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The screening accuracy of the Edinburgh Postnatal Depression Scale (EPDS) to detect perinatal depression with and without the self-harm item in pregnant and postpartum women

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ABSTRACT

Background: This study aims to examine whether the Edinburgh Postnatal Depression Scale (EPDS), excluding the self-harm item (EPDS-9), performs as effectively as the full EPDS in identifying depression among perinatal women.

Methods: A total of 3571 pregnant women and 3850 postpartum women participated in this observational study. Participants who scored ≥ 9 on the EPDS underwent further diagnostic evaluations by a clinical psychologist and/or psychiatrist.

Results: The EPDS-9 and full EPDS demonstrated a near-perfect correlation in both the antepartum (r=0.996) and postpartum (r=0.998) cohorts. EPDS-9 showed exceptional precision in identifying depression as screened by the full EPDS at cutoff points ranging 9–14, with areas under the curve ≥ 0.998 . The sensitivity of EPDS-9 and full EPDS to detect depression that requires psychotropic medications was poor. The highest accuracy for both versions was at a cutoff score of 9: sensitivity of 0.579 for the full EPDS and 0.526 for the EPDS-9. At the cutoff point of 9, EPDS-9 performed adequately in predicting the response of the participants to the self-harm item.

Conclusion: The EPDS-9 represents a solid and effective replacement for the full EPDS in clinical settings. If the presence of suicidal thoughts needs to be assessed, specialized scales should be used.

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KEYWORDS

Edinburgh Postnatal Depression Scale; perinatal depression; self-harm; suicidal ideation; screening sensitivity

Perinatal depression is a common and debilitating psychological condition among women [1,2]. It affects approximately 15% of individuals during pregnancy

(antepartum depression) and 14% following childbirth (postpartum depression) [3,4]. This condition poses severe risks to maternal health, including increased

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mortality and preterm delivery [2]. In addition, it impacts the father, the couple relationship, and the child, leading to paternal depression, impaired maternal functioning, difficult interactions with the infant, and developmental delays in the child [5-7]. These adverse outcomes impose substantial financial burdens on healthcare systems [8,9]. However, it is crucial to acknowledge that perinatal depression does not occur in isolation. Social determinants such as poverty, lack of social support [10-12], gender-based violence [13], and cultural expectations [14,15] significantly contribute to the risk and experience of perinatal depression. Furthermore, partner involvement in the relationship and behavior [16,17], including partner coercive control or violence [18], can exacerbate or even precipitate depressive symptoms, illustrating the bidirectional and complex nature of these relationships.

Mounting evidence supports early screening for depression as a crucial strategy to alleviate symptoms and prevent relapses among perinatal individuals and their families, enabling timely management and intervention [19,20]. This is particularly important in the presence of vulnerabilities due to past traumatic experiences, such as a history of childhood maltreatment or sexual abuse [21,22]. Consequently, numerous national guidelines recommend routine depression screening for pregnant and postpartum women to enhance health outcomes [23,24]. Such screenings generally employ self-administered surveys that help identify individuals who exceed specific threshold scores, which then leads to further diagnostic evaluations to confirm depression [25,26].

The Edinburgh Postnatal Depression Scale (EPDS) [27] is the most widely used self-report tool for screening depression in pregnant and postpartum individuals within primary care settings worldwide [28,29]. Its effectiveness has been validated through comparisons with both semi-structured and fully structured diagnostic interviews based on the International Classification of Diseases (ICD) and the Diagnostic and Statistical Manual of Mental Disorders (DSM) [30,31]. Additionally, the reliability of the EPDS, originally developed in English, has also been confirmed in over 60 languages [32], including Chinese [33], Spanish [34], Hindi [35], Arabic [36], and Italian [37]. However, EPDS is not without limitations, particularly when it is not utilized properly. Although its 10th item - "the thought of harming myself has occurred to me" - has been validated in perinatal populations as an indicator of suicidality [38] and is commonly used to assess suicidal ideation [39,40], the validity and the clinical significance of this item remain subject of debate. Research indicates that many women misinterpret "harming myself" as referring to non-suicidal self-harm [41]. Furthermore, when comparing the positive responses of perinatal women on EPDS item 10 with those obtained using tools specifically designed to assess suicidal ideation, the prevalence of suicidal ideation indicated by EPDS appears to be much higher than the actual prevalence [42]. It is also noteworthy that the although highest level of agreement - "yes, guite often" - on the 10th item of the EPDS correlates with affirmative responses to two items regarding suicidal ideation in the Clinical Interview Schedule-Revised, this agreement can still be accurately predicted by other EPDS items [43]. Lastly, concerning suicide risk, it is essential to note that only a few instances of self-harm ideation during pregnancy or postpartum lead to suicidal behaviors [44]. In research and clinical settings, all this leads to extensive follow-up with many women, the majority of whom are false positives. Such follow-ups consume substantial economic and clinical resources, without demonstrable patient benefit from this screening approach.

