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Research paper

# Case-finding with the anxiety sub-scale of the Edinburgh Postnatal Depression Scale in an observational cohort: Sensitivity, specificity, and cost-effectiveness

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### ABSTRACT

*Background:* The Edinburgh Postnatal Depression Scale (EPDS) is effective and cost-effective for identifying postnatal depression. Postnatal anxiety is also common and can be identified by three questions on the EPDS (anxiety sub-scale). We aimed to compare EPDS score alone with EPDS score and sub-scale score together (EPDS+) to identify common mental illness (depression or anxiety) in postnatal women.

*Methods:* The sensitivity and specificity of the EPDS and sub-scale were explored. We developed a decision tree to compare costs and health outcomes associated with case-finding for postnatal depression or anxiety over one year. Model parameters were derived from secondary data analysis, published literature, and expert consultation. Costs included case-finding and treatment. Health benefit was measured as quality-adjusted life years (QALYs). We explored the cost-effectiveness of using EPDS alone and EPDS+ (versus no case-finding).

*Results:* The greatest number of true positive outcomes and smallest number of false negative outcomes were seen with EPDS+. However, the number of false positives is also higher for EPDS+. Compared with no case-finding, EPDS alone costs £3365/QALY gained and EPDS+ costs £6405/QALY gained. The additional health gain from EPDS+ (versus EPDS alone) costs £22,104/QALY.

Limitations: The model does not include long-term impacts of maternal mental illness or impacts on other family members.

*Conclusions:* Case-finding for common mental illness in the postnatal period is cost-effective. Compared to no case-finding, EPDS alone is more cost-effective than EPDS+. If decision-makers want to maximise identification of cases, EPDS+ could be cost-effective depending on how much they are willing to pay.

### 1. Introduction

Anxiety and depression are the most common mental health conditions in the postnatal period (the first year following childbirth). Globally, the estimated prevalence of postnatal depression is close to 20 % (Hahn-Holbrook et al., 2018; Shorey et al., 2018) and international estimates range between 3 % and 38 % (Hahn-Holbrook et al., 2018). Symptoms of anxiety are estimated to affect 15 % of mothers in the first 6 months after giving birth, with the prevalence of an anxiety disorder being around 9–10 % (Dennis et al., 2017; Goodman et al., 2016).

There are short- and long-term impacts of postnatal mental illness for mothers, babies, and other family members. This includes ongoing mental health problems, reduced quality of life, relationship difficulties for mothers, and growth and development delays for the infant (Slomian et al., 2019). Therefore, it is imperative that mothers experiencing postnatal mental illness are identified and supported. Unfortunately,

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perinatal mental illness (i.e. during and beyond pregnancy) is not wellidentified or treated in current systems. Only one-third of women with a diagnosable mental disorder in the perinatal period were documented as having had contact with mental health services, according to a prospective cohort study in London (Lee-Carbon et al., 2022). In the UK, the need for more research to address this issue is recognised by national research organisations for example, the National Institute for Health and Care Research (NIHR) which called for rigorous evidence on methods of perinatal anxiety assessment (National Institute for Health and Care Research Health Services Delivery and Research Programme, 2017) and policymakers such as the National Institute for Health and Care Excellence (National Institute of Health and Care Excel-

Another consideration is that some women experience discrimination (directly and indirectly) at various stages of their maternity care (e. g., migrant populations and women from minority ethnic groups) (Higginbottom et al., 2019; MacLellan et al., 2022). There is evidence that this includes the identification of women experiencing perinatal mental health difficulties (Darwin et al., 2022). Systematic screening or case-finding is one way of potentially improving the identification of women experiencing postnatal mental health symptoms in an equitable way. There is broad support for case-finding in relation to perinatal mental health in Organisation for Economic Co-operation and Development (OECD) member countries (El-Den et al., 2022). A case-finding programme is an opportunity to make mental health "part of core healthcare business (Darwin et al., 2022)", by making it part of routine perinatal care.

There is increasing recognition of the value of transdiagnostic approaches in mental health, so rather than focussing on the diagnosis and labelling of a specific condition, the focus is on recognising that people need help with their mental health (Dalgleish et al., 2020). The core elements of psychological treatments for depression and anxiety overlap, especially interventions with a cognitive behavioural underpinning (Cuijpers et al., 2023). Furthermore, there are a number of antidepressants which are effective in both depression and anxiety disorders (Cipriani et al., 2018; Gosmann et al., 2021). It may be possible to improve the identification of women experiencing postnatal mental health symptoms by taking a transdiagnostic approach to case-finding.

