47%) were no longer eligible for trial as their EPDS score was < 13, 54 (8.6%), although scoring ≥ 13 on the EPDS, did not have an ICD-10 diagnosis of depression, a further six had commenced treatment for PND, seven were excluded by their GP or HV (all of whom had ICD-10 depression on the CIS-R) and one was past the 26-week limit for entry to the trial. This resulted in 262 women being eligible for the trial, of whom eight refused to be randomised.

A great deal of research has been undertaken regarding the sensitivity and specificity of the EPDS as a screening instrument for PND.[112] Many studies have found the EPDS wanting in terms of satisfactory psychometric properties to support its routine use as a screening instrument. In this respect an interesting finding in this study is that of the 54 women who were high scorers on the eligibility EPDS, but did not have depression, 35 of them had other ICD-10 diagnoses, mainly some form of anxiety. There has been a tendency over the years to consider all postnatal illness under the umbrella term PND. But it may well be that a case could be made for its use if it was used to screen for mental illness more generally and more attention was paid to the characteristics of the patient's symptoms including anxiety. In addition, of the 298 women who were low scorers, < 13, on the eligibility EPDS, 66 of them completed a CIS-R and of these, 19 had an ICD-10 diagnosis, mainly in the anxiety–depression spectrum.

There are one or two further comments to be made about recruitment. We had initially aimed to recruit 468 women – assuming a 50% participation rate and a 10% prevalence of PND. Our recruitment figures were slightly over ambitious – although the London centre did meet this target. As a result of the very different practice demographics, the Manchester centre had to recruit 35 rather than the originally planned 21 practices. This resulted in reduced monitoring time by the research associate and possibly less commitment from practices in terms of adhering to the protocol. Information fed back to us by practice HVs led us to believe that the detail in the initial invitation pack, which had been requested by the MREC, was off-putting to a lot of women. With the agreement of the MREC we simplified the participation procedure, which ensured that we met our revised target sample size of 248. We also overestimated the prevalence of PND – we used the lower end of the widely quoted 10–15% range[6] for our sample-size calculation. In the event, the prevalence in the women available to enter the trial was only 6.5%. However, the 10–15% figure largely comes from studies that have not used a diagnostic instrument and when these more robust criteria are used the prevalence drops to about 7%.[6] We used the EPDS followed by the CIS-R to ensure that women eligible for the trial met diagnostic criteria for ICD-10 depression, which is the morbidity level recommended by the NICE guidelines for the use of antidepressants.[53] In addition we 'lost' quite a large number of women who would have been eligible for the trial who were already on treatment (94) or excluded by their GP (seven, all of whom had ICD-10 depression on their CIS-R). If all these women had been eligible and recruited, the prevalence of PND would have been 8.7%. Finally, there were 35 women whose EPDS score was ≥ 13, but whose CIS-R determined an ICD-10 diagnosis other than depression. It is likely that in studies that have not used a second-stage instrument these women might have been described as suffering from PND and in this case our overall prevalence would have been 9.6% – not so far from the 10% estimate in our protocol. It

is well known that different assessment methods can lead to different estimates for the prevalence of depression. The CIS-R was used in the UK Psychiatric Morbidity surveys carried out in 1993 and 2000. Among women of childbearing age, the prevalence of depression in those surveys was between 3 and 4%.[2] It is possible that the higher prevalence reported here resulted from response bias, as only about 40% responded to the initial request. The information sheet was asking for people to join a trial on PND so many women who did not feel depressed may not have responded.

It is important to look at the demographic characteristics of the women who were confirmed as suffering from PND and were therefore randomised to the trial compared with the demographic associations noted in the literature. In this study, women with PND who were randomised were less likely to be married or living with a partner and tended to have less social support. They were also more likely to report previous antidepressant treatment, to have fewer qualifications, and to be in routine occupations. This pattern of associations looks very similar to that described in Chapter 1 (see Epidemiology of postnatal depression). We cannot however assume that our findings can be extrapolated to women from other ethnic groups who formed only a small minority of the trial population.

Strengths of the study

Despite the generally rather adverse conditions for primary care research that requires substantial involvement from service practitioners and the very stringent criteria laid down by the MREC in terms of information for patients, the study eventually randomised 254 women with a reasonably good balance of characteristics across the three centres and a good balance of characteristics between the two randomised groups. This study was extremely rigorous in determining a diagnosis of PND, using a two-stage assessment process that resulted in an ICD-10 diagnosis of depression as the entry criterion rather than only a high score on a screening questionnaire, in this case the EPDS. Using simply the latter would have resulted in women entering a trial, one arm of which was the prescription of antidepressants, when those women might either not have had depression of sufficient severity or have had a mental-health problem other than depression. The study used self-report questionnaires for the outcome measures to reduce observer bias – it was not possible to keep group allocation blind in this study. The listening visits were delivered by a single specially trained HV at each centre (except in Bristol) which ensured consistency within centres. The research HVs received training in this intervention from a well-known and well-respected national resource and had regular updates with one of the professionals who developed this type of counselling for women with PND and had regular supervision for the duration of the trial. A major strength of the trial was its pragmatic nature. The protocol required that for the first 4 weeks women randomised to the antidepressant group did not receive listening visits and that those randomised to listening visits did not receive antidepressants. To a large extent this was adhered to but after the 4-week assessment, women taking antidepressants were allowed access to listening visits as well as or instead of their drug treatment – 50% of them took up this option. In the listening visit group, women were allowed to have antidepressants at any time during the ensuing 14 weeks regardless of how many listening visits they had. Thirty-three per cent of women for whom there was data reported taking antidepressants as well as having listening visits. Essentially this is what happens in routine general practice – women will see their GP and their HV when they have symptoms of depression postnatally, each of whom will offer a variety of management options. One strength of the study is that randomisation to antidepressants appears to be effective at which point patient choice takes over. Each person's treatment experience then become individual and so cannot be captured in the formal aspects of a trial. However, it suggests that offering antidepressants to this patient population helps them get better more quickly. For a trial of this nature there was remarkably little attrition (overall 86% follow up at 4 weeks and 81% at 18 weeks) although not unexpectedly there was more attrition in the antidepressant group. It is worth noting that there were no notifications of adverse events in either arm throughout the trial.

A further strength of the trial is the nested qualitative study which illustrates the complexity of making the diagnosis and managing women with PND in primary care. Strengths of the qualitative study have already been outlined in Chapters 4 and 5. Briefly, the use of qualitative methods allows practitioners to raise issues that are of concern to them, and an inductive approach ensures that findings are related to the views articulated. The data were gathered from GPs and patients drawn from a large geographical area (nine PCTs). Interviewing women 1 year after the birth of their

child meant participants had to remember past views and events, making their accounts open to recall bias. These women were also individuals who had remained in the trial and therefore might have held a particularly positive view of RESPOND or the treatment they had received. However, interviewing 1 year after the birth of the study child did allow us to assess what the women's treatment experiences had been during this time period, and to identify processes or situations that had influenced their views about treatment. Using researchers from different professional and academic backgrounds is a recognised technique for increasing the trustworthiness of the analysis.[105]

Limitations of the study

The original commissioning brief suggested a trial design incorporating a placebo arm. However, although this might have enabled a simpler statistical analysis at the 18-week assessment, the use of placebo was felt unlikely to meet with the approval of women, primary care colleagues or the MREC given the current state of knowledge about the treatment of PND. There is good evidence that antidepressants are better than placebo in people who meet the criteria for depression. This study provides very strong evidence that antidepressants lead to a substantial improvement in the first 4 weeks compared with GSC. One of the main limitations of the trial was that its pragmatic design resulted in many women switching arms and it is therefore very difficult to pick out the active ingredients, as those who got better did not necessarily go for more complex treatment, or in some cases any treatment, whereas those not improving did. Indeed, the lack of evidence for differences at 18 weeks is probably the result of a combination of reduced power consequent on the original sample size not being achieved and a genuinely reducing effect over time, exacerbated by this considerable degree of switching across the two interventions by the later follow-up, especially in terms of its effect on the CACE analyses.

The study as designed was unable to include women for whom English was not a first language or at least for whom completion of the questionnaires unaided or participation in listening visits would not be possible. In a multicultural society, research of this nature is always difficult mainly because of the availability and expense of translating questionnaires and providing translators or therapists. This was a particular issue for the Manchester centre. The study design, which required a two-stage consent procedure, was clearly quite difficult for some women to understand and the amount of paperwork that we were required to present to women was more than we could reasonably expect women with a new baby, especially women who were depressed, to cope with. This resulted in poor recruitment early on which was rectified by resubmission to the MREC requesting a reduction of the information load for women. This resulted in improved recruitment rates.

We took a very pragmatic approach to the prescription of antidepressants, particularly with respect to asking GPs to adhere to the protocol. This was a deliberate strategy designed to maximise the usefulness and acceptability of the trial. However, there were some GPs who when consulted by a woman who had been randomised to antidepressants used their own clinical judgement and perhaps even prejudice and did not prescribe. This meant that fewer women than we had hoped actually received antidepressants, though it might also reflect the women's reluctance to take antidepressants. On the other hand, there were GPs who for a variety of reasons seemed to be unaware of the study (that their practice had agreed to participate in) and prescribed antidepressants to women who were in the process of being screened for eligibility for the trial. This hindered our recruitment of depressed women. We encountered some difficulties in the collection of data from practices as the result of certain practices not finding the consent forms that had been agreed by the MREC satisfactory and therefore invalid. This highlights a specific problem in primary care research whereby each practice can take its own view on the necessary procedures required to be in keeping with the Data Protection Act.

One criticism that could be made of the listening visits intervention is that we did not attempt to check fidelity to the method. The RHVs received high-quality training for this psychosocial intervention with the group who originated the method. They each had the training manual and other necessary papers to ensure that they were fully conversant with the details. The original RHVs were all women with several years in health visiting and had a particular interest in being able to step outside their routine post to be able to focus on women's mental health in the context of PND. Unfortunately, because of ill health the Bristol RHV had to leave her post early and until a replacement RHV could be found, an experienced counsellor from an organisation specialising in women's

mental health, and therefore used to seeing women with PND, filled this gap. The RHV who took on the substantive post, although not attending the Keele course, had for many years provided listening visits as part of her core post and also had a counselling qualification. As a result of the non-directive nature of this psychosocial intervention, it is unlikely that any major or systematic impact on effectiveness resulted.

There were discussions early on as the protocol was refined as to whether we should attempt to tape listening visit sessions across the three centres. The advice we had was that this was unlikely to be of benefit to the study in terms of the quality and consistency of the intervention and that we might find that women who wished to talk about very personal issues would find it off-putting and decline to continue. In the event we ensured that the RHVs had regular training updates as a group and that they had regular one-to-one supervision with a local mental-health professional, usually a community psychiatric nurse.

Finally, in concentrating on the major aims of the trial we missed an opportunity to gather information on emerging issues in the field. In particular we made no attempt to collect data on the prevalence of domestic violence, which we know to be linked to the development of PND.[37] Informally, however, we know from discussions with the RHVs that disclosures about domestic violence were made to them during the listening visits. These were made in confidence and no further details were made available to the research team.

A limitation of the qualitative study with health professionals was that we only interviewed HVs and GPs who were already involved with the RESPOND trial and it seemed difficult to engage with London GPs even though they were signed up to the main trial. PCTs were invited to participate in RESPOND if they did not have a well-established pathway of care for PND within the PCT, and therefore participating PCTs may have poorer provision of services and attitudes of the health professionals working in these areas will reflect this. The findings may not be representative of (even neighbouring) PCTs who may have developed a PND strategy and services for this group of patients. Women with PND may refuse to take part in trials because of their concerns about antidepressants,[54] and within our study we had evidence of this, we might have sampled from a biased group of women.

Interpretation of the findings in the light of previous research

Randomised controlled trials evaluating antidepressants

The interpretation of the study findings in the light of previous research is difficult because there are very few similar trials with which to compare the results. There are only three previous RCTs evaluating the use of antidepressants in the management of PND, one in the UK and two in the USA; only two of these compared an antidepressant with a psychological therapy: fluoxetine or placebo with cognitive behaviour counselling (either one or six sessions)[54] and paroxetine compared with paroxetine plus CBT.[56] In the UK study, a similar methodology to the current trial was employed using the EPDS and the CIS-R albeit with different thresholds for eligibility. The antidepressant was constrained to fluoxetine and the counselling was based on the CBT model. Significant improvement was seen in all four treatment groups. The improvement with fluoxetine was significantly greater than with placebo and the improvement after six sessions of counselling was significantly greater than after a single session. However, there did not seem to be a significant improvement for women in receiving counselling (six sessions) as well as fluoxetine. Many women were noted to be reluctant to take an antidepressant for PND. The study by Misri *et al*.[56] was very small, randomising only 35 women who had postpartum depression and comorbid anxiety. They found no difference between the two arms with about 60% having at least a 50% reduction in EPDS score at 12 weeks post randomisation. This trial, albeit lacking in power, confirmed the findings of the UK trial,[54] in that adding CBT to an antidepressant does not seem to increase effectiveness and would certainly be more costly. The final trial compared sertraline and nortryptyline[55] an SSRI and a tricyclic antidepressant. There were no differences between the two classes of drug, 46% versus 56% responding at 4 weeks, but there were more dropouts with the SSRI. The methodological quality of these three trials was regarded as poor in the recent NICE guidance.[45] None of these trials took a pragmatic approach to the choice of antidepressant nor did they compare antidepressants with GSC. Our ITT analysis found a significant, 25%, improvement in the antidepressant arm compared with usual care at 4 weeks (45% versus 20%), which at 18 weeks had

reduced to 11% (non-significant difference) when compared with listening visits (62% versus 51%). The pragmatic nature of this study makes it hard to draw direct comparisons with previous studies but there is good evidence for the effectiveness of antidepressants at both follow-ups, even though the superiority of antidepressants at 4 weeks is attenuated by 18 weeks.