In light of these considerations, it is worthwhile to reassess the inclusion of the self-harm item in the EPDS. Therefore, this study examined whether the EPDS, excluding the 10th item (EPDS-9), performs as effectively as the full EPDS in identifying depression among postpartum and pregnant women.

Methods

Study sample

The study population consisted of 3571(48%) pregnant women and 3850 (52%) postpartum women. Data were derived from an observational nationwide study conducted by the Italian Perinatal Mental Health Network, coordinated by the Istituto Superiore di Sanità (Italian National Health Institute). Recruitment occurred from November 2021 to December 2023 during routine visits at healthcare centers located throughout Italy and connected to the network. These included obstetric and gynecological wards, psychiatric hospital departments, and maternal-child health facilities. Inclusion criteria were [1] being above 18 years of age, (2a) being antepartum or (2b) having a biological newborn aged ≤ 12 months, and [3] being able to speak and read Italian. Exclusion criteria included: [1] having a diagnosis of mental retardation or cognitive disability and [2] not being able to sign a written informed consent. No sample size calculation was conducted as the objective was to involve as many women as possible. Of 7515 women approached to join the



study, 94 (1.2%) refused to participate. A total of 7421 (98.7%) completed the screening assessment and are included in this analysis. Those who screened positive underwent formal diagnostic evaluations, the results of which are also considered in this report.

Measurements

The screening battery included three self-report questionnaires designed to gather sociodemographic and clinical data, as well as to assess the presence of depressive and anxious symptoms experienced during the previous week.

Sociodemographic and clinical data form

A specialized sociodemographic and clinical data form was developed to collect key information. This included various sociodemographic variables such as age, educational level, employment status, marital status, and economic situation. Additionally, detailed data concerning the pregnancy were captured, including history of previous pregnancies, use of assisted reproductive technologies, and occurrences of miscarriages. The data form also gathered information on any past episodes of depression, usage of psychotropic drugs, and levels of perceived family and social support, assessing the availability of practical help or psychological support from partners, friends, or relatives when needed.

Edinburgh Postnatal Depression Scale

The Edinburgh Postnatal Depression Scale (EPDS) [27] is the most widely used self-report tool for assessing perinatal depression due to its high sensitivity and specificity across various cultures [45]. It comprises 10 items that encompass a broad spectrum of depressive symptoms, including hope for the future, depressed mood, feelings of guilt, anxiety, worry, sleep disturbances, and thoughts of self-harm. The EPDS is recommended to be used as a single-factor scale [46]. Each item is scored on a four-point Likert scale, ranging from 0 (absence of symptoms) to 3 (high severity of symptoms), with the total score varying between 0 and 30. Higher scores signify more severe depressive symptoms. The selection of the cutoff value is contingent upon the objectives of the assessment. For broad-based screening programs or community surveys, a cutoff value of 9 or 10 is typically deemed most appropriate. Conversely, in clinical environments and research contexts - especially in effectiveness studies where treatment is specifically targeted at individuals most likely to encounter depressive symptoms during the perinatal period - a higher cutoff value

of 12 or 13 is recommended. This distinction ensures that the screening and subsequent interventions are tailored effectively to the needs of different populations [47-49]. In this study, the Italian version of the EPDS was used [37]. In our internal consistency analysis, the EPDS showed Cronbach's α =0.86 for the antepartum sample and Cronbach's α =0.87 for the postpartum sample.