The Edinburgh Postnatal Depression Scale (EPDS), published in its current form in 1987, is a validated and frequently used tool for casefinding for depression (Cox et al., 1987). Five years later, the presence of separate dimensions for depression and anxiety within the EPDS was demonstrated (i.e. some items on the EPDS relate to symptoms of depression and others to anxiety) (Pop et al., 1992). Almost a decade later in 2001, a Dutch study carried out further work to explore the potential of the EPDS as a tool for identifying postnatal anxiety (Brouwers et al., 2001). The study reported that three items on the EPDS (questions 3, 4, and 5) represented an anxiety sub-scale (subsequently known as the EPDS-3 A). A summary of EPDS factor analyses conducted between 1992 and 2015 (Coates et al., 2017) showed that these findings were replicated by twelve of thirteen studies that used the Englishlanguage EPDS (including Ross et al. in 2003 in a group of postnatal women in Canada (Ross et al., 2003), by Jomeen et al. in 2005 in a group of pregnant women in the UK (Jomeen and Martin, 2005), by Tuhoy et al. in 2008 (using an alternative method of factor analysis) with postnatal women in the UK (Tuohy and McVey, 2008), and by Swalm et al. in 2010 in Australia who considered antenatal and postnatal data (Swalm et al., 2010). Assessing both the EPDS score and the sub-scale score together (subsequently referred to as EPDS+) may increase the identification of women who are experiencing postnatal mental illness.

The aim of this paper is twofold. Firstly, to explore the sensitivity and specificity of the EPDS anxiety sub-scale in an observational cohort of postnatal women (validation analysis). Secondly, to estimate the cost-effectiveness of case-finding for women experiencing postnatal anxiety or depression using EPDS alone versus EPDS+ (both compared with no case-finding) (cost-effectiveness analysis).

### 2. Materials and methods

#### 2.1. Data source

Secondary analysis of data from an observational cohort study was used to derive key model parameters. The BaBY PaNDA study was a longitudinal study of 391 women in England, from 20 weeks gestation to 1 year postpartum, between July 2013 and August 2014 (Littlewood et al., 2018). The study aimed to explore the identification of perinatal depression using case-finding instruments. A previous publication reports the full protocol for the BaBY PaNDA study (Littlewood et al., 2016). Ethical approval for the data collection was granted by North East - York Research Ethics Committee (REC) on 23 April 2013 (reference number: 11/NE/0022) and was subsequently approved by the relevant NHS Trusts' research and development (R&D) committees. The sample size calculation for the original BaBY PaNDA study, based on an estimated prevalence of perinatal depression of 20 % and an expected sensitivity of 95 % and a minimal acceptable lower 95 % confidence interval of 80 % to be detectable with 95 % probability, indicated that a sample size of 250 was required (Littlewood et al., 2018). The study allowed for an attrition rate of 34 % and so aimed to recruit 379 participants.

#### 2.2. Measures and outcomes

The Edinburgh Postnatal Depression Scale (EPDS) was designed as a case-finding tool to improve the detection of women experiencing postnatal depression (Cox, 2019; Cox et al., 1987). It is a 10-item, self-completed questionnaire, that asks respondents about how they have been feeling in the last week (7 days). Each item on the questionnaire is scored between 0 and 3 such that the total scores range from 0 to 30, with 30 indicating the greatest severity of depression symptoms. Cases of depression are identified using a binary threshold whereby scores over a specified cut-off indicate likely depression. Commonly-used thresholds are  $\geq 10$  or  $\geq 13$  (Cox et al., 1987; Levis et al., 2020; Matthey et al., 2006). Our previous work showed that a cut-off of  $\geq 10$  was more likely to be cost-effective than  $\geq 13$  and so we have used the lower threshold in this analysis (Camacho et al., 2023a).

The EPDS-3A represents an anxiety sub-scale within the EPDS and can be used to identify cases of postnatal anxiety. The EPDS-3A consists of items 3 ("I have blamed myself unnecessarily when things went wrong"), 4 ("I have been anxious or worried for no good reason"), and 5 ("I have felt scared or panicky for no good reason") of the EPDS. Total scores on the 3 items in the sub-scale range from 0 to 9. There is not currently an agreed optimum cut-off score. Our methods for exploring alternative cut-offs are described in the next section.

