A systematic review, evidence synthesis and meta-analysis of quantitative and qualitative studies evaluating the clinical effectiveness, the cost-effectiveness, safety and acceptability of interventions to prevent postnatal depression

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Scientific summary

Interventions to prevent postnatal depression

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Scientific summary

Background

Postnatal depression (PND) is a serious public health issue, affecting 7–13% of women in the year following childbirth. The strongest predictors of PND are antenatal anxiety, depression history, lack of social support, low self-esteem, stressful life events, poor marital relationship and domestic violence. Severe PND is associated with suicide and infanticide, especially when a woman has psychotic symptoms.

The prevention of PND is an important neglected area in the UK, with NHS effort directed towards treatment rather than prevention. A range of psychological, educational, pharmacological, social support, alternative and other interventions has been explored to minimise the development, intensity and duration of maternal depressive symptoms and their potential impact on the infant. Previous systematic reviews provided conflicting reports about the effectiveness of PND preventive interventions.

Preventive approaches relevant to PND are:

- universal preventive interventions targeting a population not at increased risk for PND
- selective preventive interventions for women perceived to be at risk for PND because of social factors
- indicated preventive interventions for women at risk of PND because of history, predisposition or above average scores on psychological measures, but not meeting diagnostic criteria.

Aims and objectives

The aims of this study were to:

1. evaluate the clinical effectiveness, cost-effectiveness, acceptability and safety of antenatal and postnatal interventions to prevent PND in pregnant and postnatal women
2. apply rigorous methods of systematic reviewing of quantitative and qualitative studies, evidence synthesis and decision-analytic modelling to evaluate the preventive impact on women, their infants and their families
3. and estimate cost-effectiveness.

The objectives were to:

(a) determine the clinical effectiveness of antenatal and postnatal interventions for preventing PND (systematic review of quantitative research)

   i. to identify moderators and mediators of the effectiveness of preventive interventions
   ii. to undertake a network meta-analysis (NMA) of available evidence, as appropriate

(b) provide a detailed service user and provider perspective on uptake, acceptability and potential harms of antenatal and postnatal interventions (systematic review of qualitative research)

   i. to examine the main service models for prevention of PND in relation to the underlying programme theory and mechanisms, focusing on group- and individual-based approaches (realist synthesis)

(c) to undertake a systematic review of economic evaluations in the area and identify other evidence needed to populate an economic model
(d) to determine the potential value of collecting further data on input parameters (expected value of information analysis).

Clinical effectiveness review methods

Data sources

A comprehensive search of MEDLINE, MEDLINE In-Process & Other Non-Indexed Citations, EMBASE, The Cochrane Library (Cochrane Systematic Reviews, Database of Abstracts of Reviews of Effects, Cochrane Central Register of Controlled Trials, NHS Economic Evaluation Database, Health Technology Assessment databases), Cumulative Index to Nursing and Allied Health Literature, PsycINFO, Science Citation Index and Conference Proceedings (Web of Science), National Institute for Health Research Health Technology Assessment Programme, Applied Social Sciences Index and Abstracts; Allied and Complementary Medicine Database and Midwives Information and Resource Service Reference Database (from inception to July 2013) in December 2012 and electronic alerts update until July 2013. The following trial databases were searched (from inception to July 2013): Current Controlled Trials, ClinicalTrials.gov and the World Health Organization's International Clinical Trials Registry Platform. Reference tracking of relevant studies was performed. Reference lists of relevant reviews were scrutinised. Searches were restricted to English-language literature with no restriction by date.

Inclusion/exclusion criteria

Population

The study population comprised all pregnant women (universal); pregnant women at risk of developing PND because of social factors (selective); pregnant women at risk of developing PND because of psychological risk factors, above average scores on psychological measures, indications of a predisposition to PND (indicated); all postnatal women in their first 6 postnatal weeks (universal) (or first postnatal year for the qualitative review); postnatal women at risk of developing PND because of social factors (selective); and postnatal women at risk of developing PND because of psychological risk factors, above average scores on psychological measures and indications of a predisposition to PND but not diagnosed with depression (indicated).

Interventions

All interventions suitable for pregnant women and women in the first 6 postnatal weeks were included.

Comparators

All usual care and enhanced usual-care control and active comparisons were considered.

Outcomes

In the review of the quantitative and the qualitative research, all outcomes reported were included. Key outcomes were measures of depressive symptoms such as the Edinburgh Postnatal Depression Scale (EPDS), depression diagnostic instruments and infant outcomes.

