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Cost-effectiveness of interventions for perinatal anxiety and/or depression: a systematic review.

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Abstract

Objectives International policy has recognised the importance of parental mental health. Anxiety and/or depression during pregnancy or year after childbirth is the most common complication of childbearing. Objectives were to systematically review and critically appraise published economic evaluations of interventions for the prevention or treatment of perinatal anxiety and/or depression (PAD).

Methods Electronic searches were conducted of the MEDLINE, PsycINFO, and NHS Economic Evaluation and Health Technology Assessment databases in September 2017 to identify relevant economic evaluations published since January 2000. Two stages of screening were used with pre-specified inclusion/exclusion criteria. A data extraction form was designed prior to the literature search to capture key data. A published checklist was used to assess the quality of publications identified.

Results Of the 168 non-duplicate citations identified, 8 studies met the inclusion criteria for the review; all but one focussing solely on postnatal depression in mothers. Interventions included prevention (3/8), treatment (3/8), or identification plus treatment (2/8). Both of the identification plus treatment interventions were likely to be cost-effective. Where the cost per quality-adjusted life year (QALY) gained was reported, interventions ranged from being dominant (cheaper and more effective than usual care) to costing £39,875/QALY.

Conclusions Complex interventions incorporating identification plus treatment of perinatal depression were most likely to be cost-effective. Uncertainty in the published data and heterogeneity across studies in terms of study settings and designs makes it difficult to draw strong conclusions. Many gaps were identified, such as a complete lack of economic evidence relating to interventions for perinatal anxiety, antenatal depression, or interventions designed for fathers.

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Strengths and limitations of this study

- This study systematically reviewed economic evaluations of interventions for perinatal depression and/or anxiety, the importance of identifying and treating these conditions is recognised in UK and international health policy.
- The current evidence base is summarised and critically appraised using two approaches and gaps in current evidence are identified.
- The review was limited to English language studies which may introduce bias, but there is scope to broaden the search to other languages in future.

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Competing interests statement

None declared.

Contributors

EMC and GES conducted the literature search and data extraction. EMC wrote the first draft of the manuscript with contribution from GES to the final version.

Data sharing statement

Search strategies and data extraction templates are available in the supplementary material. No other unpublished data from the study are available.

Background

Improving mental health is a priority for UK and international health policy; the Department of Health supports the notion that there can be "no health without mental health"[1–4]. In the UK, policy specifically aims to improve the mental health of mothers[5]; this reflects the growing recognition of the intergenerational impact of mental illness [6].

Anxiety and/or depression during pregnancy or in the first year after having a baby (perinatal anxiety and/or depression; PAD) is experienced by around 20% of mothers in high income countries [7,8]. PAD can have important implications for the life-course of mothers and children [9]; depression during pregnancy is strongly associated with both depression and anxiety following childbirth [10,11]. Other important long-term impacts include developmental delays and behavioural problems for children and family instability [4,12]. The lifetime societal burden of PAD and other perinatal mental health conditions is massive, estimated at £8.1bn for all the babies born in a single year in the United Kingdom (currently almost 700,000 [13]) [9]. This includes costs related to time off work, marriage breakdown, and social support. Evidence suggests that the costs of improving perinatal mental health services are likely to be outweighed by the benefits [7,14].

It is generally accepted that psychological therapy and/or antidepressant medication are effective at treating the symptoms of PAD for many women [7,15–17]. However less is known about the cost-effectiveness of treatments for PAD. In the UK there has been a pledge to increase healthcare spending to improve maternal mental health and therefore decision makers need to know which interventions are cost-effective so that these vital funds are allocated efficiently [18]. Systematic literature reviews can help to promote evidence-based healthcare decisions by bringing information from different sources together into a comprehensive and critically-appraised summary.

The aim of this review is to produce an up-to-date synthesis of current knowledge about the cost-effectiveness of interventions for the prevention and treatment of PAD. In particular, to identify potentially cost-effective interventions, gaps in current knowledge, and important avenues for future research.

Methods

A systematic literature search and narrative review was conducted to identify economic evaluations of interventions for PAD. The review protocol was registered on the PROSPERO register of systematic reviews (ID, CRD42016051133).

Inclusion/exclusion criteria

Explicit inclusion criteria were: (a) studies focusing on mothers and/or fathers experiencing or at risk of developing perinatal depression and/or anxiety, (b) any psychological, psychosocial and/or pharmacological intervention, (c) alternative interventions and usual care or placebo as comparators, (d) incremental assessment of cost effectiveness. Previous systematic reviews were excluded but screened for additional references.

Literature search

Electronic searches were performed on the PsycINFO, MEDLINE, NHS economic evaluation database (EED), and NHS Health Technology Assessment (HTA) database. An initial search was run in September 2016 which was updated in September 2017. The searches were restricted to English language publications from January 2000 onwards; changes in practice and resource use/costs over time mean that older references are less useful for decision making. Common search terms included words related to perinatal depression and/or anxiety and economic evaluation terms. Terms varied slightly according to database designs. The search strategies are reported in Supplementary Material (Table S1). The bibliographies of previously published systematic reviews [14,18] were hand-screened for additional references to ensure all relevant papers were captured.

Study selection

Abstracts of studies were examined independently by two reviewers (EMC and GES) to determine whether each publication met the inclusion criteria. Both reviewers independently considered the full-text of identified publications to ensure that inclusion criteria were met. At each stage any discrepancies were resolved through discussion and a consensus reached on which publications should progress to the data extraction stage.

Data extraction and quality assessment

Structured data extraction and quality assessment was undertaken, guided by the NHS EED handbook [19]. A dual-purpose (data extraction and quality assessment) form was designed a priori (see Supplementary Material, Table S2) and used to extract information on study methodology, results, limitations, evidence gaps, and quality. The quality of the studies was also assessed using a modified version of the Consensus Health Economic Criteria (CHEC) list [20]. The checklist and assessment results are included in Supplementary Material (Table S3). One reviewer (EMC) completed the data extraction process with a proportion reviewed by the second reviewer (GES).

Currency conversion and inflation

Costs were converted to Great British Pounds (£) at the average exchange rate for the cost year reported in the source study [21]. All costs were inflated to 2015/16 based on the Hospital and Community Health Services (HCHS) index [22]. Exchange and inflation rates are reported in Supplementary Material (Table S4).

Results

Initial searches identified 257 citations, following the removal of duplicates the titles and abstracts of the remaining 168 citations were screened for eligibility (Figure 1). Twenty eight papers were included for full-text review, with 8 papers identified as relevant to the review (see Supplementary Material (Table S5) for details of excluded studies). The two systematic reviews that were hand-searched resulted in no additional references [14,18]. Key characteristics of the 8 included studies are described in Table 1.

Figure 1 <to go here>

Table 1 Overview of included studies

Study	Population	Country	Intervention (all studies reported usual or routine care as the comparator)
Boath (2003) [23]	Women being treated for postnatal depression n=60	United Kingdom	***Treatment*** Psychiatric day hospital
Petrou (2006) [24]	Women who were at high risk of developing postnatal depression at 26-28 weeks of gestation. n=151	United Kingdom	***Prevention*** Counselling and support delivered by trained health visitors up to 8 weeks postnatally
Morrell (2009) [25]	Women registered with participating GP practices who became 36 weeks pregnant during the recruitment phase of the trial, had a live baby and were on a collaborating HV's caseload for 4 months postnatally n= 4084	United Kingdom	***Screening and treatment*** Health visitor (HV) training in the assessment of postnatal women, combined with either cognitive behavioural approach (CBA) or person-centred approach (PCA) sessions (once per week for up to 8 weeks) for eligible women, plus the option of a selective serotonin reuptake inhibitor - commencing around 8 weeks postnatally
Stevenson (2010) [26]	Women with postnatal depression (EPDS>12) n=not reported (model)	United Kingdom	***Treatment*** Hypothetical group CBT intervention
Dukhovny (2013) [27]	Any postpartum women in seven health regions across Ontario n=610	Canada	***Prevention*** Telephone-based volunteer lay/peer support - at least 4 phone calls starting 48 to 72 hours after randomisation and continuing through the first 12 weeks after birth
Ride (2016) [28]	First-time mothers who had recently given birth and attended one of 48 participating Maternal and Child Health Centres n=359	Australia	***Prevention*** Psychoeducational programme targeted at the partner relationship, management of infant behaviour, and parental fatigue
Grote (2017) [29]	Women at 12-32 weeks gestation, scoring 10 or higher on the PHQ-9 or with a diagnosis of probable dysthymia n=270	United States	***Treatment*** Collaborative care for depression including a choice of brief interpersonal psychotherapy, pharmacotherapy, or both
Wilkinson (2017) [30]	Hypothetical cohort of pregnant women experiencing one live birth over 2 years n=1000	United States	***Screening and treatment*** General physicians screening for and treating postpartum depression and psychosis in partnership with a psychiatrist

Characteristics of studies

As shown in Table 1, the earliest and largest number of included studies were from the United Kingdom (n=4) [23–26], the most recent two studies were from the United States [29,30], and there was one study from each of Australia [28] and Canada [27].

The interventions evaluated across the 8 studies were diverse and no two studies evaluated comparable interventions. Three studies included a preventative intervention [24,27,28], three focussed on treatment [23,26,29], and two included complex interventions incorporating both identification and treatment [25,30]. All studies focussed on postnatal depression in mothers although the study by Ride et al did also consider anxiety and fathers [28]. Two of the preventative interventions were targeted at distinct groups: high risk women [24]; first time mothers [28]. One intervention involved lay or peer support [27], two were delivered by health visitors [24,25], and the remainder were delivered across a range of settings/healthcare professionals/structures including collaborative care [29,30] and group cognitive behavioural therapy (CBT) [26]. The comparator intervention for all studies was described as usual or routine care. Usual care is likely to vary by setting which affects the external validity of the study.

The majority (n=6) of studies reported cost-effectiveness analyses with different measures of health benefits which makes it difficult to compare between studies [23,24,27–30]. The most widely used (primary or secondary) measure of health benefit was the Edinburgh Postnatal Depression Scale (EPDS) which was reported in 2 of the 6 trial-based studies [25,27]. Cost-utility analyses were reported in four studies, making results across these studies easier to compare [25,26,28,30] (two of which had also reported cost-effectiveness [28,30]). Utility was derived from the SF-6D in two studies [25,26] and from the EQ-5D in two studies [28,30]. Only two studies reported the results of an economic models [26,30] with the remainder reporting trial-based results.

Table 2 Design of included studies

Study	Evaluation type	Measure of health benefit	Evaluation details	Data source	Quality/bias considerations
Boath (2003)[23]	CEA	Recovery from PND (no longer fulfilling Research Diagnostic Criteria)	• Trial or model: trial • Perspective: health service • Time horizon: 6 months • Price year: 1992/93 • Currency: British £	Observational study - healthcare utilisation self-reported and obtained from medical records	Treatment allocation was non-randomised. Reported that no significant differences in sociodemographic characteristics or outcome measures between groups at baseline. No loss to follow-up reported
Petrou (2006)[24]	CEA	Months of postnatal depression avoided (SCID-II)	• Trial or model: trial • Perspective: health and social services • Time horizon: 18 months • Price year: 2000 • Currency: British £	RCT - health and social care utilisation was self-reported by participants	Structured clinical interviews were used to identify depression in both treatment groups. The numbers/characteristics of those declining to participate were not reported
Morrell (2009)[25]	CUA	• QALYs (derived from the SF-6D) • EPDS	• Trial or model: trial • Perspective: health and social services • Time horizon: 18 months • Price year: 2003/04 • Currency: British £	RCT - health and social care utilisation obtained from medical records (up to 6 months) and participant self-report (at 12 and 18 months)	Data was collected on women declining to take part but differences with sample were not discussed. Sample was broadly representative of general population. Missing economic data were significant at 12 and 18 months, 6 months was used as the primary time horizon
Stevenson (2010) [26]	CUA	QALYs (derived from EPDS mapped onto SF-6D)	• Trial or model: model (mathematical) • Perspective: health and social services • Time horizon: 12 months • Price year: not reported • Currency: British £	Published data sources and expert opinion informed the model. EPDS, SF-36, and costs from published RCTs.	As the model was mathematical, no structure was reported in the paper. Probabilistic sensitivity analyses were conducted
Dukhovny (2013) [27]	CEA	Cases of PND averted at 12 weeks postpartum	• Trial or model: trial • Perspective: societal • Time horizon: 12 weeks • Price year: 2011 • Currency: Canadian $	Multi-region RCT - resource utilisation was self-reported by participants	Only two people did not complete healthcare utilisation questionnaires and fewer than 0.01% of individual resource utilisation items were missing at random

Ride (2016) [28]	CEA; CUA	• Prevalence of depression and anxiety(DSM-IV criteria) • QALYs (from the EQ-5D)	• Trial or model: trial • Perspective: health and social services • Time horizon: 20 weeks • Price year: 2013/14 • Currency: Australian $	Cluster-RCT - health and social care utilisation self-reported by participants	Differences between the treatment groups were adjusted for in the analysis. The intra-cluster coefficients were small but non-negligible for QALYs which may have reduced the ability to detect an effect of the intervention
Grote (2017) [29]	CEA	• Depression severity (SCL-20) • Depression free days • PTSD Checklist	• Trial or model: trial • Perspective: health plan or insurer • Time horizon: 18 months • Price year: 2013 • Currency: US $	RCT - health and social care utilisation self-reported by participants	The costs included only related to mental health care. The perspective was 'public health' and so could have also included primary and community healthcare services. Those with partial cost data (n=12/164) were more likely to have probable PTSD and to have been randomly assigned to the intervention
Wilkinson (2017) [30]	CEA; CUA	• QALYs (derived from published literature) • EPDS	• Trial or model: model (decision tree) • Perspective: health plan (Medicaid) • Time horizon: 2 years • Price year: 2014 • Currency: US $	Systematic review of existing literature to inform the model. Some cost parameters estimated from Medicaid data	Some parameters were from studies of anxiety/depression outside of the perinatal period. Probabilistic sensitivity analyses were conducted. The model structure is pragmatic, but perhaps over simple in terms of suicide risk - only women who discontinue treatment are at risk of suicide, women who don't seek help or those who screen negative are not deemed to be at risk of suicide
CEA = cost-effectiveness analysis; CUA = cost-utility analysis; RCT = randomised controlled trial; CBT = cognitive behavioural therapy; SCID-II = Structured Clinical Interview for Depression, 2nd edition; QALY = quality adjusted life year; EPDS = Edinburgh Postnatal Depression Scale; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; SCL-20 = 20-item Symptom Checklist Depression Scale; PTSD = post-traumatic stress disorder; EPDS = Edinburgh Postnatal Depression Scale.					

Critical appraisal

A copy of the CHEC quality appraisal checklist and assessment results are included in Supplementary Material (Table S3) [20]. The median score was 15.5 (out of 18). The majority of the studies were of high quality (n=6) [24–28,30] and two were average [23,29]. The studies published prior to 2006 did not report results of incremental analysis but there is a trend towards more robust methods and reporting over time. Overall the studies reported the population, setting, intervention, and comparator well. Two studies had relatively short time horizons (12 weeks [27] and 20 weeks [28]) which may not reflect the potentially long-lasting course of PAD. Six of the studies reported sensitivity or sub-group analyses [24–28,30], demonstrating varying levels of uncertainty around their primary cost-effectiveness estimate. Not reporting uncertainty is an important limitation in economic evaluations because it indicates confidence in the results, analogous to not reporting a confidence interval for a statistical analysis. Four of the studies did not report whether there were any conflicts of interest [24,26,27,30].

Factors which increased the potential for bias in the reported results include non-randomised treatment allocation [23] and an imbalance in data completeness between treatment groups/sub-groups [29]. The study by Dukhovny et al was particularly robust owing to a high level of data completeness [27].

The model by Stevenson et al evaluating group CBT to treat postnatal depression in the UK was informed by expert opinion alongside published data available from RCTs for EPDS and SF-6D scores [26] (see Table 2). The model structure was not explicitly reported. The model by Wilkinson et al evaluating collaboration between GPs and psychiatrists to identify and treat postnatal depression included estimates for the EPDS and EQ-5D from published literature [30]. Some of the model parameters were from studies of anxiety/depression outside of the perinatal period and the model structure although pragmatic potentially oversimplified suicide risk (see Table 2). Both model-based evaluations reported probabilistic sensitivity analysis.