"Cases" of common mental illness are defined as someone who scores above the threshold for either EPDS score or the threshold for EPDS-3A score. Assessing EPDS score and EPDS-3A score together (EPDS+), enables the identification of cases of depression and/or anxiety, using a single questionnaire.

### 2.3. Validation analysis

Using data from the BaBY PaNDA study, we explored the performance of different cut-off scores on the EPDS-3A for detecting anxiety, using a GAD-7 score of  $\geq$ 8 as a comparator. A systematic review and meta-analysis reported that the optimal GAD-7 cut-off score to identify anxiety is  $\geq$ 8 (Plummer et al., 2016). Performance was measured as sensitivity, specificity, area under the curve (AUC), positive predictive value (PPV), and negative predictive value (NPV).

We also reported the number and proportion of women in the sample who would be identified as cases (of depression only, anxiety only, both conditions, either condition, neither condition) according to the EPDS (EPDS, EPDS-3A, EPDS+) compared with CIS-R (a diagnostic gold standard assessment of depression, the Clinical Interview Schedule – Revised (CIS-R) (Lewis et al., 1992)) and GAD-7. This enabled us to estimate the number/proportion of cases that would be "missed" by alternative strategies. These comparisons were restricted to participants who had data on all 3 measures.

### 2.4. Cost-effectiveness analysis

We conducted a model-based cost-effectiveness analysis. Model parameters were derived from secondary analysis of data from The BaBy PaNDA study (as described above) and from published literature (described below). An analysis plan was drafted and agreed by the project team. The cost-effectiveness analysis is based on a hypothetical one-year birth cohort. To provide an estimate of the resources required to implement a nationwide case-finding programme, total costs and QALYs were calculated based on the approximate number of women who give birth per year in England and Wales (n = 600,000, 2020 data) (Office for National Statistics, 2020). We used a decision tree to map the potential outcomes and costs associated with anxiety or depression. We compared costs and outcomes in the presence and absence of a postnatal anxiety/depression case-finding program. We have used the same decision tree model previously to estimate the cost-effectiveness analyses of case-finding for postnatal depression only and the details of the model are published in full elsewhere (Camacho et al., 2023a).

The decision tree comprised of two stages: case-finding and treatment. Both stages are shown in Fig. 1 for women with postnatal anxiety or depression. This pathway was the same for all strategies including the no case-finding option. The case-finding outcomes for women with postnatal anxiety or depression were: true positive and false negative. The treatment stage included chance nodes for depression severity, treatment response, spontaneous recovery and subsequent identification of anxiety or depression in women with a false negative case-finding outcome. For women with a false negative case-finding outcome who do not spontaneously recover from antenatal depression, there is a chance that they are subsequently identified as anxious or depressed by their primary care physician/general practitioner (GP). For women who are not anxious or depressed, there is only a case-finding stage which comprises of two branches with the outcomes true negative or false positive. The branches for women who are not anxious or depressed are shown in the supplementary material (Figure S1) alongside those for women with anxiety or depression (as already shown in Fig. 1) as a complete picture.

The point of entry into the decision tree is around 12 weeks into the postnatal period (when participants in the BaBY PaNDA source study completed the EPDS). The time horizon for the model was from the point of case-finding until one-year post-partum. The perspective for the costeffectiveness analysis was the English NHS and social care services, in line with NICE guidance (National Institute of Health and Care Excellence (NICE), 2022). The currency was British pounds (£), and the price year was 2021. The model included costs for the administration and scoring of the case-finding instruments, additional assessment of cases (either by GPs or health visitors), treatment (pharmacological, psychological, or both), and monitoring of women identified as having anxiety or depression. Treatment and monitoring costs were specified based on anxiety/depression severity - mild-to-moderate illness (£273; facilitated self-help); moderate-to-severe illness (£910 for intensive psychological therapy, £300 for sertraline, or £935 for both). Sertraline is used to treat both anxiety and depression in adults and so treatment parameters (e.g. efficacy) from our previous depression model (Camacho et al., 2023a) were assumed to be the same for anxiety or depression in this model. Each pathway in the model was assigned a health impact, measured as quality-adjusted life years (QALYs). We derived QALYs from the EQ-5D-3L (The EuroOoL Group, n.d.) that was collected as part of the BaBY PaNDA study in combination with index values for the United Kingdom (Dolan, 1997). As the time horizon for the model was less than one year, we did not apply any discounting of costs or outcomes. A full description and summary of the model parameters is reported in Table S1.

