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Best practice for perinatal mental health care: the economic case

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Abbreviations

BDI	Beck Depression Inventory
BSID	Baley Scales of Infant Development
CBT	Cognitive behavioural therapy
CES-D	Center for Epidemiological Studies Depression Scale
C-RCT	Cluster randomised controlled trial
CS	Cohort study
DASS	Depression Anxiety Stress Scales short form
EPDS	Edinburgh Postnatal Depression Scale
HAM-D	Hamilton Depression Rating Scale
ICD-10	International Classification of Diseases, Tenth Revision
IPT	Interpersonal therapy
NNT	Number-needed-to-treat
PCA	Person-centred approach
PHQ-9	9-item Patient Health Questionnaire
PTSD	Post-traumatic stress disorder
P-RCT	Pragmatic randomised controlled trial
RCT	Randomised controlled trial
RMD	Repeated measures designs
SCID	Structured Clinical Interview for Depression
SF-36	36-Item Short Form Health Survey
SR	Systematic review

Introduction

The aim of the study was to examine the potential costs and some of the potential economic benefits of early interventions that prevent or reduce perinatal mental illness and their long-term impacts on mothers and their children (thereby potentially leading to savings and other positive economic consequences). This included a comparison of the potential costs and consequences associated with such interventions compared with one or more alternative course of action (operationally defined as current practice, and sometimes referred to in studies as the 'do nothing' option). A more generalised way to describe the study is that we sought to examine the economic case for investing in early interventions that reflect best practice in England.

We defined early interventions broadly as interventions that aim to prevent or treat mental health conditions during pregnancy and up to one year postpartum. This is in line with recent NICE (2014) guidance on this topic, which describes prevention in the perinatal mental health area as being concerned with limiting the development or recurrence of mental health problems and reducing the impact of mental health problems on the child and mother. With regard to the development of the child, all perinatal mental health interventions might be regarded as primary prevention as they may avert risks of adverse events or experiences such as emotional, behavioural and cognitive conditions.

The scope of our study was defined by interventions that specifically aimed to reduce mental health problems during the perinatal period (defined as the period during pregnancy up to one year after birth). This excluded studies that did not specifically state this as the primary aim of the intervention. While the scope of our study included different perinatal mental health conditions, most evidence in this area is concerned with depression. Depression affects up to 13% of women at different trimesters and months postnatal (Gavin *et al* 2005) and often co-occurs with anxiety and other mental health problems (Lydsdottir *et al*. 2014, Wisner *et al*. 2013). The focus of this study was thus on ante- or postnatal depression but we also considered evidence on other conditions such as anxiety, posttraumatic stress disorder and psychosis. Our focus was on non-pharmacological interventions but we present evidence in relation to pharmacological interventions where this was included as part of studies on non-pharmacological interventions.

The aim of our study was to examine the costs and economic consequences of interventions that were relevant to current practice in England. The perinatal mental health area is currently undergoing substantial changes in the way services are provided; a wide range of pathways have been developed for women and families to identify mental illness in pregnancy early on and provide appropriate treatment. This includes an outline of quality standards and how different professional groups should work together. Our study sought to provide information that could potentially inform some of those changes in future provision.

During the time we were undertaking our study an important review was published by Jane Morrell and colleagues (2016). Their study is a comprehensive review of the effectiveness and cost-effectiveness of interventions that aim to prevent perinatal depression, and also included additional cost-effectiveness analysis of such interventions. We used that study to inform our own research as much as possible, although the aims of our study were different from that of Morrell *et al* in some important aspects: their focus was only on interventions that aim to prevent rather than treat postnatal depression (whilst we were interested in both) and their aim was to establish the cost-effectiveness of interventions (cost per additional quality-adjusted life year gained) rather than net benefits (i.e. economic gains expressed in pounds minus costs). The Morrell *et al* study also considered only a short-term perspective and did not model longer-term consequences (including those related to adverse child outcomes).

Method

Our method included two parts: a literature review and an economic analysis. The economic analysis also required additional searches of the literature for specific parameters.

Literature reviews and identification of relevant studies

Our study employed the following approach for identifying relevant evidence:

- We searched for the latest systematic reviews and meta-analyses of intervention studies;
- We looked at studies of interventions identified in reviews carried out as part of NICE guidance on this topic (latest review of studies in 2013);
- We carried out systematic searches, covering the years 2010 to March 2016; we searched five databases (CINAHL, EconLit, PsycINFO, Medline, Cochrane) using the following subject headings and keywords: (intervention-related terms) AND mental health-related terms) AND (perinatal period-related terms); details of those searches can be found in the Appendix;
- We carried out additional searches in Google and Google scholar to identify evidence on mother and baby (and perinatal psychiatric) units;
- We looked at studies identified by Morrell *et al.* (2016).

The final choice of studies was based on the following criteria:

- Applicability to the English health and social care system;
- Relevance to current practice in England;

- Positive findings of effectiveness (we present evidence on interventions for which evidence is less certain but do not include them in the economic analysis).

The approach of searching for and identifying relevant studies was implemented as follows. Since we were interested in good practice we only included robust studies of interventions that demonstrated positive outcomes and studies that applied to the current practice context. That meant we excluded studies from the economic analysis that were found to be neither effective nor cost-effective (e.g. by NICE guidance or the Morrell *et al* review). We still refer to those if they were considered applicable and relevant, but we did not carry out an economic analysis. We prioritised studies with higher applicability to current practice in England. For example, we looked at more recent studies and those from England, the wider UK and from high-income countries with innovative mental health practice (in particular Australia, Canada, New Zealand, US). Furthermore, we only included systematic reviews and meta-analysis published in the last couple of years. Earlier systematic reviews included largely dated studies (for example the Cochrane review by Dennis and Creedy (2004) covered studies from as early as 1980 to 2004). Where possible, we used findings from single studies (that we identified to be relevant) rather than findings from systematic reviews. We chose this approach because the problem with systematic reviews is that they summarise a wide range of interventions, which are often very different in nature and heterogeneous in terms of population groups, timing and type of interventions. Furthermore, they commonly include studies from low- and middle-income countries, and findings from those settings are less applicable to the UK.

Quality assessment

Whilst we did not carry out our own quality assessment of studies uncovered in the searches we applied a number of steps that ensured that our calculations used data from moderate-to-high quality studies. Most of the studies had been assessed in systematic reviews and we considered only studies that had passed their quality ratings (i.e. had not been rated as poor quality or as having a high risk of bias). We refer to such ratings if they were inconsistent or led to exclusion of studies. In most of the areas we only selected randomised clinical trials (RCTs) and checked that they reported no systematic differences between groups at baseline (which provided us with some confidence that the randomisation had been carried out successfully). For interventions for which RCTs were not common – namely for (1) mother and baby units and (2) for studies that were concerned with screening and service delivery – we made this transparent so that the reader can be aware of the greater level of caution that may need to be applied in the interpretation of findings. In relation to service delivery, longitudinal (cohort) or cross-sectional studies may be the more appropriate designs to assess outcomes linked to identification and treatment strategies over time or at different time points. Studies of mother-and-baby units were not

RCTs due to the nature of the work that the units do (and the potentially unethical nature of randomising people to a control group).

Economic analysis

Where possible we applied a common approach to calculating what we call the 'net benefits' of interventions, which is described here. In addition, we carried out calculations that were specific to particular studies of interventions; those are explained and presented together with the findings.

Costs of the interventions and shot-term differences in service use

We first valued resource inputs required for delivering the intervention by applying unit costs expressed at 2014/15 prices (taken from the PSSRU *Unit Costs of Health and Social Care* volume). Usually details about resource inputs were provided in studies. We made additional assumptions if such information was not provided in sufficient detail.

Next, we calculated costs linked to service use in the intervention and control groups during the period of the intervention. This referred to health and social care accessed by women in addition to the intervention under evaluation. To calculate resource implications we valued any differences in reported service contacts by applying the relevant unit costs (typically from the PSSRU source mentioned earlier). If there was no information provided we (conservatively) assumed that there had not been any impact.

Outcomes and long-term economic consequences

To assess the long-term economic consequences attached to changes in outcomes we took absolute recovery rates. This was possible because our data were from RCTs, which reported that women in both groups were comparable at baseline in terms of socio-demographic factors and other characteristics (such as depression levels), or they had adjusted for baseline differences in reporting their recovery rates. Recovery rates referred usually to short-term recovery of clinical symptoms. We did not assume that the recovery lasted for the whole year because the sustainability of outcomes is far from established, with some studies suggesting that intervention outcomes can be maintained, and others suggesting that this is not the case (e.g. Cooper *et al.* 2003). We presented evidence about long-term effectiveness where this was available and considered this in our calculations. For interventions for which long-term effectiveness had not been evaluated or findings were inconsistent, we conservatively assumed a relapse rate of 50% in the first year postpartum (in line with the approach taken by NICE 2014, p632). We then applied the costs per case averted to the additional probability of recovery due to the intervention.

Impact on mothers

Data on cost per case linked to the impact on the mother were available from our own previous research and are shown below. They present values of life-time costs. A detailed description of how they were derived can be found in Bauer *et al.* (2015, 2016). Briefly, for mothers, health and social care costs had been calculated based on additional use of such services by mothers experiencing depression (or anxiety or psychosis) during the perinatal period as well as during subsequent years linked to non-remitted mental illness or relapse. Health-related quality of life losses had been calculated based on health impairments (measured in form of health disutilities) experienced by women with depression (anxiety, psychosis) during the perinatal period as well as during subsequent years linked to non-remitted mental illness or relapse. Our estimates also included costs of life years lost due to suicide. Productivity losses had been calculated for mothers with perinatal depression (anxiety), relating to absenteeism from and presenteeism at work due to remitted and non-remitted mental illness for the proportion of women returning to full- or part-time employment after giving birth. For psychosis, estimates of yearly productivity loss were taken from existing literature and we related them to increased risk of relapse for women who experienced perinatal psychosis during the perinatal period.

Costs of perinatal depression, impact on mothers, per case (in 2014/15 prices)

Health and social care costs	Health-related quality of life losses	Productivity losses
£1,722	£18,674	£2,585

Costs of perinatal anxiety, impact on mothers, per case (in 2014/15 prices)

Health and social care costs	Health-related quality of life losses	Productivity losses
£4,407	£11,197	£5,611

Cost of perinatal psychosis, impact on mothers, per case (in 2014/15 prices)

Health and social care costs	Health-related quality of life losses	Productivity losses	Other
£24,788	£13,100	£8,559	1,992

Impact on children

Since the vast majority of the costs linked to perinatal mental illness refer to the long-term impact on the infant and child it was important to consider the potential beneficial effects in

economic terms. We valued the economic consequences of infant and child outcomes where studies had evaluated such outcomes. This included using evidence from one meta-analysis (Cuijpers *et al.* 2014), which measured the effects of psychological treatment (IPT and CBT) of maternal (and in particular perinatal) depression on child mental health. The study presented number-needed-to-treat (NNT) figures, but those did not refer to the outcomes that would have been required for the analysis (i.e. complete recovery from symptoms) and we were thus unable to take values directly. Instead, we took the relationship between the two (NNT for mothers vs. NNT for children) as an estimate of the probability that if mothers recovered because of psychological treatment their children remained unaffected by their mothers' condition. This probability was 63% and we applied this figure to interventions that were psychological treatments carried out postpartum. This figure seemed a realistic estimate as other studies of, for example, CBT for mothers with postnatal depression found that infant outcomes after intervention were similar to those of infants of non-depressed mothers (Pearson *et al.* 2013).

We applied cost estimates from our previous studies (Bauer *et al.* 2015, 2016) for measuring the impacts of perinatal depression and psychosis on the child. (We did not identify any study that would have allowed us to quantify the impact of perinatal *anxiety* on the child, and therefore we did not present those cost estimates.) For perinatal depression, we made a distinction in estimating the cost impact of depression prevented before or after birth. For interventions that were initiated towards the end of the antenatal period or during the postnatal period we removed costs linked to pre-term birth. Values are shown below: they are present values of life-time costs; a detailed description of how they have been derived can be found in Bauer *et al.* (2015, 2016).