Cost-effectiveness

Six studies reported incremental cost-effectiveness ratios (ICERs), half of which were in terms of clinical outcomes [23,24,27] and half in terms of QALY gains associated with the intervention compared with usual care [26,28,30]. Two interventions were either likely or highly likely to be cost-effective, both incorporating identification plus treatment of postnatal depression: health visitor screening and counselling [25]; general practitioner/psychiatrist collaborative screening and treatment [30]. The intervention involving health visitors was associated with lower costs and better outcomes than usual care therefore the authors did not report an ICER because the intervention dominated usual care. However when multiple imputation was used to resolve missing data (rather than a complete case analysis) the intervention was associated with more QALYs and a net cost resulting in an ICER of £15,666/QALY.

Three interventions (psychiatric day hospital (treatment) [23], health visitor counsellors (prevention) [24], telephone-delivered peer support (prevention) [27]) were classified as

possibly cost-effective because although they reported improved health outcomes with increased costs, there is no accepted threshold by which to judge ICERs when health benefits are quantified as anything other than QALYs. The ICER reported for psychiatric day hospital care was sensitive to the inclusion of primary care and medication costs, increasing from £3,843 to £56,865 per additional recovery [23]. Psychoeducation (prevention) [28] was classified as possibly cost-effective because although following currency conversion the QALY-based ICER was below the UK threshold for cost-effectiveness, the authors reported a 55% chance (i.e. not much higher than chance) that it was below the Australian threshold. Furthermore the ICER value increased by £5,055 following multiple imputation. Collaborative care (treatment) [29] was classified as possibly cost-effective because of conflicting results for sub-group analyses (Table 3). The cost-benefit analysis valued a depression-free day at US$20 (approximately £13) [29] which translated to a net benefit among mothers with PTSD and a net cost for mothers without PTSD. Group CBT was evaluated as unlikely to be a cost-effective treatment for post-natal depression [26].

Table 3 Cost-effectiveness results

Study	Interventions	Net benefit	Net cost	ICER, key conclusions, and uncertainty
Boath (2003)[23]	Psychiatric day hospital versus routine primary care	14 more women recovered in the intervention group.	The intervention was £53,824 more expensive than routine care.	£3843 per each additional recovery. The net cost is sensitive to inclusion primary care and medication costs, increasing to £56,865. ***Possibly cost-effective***
Petrou (2006)[24]	Counselling and support from health visitors versus usual care	The intervention group depressed for 2.14 weeks fewer (over 18 months) than the control group - this was not statistically significant.	The intervention group costs were £189 higher although this was not significant.	£68 per month of depression avoided. Possibly a small improvement in outcomes for a small cost. ***Possibly cost-effective***
Morrell (2009)[25]	Screening and talking therapy (CBA or PCA) delivered by health visitor versus usual care	EPDS score at 6 months was 0.9 lower ($p<0.001$) for those randomised to an intervention group. QALY gain of 0.002 associated with the intervention.	There was a non-significant net-saving of £26 for women in the intervention groups.	Improved outcomes with comparable costs. No ICER reported because of negative net cost. CBA appears to be more cost-effective than PCA. Sub-group analysis of 'at-risk' women: 6-month EPDS score 2.1 lower ($p=0.002$). Analysis of imputed data: QALY gain increased to 0.003 and net cost increased to £47, both reaching statistical significance (£15,666/QALY). ***Highly likely to be cost-effective***
Stevenson (2010)[26]	Group CBT versus usual care	Intervention associated with a QALY gain of 0.039 (PSA results).	£1568 net cost of providing gCBT (PSA results).	£39,875 per QALY gained. Intervention is not likely to be cost-effective at accepted thresholds. More research is needed to address the level of uncertainty. ***Not likely to be cost-effective***
Dukhovny (2013)[27]	Telephone-based peer support versus usual care	0.1116 more cases of postnatal depression avoided at 12 weeks in the intervention group.	£755 net cost associated with intervention ($p<0.001$).	£6768 per case of postnatal depression avoided at 12 weeks. The ICER is within the range of other postnatal depression interventions. ***Possibly cost-effective***

Ride (2016) [28]	Psychoeducational programme versus usual care	Comparable outcomes both in terms of prevalence of mental health conditions and QALYs.	£167 net cost associated with the intervention was although this was not statistically significant.	£21,987/QALY; £92 per %-point reduction in 30-day prevalence of postnatal mental health disorders. The probability the intervention if cost-effective is 0.55 at a willingness to pay threshold of AD$ 55,000 (approximately £30-35,000) - more research is needed to reduce uncertainty. Multiple imputation of missing data increased ICER to £27,042/QALY. ***Possibly cost-effective***
Grote (2017) [29]	Collaborative care for depression versus usual care	More depression free days over 18 months for the intervention group: • with PTSD 68 days ($p<0.05$) • without PTSD 13 days (NS).	Significant net cost associated with the intervention: • with PTSD £868 • without PTSD £772.	If a depression free day is valued at US$20 (approximately £13): • with PTSD net benefit of £32 • without PTSD net cost of £600. ***Possibly cost-effective***
Wilkinson (2017) [30]	Psychiatrist-supported GP screening and treating postpartum depression and psychosis	29 more healthy women in the intervention group, equating to a total of 21.43 additional QALYs over 2 years.	Total additional cost associated with the intervention £185,173.	£8642 per QALY gained, £6350 per remission achieved, £588 per additional healthy woman. ***Likely to be cost-effective***
RCT = randomised controlled trial; CBT = cognitive behavioural therapy; QALY = quality adjusted life year; CBA = cognitive behavioural approach; PCA = person centred approach; EPDS = Edinburgh Postnatal Depression Scale; AD$ = Australian dollars. Currency conversion and inflation rates used are reported in Supplementary Material (Table S4).				

Discussion

Eight studies evaluating the cost-effectiveness of interventions for PAD were included in this review. All were published between 2006 and 2017. Six studies were high quality and two average quality. Each study focussed on depression occurring in postnatal mothers (although Ride et al also considered anxiety and fathers [28]) but evaluated a different type of intervention, some of which focussed on prevention and others focussed on treatment (or identification plus treatment). Two studies identified interventions that were likely to be cost-effective, both of which incorporated identification plus treatment of postnatal depression.

The quality of the studies included in the review was mixed and generally increased over time which likely to reflect the agreement of standards for the reporting of economic evaluations. QALYs are the most widely used measure of health benefit in economic evaluations, as recommended by the National Institute for Health and Care Excellence (NICE) [31]. Interventions costing less than £20,000-30,000 per QALY gained (versus the comparator intervention) are considered to be cost-effective. Only four of the included studies reported results in terms of QALYs. Standardised methods for economic evaluations are important so that results can be directly compared, for example it may not always be appropriate to compare QALYs derived using different approaches [32]. NICE recommends that the EQ-5D is used to derive QALYs; two of the studies included derived QALYs from the SF-6D [33] and the other two studies derived QALYs from the EQ-5D [34].

There was great heterogeneity between the studies included in terms of the interventions, measure of benefit, and time horizon. However the interventions could be grouped by some characteristics such as their aim (e.g. prevention or treatment) or key actors (e.g. healthcare professional or peer support). There were inconsistent findings within the intervention sub-groups with one exception. The two studies which incorporated identification plus treatment were both likely to be cost-effective [25,30]. However the two interventions were very different. The intervention evaluated by Morrell et al involved training health visitors to identify women experiencing postnatal depression and deliver talking therapy (using either a cognitive behavioural approach or a person centred approach). Whereas the intervention evaluated by Wilkinson et al was based around collaboration between GPs and psychiatrists. Due to a large amount of missing data the health visitor intervention was only evaluated at 6 months whereas the collaborative intervention was evaluated at 2 years. This also makes it difficult to compare results between studies because it is possible that over a longer a follow up more benefits are accrued.

Strengths and limitations

There are a number of strengths and limitations of this review. Multiple major literature databases relevant to health and economic research were searched therefore it is likely that key studies have been identified. In the instance where a full text was not available online the authors were contacted and provided a copy. However, the search was restricted to English language studies introducing some bias. Searches were also restricted to published journal articles which are less likely to include inconclusive or negative cost-effectiveness

results when compared with the grey literature [35]. Two separate tools were used to critically appraise the studies which included more criteria and gave a broader perspective than a single approach. The CHEC-list [36] was used to assign a score to each study and the data extraction tool was used to identify potential sources of bias. Both approaches involve an element of subjectivity, the CHECH-list attempts to handle this by not classing a criteria as having been met if it is only partially met, however this may result in some loss of sensitivity.

Future research

The lifetime societal burden of PAD and other perinatal mental health conditions is massive, estimated at £8.1bn for each one-year cohort of births [9]. These costs include time off work, marriage breakdown, and social support. Evidence suggests that the costs of improving perinatal mental health services are likely to be outweighed by the benefits [7,14]. There is no consensus for how these spill over health effects should be incorporated into economic evaluations, but this is particularly relevant to PAD. The degree of spill over is likely to be highly context specific and so research into spill over effects of PAD would make an important contribution to this ongoing debate. One study which was excluded from this review because it focussed only on screening for postnatal depression concluded that it was not cost-effective to screen because of increased treatment costs [37]. However, identification and treatment are inextricably linked and evaluating them separately may not tell the whole story which should be borne in mind for future research. It is also necessary to address the lack of economic evidence for interventions for antenatal depression, perinatal anxiety, and PAD in fathers as these conditions are also prevalent and have impacts on individuals and families [38–40]. Future economic evaluations should be conducted and reported according to good practice guidelines so that future reviews can make clear recommendations to inform health policy.

Conclusion

The quality of the methods and reporting of economic evaluations for interventions related to PAD has improved over time. Heterogeneity in the evaluations to date means that is not possible to make any conclusions about their relative cost-effectiveness, with no clear implications for health policy. However the two interventions which were most likely to be cost-effective (compared to usual care) both incorporated identification and treatment together; this should be considered when planning future research in this area. As recognition of the impact of perinatal anxiety and PAD in fathers grows, so does the need for relevant and robust economic evidence.

Figure legend

Figure 1 - PRISMA flow diagram of studies identified

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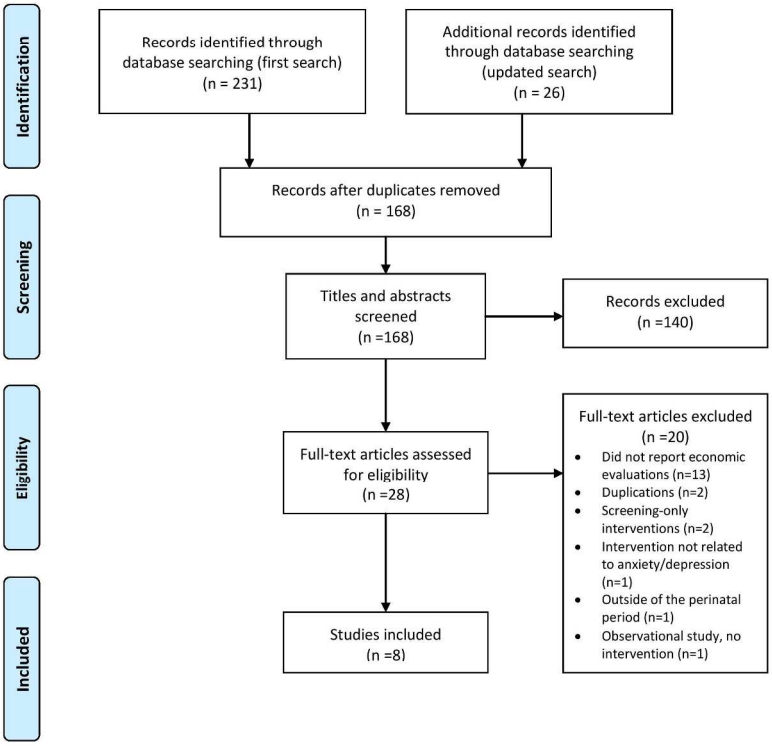

Figure 1 PRISMA flow diagram of studies identified

215x279mm (300 x 300 DPI)

Table S1 - search strategies

MEDLINE	#1 economic evaluation OR economic analys* OR cost analys* OR cost effective* analys* OR cost-effective* analys* OR cost benefit* analys* OR cost utility* analys* OR cost-benefit* analys* OR cost-utility* analys* #2 postpartum OR post-partum OR post partum #3 postnatal OR post natal OR post-natal #4 perinatal OR peri natal OR peri-natal #5 antepartum OR ante partum OR ante-partum #6 pregnan* #7 #2 OR #3 or #4 or #5 or #6 #8 depress* OR anxi* #9 #8 AND #7 #10 #1 AND #9 #11 Limit #10 to yr=2000-Current #12 #11 NOT cattle [ti] OR karyotyping[ti] OR aneuploid*[ti] OR smoking cessation[ti] OR tobacco cessation[ti]
PsycINFO	#1 anxi* OR depress* #2 postnatal OR post natal OR post-natal #3 postpartum OR post-partum OR post partum #4 antenatal OR ante natal OR ante-natal #5 perinatal OR peri natal OR peri-natal #6 antepartum OR ante partum OR ante-partum #7 pregnan* #8 #2 OR #3 OR #4 OR #5 OR #6 OR #7 #9 #1 AND #8 #10 cost analy* or *economic* or cost effective* or cost-effective* or cost benefit* or cost utility* or cost-benefit* or cost-utility* #11 #9 AND #10 #12 Limit #11 to (all journals and yr="2000-Current")
NHS EED/HTA	*Title search* (depress* OR anxi*) AND ((postpartum OR post-partum OR post partum) OR (postnatal OR post natal OR post-natal) OR (perinatal OR peri natal OR peri-natal) OR (antepartum OR ante partum OR ante-partum) OR pregnan*)

Table S2 - Data extraction and quality assessment form

Subject of the study	
Intervention(s)	
Comparator(s)	
Intervention type	
Disease	
Study question/hypothesis	
Key elements of the study	
Type of economic analysis	
Study population	
Details of model (if applicable)	
Setting	
Country	
Dates to which data relate	
Link between cost and health benefit data	
Clinical evidence	
Clinical and epidemiological inputs	
Data sources	
Methods to obtain data	
Measures of health benefit	
Summary measure of health benefit	
Method of utility valuation	
Time horizon	
Discount rate for health benefit	
Direct costs	
Direct costs included	
Who bears the direct costs?	
Source of resource use data	
Resource use reported separately from costs	
Sources of unit prices	
Currency and price year	
Adjustment for inflation; other adjustments	
Costs excluded	
Time horizon	
Discount rate for direct costs	
Indirect costs	
Inclusion of indirect (productivity)	
Source of cost and quantity data	
Resource use reported separately from costs	
Time horizon	
Discounting of indirect costs	
Statistical analysis of costs	
Descriptive statistics/point estimates reported	
Significance testing reported	
Study powered to detect differences in cost	
Analysis of uncertainty	
If model: exploration of parameter uncertainty	

If model: exploration of structural uncertainty	
All studies: exploration of alternative subgroups / settings	
Estimated benefits	
Total benefit: intervention arm(s)	
Total benefit: comparator arm(s)	
Net (incremental) benefit	
Result of statistical test for difference in benefits	
Were adverse effects included?	
Estimated costs	
Total cost: intervention arm(s)	
Total cost: comparator arm(s)	
Net (incremental) cost (intervention versus comparator)	
Result of statistical test for difference in costs	
Did the duration of costs match the time horizon?	
Synthesis of benefits & costs, and conclusions	
Synthesis of benefits and costs conducted (e.g. ICER)	
ICER	
Probability cost-effective	
Important differences in results for subgroups or sensitivity analyses	
Summary of authors' conclusions	
Critical review	
Is the choice of comparator suitably justified?	
If model: was the model structure suitable?	
If model: was a model schematic presented?	
If model: was the model adequately reported?	
Validity of primary effectiveness data	
Validity of secondary effectiveness data	
Validity of estimated health benefit	
Validity of estimated costs	
Do the authors discuss the generalisability of their findings?	
Do the authors compare their findings to previous studies?	
Are the authors' conclusions justified?	
Implications	
Do the authors describe policy implications of their findings? Are they appropriate?	

