

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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Executive summary

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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 Golombok–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 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.

Publication

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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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