Briefly, costs included a range of public sector costs (health and social care, education, criminal justice), health-related quality of life and productivity losses linked to a range of adverse, partly overlapping child outcomes. Adverse child outcomes included pre-term birth, infant death, emotional and conduct problems, special educational needs, and leaving school without qualifications. Health-related quality of life losses were calculated based on health impairments (measured in form of disutilities) experienced by children with cognitive, emotional or behavioral problems. Productivity losses were calculated based on their reduced probability of leaving school with qualifications. We extracted relative risk data for those outcomes from the literature and calculated the absolute additional probabilities for children exposed to perinatal mental illness to develop adverse child outcome. Different methods were applied to calculate life-time costs depending on the available data from previous research, which for some outcomes, such as conduct problems, included already published present values of long-term costs. For other outcomes such as emotional problems, we calculated present values based on annual cost estimates that had been published in studies. For some outcomes, such as pre-term birth, additional calculations were carried out to include costs that had not been included in published

estimates. Health and social care costs mainly referred to neonatal care as well as mental health treatment during childhood and adolescence. Costs of education referred to special educational needs provision. Criminal justice sector costs related to (severe) conduct problems. Productivity losses referred to reduced employment opportunities for children who leave school without qualifications as well as to productivity losses related to mental illness during adulthood.

Cost of perinatal depression, impact on children (pre-term birth excluded), per case (in 2014/15 prices)

Health and social care	Education	Criminal justice	Health-related quality of life losses	Productivity losses	Other (societal)
£1,894	£3,230	£2,014	£30,771	£5,539	£7,596

Cost of perinatal depression, impact on children (pre-term birth included), per case (in 2014/15 prices)

Health and social care	Education	Criminal justice	Health-related quality of life losses	Productivity losses	Other (societal)
£2,888	£3,230	£2,014	£31,192	£5,560	£7,600

Cost of perinatal psychosis, impact on children, per case in 2014/15 prices

Health and social care	Education	Criminal justice	Health-related quality of life losses	Productivity losses	Other (societal)
£354	£7	-	£4,851	£7	£5

Net benefit

We then simply summed up values. First, we considered the health and social care perspective by aggregating: costs of the interventions; short-term differences in service use; economic benefits linked to improved outcomes for mothers and children and averting health and social care costs. We then calculated this measure of 'net benefit' from a wider government perspective, which also included benefits linked to averted education and criminal justice costs. Finally we calculated the 'net benefit' from a wider societal

perspective, which included all costs and economic gains including those from a government perspective, health-related quality of life, productivity and other costs to individuals (which included for example out-of-pocket expenditure or victim of crime costs).

Results

We present our results in two parts. First, in Part A, we summarise the evidence from studies that we identified in our review. We conclude whether evidence could be used for our economic analysis. In Part B, we then present the economic calculations we carried out for those interventions and the calculated net benefits.

We distinguished universal and selective preventative interventions, interventions addressing mild or sub-threshold problems, interventions that addressed primarily moderate symptoms and interventions that specifically targeted women with severe and very severe illness. Categories were informed by the preventive intervention classifications – universal, selective or indicated (Mrazek *et al*. 1994) – plus other categories to include more severely affected women and models of service delivery.

- *Universal interventions* included those that were universally provided to all women during the perinatal period.
- *Selective preventive interventions* were those targeted at high-risk groups based on identified *social* risks (i.e. vulnerable groups with higher probability of developing mental illness). This did not include studies of interventions in which women were identified at higher psychological risk because of elevated symptoms.
- *Interventions addressing mild or sub-threshold symptoms* included those that were indicated preventative: Women were identified with above-average scores on psychological measures (such as a score greater than 9 on the EPDS) or other indications of a predisposition to perinatal mental illness; women meeting diagnostic criteria at that time were excluded from such studies.
- *Interventions addressing moderate to major symptoms* referred to studies that applied an EPDS cut-off point of 13 or more for recruiting women usually combined with a diagnostic tool. The majority of women in these studies had moderate to major depression. The majority of interventions in this area complemented other treatments and some had aims to increase access to specialist provision.
- *Interventions addressing major symptoms only* were those that specifically targeted women meeting diagnostic criteria for severe mental illness. Studies in this area usually evaluated very intensive interventions and included, as an important part of provision in England and UK, mother and baby inpatient units.

- With *service delivery models* we referred to programmes that have been developed to increase access to treatment, for example through screening and additional incentives and training for practitioners to signpost and refer to services and enhance service provision. This also included the role of midwives and health visitors. Studies in this area evaluated the increase in access to services involving populations at a wider geographical level. Some of them measured changes in service use as well as outcomes linked to those changes, and some were economic studies that evaluated the cost effectiveness of programmes.

As is the case with most categorisations, there were studies that could not be neatly categorised and which fell into more than one group, as we explain below.

We also report the time when the intervention was initiated (i.e. the time when women were contacted and recruited into the study), the time when the intervention started and when it was completed (indicating whether the support took place during the ante- and/or postnatal period.

Part A: Summary of the evidence

A.1 Universal interventions

Parenting education

We identified two US studies by the same lead researcher (Feinberg *et al.* 2008; N=169, Feinberg *et al.* 2015; N=148; *initiated and started during pregnancy, completed postnatal*), which found positive outcomes of a parent education programme (Family Foundation), which was designed as a universal prevention programme with particular focus on involving fathers. Half of altogether eight classes took place before birth and the remaining classes took place 3 to 6 months after birth. Findings of the study were included in the economic analysis (B1.1).

Infant sleep intervention

Hiscock *et al.* (2014; AUS; RCT; N=781; *initiated, started and completed postnatal*) evaluated a universal prevention programme offered by nurses to women during first home visits after birth (covering 93% of all births) for addressing postnatal depression as well as infant sleep and crying problems. They found that the programme reduced mothers' depression; it also improved sleep and crying problems in infants who were frequent feeders. We included findings of these studies in our analysis (B1.2).

Yoga

Newham *et al.* (2014; UK; RCT; N=59; *initiated, started and completed during pregnancy*) evaluated an 8 weeks course of yoga for low-risk women during pregnancy and found that the intervention led to a significant reduction in pregnancy-specific anxiety and prevented increases in depression. The quality of the study was unclear and findings were not presented in a way that they could be used for our analysis.

A.2 Selective preventive

Peer support, mentoring and befriending

Barnes *et al.* (2009, UK; RCT; N=527; *initiated during pregnancy, started and completed postnatal*) examined peer support provided by Home-Start volunteers to women identified during pregnancy as having a social disadvantage (assessed with the Social Disadvantage Screening Index). The intervention started on average 0.2 months after birth. The study did not find that the intervention reduced symptoms of depression (using the EPDS) at 2 to 12 months after birth. The study had methodological limitations that could have led to selection and outcome bias (Dennis and Dowswell, 2013) which means no definite conclusions could be drawn regarding the absence of an effect.

However, another UK study by Cupples *et al.* (2011, UK; RCT; N=324; *initiated and started during pregnancy, completed postnatal*) also found that home visits by peer mentors did not lead to significant differences in depression (measured via BSID and SF-36) or infant development at one year. The mentoring sessions (mean number of contacts 8.5) were offered twice monthly during pregnancy and monthly for the first postpartum year to women living in socio-economically deprived areas. Peer mentors were mothers with at least one child under 10 years, who were matched based on age and locality. They received an initial 2-hour training session, follow-up training sessions every 6-8 weeks and ongoing supervision from a midwife.

Harris *et al.* (2006, UK; RCT; N=65; *initiated and started during pregnancy, completed postnatal*) evaluated the Newpin befriending intervention and found positive impacts that were statistically significant. We did not have full text access but information was available from Dennis and Dowswell (2013) and Morrell *et al.* (2016). The intervention took place during the ante- and postnatal period and consisted of individual sessions in the person's home as well as psycho-educational group meetings led by trained volunteers who themselves were mothers. Pregnant women were screened and those thought to be at risk for depression were contacted about the study. Quality ratings by the two systematic reviews were in slight disagreement: whilst Dennis and Dowswell rated the study as having high risk of bias, Morrell and colleagues rated the study as having low or unclear risk of bias

(overall unclear). We included the study in our analysis but findings need to be interpreted with some caution (B2.1).

Parenting and mother-infant support

We identified a UK study of an antenatal parenting support intervention (Mellow Bumps), which aimed to promote the mother-infant interaction among women identified as high-risk and demonstrated positive maternal mental health outcomes (Wilson *et al.* 2013; UK, exploratory RCT; N=31; *initiated, started and completed during pregnancy*); however, changes did not reach significance so that we did not use their findings for the economic analysis.

CBT addressing multiple risks

We identified a large US study (El-Mohandes *et al.* 2008; US; RCT; N=1,070; *initiated, started and completed during pregnancy*), which evaluated CBT to address depression in women identified at high social risk. The intervention was provided during pregnancy and aimed to address a range of risk factors including depression, smoking and domestic violence. The study sought to measure the effect of the intervention on a range of birth outcomes. The intervention significantly reduced very pre-term birth outcomes. It also improved other pregnancy outcomes although the latter did not reach clinical significance. We included findings from this study in our analysis (B2.2)

Integrated healthy lifestyle intervention

We identified one US study of a healthy lifestyle intervention that was culturally and linguistically tailored with a focus on social support and provided by community health workers (MOMs; Kieffer *et al.* 2013; US; N=275*; initiated, started and completed during pregnancy*). The intervention was offered to pregnant women from a particular ethnic group and on low incomes. Findings showed that women's depressive symptoms did not reduce significantly at postpartum follow up compared to a standard educational intervention about healthy pregnancy.

A.3 Interventions addressing mild or subthreshold symptoms (indicated preventative)

Peer support

We identified a Canadian (economic) evaluation of telephone-based peer-support provided to women who scored 9 or higher on the EPDS (Dennis 2009, Dukhovny *et al.* 2013; CAN; RCT; N=701; *initiated, started and completed postnatal*). The intervention consisted of individualised telephone-based peer-support targeted on women after birth. Volunteers

were mothers with lived experience who were recruited from the community and who attended a four-hour training session. The mean number of contacts was 8.8 (mean duration was 14.1 minutes). Findings suggested that this type of peer-support could be cost-effective and we included their findings in our analysis (B3.1).

Parenting and mother-infant support

A UK RCT (Petrou *et al.* 2006; Cooper *et al.* 2015; UK; RCT; N=66; 180; *initiated and started during pregnancy, completed postnatal*) examined the benefits of home visits by health visitors with focus on promoting parent-infant interaction; the interventions were initiated during pregnancy to women scoring 24 or more on the Cooper Predictive Index of Postnatal Depression (Cooper *et al.* 1996). The economic evaluation presented cost-effectiveness results per month of depression avoided and concluded that the intervention was likely to be cost-effective (Petrou *et al.* 2006). We thus included their findings in our analysis (B3.2). However, findings need to be interpreted with caution because of the non-significant difference in the outcome and the findings from the main study by Cooper *et al.* (2015), which did not confirm any positive outcomes. The intervention involved 11 home visits provided by health visitors, two antenatally and nine postnatally. Visits were supportive in nature, with specific measures to enhance maternal sensitivity to infant communicative signals, including items from the Neonatal Behavioral Assessment Scale. The intervention had no impact on maternal mood, the quality of the maternal parenting behaviours, or infant outcome, although there were suggestions, on some self-report measures, that those women with a lower level of antenatal risk experienced benefits.

We identified an Australian study (Milgrom *et al.* 2011; AUS; RCT; N=143; *initiated, started and completed during pregnancy*), which evaluated a facilitated self-help intervention (Towards Parenthood) focused on the mother-infant relationship but implemented a wider approach that aimed at reducing the impact of risk factors, strengthening relationships and providing problem-solving skills in regards to emotional health and the demands of parenting. Women were recruited from hospital by midwives during pregnancy (20–32 weeks) and screened with the EPDS and risk assessment checklist. Women who scored above 12 on the EPDS and/or with high scores on the checklist were all invited to participate. Although women did not necessarily have elevated EPDS scores we categorised the intervention under this section as the baseline prevalence of above threshold depression (BDI-II >13), anxiety (DASS anxiety >7) and stress (DASS stress > 14) was 30%, 41% and 35%. Findings suggested that the intervention was effective and we included them in our analysis (B3.3).

Werner *et al.* (2015; US; RCT; N=54; *initiated and started during pregnancy, completed postnatal*) evaluated an intervention called Practical Resources for Effective Postpartum Parenting (PREPP); the aim was to determine if a behavioural intervention primarily targeting maternal caregiving could increase infant sleep and reduce fussing or crying, and

thereby reduce the incidence or severity of postpartum maternal depression. This was an integrated intervention that incorporated caregiving techniques, traditional psychotherapy approaches, psycho-education, as well as mindfulness meditation training. Women were recruited during pregnancy; those scoring above 24 on the Cooper Predictive Index of Postnatal Depression (Cooper *et al.* 1996) were invited to participate. The intervention consisted of three personal sessions provided by a clinical psychologist during pregnancy and after birth. Findings suggest that the intervention had short-term benefits in reducing maternal anxiety and depression, and that infants had fewer bouts of fussing and crying. Outcomes were not measured via EPDS scores and did not present changes in number of women who recovered so that findings could not be used for the economic analysis.