Table S3 - Criteria list for assessment of methodological quality of economic evaluations: Consensus on Health Economic Criteria [9]

	Boath (2003) [1]	Petrou (2006) [2]	Morrell (2009) [3]	Stevenson (2010) [4]	Dukhovny (2013) [5]	Ride (2016) [6]	Grote (2017) [7]	Wilkinson (2017) [8]
1. Is the study population clearly described?	✓	✓	✓	✓	✓	✓	✓	✓
2. Are competing alternatives clearly described?	✗	✓	✓	✓	✓	✓	✓	✓
3. Is the economic study design appropriate to the stated objective?	✓	✓	✓	✓	✓	✓	✓	✓
4. Is the chosen time horizon appropriate to include relevant costs and consequences?	✓	✓	✓	✓	✗	✗	✓	✓
5. Is the actual perspective chosen appropriate?	✓	✓	✓	✓	✓	✓	✓	✓
6. Are all important and relevant costs for each alternative identified?	✓	✓	✓	✓	✓	✓	✗	✓
7. Are all costs measured appropriately?	✓	✓	✓	✓	✓	✓	✓	✓
8. Are costs valued appropriately?	✓	✓	✓	✓	✓	✓	✓	✓
9. Are all important and relevant outcomes for each alternative identified?	✓	✓	✓	✓	✓	✓	✓	✓
10. Are all outcomes measured appropriately?	✓	✓	✓	✓	✓	✓	✓	✓
11. Are outcomes valued appropriately?	✗	✗	✓	✓	✗	✓	✗	✓
12. Is an incremental analysis of costs and outcomes of alternatives performed?	✗	✓	✓	✓	✓	✓	✓	✓
13. Are all future costs and outcomes discounted appropriately?	✓	✓	✓	✓	✓	✓	✗	✓
14. Are all important variables, appropriately subjected to sensitivity analysis?	✗	✓	✓	✓	✓	✓	✗	✓
15. Do the conclusions follow from the data reported?	✓	✓	✓	✓	✓	✓	✓	✓
16. Does the study discuss the generalizability of the results to other settings and patient/client groups?	✓	✗	✓	✗	✓	✗	✗	✓

	Boath (2003)	Petrou (2006)	Morrell (2009)	Stevenson (2010)	Dukhovny (2013)	Ride (2016)	Grote (2017)	Wilkinson (2017)
17. Does the article indicate that there is no potential conflict of interest of study researcher(s) and funder(s)?	✓	✗	✓	✗	✗	✓	✓	✗
18. Are ethical and distributional issues discussed appropriately?	✗	✓	✓	✓	✓	✓	✗	✓
TOTAL SCORE	13	15	18	16	15	16	12	17
Each criteria met is awarded one point: 15 or greater = high quality, 8-14 = average quality, less than 8 = poor quality. Item 13 – studies where discounting is not applicable (i.e. time horizon less than one year) have been assumed to meet criteria.								

Table S4 - Currency conversion and inflation rates applied

	Price year in study	Original currency	Exchange rate#	HCHS year	HCHS index (1987/88 = 100.0)	HCHS inflation factor to 2015/16*
Boath (2003) [1]	1992/93	GBP	n/a	1992/93	150.3	1.98
Petrou (2006) [2]	2000	GBP	n/a	1999/2000	188.5	1.58
Morrell (2009) [3]	2003/04	GBP	n/a	2003/04	225.6	1.32
Stevenson (2010) [4]	2010	GBP	n/a	2009/10	268.6	1.11
Dukhovny (2013) [5]	2011	Canadian $	0.63	2010/11	276.7	1.07
Ride (2016) [6]	2013/14	Australian $	0.59**	2013/14	290.5	1.02
Grote (2017) [7]	2013	US $	0.64	2012/13	287.3	1.03
Wilkinson (2017) [8]	2014	US $	0.61	2013/14	290.5	1.02

GBP = Great British Pound/United Kingdom £ sterling; US = United States
#per 1GBP;
*HCHS index 2015/16 = 297.0
*The exchange rate between Australian dollars ($) and GBP was notably different in 2013 (0.62 $/£) and 2014 (0.55 $/£) therefore the midpoint (0.59 $/£) was used.

Table S5 - reasons for exclusion of full texts screened

Title	Year	Lead author	Reason
A randomized comparison of home and clinic follow-up visits after early postpartum hospital discharge.	2000	Lieu [10]	No economic evaluation reported
Costs and effectiveness of community postnatal support workers: a randomised controlled trial.	2000	Morrell [11]	No economic evaluation reported
Costs and benefits of community postnatal support workers: a randomised controlled trial.	2000	Morrell [12]	Duplicate - HTA report for same study reported elsewhere
The treatment of postnatal depression by health visitors: impact of brief training on skills and clinical practice.	2003	Appleby [13]	No economic evaluation reported
The Social Support and Family Health Study: a randomised controlled trial and economic evaluation.	2004	Wiggins [14]	No economic evaluation reported
Improving infant sleep and maternal mental health: a cluster randomised trial.	2007	Hiscock [15]	No economic evaluation reported
Stepped care treatment of postpartum depression: A primary care-based management model.	2008	Gjerdingen [16]	No economic evaluation reported
Screening for postnatal depression within the Well Child Tamariki Ora Framework.	2008	Suebwongpat [17]	Intervention – screening only
Screening for postnatal depression in primary care: Cost effectiveness analysis.	2009	Paulden [18]	Intervention – screening only
Postpartum follow-up: can psychosocial support reduce newborn readmissions?	2010	Barilla [19]	Intervention - aim of intervention not related to anxiety/depression, no measure of anxiety/depression collected
A model for maternal depression.	2010	Connelly [20]	No economic evaluation reported, review of existing evidence
A pragmatic randomised controlled trial to compare antidepressants with a community-based psychosocial intervention for the treatment of women with postnatal depression: the RESPOND trial	2010	Sharp [21]	No economic evaluation reported
Group cognitive behavioural therapy for postnatal depression: a systematic review of clinical effectiveness, cost-effectiveness and value of information analyses.	2010	Stevenson [22]	Duplicate - HTA report for same study reported elsewhere
Supporting women with postnatal depression through psychological therapies	2011	Centre for Reviews and Dissemination [23]	No economic evaluation reported, review of existing evidence

Peer support and interpersonal psychotherapy groups experienced decreased prenatal depression, anxiety and cortisol.	2013	Field [24]	No economic evaluation reported
Effects of an infant-focused relationship-based hospital and home visiting intervention on reducing symptoms of postpartum maternal depression: A pilot study.	2014	Nugent [25]	No economic evaluation reported
Antidepressant treatment of depression during pregnancy and the postpartum period	2014	McDonagh [26]	No economic evaluation reported, review of existing evidence
Enhanced engagement: An intervention pilot for mental health promotion among low-income women in a community home visiting program.	2015	Price [27]	Patient group - not restricted to the postpartum period
Perinatal depression and child development: exploring the economic consequences from a South London cohort.	2015	Bauer [28]	Intervention - observational study, no intervention
Improving perinatal depression care: The Massachusetts Child Psychiatry Access Project for Moms.	2016	Byatt [29]	No economic evaluation reported, no comparator intervention

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	3
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	3-4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplementary material
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	4
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	4 Supplementary material
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	4
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	4
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	3-4 (narrative review)

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	4
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	n/a
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	4, figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	9, Table 2
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Table 3
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	n/a
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Table 2
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	n/a
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	13
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	13
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	13-14
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	2

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

BMJ Open

Cost-effectiveness of interventions for perinatal anxiety and/or depression: a systematic review.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-022022.R1
Article Type:	Research
Date Submitted by the Author:	26-Apr-2018
Complete List of Authors:	Camacho , Elizabeth; University of Manchester, Manchester Centre for Health Economics, Division of Population Health, Health Services Research and Public Health Shields, Gemma; University of Manchester, Manchester Centre for Health Economics, Division of Population Health, Health Services Research and Public Health
Primary Subject Heading:	Mental health
Secondary Subject Heading:	Health economics
Keywords:	HEALTH ECONOMICS, MENTAL HEALTH, Depression & mood disorders < PSYCHIATRY

Cost-effectiveness of interventions for perinatal anxiety and/or depression: a systematic review.

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Abstract

Objectives Anxiety and/or depression during pregnancy or year after childbirth is the most common complication of childbearing. Economic evaluations of interventions for the prevention or treatment of perinatal anxiety and/or depression (PAD) were systematically reviewed with the aim of guiding researchers and commissioners of perinatal mental health services towards potentially cost-effective strategies.

Methods Electronic searches were conducted of the MEDLINE, PsycINFO, and NHS Economic Evaluation and Health Technology Assessment databases in September 2017 to identify relevant economic evaluations published since January 2000. Two stages of screening were used with pre-specified inclusion/exclusion criteria. A data extraction form was designed prior to the literature search to capture key data. A published checklist was used to assess the quality of publications identified.

Results Of the 168 non-duplicate citations identified, 8 studies met the inclusion criteria for the review; all but one focussing solely on postnatal depression in mothers. Interventions included prevention (3/8), treatment (3/8), or identification plus treatment (2/8). Two interventions were likely to be cost-effective, both incorporated identification plus treatment. Where the cost per quality-adjusted life year (QALY) gained was reported, interventions ranged from being dominant (cheaper and more effective than usual care) to costing £39,875/QALY.

Conclusions Uncertainty and heterogeneity across studies in terms of setting and design make it difficult to make direct comparisons or draw strong conclusions. However the two interventions incorporating identification plus treatment of perinatal depression were both likely to be cost-effective. Many gaps were identified in the economic evidence, such as the cost-effectiveness of interventions for perinatal anxiety, antenatal depression, or interventions for fathers.

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Strengths and limitations of this study

- A pre-specified protocol was registered on the International Prospective Register of Systematic Reviews (PROSPERO).
- The current evidence base was summarised and critically appraised using two approaches to minimise subjectivity.
- The review was limited to English language studies which may introduce bias and it is possible that some studies were not identified despite the comprehensive search strategy.

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Competing interests statement

None declared.

Contributors

EMC and GES conducted the literature search and data extraction. EMC wrote the first draft of the manuscript with contribution from GES to the final version.

Data sharing statement

Search strategies and data extraction templates are available in the supplementary material. No other unpublished data from the study are available.

Background

Improving mental health is a priority for UK and international health policy; the Department of Health supports the notion that there can be "no health without mental health"[1–4]. In the UK, policy specifically aims to improve the mental health of mothers[5]; this reflects the growing recognition of the potential intergenerational effects of mental illness [6].

Anxiety and/or depression during pregnancy or in the first year after having a baby (perinatal anxiety and/or depression; PAD) is experienced by around 20% of mothers in high income countries [7,8]. The gold standard for clinical diagnosis of PAD is a structured interview [9], typically conducted by a psychiatrist. The current recommendation in the UK is that at first contact with maternity services and in the weeks following childbirth healthcare professionals consider asking women the Whooley and Generalised Anxiety Disorder scale (GAD-2) case-finding questions [7]. However the Edinburgh Postnatal Depression Scale (EPDS) [10] is the most frequently used instrument used to detect PAD in research settings [11], which has validated cut-off scores to identify antenatal and postnatal women experiencing PAD [12].

PAD can have important implications for the life-course of mothers and children [13]; depression during pregnancy is strongly associated with both depression and anxiety following childbirth [14,15]. Other important potential long-term considerations include developmental delays and behavioural problems for children and family instability [4,16]. The lifetime societal burden of PAD and other perinatal mental health conditions is massive, estimated at £8.1bn for all the babies born in a single year in the United Kingdom (almost 700,000 in 2016 [17]) [13]. This includes costs related to time off work, marriage breakdown, and social support. Evidence suggests that the costs of improving perinatal mental health outcomes are likely to be outweighed by the benefits [7,18]; high quality economic evidence is needed to identify the most efficient ways of doing so.

Systematic reviews of the evidence [19–21] suggest that psychological therapy and/or antidepressant medication are effective at treating the symptoms of PAD for many women which is reflected in current clinical guidance [7]. However less is known about the cost-effectiveness of treatments for PAD. A systematic review of literature published before July 2013 and relating to *preventative* interventions for perinatal depression concluded that midwifery redesigned postnatal care, a person-centred approach-based intervention, and an interpersonal therapy-based intervention showed some evidence of cost-effectiveness but with considerable uncertainty [22]. A recent report on the long-term cost-effectiveness of perinatal mental health interventions included a selective review of interventions which had previously been found to be cost-effective and concluded that all of the interventions led to a long-term net monetary benefit from a societal perspective [18].

Different perinatal mental health conditions often co-occur [14,23] and in the UK there has been a move towards commissioning the healthcare services for conditions under this umbrella together. Furthermore, widely used screening instruments such as the EPDS [10] were not designed to differentiate between different perinatal mental health conditions which may mean that people with different (albeit related) conditions are treated with the

same interventions. As such it is likely to be more relevant and useful to commissioners and researchers to present synthesised evidence from a broad range of interventions for PAD. There has not been a recent review which aimed to bring all of the economic evidence on preventative *and* treatment interventions for PAD into a single narrative.

This review sought to produce an up-to-date synthesis of current knowledge about the cost-effectiveness of interventions for the prevention or treatment of PAD. Particular objectives were to identify characteristics of potentially cost-effective interventions, gaps in current knowledge, and important avenues for future research. In the UK there has been a pledge to increase healthcare spending to improve maternal mental health and therefore decision makers need to know which interventions are likely to be cost-effective so that these vital funds are allocated efficiently [22]. The aim of this review is to provide an evidence-base that could potentially inform these decisions by bringing information from different sources together into a comprehensive and critically-appraised summary with recommendations for commissioners and researchers.

Methods

A systematic literature search and narrative review was conducted to identify economic evaluations of interventions for PAD. The research questions addressed by this review were:
1) What are the characteristics of existing interventions for PAD that are likely to be cost-effective?
2) Where do the evidence and knowledge gaps indicate future research should be focussed?

The review protocol was registered on the PROSPERO register of systematic reviews (ID, CRD42016051133).

Inclusion/exclusion criteria

Explicit inclusion criteria were: (a) studies focusing on mothers and/or fathers experiencing or at risk of developing perinatal depression and/or anxiety, (b) any psychological, psychosocial and/or pharmacological intervention, (c) alternative interventions and usual care or placebo as comparators, (d) incremental assessment of cost effectiveness. Previous systematic reviews were excluded but screened for additional references.

Literature search

Electronic searches were performed on the PsycINFO, MEDLINE, NHS economic evaluation database (EED), and NHS Health Technology Assessment (HTA) database. An initial search was run in September 2016 which was updated in September 2017. The searches were restricted to English language publications from January 2000 onwards; changes in practice and resource use/costs over time mean that older references are less useful for decision making. Common search terms included words related to perinatal depression and/or anxiety and economic evaluation terms. Terms varied slightly according to database designs. The search strategies are reported in Supplementary Material (Table S1). The bibliographies of previously published systematic reviews [18,22] were hand-screened for additional references to ensure all relevant papers were captured.

Study selection

Abstracts of studies were examined independently by two reviewers (EMC and GES) to determine whether each publication met the inclusion criteria. Both reviewers independently considered the full-text of identified publications to ensure that inclusion criteria were met. At each stage any discrepancies were resolved through discussion and a consensus reached on which publications should progress to the data extraction stage.

Data extraction and quality assessment

Structured data extraction and quality assessment was undertaken, guided by the NHS EED handbook [24]. A dual-purpose (data extraction and quality assessment) form was designed a priori (see Supplementary Material, Table S2) and used to extract information on study methodology, results, limitations, evidence gaps, and quality. The quality of the studies was also assessed using a modified version of the Consensus Health Economic Criteria (CHEC) list [25]. The checklist and assessment results are included in Supplementary Material (Table S3). One reviewer (EMC) completed the data extraction process with half reviewed by the second reviewer (GES). No issues were identified that suggested that the second reviewer needed to review all data extracted.