The evidence for the treatment of moderate depression with antidepressants in women outside the postpartum period is well made[53] and so it is not surprising that antidepressants have been found to be effective in this trial and others. Given the lack of evidence for a distinct hormonal or other aetiology for PND, its responsiveness to antidepressants is in line with it being a typical depressive disorder. There are a number of possible mechanisms whereby gender may influence treatment response. Drugs with effects on the serotonergic system may be relevant for younger women because serotonergic agents have demonstrated efficacy in disorders such as premenstrual dysphoric disorder.[113] Second, the presence of atypical depression, for example with weight gain rather than loss, may modify treatment responsivity and women are more likely to present with atypical depressive symptoms.[114] Another explanation is that female reproductive hormones may play a permissive or inhibitory role in antidepressant activity. For example, oestrogen may enhance serotonergic activity.[115] There has been one trial finding some evidence in favour of oestrogen as a treatment for PND.[116] However, PND is different, at least in some ways, in that it occurs at a particular time and has repercussions not only for the mother but also for her infant.[27,31,38] The impact on the infant may be the result of biological as well as psychosocial mechanisms. The other issue that makes PND and considerations about its treatment with antidepressants special is the need to consider risk to the infant if the mother is breastfeeding. Several studies have been undertaken to address this risk – the overall conclusion being that most antidepressants are safe for infants, the exceptions being fluoxetine (because of its long half-life), citalopram and doxepin.[59]

Randomised controlled trials evaluating psychosocial interventions

There is much more evidence regarding the effectiveness of different psychological and psychosocial interventions for PND.[62] In this systematic review there was significant heterogeneity among the four trials evaluating non-directive counselling; however, overall there was evidence of significant benefit in reducing depressive symptomatology both immediately post-treatment and at 1 year. In two trials that compared non-directive counselling (listening visits) with CBT there was no difference at the final assessment.[71,72] In the first of these trials, which had several methodological flaws, there was no difference between the proportions free of depression as assessed by the Structured Clinical Interview for DSM-III-R (SCID)[117] at 4.5 months (54% with non-directive counselling and 57% with CBT).[71] In the second trial, at 6 months, there was no difference in mean EPDS score between the women who received CBT and those who received person-centred counselling.[72,72] Non-directive counselling is a form of counselling that is based on the understanding that, in many situations, people can resolve their own problems without being provided with a solution by the counsellor. In particular, the counsellor's role is to encourage the person to express their feelings but not suggest what decision the person should make. By listening and reflecting back what the person reveals to them, the counsellor helps them to explore and understand their feelings. With this understanding, the person is able to make the decision that is best for them. This treatment modality may be an important option for mothers with mild to moderate postpartum depression. Previous trials have demonstrated the feasibility of population-based screening and the application of home visiting using trained health professionals. The results from this study add to the evidence base for the effectiveness of HV-delivered listening visits, even for women with moderate to severe depression, where at 18 weeks the improvement in women who received listening visits was very similar to that in women who received antidepressants.

The qualitative work demonstrated that many women viewed listening visits as a preferred intervention and some expressed scepticism about the value of antidepressants. However, the study has demonstrated that antidepressants are an effective treatment for depression, at least in the short term, despite these rather negative attitudes.

What the qualitative studies add

The qualitative studies describe the difficulties in making the diagnosis of PND in primary care with

women and provide further evidence of the need to spend time negotiating a diagnosis of depression with a woman. Women with PND may view listening visits as helpful but insufficient to manage their depression. The extent to which women perceive listening visits as beneficial appears to be linked to the causes of their depression, the way in which the visits are delivered and by whom. Women's views of antidepressants can change in response to their treatment options and experiences, the views of friends and relatives and their contact with health professionals. GPs need to assess women's concerns about antidepressants before prescribing them and should provide regular follow-up for women on medication. This should lead to greater treatment adherence and hence to earlier resolution of symptoms. Women described making a conscious decision about whether or not to disclose their feelings to their GP or HV. Health professionals described strategies used to hinder disclosure and described a reluctance to make a diagnosis of PND, as they had few personal resources to manage women with PND themselves, and no services to which to refer women for further treatment.

Ongoing organisational changes within primary care, such as the implementation of corporate working by HVs, was reported to affect the care provided to women after delivery, which in turn impacts on the diagnosis and management of PND. Improving the detection and management of PND in primary care requires recognition of the context in which women consult, and system changes that ensure that health professionals work in an environment that can facilitate disclosure and that the necessary resources for management are available.

Implications for further research

For a variety of reasons we found it difficult to recruit our original target number. This is not uncommon in mental-health trials in the primary care setting, particularly where a drug treatment is being compared with a psychological treatment approach. Yet in everyday general practice antidepressants are prescribed very commonly – very often at the behest of the patient. This dichotomy needs exploring further, possibly using qualitative methods – the effectiveness of antidepressants in many instances cannot be denied but further refinement of specific populations for whom they are appropriate, which drug and at what dose need further investigation.

In the case of PND there needs to be further work looking at the symptomatology in terms of the anxiety–depression spectrum. Just as there has been recognition of the importance of antenatal depression as a diagnostic entity and the need for research to investigate treatment, there is a need to investigate the diagnostic spectrum in PND and ensure, at least from a pharmacological point of view, that drugs with the correct profile are being used. Considering the effectiveness of non-directive counselling (listening visits), the current trial for methodological reasons used RHVs and not women's own PHVs. A trial comparing the delivery of listening visits by these different professionals might be worthwhile, particularly with respect to the issues of delay in accessing treatment and cost-effectiveness. With respect to other psychological treatments for PND, the use of CBT, now likely to be made more widely available through Improving Access to Psychological Therapies (UK)[118] needs to be assessed more closely – in terms of mode of delivery, e.g. if in person by whom – usual PHV, RHV or generic counsellor, through self-directed computer programmes or online.[119] One result of our extension request from the HTA, was to drop the 44-week assessment and the associated cost-effectiveness analysis. We still think it is important to investigate the cost-effectiveness of antidepressants compared with listening visits. We also believe that it is important to have information on the longer-term outcome for these two interventions. The screening phase of this study revealed a significant amount of postnatal psychiatric morbidity other than depression. A formal more inclusive epidemiological study of postnatal mental illness needs to be undertaken to ensure that primary care professionals are aware of the diversity of disorder and have the training and resources to offer treatment not only for depression but for some of the other common mental disorders that occur in pregnancy, particularly anxiety. The psychometric properties of the commonly used screening methods for PND need to be assessed for disorders other than depression, followed by trials to evaluate the effectiveness of treatments used for PND in the other common postnatal psychiatric disorders.

Conclusions

This trial successfully randomised 254 women with PND into two different treatment groups and assessed outcomes with good follow-up rates at 4 weeks and 18 weeks post randomisation. Antidepressants offer significantly greater

improvement compared with GSC at 4 weeks, equivalent to what NICE calls watchful waiting.[53] At 18 weeks women randomised to antidepressants still seem to have an increased chance of improvement compared with those randomised to listening visits although this difference is no longer significant. However, by 18 weeks, many of the women in the group receiving listening visits first were also receiving antidepressants. As this was a pragmatic trial it allowed women who started to improve spontaneously or improve early on their allocated treatment to make a choice to wait and see as to whether they should stop their allocated treatment or swap to the other group whereas those not improving tended to add treatments. The results from the analysis of the secondary outcome measures tended to be in the same direction as those of the primary outcomes, which lends strength to the reliability of the conclusions. GPs can be reassured that prescribing antidepressants at about 10 weeks postnatal gives a much better chance of improvement over the next 4 weeks than GSC. The nested qualitative studies found that both treatments are acceptable to women although there was a preference for listening visits as a first choice. However, women did report that their resistance to taking antidepressants was lessened by the experience of having listening visits, which in many cases were not sufficient to induce remission of symptoms and led women to recognise their need for further help such as antidepressants. The role of the RHV may well have been instrumental in facilitating this change of opinion. The interviews with GPs and HVs revealed a rather disturbing lack of collaborative working in the care of postnatal women with neither group believing that the diagnosis of PND was their responsibility. The move to corporate working with its loss of collocation may be the cause of this finding. Systems of working can influence clinical care and need to be taken into consideration in any reorganisation of services. PND remains a prevalent mental-health problem with important negative consequences for mother and child. Most of the morbidity is expressed in the primary care setting. PCTs must ensure that their commissioners make robust arrangements for the care of women suffering from PND particularly with the implementation of Improving Access to Psychological Therapies (UK).[118]

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Contribution of authors

Deborah Sharp (Professor of Primary Health Care) was the Chief Investigator, wrote the original trial protocol, was Principal Investigator in Bristol and oversaw the study and the writing of the draft final report. Carolyn Chew-Graham (Senior Lecturer, Primary Care) was a Principal Investigator, contributed to the original protocol, cosupervised the trial in Manchester and was responsible for the qualitative study with health professionals, supervising the data collection, analysing the data,

and drafting the relevant sections of the report. Andre Tylee (Professor of Primary Care Mental Health) was a Principal Investigator, contributed to the original protocol, cosupervised the London arm of the trial and contributed to the report. Glyn Lewis (Professor of Psychiatric Epidemiology) was a Principal Investigator, contributed to the original protocol, cosupervised the trial co-ordinators in Bristol and contributed to the final report. Louise Howard (Senior Lecturer, Women's Mental Health) was a Principal Investigator, contributed to the original protocol, cosupervised the London arm of the trial and contributed to the draft final report. Ian Anderson (Professor of Psychiatry) was a Principal Investigator, contributed to the original protocol, cosupervised the Manchester arm of the trial, provided psychopharmacological expertise and contributed to the draft final report. Kathryn Abel (Senior Lecturer, Psychiatry) was a Principal Investigator, contributed to the original protocol, cosupervised the Manchester arm of the trial, contributed expertise in perinatal psychiatry and women's mental health and contributed to the draft final report. Katrina Turner (Lecturer, Primary Health Care) was responsible for the qualitative study with the women, supervised the research associate, analysed the data, and drafted the relevant Methods and Results sections of the report. Sandra Hollinghurst (Health Economist) was responsible for managing the health economic data collection and analysis and drafting the relevant sections of the report. Deborah Tallon (Research Associate, Psychiatry) contributed to data collection in Bristol and the draft final report. Anne McCarthy (Trial Co-ordinator June 2004 to November 2006) was responsible for setting up the study in all three centres, managing the data collection and contributing to the draft final report. Tim Peters (Professor of Primary Care Health Services Research) was a Principal Investigator and the trial statistician, contributed to the original protocol and the draft final report.

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Chew-Graham C, Sharp D, Chamberlain E, Folkes L, Turner KM. Disclosure of symptoms of postnatal depression, the perspectives of health professionals and women: a qualitative study. *BMC Fam Pract* 2009;**10**:7. www.biomedcentral.com/1471–2296/10/7.

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Turner, KM, Sharp D, Folkes L, Chew-Graham C. Women's views and experiences of antidepressants as a treatment for postnatal depression: a qualitative study. (Accepted for publication subject to revision, *Family Practice*).

Presentations relating to this research project

Turner K, Chew-Graham C, Folkes L, Sharp D. Women's experiences of listening visits as a treatment for postnatal depression: a qualitative study. Oral presentation at the Society for Academic Primary Care's South West conference, Winchester, March 2009.

Turner K, Chew-Graham C, Folkes L, Sharp D. Women's experiences of listening visits as a treatment for postnatal depression: a qualitative study. Oral presentation at the West Hub Mental Health Research Network conference, Bristol, February 2009.

Sharp D, on behalf of the RESPOND team. The epidemiology of postnatal depression – data from phase 1 of an RCT based in UK general practice. Oral presentation at the Annual Scientific Meeting of the Society for Academic Primary Care, Galway, July 2008.