Group CBT

One US study (Tandon *et al.* 2014; US; RCT; N=78*; initiated, started and completed during pregnancy or postnatal period*) evaluated the effectiveness of group-based CBT incorporated into a home visitation programme targeted on women with elevated symptoms of depression (CES-D of 16 and more) during pregnancy and up to 6 months postpartum. Women experiencing a depressive episode (assessed with the Maternal Mood Screener, a checklist that has shown good concordance with diagnostic interviews) were referred to further assessment and mental health treatment. Women were from a particular ethnic group (African American) and on low incomes. The intervention consisted of six two-hour intervention sessions delivered weekly in a group format by either a licensed clinical social worker or clinical psychologist. Primary outcome was the number of women who did not experience major depression during the follow-up. The intervention was effective and we included findings in our analysis (B3.4).

A.4 Interventions addressing moderate to severe symptoms

Facilitated-self help

Two UK studies by the same lead researcher (O'Mahen *et al.* 2013a; N=910, O'Mahen *et al.* 2014; N=83; UK; RCTs; *initiated, started and completed during postnatal period*) evaluated the same type of facilitated self-help in form of a computer-delivered, behavioural activation intervention provided during the postnatal period. Women with a new born not older than a year were recruited into the studies. Women in the second trial had a diagnostic assessment over the phone and were only eligible if they met ICD-10 criteria for *major depressive disorder*, whilst women in the first and larger trial were recruited if they scored greater than 12 on the EPDS. Findings suggested that those interventions were effective in reducing depression. We included findings from both studies in the economic analysis (B4.1).

Multi-disciplinary, specialist care

We identified one economic evaluation carried in form of a prospective cohort study, which compared costs and outcomes of a parent and baby day unit for mothers with moderate to major depression versus standard care in England and found that the intervention was likely to be cost-effective (Boath *et al.* 2003; UK; CS; N=60; *initiated, started and completed during ante- and/or postnatal period*). Although the setting of a day hospital was less relevant to the current practice context in England, the types of services offered were particularly innovative at that time and we considered those to reflect current good practice; we thus included their findings in the economic analysis (B4.2).

CBT (including mindfulness-based) during pregnancy

A systematic review by O'Connor *et al.* (2016) showed pooled results for CBT for n=11,869 pregnant women with absolute increases in remission rates compared with usual care ranging from 6.2% to 34.6%; recent studies of CBT during pregnancy as identified in the review with applicability to the current UK context showed absolute rates of as large as 30% (McGregor *et al.* 2014; Canada); however, the study was not a RCT (and effects might have been overestimated as a result) and we did not include findings in our analysis. However, we identified a small recent RCT from the UK (Burns *et al.* 2013; UK; RCT; N=36*; initiated, started and completed during pregnancy*), which evaluated individual CBT provided in women's homes. Women who met a diagnosis of depression (assessed using the CIS-R) were recruited through routine contact with midwives. The vast majority (83%) had an ICD-10 diagnosis of moderate (56%) or severe (28%) depression. Women were excluded if they were currently receiving CBT or any individual or group psychological therapy for depression or if they had a psychotic illness. Findings suggested that the intervention was effective for treating antenatal depression and we included findings in our analysis (B4.3).

A growing body of evidence is emerging (primarily from the US) that supports the effectiveness of mindfulness-based CBT in reducing anxiety (as well as depression) during pregnancy. For example, in an open-treatment pilot study (Goodman *et al.* 2014, US; RMD; N=24; *initiated, started and completed during pregnancy*) women identified with generalised anxiety disorder completed the intervention with high attendance, good compliance and statistically and clinically significant improvements in anxiety, worry, depression, self-compassion and mindfulness. Of the 17 women who met criteria for generalised anxiety disorder at baseline, only one continued to meet criteria post-intervention. However, since the study did not have a control group and was not an RCT we did not consider the findings robust enough for our analysis.

CBT during postnatal period

We identified one recent UK study by Marss (2013; UK; RMD; N=36), which found that CBT group intervention provided to women who scored 12 or above on the EPDS postpartum

could reduce depression; however the study did not have a control group so we did not use its data. Morrell *et al.* (2009; UK; RCT; N=2,241; *initiated, started and completed postnatal*) evaluated CBT and a person-centred approach provided to women with scores of 12 and above on the EPDS during the postnatal period. The interventions were provided by health visitors. Findings suggested that both approaches were able to achieve significant reductions in depression and that they were cost-effective so that they could inform our analysis (B4.4).

Stevenson *et al.* (2010) presented a systematic review and an economic model of health visitor-provided CBT; the latter was based primarily on data from an older UK RCT by Honey *et al.* (2002; UK; RCT; N=45; *initiated, started and completed postnatal*). In their model they evaluated the cost-effectiveness of CBT provided for women at some point during the year after birth (on average 5 months postpartum); women were randomised who had a score of 12 or above on the EPDS (not confirmed by diagnostic interview). Their findings did not confirm the short-term cost-effectiveness of the intervention. The model applied a range of means to ensure that the potential uncertainty of values was accounted for and we thus used their findings to explore in our analysis whether the interventions was likely to lead to positive net benefits (if longer-term impact was considered). It is interesting to note other evidence suggested that health visitors can provide additional CBT support without necessarily leading to higher costs (Appleby *et al.* 2003). We therefore included findings from the economic evaluation in our analysis (B4.5).

Furthermore, we identified one RCT from Australia (Milgrom *et al.* 2005; AUS; RCT; N=49; *initiated, started and completed postnatal*), which was applicable to the UK context and evaluated group-based CBT taking place in clinics for women identified with scores of 12 and above on the EPDS. The findings showed that the intervention was effective in reducing depression and we included them in our analysis (B4.6).

Interpersonal therapy (IPT)

A Cochrane systematic review by Dennis and Dowswell (2013; SR; N=17,000) found that IPT was likely to be an effective intervention in the prevention of postpartum depression. The HTA review and economic analysis by Morrell and colleagues (2016; SR) also found that IPT was effective and cost-effective. We were unable to identify evidence from the UK and instead looked for evidence from other countries.

We identified evidence for the effectiveness of IPT for moderate to major depression targeted at vulnerable groups. A US study by Zlotnick *et al.* (2011; US; RCT; N=54; *initiated and started during pregnancy, completed postnatal*) was focused on IPT enhancement of social support and used empowerment based strategies especially relevant for women with intimate partner violence; the intervention aimed to improve women's mental health such as symptoms of depression, post-traumatic stress disorder (PTSD), and anxiety by providing

social support as a protective factor against the negative effects of partner violence. Whilst the intervention reduced symptoms of PTSD and depression during pregnancy and (for PTSD) up to 3 months postpartum, it did not significantly reduce the likelihood of women experiencing a major depressive episode, PTSD, or intimate partner violence. We thus were not able to calculate potential economic benefits. However, we identified another US study (Grote *et al.* 2009; RCT; US; N=52; *initiated, started and completed during pregnancy*) focused on socioeconomically disadvantaged women from one particular ethnic group. Enhanced IPT was provided which included a multicomponent model of care designed to treat antenatal depression for women identified at clinic with depression (EPDS>12). As many as 56% of the intervention group participants had at least one anxiety disorder, including 28% with PTSD and 20% with panic disorder. Similar rates were found in the control group. The study found that the intervention was effective in reducing major depression and we included the study's findings in our economic analysis (B4.7).

Complementary therapies incl. yoga, massage

Evidence showed that a number of complementary therapies provided alongside usual care or specific psychological therapies were effective in reducing anxiety and depression during pregnancy. A small study by Mitchell *et al.* (2012; US; RCT; N=24; *initiated, started and completed during pregnancy*) showed that a 12-week yoga intervention (two times a week) targeted at pregnant women meeting diagnostic criteria for depression on the Structured Clinical Interview for Depression could reduce depressive symptoms. Similarly a larger study by Field *et al.* (2013; US; RCT; N=92; *initiated, started and completed during pregnancy*) found that a 12-week yoga intervention (1 time a week) provided to this target group was effective in reducing depression, anxiety and sleep disturbances. Two single studies from the same group of researchers showed significant reduction in cortisol levels in pregnancy and improvements of maternal anxiety and depression after yoga and massage therapy (Field *et al.* 2009; US; RCT; N=112; Field *et al.* 2012; US; RCT; N=84; *initiated, started and completed during pregnancy*). In addition, infants of women in yoga and massage therapy groups had greater gestational age and birth weight than the control group (Field *et al.* 2012). The quality of the studies in this area was unclear and findings were not presented in a way that we could use them in our analysis.

A.5 Interventions addressing major symptoms

Facilitated exercise

A pragmatic RCT (Daley *et al.* 2015; UK; P-RCT; N=94; *initiated, started and completed postnatal*) reported that an exercise intervention targeted at women meeting diagnostic ICD-10 criteria for major depression reduced postnatal depression (measured via EPDS); 34% of women had thoughts of self- harming at baseline. The intervention involved

encouragement to exercise and to seek out social support to exercise; women participating in the trial had a diagnosis of major depression. Outcomes included EPDS score as a binary variable (recovered and improved) at 6 and 12 months post-randomisation so that we could include findings in our analysis (B5.1).

Massage therapy

Field *et al.* (2009; US; N=112; *initiated, started and completed during pregnancy*) compared group massage therapy session for women with major depression during pregnancy based on the SCID; they were provided in combination with IPT whilst mothers in the control group received group-based IPT only. Group therapy sessions in the intervention group were held for one hour and twenty minutes (versus one hour in the control group) once per week for a total of 6 sessions. Group massage therapy sessions were led by trained massage therapists. The group who received both therapies showed a greater decrease in depression, depressed affect and somatic vegetative symptom scores on the CES-D, a greater decrease in anxiety scale (STAI) scores and a greater decrease in cortisol levels. The intervention did not have an effect on neonatal outcomes which contradicted earlier results which showed reduced prematurity and low birthweight (Field *et al*. 2004). Results of the study were not reported in a way that they could have been used for our analysis.

CBT

We identified one US study (Ammerman *et al.* 2013b; US; RCT; N=93; *initiated, started and completed postnatal*), which evaluated CBT provided to women who had been identified with major depressive disorder at 3 months postpartum. The intervention was provided as part of a home visitation programme for vulnerable groups of mothers in their own home. The study found that the intervention was effective in reducing major depression and we included findings in our analysis (B5.2).

IPT

We identified one study from Australia (Mulcahy *et al.* 2010; AUS; N=50; *initiated, started and completed postnatal*), which evaluated a group-based IPT intervention provided to women with major postnatal depression assessed with Millon Clinical Multiaxial Inventory-III (MCMI-III; Millon *et al*. 1997) and a score of 14 or more on the Hamilton Depression Rating Scale- 17 item (HAM-D; Hamilton 1960); the intervention specifically targeted social role transitions and interpersonal relationships but also grief and loss issues associated with becoming a parent. The study measured a range of mother and infant outcomes including depressive symptoms, marital adjustment, social support, and mother-infant bond. The intervention led to significantly greater reductions in mean depression scores, and had continued improvements at 3 months post therapy. Furthermore, the group was more likely to report better marital functioning and perceptions of the mother-infant bond. Data from the same study had also been analysed by Reay *et al.* (2012) in a long-term follow up (mean

age of children 2.6yrs) and showed that outcomes were sustained i.e. that mothers in the intervention group were less likely to develop a persistent course of depression compared to mothers in the control condition. Interestingly, mothers who received combined IPT and antidepressant medication did not show a significantly greater rate of mean improvement in depression compared to those who received IPT alone. Findings of the two studies (Mulcahy *et al.* 2010, Reay *et al.* 2012) were included in our analysis (B5.3).

Mother and baby units

Inpatient specialist services allow mothers with severe perinatal mental illness during the ante- or postnatal period to be admitted jointly with their infant, while the mother is treated, to promote the formation of their relationship. Units offer a wide range of interventions including a wide range of psychological treatments and therapies such as art, relaxation, behavioural, and mindfulness-based cognitive therapy, M-wave biofeedback therapy, mother–infant attachment therapy, family and partner-assisted interpersonal psychotherapy, therapeutic yoga, spiritual support, nursery nurse inputs and infant massage (Meltzer-Brody *et al*. 2014). Most mothers get medication at mother and baby units (e.g. 87%, Kimmel *et al*. 2016) and some get ECT (e.g. 10%, Kimmel *et al*. 2016).