Currency conversion and inflation

Costs were converted to Great British Pounds (£) at the average exchange rate for the cost year reported in the source study [26]. All costs were inflated to 2015/16 based on the Hospital and Community Health Services (HCHS) index [27]. Exchange and inflation rates are reported in Supplementary Material (Table S4).

Patient and public involvement

Neither patients nor the public were involved in this research.

Results

Initial searches identified 257 citations, following the removal of duplicates the titles and abstracts of the remaining 168 citations were screened for eligibility (Figure 1). Twenty eight papers were included for full-text review, with 8 papers identified as relevant to the review (see Supplementary Material (Table S5) for details of excluded studies). The two systematic reviews that were hand-searched resulted in no additional references [18,22]. Key characteristics of the 8 included studies are described in Table 1.

Figure 1 <to go here>

Table 1 Overview of included studies

Study	**Population**	**Country**	**Intervention** (all studies reported usual or routine care as the comparator)
Boath (2003) [28]	Women being treated for postnatal depression n=60	United Kingdom	***Treatment*** Access to psychiatric day hospital, Monday-Friday 08:30-16:30, over 6 months. Day hospital was staffed by a multi-disciplinary team of four psychiatric nurses, an occupational therapist, a nursery nurses, a lead psychiatric consultant, two clinical assistants, and a senior registrar
Petrou (2006) [29]	Women who were at high risk of developing postnatal depression at 26-28 weeks of gestation. n=151	United Kingdom	***Prevention*** Counselling and support delivered by trained health visitors during home visits at 3, 7, and 17 days post delivery, then weekly up to 8 weeks postnatally
Morrell (2009) [30]	Women registered with participating GP practices who became 36 weeks pregnant during the recruitment phase of the trial, had a live baby and were on a collaborating HV's caseload for 4 months postnatally n= 4084	United Kingdom	***Screening and treatment*** Health visitor (HV) training in the assessment of postnatal women, combined with either cognitive behavioural approach (CBA) or person-centred approach (PCA) sessions (once per week for up to 8 weeks) for eligible women, plus the option of a selective serotonin reuptake inhibitor - commencing around 8 weeks postnatally
Stevenson (2010) [31]	Women with postnatal depression (EPDS>12) n=not reported (model)	United Kingdom	***Treatment*** Hypothetical group CBT intervention, one 2-hour session per week for 8 weeks, 4-6 women per group
Dukhovny (2013) [32]	Any postpartum women in seven health regions across Ontario n=610	Canada	***Prevention*** Telephone-based volunteer lay/peer support - at least 4 phone calls starting 48 to 72 hours after randomisation and continuing through the first 12 weeks after birth
Ride (2016) [33]	First-time mothers who had recently given birth and attended one of 48 participating Maternal and Child Health Centres n=359	Australia	***Prevention*** Psychoeducational programme targeted at the partner relationship, management of infant behaviour, and parental fatigue, delivered as a one-off 6-hour session by nurses based at Maternal and Child Health Centres

Grote (2017) [34]	Women at 12-32 weeks gestation, scoring 10 or higher on the PHQ-9 or with a diagnosis of probable dysthymia n=270	United States	***Treatment*** Collaborative care for depression including a choice of brief interpersonal psychotherapy (8 initial sessions plus maintenance sessions through baby's first year), pharmacotherapy, or both, co-ordinated by Depression Care Specialists (master's-level social workers) in collaboration with obstetric care providers
Wilkinson (2017) [35]	Hypothetical cohort of pregnant women experiencing one live birth over 2 years n=1000	United States	***Screening and treatment*** Over first year postpartum, general physicians screening for and treating postpartum depression and psychosis in partnership with a psychiatrist

Characteristics of studies

As shown in Table 1, the earliest and largest number of included studies were from the United Kingdom (n=4) [28–31], the most recent two studies were from the United States [34,35], and there was one study from each of Australia [33] and Canada [32].

The interventions evaluated across the 8 studies were diverse and no two studies evaluated comparable interventions. Three studies included a preventative intervention [29,32,33], three focussed on treatment [28,31,34], and two included complex interventions incorporating both identification and treatment [30,35]. All studies focussed on postnatal depression in mothers although the study by Ride et al did also consider anxiety and fathers [33]. Two of the preventative interventions were targeted at distinct groups: high risk women [29]; first time mothers [33]. One intervention involved lay or peer support [32], two were delivered by health visitors [29,30], and the remainder were delivered across a range of settings/healthcare professionals/structures including collaborative care [34,35] and group cognitive behavioural therapy (CBT) [31]. The comparator intervention for all studies was described as usual or routine care. Usual care is likely to vary by setting which affects the external validity of the study.

The majority (n=6) of studies reported cost-effectiveness analyses with different measures of health benefits which makes it difficult to compare between studies [28,29,32–35]. The most widely used (primary or secondary) measure of health benefit was the Edinburgh Postnatal Depression Scale (EPDS) which was reported in 2 of the 6 trial-based studies [30,32]. Cost-utility analyses were reported in four studies, making results across these studies easier to compare [30,31,33,35] (two of which had also reported cost-effectiveness [33,35]). Utility was derived from the SF-6D in two studies [30,31] and from the EQ-5D in two studies [33,35]. Only two studies reported the results of an economic models [31,35] with the remainder reporting trial-based results.

Table 2 Design of included studies

Study	Evaluation type	Measure of health benefit	Evaluation details	Data source	Quality/bias considerations
Boath (2003) [28]	CEA	Recovery from PND (no longer fulfilling Research Diagnostic Criteria)	• Trial or model: trial • Perspective: health service • Time horizon: 6 months • Price year: 1992/93 • Currency: British £	Observational study - healthcare utilisation self-reported and obtained from medical records	Treatment allocation was non-randomised. Reported that no significant differences in sociodemographic characteristics or outcome measures between groups at baseline. No loss to follow-up reported
Petrou (2006) [29]	CEA	Months of postnatal depression avoided (SCID-II)	• Trial or model: trial • Perspective: health and social services • Time horizon: 18 months • Price year: 2000 • Currency: British £	RCT - health and social care utilisation was self-reported by participants	Structured clinical interviews were used to identify depression in both treatment groups. The numbers/characteristics of those declining to participate were not reported
Morrell (2009) [30]	CUA	• QALYs (derived from the SF-6D) • EPDS	• Trial or model: trial • Perspective: health and social services • Time horizon: 18 months • Price year: 2003/04 • Currency: British £	RCT - health and social care utilisation obtained from medical records (up to 6 months) and participant self-report (at 12 and 18 months)	Data was collected on women declining to take part but differences with sample were not discussed. Sample was broadly representative of general population. Missing economic data were significant at 12 and 18 months, 6 months was used as the primary time horizon
Stevenson (2010) [31]	CUA	QALYs (derived from EPDS mapped onto SF-6D)	• Trial or model: model (mathematical) • Perspective: health and social services • Time horizon: 12 months • Price year: not reported • Currency: British £	Published data sources and expert opinion informed the model. EPDS, SF-36, and costs from published RCTs.	As the model was mathematical, no structure was reported in the paper. Probabilistic sensitivity analyses were conducted
Dukhovny (2013) [32]	CEA	Cases of PND averted at 12 weeks postpartum	• Trial or model: trial • Perspective: societal • Time horizon: 12 weeks • Price year: 2011 • Currency: Canadian $	Multi-region RCT - resource utilisation was self-reported by participants	Only two people did not complete healthcare utilisation questionnaires and fewer than 0.01% of individual resource utilisation items were missing at random

Ride (2016) [33]	CEA; CUA	• Prevalence of depression and anxiety(DSM-IV criteria) • QALYs (from the EQ-5D)	• Trial or model: trial • Perspective: health and social services • Time horizon: 20 weeks • Price year: 2013/14 • Currency: Australian $	Cluster-RCT - health and social care utilisation self-reported by participants	Differences between the treatment groups were adjusted for in the analysis. The intra-cluster coefficients were small but non-negligible for QALYs which may have reduced the ability to detect an effect of the intervention
Grote (2017) [34]	CEA	• Depression severity (SCL-20) • Depression free days • PTSD Checklist	• Trial or model: trial • Perspective: health plan or insurer • Time horizon: 18 months • Price year: 2013 • Currency: US $	RCT - health and social care utilisation self-reported by participants	The costs included only related to mental health care. The perspective was 'public health' and so could have also included primary and community healthcare services. Those with partial cost data (n=12/164) were more likely to have probable PTSD and to have been randomly assigned to the intervention
Wilkinson (2017) [35]	CEA; CUA	• QALYs (derived from published literature) • EPDS	• Trial or model: model (decision tree) • Perspective: health plan (Medicaid) • Time horizon: 2 years • Price year: 2014 • Currency: US $	Systematic review of existing literature to inform the model. Some cost parameters estimated from Medicaid data	Some parameters were from studies of anxiety/depression outside of the perinatal period. Probabilistic sensitivity analyses were conducted. The model structure is pragmatic, but perhaps over simple in terms of suicide risk - only women who discontinue treatment are at risk of suicide, women who don't seek help or those who screen negative are not deemed to be at risk of suicide
CEA = cost-effectiveness analysis; CUA = cost-utility analysis; RCT = randomised controlled trial; CBT = cognitive behavioural therapy; SCID-II = Structured Clinical Interview for Depression, 2nd edition; QALY = quality adjusted life year; EPDS = Edinburgh Postnatal Depression Scale; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; SCL-20 = 20-item Symptom Checklist Depression Scale; PTSD = post-traumatic stress disorder; EPDS = Edinburgh Postnatal Depression Scale.					

Critical appraisal

A copy of the CHEC quality appraisal checklist and assessment results are included in Supplementary Material (Table S3) [25]. The median score was 15.5 (out of 18). The majority of the studies were of high quality (n=6) [29–33,35] and two were average [28,34]. The studies published prior to 2006 did not report results of incremental analysis but there is a trend towards more robust methods and reporting over time. Overall the studies reported the population, setting, intervention, and comparator well. Two studies had relatively short time horizons (12 weeks [32] and 20 weeks [33]) which may not reflect the potentially long-lasting course of PAD. Six of the studies reported sensitivity or sub-group analyses [29–33,35], demonstrating varying levels of uncertainty around their primary cost-effectiveness estimate. Not reporting uncertainty is an important limitation in economic evaluations because it indicates confidence in the results, analogous to not reporting a confidence interval for a statistical analysis. Four of the studies did not report whether there were any conflicts of interest [29,31,32,35].

Factors which increased the potential for bias in the reported results include non-randomised treatment allocation [28] and an imbalance in data completeness between treatment groups/sub-groups [34]. The study by Dukhovny et al was particularly robust owing to a high level of data completeness [32].

The model by Stevenson et al evaluating group CBT to treat postnatal depression in the UK was informed by expert opinion alongside published data available from RCTs for EPDS and SF-6D scores [31] (see Table 2). The model structure was not explicitly reported. The model by Wilkinson et al evaluating collaboration between GPs and psychiatrists to identify and treat postnatal depression included estimates for the EPDS and EQ-5D from published literature [35]. Some of the model parameters were from studies of anxiety/depression outside of the perinatal period and the model structure although pragmatic potentially oversimplified suicide risk (see Table 2). Both model-based evaluations reported probabilistic sensitivity analysis.

Cost-effectiveness

Six studies reported incremental cost-effectiveness ratios (ICERs), half of which were in terms of clinical outcomes [28,29,32] and half in terms of QALY gains associated with the intervention compared with usual care [31,33,35]. Two interventions were either likely or highly likely to be cost-effective, both incorporating identification plus treatment of postnatal depression: health visitor screening and counselling [30]; general practitioner/psychiatrist collaborative screening and treatment [35]. The intervention involving health visitors was associated with lower costs and better outcomes than usual care therefore the authors did not report an ICER because the intervention dominated usual care. However when multiple imputation was used to resolve missing data (rather than a complete case analysis) the intervention was associated with more QALYs and a net cost resulting in an ICER of £15,666/QALY.

Three interventions (psychiatric day hospital (treatment) [28], health visitor counsellors (prevention) [29], telephone-delivered peer support (prevention) [32]) were classified as

possibly cost-effective because although they reported improved health outcomes with increased costs, there is no accepted threshold by which to judge ICERs when health benefits are quantified as anything other than QALYs. The ICER reported for psychiatric day hospital care was sensitive to the inclusion of primary care and medication costs, increasing from £3,843 to £56,865 per additional recovery [28]. Psychoeducation (prevention) [33] was classified as possibly cost-effective because although following currency conversion the QALY-based ICER was below the UK threshold for cost-effectiveness, the authors reported a 55% chance (i.e. not much higher than chance) that it was below the Australian threshold. Furthermore the ICER value increased by £5,055 following multiple imputation. Collaborative care (treatment) [34] was classified as possibly cost-effective because of conflicting results for sub-group analyses (Table 3). The cost-benefit analysis valued a depression-free day at US$20 (approximately £13) [34] which translated to a net benefit among mothers with PTSD and a net cost for mothers without PTSD. Group CBT was evaluated as unlikely to be a cost-effective treatment for post-natal depression [31].

Table 3 Cost-effectiveness results

Study	Interventions	Net benefit	Net cost	ICER, key conclusions, and uncertainty
Boath (2003)[28]	Psychiatric day hospital versus routine primary care	14 more women recovered in the intervention group.	The intervention was £53,824 (p<0.001) more expensive than routine care.	£3843 per each additional recovery. The net cost is sensitive to inclusion primary care and medication costs, increasing to £56,865. ***Possibly cost-effective***
Petrou (2006)[29]	Counselling and support from health visitors versus usual care	The intervention group depressed for 2.14 weeks fewer (over 18 months) than the control group - this was not statistically significant (p=0.41).	The intervention group costs were £189 higher although this was not significant (95% CI -£843 to £1237).	£68 per month of depression avoided. Possibly a small improvement in outcomes for a small cost. ***Possibly cost-effective***
Morrell (2009)[30]	Screening and talking therapy (CBA or PCA) delivered by health visitor versus usual care	EPDS score at 6 months was 0.9 lower (p<0.001) for those randomised to an intervention group. QALY gain of 0.002 (95% CI -0.001 to 0.005) associated with the intervention.	There was a non-significant net-saving of £26 (95% CI -£100 to £47) for women in the intervention groups.	Improved outcomes with comparable costs. No ICER reported because of negative net cost. CBA appears to be more cost-effective than PCA. Sub-group analysis of 'at-risk' women: 6-month EPDS score 2.1 lower (p=0.002). Analysis of imputed data: QALY gain increased to 0.003 (95% CI 0.001 to 0.006) and net cost saving increased to £47 (95% CI -£68 to -£4), both reaching statistical significance (£15,666/QALY). ***Highly likely to be cost-effective***
Stevenson (2010)[31]	Group CBT versus usual care	Intervention associated with a QALY gain of 0.039 (PSA results).	£1568 net cost of providing gCBT (PSA results).	£39,875 per QALY gained. Intervention is not likely to be cost-effective at accepted thresholds. More research is needed to address the level of uncertainty. ***Not likely to be cost-effective***
Dukhovny (2013)[32]	Telephone-based peer support versus usual care	0.1116 more cases of postnatal depression avoided at 12 weeks in the intervention group.	£755 net cost associated with intervention (p<0.001).	£6768 per case of postnatal depression avoided. The ICER is within the range of other postnatal depression interventions. ***Possibly cost-effective***

Ride (2016) [33]	Psychoeducational programme versus usual care	Comparable outcomes both in terms of prevalence of mental health conditions (p=0.883) and QALYs (p=0.967).	£167 net cost associated with the intervention was although this was not statistically significant (p=0.333).	£21,987/QALY; £92 per %-point reduction in 30-day prevalence of postnatal mental health disorders. The probability the intervention if cost-effective is 0.55 at a willingness to pay threshold of AD$ 55,000 (approximately £30-35,000) - more research is needed to reduce uncertainty. Multiple imputation of missing data increased ICER to £27,042/QALY. ***Possibly cost-effective***
Grote (2017) [34]	Collaborative care for depression versus usual care	More depression free days over 18 months for the intervention group: • with PTSD 68 days (95% CI 5 to 132) • without PTSD 13 days (95% CI -72 to 99).	Significant net cost associated with the intervention: • with PTSD £868 (95% CI £543 to £1192) • without PTSD £772 (95% CI £473 to £1072).	If a depression free day is valued at US$20 (approximately £13): • with PTSD net benefit of £32 • without PTSD net cost of £600. ***Possibly cost-effective***
Wilkinson (2017) [35]	Psychiatrist-supported GP screening and treating postpartum depression and psychosis	29 more healthy women in the intervention group, equating to a total of 21.43 additional QALYs over 2 years.	Total additional cost associated with the intervention £185,173.	£8642 per QALY gained, £6350 per remission achieved, £588 per additional healthy woman. ***Likely to be cost-effective***
RCT = randomised controlled trial; CBT = cognitive behavioural therapy; QALY = quality adjusted life year; CBA = cognitive behavioural approach; PCA = person centred approach; EPDS = Edinburgh Postnatal Depression Scale; AD$ = Australian dollars. Currency conversion and inflation rates used are reported in Supplementary Material (Table S4). 95% CI = 95% confidence interval.				