Turner K, Folkes L, Sharp D, Chew-Graham C. Women's views and experiences of antidepressants as a treatment for postnatal depression: a qualitative study. Oral presentation at the Annual Scientific Meeting of the Society for Academic Primary Care, Galway, July 2008.

Sharp D. The epidemiology of postnatal depression – data from phase 1 of an RCT based in UK general practice. Oral presentation at the Mental Health Research Network conference, London, 2008.

Turner K, Folkes L, Sharp D, Chew-Graham C. Women's views and experiences of antidepressants as a treatment for postnatal depression: a qualitative study. Oral presentation at the Society for Academic Primary Care South West conference, Warwick, March 2008.

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Appendix 1

Consort Statement 2001 checklist

PAPER SECTION and topic	Item	Descriptor	Where reported
TITLE and ABSTRACT	1	How participants were allocated to interventions (e.g. 'random allocation', 'randomised', or 'randomly assigned')	Title and abstract
INTRODUCTION Background	2	Scientific background and explanation of rationale	Chapter 1
METHODS			
Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected	pp. 8–12
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered	pp. 12–14
Objectives	5	Specific objectives and hypotheses	p. 5
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (e.g. multiple observations, training of assessors)	pp. 14, 15
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules	p. 16
Randomisation – Sequence generation	8	Method used to generate the random allocation sequence, including details of any restrictions (e.g. blocking, stratification)	p. 9
Randomisation – Allocation concealment	9	Method used to implement the random allocation sequence (e.g. numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned	p. 9
Randomisation – Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups	p. 9
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated	p. 9
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses	pp. 16–18
RESULTS			
Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analysed for the primary outcome. Describe protocol deviations from study as planned, together with reasons	pp. 23–39, Appendices 15 and 16
Recruitment	14	Dates defining the periods of recruitment and follow-up	pp. 7, 8
Baseline data	15	Baseline demographic and clinical characteristics of each group	pp. 30–33
Numbers analysed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by 'intention-to-treat'. State the results in absolute numbers when feasible (e.g., 10/20, not 50%)	pp. 31–33
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (e.g. 95% confidence interval)	pp. 39–51

Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those prespecified and those exploratory	pp. 51, 52
Adverse events	19	All important adverse events or side effects in each intervention group	pp. 89, 90
DISCUSSION			
Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes	pp. 83–93
Generalisability	21	Generalisability (external validity) of the trial findings	pp. 86–89
Overall evidence	22	General interpretation of the results in the context of current evidence	pp. 91–93
www.consort-statement.org			

Appendix 2

Patient screening invitation letter from general practitioner

On GP practice headed paper

_ _/_ _/200_

Dear

RESPOND: a study to evaluate treatments for post-natal depression (PND)

Participant Information sheet

Our practice is helping the University of Bristol in a multi-centre research study comparing different treatments for postnatal depression (PND). **We have agreed to contact all our patients who have recently had a baby to ask if they are willing to take part, regardless of whether they have PND or not.** Receiving this letter does not mean that you have PND and if you do not wish to be a part of this study, it will in no way affect your usual treatment.

Study purpose and reason for invitation

About 10% of women suffer from PND. However, it is unclear as to which treatments for PND are the most effective. The Department of Health has asked us to compare different types of treatment for PND. The study is designed so that you will have the opportunity to try the second treatment if your response to the first is insufficient. The treatments being compared are antidepressant drug therapy and health visitor "active listening" visits. We are inviting all new mothers, regardless of whether they have PND or not, to take part in the study.

What will happen if I do take part?

1. We are asking you to complete the enclosed questionnaire and consent form and return it to us.
(These data will be used anonymously to measure the rate of PND among all new mothers).
2. If you have a high score on this questionnaire, we would like to visit you at home and ask you to complete a second questionnaire.
3. If at the home visit you continue to have a high score on the questionnaire, we will invite you to take part in the main study and allocate you (randomly) to one of the two treatments.
4. Over the following 10 months we will ask you, on three occasions, to complete another questionnaire.

Do I have to take part?

It is up to you to decide whether or not to take part. If you decide to take part, please complete the enclosed questionnaire and consent form. All information collected will be stored anonymously and securely and no-one will be able to identify you from the published findings. Once the study has been completed our records of your name and address will be destroyed. Remember you are free to withdraw from the study at any time without giving a reason or affecting your medical care.

Your GP retains full responsibility for you and the routine care you receive. If you take part in the study, your Health Visitor will be informed of the score from your questionnaire.

If you require a more extensive information sheet **please contact the Respond Team in Bristol on (0117)** xxxxxxx or contact the lead researcher in Bristol, Professor Debbie Sharp, on (0117) xxxxxxx or your General Practitioner or Health Visitor.

Thank you very much for your time to consider taking part in this study.

Yours sincerely

GP name

This is a collaborative study between the Universities of Bristol, Manchester and London (Institute of Psychiatry) funded by the Department of Health.

Version 5 01122005

Appendix 3

Patient consent form for screening

RESPOND

Centre

Practice

Practice unique identifier

Participant's unique identifier [ ]

CONSENT FORM FOR **YOU** TO KEEP

PATIENT CONSENT FORM A

Antidepressant drug therapy vs a community based psychosocial intervention for the treatment of moderate postnatal depression: a pragmatic randomised controlled trial

I confirm that I

- have read and understood the patient information sheet (version 5, 01122005)
- have received enough information about the study
- have had the opportunity to discuss the study and ask questions and have received satisfactory answers to my questions (please phone the **Respond Team on (0117)** xxx xxxx if necessary)

YES / NO

I understand that I am agreeing to

- complete the Edinburgh Postnatal Depression Scale questionnaire and return it to the study centre
- allow the score from it to be used anonymously for statistical purposes
- allow the study centre to contact me again if necessary
- be free to withdraw from the study at any time, without having to give a reason and without affecting my current or future medical care
- the details of my participation up until the time of withdrawal being stored anonymously on file and may be used in the final analysis of data.

YES / NO

- I agree to participate in this study **YES /NO**

Signed_____

Name (block letters)_____

Date_____

(ISRCTN 16479417)

Appendix 4
Self-harm protocol

1. RESPOND SELF-HARM RISK PROTOCOL

1.1 OVERVIEW

Risk of self-harm is defined as:

a) a score of 2 or 3 in the relation to question 10 on the EPDS ***'The thought of harming myself has occurred to me:'***. An answer of ***'Sometimes'*** scores 2 and an answer of ***'Yes, quite often'*** scores 3.
b) The outcome of the suicide intent questions on the CIS-R is:
   i) **CIS-R SUICIDE INTENT:** Patient feels life isn't worth living
   ii) **CIS-R SUICIDE INTENT:** Patient has had suicidal thoughts
   iii) **CIS-R SUICIDE INTENT:** Patient has had suicidal plans

Whenever these instances occur, or if at any time, the researcher believes that there is a significant risk of a patient who is participating in the study self-harming that has not been communicated to their GP, the researcher will consult the Centre's PI or nominated deputy if unavailable.

The PI or deputy will examine the patient's data and if it is considered necessary, will assess the patient. If it is concluded that there is a significant risk, the patient's GP will be notified **with or without** the patient's consent. However, the PI or his deputy would contact the GP without first assessing the patient him/herself if the situation was urgent, again with or without the patient's consent.

1.2 ACTION

At EPDS-2

On receipt of the EPDS-2 questionnaire, the research associate will screen woman's response to item 10 relating to self-harm to assess risk. Regardless of consent status or total EPDS score, women who score 2 or 3 should be contacted by the researcher and the Self-harm Pro forma outlined below should be actioned. If for any reason the woman cannot be contacted, the researcher should inform the centre's PI or nominated deputy to discuss.

At the Home Visit interview

After the woman has completed the baseline questionnaires, the research associate will screen woman's response to item 10 on the EPDS0 questionnaire and the outcome of suicide intent questions on the CIS-R questionnaire. If risk of self-harm as defined in 1.1 is evident, the Self-harm Pro forma below should be actioned regardless of whether the woman is eligible to continue to randomisation.

Women eligible to continue in study:

If the woman agrees for the information to be passed to GP, randomisation should be delayed until woman's response has been discussed with GP and the GP is happy for the woman to participate in the study.

If the woman does not agree for information to be passed to GP, randomisation may proceed but the researcher should delay randomisation until they discussed with PI if they have any concerns about the woman's intent.

4-, 18-, and 44-week follow-up points after randomisation

On receipt of an EPDS questionnaire, the research associate will screen woman's response to item 10 relating to self-harm to assess risk. Women who score 2 or 3 should be contacted by the researcher and the Self-harm Pro forma outlined below should be actioned. If for any reason the woman cannot be contacted, the researcher should inform the centre's PI or nominated deputy to discuss.

.

RESPOND SELF-HARM ACTION PRO FORMA

If at any time-point during the study period, a woman expresses risk of self-harm is as defined above the following procedure MUST be implement:

a) The RA should contact the woman as soon as possible and advise her to discuss these thoughts with her HV/GP. If this is the first-time that woman has expressed these thoughts or if the GP has not previously been informed, offer to pass this information to the HV/GP concerned. (see suggested script).
b) If the woman agrees, the HV/GP should be contacted by telephone to discuss and giving the option of withdrawing the woman from the study.
c) If the woman refuses to give her permission, the researcher should notify the PI who will then decide the next course of action.
d) The attached ACTION PRO FORMA form should be completed by the researcher, signed by the PI, and stored with the woman's confidential data.
e) If the woman cannot be contacted, the RA should inform the centre's PI or nominated deputy to discuss.

Suggested script

Thank you for completing the questionnaire we sent recently. It is a big help and it allows us to see how women feel in the weeks/months following the birth of their baby.

EPDS-2 script e.g.
The answers you gave suggested that you were feeling a bit down when you filled it in. I was wondering whether I could come and see you at home, to find out how you are feeling now. This will involve you completing a couple more questionnaires to see how you are feeling now. If you are still feeling low, the next part of our study might be suitable for you.

You may remember that the next part of the study is comparing two treatments that are helpful for women who are feeling low after having a baby. I can go through the study in more detail when I see you at home, but did you have any questions about it now?

When would be a convenient time to come and visit you? The appointment shouldn't take more than an hour.

I notice that during the last few weeks you have had thoughts of harming yourself and I wondered how you are feeling now?

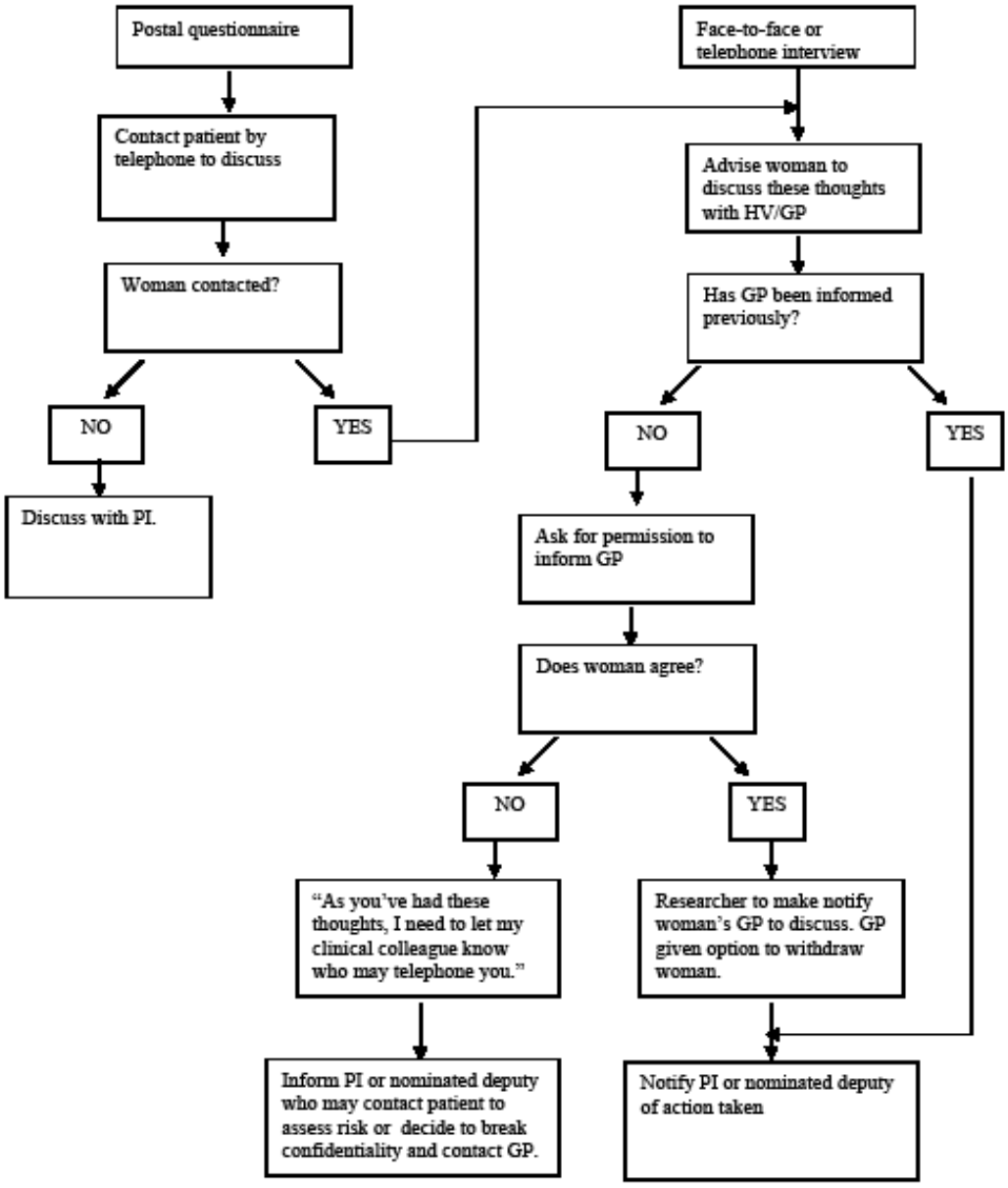
I will pass this information on to my clinical colleague in charge of the study and she/he may want to call you just to check that you are ok. It is also a good idea to talk to your own doctor or health visitor about these feelings, but sometimes it is a bit difficult to bring the subject up. If you like I can contact your health visitor or GP and let them know how you are feeling.