The EPDS-9 refers to the EPDS excluding the 10th item, which concerns thoughts of self-harm.

Ethical approval

Before participating in the study, the women received oral and written information on the content and objectives of the study. Those willing to participate in the study were asked to sign the informed consent form and were able to withdraw from the study at any time. This study was approved by the Ethics Committee of the Italian National Institute of Health (No. 0024542, approved on 21 June 2021).

Procedure

Participants were screened once during the perinatal period, which ranged from the first stage of pregnancy up to 12 months postpartum. Screenings occurred during routine antepartum or postpartum checkups and included a sociodemographic and clinical data form, the EPDS, and the Generalized Anxiety Disorder (GAD)-7 scale [50]. Individuals who screened positive on the EPDS, identified by a cutoff score of 9 on the EPDS, underwent formal diagnostic evaluations by a clinical psychologist and/or a psychiatrist. In contrast, scores on the GAD-7 did not lead to any decisions for formal diagnostic evaluations. Participants diagnosed with a mood disorder received appropriate psychological interventions and/or psychotropic medications as needed. Data from these evaluations, conducted in the days following the EPDS administration, were used in the current analysis.

Statistical analysis

The analysis began by calculating the correlation between EPDS-9 and EPDS-10. Subsequently, the differentiating performance of EPDS-9 compared to EPDS-10 in screening for depression was assessed separately for postpartum and pregnant women. This was done by estimating the area under the curve (AUC), sensitivity, and specificity. Next, using the clinical decision to prescribe psychotropic medication as the

criterion for defining depression, we employed equivalence tests to compare the differentiating performance of EPDS-9 against EPDS-10. Lastly, the ability of EPDS-9 to predict responses on the 10th item (i.e. self-harm) was evaluated. All analyses were conducted using the R software environment (version 4.3.1).

Results

Participants characteristics are detailed in Table 1.

EPDS-9 and full EPDS demonstrated a near-perfect correlation in both the antepartum (r=0.996) and

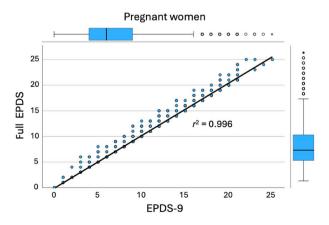
Table 1. Participant characteristics (N=7421).

	Pregnant women (n=3571)	Postpartum women $(n=3850)$
	% (n)	% (n)
A (
Age (mean ±SD)	32.9 (5.5)	33.2 (5.1)
Nationality	020/ (2204)	040/ (2542)
Italian	92% (3291)	91% (3513)
Non-Italian	8% (280)	9% (337)
Educational level		
Primary	1% (45)	1% (29)
Middle school	12% (448)	9% (362)
High school	43% (1540)	44% (1738)
Degree	44% (1582)	47% (1866)
Marital status		
Single	7% (249)	6% (257)
Separated. divorced. or widowed	1% (34)	1% (45)
Married or cohabiting	92% (3344)	93% (3719)
Family situation		
Lives alone	1% (37)	1% (31)
With others/parent	0% (4)	0% (2)
Lives with partner	99% (3449)	99% (3907)
Economic status	(,	,
Some or many problems	10% (345)	6% (218)
A few problems	64% (2250)	55% (2180)
Average to high status	27% (948)	39% (1544)
Occupational status		2772 (1211)
Housewife	10% (350)	10% (412)
Student or unemployed	24% (875)	13% (524)
Temporary employee	6% (228)	6% (236)
Permanent employee	60% (2142)	61% (2821)
Primiparous	00/0 (2172)	01/0 (2021)
No	56% (1946)	56% (2220)
Yes	44% (1536)	44% (1744)
162	77 (1330)	44 70 (1/ 44)

postpartum (r=0.998)cohorts (see **Figure** Furthermore, EPDS-9 achieved exceptional precision in identifying depression as screened by full EPDS at six cutoff points (ranging from 9 to 14). This was evidenced by areas under the curve (AUCs) of at least 0.998 in both the antepartum and postpartum samples (Table 2). The optimal operating points for EPDS-9 relative to full EPDS-based depression screening at these cutoff points are presented in Table 2. Notably, at the cutoff point of 9, the sensitivity tab was 0.98 and the specificity was 1.00 in both the postpartum and pregnant cohorts.