Discussion

Eight studies evaluating the cost-effectiveness of interventions for PAD were included in this review. All were published between 2006 and 2017. Six studies were high quality and two average quality. Each study focussed on depression occurring in postnatal mothers (although Ride et al also considered anxiety and fathers [33]) but evaluated a different type of intervention, some of which focussed on prevention and others focussed on treatment (or identification plus treatment). Two studies identified interventions that were likely to be cost-effective, both of which incorporated identification plus treatment of postnatal depression.

The quality of the studies included in the review was mixed and generally increased over time which is likely to reflect the agreement of standards for the reporting of economic evaluations. The use of a standardised checklist, such as the commonly used CHEERS checklist for the reporting of economic evaluations [36], would facilitate the synthesis of data in future reviews. In order to meaningfully compare studies, the most critical information required is: a full description of the intervention and comparator, inclusion/exclusion criteria, time horizon and perspective of the evaluation, the net outcome, the net cost, ICER, and cost-effectiveness acceptability (reported as the likelihood an intervention is cost-effective at appropriate willingness to pay thresholds), and summary of uncertainty.

QALYs are the most widely used measure of health benefit in economic evaluations, as recommended by the National Institute for Health and Care Excellence (NICE) [37]. Interventions costing less than £20,000-30,000 per QALY gained (versus the comparator intervention) are considered to be cost-effective. Only four of the included studies reported results in terms of QALYs. Standardised methods for economic evaluations are important so that results can be directly compared, for example it may not always be appropriate to compare QALYs derived using different approaches [38]. NICE recommends that the EQ-5D is used to derive QALYs; two of the studies included derived QALYs from the SF-6D [39] and the other two studies derived QALYs from the EQ-5D [40].

There was great heterogeneity between the studies included in terms of the interventions, measure of benefit, and time horizon. However the interventions could be grouped by some characteristics such as their aim (e.g. prevention or treatment) or key actors (e.g. healthcare professional or peer support). There were inconsistent findings within the intervention sub-groups with one exception. The two studies which incorporated identification plus treatment were both likely to be cost-effective [30,35]. However the two interventions were very different. The intervention evaluated by Morrell et al involved training health visitors to identify women experiencing postnatal depression and deliver talking therapy (using either a cognitive behavioural approach or a person centred approach) whereas the intervention evaluated by Wilkinson et al was based around collaboration between GPs and psychiatrists. Due to a large amount of missing data the health visitor intervention was only evaluated at 6 months whereas the collaborative intervention was evaluated at 2 years. This also makes it difficult to compare results

between studies because it is possible that over a longer a follow up more benefits are accrued.

Strengths and limitations

There are a number of strengths and limitations of this review. Multiple major literature databases relevant to health and economic research were searched therefore it is likely that key studies incorporating the search terms have been identified. In the instance where a full text was not available online the authors were contacted and provided a copy. The search was however restricted to English language studies, introducing some bias. Searches were also restricted to published journal articles which are less likely to include inconclusive or negative cost-effectiveness results when compared with the grey literature [41]. The exclusion of studies published prior to the year 2000 may also have introduced bias; however a post hoc search of the NHS EED database returned no relevant studies from before this time.

Despite a robust search strategy there may be relevant studies that were not identified by this review. For example, the definition of the perinatal period adopted by researchers (from conception up to 4 weeks [42], 6 weeks [43], or 12 months postpartum [7]) will influence whether interventions for PAD are described as 'perinatal' or 'early childhood'. After this review was completed a paper was brought to the authors' attention which involved an intervention for depression in mothers in the first year postpartum. However, as it was described as an 'early childhood program' and was not explicitly referred to as an intervention for postnatal or postpartum depression it was not identified in this search [44]. The intervention (in-home CBT) was nested within a complex home-visiting support program which aimed to improve the health and wellbeing of low-income parents and babies which was the 'standard care' comparator in the economic evaluation. The study reported the results of an economic model which extrapolated the results from an RCT and concluded that in-home CBT was likely to be cost-effective compared to this standard care as a treatment for depression.

Two separate tools were used to critically appraise the studies which included more criteria and gave a broader perspective than a single approach, although one was developed specifically for this review and not formally validated. The CHEC-list [45] was used to assign a score to each study and the data extraction tool was used to identify potential sources of bias. Both approaches involve an element of subjectivity, the CHECH-list attempts to handle this by not classing a criteria as having been met if it is only partially met, however this may result in some loss of sensitivity.

Future research

One study which was excluded from this review because it focussed only on screening for postnatal depression concluded that it was not cost-effective to screen because of increased treatment costs [46]. However, identification and treatment are inextricably linked and evaluating them separately may not tell the whole story which should be borne in mind for future research. It is also necessary to address the lack of economic evidence for interventions for antenatal depression, perinatal anxiety, and PAD in fathers as these

conditions are also prevalent and may be associated with negative outcomes for individuals and families [47–49]. Future economic evaluations should be conducted and reported according to good practice guidelines so that future reviews can make clear recommendations to inform health policy.

Conclusion

Heterogeneity in the evaluations to date means that is not possible to make any conclusions about their relative cost-effectiveness, with no clear implications for health policy. However the two interventions which were likely to be cost-effective (compared to usual care) both incorporated identification and treatment together; this appears to be the most fruitful direction for future research and could inform perinatal mental health service strategy. As recognition of the incidence of perinatal anxiety in mothers, and all PAD conditions in fathers, grows so does the need for relevant and robust economic evidence, therefore this is also a recommended area for future research. The quality of the methods and reporting of economic evaluations for interventions related to PAD has improved over time, but it is important that new studies adhere to reporting guidelines which will facilitate future evidence synthesis.

Figure legend

Figure 1 - PRISMA flow diagram of studies identified

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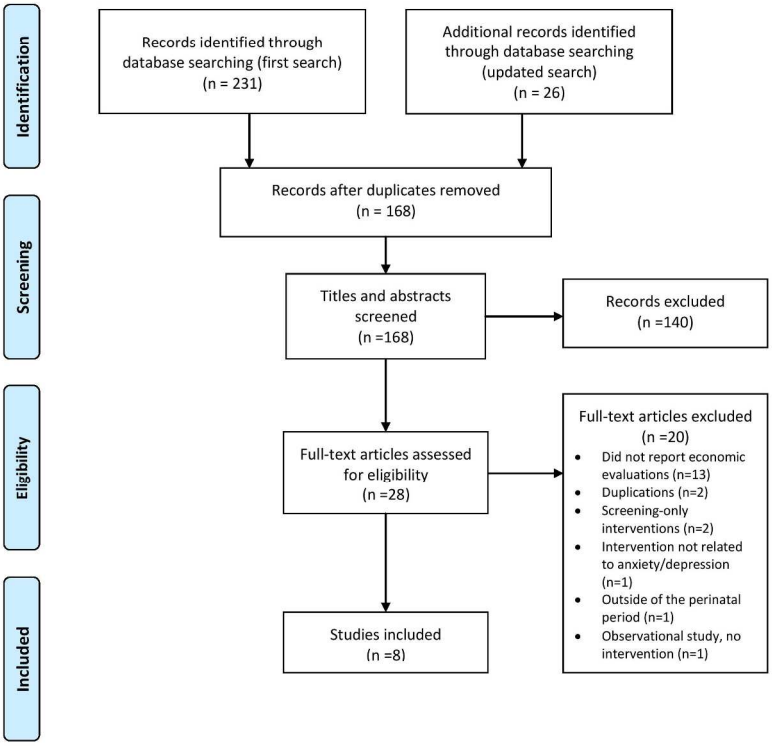

Figure 1 PRISMA flow diagram of studies identified

215x279mm (300 x 300 DPI)

Table S1 - search strategies

MEDLINE	#1 economic evaluation OR economic analys* OR cost analys* OR cost effective* analys* OR cost-effective* analys* OR cost benefit* analys* OR cost utility* analys* OR cost-benefit* analys* OR cost-utility* analys* #2 postpartum OR post-partum OR post partum #3 postnatal OR post natal OR post-natal #4 perinatal OR peri natal OR peri-natal #5 antepartum OR ante partum OR ante-partum #6 pregnan* #7 #2 OR #3 or #4 or #5 or #6 #8 depress* OR anxi* #9 #8 AND #7 #10 #1 AND #9 #11 Limit #10 to yr=2000-Current #12 #11 NOT cattle [ti] OR karyotyping[ti] OR aneuploid*[ti] OR smoking cessation[ti] OR tobacco cessation[ti]
PsycINFO	#1 anxi* OR depress* #2 postnatal OR post natal OR post-natal #3 postpartum OR post-partum OR post partum #4 antenatal OR ante natal OR ante-natal #5 perinatal OR peri natal OR peri-natal #6 antepartum OR ante partum OR ante-partum #7 pregnan* #8 #2 OR #3 OR #4 OR #5 OR #6 OR #7 #9 #1 AND #8 #10 cost analy* or *economic* or cost effective* or cost-effective* or cost benefit* or cost utility* or cost-benefit* or cost-utility* #11 #9 AND #10 #12 Limit #11 to (all journals and yr="2000-Current")
NHS EED/HTA	*Title search* (depress* OR anxi*) AND ((postpartum OR post-partum OR post partum) OR (postnatal OR post natal OR post-natal) OR (perinatal OR peri natal OR peri-natal) OR (antepartum OR ante partum OR ante-partum) OR pregnan*)

Table S2 - Data extraction and quality assessment form

Subject of the study	
Intervention(s)	
Comparator(s)	
Intervention type	
Disease	
Study question/hypothesis	
Key elements of the study	
Type of economic analysis	
Study population	
Details of model (if applicable)	
Setting	
Country	
Dates to which data relate	
Link between cost and health benefit data	
Clinical evidence	
Clinical and epidemiological inputs	
Data sources	
Methods to obtain data	
Measures of health benefit	
Summary measure of health benefit	
Method of utility valuation	
Time horizon	
Discount rate for health benefit	
Direct costs	
Direct costs included	
Who bears the direct costs?	
Source of resource use data	
Resource use reported separately from costs	
Sources of unit prices	
Currency and price year	
Adjustment for inflation; other adjustments	
Costs excluded	
Time horizon	
Discount rate for direct costs	
Indirect costs	
Inclusion of indirect (productivity)	
Source of cost and quantity data	
Resource use reported separately from costs	
Time horizon	
Discounting of indirect costs	
Statistical analysis of costs	
Descriptive statistics/point estimates reported	
Significance testing reported	
Study powered to detect differences in cost	
Analysis of uncertainty	
If model: exploration of parameter uncertainty	

If model: exploration of structural uncertainty	
All studies: exploration of alternative subgroups / settings	
Estimated benefits	
Total benefit: intervention arm(s)	
Total benefit: comparator arm(s)	
Net (incremental) benefit	
Result of statistical test for difference in benefits	
Were adverse effects included?	
Estimated costs	
Total cost: intervention arm(s)	
Total cost: comparator arm(s)	
Net (incremental) cost (intervention versus comparator)	
Result of statistical test for difference in costs	
Did the duration of costs match the time horizon?	
Synthesis of benefits & costs, and conclusions	
Synthesis of benefits and costs conducted (e.g. ICER)	
ICER	
Probability cost-effective	
Important differences in results for subgroups or sensitivity analyses	
Summary of authors' conclusions	
Critical review	
Is the choice of comparator suitably justified?	
If model: was the model structure suitable?	
If model: was a model schematic presented?	
If model: was the model adequately reported?	
Validity of primary effectiveness data	
Validity of secondary effectiveness data	
Validity of estimated health benefit	
Validity of estimated costs	
Do the authors discuss the generalisability of their findings?	
Do the authors compare their findings to previous studies?	
Are the authors' conclusions justified?	
Implications	
Do the authors describe policy implications of their findings? Are they appropriate?	

Table S3 - Criteria list for assessment of methodological quality of economic evaluations: Consensus on Health Economic Criteria [9]

	Boath (2003) [1]	Petrou (2006) [2]	Morrell (2009) [3]	Stevenson (2010) [4]	Dukhovny (2013) [5]	Ride (2016) [6]	Grote (2017) [7]	Wilkinson (2017) [8]
1. Is the study population clearly described?	✓	✓	✓	✓	✓	✓	✓	✓
2. Are competing alternatives clearly described?	✗	✓	✓	✓	✓	✓	✓	✓
3. Is the economic study design appropriate to the stated objective?	✓	✓	✓	✓	✓	✓	✓	✓
4. Is the chosen time horizon appropriate to include relevant costs and consequences?	✓	✓	✓	✓	✗	✗	✓	✓
5. Is the actual perspective chosen appropriate?	✓	✓	✓	✓	✓	✓	✓	✓
6. Are all important and relevant costs for each alternative identified?	✓	✓	✓	✓	✓	✓	✗	✓
7. Are all costs measured appropriately?	✓	✓	✓	✓	✓	✓	✓	✓
8. Are costs valued appropriately?	✓	✓	✓	✓	✓	✓	✓	✓
9. Are all important and relevant outcomes for each alternative identified?	✓	✓	✓	✓	✓	✓	✓	✓
10. Are all outcomes measured appropriately?	✓	✓	✓	✓	✓	✓	✓	✓
11. Are outcomes valued appropriately?	✗	✗	✓	✓	✗	✓	✗	✓
12. Is an incremental analysis of costs and outcomes of alternatives performed?	✗	✓	✓	✓	✓	✓	✓	✓
13. Are all future costs and outcomes discounted appropriately?	✓	✓	✓	✓	✓	✓	✗	✓
14. Are all important variables, appropriately subjected to sensitivity analysis?	✗	✓	✓	✓	✓	✓	✗	✓
15. Do the conclusions follow from the data reported?	✓	✓	✓	✓	✓	✓	✓	✓
16. Does the study discuss the generalizability of the results to other settings and patient/client groups?	✓	✗	✓	✗	✓	✗	✗	✓

	Boath (2003)	Petrou (2006)	Morrell (2009)	Stevenson (2010)	Dukhovny (2013)	Ride (2016)	Grote (2017)	Wilkinson (2017)
17. Does the article indicate that there is no potential conflict of interest of study researcher(s) and funder(s)?	✓	✗	✓	✗	✗	✓	✓	✗
18. Are ethical and distributional issues discussed appropriately?	✗	✓	✓	✓	✓	✓	✗	✓
TOTAL SCORE	13	15	18	16	15	16	12	17
Each criteria met is awarded one point: 15 or greater = high quality, 8-14 = average quality, less than 8 = poor quality. Item 13 – studies where discounting is not applicable (i.e. time horizon less than one year) have been assumed to meet criteria.								