RESPOND SELF-HARM ACTION PRO FORMA

Risk of self-harm is defined as a score of 2 or 3 in the relation to question 10 on the EPDS or the outcome of the suicide intent questions on the CIS-R is one of the following:

a) CIS-R SUICIDE INTENT: Patient feels life isn't worth living
b) CIS-R SUICIDE INTENT: Patient has had suicidal thoughts
c) CIS-R SUICIDE INTENT: Patient has had suicidal plans

If at any time point during the study period risk of self-harm has been expressed by a woman either in postal, telephone or face-to-face interview then the following action must be taken and recorded by the researcher:



*** Nominated Bristol PI Debbie Sharp 0117** xxx-xxxx **& Deputy Glyn Lewis 0117** xxx-xxxx

Appendix 5

Patient information sheet for baseline home visits

RESPOND

Professor D. Sharp
Academic Unit of Primary Care
University of Bristol
Cotham House
Cotham Hill
Bristol BS6

(0117) xxxxxxx

05 August 2008

Patient Information Sheet B (i)

Antidepressant drug therapy vs a community based psychosocial intervention for the treatment of moderate postnatal depression: a pragmatic randomised controlled trial
RESPOND
ISRCTN 16479417

Thank you for helping us with the first part of this study and completing the EPDS forms. As discussed on the phone your EPDS score showed that you might be experiencing symptoms of postnatal depression so we have arranged for our research associate, Laura Bridges, to come and visit you at home on

Date: at Time:

If you are unable to make this appointment, please could you call the RESPOND team on 0117 xxxxxxx or 07795 xxxxxx to arrange a more convenient time for her to visit?

What happens now?
If an updated EPDS at the home visit and your answers to the further questions show you are experiencing symptoms of postnatal depression, we would like you to participate in our study comparing antidepressants and counselling from a Health Visitor in the treatment of postnatal depression. Antidepressants and Health Visitor counselling are both accepted treatments for postnatal depression. This study aims to increase our understanding of under what circumstances and for which women these two treatments are most effective.

The study design allows everyone to try both treatments – antidepressants and counselling. However, the order in which women receive the treatments will differ. We will randomise women, effectively like tossing a coin, to see which treatment is offered first. If after a

certain time you do not respond to that treatment, you will be offered the alternative treatment.

The type of antidepressant will be agreed between you and your doctor. He or she will follow you up at monthly intervals whilst you are taking the tablets.

The counselling will begin four weeks after seeing the Research Associate and comprise a course of 4 to 8 sessions from a special Health Visitor who will come to your home. She will help you talk about your difficulties and look at ways of overcoming them. Whilst in the study, your GP will be able to offer additional treatment as s/he thinks fit.

We will ask you to complete self-report questionnaires 4, 18 and 44 weeks after entering the study. At about the time of your baby's first birthday, we would like to visit you at home to see how you are feeling and do a brief developmental assessment of your baby. The assessment of the baby will be looking at how they are progressing in terms of sitting up, crawling, holding and playing with small objects, starting to talk, etc.

The questionnaires will focus on how you are feeling, how you are coping at home and looking after your family, and your relationship with the baby and your partner. They will take about 30-40 minutes to complete.

Having a baby also has an impact on your partner and their views on how you are feeling are also important. We hope that you will allow us to contact your partner so they can fill in some very similar questionnaires, at the same time points.

We would need to look at the GP records for you and your baby to count up the number of consultations, referrals and prescriptions you and he/she have had since the baby was born.

[1]Finally, we will ask you to agree to possibly being approached by our Research Associate to be interviewed so we may hear your views on the treatment of postnatal depression.

Do I have to take part?
It is up to you to decide whether or not to take part. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a further consent form. If you decide to take part, you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive. If you do not wish to take part we will suggest that you consult your GP to see if you need treatment.

What about antidepressants and breastfeeding?
The evidence shows that the amount of antidepressants that get into breast milk and into the baby is so low it is unlikely to do any harm. Babies who have been in the womb or been breastfed, while their mothers have been on antidepressants, have had no serious problems reported. However, we recognise that this might be an area of concern. If you are breastfeeding, your GP will talk to you about any advantages and disadvantages of antidepressants in this situation, and which antidepressant would be the best one to take. You can then decide about participating in the study where you have a 50:50 chance of being offered an antidepressant as the first treatment.

Version 3, 27/07/07

What are the side-effects of the antidepressants?
The choice of antidepressant will be made by your GP in consultation with you and s/he will explain any possible side-effects. You will also be given a leaflet explaining the possible side-effects. The antidepressants, known as selective serontonin re-uptake inhibitors (SSRIs), are generally well tolerated, but you can have side-effects in the first couple of weeks, e.g. feeling sick/nauseated, and sometimes feeling more on edge or anxious and sexual side effects. Usually these are mild and settle down, but if you are concerned in any way, you should consult your GP.

Confidentiality
All the information collected will be stored securely according to the Data Protection Act. We will not release any identifiable information to any other organisation. No-one will be able to identify any of the participants from the published findings. Once the study has been completed our record of your name and address will be destroyed.

Will taking part in the study affect my treatment?
If you agree to take part in this study, the routine care you receive from your general practice will not change in any way at all. Your GP will retain full clinical responsibility for your care. As usual, you will be able to consult with your GP at any time you wish.

Further questions
If there is any further information that you require, please contact the RESPOND Team at the telephone number 0117 xxxxxxx or contact the study lead researcher Professor Debbie Sharp at Bristol at the telephone number (0117) xxx-xxxx

Thank you for considering helping us with this study.

Yours sincerely

Professor D. Sharp

Version 3, 27/07/07

Appendix 6

Patient consent form for home visit

Professor D. Sharp, Cotham House, Bristol BS6
participant unique ID [ ]
participant DOB [ ]

RESPOND

PATIENT CONSENT FORM B
(ISRCTN 16479417)

Antidepressant drug therapy vs a community based psychosocial intervention for the treatment of moderate postnatal depression: a pragmatic randomised controlled trial

		(Please circle one)	
1.	Have you read and understood the patient information sheet (Version 3, 27/07/07)	**YES**	**NO**
2.	Have you received enough information about the study?	**YES**	**NO**
3.	Have you had an opportunity to discuss this study and ask any questions?	**YES**	**NO**
4.	Have you had satisfactory answers to all of your questions?	**YES**	**NO**
5.	Have you had sufficient time to come to your decision?	**YES**	**NO**
6.	Do you understand that if you consent to this part of the study, you are agreeing to participate in a study comparing two treatments for postnatal depression: antidepressants and counselling from a Health Visitor?	**YES**	**NO**
7.	Do you understand that if you consent to this part of study, you are agreeing to let the Research Associate, or other responsible members of the research team, to look at the medical records for you and your baby?	**YES**	**NO**
8.	Do you understand that you are free to withdraw from the study: • At any time? • Without having to give a reason? • Without affecting your current or future medical care? • That details of your participation up to the time of withdrawal will be stored anonymously on file and may be used in the final analysis of data?	**YES**	**NO**
9.	Do you agree to possibly being contacted by a Research Associate to talk about your views on the treatment of postnatal depression?	**YES**	**NO**
10.	Do you agree to participate in this study?	**YES**	**NO**

PATIENT'S Signature ……..

Name (BLOCK LETTERS) ……Date……..
Version 3 July 27 2007

Appendix 7

Adapted and less well-known questionnaires

Social support		
10.6.1	There are members of my family or friends who can be relied on no matter what happens.	Not true[1] Partly true[2] Certainly true[3]
10.6.2	There are members of my family or friends who give me support and encouragement.	Not true[1] Partly true[2] Certainly true[3]
10.6.3	There are members of my family or friends who I can talk to whenever I like.	Not true[1] Partly true[2] Certainly true[3]

MAMA

These questions are asking you to reflect on your experiences of motherhood.

Please complete each question by putting a circle around the answer, which most closely applies to you. Work quickly and please remember to ANSWER EVERY QUESTION. We want to know how you have been FEELING DURING THE PAST MONTH. If you have not considered some of the questions during the past month, go ahead and answer them on your present feelings.

Here are some examples of completed questions:

Have you felt attractive? Never Rarely (Often) Very often

Have you felt proud of your appearance? Very much (A lot) A little Not at all

IN THE PAST MONTH

4.1.	Have you been worrying that you might not be a good mother?	Not at all	A little	A lot	Very much
4.2.	Have you worried about hurting your baby?	Not at all	A little	A lot	Very much
4.3.	Have you had enough time for yourself since you had the baby?	Not at all	A little	A lot	Very much
4.4.	Have you regretted having the baby?	Never	Rarely	Often	Very often
4.5.	Have you felt proud of being a mother?	Very much	A lot	A little	Not at all
4.6.	Have you been feeling happy that you have a baby?	Not at all	A little	A lot	Very much
4.7.	Has the thought of having several children appealed to you?	Not at all	A little	A lot	Very much
4.8.	Have you felt disappointed by motherhood?	Very much	A lot	A little	Not at all
4.9.	Have you enjoyed caring for your baby's needs?	Not at all	A little	A lot	Very much
4.10.	Have you been wondering whether your baby will be healthy and normal?	Not at all	A little	A lot	Very much
4.11.	Has life been more difficult since the baby was born?	Not at all	A little	A lot	Very much
4.12.	Have you enjoyed feeding your baby?	Not at all	A little	A lot	Very much

PAPA

These questions are asking you to reflect on your experiences of fatherhood.

Please complete each question by putting a circle around the answer which most closely applies to you. Work quickly and please remember to answer each question. We want to know how **YOU** have been feeling during the past **MONTH**. If you have not considered some of the questions during the past month go ahead and answer them on your present feelings.

Here are some examples of completed questions:

Have you helped in the running of the house?	Never	Rarely	(Often)	Very often
Has the thought of having more children appealed to you?	Very much	(A lot)	A little	Not at all

All the information will be treated in the strict confidence.

IN THE PAST MONTH

4.1	Has there been tension between you and your partner – irritability, unpleasant silence, etc?	Never	Rarely	Often	Very often
4.2	Have you been worrying that you might not be a good father?	Not at all	A little	A lot	Very much
4.3	Have arguments between you and your partner come close to blows?	Very often	Often	Rarely	Never
4.4	Have you worried about hurting your baby?	Not at all	A little	A lot	Very much
4.5	Have you had enough time for yourself since you had the baby?	Not at all	A little	A lot	Very much
4.6	Have you found it easy to show affection to your partner?	Very often	Often	Rarely	Never
4.7	Have you regretted having the baby?	Never	Rarely	Often	Very often
4.8	Have you felt proud of being a father?	Very much	A lot	A little	Not at all
4.9	Have you been feeling happy that you have the baby?	Not at all	A little	A lot	Very much

4.10	Have you helped in the running of the house?	Very much	A lot	A little	Not at all
4.11	Has the thought of having more children appealed to you?	Not at all	A little	A lot	Very much
4.12	Have you felt that your partner was paying you too little attention?	Very often	Often	Rarely	Never
4.13	Have you felt disappointed by fatherhood?	Very much	A lot	A little	Not at all
4.14	Has your partner seemed to ignore how you were feeling?	Very often	Often	Rarely	Never
4.15	Has your partner tried to share your interests?	Never	Rarely	Often	Very often
4.16	Have you enjoyed caring for your baby's needs?	Not at all	A little	A lot	Very much
4.17	Have you felt that you wanted to spend time away from your partner?	Never	Rarely	Often	Very often
4.18	Have you been feeling close to your partner since the baby was born?	Never	Rarely	Often	Very often
4.19	Have you felt like putting your arms round your partner and cuddling her?	Very much	A lot	A little	Not at all
4.20	Have you been wondering whether your baby will be healthy and normal?	Not at all	A little	A lot	Very much
4.21	Has your partner shown affection to you?	Very often	Often	Rarely	Never
4.22	Has life been more difficult since the baby was born?	Not at all	A little	A lot	Very much
4.23	Have you wished you could rely more on your partner to look after you?	Very often	Often	Rarely	Never
4.24	Have you enjoyed feeding and looking after your baby?	Not at all	A little	A lot	Very much

SF-12 Social Functioning Questionnaire

This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. For each of the following questions PLEASE MARK AN "X" IN THE ONE BOX that best describes your answer. If you are unsure about how to answer a question, please give the best answer you can.