We identified a few studies, which examined the feasibility and effectiveness of particular interventions in mother and baby units; such as parenting programmes (Butler *et al.* 2014; UK; qualitative design; N=15) and heart rate variability biofeedback therapy (Beckham *et al.* 2013; US; RMD; N=15); both interventions had the potential to achieve additional positive outcomes but results were not reported in a way that they could be used for our analysis and further research is needed to confirm their effectiveness.

The majority of studies, however, evaluated changes in mothers' and infant health from admission to discharge (without employing a control group). A few studies employed long-term follow-ups and a couple compared the results against natural and non-randomised control groups.

One cohort study (Meltzer-Brody *et al.* 2014; US; N=91) showed that mothers' symptoms of depression (measured via EPDS) and anxiety (measured via Generalised Anxiety Disorder Scale) improved and active suicide ideation (measured via Patient Health Questionnaire) reduced between admission and discharge. Overall functioning also improved (measured via the Work and Social Adjustment Scale). Positive outcomes were confirmed study by Christl *et al.* (2015; AUS; N=191) showing improvements from admission to discharge in terms of depression (measured via EPDS) and functioning; the majority of women (73%) recovered symptomatically. A systematic review of mother and baby units (Gillham and Wittkowski 2015; SR; 13 out of 23 studies from UK) found a range of outcomes indicating positive effects on maternal mental health that could be sustained in the long-term. A very recent US study that looked specifically at women with bipolar and psychotic mood disorders

(Kimmel *et al.* 2016; US; N=47) found that women stayed on average 10 days in the unit and improved significantly in terms of depression, anxiety and functioning.

In term of infant and child outcomes, a range of studies also found positive outcomes. A UK study (Kenny *et al.* 2013; N=138) found that mother-infant interactions improved between admission and discharge; the study made comparisons with a community sample of women with similar severity of conditions and a non-depressed sample and found that improvements in maternal sensitivity, responsiveness and infant cooperativeness were significantly stronger than in the community sample and similar to the non-depressed sample. An earlier UK study (Wai Wan *et al.* 2007; N=16) compared outcomes of children (4 to 6yrs) whose mothers had been admitted to a mother and baby unit with those of offspring of mothers not admitted as well as with standardised child norms; findings suggest that children had similar outcomes to comparison children or standardised child norms, which could indicate that treatment in the mother and baby unit can lead to long-term improvements. Christl *et al.* (2015) reported that parenting confidence and infant attachment improved significantly during their stay in the mother and baby unit. The review by Gillham and Wittkowski (2015) confirmed significant improvements in mother–infant relationships and an absence of adverse effects on child development; they also reported long-term follow-up data in which 21 % of women were clinically depressed at 4 to 6 years.

We used data from the different studies as it was feasible for the modelling (i.e. result needed to be presented in a way that they could be used to derive recovery rates; B5.4).

A.5 Service delivery models

Bowen *et al.* (2012, Canada; N=649) investigated access to services and the effects of different treatment options if women were encouraged to seek assessment and treatment. Women who were assessed for treatment and scored 12 or more on the EPDS were encouraged to seek assessment and treatment. The unadjusted prevalence of depressive symptoms (EPDS score 12 or more) was 14% in early pregnancy, 10% in late pregnancy, and 8% postpartum. 12% of women were engaged in treatment. 21% of women who were depressed in early pregnancy were also depressed in postpartum and 27% of women who were depressed in late pregnancy experienced depression in postpartum. The predicted mean EPDS score decreased over the course of the pregnancy into the postpartum period, most significantly when women were engaged in counselling or taking psychotropic medication. Counselling was the more common method of treatment during pregnancy, and medication was the most common in the postpartum period.

In a very recent review, Byatt *et al.* (2015) summarised findings of studies that evaluated mental health care use after screening for depression in perinatal care setting. They found

that when no intervention was in place, an average of 22% of women who screened positive for depression had at least one mental health visit; rate of mental health service use increased with patient engagement strategies to 44%, with on-site assessments to 49% and with perinatal care provider training to 54%. High rates of mental health care use (81%) were associated with implementation of additional interventions. The authors found that the quality of studies varied widely and referred in their conclusions to one high quality study by Yawn *et al.* (2012; N=1,897) who evaluated a practice-based training and network programme for the screening, diagnosis and management of postnatal depression. Among the 654 women with elevated postpartum depression screening scores (using a multi-step screening and diagnosis process with the EPDS and PHQ-9), those in the intervention practices were more likely to receive a diagnosis and therapy for postpartum depression: 66% vs. 41% (diagnosis); 56% vs. 35% (medication); 20% vs. 11% (counselling); 60% vs. 37% (counselling and medication). They also had lower depressive symptom levels at 6 and 12 months postpartum although this did not reach statistical significance.

Another very recent systematic review by O'Connor *et al.* (2016, 6 trials, N=11,869) looked at programmes involving depression screening, with or without additional treatment components, compared with usual care; they found an absolute reduction of 2.1% to 9.1% in the risk of depression at follow-up (3 to 5 months) among pregnant and postpartum women. Since the studies did not provide sufficient details about the resource inputs to cost the programmes and because of the availability of a recent England specific economic model (NICE 2014) we did not carry out economic analysis.

This economic model found that screening with access to self-help as well as structured psychological therapy was cost-effective (NICE 2014). The research found that screening through the initial Whooley questions that was followed by the assessment with the PHQ-9 was the most cost-effective screening strategy. Mean total costs per woman were £77 in 2014/15 prices and mean total QALYs per woman were 0.75; in comparison to standard care the incremental cost-effectiveness ratio was £11,972 and thus well under the NICE threshold of £25,000. The model did not consider a strategy of applying EPDS and then PHQ-9 as evaluated by Yawn and colleagues so it is possible that this would be more cost-effective.

In the literature, there is still a debate whether the use of screening strategies and standard treatment itself would lead to better outcomes, as a large proportion of women will not take up the screening (Reay *et al.* 2011). Instead collaborative approaches and additional enhancements have been recommended (Truitt *et al.* 2013). A large cluster-randomised trial (Lumley *et al.* 2006; N=18,555) involving 16 rural and metropolitan communities in Australia, which aimed to reduce the relative risk of depression in mothers six months after birth by 20% did not lead to any significant improvements. The model (PRISM; Programme of Resources, Information and Support for Mothers) involved primary care and community-

based strategies embedded in existing services and included awareness raising and information materials to mothers as well as service providers; it provided additional incentives for local services to raise awareness and signpost to services. It was less clear in how far the focus had been on supporting collaborative approaches. Some of the intervention studies (Milgrom *et al.* 2011, Ammerman *et al.* 2013) included collaborative elements of provision and showed that this was effective. However, because the focus of the evaluation had not been on collaborative care its contribution could not be established.

A UK cluster randomised controlled trial (McArthur *et al.* 2003; UK; C-RCT; 36 general practices; N=2,064; *initiated, started and completed during pregnancy*) evaluated a redesigned community postnatal care service led by midwives and tailored to the health and psychological needs of women postnatal. Participants were all women eligible for postnatal care. Outcomes were measured at 4 and 12 months via the SF-36 and EPDS. The intervention was found to be effective. Whilst the study is relatively old we still considered it relevant to the current context of service delivery. It is possible that some or most midwifery teams already deliver this type of redesigned care but it is important to understand potential net benefits of working in this way. Whilst this study looked at redesigned care, it also presented a universal intervention and we thus categorised it in the economic analysis as such (B1.3).

In many of the intervention studies we identified in our review, midwives had an important role in identifying women with mental health symptoms during pregnancy and referring them to certain types of specialist provision (e.g. CBT). Recent evidence from the UK also suggests the feasibility of training midwifes to provide psychological interventions (Brugha *et al.* 2016). However, we also identified evidence that suggested that *only* providing continuity of midwifery care (in the form of a named midwife who as far as possible followed the woman through pregnancy care, delivery and postnatally) and providing additional visits did not lead to changes in outcomes (Marks *et al.* 2003).

Similarly, in the studies we identified in our review health visitors had an important role in the early identification of mental health conditions during the postpartum period. Based on good quality evidence (in particular Morrell *et al.* 2009) there have been also developments in England in building health visitors' capacities to identify women with depressive symptoms postnatally and provide early psychological interventions. This includes additional visits and activities from trained health visitors with the aim being to identify and – under clinical supervision - support women at risk of postnatal depression. Evidence from the same study by Morrell and colleagues also suggests that there are wider universal benefits for all women if health visitors are trained, probably due to increased awareness, confidence and skills of health visitors to focus on women's psychological wellbeing during visits (Brugha *et al*. 2010). Training and supervision seems to be an essential component as

studies show that simply increasing the number of visits by health visitors in itself did not lead to better outcomes (Christie and Bunting 2011; N=295; UK).

Part B: Economic analysis

B.1 Universal interventions

B.1.1 Family Foundation (Feinberg *et al.* 2008; N=169, Feinberg *et al.* 2015; N=148; *initiated and started during pregnancy, completed postnatal*)

Description

This was a universal, psychosocial intervention that aimed to reduce maternal distress by supporting the inter-parental (couple) relationship; the group-format programme was designed to prepare couples to enter parenthood together in a supportive manner. The intervention consisted of a series of classes for first-time, expectant couples; half of the eight classes took place before birth and the remaining classes took place 3 to 6 months after birth; each group consisted of 6 to 10 couples; two facilitators (male and female) led each class.

Costs of intervention

We estimated the costs of the intervention at £304 per couple; this was based on unit costs for two psychological wellbeing practitioners (Band 5) of £76 per hour, eight sessions, assumed duration of 2 hours per session and an average of eight couples.

Short-term changes in resource use

The study found short-term changes in C-section: 21% vs. 40% had a C-section in the intervention compared to the standard care group. In the UK, Caesarean sections have been found to cost an average of £2,369 (NICE 2011) while a natural birth (vaginal delivery) costs an average £1,824 (NHS Reference Costs 2013-2014). In 2014/15 theses costs were £2,458 versus £1,876.

Outcomes (and economic consequences)

Intervention found in earlier study (Feinberg *et al.* 2008) to reduce maternal depression and anxiety but outcomes were not presented in a way that we could use for the economic analysis. The study indicated significant positive effects on coparental support, distress in the parent–child relationship, and several indicators of infant regulation.

Net benefit

Based on the one outcome only, which was the number of Caesarean sections, there was a positive net benefit of £111 per woman from a health and social care perspective.

B.1.2 The Baby Business programme (Hiscock *et al.* 2014; AUS; RCT; N=781; *initiated, started and completed postnatal*)

Description

The intervention was a universal parenting support and mother-baby intervention that aimed to reduce mothers' depression by providing information about normal infant sleep and cry patterns, settling techniques, medical causes of crying and parent self-care. The intervention was delivered via a booklet and DVD (at infant age 4 weeks), telephone consultation (at infant age 8 weeks), and parent group (at infant age 13 weeks) versus standard care (which was described as child-well care). Intervention families were also offered an individual telephone consultation at infant age 6 to 8 weeks (peak infant crying time) and a 1.5-hour parent group session at approximately infant age 12 weeks. In both intervention and standard care groups, parents were encouraged to discuss cry or sleeping problems and to develop a tailored management plan (e.g. establish a bedtime routine) to address any problems. Telephone consultations and group sessions were delivered by trained health professionals (nurses, psychologists) with a background in infant care and followed standardised scripts. Staff conducting the telephone and group interventions met on a regular basis with a paediatrician and clinical psychologist to monitor fidelity to content and troubleshoot clinical issues.

Costs of the intervention

The total cost of providing the intervention was £97 per family (in 2014/15 prices). This included the costs of training health professionals, delivering consultation phone calls, running the parent group sessions, distribution of intervention materials, and overhead costs. Training cost was estimated as the time of trainers and trainees plus training materials. Consultation phone call cost included time spent making appointments, rescheduling families, and preparing for and delivering calls (20 minutes). Parent group costs included time spent booking appointments, rescheduling families, preparing (15 minutes), facilitating the group session (about 1 hour), and travel expenses.

Outcomes (and long-term economic consequences)

Relative to mothers in the control group, mothers in the intervention group were less likely to score > 9 on the EPDS at 6 months (7.9%, vs 12.9%); earlier research of a similar programme designed by the same researchers (Hiscock *et al.* 2008) showed long-term benefits. At 2 years mothers in the intervention group were less likely than control mothers to report clinical depression symptoms (clinical cut off point of EPDS < 12): 4.2% versus 13.2%. Since this figure provided the longer-term estimate of remission at the clinical cut-off point we used this additional probability of 9% for the analysis. The estimated economic benefits in relation to reduced impact on mothers are shown below.