Table S4 - Currency conversion and inflation rates applied

	Price year in study	Original currency	Exchange rate#	HCHS year	HCHS index (1987/88 = 100.0)	HCHS inflation factor to 2015/16*
Boath (2003) [1]	1992/93	GBP	n/a	1992/93	150.3	1.98
Petrou (2006) [2]	2000	GBP	n/a	1999/2000	188.5	1.58
Morrell (2009) [3]	2003/04	GBP	n/a	2003/04	225.6	1.32
Stevenson (2010) [4]	2010	GBP	n/a	2009/10	268.6	1.11
Dukhovny (2013) [5]	2011	Canadian $	0.63	2010/11	276.7	1.07
Ride (2016) [6]	2013/14	Australian $	0.59**	2013/14	290.5	1.02
Grote (2017) [7]	2013	US $	0.64	2012/13	287.3	1.03
Wilkinson (2017) [8]	2014	US $	0.61	2013/14	290.5	1.02

GBP = Great British Pound/United Kingdom £ sterling; US = United States
#per 1GBP;
*HCHS index 2015/16 = 297.0
*The exchange rate between Australian dollars ($) and GBP was notably different in 2013 (0.62 $/£) and 2014 (0.55 $/£) therefore the midpoint (0.59 $/£) was used.

Table S5 - reasons for exclusion of full texts screened

Title	Year	Lead author	Reason
A randomized comparison of home and clinic follow-up visits after early postpartum hospital discharge.	2000	Lieu [10]	No economic evaluation reported
Costs and effectiveness of community postnatal support workers: a randomised controlled trial.	2000	Morrell [11]	No economic evaluation reported
Costs and benefits of community postnatal support workers: a randomised controlled trial.	2000	Morrell [12]	Duplicate - HTA report for same study reported elsewhere
The treatment of postnatal depression by health visitors: impact of brief training on skills and clinical practice.	2003	Appleby [13]	No economic evaluation reported
The Social Support and Family Health Study: a randomised controlled trial and economic evaluation.	2004	Wiggins [14]	No economic evaluation reported
Improving infant sleep and maternal mental health: a cluster randomised trial.	2007	Hiscock [15]	No economic evaluation reported
Stepped care treatment of postpartum depression: A primary care-based management model.	2008	Gjerdingen [16]	No economic evaluation reported
Screening for postnatal depression within the Well Child Tamariki Ora Framework.	2008	Suebwongpat [17]	Intervention – screening only
Screening for postnatal depression in primary care: Cost effectiveness analysis.	2009	Paulden [18]	Intervention – screening only
Postpartum follow-up: can psychosocial support reduce newborn readmissions?	2010	Barilla [19]	Intervention - aim of intervention not related to anxiety/depression, no measure of anxiety/depression collected
A model for maternal depression.	2010	Connelly [20]	No economic evaluation reported, review of existing evidence
A pragmatic randomised controlled trial to compare antidepressants with a community-based psychosocial intervention for the treatment of women with postnatal depression: the RESPOND trial	2010	Sharp [21]	No economic evaluation reported
Group cognitive behavioural therapy for postnatal depression: a systematic review of clinical effectiveness, cost-effectiveness and value of information analyses.	2010	Stevenson [22]	Duplicate - HTA report for same study reported elsewhere
Supporting women with postnatal depression through psychological therapies	2011	Centre for Reviews and Dissemination [23]	No economic evaluation reported, review of existing evidence

Peer support and interpersonal psychotherapy groups experienced decreased prenatal depression, anxiety and cortisol.	2013	Field [24]	No economic evaluation reported
Effects of an infant-focused relationship-based hospital and home visiting intervention on reducing symptoms of postpartum maternal depression: A pilot study.	2014	Nugent [25]	No economic evaluation reported
Antidepressant treatment of depression during pregnancy and the postpartum period	2014	McDonagh [26]	No economic evaluation reported, review of existing evidence
Enhanced engagement: An intervention pilot for mental health promotion among low-income women in a community home visiting program.	2015	Price [27]	Patient group - not restricted to the postpartum period
Perinatal depression and child development: exploring the economic consequences from a South London cohort.	2015	Bauer [28]	Intervention - observational study, no intervention
Improving perinatal depression care: The Massachusetts Child Psychiatry Access Project for Moms.	2016	Byatt [29]	No economic evaluation reported, no comparator intervention

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	3
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	3-4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplementary material
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	4
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	4 Supplementary material
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	4
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	4
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	3-4 (narrative review)

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	4
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	n/a
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	4, figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	9, Table 2
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Table 3
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	n/a
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Table 2
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	n/a
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	13
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	13
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	13-14
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	2

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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Cost-effectiveness of interventions for perinatal anxiety and/or depression: a systematic review.

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Cost-effectiveness of interventions for perinatal anxiety and/or depression: a systematic review.

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Abstract

Objectives Anxiety and/or depression during pregnancy or year after childbirth is the most common complication of childbearing. Economic evaluations of interventions for the prevention or treatment of perinatal anxiety and/or depression (PAD) were systematically reviewed with the aim of guiding researchers and commissioners of perinatal mental health services towards potentially cost-effective strategies.

Methods Electronic searches were conducted of the MEDLINE, PsycINFO, and NHS Economic Evaluation and Health Technology Assessment databases in September 2017 to identify relevant economic evaluations published since January 2000. Two stages of screening were used with pre-specified inclusion/exclusion criteria. A data extraction form was designed prior to the literature search to capture key data. A published checklist was used to assess the quality of publications identified.

Results Of the 168 non-duplicate citations identified, 8 studies met the inclusion criteria for the review; all but one focussing solely on postnatal depression in mothers. Interventions included prevention (3/8), treatment (3/8), or identification plus treatment (2/8). Two interventions were likely to be cost-effective, both incorporated identification plus treatment. Where the cost per quality-adjusted life year (QALY) gained was reported, interventions ranged from being dominant (cheaper and more effective than usual care) to costing £39,875/QALY.

Conclusions Uncertainty and heterogeneity across studies in terms of setting and design make it difficult to make direct comparisons or draw strong conclusions. However the two interventions incorporating identification plus treatment of perinatal depression were both likely to be cost-effective. Many gaps were identified in the economic evidence, such as the cost-effectiveness of interventions for perinatal anxiety, antenatal depression, or interventions for fathers.

Review registration PROSPERO ID: CRD42016051133.

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Strengths and limitations of this study

- A pre-specified protocol was registered on the International Prospective Register of Systematic Reviews (PROSPERO).
- The current evidence base was summarised and critically appraised using two approaches to minimise subjectivity.
- The review was limited to English language studies which may introduce bias and it is possible that some studies were not identified despite the comprehensive search strategy.

Funding statement

This research received no specific grant from any finding agency in the public, commercial, or not-for-profit sectors.

Competing interests statement

None declared.

Contributors

EMC and GES conducted the literature search and data extraction. EMC wrote the first draft of the manuscript with contribution from GES to the final version.

Data sharing statement

Search strategies and data extraction templates are available in the supplementary material. No other unpublished data from the study are available.

Background

Improving mental health is a priority for UK and international health policy; the Department of Health supports the notion that there can be "no health without mental health"[1–4]. In the UK, policy specifically aims to improve the mental health of mothers[5]; this reflects the growing recognition of the potential intergenerational effects of mental illness [6].

Anxiety and/or depression during pregnancy or in the first year after having a baby (perinatal anxiety and/or depression; PAD) is experienced by around 20% of mothers in high income countries [7,8]. The gold standard for clinical diagnosis of PAD is a structured interview [9], typically conducted by a psychiatrist. The current recommendation in the UK is that at first contact with maternity services and in the weeks following childbirth healthcare professionals consider asking women the Whooley and Generalised Anxiety Disorder scale (GAD-2) case-finding questions [7]. However the Edinburgh Postnatal Depression Scale (EPDS) [10] is the most frequently used instrument used to detect PAD in research settings [11], which has validated cut-off scores to identify antenatal and postnatal women likely to be experiencing PAD [12].

PAD can have important implications for the life-course of mothers and children [13]; depression during pregnancy is strongly associated with both depression and anxiety following childbirth [14,15]. Other important potential long-term considerations include developmental delays and behavioural problems for children and family instability [4,16]. The lifetime societal burden of PAD and other perinatal mental health conditions is massive, estimated at £8.1bn for all the babies born in a single year in the United Kingdom (almost 700,000 in 2016 [17]) [13]. This includes costs related to time off work, marriage breakdown, and social support. Evidence suggests that the costs of improving perinatal mental health outcomes are likely to be outweighed by the benefits [7,18]; high quality economic evidence is needed to identify the most efficient ways of doing so.

Systematic reviews of the evidence [19–21] suggest that psychological therapy and/or antidepressant medication are effective at treating the symptoms of PAD for many women which is reflected in current clinical guidance [7]. However less is known about the cost-effectiveness of treatments for PAD. A systematic review of literature published before July 2013 and relating to *preventative* interventions for perinatal depression concluded that midwifery redesigned postnatal care, a person-centred approach-based intervention, and an interpersonal therapy-based intervention showed some evidence of cost-effectiveness but with considerable uncertainty [22]. A recent report on the long-term cost-effectiveness of perinatal mental health interventions included a selective review of interventions which had previously been found to be cost-effective and concluded that all of the interventions led to a long-term net monetary benefit from a societal perspective [18].

Different perinatal mental health conditions often co-occur [14,23] and in the UK there has been a move towards commissioning the healthcare services for conditions under this umbrella together. Furthermore, widely used screening instruments such as the EPDS [10] were not designed to differentiate between different perinatal mental health conditions which may mean that people with different (albeit related) conditions are treated with the

same interventions. As such it is likely to be more relevant and useful to commissioners and researchers to present synthesised evidence from a broad range of interventions for PAD. There has not been a recent review which aimed to bring all of the economic evidence on preventative *and* treatment interventions for PAD into a single narrative.

This review sought to produce an up-to-date synthesis of current knowledge about the cost-effectiveness of interventions for the prevention or treatment of PAD. Particular objectives were to identify characteristics of potentially cost-effective interventions, gaps in current knowledge, and important avenues for future research. In the UK there has been a pledge to increase healthcare spending to improve maternal mental health and therefore decision makers need to know which interventions are likely to be cost-effective so that these vital funds are allocated efficiently [22]. The aim of this review is to provide an evidence-base that could potentially inform these decisions by bringing information from different sources together into a comprehensive and critically-appraised summary with recommendations for commissioners and researchers.

Methods

A systematic literature search and narrative review was conducted to identify economic evaluations of interventions for PAD. The research questions addressed by this review were:
1) What are the characteristics of existing interventions for PAD that are likely to be cost-effective?
2) Where do the evidence and knowledge gaps indicate future research should be focussed?

The review protocol was registered on the PROSPERO register of systematic reviews (ID, CRD42016051133).

Inclusion/exclusion criteria

Explicit inclusion criteria were: (a) studies focusing on mothers and/or fathers experiencing or at risk of developing perinatal depression and/or anxiety, (b) any psychological, psychosocial and/or pharmacological intervention, (c) alternative interventions and usual care or placebo as comparators, (d) incremental assessment of cost effectiveness. Previous systematic reviews were excluded but screened for additional references.

Literature search

Electronic searches were performed on the PsycINFO, MEDLINE, NHS economic evaluation database (EED), and NHS Health Technology Assessment (HTA) database. An initial search was run in September 2016 which was updated in September 2017. The searches were restricted to English language publications from January 2000 onwards; changes in practice and resource use/costs over time mean that older references are less useful for decision making. Common search terms included words related to perinatal depression and/or anxiety and economic evaluation terms. Terms varied slightly according to database designs. The search strategies are reported in Supplementary Material (Table S1). The bibliographies of previously published systematic reviews [18,22] were hand-screened for additional references to ensure all relevant papers were captured.

Study selection

Abstracts of studies were examined independently by two reviewers (EMC and GES) to determine whether each publication met the inclusion criteria. Both reviewers independently considered the full-text of identified publications to ensure that inclusion criteria were met. At each stage any discrepancies were resolved through discussion and a consensus reached on which publications should progress to the data extraction stage.

Data extraction and quality assessment

Structured data extraction and quality assessment was undertaken, guided by the NHS EED handbook [24]. A dual-purpose (data extraction and quality assessment) form was designed a priori (see Supplementary Material, Table S2) and used to extract information on study methodology, results, limitations, evidence gaps, and quality. The quality of the studies was also assessed using a modified version of the Consensus Health Economic Criteria (CHEC) list [25]. The checklist and assessment results are included in Supplementary Material (Table S3). One reviewer (EMC) completed the data extraction process with half reviewed by the second reviewer (GES). No issues were identified that suggested that the second reviewer needed to review all data extracted.

Currency conversion and inflation

Costs were converted to Great British Pounds (£) at the average exchange rate for the cost year reported in the source study [26]. All costs were inflated to 2015/16 based on the Hospital and Community Health Services (HCHS) index [27]. Exchange and inflation rates are reported in Supplementary Material (Table S4).

Patient and public involvement

Neither patients nor the public were involved in this research.

Results

Initial searches identified 257 citations, following the removal of duplicates the titles and abstracts of the remaining 168 citations were screened for eligibility (Figure 1). Twenty eight papers were included for full-text review, with 8 papers identified as relevant to the review (see Supplementary Material (Table S5) for details of excluded studies). The two systematic reviews that were hand-searched resulted in no additional references [18,22]. Key characteristics of the 8 included studies are described in Table 1.

Figure 1 <to go here>

Table 1 Overview of included studies

Study	**Population**	**Country**	**Intervention** (all studies reported usual or routine care as the comparator)
Boath (2003) [28]	Women being treated for postnatal depression n=60	United Kingdom	***Treatment*** Access to psychiatric day hospital, Monday-Friday 08:30-16:30, over 6 months. Day hospital was staffed by a multi-disciplinary team of four psychiatric nurses, an occupational therapist, a nursery nurses, a lead psychiatric consultant, two clinical assistants, and a senior registrar
Petrou (2006) [29]	Women who were at high risk of developing postnatal depression at 26-28 weeks of gestation. n=151	United Kingdom	***Prevention*** Counselling and support delivered by trained health visitors during home visits at 3, 7, and 17 days post delivery, then weekly up to 8 weeks postnatally
Morrell (2009) [30]	Women registered with participating GP practices who became 36 weeks pregnant during the recruitment phase of the trial, had a live baby and were on a collaborating HV's caseload for 4 months postnatally n= 4084	United Kingdom	***Screening and treatment*** Health visitor (HV) training in the assessment of postnatal women, combined with either cognitive behavioural approach (CBA) or person-centred approach (PCA) sessions (once per week for up to 8 weeks) for eligible women, plus the option of a selective serotonin reuptake inhibitor - commencing around 8 weeks postnatally
Stevenson (2010) [31]	Women with postnatal depression (EPDS>12) n=not reported (model)	United Kingdom	***Treatment*** Hypothetical group CBT intervention, one 2-hour session per week for 8 weeks, 4-6 women per group
Dukhovny (2013) [32]	Any postpartum women in seven health regions across Ontario n=610	Canada	***Prevention*** Telephone-based volunteer lay/peer support - at least 4 phone calls starting 48 to 72 hours after randomisation and continuing through the first 12 weeks after birth
Ride (2016) [33]	First-time mothers who had recently given birth and attended one of 48 participating Maternal and Child Health Centres n=359	Australia	***Prevention*** Psychoeducational programme targeted at the partner relationship, management of infant behaviour, and parental fatigue, delivered as a one-off 6-hour session by nurses based at Maternal and Child Health Centres

Grote (2017) [34]	Women at 12-32 weeks gestation, scoring 10 or higher on the PHQ-9 or with a diagnosis of probable dysthymia n=270	United States	***Treatment*** Collaborative care for depression including a choice of brief interpersonal psychotherapy (8 initial sessions plus maintenance sessions through baby's first year), pharmacotherapy, or both, co-ordinated by Depression Care Specialists (master's-level social workers) in collaboration with obstetric care providers
Wilkinson (2017) [35]	Hypothetical cohort of pregnant women experiencing one live birth over 2 years n=1000	United States	***Screening and treatment*** Over first year postpartum, general physicians screening for and treating postpartum depression and psychosis in partnership with a psychiatrist

Characteristics of studies

As shown in Table 1, the earliest and largest number of included studies were from the United Kingdom (n=4) [28–31], the most recent two studies were from the United States [34,35], and there was one study from each of Australia [33] and Canada [32].