The clinical decision by psychiatrists or clinical psychologists to treat participants with psychotropic medication was used as a depression diagnosis. This diagnosis was used as a criterion to compare the performance of EPDS-9 and full EPDS. The ROC curves for both scales were almost identical when differentiating the current state of depression (Table 3). Equivalence tests did not reveal significant differences between AUCs for postpartum (AUC difference = 0.005, 95% CI = [-0.004, 0.014], p=0.275) or pregnant people (AUC difference 0.000, 95% CI = [-0.003, 0.003], p=0.967). The diagnostic accuracy of both versions of the EPDS is low. The sensitivity of the EPDS-9 and the full EPDS in detecting depression requiring medication is highest at a cutoff score of 9. For the full EPDS, sensitivity is 0.610 for antepartum depression and 0.579 for postpartum depression. For the EPDS-9, sensitivity is 0.610 for antepartum depression and 0.526 for postpartum depression. Detailed sensitivity and specificity values for each cutoff are provided in Table 3.

The predictive capacity of EPDS-9 for responses to the EPDS self-harm item was also evaluated. The AUC values for EPDS-9 against self-harm responses at the frequency of symptoms ("hardly ever", "sometimes", "often") are presented in Table 4. For responses of hardly ever, the AUC was 0.794 in the antepartum



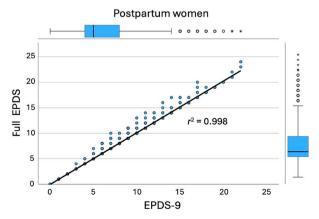


Figure 1. Scatterplot of the correlation between EPDS-9 and full EPDS.



Table 2. Optimal operating points for EPDS-9 against full EPDS-based screening depression.

		EP	DS-10 based scre	ening of depress	ion	
	Cutoff = 9	Cutoff = 10	Cutoff =11	cutoff = 12	Cutoff = 13	Cutoff =14
Pregnant women	Sn = 0.989 Sp = 1 AUC = 0.999	Sn = 0.976 Sp = 1 AUC = 0.998	Sn = 0.970 Sp = 1 AUC = 0.999	Sn = 0.966 Sp = 1 AUC = 0.998	Sn = 0.935 Sp = 1 AUC = 0.998	Sn = 0.902 Sp = 1 AUC = 0.998
Postpartum women	Sn = 0.984 Sp = 1 AUC = 0.999	Sn = 0.984 Sp = 1 AUC = 0.998	Sn = 0.967 Sp = 1 AUC = 0.998	Sn = 0.965 Sp = 1 AUC = 0.999	Sn = 0.950 Sp = 1 AUC = 0.999	Sn = 0.936 Sp = 1 AUC = 0.999

Note. AUC: area under the receiver operating characteristic curve; Sn: sensitivity; Sp: specificity.

group and 0.802 in the postpartum group. For the frequency of sometimes, the AUCs were 0.770 in antepartum and 0.818 in postpartum. For the frequency of often, the AUCs increased to 0.836 in antepartum and 0.912 in postpartum. Equivalence testing indicated no significant differences between the AUCs across the frequencies: hardly ever (AUC difference = -0.008, 95% CI = [-0.084, 0.068], p = 0.845), sometimes (AUC difference = -0.048, 95% CI = [-0.138, 0.041], p=0.293), and often (AUC difference = -0.076, 95% CI = [-0.221, 0.070], p = 0.307). Sensitivity and specificity details for each cutoff are provided in Table 4. Notably, at a cutoff of 9, the sensitivity of the EPDS-9 against self-harm at the frequency of often was 0.875 for pregnant women and 0.833 for postpartum individuals. This indicates that only 13% of pregnant women (2 out of 16) and 17% of postpartum women (1 out of 6) experiencing frequent self-harm thoughts scored below 9 on the EPDS-9.