Health and social care costs	Health-related quality of life losses	Productivity losses
£155	£1,681	£233

There was also evidence of a positive impact on the infant: Mothers were more likely to

spend 20 or more minutes attending infant wakings (41% vs. 51%) and change formula (13% vs. 23%). Infants in the intervention group were significantly less likely to have daytime sleep or cry problems at 4 months and fewer infants had sleep problems (27% vs. 33%). Since it is unclear whether sleep problems are causing long-term adverse effects (with a recent study by Price *et al.* 2012 not finding any long-term negative effects on the child) we did not carry out any calculations.

Net benefit

From a health and social care perspective, there was a net benefit of £58 per woman. Economic benefits from a societal perspective were £1,972.

B.1.3 Midwifery-led service delivery model (McArthur *et al.* 2003; UK; C-RCT; 36 general practices; N=2,064; *initiated, started and completed during pregnancy*)

Description

The redesigned care focused on the identification and management of women's physical and mental health problems and was midwifery-led with general practitioner (GP) contact only if required. Symptom checklists were used at the first home visit, 10 and 28 days, and the Edinburgh Postnatal Depression Scale (EPDS) at 28 days, to maximise identification of problems. Evidence-based guidelines, including clear GP referral criteria, were applied. The length and duration of visits were extended, with home visits to 28 days and a follow up check at 10 to 12 weeks.

Short-term differences in service use and costs (including costs of the intervention)

Costs were measured by collecting information about all health and social care contacts for both women in the intervention and control group. Assuming a worst case scenario, the authors report that the costs of service use in the intervention group were £145 higher compared to the control group (in 2014/15 prices); mean total costs of service use (before considering costs of the intervention) ranged between £805 to £830 in the intervention group (in 2014/15 prices). This was based on a range of differences in service use between women in the control and intervention group. Women in the intervention group had on average 0.68 fewer GP consultations during the first year postpartum and this was a conservative estimate, which showed statistical significance. There were also a significantly lower number of GP prescriptions issued in the intervention group (-0.75; $p<0.01$). Referrals to allied health professionals in primary care were greater in the control group (although this was not significant). There were a significantly higher number of secondary care referrals to allied health professionals (OR 1.6, 95% 1.03 to 2.49) and of secondary care consultations for the baby in the intervention group (OR 1.37, 95% CI 0.93 to 2.03). Also, the mean number of visits of midwives as recorded by midwives was significantly greater in the intervention than the control group (6.0 versus 4.3) and visits lasted significantly longer (78 versus 31 minutes).

Outcomes (economic consequences)

Number of women with scores in EPDS of 13 or higher at 12-months follow-up was significantly lower in the intervention group (12.2% vs. 21.6%; p<0.001). Since this estimate referred to the 12-month period we did not apply any relapse rate to account for women relapsing in the first year postpartum; we used the additional probability of 9.4% for women to recover when they received the redesigned care. The economic benefits are shown below.

Health and social care costs	Health-related quality of life losses	Productivity losses
£162	£1,755	£243

Net benefit

The study did not present net benefit estimates so we carried out our own calculations. Based on the information on costs linked to resource use and economic gains, the new intervention was likely to achieve a small net benefit of £17 from a health and social care perspective. From a societal perspective the net benefit was £2,015.

B.2 Selective preventive interventions

B.2.1 Newpin Befriending (Harris *et al.* 2006; UK; RCT; N=65; *initiated and started during pregnancy, completed postnatal*)

Description

This befriending intervention was provided by volunteers and aimed to prevent the onset of depression by providing social support; the intervention took place during the ante and postnatal period and consisted of individual sessions in the person's home in form of 1-to-1 befriending as well as psycho-educational group meetings led by trained volunteers who themselves were mothers. Pregnant women were screened and those thought to be at risk for depression were contacted about the study. Women with psychotic illness, major depression, serious suicidal risk or poor fluency in English were excluded.

Costs of the intervention

We did not have access to full text and did not have details of resource inputs. The costs of peer support for mothers during the perinatal period were estimated by Morrell *et al.* (2016) at £150 and we took this estimate for the befriending intervention in the absence of better information.

Outcomes (and economic consequences)

The following outcomes were measured: onset of major depression, minor depression requiring medication, or - if already depressed - a failure to recover during the period from baseline to follow-up. Outcome data were measured using the Schedules for assessment in Neuropsychiatry which yields a diagnosis of depression according to DSM-IV criteria. Morrell *et al.* (2016) reported findings from personal communication which

showed an onset of major depression of 27% (8/30) for the Newpin befriender group and 54% (19/35) for the control group (p=0.045). Applying a relapse rate of 50% the additional chance that a woman would not develop major depression during the first year postpartum due to the intervention was then 13.5%. The associated economic benefits were:

Health and social care costs	Health-related quality of life losses	Productivity losses
£195	£2,119	£294

Net benefit

Befriending led to a positive net benefit of £45 from a health and social care perspective and £2,413 from a societal perspective; this was based on specific assumptions, in particular that peer support could be implemented at a low cost of £150 per women.

B.2.2 CBT addressing multiple risks (El-Mohandes *et al.* 2008; US; RCT; N=1,070; *initiated, started and completed during pregnancy)*

Description

This integrated behavioural intervention addressed risk factors during the perinatal period more widely (such as depression, smoking, domestic violence) and included CBT for addressing depression. Eight individualised counselling sessions lasting on average 35 minutes were provided by an intervention specialist. The intervention was provided during the antenatal period and aimed to improve four infant outcomes: very low birth weight; low birth weight; pre-term birth; very pre-term birth.

Costs of intervention

We estimated costs of the intervention at £499. This was based on eight sessions (35 minutes each) and unit costs of CBT (PSSRU 2015, p90).

Outcomes (and economic consequences)

All outcomes were better in the comparison group but the difference only reached significance for very pre-term birth, with 2.2% in the IG versus 5.0% in the CG. On average, 36 mothers needed to receive the intervention to prevent one case of very pre-term birth. The net values of life-time costs for very pre-term birth (per case) are as shown below (in second row) together with economic benefits linked to the additional reduction in risk of very pre-term birth of 2.8% (in first row).

Costs of very pre-term birth	Health and social care	Education	Productivity	Out-of-pocket expenditure
Total cost per case	£107,178	£4,975	£2,443	£3,973
Reduced cost due to intervention	£3,001	£141	£68	£111

Net benefit
We estimated a positive net benefit of £2,502 per woman from a health and social care perspective only, and this economic advantage was even higher (£2,643) from a public sector perspective if cost savings to the education sector were considered. From a societal perspective the net benefit was as high as £2,823. This did not yet include quality of life losses which are substantial for this group.

B.3 Interventions addressing mild or subthreshold symptoms

B3.1 Peer support, in UK known as 'Mum-4-mum' (Dennis *et al.* 2009, Dukhovny *et al.* 2013; CAN; RCT; N=701; *initiated, started and completed postnatal*)
Description
The intervention consisted of individualised telephone-based peer-support targeted on women after birth with EPDS > 9; volunteers were mothers with lived experience who were recruited from the community; they attended a four-hour training session; the mean number of contacts was 8.8; the mean length of contact was 14.1 minutes, ranging from 1 to 180 minutes; women in the control group accessed standard community postpartum care including access to services from public health nurses and other providers and drop in centres.
Costs of the intervention
Costs of the intervention were £373 in 2014/15 prices (uprated from costs presented in Morrell *et al.* 2009).
Short-term changes in resources use
The mean cost per woman was £3,054 in the peer-support group and £2,295 in the usual care group (difference of £759, $p < 0.0001$). This referred to a wide range of resources from a societal perspective including health service use, volunteer time, time taken off work, child care, and other out-of-pocket expenditure.
Outcomes
At 12 weeks, 14% (40/297) of women in the intervention group and 25% (78/315) in the control group had an EPDS >12; at 24 weeks 11% (33/289) of women in the intervention group and 14% (43/311) in the control group had a score >12. In addition, there was a positive trend in favour of the intervention group for maternal anxiety but not loneliness. We did not have to calculate economic consequences as the study included an economic evaluation and findings were presented and could directly inform net benefits.
Net benefit
The study found a 95% probability that the programme would cost less than £13,714 per case of postpartum depression averted. We compared this against the costs per case of perinatal depression (see Table in method section). From a health and social care perspective there was a net cost of £11,992; from a societal perspective there was a net benefit of £9,267.

B3.2 Parenting and mother-infant support (Petrou *et al*. 2006; Cooper *et al*, 2015; UK; RCT; N=66; 180; *initiated and started during pregnancy, completed postnatal*)
Description
The study evaluated counselling and specific support for mother-infant relationships; home visits (mean of 10.5) were carried out by trained health visitors; it aimed to reduce postnatal depression and enhance mother-infant relationship; the intervention was provided to pregnant women scoring 24 or more predictive index of postnatal depression.
Costs
The study found that on average costs were £178 higher in the intervention group (in 2014/15 prices).
Outcomes
Women in the preventive intervention group spent on average 0.49 months (2.14 weeks) longer without depression but this difference was not significant. Based on an incremental health utility for postnatal depression of 0.26 (Bauer *et al.* 2015) and a cost per QALY threshold of £25,000, economic benefits from this change in outcomes were £268.
Net benefit
From a health and social care perspective there was an additional net cost of £178; from a societal perspective there was a small net benefit of £90.

B3.3 Mother-infant support 'Towards Parenthood' (Milgrom *et al*. 2011; AUS; RCT; N=143*; initiated, started and completed during pregnancy*)
Description
Facilitated self-help included 'Towards Parenthood' intervention and community networking delivered over 8 weeks. Women received a self-help workbook and were encouraged to read material each week and then discuss the content with a (trainee) psychologist in weekly telephone support sessions; telephone calls lasted approximately half an hour. Both intervention and control groups received community networking information to encourage and enable help-seeking; this included information about professional services (e.g. GPs, midwives, social workers, psychology services) and non-clinical community supports (e.g. playgroups, mother's groups); they also received an information booklet about emotional health during pregnancy and early parenthood. In addition, each participant's GP and other appropriate health professionals were contacted by letter and/or phone and provided with contact details for all other health professionals in contact with the woman to encourage collaborative case management. GPs were advised of their patient's screening score (this was clearly explained on participants' consent forms) and received an 'Antenatal and Postnatal Depression Management Guide'.
Costs of the intervention
We estimated that costs were £437 per woman (in 2014/15 prices). This estimate was

based on eight telephone-based support sessions (30 minutes per session) provided by psychological therapist (an average was taken between speciality doctor, clinical psychologist and mental health nurse from PSSRU 2015; p90; £107/hr); plus facilitated self-help manual costing £9.09 (*Overcoming Depression: A 'Books on Prescription' Title: A Self-help Guide Using Cognitive Behavioral Techniques* by Paul Gilbert; Amazon.co.uk).

Outcomes (and economic consequences)

Prevalence of depression (BDI-II of 14 and above) decreased by 17% in the intervention group and increased by 5% in the control group; n=21 (30%) women in IG and n=24 (33%) had a high depression score at baseline, whilst n=6 (13%) and n=16 (38%) had high depression scores post intervention. If we applied the relapse rate of 50% then the additional probability that a woman would have a lasting recovery was 11%. The associated economic benefits were as follows:

Health and social care costs	Health-related quality of life losses	Productivity losses
£189	£2,054	£284

In addition, the prevalence of anxiety (measured with DASS anxiety score of 8 and above) decreased substantially from n=29 (41%) cent to n=3 (6%) in the intervention group compared to a decrease in standard care group from n=23 (32%) to n=11 (26%). We avoided double counting and conservatively only counted the probability of recovery from anxiety of 18% in IG and of 6% in the standard care group. After applying a 50% risk of relapse, the additional probability that a woman would only experience a very short episode of perinatal anxiety was 6%. The economic benefits were then as follows.

Health and social care costs	Health-related quality of life losses	Productivity losses
£264	£672	£336

Net benefit

From a health and social care public sector perspective there was a small benefit of £16 per woman. From a societal perspective the net benefit amounted to £3,362.