3.1 In general, would you say your health is:

Excellent[1]	Very good[2]	Good[3]	Fair[4]	Poor[5]
☐	☐	☐	☐	☐

3.2 The following questions are about activities you might do during a typical day. Does your health limit you in these activities? If so, how much?

	Yes, limited a lot[1]	Yes, limited a little[2]	No, not limited at all[3]
(a) Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐	☐	☐
(b) Climbing several flights of stairs	☐	☐	☐

3.3 During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	All of the time[1]	Most of the time[2]	Some of the time[3]	A little of the time[4]	None of the time[5]
(a) Accomplished less than you would like	☐	☐	☐	☐	☐
(b) Were limited in the kind of work or other activities	☐	☐	☐	☐	☐

3.4 During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	All of the time[1]	Most of the time[2]	Some of the time[3]	A little of the time[4]	None of the time[5]
(a) Accomplished less than you would like	☐	☐	☐	☐	☐
(b) Did work or activities less carefully than usual	☐	☐	☐	☐	☐

3.5 During the past 4 weeks, how much did pain interfere with your normal work (including both outside the home and housework)?

Not at all[1]	A little bit[2]	Moderately[3]	Quite a bit[4]	Extremely[5]
☐	☐	☐	☐	☐

3.6 These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling.

How much of the time during the past 4 weeks...

	All of the time[1]	Most of the time[2]	Some of the time[3]	A little of the time[4]	None of the time[5]
(a) Have you felt calm and peaceful?	☐	☐	☐	☐	☐
(b) Did you have a lot of energy?	☐	☐	☐	☐	☐
(c) Have you felt downhearted and depressed?	☐	☐	☐	☐	☐
(d) Have you been a very nervous person?	☐	☐	☐	☐	☐
(e) Have you been a happy person?	☐	☐	☐	☐	☐
(f) Have you felt so down in the dumps that nothing could cheer you up?	☐	☐	☐	☐	☐

3.7 During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc.)?

All of the time[1]	Most of the time[2]	Some of the time[3]	A little of the time[4]	None of the time[5]
☐	☐	☐	☐	☐

Adherence

These questions ask you about how easy it is to remember to take your medication. If you have been prescribed antidepressant drugs as part of this study please complete the following section. **If you have not been prescribed antidepressants please go to section 9.**

7.1 In the past 4 weeks...

(a) Did you ever forget to take you antidepressants? YES1 NO2

If NO go to question. 7.2

If YES

(b) How many times did you miss a dose?

(c) Did you ever miss more than one dose at a time? YES1 NO2

(d) What was the most times you missed a dose before starting them again?

7.2 If you felt better did you sometimes stop taking your antidepressants? YES1 NO2

7.3 If you felt worse did you sometimes stop taking your antidepressants? YES1 NO2

7.4 Below are four examples of people describing how they take their antidepressants.

Thinking back over the past 4 weeks, please circle the number next to the ONE description that you feel comes closest to your experience of taking antidepressants.

Please remember, we are interested in knowing about your experiences and we are not looking for a particular answer. **PLEASE CIRCLE ONE NUMBER ONLY.**

Level	During the past 4 weeks
1	"I took all my antidepressant tablets at the same time every day"
2	"I managed to take all my antidepressant tablets – but not always at the same time of day"
3	"I sometimes did not take all of my antidepressant tablets, but I never missed more than one dose at a time"
4	"I missed many of my antidepressant tablets and on one or two occasions I missed my tablets for two or more days"

Adapted from Morisky *et al.*[95] and Schroeder *et al.*[96]

Relationship Questionnaire

These questions ask you about your current relationship.

Each statement is followed by a series of possible responses: strongly disagree, disagree, agree and strongly agree. Please read each statement carefully and decide which response best describes how you feel about your relationship with your partner; then circle the corresponding response.

Please respond to **every** statement. If none of the responses seem **completely** accurate, circle the one you feel is most appropriate. Do not spend too long on each question.

Please answer this questionnaire without discussing any of the statements with your partner. In order for us to obtain valid information it is important for you to be as honest and as accurate as possible.

All information will be treated in the strictest confidence.

5.1	My partner is usually sensitive to and aware of my needs	Strongly disagree	Disagree	Agree	Strongly agree
5.2	My partner doesn't seem to listen to me any more	Strongly disagree	Disagree	Agree	Strongly agree
5.3	I am dissatisfied with our relationship	Strongly disagree	Disagree	Agree	Strongly agree
5.4	I enjoy just sitting and talking with my partner	Strongly disagree	Disagree	Agree	Strongly agree
5.5	I sometimes feel lonely even when I am with my partner	Strongly disagree	Disagree	Agree	Strongly agree
5.6	There is plenty of "give and take" in our relationship	Strongly disagree	Disagree	Agree	Strongly agree
5.7	Our relationship is still full of joy and excitement	Strongly disagree	Disagree	Agree	Strongly agree
5.8	I wish there was more warmth and affection between us	Strongly disagree	Disagree	Agree	Strongly agree
5.9	I suspect we may be on the brink of separation	Strongly disagree	Disagree	Agree	Strongly agree
5.10	We can always make up quickly after an argument	Strongly disagree	Disagree	Agree	Strongly agree

Adapted from Rust *et al.*[81]

Appendix 8

Intervention leaflets (two-sided fan-folded)

Are there side effects?

Like all medicines, antidepressants may cause some unwanted effects. However, most people have either minor or no side effects. Possible side effects vary between different tablets and your doctor will be able to advise you about these. The most common side effects of SSRI tablets include diarrhoea, feeling or being sick and headaches. These side effects are not dangerous, usually wear off after a week or so, and you may be able to treat them yourself. If side effects are a problem, your GP can alter your tablets, or give you something to help.

Are they addictive?

Antidepressants don't cause the addictions that you get with tranquillisers, alcohol or nicotine, in that you don't need to keep increasing the dose to get the same effect, and you won't find yourself craving them if you stop taking them. Most people can stop treatment without any problem, but at the end of treatment you should reduce the dose gradually over about four weeks before stopping as some people develop 'withdrawal' symptoms if the tablets are stopped too quickly.

What about breastfeeding?

Having depression can exhaust you, stop you from breastfeeding, upset your relationship with your baby and even hold back your baby's development. In this case, antidepressants can be helpful.

Your baby will only get very small amounts of antidepressant from your breast milk. Babies older than a few weeks have very effective kidneys and livers. They are able to break down and get rid of medicines just as adults do, so the risk to the baby is very small. Some antidepressants are better than others in this regard and it is worth discussing this with your doctor. On balance, bearing in mind all the advantages of breastfeeding, it seems better to carry on with it while taking antidepressants.

Contact details

For further information, please contact the Respond Team on 0117xxxxxxx.

University of BRISTOL

RESPOND

Antidepressants

MANCHESTER 1824
The University of Manchester

KING'S College LONDON
University of London

The RESPOND study...

... is comparing the use of antidepressant medication and Health Visitor listening visits for the treatment of mild to moderate postnatal depression in the community.

It intends to look at how well the treatments work, how cost-effective each is and which is preferred by the women involved and the people who treat them.

Women involved in the study will first receive either medication or listening visits to treat their postnatal depression. If they do not make progress with their initial treatment they will be able to either add in the other treatment or swap to the other treatment.

The study is taking place in 3 centres in the UK - Bristol, London and Manchester and will last for 3 years. By then we hope to have screened all new mums from the 74 GP practices involved, for postnatal depression, and included about 250 of them in the treatment trial.

At the end of this time we will know more about the best treatment for women who have mild to moderate postnatal depression.

What happens if I am allocated antidepressants?

The researcher will contact your GP to tell them that you are taking part in the trial and have been allocated antidepressants. The researcher will ask you to make an appointment with your GP, who will discuss the prescription with you, and decide which are the best tablets for you to take. The GP will remain responsible for your care and will monitor how well you respond to the tablets.

What are antidepressants?

Antidepressants are drugs that relieve the symptoms of depression. There are four main types but the most commonly prescribed are SSRIs (Selective Serotonin Reuptake Inhibitors).

Antidepressants work by increasing the activity of chemical messengers, called neurotransmitters, in the brain. Antidepressants usually influence the neurotransmitters Serotonin or Noradrenaline. However, there is still some uncertainty about how the changes in these neurotransmitters lead to improvement of mood.

How well do they work?

About 6 in 10 people with depression improve within a few weeks of starting antidepressants. However, up to 3 in 10 people improve with dummy tablets (placebo) as some people get better in this time naturally. So, you are roughly twice as likely to improve with antidepressants compared to no treatment.

Antidepressants take 2-4 weeks to work fully. It is best to wait 4 weeks before deciding if the treatment is helping or not. There are different types of antidepressants and some people don't respond to the first ones they try. If the tablets are not helping after 4 weeks, your GP may suggest you take a higher dose, or try a different sort of tablet.

A normal course of antidepressants lasts up to six months or more after symptoms have eased. If you stop too soon, your symptoms may return. Some people with recurrent depression need longer courses of treatment.

Depression is unpleasant and can seriously affect your ability to work, enjoy life and your new baby. Antidepressants can help you get better quicker. People on antidepressants, particularly the newer ones, should be able to socialise, work and carry on their normal activities.

DOI: 10.3310/hta14430

The RESPOND study...

... is about the use of antidepressant medication and Health Visitor listening visits for the treatment of mild to moderate postnatal depression in the community.

It intends to look at how well the treatments work, how cost-effective each is and which is preferred by the women involved and the people who treat them.

Women involved in the study will first receive either medication or listening visits to treat their postnatal depression. If they do not make progress with their initial treatment they will be able to either add in the other treatment or swap to the other treatment.

The study is taking place in 3 centres in the UK - Bristol, London and Manchester and will last for 3 years. By then we hope to have screened around 9000 women for postnatal depression and involved approximately 450 of them in the trial.

At the end of this time we will know more about the best treatment for women who have mild to moderate postnatal depression.

The Research Health Visitor

The Research Health Visitor is an experienced Health Visitor who has been specially trained by the study to provide listening visits to women who are experiencing mild to moderate postnatal depression.

Her role is to provide the time and space for you to speak about whatever is bothering you and to help you to find your own ways of enjoying your life and your baby once again.

She works alongside your normal Health Visitor and would expect you to continue to see your own Health Visitor at home or in clinic as you normally would during her series of visits.

Your GP knows the Research Health Visitor is visiting you and continues to be in charge of your care. You are free to see them as usual also.

The Research Health Visitor however will not speak to your GP or Health Visitor about the content of the visits unless you allow this. The only time this would happen would be if they had serious concerns for your wellbeing. If this were the case they would tell you so immediately.

What you can expect

- a once a week visit for 4 weeks initially
- if necessary we will discuss with you the possibility of further treatment
- to speak about whatever is important to you and to be listened to
- the visits will last around 1 hour
- to be seen at home unless you want to meet elsewhere

What you won't get

- someone telling you what to do
- someone judging you
- someone who doesn't believe you are important

Appendix 9

Antidepressant prescribing guidelines for general practitioners

Guidelines for antidepressant use in the RESPOND trial

A Background

The Department of Health/HTA funded RESPOND trial will compare antidepressant drug therapy versus Health Visitor delivered non-directive counselling for the treatment of postnatal depression (affecting 8-15% of postpartum women) in primary care.

B Diagnosis

Women in the RESPOND trial attending their GP for prescription of an antidepressant will have a confirmed diagnosis of postnatal depression – an EPDS ≥12 and a score on the standardised psychiatric interview (CIS-R) denoting symptoms severe enough to consider treatment with an antidepressant.

C General issues in prescribing

1. Patients should be advised not to suddenly stop medication without discussing it with their GP.
2. Usual criteria for referral to secondary care psychiatric services should be applied (significant suicide risk or risk to baby; consideration in more severe depression, treatment non-response and complex cases).
3. Patients expressing suicidal ideation but not intent are still eligible for the study but require careful monitoring (see E below).
4. St John's Wort should not be taken at the same time as an SSRI.