Discussion

Our findings indicate that the EPDS without the self-harm item (EPDS-9) shows a near-perfect correlation with the full EPDS in both pregnant and postpartum women. The two versions of the EPDS demonstrate equivalent effectiveness, albeit less than acceptable, in identifying participants, whether in the antepartum or postpartum period, who have a depression diagnosis that requires psychotropic medication. Lastly, the performance of the EPDS-9 is only marginally acceptable [51], or even less than acceptable depending on the cutoff, in predicting perinatal women's responses to the self-harm item. These results suggest that while the EPDS-9 can be an effective screening tool for antepartum and postpartum depression, it has low sensitivity in identifying cases requiring psychotropic medication and is inadequate for detecting thoughts of intentional self-harm among Italian women.

Although healthcare providers and researchers often intend the self-harm item to assess suicidal ideation [39,40], respondents frequently interpret it as referring to non-suicidal self-harm [41]. This misinterpretation can lead to an overestimation of risks, resulting in the unnecessary consumption of healthcare resources. Our findings indicate that the inclusion or exclusion of the self-harm item does not impair the EPDS's performance in identifying perinatal women with depression. This aligns with a recent individual participant data meta-analysis, which demonstrated that the EPDS-9 and the full EPDS have similar screening accuracy for detecting major depression among pregnant and postpartum women [31].

When evaluating the predictive potential of the EPDS-9 for responses to the self-harm item, we found that the strongest agreement ("yes, quite often") was the only acceptable one. Interestingly, the AUC of EPDS-9 against the self-harm item varied depending on the frequency level, suggesting that EPDS-9's predictive ability decreases with this more conservative threshold. Furthermore, the variations in AUC values for self-harm frequencies above "sometimes" and "often" highlight the importance of considering frequency when examining self-harm predictions. These results are consistent with a previous Italian study [52] based on a smaller sample but contrast with a recent Japanese study [53], which reported that the response "yes, quite often" on the self-harm item is perfectly predicted by the EPDS-9.

It may be important here to remember that the EPDS was originally developed in English [27]. Our study, along with Chen et al.'s (2023) study, utilized translated versions of the scale. While the Italian and Japanese translations have been validated [37,54] and proven reliable for assessing perinatal depression [46,55], including a similar factor structure encompassing anxiety and anhedonia [56,57], the translation process may still introduce inconsistencies. This issue underscores the importance of establishing cross-cultural validity for psychological assessments. In fact, cultural differences in the experience and expression of affective disorders are essential to consider in clinical assessments [58,59]. Variations in how depression symptoms manifest and the willingness to disclose self-harm are significant, as suggested by numerous studies. Depression and other mental health issues may present differently across cultures due to social norms, belief systems, and the stigma associated with mental health

Table 3. Comparison of sensitivity and specificity values between EPDS-9 and full EPDS against self-reported depression diagnosis.

	Cutof	Cutoff = 9	Cutoff =	= 10	Cutoff	Cutoff = 11	Cutoff	Cutoff = 12	Cutoff	Cutoff = 13	Cutoff	Cutoff = 14
	EPDS-10	EPDS-9	EPDS-10	EPDS-9	EPDS-10	EPDS-9	EPDS-10	EPDS-9	EPDS-10	EPDS-9	EPDS-10	EPDS-9
Pregnant women	Sn = 0.610	Sn = 0.610 Sn = 0.576	Sn = 0.576	Sn = 0.559		Sn = 0.475	Sn = 0.407	Sn = 0.390	Sn = 0.373	Sn = 0.375	Sn = 0.322	Sn = 0.322
1	Sp = 0.697		Sp = 0.774	Sp = 0.779		Sp = 0.834	Sp = 0.872	Sp = 0.873	Sp = 0.908	Sp = 0.915	Sp = 0.933	Sp = 0.940
	$A\dot{U}C = 0.701$	AUC = 0.695	AUC = 0.644	AUC = 0.640	$A\dot{U}C = 0.679$	AUC = 0.672	AUC = 0.693	AUC = 0.682	AUC = 0.642	AUC = 0.629	AUC = 0.623	AUC = 0.588
Postpartum women	Sn = 0.579	Sn = 0.526	Sn = 0.421	Sn = 0.421		Sn = 0.395	Sn = 0.368	Sn = 0.342	Sn = 0.263	Sn = 0.263	Sn = 0.132	Sn = 0.132
•	Sp = 0.821	Sp = 0.824	Sp = 0.875	Sp = 0.880		Sp = 0.913	Sp = 0.939	Sp = 0.941	Sp = 0.957	Sp = 0.960	Sp = 0.970	Sp = 0.972
	AUC = 0.610	AUC = 0.598	AUC = 0.686	AUC = 0.682		AUC = 0.611	AUC = 0.480	AUC = 0.479	AUC = 0.446	AUC = 0.448	AUC = 0.645	AUC = 0.579
			:		: ;							

Note. AUC: area under the receiver operating characteristic curve; Sn: sensitivity; Sp: specificity.