The interventions evaluated across the 8 studies were diverse and no two studies evaluated comparable interventions. Three studies included a preventative intervention [29,32,33], three focussed on treatment [28,31,34], and two included complex interventions incorporating both identification and treatment [30,35]. All studies focussed on postnatal depression in mothers although the study by Ride et al did also consider anxiety and fathers [33]. Two of the preventative interventions were targeted at distinct groups: high risk women [29]; first time mothers [33]. One intervention involved lay or peer support [32], two were delivered by health visitors [29,30], and the remainder were delivered across a range of settings/healthcare professionals/structures including collaborative care [34,35] and group cognitive behavioural therapy (CBT) [31]. The comparator intervention for all studies was described as usual or routine care. Usual care is likely to vary by setting which affects the external validity of the study.

The majority (n=6) of studies reported cost-effectiveness analyses with different measures of health benefits which makes it difficult to compare between studies [28,29,32–35]. The most widely used (primary or secondary) measure of health benefit was the Edinburgh Postnatal Depression Scale (EPDS) which was reported in 2 of the 6 trial-based studies [30,32]. Cost-utility analyses were reported in four studies, making results across these studies easier to compare [30,31,33,35] (two of which had also reported cost-effectiveness [33,35]). Utility was derived from the SF-6D in two studies [30,31] and from the EQ-5D in two studies [33,35]. Only two studies reported the results of an economic models [31,35] with the remainder reporting trial-based results.

Table 2 Design of included studies

Study	Evaluation type	Measure of health benefit	Evaluation details	Data source	Quality/bias considerations
Boath (2003) [28]	CEA	Recovery from PND (no longer fulfilling Research Diagnostic Criteria)	• Trial or model: trial • Perspective: health service • Time horizon: 6 months • Price year: 1992/93 • Currency: British £	Observational study - healthcare utilisation self-reported and obtained from medical records	Treatment allocation was non-randomised. Reported that no significant differences in sociodemographic characteristics or outcome measures between groups at baseline. No loss to follow-up reported
Petrou (2006) [29]	CEA	Months of postnatal depression avoided (SCID-II)	• Trial or model: trial • Perspective: health and social services • Time horizon: 18 months • Price year: 2000 • Currency: British £	RCT - health and social care utilisation was self-reported by participants	Structured clinical interviews were used to identify depression in both treatment groups. The numbers/characteristics of those declining to participate were not reported
Morrell (2009) [30]	CUA	• QALYs (derived from the SF-6D) • EPDS	• Trial or model: trial • Perspective: health and social services • Time horizon: 18 months • Price year: 2003/04 • Currency: British £	RCT - health and social care utilisation obtained from medical records (up to 6 months) and participant self-report (at 12 and 18 months)	Data was collected on women declining to take part but differences with sample were not discussed. Sample was broadly representative of general population. Missing economic data were significant at 12 and 18 months, 6 months was used as the primary time horizon
Stevenson (2010) [31]	CUA	QALYs (derived from EPDS mapped onto SF-6D)	• Trial or model: model (mathematical) • Perspective: health and social services • Time horizon: 12 months • Price year: not reported • Currency: British £	Published data sources and expert opinion informed the model. EPDS, SF-36, and costs from published RCTs.	As the model was mathematical, no structure was reported in the paper. Probabilistic sensitivity analyses were conducted
Dukhovny (2013) [32]	CEA	Cases of PND averted at 12 weeks postpartum	• Trial or model: trial • Perspective: societal • Time horizon: 12 weeks • Price year: 2011 • Currency: Canadian $	Multi-region RCT - resource utilisation was self-reported by participants	Only two people did not complete healthcare utilisation questionnaires and fewer than 0.01% of individual resource utilisation items were missing at random

Ride (2016) [33]	CEA; CUA	• Prevalence of depression and anxiety(DSM-IV criteria) • QALYs (from the EQ-5D)	• Trial or model: trial • Perspective: health and social services • Time horizon: 20 weeks • Price year: 2013/14 • Currency: Australian $	Cluster-RCT - health and social care utilisation self-reported by participants	Differences between the treatment groups were adjusted for in the analysis. The intra-cluster coefficients were small but non-negligible for QALYs which may have reduced the ability to detect an effect of the intervention
Grote (2017) [34]	CEA	• Depression severity (SCL-20) • Depression free days • PTSD Checklist	• Trial or model: trial • Perspective: health plan or insurer • Time horizon: 18 months • Price year: 2013 • Currency: US $	RCT - health and social care utilisation self-reported by participants	The costs included only related to mental health care. The perspective was 'public health' and so could have also included primary and community healthcare services. Those with partial cost data (n=12/164) were more likely to have probable PTSD and to have been randomly assigned to the intervention
Wilkinson (2017) [35]	CEA; CUA	• QALYs (derived from published literature) • EPDS	• Trial or model: model (decision tree) • Perspective: health plan (Medicaid) • Time horizon: 2 years • Price year: 2014 • Currency: US $	Systematic review of existing literature to inform the model. Some cost parameters estimated from Medicaid data	Some parameters were from studies of anxiety/depression outside of the perinatal period. Probabilistic sensitivity analyses were conducted. The model structure is pragmatic, but perhaps over simple in terms of suicide risk - only women who discontinue treatment are at risk of suicide, women who don't seek help or those who screen negative are not deemed to be at risk of suicide
CEA = cost-effectiveness analysis; CUA = cost-utility analysis; RCT = randomised controlled trial; CBT = cognitive behavioural therapy; SCID-II = Structured Clinical Interview for Depression, 2nd edition; QALY = quality adjusted life year; EPDS = Edinburgh Postnatal Depression Scale; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; SCL-20 = 20-item Symptom Checklist Depression Scale; PTSD = post-traumatic stress disorder; EPDS = Edinburgh Postnatal Depression Scale.					

Critical appraisal

A copy of the CHEC quality appraisal checklist and assessment results are included in Supplementary Material (Table S3) [25]. The median score was 15.5 (out of 18). The majority of the studies were of high quality (n=6) [29–33,35] and two were average [28,34]. The studies published prior to 2006 did not report results of incremental analysis but there is a trend towards more robust methods and reporting over time. Overall the studies reported the population, setting, intervention, and comparator well. Two studies had relatively short time horizons (12 weeks [32] and 20 weeks [33]) which may not reflect the potentially long-lasting course of PAD. Six of the studies reported sensitivity or sub-group analyses [29–33,35], demonstrating varying levels of uncertainty around their primary cost-effectiveness estimate. Not reporting uncertainty is an important limitation in economic evaluations because it indicates confidence in the results, analogous to not reporting a confidence interval for a statistical analysis. Four of the studies did not report whether there were any conflicts of interest [29,31,32,35].

Factors which increased the potential for bias in the reported results include non-randomised treatment allocation [28] and an imbalance in data completeness between treatment groups/sub-groups [34]. The study by Dukhovny et al was particularly robust owing to a high level of data completeness [32].

The model by Stevenson et al evaluating group CBT to treat postnatal depression in the UK was informed by expert opinion alongside published data available from RCTs for EPDS and SF-6D scores [31] (see Table 2). The model structure was not explicitly reported. The model by Wilkinson et al evaluating collaboration between GPs and psychiatrists to identify and treat postnatal depression included estimates for the EPDS and EQ-5D from published literature [35]. Some of the model parameters were from studies of anxiety/depression outside of the perinatal period and the model structure although pragmatic potentially oversimplified suicide risk (see Table 2). Both model-based evaluations reported probabilistic sensitivity analysis.

Cost-effectiveness

Six studies reported incremental cost-effectiveness ratios (ICERs), half of which were in terms of clinical outcomes [28,29,32] and half in terms of QALY gains associated with the intervention compared with usual care [31,33,35]. Two interventions were either likely or highly likely to be cost-effective, both incorporating identification plus treatment of postnatal depression: health visitor screening and counselling [30]; general practitioner/psychiatrist collaborative screening and treatment [35]. The intervention involving health visitors was associated with lower costs and better outcomes than usual care therefore the authors did not report an ICER because the intervention dominated usual care. However when multiple imputation was used to resolve missing data (rather than a complete case analysis) the intervention was associated with more QALYs and a net cost resulting in an ICER of £15,666/QALY.

Three interventions (psychiatric day hospital (treatment) [28], health visitor counsellors (prevention) [29], telephone-delivered peer support (prevention) [32]) were classified as

possibly cost-effective because although they reported improved health outcomes with increased costs, there is no accepted threshold by which to judge ICERs when health benefits are quantified as anything other than QALYs. The ICER reported for psychiatric day hospital care was sensitive to the inclusion of primary care and medication costs, increasing from £3,843 to £56,865 per additional recovery [28]. Psychoeducation (prevention) [33] was classified as possibly cost-effective because although following currency conversion the QALY-based ICER was below the UK threshold for cost-effectiveness, the authors reported a 55% chance (i.e. not much higher than chance) that it was below the Australian threshold. Furthermore the ICER value increased by £5,055 following multiple imputation. Collaborative care (treatment) [34] was classified as possibly cost-effective because of conflicting results for sub-group analyses (Table 3). The cost-benefit analysis valued a depression-free day at US$20 (approximately £13) [34] which translated to a net benefit among mothers with PTSD and a net cost for mothers without PTSD. Group CBT was evaluated as unlikely to be a cost-effective treatment for post-natal depression [31].

Table 3 Cost-effectiveness results

Study	Interventions	Net benefit	Net cost	ICER, key conclusions, and uncertainty
Boath (2003)[28]	Psychiatric day hospital versus routine primary care	14 more women recovered in the intervention group.	The intervention was £53,824 (p<0.001) more expensive than routine care.	£3843 per each additional recovery. The net cost is sensitive to inclusion primary care and medication costs, increasing to £56,865. ***Possibly cost-effective***
Petrou (2006)[29]	Counselling and support from health visitors versus usual care	The intervention group depressed for 2.14 weeks fewer (over 18 months) than the control group - this was not statistically significant (p=0.41).	The intervention group costs were £189 higher although this was not significant (95% CI -£843 to £1237).	£68 per month of depression avoided. Possibly a small improvement in outcomes for a small cost. ***Possibly cost-effective***
Morrell (2009)[30]	Screening and talking therapy (CBA or PCA) delivered by health visitor versus usual care	EPDS score at 6 months was 0.9 lower (p<0.001) for those randomised to an intervention group. QALY gain of 0.002 (95% CI -0.001 to 0.005) associated with the intervention.	There was a non-significant net-saving of £26 (95% CI -£100 to £47) for women in the intervention groups.	Improved outcomes with comparable costs. No ICER reported because of negative net cost. CBA appears to be more cost-effective than PCA. Sub-group analysis of 'at-risk' women: 6-month EPDS score 2.1 lower (p=0.002). Analysis of imputed data: QALY gain increased to 0.003 (95% CI 0.001 to 0.006) and net cost saving increased to £47 (95% CI -£68 to -£4), both reaching statistical significance (£15,666/QALY). ***Highly likely to be cost-effective***
Stevenson (2010)[31]	Group CBT versus usual care	Intervention associated with a QALY gain of 0.039 (PSA results).	£1568 net cost of providing gCBT (PSA results).	£39,875 per QALY gained. Intervention is not likely to be cost-effective at accepted thresholds. More research is needed to address the level of uncertainty. ***Not likely to be cost-effective***
Dukhovny (2013)[32]	Telephone-based peer support versus usual care	0.1116 more cases of postnatal depression avoided at 12 weeks in the intervention group.	£755 net cost associated with intervention (p<0.001).	£6768 per case of postnatal depression avoided. The ICER is within the range of other postnatal depression interventions. ***Possibly cost-effective***

Ride (2016) [33]	Psychoeducational programme versus usual care	Comparable outcomes both in terms of prevalence of mental health conditions (p=0.883) and QALYs (p=0.967).	£167 net cost associated with the intervention was although this was not statistically significant (p=0.333).	£21,987/QALY; £92 per %-point reduction in 30-day prevalence of postnatal mental health disorders. The probability the intervention if cost-effective is 0.55 at a willingness to pay threshold of AD$ 55,000 (approximately £30-35,000) - more research is needed to reduce uncertainty. Multiple imputation of missing data increased ICER to £27,042/QALY. ***Possibly cost-effective***
Grote (2017) [34]	Collaborative care for depression versus usual care	More depression free days over 18 months for the intervention group: • with PTSD 68 days (95% CI 5 to 132) • without PTSD 13 days (95% CI -72 to 99).	Significant net cost associated with the intervention: • with PTSD £868 (95% CI £543 to £1192) • without PTSD £772 (95% CI £473 to £1072).	If a depression free day is valued at US$20 (approximately £13): • with PTSD net benefit of £32 • without PTSD net cost of £600. ***Possibly cost-effective***
Wilkinson (2017) [35]	Psychiatrist-supported GP screening and treating postpartum depression and psychosis	29 more healthy women in the intervention group, equating to a total of 21.43 additional QALYs over 2 years.	Total additional cost associated with the intervention £185,173.	£8642 per QALY gained, £6350 per remission achieved, £588 per additional healthy woman. ***Likely to be cost-effective***
RCT = randomised controlled trial; CBT = cognitive behavioural therapy; QALY = quality adjusted life year; CBA = cognitive behavioural approach; PCA = person centred approach; EPDS = Edinburgh Postnatal Depression Scale; AD$ = Australian dollars. Currency conversion and inflation rates used are reported in Supplementary Material (Table S4). 95% CI = 95% confidence interval.				

Discussion

Eight studies evaluating the cost-effectiveness of interventions for PAD were included in this review. All were published between 2006 and 2017. Six studies were high quality and two average quality. Each study focussed on depression occurring in postnatal mothers (although Ride et al also considered anxiety and fathers [33]) but evaluated a different type of intervention, some of which focussed on prevention and others focussed on treatment (or identification plus treatment). Two studies identified interventions that were likely to be cost-effective, both of which incorporated identification plus treatment of postnatal depression.

The quality of the studies included in the review was mixed and generally increased over time which is likely to reflect the agreement of standards for the reporting of economic evaluations. The use of a standardised checklist, such as the commonly used CHEERS checklist for the reporting of economic evaluations [36], would facilitate the synthesis of data in future reviews. In order to meaningfully compare studies, the most critical information required is: a full description of the intervention and comparator, inclusion/exclusion criteria, time horizon and perspective of the evaluation, the net outcome, the net cost, ICER, and cost-effectiveness acceptability (reported as the likelihood an intervention is cost-effective at appropriate willingness to pay thresholds), and summary of uncertainty.

QALYs are the most widely used measure of health benefit in economic evaluations, as recommended by the National Institute for Health and Care Excellence (NICE) [37]. Interventions costing less than £20,000-30,000 per QALY gained (versus the comparator intervention) are considered to be cost-effective. Only four of the included studies reported results in terms of QALYs. Standardised methods for economic evaluations are important so that results can be directly compared, for example it may not always be appropriate to compare QALYs derived using different approaches [38]. NICE recommends that the EQ-5D is used to derive QALYs; two of the studies included derived QALYs from the SF-6D [39] and the other two studies derived QALYs from the EQ-5D [40].

There was great heterogeneity between the studies included in terms of the interventions, measure of benefit, and time horizon. However the interventions could be grouped by some characteristics such as their aim (e.g. prevention or treatment) or key actors (e.g. healthcare professional or peer support). There were inconsistent findings within the intervention sub-groups with one exception. The two studies which incorporated identification plus treatment were both likely to be cost-effective [30,35]. However the two interventions were very different. The intervention evaluated by Morrell et al involved training health visitors to identify women experiencing postnatal depression and deliver talking therapy (using either a cognitive behavioural approach or a person centred approach) whereas the intervention evaluated by Wilkinson et al was based around collaboration between GPs and psychiatrists. Due to a large amount of missing data the health visitor intervention was only evaluated at 6 months whereas the collaborative intervention was evaluated at 2 years. This also makes it difficult to compare results

between studies because it is possible that over a longer a follow up more benefits are accrued.

Strengths and limitations

There are a number of strengths and limitations of this review. Multiple major literature databases relevant to health and economic research were searched therefore it is likely that key studies incorporating the search terms have been identified. In the instance where a full text was not available online the authors were contacted and provided a copy. The search was however restricted to English language studies, introducing some bias. Searches were also restricted to published journal articles which are less likely to include inconclusive or negative cost-effectiveness results when compared with the grey literature [41]. The exclusion of studies published prior to the year 2000 may also have introduced bias; however a post hoc search of the NHS EED database returned no relevant studies from before this time.