D Choice of antidepressant

1. Patient preference and particular patient characteristics, as well as past experience of treatment, should inform the choice of drug, taking into account special issues relevant to postnatal depression such as breastfeeding, sedation, suicidal ideation etc.
2. We suggest an SSRI will usually be the drug of choice as they are as effective as TCAs and are less likely to be discontinued due to side effects and are less toxic in overdose.
3. See C1 above. We are not generally advising or prohibiting any particular SSRI, but the following should be taken into account:
   i) If the woman is breastfeeding we <u>do not</u> advise fluoxetine due to its long half-life and higher levels in breast milk, although harmful effects on breastfed babies have not been detected in case reports.
   ii) If the woman is breastfeeding, the preferred drugs are sertraline, paroxetine and citalopram with no harmful effects on the baby observed in case series.
   iii) For second-line drugs (see G below), there is less experience and information about safety in breastfeeding, so extra caution is required.

E Monitoring/duration of treatment

1. Careful monitoring of symptoms, side-effects, suicide risk and risk to baby should be routinely undertaken, especially early in treatment when they may worsen or appear for the first time.
2. For patients expressing suicidal ideation but not intent, consideration should be given to the appropriate length of each prescription and support in administration of the medication.
3. We believe it is best practice to have an early follow up after the initial prescription and then to see women for each repeat prescription. We would like women to be seen at 2 weeks, 4 weeks, 8 weeks, 12 weeks, 16 weeks, 20 weeks, 24 weeks and 28 weeks.

Version 3, 13.01.05

4. It should be explained to the women that once remission has been achieved it is recommended that the medication will need to be continued at the same dose for at least 4 to 6 months to reduce the likelihood of relapse.
5. If the woman has a history of recurrent depression she may need to continue treatment for a longer period.
6. It should be explained that if a satisfactory response is not occurring by 6 to 8 weeks, it is possible that either dose will be increased or a medication from a different class will be tried (see below). In practice if there has been NO response by 4 weeks a dose increase or change of medication at this point is reasonable as subsequent response is unlikely.
7. It is important to monitor for relapse and discontinuation symptoms when reducing or stopping medication.
8. The dose would normally be reduced over 4 weeks unless fluoxetine is used as it has a long half-life and can be stopped abruptly.
9. If discontinuation symptoms are mild, practitioners should reassure the patient and arrange for monitoring. If severe symptoms are experienced, consider re-starting the original drug (or for SSRIs start fluoxetine) and reduce gradually while monitoring symptoms.
10. Patients should be advised to seek help from their GP for severe discontinuation symptoms.

F Explanation to be offered with first prescription

1. The tablets are to help treat your postnatal depression
2. They do not work immediately – it will be 10-14 days before you begin to notice any improvement.
3. I would like to see you again in 2 weeks.
4. You might notice a few side effects which tend to be worse early on, e.g. dry mouth, feeling sick. These are likely to be transient. You will find full details in the Patient Information Leaflet.
5. Occasionally people can get much worse and even begin to feel like harming themselves or others. In this situation contact me or another GP or your health visitor straight away.
6. If the side effects are difficult to bear, please make an appointment to see me or another GP.

G Drugs to consider

1st line drug

Drug	Starting dose	Review for side effects	1st review efficacy	If no improvement at 4 weeks or only slightly better at 6/8 wks
Fluoxetine (not if breastfeeding)	20mg	2 wks	4 wks	Increase to 40mg or change drug
Sertraline	50mg	2 wks	4 wks	Increase to 100mg or change drug
Paroxetine	20mg	2 wks	4 wks	Change drug*
Citalopram	20mg	2 wks	4 wks	Increase to 40mg or change drug
Escitalopram**	10mg	2 wks	4 wks	Increase to 20mg or change drug

2nd line drug

Drug	Starting dose	Review for side effects	1st review efficacy	If not/only slightly better at 6/8 wks
Lofepramine	70mg bd	2 wks	4 wks	Increase to 210mg/day
Reboxetine**	4mg	2 wks	4 wks	Increase to 8mg

* recent MCA guidance not to increase paroxetine dose above 20mg for depression
** lack of data re breastfeeding

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Appendix 10

Letter sent at 4 weeks to general practitioners of women allocated antidepressants

RESPOND

Clare Richards
Community Based Medicine
The Grange
1 Woodland Road
Bristol BS8 1AU

Tel: (0117) 3310950
Fax: (0117) 3310964
Clare.Richards@bristol.ac.uk

08-06-2006

Dear Dr Name

RE:
DoB:
Postcode:

The above named woman is participating in the RESPOND study comparing treatments for postnatal depression. Four weeks ago she was randomised to the antidepressant arm of the trial and is now due to make an appointment to see you for her four week follow up appointment. This will enable you to decide jointly how the treatment is going. At this stage of the trial, there are a number of options open to patients on antidepressants:

- If the depression is improving continue treatment as prescribed.

OR

- If treatment is not improving or the woman would like to consider other treatments you can:
  1. Change the dose of the antidepressant that the patient is taking.
  2. Change the type of antidepressant that the patient is taking.
  3. Add Health Visitor counselling (from our Research Health Visitor) to the antidepressant drug therapy.
  4. Stop the antidepressant drug therapy and replace it with Health Visitor counselling (from our Research Health Visitor)
  5. Review again in two weeks
  6. Stop all treatments

If you have any questions please do not hesitate to contact me. If you and the patient decide to take up the offer of Health Visitor counselling from our Research Health Visitor then please get in touch so that we can make the necessary arrangements.

Yours sincerely

Clare Richards
Research Associate

1.09 GP reminder that woman on ADs is due her 4 week follow up appointment

Appendix 11

Interview schedule for completers

Entering trial

- How did you hear about RESPOND?
- Why did you decide to take part?
- How did you feel about being asked to take part in a trial about PND?
- How did you feel when you found out that you were eligible to take part in the trial?

Diagnosis

- How did you feel about being diagnosed as having PND? Did you think you would be? Prompt surprise, relief, agreement with diagnosis.
- How were you feeling at the time? Why do you think you felt like this?
- What care were you receiving at this time? (GP, HV etc.) Did you have any other forms of support (family, friends, clinics, groups)?

Randomisation

- How was it decided what type of care you got in the trial? Why was it decided like this? Prompt for understanding of trial aims and process.
- Did you think you were more likely to get one type of care rather than another? Why? Was it down to chance?

Treatment: expectations

- In what ways did you think each of the treatments might help you?
  - Antidepressants: prompt for understanding, expectations, prior experience, concerns including breastfeeding and antidepressants, side effects, stigma.
  - Listening visits: as before and include time, relationship.
- What type of care were you hoping to get? Why?
- What type of care were you allocated first? How did you feel about this? Prompt for acceptance, disappointment, preferred treatment etc.
- What treatments have you received since being in RESPOND?

If received antidepressants:

- What did you see as the advantages and disadvantages of this treatment?
- Prior knowledge of antidepressants – taken them before, if so why? Also explore previous postnatal depression and treatment.
- Have you ever missed taking your tablets for any reason? If so, when was this and why?
- Are you still taking medication? If not, why did you stop taking the medication? If so, why still taking antidepressants?
- How would you describe your experience of this treatment? Helpful? Unhelpful? Was it as you expected? What changes have you noticed since taking them? Was treatment effective?

If received listening visits:

- What support did you get while waiting for the visits to start, from your HV/GP? Was this helpful?
- Did you receive any other forms of help or support during this time?
- Tell me about your listening visits. What did they entail? How did you find them? Did you have any concerns? Prompt for structure, agenda setting, who was present.
- How were the listening visits different to the visits you had from your own HV? Prompt for support received, role of HV, relationship with own HV/RHV.
- Did you miss any appointments? If so, why?
- How many visits did you receive? If over four, why did you decide to have more visits?
- *If a non-complier: why did you decide not to continue with the visits?* Prompt for treatment expectations versus reality, practical issues, helpfulness of intervention, changing needs.
- How do you feel about the visits finishing?
- How would you describe your experience of this treatment? What things were helpful? Unhelpful? Effective? Was it as you expected?

General supportive care (all women)

- Have you had much contact with you GP since [child's] birth? Prompt for information, advice, support received, options presented, acceptability and satisfaction with the care received.

- Have you had much contact with your HV since [child's] birth? Prompt for information, advice, support received, acceptability and satisfaction with care received.
- In what other ways did you manage your depression? Have you spoken to others (experts, family, friends, other health professionals, agencies) or looked for any information on PND through the library, media, or internet?

For women who crossed over

- Why did you decide to have this other treatment? Prompt for expectations of listening visits (support, non-invasive etc.), attitude/ experience of antidepressants, and whether they perceived that their needs had changed.

Comparing care (all women)

- Thinking about all the care that you have received during the trial, what has been most useful and why?
- How are you feeling now?

Experiences of the trial

- What were your experiences of being involved in the RESPOND trial?
- Negative and positive?
- Are there any ways you think the trial could have been improved?
- Is there anything else you would like to say about postnatal depression, your experiences of a particular treatment, views on treatments available and/or the trial?

Appendix 12

Interview schedule for decliners

Entering trial

- How did you hear about RESPOND?
- How did you feel about being asked to take part in a trial about PND?
- Why did you decide to return the initial questionnaire?
- How did you feel when you found out that you were eligible to take part in the trial?

Diagnosis

- How did you feel about being diagnosed as having PND? Did you think you would be? Prompt surprise, relief, agreement with diagnosis.
- How were you feeling at the time? Why do you think you felt like this?
- What care were you receiving at this time? (GP, HV etc.) Did you have any other forms of support (family, friends, clinics, groups)?

Randomisation

- How was it decided what type of care you got in the trial? Why was it decided like this? Prompt for understanding of trial aims and process?
- Did you think you were more likely to get one type of care rather than another? Why? Was it down to chance?

Declining

- Why did you decide not to take part in the RESPOND trial? Prompt for felt better, concerns and expectations about treatment, the attitudes of others.
- Is there anything that would have encouraged you to take part in the trial?

Treatments

- What did you know about the different treatments offered in the trial?
- What ways do you think the treatments might have been helpful for you at that time? What ways do you think they might have been unhelpful?

Antidepressants

- Prompt for understanding, expectations, prior experience, and concerns, including breastfeeding and antidepressants, side effects, stigma.

Listening visits

- Prompt as above and include time, relationship.

General supportive care

- Have you had much contact with you GP since [child's] birth? Prompt for information, advice, support received, options presented, acceptability and satisfaction with the care received.
- Have you had much contact with your HV since [child's] birth? Prompt for information, advice, support received, acceptability and satisfaction with care received.

Management of postnatal depression and comparing care received

- In what other ways did you manage your depression? Have you spoken to others (experts, family, friends, other health professionals, agencies) or looked for any information on PND through the library, media, or internet?
- Thinking about all the care that you have received what has been most useful and why?
- How are you feeling now?

Appendix 13

Interview schedule for general practitioners

Introduction to study

Sort consent and audio equipment

OK–if we could start with a bit of background information…

Could you describe the area in which you practice?

Demographics, types of patients…any particular ethnic groups?

Can you tell me about the sorts of mental-health problems you see in your patients?

Now, you're part of the study in Manchester because you have a fairly large annual birth rate.

Do you see many women with PND?

How do women with PND present in the surgery?

Could you talk me through what happens in consultation with woman who presents with PND? Can you recall a specific case?

Is knowing the patient important in making the diagnosis? Why? How?

How do you make the diagnosis? What questions do you ask? What role does the PHV play in making a diagnosis? What do HVs do? (Aim for GPs understanding of their role)

Do you routinely screen for PND? If so what methods do you use? Schedules?

How do you negotiate a diagnosis of PND with a woman and her family? Health visitors we have interviewed have mentioned the role of the partner in PND, do you think it is important? (Prompts: in facilitating treatment/causation of depression/ management of or maintaining depression)

What difficulties do you find? Is ethnicity of the woman important?

How do you view postnatal depression?

Compared to other depressions? Do you think it is different? If so, how?

Do you feel that you use antidepressants in a different way in PND? Some GPs say they wait before prescribing in PND, what do you do?

Some people we have interviewed say that PND is a reaction to the life event of becoming a parent, how does this square with PND being a major cause of maternal morbidity and developmental delay in the child?

How is PND managed within the practice?

Do you offer antidepressants? When? How do you assess severity?

In your experience what are women's attitudes to antidepressants?

Do you have access to talking therapies for women with PND?

Do you offer self-help materials?

Do you refer to voluntary agencies? Mother and toddler groups? Church groups?

What role does the PHV play in management of PND?

Some GPs and HVs we have interviewed imply that there is a confusion in the role of HVs, because they are seeing both the woman and her baby, what do you think?

How would you describe your working relationship with the PHVs?

Has it changed since corporate working was introduced?

Some patients have described a lack of continuity nowadays.

Whose overall responsibility is a woman with PND?