Table 4. Sensitivity and specificity values of EPDS-9 against thoughts of self-harm.

		Cutoff = 9			Cutoff = 10			Cutoff = 11	
	≥ hardly ever	≥ sometimes	> often	≥ hardly ever	≥ sometimes	> often	≥ hardly ever	≥ sometimes	≥ often
Pregnant women	Sn = 0.804	Sn = 0.661	Sn = 0.875	Sn = 0.670	Sn = 0.644	Sn = 0.750	Sn = 0.567	Sn = 0.559	Sn = 0.688
	Sp = 0.719	Sp = 0.0719	Sp = 0.719	5p = 0.796	Sp = 0.796	8p = 0.796	Sp = 0.850	Sp = 0.850	Sp = 0.850
	AUC = 0.638	AUC = 0.594	AUC = 0.723	AUC = 0.559	AUC = 0.593	AUC = 0.645	AUC = 0.585	AUC = 0.563	AUC = 0.582
Postpartum women	Sn = 0.625	Sn = 0.640	5n = 0.833	Sn = 0.500	Sn = 0.360	Sn = 0.833	Sn = 0.429	Sn = 0.320	Sn = 0.677
	Sp = 0.831	5p = 0.831	5p = 0.831	Sp = 0.885	Sp = 0.885	Sp = 0.885	Sp = 0.917	Sp = 0.917	Sp = 0.917
	AUC = 0.511	AUC = 0.410	AUC = 0.611	AUC = 0.496	AUC = 0.342	AUC = 0.506	AUC = 0.525	AUC = 0.329	AUC = 0.493
		Cutoff $= 12$			Cutoff = 13			Cutoff = 14	
	≥ hardly ever	≥ sometimes	> often	≥ hardly ever	≥ sometimes	> often	≥ hardly ever	≥ sometimes	> often
Pregnant women	Sn = 0.516	Sn = 0.509	Sn = 0.688	Sn = 0.443	5n = 0.373	Sn = 0.500	Sn = 0.361	Sn = 0.271	Sn = 0.500
	5p = 0.893	5p = 0.893	5p = 0.893	Sp = 0.927	Sp = 0.927	Sp = 0.927	Sp = 0.949	Sp = 0.949	Sp = 0.949
	AUC = 0.592	AUC = 0.477	AUC = 0.500	AUC = 0.506	AUC = 0.436	AUC = 0.485	AUC = 0.455	AUC = 0.412	AUC = 0.441
Postpartum women	Sn = 0.339	Sn = 0.280	Sn = 0.500	Sn = 0.268	Sn = 0.200	Sn = 0.500	Sn = 0.214	Sn = 0.160	Sn = 0.333
	Sp = 0.945	Sp = 0.945	Sp = 0.945	Sp = 0.962	Sp = 0.962	Sp = 0.962	Sp = 0.975	Sp = 0.975	Sp = 0.975
	AUC = 0.484	AUC = 0.459	AUC = 0.390	AUC = 0.461	AUC = 0.404	AUC= 0.288	AUC = 0.467	AUC = 0.375	AUC = 0.233

Note. AUC: area under the receiver operating characteristic curve; Sn: sensitivity; Sp: specificity.

[59,60]. Furthermore, cultural factors can significantly impact the willingness to disclose self-harm and suicidal ideation. High levels of stigma associated with mental health conditions or self-harm behaviors in some cultures can make individuals less likely to report these experiences openly [61]. In cultures that prioritize collective identity over individualism, self-stigma may lead to lower levels of openness about mental health struggles, including self-harm [62]. Therefore, it appears critical to consider cultural factors when interpreting the effectiveness of measures like the EPDS-9 and the full EPDS in different cultural and perinatal populations (pregnant versus postpartum individuals). The differences in predictive accuracy of EPDS-9 for self-harm responses between culturally different samples highlight the need for culturally sensitive approaches in detecting perinatal depression.