The costs, outcomes, and probabilities were entered into the model to estimate incremental cost-effectiveness ratios (ICERs). Three strategies were compared: no case-finding, case-finding with EPDS only, and case-finding with both the EPDS and EPDS-3A (subsequently referred to as the EPDS+ strategy). In the 'no case-finding' comparator, women can only be identified as having depression if they consult their GP.

### 2.5. Secondary analyses

Probabilistic analyses were used to quantify decision uncertainty in the analysis. Each of the deterministic probability and utility parameters in the model were selected randomly (simulated) 10,000 times from a defined distribution. Beta distributions were used for probability and utility value parameters. Unit costs were assumed to be fixed. For each simulation net costs and QALYs were calculated. These values were used to generate means with 95 % confidence intervals for net costs and



Fig. 1. Case-finding and treatment pathway for women with postnatal anxiety or depression.

QALYs and to calculate the probability that either strategy would be cost-effective at willingness to pay thresholds of £0, £20,000, and  $\pm$ 30,000/QALY.

We also conducted one-way sensitivity analyses to explore the impact of key model assumptions on the cost-effectiveness results. For the branch of the decision tree corresponding to a false-positive casefinding outcome, we explored including a utility decrement (2 % and 10 %) and alternative costs associated with unnecessary treatment initiation (10 % and 30 % of the full treatment/monitoring cost for mild symptoms). For the no case-finding strategy, consultation with experts (clinical and by lived experience) suggested that the average appointment length (9.22 min (Jones and Burns, 2021)) is likely to underestimate how long a GP would spend assessing someone at an initial presentation with postnatal depression or anxiety. Expert consensus was that for a telephone appointment 10–15 min would be more typical, and 15-20 min for a face-to-face appointment. We used the average appointment length in the base case model and explored alternatives in sensitivity analyses. In the absence of robust published data, we assumed (based on expert opinion) that 10 % of women who were initially incorrectly classified as not being anxious or depressed would subsequently be appropriately identified by their GP. We explored alternative values of 5 % and 25 %.

#### 2.6. Stakeholder involvement and engagement

Four mothers with lived experience of postnatal mental illness contributed to this research. We provided our lived experience contributors with an introduction to economic evaluation in healthcare and decision analytic modelling to enable them to comment on the model. This enabled us to incorporate greater real-world validity in the model from the lived experience perspective. In addition, consultation with clinical experts (2 GPs in addition to the study team) helped to ensure that the model reflects current NHS practice.

### 3. Results

The characteristics of the BaBY PaNDA cohort are summarised in Table 1. Over one-third of the sample self-reported a history of anxiety or depression, with 16.7 % screening positive for either condition at around 3–4 months postnatally.

### 3.1. Validation analysis

Table 2 shows the sensitivity, specificity, PPV, NPV, and AUC for the EPDS-3A compared with a GAD-7 score of  $\geq$ 8. A cut-off score of  $\geq$ 5 on the EPDS-3A had the best balance between sensitivity (88.6) and specificity (91.0) (and highest AUC [0.898]) for identifying postnatal anxiety. Using a cut-off score of  $\geq$ 4 increases sensitivity (to 93.2) but still has reasonable specificity (76.4) and so may be an acceptable trade-off to policymakers if their goal is to identify more women who experience postnatal anxiety.

Table 3 compares the number of people who would be identified as requiring additional follow-up for postnatal anxiety or depression according to different instruments. According to the CIS-R and GAD-7, less

#### Table 1

Cohort characteristics		
Age at study entry (years), mean (SD)	31.2 (5.1) <i>n</i> = 390	
History of anxiety (self-report), n (%)	138/369 (35.9)	
History of depression (self-report), n (%)	133/370 (34.0)	
Current anxiety (GAD-7 $\geq$ 8), <i>n</i> (%)	44/345 (12.8)	
Current depression (CIS-R), n(%)	35/334 (10.5)	
Current anxiety or depression (GAD-7 and CIS-R)	56/336 (16.7 %)	
GAD-7 = Generalized Anxiety Disorder 7-item scale; CIS-R = Clinical Interview		
Schedule – Revised		

### Table 2

Sensitivity, specificity, AUC, PPV, and NPV for the EPDS-3A compared with the GAD-7 for identifying postnatal anxiety (n = 345).