Do you think that women fall through the net? (Or, some HVs have suggested that women are falling through the net, is that how you see it?)

There seems to be a tension in that GPs describe making a diagnosis and referring the patient to the HV, whereas HVs describe being worried about a woman, thinking she has PND and referring woman to GP–are you aware of such a tension?

Some GPs and HVs feel that women with PND seem to fall between services with no one taking responsibility for the individual in either diagnosis/detection or treatment what do you think?

GPs/HVs we have interviewed say that part of any intervention should mean that control is given back to women, what do you think about this? How could this be done?

What do you think causes PND?

Can you think of ways PND may be prevented? Or detected earlier?

Have you had any PND training? If so, did it prepare you for dealing with real cases of PND?

If you had unlimited resources how would you like to manage women with PND?

Some GPs say that ideal care for women with PND would be more social interventions–support networks, empowering women, self-management rather than a medical model of care–what do you think of this?

Now I'd like to ask you about your experiences of being part of the RESPOND study…

Can I first ask why you agreed to be part of the study?

You've had xxx patients randomised, xxx to antidepressants and xxx to active listening. What has your experience of this been?

What have you got out of being in the trial? Is there anything else you would like to add?

Appendix 14

Interview schedule for practice health visitors

Introduction to study and consent and tape

Can I start by asking, what do you enjoy about your work? Anything you don't enjoy?

Can you describe the set-up of the HV service within your PCT and your local area? Do you work with one particular GP or practice, or corporately with a number of practices? Where are you based?

Could you run through the contacts you have with women prenatally and postnatally? How are these contacts organised? Are women able to choose which HV they see?

Do you see many women with PND? How do women with PND present?

What do you think causes PND? Some HVs talk about women with PND seeing themselves as a 'failure'–might health professionals also see women in that way?

Could you talk me through what happens in your contact/consultation with a woman who presents with low mood? What questions do you ask? How do you negotiate a diagnosis of PND with a woman (and her partner)? Do you have any difficulties with this? Are there any issues in your area relating to the ethnicity of the woman?

Do you routinely screen for PND at postnatal visits/checks? (If so, explore use of EPDS, training, support and supervision with its use)

What do you do when you suspect a woman may have PND (manage it alone, liaison with GP, pass patient on to GP, refer to support groups, refer to website/other self-help)?

Could you talk me through what happens when you feel that a woman has PND?

What support do you offer to the woman? (Explore content of any intervention mentioned, how trained in this, supervision issues)

Do you think that because you have a responsibility for baby as well as mum, that this causes any tension in your interactions with a mother with PND?

When do you think that PND became an important part of the HVs work? Has this changed?

Some health visitors have talked about offering listening visits. Can you run me through what would happen in a listening visit? What do you feel you actually do?

(Omit this section on antidepressants if short of time)

- What do you feel the place of antidepressants is in management of PND?
- In your experience, what are women's attitudes to antidepressants?
- Do you have access to talking treatments for women with PND?
- Do you offer self-help material?
- Do you refer to voluntary agencies? (What services/groups are offered by the practice?)

Some women have mentioned the lack of continuity in health visiting since corporate working began. How does having a corporate caseload affect working with women?

Some HVs have referred to how they used to have long-term relationships with women in the community when they were practice-based. What has happened to this side of health visiting now? Is there continuity of relationships/support for women?

Does what you want to do conflict with organisational changes being imposed on health visiting?

What role does the patient's GP play in making the diagnosis? (Explore variation)

How is this communicated to you?

Does the GP ask you to take over management?

Do you feel you manage a woman with PND collaboratively with the GP?

Whose responsibility are postnatal women? (GP, HV team manager, HV?)

When you speak to the GP do you hand over the women to them or just ask for advice?

Can you give me an example of where things have gone well? And an example of where things have not gone so well?

Some HVs have said that women fall through the net? Do you feel this can or does happen?

Some GPs and HVs feel that women with PND seem to fall between services with no one taking responsibility for the individual in either diagnosis/ detection or treatment, what do you think?

What happens if you find you have problems with a woman assigned to you? Has this ever happened, where you just haven't clicked?

GPs and HVs we have interviewed say that part of any intervention should mean that control is given back to women, what do you think about this? How could this be done?

What role (if any) does the midwife have in diagnosing depression antenatally? Is this ever communicated to you?

Some people we have interviewed say that PND is a reaction to the life event of becoming a parent, how does this square with PND being a major cause of maternal morbidity and developmental delay in the child?

How would you like to manage women with PND (if resources were not an issue)?

Can I ask why you agreed to participate in the RESPOND study? You have had xx women randomised in the study–*x* to antidepressants and x to HV listening visits.

What has been your experience of this? (Explore antidepressants and supportive listening)

Have you seen anyone who has completed the intervention in the trial? How did they find it? What do you think is involved in the listening visits? How have you managed the case afterwards?

Some HVs we have spoken to suggest that they would value a more medical model of intervention for women with PND–do you agree?

What have you got out of being in the trial?

Anything else you wish to add?