B3.4 Group CBT 'The Mothers and Babies Course' (Tandon *et al*. 2014; US; RCT; N=78*; initiated, started and completed during pregnancy or postnatal period*)

Description

This CBT-based group intervention (the Mothers and Babies Course) was designed to prevent the development of major depression in low-income women who were recruited from pregnancy and up to 6 months postpartum; the course consisted of six two-hour intervention sessions delivered weekly in a group format by either a clinical social worker or

clinical psychologist; the number of women per group ranged from six to nine. All women participated in home visiting programmes and the majority were African American. Home visitors reinforced group material for five to ten minutes during each of their regularly scheduled home visits with intervention participants using visual tools. Booster sessions were conducted at 3-months and 6-months post-intervention. Intervention participants were provided with transportation, childcare (if needed), and a meal at each session. Whilst women were recruited who had elevated depressive symptoms (CES-D ≥ 16) and/or a lifetime depressive episode, the study excluded women with moderate to major depression who were sent to additional specialist mental health treatment.

Costs of the intervention

We estimated the costs of the intervention at £414 per woman; this was based on one clinical psychologist providing eight sessions of 2 hours each (including booster sessions) to on average 8 women (£282). In addition the costs of health visitor were included (£50) based on six sessions and 7.5 minutes of health visitors' client-related time. Since this group course was targeted at low-income groups which required additional incentives, we also added in the additional costs for crèche (£42, PSSRU 2015 p99) and food (£40, PSSRU p99) but not for transport as it was assumed that most women had publicly funded travel passes.

Outcomes (and long-term economic consequences)

At the six-month follow-up, 15% of women who received the intervention had experienced a major depressive episode as compared with 32% of women receiving usual care. Since this intervention was preventing major depression we did not apply a relapse rate but used the difference in affected women of 17% to calculate potential economic benefits.

Health and social care costs	Health-related quality of life losses	Productivity losses
£293	£3,175	£440

We estimated the economic benefits linked to a reduced likelihood of developing child problems due to the intervention of 10.7%.

Health and social care	Education	Criminal justice	Health-related quality of life losses	Productivity losses	Other (societal)
£203	£346	£214	£3,293	£593	£813

Net benefit

From a health and social care perspective the net benefit was £82. This increased to £642 from a broader government perspective. From a societal perspective the net benefit was

£8,956.

B.4 Interventions addressing primarily moderate symptoms

B4.1 Facilitated self-help 'Netmums' (O'Mahen *et al.* 2013a; N=910, O'Mahen *et al.* 2014; N=83; UK; RCTs; *initiated, started and completed during postnatal period*)
Description
The intervention referred to web-based, behavioural activation following principles of CBT. The intervention specifically aimed to address barriers to treatment. Women were recruited via a UK website called 'Netmums'; eligible participants were women with EPDS score of >12 in the postnatal period; women in both groups also had access to pharmacological treatment (but were excluded if they were already engaged in psychological treatment). The intervention consisted of 11 online sessions that lasted on average 40mins and were completed weekly and 1 to 2 support sessions delivered over 15 weeks. In the second study (O'Mahen *et al.* 2014) treatment materials were modified taking a modular approach, and offering additional guided support. The intervention consisted of 8 computer sessions and 12 telephone sessions; the first telephone session had a mean duration of 50 minutes; sessions two to 12 had a mean duration of 29 minutes.
Costs of interventions
Costs were estimated in the latest NICE guidance at £230 in 2014/15 prices. This estimate was based on seven telephone-based support sessions (25 minutes per session) provided by psychological wellbeing practitioner (Band 5) trained in perinatal issues; plus facilitated self-help manual costing £9.09 (*Overcoming Depression: A 'Books on Prescription' Title: A Self-help Guide Using Cognitive Behavioral Techniques* by Paul Gilbert; Amazon.co.uk). Since the unit costs of psychological wellbeing practitioner were not available they were approximated using a unit cost of a mental health nurse (Band 5) £76 per hour (Curtis, 2013 uprated to 2014/15 prices). We also estimated costs ourselves taking a more conservative approach and valued the newer modified intervention. Costs of the intervention were then £476; this was based on 12 telephone sessions with the mean durations described above and the costs of the self-help manual.
Short-term changes in resource use
There were no differences in health service utilisation between the intervention and control groups at baseline or at follow up. At baseline, 63% of the total randomised sample was taking an antidepressant medication (none was in mental health therapy because this was an exclusion criterion of the trial).
Outcomes (and long-term economic consequences)
In the first (second) study a reliable and clinically significant improvement (EPDS <12) was seen in 61% (62%) of those in the IG compared with 41% (29%) in the CG. If we applied a relapse rate of 50% to the data then the estimated probability that a woman would recover

due to the intervention was 10%. If this figure was applied then the potential long-term economic consequences (at present value) were as follows:

Health and social care costs	Health-related quality of life losses	Productivity losses
£172	£1,867	£259

No infant outcomes were measured and we could not identify any evidence of positive infant outcomes from other evaluations of computerised or web-based CBT.

Net benefit

There was a small negative net benefit of -£58 (-£304) from a health and social care perspective if the lower (higher) estimate of the costs of the intervention were applied. However, if a societal perspective was taken then the net benefit was a large positive one of £2,073 (£1,822).

B4.2 Multi-disciplinary, specialist care in 'Parent and baby day unit' (Boath *et al.* 2003; UK; CS; N=60; *initiated, started and completed during ante- and/or postnatal period*)

Description

The unit offered multi-disciplinary care to women with major postnatal depression. The unit was consultant-led and nurse-managed and staffed by a multi-disciplinary team consisting of four psychiatric nurses (Grades G, F, E and D), one senior occupational therapist, one nursery nurse, a receptionist / secretary and a quarter-time domestic assistant. The medical staffing consisted of a lead consultant (one session per week), two clinical assistants (three sessions) and a senior registrar (two sessions). The unit offered individual, couple and family counselling, group therapy, creative therapy, hobbies and activities, stress management, assertiveness training, yoga and relaxation, a group for parents and older children and pharmacotherapy. The ethos of the unit was to foster social support and to improve social networks. The informal atmosphere of the unit was used to promote social interaction between clients and they were encouraged to spend time in the nursery. Women in the standard care group had access to a GP and health visitor and to psychiatric inpatient care.

Costs of the intervention

Mean costs of parent and baby care in 1992/3 prices were £991 (95% CI, £611to £1,371). Uprated to 2014/15 prices this amount was £1,870.

Short-term differences in service use and costs

There were no significant differences between the two groups in costs related to GP and health visitors or medication. However, the study found additional costs in the control group in form of specialist provision. Three of the 30 women in the standard care group were referred to a Community Psychiatric Nurse. Two of the three women were referred to psychiatric inpatient care. Total costs of the three women who received treatment beyond

primary care were £9,269 and mean costs were £309 (this was £583 in 2014/15 prices).

Outcomes (and economic consequences)

At 6 months follow up, 21 of the 30 women (70%) were no longer depressed (measured with the Clinical Interview Schedule; Goldberg *et al.* 1970) compared with seven women (23%) in the standard care group. The study reported no significant difference in other characteristics between women in the two groups. The estimated additional probability that a woman in the intervention group would recover at 6 months postpartum was thus 47%. As before, we applied a 50% chance that women would relapse in the course of the next 6 months: the additional chance of recovery used for the calculation of long-term cost savings was 23.5%. The associated economic benefits are shown below.

Health and social care costs	Health-related quality of life losses	Productivity losses
£405	£4,388	£608

The original study did not measure the impact on the infant or child. We applied the same approach as before to estimate the economic gains linked to averted negative child impact (the additional probability of averted child impact due to the intervention was 14.8%).

Health and social care	Education	Criminal justice	Health-related quality of life losses	Productivity losses	Other (societal)
£280	£478	£298	£4,554	£820	£1,124

Net benefit

Before considering the economic gains due to improved outcomes, the net benefit was negative as the intervention generated additional costs of £1,287. When gains were considered from a health and social care perspective this reduced to costs of £602. If a broader government perspective was taken the net benefit became positive (£174). From a societal perspective the net benefit was as large as £11,668.

B4.3 Individual CBT during pregnancy in women's home (Burns *et al.* 2013; UK; RCT; N=36*; initiated, started and completed during pregnancy*)

Description

Women in this study were recruited through routine contact with midwives if they screened positive on a 3-question depression screen (Whooley questions) and met ICD-10 criteria for depression assessed using the Clinical Interview Schedule – Revised version (CIS-R). 72% of women completed 9 or more sessions of CBT before the end of pregnancy; the majority of those women (77%) attended all 12 sessions.

Costs of the intervention

We calculated the mean costs per woman of £784; this was based on the full twelve sessions and the assumption that each session lasted 55 minutes and that CBT therapists had travel time of 40 minutes per visit; unit for CBT were taken from PSSRU (2015).

Short-term differences in service use

The study showed that women in the control group were more likely to be referred to specialist perinatal psychiatry treatment (86% vs.14%). All those referrals were to a specialist psychological treatment service, although there was no information available on whether treatment was started or completed. We calculated the additional cost for specialist perinatal mental health services for women in the control group. The costs for the five women were £12,270 so that the average cost per woman in the control group (N=13) was £944. This was based on costs of community specialist provision of £2,454.

Women in both groups continued to receive usual care from their midwife and GP. No comparisons were presented for differences in the two groups so that we did not calculate costs. There were some differences in the use of antidepressants between the two groups with more women in the intervention group more likely to stop taking antidepressants during pregnancy and after giving birth. However, those numbers were small and we did not include them in the calculations.

Outcomes (and economic consequences)

At 15 weeks post-randomisation (the end of pregnancy), there were more women in the intervention group (69%) who recovered (i.e. no longer met ICD-10 criteria for depression), than those receiving only usual care (39%). We assumed as outlined before that 50% of women who recovered during the antenatal period would relapse during the postnatal period so that the additional chance of recovery for a woman participating in the intervention was 15%.

Health and social care costs	Health-related quality of life losses	Productivity losses
£258	£2,801	£388

The study did not measure the impact on the infant or child. We applied the approach described before to estimate economic gains linked to averted negative child impact. The additional probability that a child would not experience negative impact due to the intervention was 9.5%. The potential economic gains are shown below.

Health and social care	Education	Criminal justice	Health-related quality of life losses	Productivity losses	Other (societal)
£180	£307	£191	£2,923	£526	£722

Net benefit

Even before considering any economic gains of improved outcomes, the intervention achieved a positive net benefit of £160 due to higher short-term health and social care costs in the control group. After considering outcome-related gains from a health and social care perspective the net benefit increased to £598. From a broader government perspective the net benefit was £1,096 and from a societal perspective £8,456.

B4.4 Psychological interventions (CBT, PCA) during postnatal period, PONDER trial (Morrell *et al.* 2009; UK; RCT; N=2,241; *initiated, started and completed postnatal*)

Description

The study evaluated health visitor training in the assessment for postnatal depression combined with psychological interventions using CBT and PCA approaches for eligible women (EPDS score of 12 or more) provided by health visitors.

Short-term changes in costs (including costs of the intervention)

Costs of providing the intervention were not presented separately. Instead, the study presented all costs linked to health and social care use in the intervention and control group. Mean total costs in the intervention group were lower than in the control group (£427 vs. £471, in 2014/15 prices). This included health visitor contacts, GP contacts, mother and baby unit or psychiatric unit admissions, community mental health contacts, clinical mental health contacts, A&E attendances, social services contacts and antidepressant and other prescriptions. Costs for health visitors included the costs of training for the intervention group and translated into a cost per hour of client time of £100 vs. £97 in comparison group (in 2014/15 prices).

Outcomes (and economic consequences)

At 6 months postnatally, 93 of the 271 (34%) women in the intervention group and 67 of the 147 women in the control group (46%) had an EPDS score of 12 or more at 6 weeks; at 6 months 12% versus 16% had an EPDS of > 12; the exact difference in scores between intervention and standard care group was 4.7% (p=0.003); the study showed that outcomes were sustained at 12 months so that for our analysis of economic benefits we applied the additional probability of recovery due to the intervention of 4.7%.

Health and social care costs	Health-related quality of life losses	Productivity losses
£81	£878	£122

The study did not evaluate the impact on the infant or child. We applied the approach as before to estimate potential economic gains due to averted negative effects on the child. The additional probability that a child would not experience a negative impact due to the intervention was 2.9%. The associated economic gains are shown below.

Health and social care	Education	Criminal justice	Health-related quality of life losses	Productivity losses	Other (societal)
£55	£94	£58	£892	£161	£220

Net benefit

Even before considering economic gains of improved outcomes the intervention had a positive net benefit of £44 from a health and social care perspective due to reductions in short-term service use. If the gains from improved outcomes were considered then the net benefit increased to £180 from a health and social care perspective and to £332 from a wider government perspective (which included gains to education and criminal justice sectors). From a societal perspective the gain was £2,605.