EPDS -3A cut-off	Sensitivity	Specificity	AUC	PPV	NPV
$\geq 3$	93.2	60.5	0.768	25.6	98.4
$\geq 4$	93.2	76.4	0.848	36.6	98.7
$\geq$ 5	88.6	91.0	0.898	59.1	98.2
$\geq 6$	75.0	97.0	0.860	78.6	96.4
$\geq$ 7	47.7	99.3	0.735	91.3	92.9
$\geq 8$	29.5	99.7	0.646	92.9	90.6
$\geq 9$	15.9	100	0.580	100	89.1

GAD-7 score of  $\geq$ 8 used to indicate anxiety.

AUC = area under the curve; PPV = positive predictive value; NPV = negative predictive value.

### Table 3

Classification of cases using the EPDS versus CIS-R and GAD-7.

	Number of cases (case- finding)	Number of cases ("diagnosis")
Depression only	15 (EPDS); 4.5 %	12 (CIS-R); 3.6 %
Anxiety only	14 (EPDS-3A); 4.2 %	19 (GAD-7); 5.7 %
Both conditions	51 (EPDS+); 15.3 %	23 (CIS-R and GAD-7); 6.9 %
Either depression or anxiety	80; 24.0 %	54; 16.2 %
Neither condition	254; 76.0 %	280; 83.8 %

Data presented in this table are restricted to participants with complete data for the EPDS, CIS-R, and GAD-7; n = 334.

than half (43 %) of the 54 women with either depression or anxiety meet the criteria for both conditions. Whereas according to the EPDS+ (i.e. considering both the total and sub-scale scores), almost two-thirds (64 %) of the 80 women scoring above the cut-off for either condition score above for both conditions. The EPDS marginally over-identifies women with depression only and the EPDS-3 A marginally under-identifies postnatal anxiety only compared with the CIS-R and GAD-7 respectively. However, using the EPDS+ appears to markedly over-identify women with both anxiety and depression compared to the CIS-R and GAD-7 (15.3 % versus 6.9 %).

By adding assessment of the EPDS-3A score to assessment of total EPDS score, 14 women with anxiety would be identified as requiring additional follow-up that would not have been otherwise (18 % of the 80 women with either condition). Adding the GAD-7 to assessment with the CIS-R would identify 19 additional women requiring support (35 % of the 54 with either condition). Of the 35 women (with data for the EPDS, CIS-R, and GAD-7) who had depression according to the CIS-R, the EPDS identified 29 (83 %) of them as depressed. None of the 6 depressed women who were missed by the EPDS would have been identified by the addition of the EPDS-3 A. Of the 42 women who had anxiety according to the GAD-7, 37 (88 %) would have been detected using the EPDS alone. Of the 5 who were missed by the EPDS, 3 (60 %) would have been captured by the addition of the EPDS-3 A.

### 3.2. Cost-effectiveness analysis

Table 4 summarises the sensitivity, specificity, outcomes, costs and QALYs associated with case-finding for anxiety *or* depression among women in the postnatal period using the EPDS and EPDS+ strategies (compared with no case-finding) for a hypothetical one-year cohort of women giving birth in the UK. Compared with no case-finding, the EPDS strategy improves health at a cost of £3365/QALY gained. If decision-makers are willing to pay £20,000 to improve health by one QALY, then the EPDS strategy is most likely to be cost-effective.

The greatest number of true positive outcomes (i.e. where women are correctly identified as having anxiety or depression) and smallest number of false negative outcomes (i.e. where a woman experiencing

#### Table 4

Sensitivity, specificity, resources, and outcomes in a hypothetical cohort of 600,000 women.

Strategy	No case-finding	EPDS	EPDS+		
Prevalence of	16.7 %				
depression/					
anxiety					
Number with	100,200				
depression/					
anxiety	50.1.0/	00.1.4/	07 5 0/		
Sensitivity	50.1 %	82.1 %	87.5 %		
Specificity	81.3 %	92.1 %	88.2 %		
True positives	50,200	82,264	87,675		
True negatives	406,337	460,316	440,824		
False negatives	50,000	17,936	12,525		
False positives	93,463	39,484	58,976		
Total costs (£)	36,705,056	40,296,936	44,344,311		
Total QALYs	427,363	428,429	428,609		
Mean costs and QALYs (per person) <sup>a</sup>					
Costs (£)	61.19	67.15	74.00		
	(50.55–73.80)	(47.64-88.17)	(53.44–95.63)		
QALYs	0.7122	0.7139	0.7142		
	(0.6993-0.7249)	(0.7013-0.7266)	(0.7023-0.7265)		
ICER (£/QALY) <sup>b</sup>	_	3365	22,104		
		(vs. no case	(vs. EPDS)		
		finding)			
Probability cost-effective at maximum WTP <sup>a</sup>					
£0/OALY	0.753	0.199	0.048		
£20.000/OALY	0.079	0.466	0.455		
£30.000/OALY	0.064	0.422	0.513		

QALYs = quality adjusted life years; ICER = incremental cost-effectiveness ratio; WTP = willingness to pay.