Despite a robust search strategy there may be relevant studies that were not identified by this review. For example, the definition of the perinatal period adopted by researchers (from conception up to 4 weeks [42], 6 weeks [43], or 12 months postpartum [7]) will influence whether interventions for PAD are described as 'perinatal' or 'early childhood'. After this review was completed a paper was brought to the authors' attention which involved an intervention for depression in mothers in the first year postpartum. However, as it was described as an 'early childhood program' and was not explicitly referred to as an intervention for postnatal or postpartum depression it was not identified in this search [44]. The intervention (in-home CBT) was nested within a complex home-visiting support program which aimed to improve the health and wellbeing of low-income parents and babies which was the 'standard care' comparator in the economic evaluation. The study reported the results of an economic model which extrapolated the results from an RCT and concluded that in-home CBT was likely to be cost-effective compared to this standard care as a treatment for depression.

Two separate tools were used to critically appraise the studies which included more criteria and gave a broader perspective than a single approach, although one was developed specifically for this review and not formally validated. The CHEC-list [45] was used to assign a score to each study and the data extraction tool was used to identify potential sources of bias. Both approaches involve an element of subjectivity, the CHECH-list attempts to handle this by not classing a criteria as having been met if it is only partially met, however this may result in some loss of sensitivity.

Future research

One study which was excluded from this review because it focussed only on screening for postnatal depression concluded that it was not cost-effective to screen because of increased treatment costs [46]. However, identification and treatment are inextricably linked and evaluating them separately may not tell the whole story which should be borne in mind for future research. It is also necessary to address the lack of economic evidence for interventions for antenatal depression, perinatal anxiety, and PAD in fathers as these

conditions are also prevalent and may be associated with negative outcomes for individuals and families [47–49]. Future economic evaluations should be conducted and reported according to good practice guidelines so that future reviews can make clear recommendations to inform health policy.

Conclusion

Heterogeneity in the evaluations to date means that is not possible to make any conclusions about their relative cost-effectiveness, with no clear implications for health policy. However the two interventions which were likely to be cost-effective (compared to usual care) both incorporated identification and treatment together; this appears to be the most fruitful direction for future research and could inform perinatal mental health service strategy. As recognition of the incidence of perinatal anxiety in mothers, and all PAD conditions in fathers, grows so does the need for relevant and robust economic evidence, therefore this is also a recommended area for future research. The quality of the methods and reporting of economic evaluations for interventions related to PAD has improved over time, but it is important that new studies adhere to reporting guidelines which will facilitate future evidence synthesis.

Figure legend

Figure 1 - PRISMA flow diagram of studies identified

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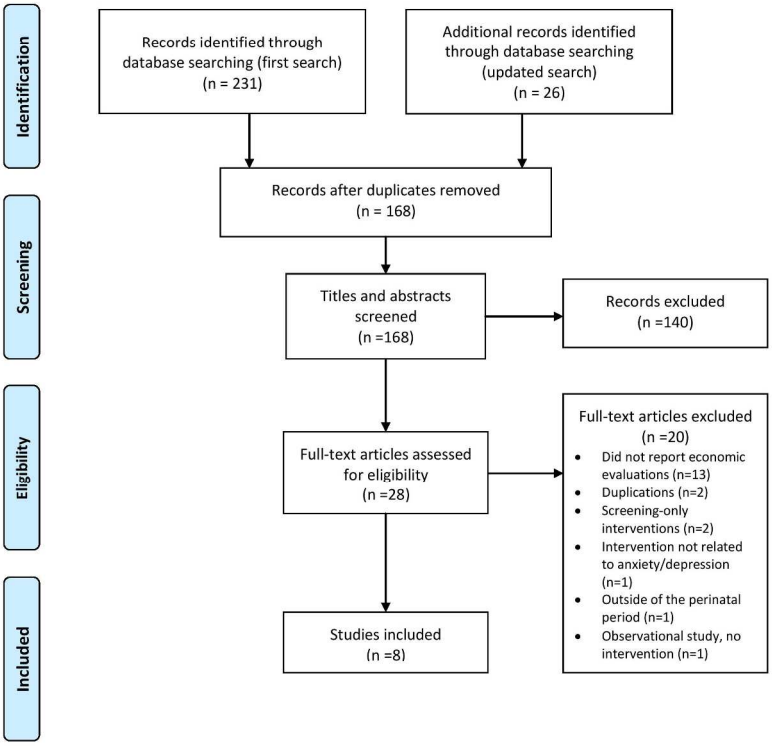

Figure 1 PRISMA flow diagram of studies identified

215x279mm (300 x 300 DPI)

Table S1 - search strategies

MEDLINE	#1 economic evaluation OR economic analys* OR cost analys* OR cost effective* analys* OR cost-effective* analys* OR cost benefit* analys* OR cost utility* analys* OR cost-benefit* analys* OR cost-utility* analys* #2 postpartum OR post-partum OR post partum #3 postnatal OR post natal OR post-natal #4 perinatal OR peri natal OR peri-natal #5 antepartum OR ante partum OR ante-partum #6 pregnan* #7 #2 OR #3 or #4 or #5 or #6 #8 depress* OR anxi* #9 #8 AND #7 #10 #1 AND #9 #11 Limit #10 to yr=2000-Current #12 #11 NOT cattle [ti] OR karyotyping[ti] OR aneuploid*[ti] OR smoking cessation[ti] OR tobacco cessation[ti]
PsycINFO	#1 anxi* OR depress* #2 postnatal OR post natal OR post-natal #3 postpartum OR post-partum OR post partum #4 antenatal OR ante natal OR ante-natal #5 perinatal OR peri natal OR peri-natal #6 antepartum OR ante partum OR ante-partum #7 pregnan* #8 #2 OR #3 OR #4 OR #5 OR #6 OR #7 #9 #1 AND #8 #10 cost analy* or *economic* or cost effective* or cost-effective* or cost benefit* or cost utility* or cost-benefit* or cost-utility* #11 #9 AND #10 #12 Limit #11 to (all journals and yr="2000-Current")
NHS EED/HTA	*Title search* (depress* OR anxi*) AND ((postpartum OR post-partum OR post partum) OR (postnatal OR post natal OR post-natal) OR (perinatal OR peri natal OR peri-natal) OR (antepartum OR ante partum OR ante-partum) OR pregnan*)

Table S2 - Data extraction and quality assessment form

Subject of the study	
Intervention(s)	
Comparator(s)	
Intervention type	
Disease	
Study question/hypothesis	
Key elements of the study	
Type of economic analysis	
Study population	
Details of model (if applicable)	
Setting	
Country	
Dates to which data relate	
Link between cost and health benefit data	
Clinical evidence	
Clinical and epidemiological inputs	
Data sources	
Methods to obtain data	
Measures of health benefit	
Summary measure of health benefit	
Method of utility valuation	
Time horizon	
Discount rate for health benefit	
Direct costs	
Direct costs included	
Who bears the direct costs?	
Source of resource use data	
Resource use reported separately from costs	
Sources of unit prices	
Currency and price year	
Adjustment for inflation; other adjustments	
Costs excluded	
Time horizon	
Discount rate for direct costs	
Indirect costs	
Inclusion of indirect (productivity)	
Source of cost and quantity data	
Resource use reported separately from costs	
Time horizon	
Discounting of indirect costs	
Statistical analysis of costs	
Descriptive statistics/point estimates reported	
Significance testing reported	
Study powered to detect differences in cost	
Analysis of uncertainty	
If model: exploration of parameter uncertainty	

If model: exploration of structural uncertainty	
All studies: exploration of alternative subgroups / settings	
Estimated benefits	
Total benefit: intervention arm(s)	
Total benefit: comparator arm(s)	
Net (incremental) benefit	
Result of statistical test for difference in benefits	
Were adverse effects included?	
Estimated costs	
Total cost: intervention arm(s)	
Total cost: comparator arm(s)	
Net (incremental) cost (intervention versus comparator)	
Result of statistical test for difference in costs	
Did the duration of costs match the time horizon?	
Synthesis of benefits & costs, and conclusions	
Synthesis of benefits and costs conducted (e.g. ICER)	
ICER	
Probability cost-effective	
Important differences in results for subgroups or sensitivity analyses	
Summary of authors' conclusions	
Critical review	
Is the choice of comparator suitably justified?	
If model: was the model structure suitable?	
If model: was a model schematic presented?	
If model: was the model adequately reported?	
Validity of primary effectiveness data	
Validity of secondary effectiveness data	
Validity of estimated health benefit	
Validity of estimated costs	
Do the authors discuss the generalisability of their findings?	
Do the authors compare their findings to previous studies?	
Are the authors' conclusions justified?	
Implications	
Do the authors describe policy implications of their findings? Are they appropriate?	

Table S3 - Criteria list for assessment of methodological quality of economic evaluations: Consensus on Health Economic Criteria [9]

	Boath (2003) [1]	Petrou (2006) [2]	Morrell (2009) [3]	Stevenson (2010) [4]	Dukhovny (2013) [5]	Ride (2016) [6]	Grote (2017) [7]	Wilkinson (2017) [8]
1. Is the study population clearly described?	✓	✓	✓	✓	✓	✓	✓	✓
2. Are competing alternatives clearly described?	✗	✓	✓	✓	✓	✓	✓	✓
3. Is the economic study design appropriate to the stated objective?	✓	✓	✓	✓	✓	✓	✓	✓
4. Is the chosen time horizon appropriate to include relevant costs and consequences?	✓	✓	✓	✓	✗	✗	✓	✓
5. Is the actual perspective chosen appropriate?	✓	✓	✓	✓	✓	✓	✓	✓
6. Are all important and relevant costs for each alternative identified?	✓	✓	✓	✓	✓	✓	✗	✓
7. Are all costs measured appropriately?	✓	✓	✓	✓	✓	✓	✓	✓
8. Are costs valued appropriately?	✓	✓	✓	✓	✓	✓	✓	✓
9. Are all important and relevant outcomes for each alternative identified?	✓	✓	✓	✓	✓	✓	✓	✓
10. Are all outcomes measured appropriately?	✓	✓	✓	✓	✓	✓	✓	✓
11. Are outcomes valued appropriately?	✗	✗	✓	✓	✗	✓	✗	✓
12. Is an incremental analysis of costs and outcomes of alternatives performed?	✗	✓	✓	✓	✓	✓	✓	✓
13. Are all future costs and outcomes discounted appropriately?	✓	✓	✓	✓	✓	✓	✗	✓
14. Are all important variables, appropriately subjected to sensitivity analysis?	✗	✓	✓	✓	✓	✓	✗	✓
15. Do the conclusions follow from the data reported?	✓	✓	✓	✓	✓	✓	✓	✓
16. Does the study discuss the generalizability of the results to other settings and patient/client groups?	✓	✗	✓	✗	✓	✗	✗	✓

	Boath (2003)	Petrou (2006)	Morrell (2009)	Stevenson (2010)	Dukhovny (2013)	Ride (2016)	Grote (2017)	Wilkinson (2017)
17. Does the article indicate that there is no potential conflict of interest of study researcher(s) and funder(s)?	✓	✗	✓	✗	✗	✓	✓	✗
18. Are ethical and distributional issues discussed appropriately?	✗	✓	✓	✓	✓	✓	✗	✓
TOTAL SCORE	13	15	18	16	15	16	12	17
Each criteria met is awarded one point: 15 or greater = high quality, 8-14 = average quality, less than 8 = poor quality. Item 13 – studies where discounting is not applicable (i.e. time horizon less than one year) have been assumed to meet criteria.								

Table S4 - Currency conversion and inflation rates applied

	Price year in study	Original currency	Exchange rate#	HCHS year	HCHS index (1987/88 = 100.0)	HCHS inflation factor to 2015/16*
Boath (2003) [1]	1992/93	GBP	n/a	1992/93	150.3	1.98
Petrou (2006) [2]	2000	GBP	n/a	1999/2000	188.5	1.58
Morrell (2009) [3]	2003/04	GBP	n/a	2003/04	225.6	1.32
Stevenson (2010) [4]	2010	GBP	n/a	2009/10	268.6	1.11
Dukhovny (2013) [5]	2011	Canadian $	0.63	2010/11	276.7	1.07
Ride (2016) [6]	2013/14	Australian $	0.59**	2013/14	290.5	1.02
Grote (2017) [7]	2013	US $	0.64	2012/13	287.3	1.03
Wilkinson (2017) [8]	2014	US $	0.61	2013/14	290.5	1.02

GBP = Great British Pound/United Kingdom £ sterling; US = United States
#per 1GBP;
*HCHS index 2015/16 = 297.0
*The exchange rate between Australian dollars ($) and GBP was notably different in 2013 (0.62 $/£) and 2014 (0.55 $/£) therefore the midpoint (0.59 $/£) was used.

Table S5 - reasons for exclusion of full texts screened

Title	Year	Lead author	Reason
A randomized comparison of home and clinic follow-up visits after early postpartum hospital discharge.	2000	Lieu [10]	No economic evaluation reported
Costs and effectiveness of community postnatal support workers: a randomised controlled trial.	2000	Morrell [11]	No economic evaluation reported
Costs and benefits of community postnatal support workers: a randomised controlled trial.	2000	Morrell [12]	Duplicate - HTA report for same study reported elsewhere
The treatment of postnatal depression by health visitors: impact of brief training on skills and clinical practice.	2003	Appleby [13]	No economic evaluation reported
The Social Support and Family Health Study: a randomised controlled trial and economic evaluation.	2004	Wiggins [14]	No economic evaluation reported
Improving infant sleep and maternal mental health: a cluster randomised trial.	2007	Hiscock [15]	No economic evaluation reported
Stepped care treatment of postpartum depression: A primary care-based management model.	2008	Gjerdingen [16]	No economic evaluation reported
Screening for postnatal depression within the Well Child Tamariki Ora Framework.	2008	Suebwongpat [17]	Intervention – screening only
Screening for postnatal depression in primary care: Cost effectiveness analysis.	2009	Paulden [18]	Intervention – screening only
Postpartum follow-up: can psychosocial support reduce newborn readmissions?	2010	Barilla [19]	Intervention - aim of intervention not related to anxiety/depression, no measure of anxiety/depression collected
A model for maternal depression.	2010	Connelly [20]	No economic evaluation reported, review of existing evidence
A pragmatic randomised controlled trial to compare antidepressants with a community-based psychosocial intervention for the treatment of women with postnatal depression: the RESPOND trial	2010	Sharp [21]	No economic evaluation reported
Group cognitive behavioural therapy for postnatal depression: a systematic review of clinical effectiveness, cost-effectiveness and value of information analyses.	2010	Stevenson [22]	Duplicate - HTA report for same study reported elsewhere
Supporting women with postnatal depression through psychological therapies	2011	Centre for Reviews and Dissemination [23]	No economic evaluation reported, review of existing evidence

Peer support and interpersonal psychotherapy groups experienced decreased prenatal depression, anxiety and cortisol.	2013	Field [24]	No economic evaluation reported
Effects of an infant-focused relationship-based hospital and home visiting intervention on reducing symptoms of postpartum maternal depression: A pilot study.	2014	Nugent [25]	No economic evaluation reported
Antidepressant treatment of depression during pregnancy and the postpartum period	2014	McDonagh [26]	No economic evaluation reported, review of existing evidence
Enhanced engagement: An intervention pilot for mental health promotion among low-income women in a community home visiting program.	2015	Price [27]	Patient group - not restricted to the postpartum period
Perinatal depression and child development: exploring the economic consequences from a South London cohort.	2015	Bauer [28]	Intervention - observational study, no intervention
Improving perinatal depression care: The Massachusetts Child Psychiatry Access Project for Moms.	2016	Byatt [29]	No economic evaluation reported, no comparator intervention

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	3
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	3-4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplementary material
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	4
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	4 Supplementary material
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	4
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	4
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	3-4 (narrative review)

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	4
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	n/a
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	4, figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	9, Table 2
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Table 3
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	n/a
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Table 2
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	n/a
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	13
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	13
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	13-14
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	2

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