B4.5 Group CBT during postnatal period (Stevenson *et al.* 2010; UK; economic model; *initiated, started and completed postnatal*)

Description

Women assessed by health visitors as scoring above 12 on EPDS were referred to brief psycho-educational group which consists of eight weekly, 2-hour meetings, run by two health visitors. The number of participants per group was five.

Costs of intervention

Stevenson *et al* estimated the costs of providing intervention based on the resources reported in the study (£1,317) and from an assessment made by a group of experts regarding the likely resources required (£1,246); the price year was not reported and we assumed that it was the most recent one before publication of the data i.e. 2009/10. Our uprated costs in 2014/15 prices were £1,437 and £1,360. Costs included a comprehensive range of resource inputs including initial assessment and preparation time. For our analysis we took the higher cost estimate of £1,437 following a conservative approach.

Outcomes (and economic consequences)

A significantly higher number of women in the intervention group scored below the cut-off for major probable postnatal depression at 8 months (65% versus 36%, $p<0.05$); the additional chance of recovery was thus 29% and after accounting for the 50% chance of relapse in the following months (until one year postpartum) we estimated that the additional chance of recovery was 14.5%. The economic benefits linked to these improvements are shown below.

Health and social care costs	Health-related quality of life losses	Productivity losses
£250	£2,708	£375

Impact on the infant or child was not considered in the study. We applied the evidence of the impact of psychological treatment as described in the Methods section (i.e. we assumed that for 63% of children whose mothers recovered there were not negative outcomes); this translated to an additional probability of 9.1% for children whose mothers participated in the intervention to not experience adverse effects. Potential additional economic gains because of the reduced impact on children are shown below.

Health and social care	Education	Criminal justice	Health-related quality of life losses	Productivity losses	Other (societal)
£172	£294	£183	£2,800	£504	£691

Net benefit

From a health and social care perspective there was a net cost of £1,015. From a broader government perspective (which included the costs to the education and criminal justice sector) net costs reduced to £538. From a societal perspective the net benefit was large and positive (£6,540).

B4.6 Group CBT during postnatal period (Milgrom *et al.* 2005; AUS; RCT; N=49; *initiated, started and completed postnatal)*

Description

Group-based CBT took place in clinics, which also included a partner session, relaxation and time management; nine 90-minute sessions were delivered by senior therapists and 5 to 10 women were attending the course. Women were randomised postpartum if they scored above 12 on the EPDS and met criteria for DSM-IV diagnosis of depression.

Costs of the intervention

We estimated the costs of the intervention at £476 per woman; this was based on unit costs for two clinical psychologists (Band 8 median) of £141 per hour of client contact (in 2014/15 prices) and an average of 8 participating women.

Outcomes (and economic consequences)

The following remission rates were found in the intervention versus standard care group at 3 months: 55% vs. 28% (Milgrom *et al.* 2005; also reported in review by O'Connor *et al.* 2016). After applying the 50% relapse risk, the additional probability of remitted depression early on was 13.5%, leading to the following economic benefits.

Health and social care costs	Health-related quality of life losses	Productivity losses
£195	£2119	£294

As before we estimated the potential economic gains because of averted child problems. The additional probability that a child would not develop problems due to the intervention was 8.5%. The respective economic gains are shown below.

Health and social care	Education	Criminal justice	Health-related quality of life losses	Productivity losses	Other (societal)
£161	£275	£171	£2,616	£471	£646

Net benefit

From a health and social care perspective, there was a net cost of £120; however, this turned into a net benefit of £326 when a wider government perspective was taken. From a societal perspective the net benefit was £6,472.

B4.7 Enhanced IPT (Grote *et al.* 2009; RCT; US; N=52; *initiated, started and completed during pregnancy)*

Description

Enhanced IPT included a multicomponent model of care designed to treat antenatal depression; the intervention consisted of an engagement session, followed by eight 'acute IPT' sessions before the birth and 'maintenance IPT' up to six months postpartum. IPT was specifically enhanced to make it culturally relevant to socioeconomically disadvantaged women (here, African American women primarily). Women (N=53) received the intervention if they had been identified at a clinic with depression (EPDS > 12). 56% of participants in the intervention group had at least one anxiety disorder, including 28% with PTSD and 20% with panic disorder. Similar rates were found in the control group.

Costs of the intervention

We estimated that costs of the intervention were £2,115. This was based on unit costs of a clinical psychologist of £141 and 15 sessions (including engagement sessions) lasting an hour each.

Outcomes (and long-term economic consequences)

At 3 months a significantly larger proportion of women in the intervention group (95%) no longer met criteria for major depression compared with those in usual care (58%); at 6 months no women had major depression in the intervention group, compared with 70% of those in usual care. We applied a relapse rate of 50% and the additional chance of recovery throughout most parts of the postnatal period due to the intervention was then 18.5%.

Health and social care costs	Health-related quality of life losses	Productivity losses
£319	£3,455	£478

Mothers in the intervention group were significantly more likely than mothers in the usual care group to report that they and their family members thought they were doing a good job in taking care of their baby's needs and engaging in physical contact and play with their baby. We applied the approach as before to estimate economic gains of reduced child impact but this time used the estimate for impact on children that included pre-term birth (since the main parts of the intervention took place during the antenatal period). The additional chance that a child would not experience adverse effects due to the intervention was 11.7%. The associated economic benefits are shown below.

Health and social care	Education	Criminal justice	Health-related quality of life losses	Productivity losses	Other (societal)
£338	£378	£236	£3,618	£651	£889

Net benefit

There was a net cost of £1,458 from a health and social care perspective. This reduced to a net cost of £844 from a wider government perspective. From a societal perspective the net benefit was £8,247.

B.5 Interventions addressing major symptoms

B5.1 Facilitated exercise (Daley *et al.* 2015; UK; P-RCT; N=94; *initiated, started and completed postnatal*)

Description

Women were randomised in the 6 months following birth to receive usual care plus a facilitated exercise intervention or usual care only. The intervention involved two face-to-face consultations and two telephone support calls with a physical activity facilitator over 6 months to support participants to engage in regular exercise. At baseline, 34% of women reported thoughts of self-harming.

Costs of the intervention

We were not able to identify a suitable unit cost for a physical activity coordinator and instead applied the costs for a physical activity intervention of £179 (PSSRU 2015, p111).

Outcomes (and long-term economic consequences)

Based on EPDS score, a larger proportion of the intervention group had recovered (46.5% vs.

23.8%) compared with usual care at 6 months follow-up. We applied a relapse rate of 50% for the next 6 months so that the additional probability that a woman would recover was 11.4%. The economic benefit linked to this outcome is shown below.

Health and social care costs	Health-related quality of life losses	Productivity losses
£196	£2,129	£295

Net benefit

From a health and social care perspective there was a small net benefit per woman of £17. From a societal perspective the net benefit was £2,441.

B5.2 Individual CBT as part of home visitation programme (Ammerman *et al.* 2013b; US; RCT; N=93; *initiated, started and completed postnatal*)

Description

CBT was provided as part of a home visitation programme for vulnerable mothers who had been identified with major depressive disorder at 3 months postpartum. Women in the control group received ongoing home visits with access to treatment in the community. CBT was delivered in the home by therapists. Treatment consisted of 15 sessions that were scheduled weekly and lasted 60 minutes plus a booster session at one month posttreatment. Treatment content focused on issues relevant to this population, such as transition to adult roles, stress management, parenting challenges, and family relationships. Another focus was on facilitating communication and collaboration with home visitors (shared web-based system and telephone contact). In addition, the home visitor attended the 15th session with the mother and therapist. Weekly supervision was provided by doctoral-level clinicians and included review of audiotaped sessions.

Costs of the intervention

We estimated the costs of the interventions at £2,853. This was based on 16 sessions (including booster session) lasting 60 minutes each, assuming a unit cost of £107 per hour of CBT (PSSRU 2015) and an estimated travelling time of 40 minutes per session.

Short-term differences in service use

Estimated costs of treatment in the control group were £277 per woman. This was based on the following information reported in the study: 35% of mothers in the control group accessed treatment in the community; 21% received medication and 16% received psychotherapy; this figure increased between end of treatment and follow up to 44.7% (18.4% received medication and 36.8% received psychotherapy). Over the whole period of the trial it was reported that 15.8% of mothers in the control group received appropriate and sufficient treatment. We applied costs from NICE guidance for intensive psychology therapy (£1,623, in 2014/15 prices) and for pharmacological treatment (£218, in 2014/15 prices); both costs included the additional care required and were thus costs of adequate treatment.

Conservatively we only applied the costs to the proportion of women that accessed treatment and could be assumed to receive adequate treatment (45%). We thus estimated that 8% of women got pharmacological treatment adhering to NICE standards and 16% of women got psychotherapy adhering to NICE standards.

Outcomes (and economic consequences)

Mothers in the intervention group showed improvements in all indicators of depression relative to the control group and these gains were maintained at follow-up. 71% of mothers receiving CBT no longer met criteria for major depressive disorder compared to 30% in the control group at 3 months follow-up. After applying a relapse rate of 50% for the rest of the postpartum year, the additional probability that a woman recovered from major depression was 10.5%.

Health and social care costs	Health-related quality of life losses	Productivity losses
£181	£1,961	£271

We estimated economic gains of CBT because of a reduced probability of child problems of 6.6%. The economic gains are shown below.

Health and social care	Education	Criminal justice	Health-related quality of life losses	Productivity losses	Other (societal)
£125	£213	£133	£2,031	£336	£501

Net benefit

The additional health and social care costs in the intervention group (before considering any gains from improved outcomes) were £2,576. From a health and social care perspective this reduced to £2,270 after such benefits were considered. It reduced further to £1,924 from a broader government perspective. From a societal perspective there was a positive net benefit, which amounted to £3,176.

B5.3 Group IPT during postnatal period (Mulcahy *et al.* 2010; AUS; N=50; *initiated, started and completed postnatal*)

Description

The intervention was an eight-week Interpersonal Psychotherapy (IPT) programme, modified for a group setting. Mothers were randomised if they had a DSM-IV diagnosis of major postnatal depression. The intervention specifically targeted interpersonal relationships, social role transitions, conflicts and issues with key relationships, as well as grief and loss issues associated with becoming a parent. It consisted of two individual sessions, eight group

therapy sessions (2 hours duration) and an additional two-hour partner's evening; provided by experienced mental health clinicians trained in both individual and group IPT. Groups were run at local community centres, with accredited childcare staff in close proximity to the group facilities providing free childcare. IPT had received a wide range of training and received comprehensive supervision.

Costs of the intervention

We estimated the costs of the intervention at £691 per woman; this was based on one clinical psychologist providing eight sessions of two hours each – including partner session - to on average of 8 women (£317), two individual sessions of one hour provided by a clinical psychologist (£282); as before we added costs for crèche for 9 group sessions (£47, PSSRU 2015 p99) and also for food (£45, PSSRU, p99) but not for transport as it was assumed that most women had publicly funded travel passes.

Short-term differences in service use and costs

The study did not find significant differences between the two groups in relation to their usage of antidepressant medication, maternal and child health nurse support, self-help support groups or alternative therapies for treating their depression. However, significantly fewer women in the intervention group received psychotherapy (8% vs 34%) or counselling (21% vs 52%) compared to women in the control group. We estimated the costs linked to the probability of additional use of psychotherapy in the control group (26%) by applying the unit costs from NICE guidance for intensive psychological treatment of £1,623 (in 2014/15 prices); costs per woman were £422. For counselling we based estimates on the additional probability of 30% and the unit costs of therapist and assumed conservatively that women had access to on average 3 sessions; costs per woman were £88. Taken together the average costs of mental health service use were £510 higher in the control than in the intervention group.

Outcomes (and long-term economic consequences)

70% of women recovered in the intervention group versus 33.3% in the comparison group ($p< 0.011$); recovery was defined as a decrease on EPDS score at 8 weeks of four points from above to below the clinical cut off of 13. The additional chance that a woman would recover was thus 37%. We applied a 50% relapse rate so that the additional chance of full recovery during the postnatal period was 18.5%. Economic benefits linked to those improvements are shown below.

Health and social care costs	Health-related quality of life losses	Productivity losses
£319	£3,455	£478

In addition, the intervention group showed significant improvement in marital functioning, social support, and infant caregiving from the beginning to end of treatment (8wks), whilst the treatment-as-usual women did not show any statistically significant improvement.

As before we calculated the economic benefits of the reduced probability that children did not experience any adverse effects due to the intervention (which was 11.7%).