<sup>a</sup> Based on 10,000 iterations.

<sup>b</sup> Costs and QALYs reported are rounded values whereas ICERs are calculated based on non-rounded values.

anxiety or depression is missed) are seen with the EPDS+ strategy. However, the number of false positives (i.e. women incorrectly flagged as requiring additional support for anxiety or depression) is also higher for the EPDS+ strategy compared with the EPDS. It is this trade-off which results in the EPDS strategy being more cost-effective than EPDS +. However, if decision-makers are willing to pay more (e.g. one commonly discussed threshold is £30,000/QALY) to improve the health of postnatal women, then the EPDS+ strategy is most likely to be costeffective. Compared with no case-finding, the cost per additional QALY gained with the EPDS+ strategy is £6405.

Fig. 2 shows the cost-effectiveness acceptability curve comparing the three strategies (no case-finding, EPDS, and EPDS+). It clearly shows how the optimal strategy depends on how much decision-makers are willing to pay to improve health. As long as decision-makers are willing to pay at least around £7500/QALY, then it is likely that one of the case-finding strategies is cost-effective compared with no case-finding. As the willingness to pay threshold increases beyond £20,000, the EPDS+ strategy becomes more favourable.

The results of our sensitivity analyses are shown in full in supplementary material (Table S2). Generally, alternative assumptions had little impact on the results compared with the base case model. When a utility decrement is included for false positive outcomes, EPDS remains the most cost-effective strategy, with a small ICER compared with no case-finding (around £3000/QALY). However, when the utility decrement is 10 %, the ICER for EPDS+ (vs EPDS) increases from around £22,000/QALY to over £80,000/QALY. Also in favour of case-finding with EPDS, including the cost of longer GP consultations makes this strategy dominant over no case-finding (i.e. lower cost, higher QALYs). The only sensitivity analysis which changed the overall finding was when the cost associated with initiating treatment for a false positive outcome is reduced. Under this assumption, the EPDS+ is more likely to be cost-effective than EPDS (probability 0.475 vs. 0.445 at a threshold of  $\pm 20,000/QALY$ ) and the ICER comparing EPDS+ with EPDS falls to just below  $\pm 20,000/QALY$ .

#### 4. Discussion

When identifying cases of postnatal anxiety or depression, the EPDS+ (EPDS total score with anxiety subscale score) shows greater sensitivity but lower specificity than the EPDS total score alone. Although the EPDS was designed to identify postnatal depression, almost 90 % of women in our dataset who had anxiety had a total EPDS score above the threshold for depression. Of the small group with anxiety who scored below the depression threshold, 60 % would be identified by the EPDS+ strategy. There are some additional gains associated with the EPDS+ (beyond the EPDS), however they are small and must be balanced with an increased number of false positive outcomes. Either case-finding strategy (EPDS or EPDS+) has more true positives and true negatives and fewer false positives and negatives than not case-finding. Between 32,000 and 37,000 women per year in the UK who are experiencing depression or anxiety in the postnatal period would be identified by implementing a case-finding strategy. However, identifying and treating these women does come at a cost.

### 4.1. Validation analysis

The National Screening Committee in the UK noted a lack of evidence on the effectiveness of tools for identifying anxiety (Solutions for Public Health, 2019). Our analysis contributes to addressing this evidence gap. The EPDS-3 A, with a cut-off score of >5, has good sensitivity and specificity as a standalone instrument to detect anxiety (vs. GAD-7 cut-off score of  $\geq$ 8). Using the GAD-7 to measure the sensitivity and specificity of the EPDS-3A is a notable limitation of our analysis of the validity of the EPDS-3A as it is not a diagnostic gold standard for anxiety. A meta-analysis identified the optimal GAD-7 cut-off score of  $\geq 8$ (Plummer et al., 2016). However, this was based on general population samples rather than being restricted to postnatal samples. A longitudinal cohort study of pregnant and postnatal women reported that a GAD-7 cut off of  $\geq 6$  was optimal using diagnostic interviews as the comparison (Ayers et al., 2024a). We used the value from the meta-analysis in this analysis as it includes data from multiple studies. Furthermore, the sensitivity and specificity reported from the meta-analysis were 0.83 and 0.84 respectively. However, the single study of postnatal women reported that their optimal values were 0.65 and 0.76 for sensitivity and specificity, respectively. This may suggest that the GAD-7 performs less well in postnatal women than in the general population or may be related to the characteristics of the sample in the study of postnatal women. If the former is the case, this strengthens the argument for the need for postnatal-specific measures of anxiety.