Amended ECC and CR 14 September 2006 and CCG 30 June 2005

Amended 20 September 2006 and 27 September 2006 CCG

Amended 28 November 2006 ECC

Amended 12 December 2006 ECC

Amended 20 December 2006 ECC and CCG

Appendix 15

Screening CONSORT diagrams for each centre

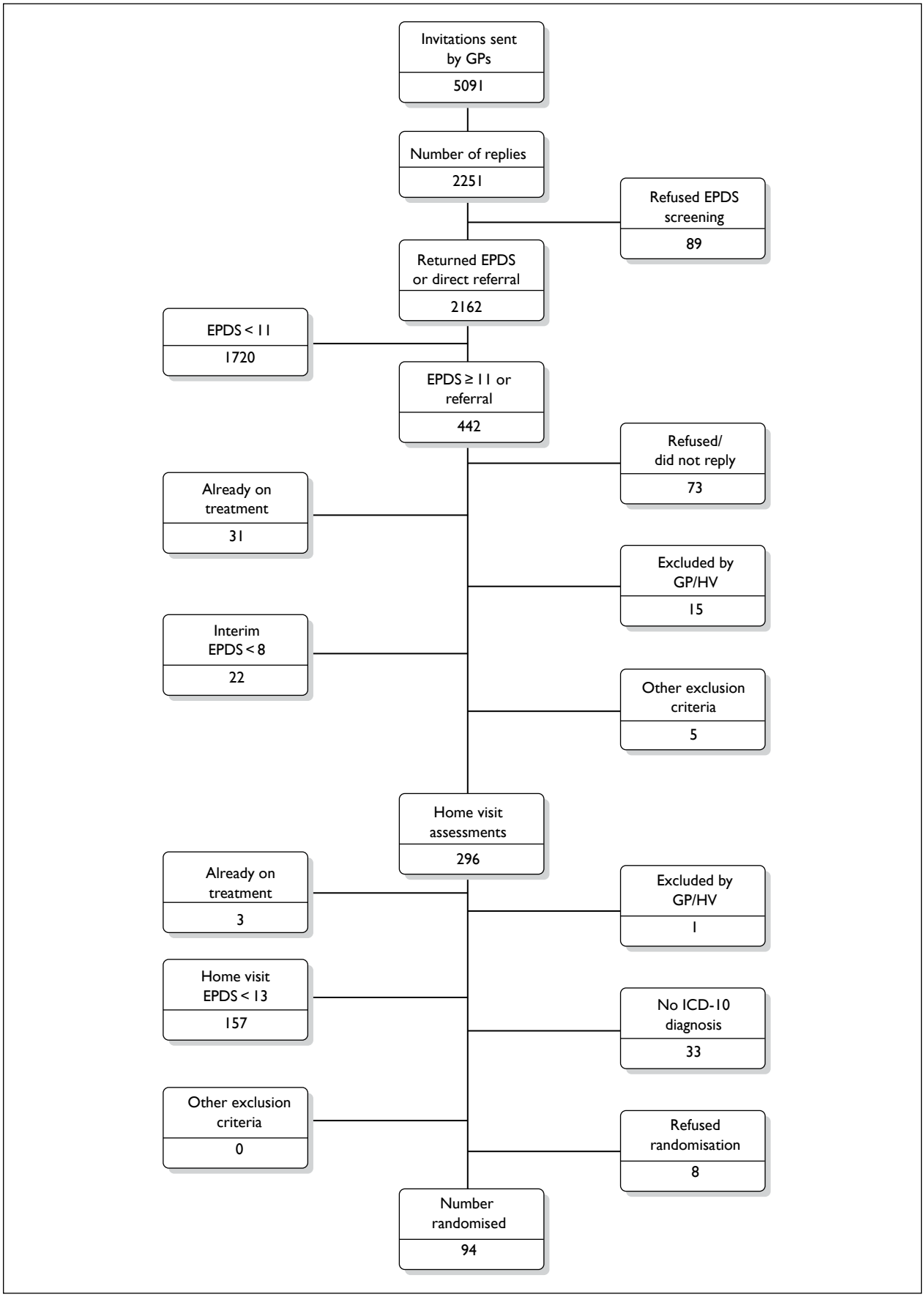

FIGURE 6 *Screening CONSORT diagram – Bristol.*

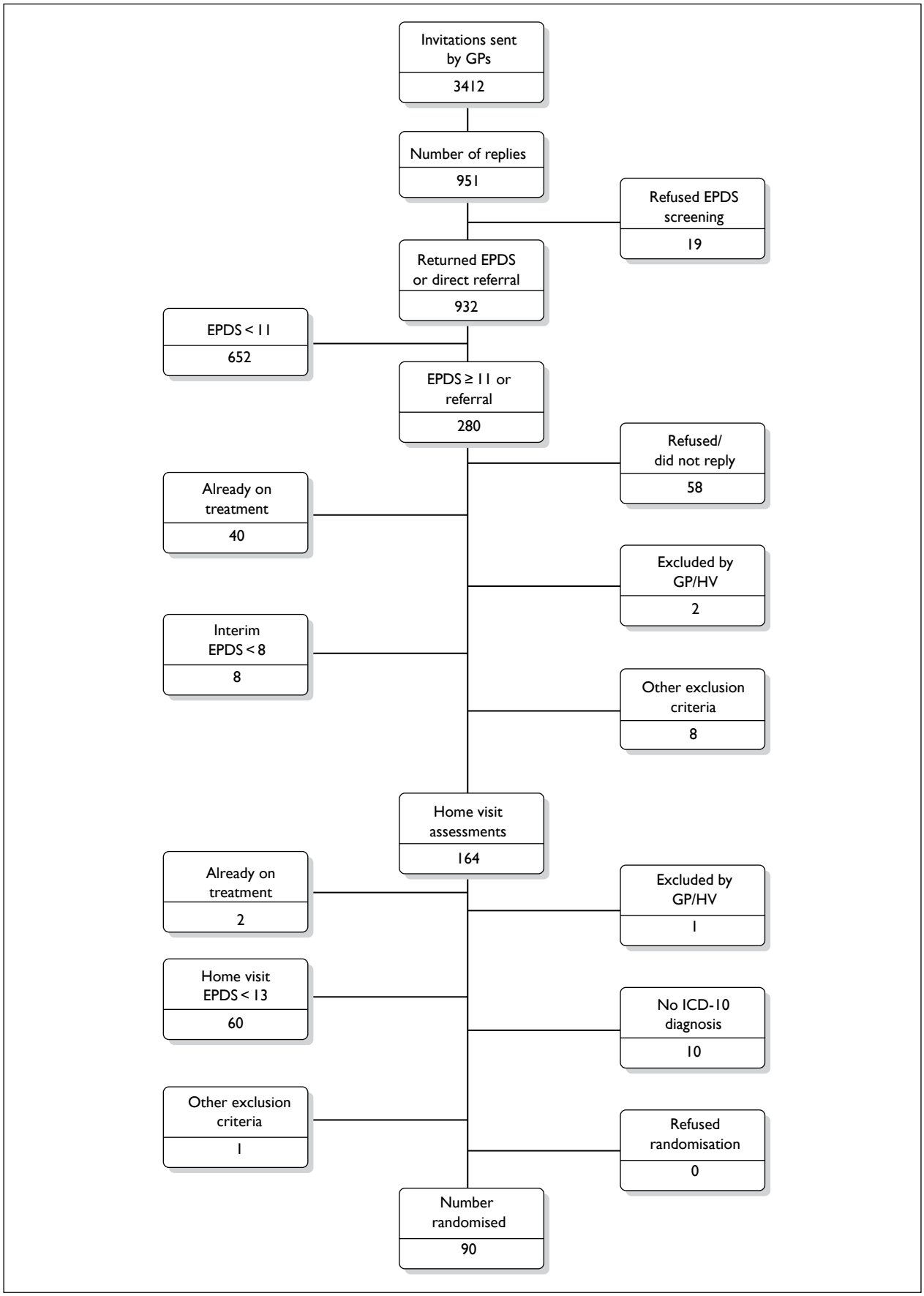

FIGURE 7 *Screening CONSORT diagram – Manchester.*

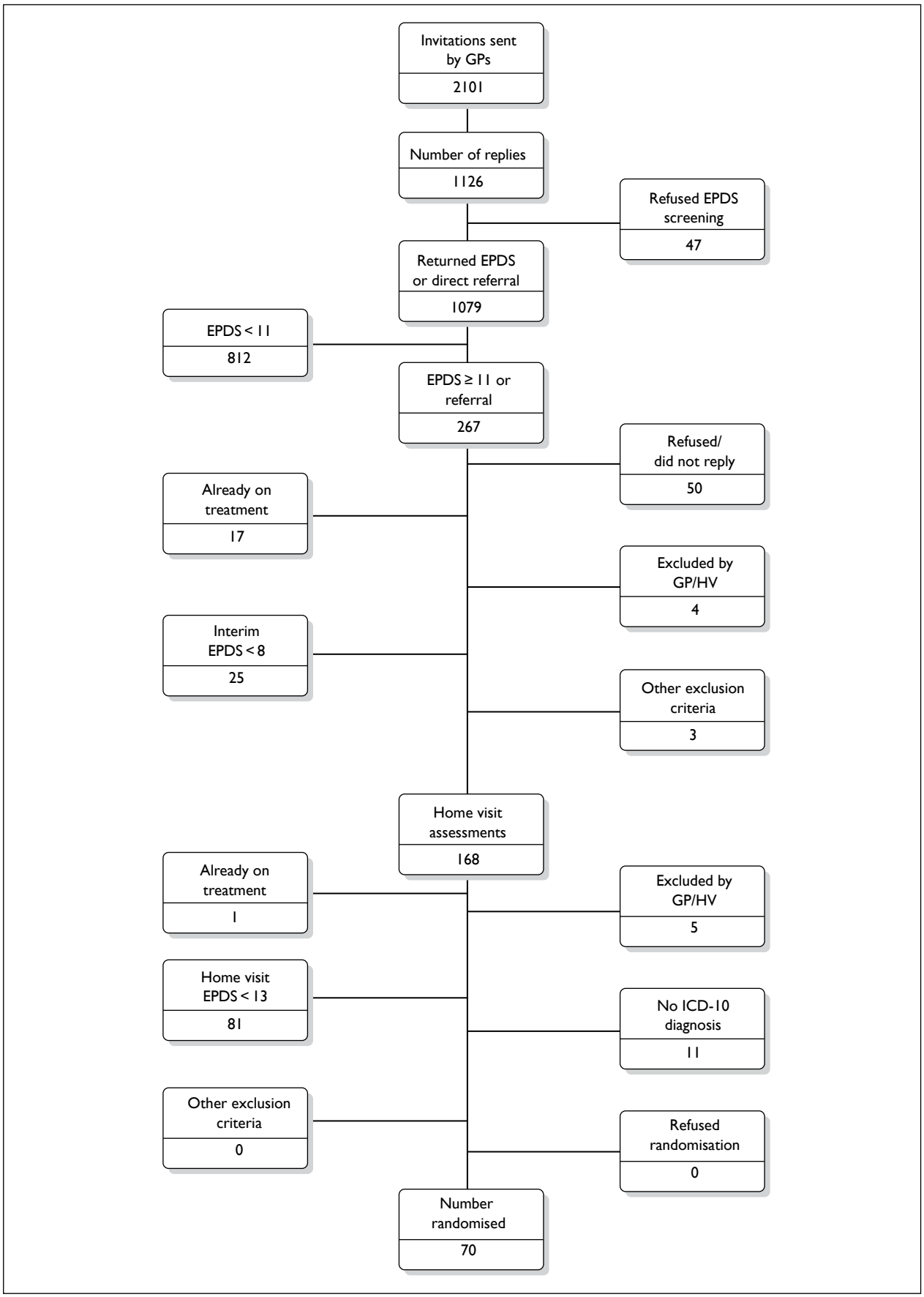

FIGURE 8 *Screening CONSORT diagram – London.*

Appendix 16

Intervention CONSORT diagrams for each centre

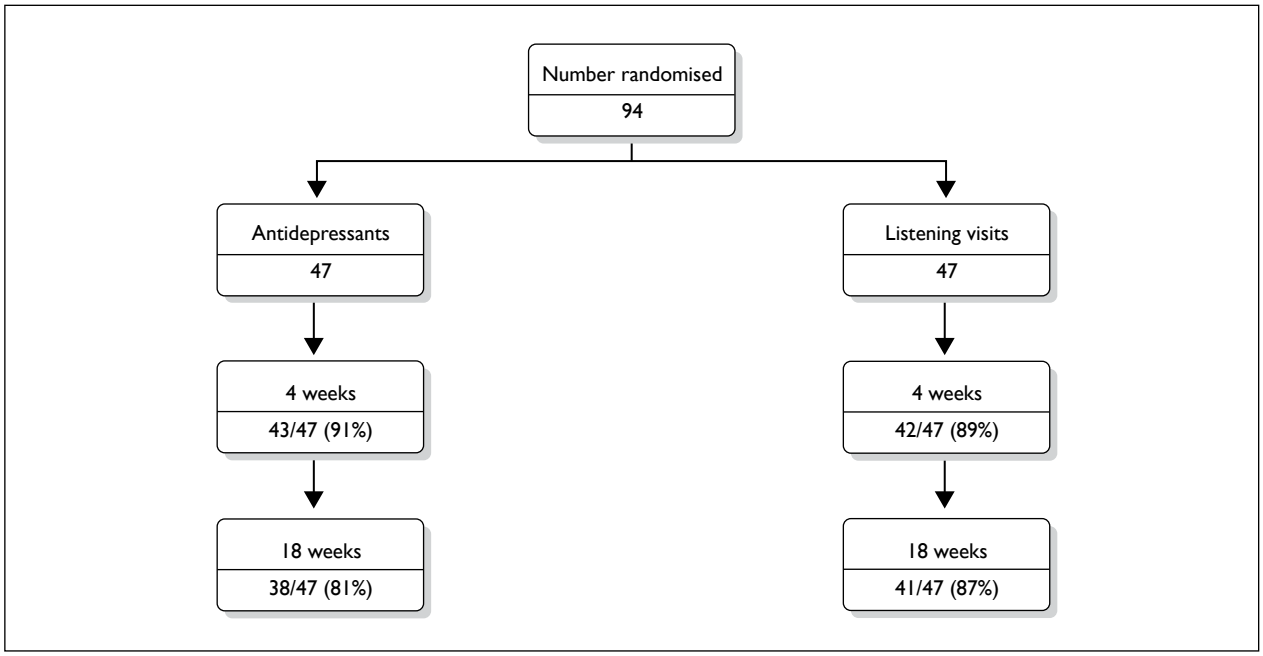

FIGURE 9 *Intervention CONSORT diagram – Bristol.*

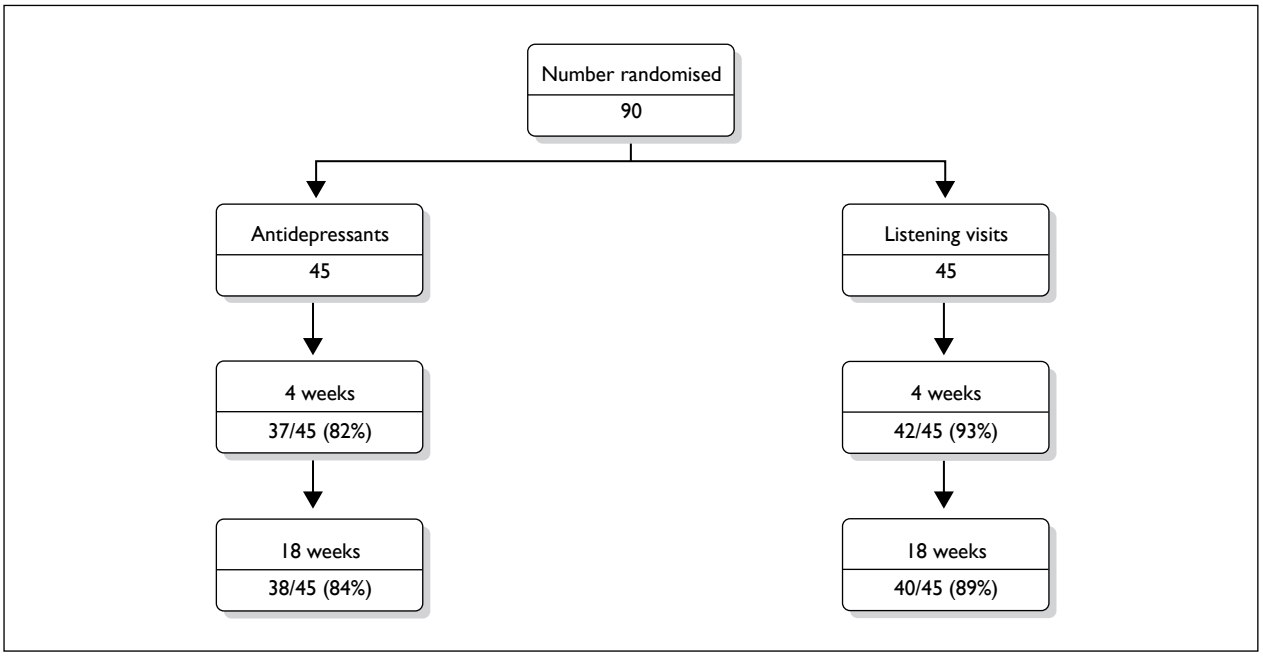

FIGURE 10 *Intervention CONSORT diagram – Manchester.*

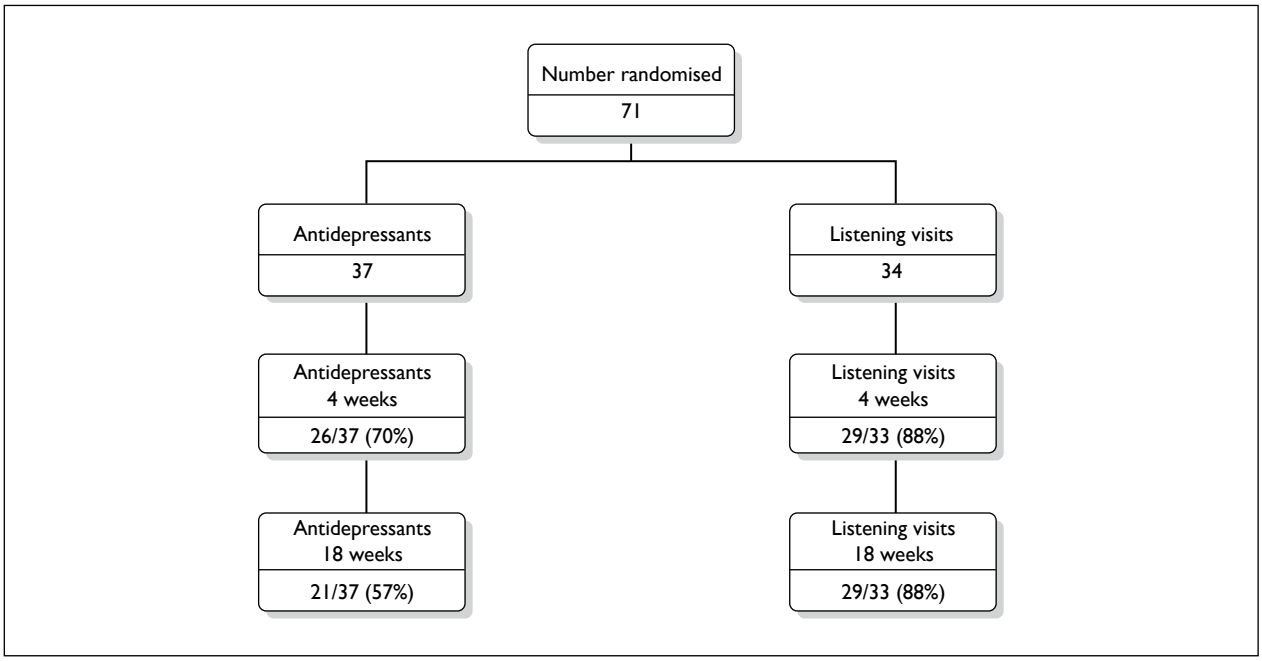

FIGURE 11 *Intervention CONSORT diagram – London.*

Health Technology Assessment reports published to date

Volume 1, 1997

No. 1
Home parenteral nutrition: a systematic review.
By Richards DM, Deeks JJ, Sheldon TA, Shaffer JL.

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Volume 2, 1998

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The Correspondence Page on the HTA website (www.hta.ac.uk) is a convenient way to publish your comments. If you prefer, you can send your comments to the address below, telling us whether you would like us to transfer them to the website.

We look forward to hearing from you.

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