Data extraction

The general principles recommended in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement were used. For the quantitative studies, two independent reviewers screened all records and extracted data; disagreements were resolved through consensus. The risk of bias of included randomised controlled trials (RCTs) was assessed using Cochrane's risk-of-bias tool. For the included qualitative studies, data extraction was undertaken by one reviewer using a tailored data extraction framework, developed to elicit data extraction elements related directly to the review question and 20% of extractions were checked by a second reviewer. The methodological quality of individual

studies was appraised by two reviewers independently using an abbreviated version of the Critical Appraisal Skills Programme (CASP) quality assessment tool for qualitative studies and the CERQual (Confidence in the Evidence from Reviews of Qualitative research) approach was used to assess the certainty of the findings.

Data synthesis

Extracted data and quality assessment variables were presented in tables with narrative description. The evidence was synthesised using a NMA, which enabled a simultaneous comparison of all evaluated interventions in a single coherent analysis. Evidence from RCTs presenting data at any assessment time up to 12 months postnatally was relevant to the decision problem. The analysis of the EPDS score data was conducted in two stages: (1) a treatment-effects model, in which the effect of each intervention was estimated relative to usual care; and (2) a baseline (i.e. usual-care) model, in which the absolute response to usual care was estimated. The estimates of treatment effects relative to usual care were combined with the baseline model to provide estimates of absolute responses for each intervention; these estimates were used as inputs to the economic model.

Qualitative meta-synthesis was undertaken by highlighting women's and service providers' issues around the acceptability of interventions, elucidating evidence around personal and social support strategies (PSSSs) employed by women, using the data extraction framework and thematic synthesis to aggregate the findings. Evidence about interventions from women and from service providers and evidence about PSSSs were presented separately.

Clinical effectiveness summary results

For the quantitative studies, 3072 records were identified through electronic searches. In total, 122 papers (representing 86 unique studies of preventive interventions) were included, of which 37 studies were of universal preventive interventions, 20 were of selective interventions and 30 were of indicated interventions (one study included both indicated and universal preventive interventions). The highest levels of assessed risk of bias were for selection bias [9 of 86 RCTs (10.5%)] and for attrition and/or analysis bias [8 of 86 RCTs (9.3%)]. The universal preventive intervention studies had greater risks of bias than the selective and indicated preventive interventions; this was most notable for selection bias and attrition bias. There was a consistent lack of clarity about the allocation method, the use of a non-random process, how the baseline was defined and how this affected initiation of an intervention.

A further 23 relevant systematic reviews were identified which revealed one additional study.

Universal preventive interventions

The results were inconclusive from the set of interventions which formed a network. The most beneficial interventions at 12 months, shown by difference in the mean EPDS score, appeared to be midwifery redesigned postnatal care [–1.43, 95% credible interval (CrI) –4.00 to 1.36], person-centred approach (PCA)-based intervention (–0.97, 95% CrI –3.54 to 1.71) and cognitive–behavioural therapy (CBT)-based intervention (–0.78, 95% CrI –3.41 to 1.91).

Selective preventive interventions

Not all interventions were evaluable and the treatment effects were inconclusive. Interpersonal psychotherapy (IPT)-based intervention appeared to be beneficial as indicated by difference in mean 3-month EPDS score (–1.85, 95% CrI –5.60 to 2.14). Education on preparing for parenting appeared to be beneficial, as indicated by the difference in mean 6-month EPDS score (–1.32, 95% CrI –3.54 to 1.10).

Indicated preventive interventions

Not all interventions were evaluable, and the NMA showed that, in general, the treatment effects were inconclusive. The difference in mean 6-month EPDS score was –4.25 (95% CrI –7.78 to 0.43) for IPT-based intervention. The difference in 12-month mean EPDS score was –2.18 (95% CrI –5.39 to 1.15) for PCA-based intervention and –2.18 (95% CrI –5.39 to 1.15) for CBT-based intervention. The difference in the 6-week mean EPDS score was –1.12 (95% CrI –4.35 to 1.93) for promoting parent–infant interaction for peer support and the difference in 3-month EPDS score was –0.93 (95% CrI –5.11 to 3.32).

Cost-effectiveness review methods

A comprehensive search of published economic evaluations was performed. One reviewer independently screened titles and abstracts with discussion about uncertainty and consensus agreement. A mathematical model was constructed to explore the cost-effectiveness of interventions contained within the NMA versus usual care. An area under the curve approach was employed alongside mapping from the EPDS values to a preference-based utility score; Short Form 6-Dimensions (SF-6D). The time horizon was 1 year, amended to 2 years in a sensitivity analysis. Expected value of partial perfect information (EVPPI) analyses were undertaken for efficacy data and for mapping the EPDS values to utility.