It is notable that studies using other measures of anxiety compared with the EPDS-3A found similar results to ours. For example Smith-Neilsen et al compared the EPDS-3A with the Hopkins symptom checklist and also found that of  $\geq$ 5 was the optimal cut-off score (Smith-Nielsen et al., 2021). They reported an AUC of 0.926 at this cut-off, which is close to ours of 0.898. Another study compared the EPDS-3A with the Screening Assessment for Guiding Evaluation-Self-Report (SAGE-SR) and also reported that  $\geq 5$  was the optimal cut-off score (Austin et al., 2022), although this was for an antenatal population and the AUC was 0.809. One study compared self-reported postnatal anxiety with EPDS-3A scores and found that anxiety was greatest at an EPDS-3A score of  $\geq$ 5 (Fellmeth et al., 2022). A recent study of longitudinal data compared the efficacy of 5 different measures of anxiety in the perinatal period with the Mini-International Neuropsychiatric Interview (MINI): GAD-2, GAD-7, Whooley questions, Clinical Outcomes in Routine Evaluation (CORE-10), and Stirling Antenatal Anxiety Scale (SAAS)) (Ayers et al., 2024a). The CORE-10 and SAAS had the best diagnostic accuracy for anxiety, however, the study did not evaluate the EPDS-3A.

# - No case-finding 0.8 -D- EPDS -C> EPDS+ 07 0.6 05 % Iterations Cost-Effective 04 0.3 0.2 0.1 0 0 5000 10000 15000 20000 25000 30000 35000 40000 Willingness-to-Pay (£)

**CE Acceptability Curve** 

Fig. 2. Cost-effectiveness acceptability curve (CEAC) for case-finding with EPDS or EPDS+ versus standard care (no case finding).

We have used the 3-item anxiety sub-scale of the EPDS (questions 3, 4, and 5) for this analysis as most factor analyses of the English-language EPDS identified a sub-scale with these items (summarised in (Coates et al., 2017)). However, the analysis of around 12,000 participants in a British longitudinal study reported in the same paper found that question 6 could also be part of the anxiety sub-scale (i.e. questions 3–6) (Coates et al., 2017). The same 4-item sub-scale was also identified in a very large analysis (over 90,000 participants) of the Japanese EPDS (Matsumura et al., 2020) but the findings from factor analyses of other non-English language versions of the EPDS were less consistent and found a number of different question combinations including 3–5, 3–6, 3–7, 3–5 + 8, and 4–6 (summarised in (Coates et al., 2017)). More research is needed to better understand which questions should be included in the anxiety sub-scale for different populations/languages.

### 4.2. Cost-effectiveness analysis

There is a growing body of literature suggesting that case-finding or screening for antenatal or postnatal depression is likely to be costeffective (Camacho et al., 2023a, 2023b; Heslin et al., 2022; Littlewood et al., 2018; National Institute of Health and Care Excellence (NICE), 2014; Premji et al., 2021; Wilkinson et al., 2017). No literature was identified (by the authors) about the cost-effectiveness of casefinding for anxiety, either antenatally or postnatally, which is a key evidence gap. Our analysis is the first to take a transdiagnostic approach and look at using a single case-finding tool to identify symptoms of anxiety or depression or both. A key strength of the EPDS is that it is already widely used, generally acceptable (Littlewood et al., 2018), and does not require any additional questions to capture symptoms of anxiety alongside depression.

We found that by capitalising upon the potential of the EPDS to identify anxiety (in addition to depression), there were additional health gains compared to using the total EPDS score alone. However, there are also additional costs and whether this use of resources is considered good value for money depends on how much decision-makers are willing to pay to improve the health of new mothers (and their children in the longer-term).