Health and social care	Education	Criminal justice	Health-related quality of life losses	Productivity losses	Other (societal)
£222	£378	£236	£3,600	£643	£889

Net benefit

From a health and social care perspective there was a net benefit of £360, which increased to £974 of from a wider government perspective. From a societal perspective the net benefit was £10,039.

B5.4 Mother and baby unit (different data sources including from US, AUS, UK)

Description

Most mothers get medication at mother and baby units (e.g. 87%, Kimmel *et al.* 2016) and some get ECT (e.g. 10%, Kimmel *et al.* 2016). Interventions provided at these units could include a wide range of psychological treatments and therapies such as art, relaxation, behavioural, and mindfulness-based cognitive therapy, M-wave biofeedback therapy, mother–infant attachment therapy, family and partner-assisted interpersonal psychotherapy, therapeutic yoga, spiritual support, nursery nurse inputs and infant massage (Meltzer-Brody *et al.* 2014).

Costs of intervention

The average cost per mother treated in a mother and baby unit is £34,450 (NHS benchmarking network).

Outcomes (and long-term economic consequences)

Kimmel *et al.* (2016) presented admission score on the EDPS of 20.4 at admission and 8.8 at discharge, with a mean difference of −11.6 ($p<0.001$). From these data we calculated the probability that a woman recovered during her stay at the unit (assuming a normal distribution of women's EPDS scores). Since all women had been above the cut-off score (EPDS> 12) when they were admitted, we only needed to derive the probability of having a score on the EPDS of >12 from the distribution of EPDS scores at discharge. The probability that a woman would recover was 72%. This number is almost identical to the one found in Christl *et al.* (2015). We applied long-term follow-up data from Gillham and Wittkowski (2015) and thus estimated that about 50% of mothers admitted to the mothers and baby unit recovered permanently.

Health and social care costs	Health-related quality of life losses	Productivity losses

£861	£9,337	£1,293

In addition, we estimated benefits linked to women whose mental illness had the severity of psychosis (10.6% on mother and baby unit, Kimmel *et al.* 2016). Again, we assumed the same 50% probability as before that mothers recovered permanently due their admission at the mother and baby unit.

Health and social care costs	Health-related quality of life losses	Productivity losses	Other
£1,314	£694	£454	106

In the review by Gillham and Wittkowski (2015), one study found that 76% of children were rated as having good health or no problems, and recorded difficulties were often transitory. A further study used a range of standardised tools with children whose mothers had been discharged 4 to 6 years previously. No concerns with behavioural, emotional, or cognitive functioning were revealed. However, only 28% of eligible mothers participated, limiting the power of this study. Conservatively we took the data from the review (rather than 100%) and applied the 76% directly to estimate potential gains due to negative child impact averted.

Health and social care	Education	Criminal justice	Health-related quality of life losses	Productivity losses	Other (societal)
£1,439	£2,455	£1,531	£23,386	£4,210	£5,773

As before, we assumed that 10.6% of the sample had psychosis and that thus additional economic benefits occurred from averted negative child impact not only due to depression but also due to psychosis.

Health and social care	Education	Criminal justice	Health-related quality of life losses	Productivity losses	Other (societal)
£28	£1	-	£367	£1	£0

Net benefit

From a health and social care perspective mother and baby units generated net costs of £30,080. From a wider government perspective net costs reduced to £26,821. From a societal perspective there was a net benefit of £18,801.

B3.5 Summary

A summary of the findings of the economic analysis is presented below.

	Net benefit health and social care perspective	*Net benefit government perspective*	*Net benefit societal perspective*
Universal preventive interventions			
B1.1 Parenting education 'Family Foundation' (US), antenatal	111	111	111
B1.2 Infant sleep intervention 'Baby Business programme'(AUS), postnatal	58	58	1,972
B1.3 Midwifery-led service delivery model (UK), antenatal	17	17	2,015
Selective preventive interventions			
B2.1 'Newpin' befriending (UK), perinatal	45	45	2,413
B2.2 Individual CBT addressing multiple risks (US), antenatal	2,502	2,643	2,823
Interventions addressing mild or subthreshold symptoms			
B3.1 Peer support (CAN), known in UK as 'Mum-4-mum', postnatal	-11,992	-11,992	9,267
B3.2 Parenting and mother-infant support (UK), postnatal	-178	-178	90
B3.3 Facilitated self-help 'Towards Parenthood' (AUS), antenatal	16	16	3,362
B3.4 Group CBT, 'Mothers and Babies Course' (US), perinatal	82	642	8,956
Interventions addressing moderate to major symptoms			
B4.1 Facilitated self-help CBT 'Netmums' (UK), postnatal	-181	-181	1,948
B4.2 Multi-disciplinary specialist care (UK), ante- and/or postnatal	-602	174	11,668
B4.3 Individual CBT in women's home (UK), antenatal	598	1,096	8,456
B4.4 Individual CBT or person-centred approach in women's home (UK), postnatal	180	332	2,605
B4.5 Group CBT (UK), postnatal	-1,015	-538	6,540
B4.6 Group CBT (AUS), postnatal	-120	326	6,472

B4.7 Enhanced IPT (US), perinatal	-1,458	-844	8,247
Interventions addressing major symptoms			
B5.1 Facilitated exercise (UK), postnatal	17	17	2,441
B5.2 Individual CBT in women's home, postnatal (US)	-2,270	-1,924	3,176
B5.3 Group IPT (AUS), postnatal	360	974	10,039
B5.4 Mother and baby inpatient unit (different countries), mostly postnatal	-30,080	-26,821	18,801

Conclusions

Our study sought to examine the potential costs and economic consequences of best practice interventions in the perinatal period that specifically aimed to improve women's mental health. We included a wide range of interventions concerned with the prevention and early treatment of mental illness. Interventions included elements of care and support that were specifically addressing the needs of women and their families during the perinatal period. The findings of our study need to be interpreted in the context of the study's limitations and the many gaps in the evidence. We discuss those first and then set out the main findings and implications of the study.

Limitations and current gaps in evidence

Our study was led by the available evidence, which was centred on interventions that addressed depression (sometimes in addition to other perinatal mental health problems, in particular stress and anxiety, but this was also not always reported in studies).

Some studies used an assessment (rather than diagnostic) tool for determining case-ness. Elevated scores indicate depression but can also indicate the (co-)existence of other mental health problems such as anxiety disorders. Interventions in this area may thus be effective for other conditions, but because this information is not available no definite conclusions can be drawn. At the same time, results might be more optimistic than results from studies that used diagnostic tools to determine recovery rates.

There were some important gaps in evidence regarding how to address major mental illness i.e. evidence that would clarify which types of *specialist* provision are effective and cost-effective. This is partly due to the challenges of evaluating interventions in this area, in particular the challenge of having suitable control groups (as it could be unethical not to provide women with specialist provision).

Since we only reviewed studies that used mothers' mental health as the primary outcome, there might be other interventions that are successful and possibly cost-effective in reducing perinatal mental health, including interventions that address related risk factors such as substance misuse or intimate partner violence. Those interventions might play an important role in reducing perinatal mental illness for some women.

Similarly, there are likely to be other areas of evidence that were relevant to this topic but which we did not address because they were outside the scope of this study. This included some evidence on parent infant psychotherapy, which usually included parents of infants older than one year (even if the mean age of infants in some studies was less than one year).

Inconsistencies in the nature and depth of information provided by studies also meant that findings were not directly comparable between them, and so it was not possible to derive definitive conclusions about whether one intervention achieves greater net benefits than others.

The evidence on child outcomes is patchy. There are currently important gaps in evidence about when interventions need to take place and which factors they need to address in order to improve infant outcomes to such an extent that long-term adverse impacts are reduced. In particular, findings on savings due to reduced adverse child impact need to be seen as tentative, representing potential impact. On the other hand, it is possible that interventions that did not lead to improvement in child outcomes may well be effective for certain sub-groups.

We prioritised the use of RCTs over other study designs in our interpretation of evidence and in our analyses. RCTs confer a number of well-known advantages, but there are areas where other study designs play an important role in gathering evidence that cannot be established with RCTs. This might be true for some complex interventions that are provided flexibly in response to individuals' needs, addressing a whole range of outcomes such as social support. Those areas of interventions might be highly beneficial and even cost-effective, but this is more difficult to demonstrate.

Because the focus was on best practice, we made a choice to include interventions from countries such as the US and Canada, even though the transferability of interventions to the UK context needs to yet be established.

Net benefits were often strongly influenced by intervention costs, and it is assumed that interventions can and will be delivered at those costs. We often had to make assumptions about these intervention costs, as there was not much detailed information available from current UK practice. There is a need in particular for specialist community teams and other providers (such as those that are part of the Improving Access to Psychological Therapies – IAPT - programme) to gather information in a way that allows them to gauge costs per woman and per intervention.

Although in the given time-frame for this study we were not able to carry out a *systematic* review following the standards outlined in research method guidelines and protocols (e.g. Cochrane Handbook or Centre for Review and Dissemination's guidance), we made substantial efforts to carry out both broad and specific searches in order to cover the relevant literature comprehensively.

Main findings and implications

Each of the interventions included in our economic analysis – which had, given the design of our study, been shown previously to be effective in helping women to recover from mental illness or to prevent their mental illness altogether – led to positive net benefits from a societal perspective.

In addition, each of the *universal and selective preventative* interventions achieved a positive net benefit from a health and social care perspective, and thus could offset costs (i.e. the monetary value of the outcomes achieved exceeded the costs). This was due largely to the low costs of interventions in this area, which meant that even small effects led to overall positive benefits. Targeting women *at high social risk* with interventions that address multiple risk factors and that provide additional incentives and strategies for recruiting mothers might be particularly promising, although evidence on this particular aspect came from the US and would need to be tested in a UK context. Findings suggested that interventions targeting women with *mild or sub-threshold problems* – i.e. in our study, facilitated self-help and group-based CBT - were achieving positive net benefits from a health and social care perspective when they were initiated during the antenatal period and were provided either during the antenatal or the whole perinatal period. Interventions primarily addressing *moderate symptoms* and interventions specifically addressing *major symptoms* often required initially a more substantive investment – either by government or by the independent sector – in order to improve individuals' health and wellbeing (and provide a return on investment from a societal perspective). Some of those more costly interventions appeared to achieve substantial impact on women and their children (in relation to their quality of life and ability to generate earnings from wages).

Overall, although the net benefits were greater when adopting a societal perspective, there is also a strong economic case for many of the effective interventions from the two narrower perspectives explored in this study (health and social care, and governmental). However, it is important to bear in mind that most of the net benefits refer to economic gains realised over the medium- or long-term. As is typical for interventions in the early and prevention areas, only a few interventions were able to offset costs in the very short-term (e.g. typically during the follow-up periods of the trials) by reducing health and social care costs. It is therefore important for the health system to consider the longer-term economic advantages when considering investment to prevent or address the mental health needs of mothers during the perinatal period.

Our findings suggest that investing in a comprehensive range of interventions during the perinatal period is likely to offer good value for money. These interventions might include:

- Multi-step screening and collaborative care to identify and refer women (with a particular role for midwifes);

- Universally provided parent education and infant sleep interventions;
- Mother-infant (as part of wider) support for women with elevated symptoms of perinatal depression;
- Intensive psychological support (including CBT and IPT) during the postnatal period for women with moderate and severe symptoms;
- Multi-disciplinary support for those women with moderate to severe symptoms, offering a range of different support including exercise, yoga; and online support for some of them.

Our study did not seek to determine which professional groups or teams should be providing interventions or whether they should be provided by specialist or non-specialist staff. However, it is important to note that in many of the studies on interventions that were provided by non-mental health professionals, there was supervision by a clinical psychologist or similar. Training and supervision of non-mental health staff is possibly an important contributor to the clinical effectiveness on which we based our findings.

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Appendix

Documentation for our systematic searches

Databases: CINAHL, EconLit, PsycINFO, Medline, Cochrane

Years: 2010 to 31/03/2016

Search limits: Peer-reviewed journals

Search strategy:

Keyword and subject headings

Search terms 1: service OR approach OR intervention* OR model OR care OR treatment OR program* OR support OR provision

AND

Search terms 2: anxiety OR depression OR psychosis OR PTSD OR Post-traumatic stress disorder OR mental illness

AND

Search terms 3: Postnatal OR antenatal OR perinatal OR pregnancy OR postpartum

The yield was 4127 (excluding Cochrane n=81)

We added NOT qualitative AND effect OR outcome (abstract), NOT low income (abstract), NOT perception OR views OR experiences OR opinion (title)