Cost-effectiveness summary results

No economic evaluations were identified as appropriate for answering the decision problem and hence a de novo model was constructed. The cost of the interventions relative to usual care ranged from cost saving to an increase of £1200 per woman. Assuming a willingness to pay of £20,000 per quality-adjusted life-year (QALY), the most cost-effective interventions were estimated to be midwifery redesigned postnatal care, PCA-based intervention and CBT-based intervention (universal); education on preparing for pregnancy (selective); and PCA-based intervention (indicated). If a benefit of 2 years was assumed, then an IPT-based intervention was the most cost-effective indicated preventive intervention. However, there was considerable uncertainty in these results. The EVPPI for efficacy data was very large, in excess of £150M for each population.

Qualitative review summary results

For the qualitative studies, 2152 records were identified through all searches. There were 56 records included (representing 44 unique studies) which were examined at full text. In addition, 27 papers (representing 21 unique studies of preventive interventions) were included, of which 14 studies were of universal preventive interventions, three were of selective interventions and four were of indicated interventions. The studies varied in quality. Only six studies showed evidence of researcher reflexivity. No findings were assessed as being of high certainty by the CERQual approach. The remaining 29 papers (23 studies) were concerned with PSSSs to prevent PND.

Social support interventions provided emotional and informational support to women, and group-based approaches may be a useful supplement, provided that they do not prove to be too resource intensive or create unrealistic expectations of services. Continuity of care was confirmed as an important operator across several interventions in that it enabled women to build up a relationship of trust with their health-care provider.

Discussion

We undertook a rigorous systematic review and identified all relevant publications concerning the clinical effectiveness and cost-effectiveness interventions to prevent PND. Although we appraised and summarised a very large number of studies, the results of the review were inconclusive. It is possible that usual care could be the most effective intervention in all three populations.

Strengths

The analysis approach differs from that used in previous Cochrane reviews, which did not distinguish between interventions within studies in terms of control, comparator or preventive approach. Previous reviews used standardised effect sizes rather than EPDS values and also tended to not take into account the assessment time, often taking the latest assessment time. The qualitative review identified helpful features from the women's and service providers' perspectives, as well as preferences for potential improvement.

Limitations

The NMA offers an advance on previous reviews. Nevertheless, there are some limitations with the current analysis: (1) some studies were omitted because they did not provide EPDS values, which may have introduced reporting or selection bias; (2) no adjustment was made for the lack of quality associated with some trials, and treatment effects may therefore be overstated; (3) the analysis assumed independence of outcomes within studies and independence of intervention effects between studies; and (4) infant outcomes were not examined in detail because of insufficient infant outcome data.

Limitations with the cost-effectiveness analyses are that (1) interventions that did not report EPDS values were omitted from the analyses; (2) the incremental costs for each strategy have, by necessity, been estimated in a simplistic manner and costs of restructuring services have not been included; (3) the possibility of erroneous grouping of trials as a single intervention within indicated preventive interventions; and (4) simplistic assumptions have been made in estimating the area under the curve when data were not available for all time points.

Limitations with providing a conclusion regarding the most cost-effective intervention are (1) absolute QALY gains estimated are small for all interventions; and (2) there is considerable uncertainty in the direction of the estimates of QALY change compared with usual care for all interventions.

The values of future research into the relative effectiveness of interventions were shown to be very high in all populations, in the order of hundreds of millions of pounds, which would be sufficient to cover the cost of such research. Although the relationship between EPDS values and utility was not shown to influence the decision, given current information, future research should include collection of utility data. In addition, detailed costing data for each intervention should be recorded.

Research recommendations

Owing to the uncertainty associated with the results and the limitations highlighted above, our overall research recommendations and conclusions are tentative. Given the poor quality of the clinical effectiveness and cost-effectiveness evidence available, replication of some studies is needed within good-quality RCTs:

- as a universal preventive intervention: midwifery redesigned postnatal care, PCA-based intervention and CBT-based intervention
- as a selective preventive intervention: education on preparing for parenting, peer support and IPT-based intervention
- as an indicated preventive intervention: promoting parent–infant interaction; peer support (telephone-based and Newpin volunteer support); and CBT-, PCA- and IPT-based interventions.

Conclusions

As far as we are aware this is the most comprehensive review of the clinical effectiveness and cost-effectiveness, acceptability and safety of antenatal and postnatal interventions for pregnant and postnatal women to prevent PND. Despite this, no definitive conclusions can be drawn regarding the most clinically effective or cost-effective intervention because of the uncertainty about the relative effectiveness of the interventions. Several interventions would warrant replication. Future RCTs estimating the effectiveness of interventions considered acceptable to pregnant and postnatal women and the clinical community should be undertaken using the EPDS. Given the EVPPI values, future trials assessing the relative efficacies of promising interventions would appear to represent value for money.

Study registration

This study is registered as PROSPERO CRD42012003273.

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