The benefit of identifying more cases of mental health conditions can only be realised if timely access to effective support and treatment is available. The UK National Screening Committee do not currently recommend screening (or case-finding) for postnatal mental health conditions (Solutions for Public Health, 2019). One reason cited for this is a lack of evidence on the effectiveness of treatments. Subsequently, this must be addressed. In our model, treatment of anxiety and depression is a key driver of cost. These costs would be better offset if the likelihood of recovery were higher (in the model there is a 54-63 % chance of recovery following treatment). Further work is needed to improve mental health care in the postnatal period, that recognises and meets the different needs of different people, and increase the likelihood of recovery. A recent systematic review of non-pharmacological interventions for perinatal anxiety highlighted the importance of providing women with a choice of treatment options and of patientcentred care (Silverwood et al., 2023). Specialist perinatal mental health teams provide a vital avenue for support and are now established throughout England (Maternal Mental Health Alliance, 2023). The level of service provided varies vastly across the country with only 10 out of 62 areas (6 of which are in London) delivering all four main ambitions from the Government's Long Term Plan for perinatal mental health. In Wales, all areas provide a specialist perinatal service, although none at the highest level. In Northern Ireland 3 of 5 areas provide a specialist perinatal service, again with none at the highest level. In Scotland, 11 out of 14 areas proved a service, with only 2 at the highest level. This demonstrates clear geographical health inequalities which must be addressed so that everyone can access high-quality, appropriate, support

### regardless of location.

The strengths and limitations of the cost-effectiveness model have been discussed in full elsewhere (Camacho et al., 2023a). Briefly, key limitations are that the time horizon (not going beyond the first postnatal year) and perspective (mothers only) include a limited scope of the impacts of anxiety/depression when broader impacts are known to be considerable (Bauer et al., 2016). We have assumed a single time point for case-finding and not explored the cost-effectiveness of serial casefinding or when the optimal timing of case-finding may be. A recent longitudinal cohort study suggested that early pregnancy is the optimal time to screen for anxiety, based on the performance of screening questionnaires compared with diagnostic interview and that this is when anxiety symptoms were found to be highest (Ayers et al., 2024b). However, the authors warn against the normalisation of anxiety in early pregnancy and recognise the challenges of identifying cases of anxiety in this period which remit without treatment. Repeated completion of casefinding instruments may also help to increase our understanding of this. It may also be able to reduce the rate of false positive outcomes (and associated treatment costs) if treatment is not initiated where only the first test is positive. It would be useful to better understand the implications of false positive case-finding outcomes on utility values and treatment costs in the real world, as these are notable areas of uncertainty in our model and can have an impact on the cost-effectiveness results.

In our model we have assumed that health visitors conduct casefinding as part of their routine contacts with families with a new baby. Health visitors are nurses or midwives based in public health services, supporting families through early childhood. In the current programme in the UK, health visitors are expected to have contact with all families, typically face-to-face in the family home. This provides an opportunity to capitalise upon existing systems and processes to increase the identification of mental health conditions. While at-home visits may enable some women to disclose mental health symptoms, others may feel more able to do so in a different setting (e.g. due to stigma or domestic abuse/violence). There are other routine healthcare contacts in the perinatal period, for example with midwives (e.g. antenatally) or primary care physicians (e.g. routine postnatal health checks with General Practitioners) which could also incorporate case-finding for mental health conditions as standard.

### 5. Conclusion

Case-finding for postnatal mental health conditions using the EPDS is cost-effective compared with no case-finding. Additional consideration of the anxiety subscale score could be used to identify more cases of postnatal mental health conditions than the total score alone. However, the cost of treating the increased number of false positive cases makes it less cost-effective.

### CRediT authorship contribution statement

Elizabeth M. Camacho: Writing – review & editing, Writing – original draft, Project administration, Funding acquisition, Formal analysis, Conceptualization. Gemma E. Shields: Writing – review & editing, Writing – original draft, Funding acquisition, Formal analysis. Emily Eisner: Writing – review & editing, Writing – original draft, Investigation, Funding acquisition. Elizabeth Littlewood: Writing – review & editing, Writing – original draft, Investigation, Funding acquisition, Conceptualization. Kylie Watson: Writing – review & editing, Writing – original draft, Investigation, Funding acquisition, Conceptualization. Kylie Watson: Writing – review & editing, Writing – original draft, Investigation, Funding acquisition. Carolyn A. Chew-Graham: Writing – review & editing, Writing – original draft, Investigation, Funding acquisition. Dean McMillan: Writing – review & editing, Writing – original draft, Investigation, Funding acquisition. Simon Gilbody: Writing – review & editing, Writing – original draft, Investigation, Funding acquisition.

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### Declaration of competing interest

All authors report no conflicts of interest.

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#### Appendix A. Supplementary data

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