Furthermore, although some literature indicates that low literacy levels and cultural factors may complicate the completion of screening instruments such as the EPDS for some women [63], it is important to note that only 1% of our entire sample had a primary educational level, and 8% and 9% of the antepartum and postpartum samples, respectively, were non-Italian.

A recently published cohort study involving 952,061 perinatal women with follow-up up to 18 years has shown that the risk of suicidal behavior is three times higher for mothers with clinically diagnosed perinatal depression compared to those without this mood disorder [64]. This highlights suicidality as a critical issue in perinatal care. However, while there is strong evidence supporting the importance of depression screening during pregnancy and postpartum, significant gaps remain in the evidence for suicide risk screening [65]. This may be because three of the four most widely used screening tools (Whooley questions, CES-D, and EPDS; versus PHQ-9 [65]) do not specifically address suicidality. Therefore, screening should focus on perinatal women at high risk of depression. Given the consistent evidence that (i) EPDS-9 and full EPDS show a near-perfect correlation, (ii) responses to the self-harm item are predicted with moderate accuracy by the EPDS-9, and (iii) the EPDS self-harm item is often misinterpreted, the EPDS self-harm item can be discarded in clinical screenings, especially when there are concerns its administration. Instead, validated, standalone self-report measures specifically developed for assessing perinatal suicide should be adopted.

Based on our results and consistent with previous studies [53], a cutoff score of 9 appears to be optimal for sensitivity in the EPDS-9.

Strengths and limitations

The primary strength of this study was the substantial sample size, encompassing both antepartum and postpartum cohorts from various regions across Italy. Additionally, we recruited participants from diverse settings, including obstetric and gynecological wards and maternal-child health facilities. However, two main limitations should be noted. First, we did not employ DSM- or ICD-based semi-structured or structured diagnostic interviews to define clinical depression. Instead, unstructured diagnostic evaluations were conducted for participants who scored ≥9 on the EPDS, and we collected data on the outcomes of these evaluations. Second, no follow-up assessments were performed to evaluate the longitudinal predictive power of the EPDS-9. Future studies are needed to compare the performance of EPDS-9 against diagnostic structured interviews and to determine whether our findings are applicable over longer observation periods and across different cultural contexts.

Conclusion

In conclusion, our findings indicate that the EPDS without the self-harm item performs equivalently to the full EPDS in assessing depressive symptom severity in both antepartum and postpartum cohorts. Additionally, both versions of the EPDS show equal accuracy in screening for depression that requires medication. The EPDS without the self-harm item only performs with moderate accuracy in predicting frequent thoughts of self-harm in perinatal women. Given these results and the growing evidence that many respondents misinterpret the EPDS's "harming myself" item as referring to non-suicidal self-harm [41], omitting this item may help avoid confusion among respondents and reduce unnecessary healthcare resource consumption, such as psychiatric visits and psychological assessments. The EPDS-9 represents a solid and effective replacement for the full EPDS in clinical settings. If the presence of suicidal thoughts needs to be assessed, specialized scales should be used.

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Data availability statement

Both the data and the analysis code that support the findings of this study are available from the corresponding author upon reasonable request.

References

- [1] Howard LM, Khalifeh H. Perinatal mental health: a review of progress and challenges. World Psychiatry. 2020;19(3):313-327. doi:10.1002/wps.20769
- [2] Howard LM, Molyneaux E, Dennis C-L, et al. Non-psychotic mental disorders in the perinatal period. Lancet. 2014;384(9956):1775-1788. doi:10.1016/S0140-6736(14)61276-9
- [3] Liu X, Wang S, Wang G. Prevalence and risk factors of postpartum depression in women: a systematic review and meta-analysis. J Clin Nurs. 2022;31(19-20):2665-2677. doi:10.1111/jocn.16121
- [4] Yin X, Sun N, Jiang N, et al. Prevalence and associated factors of antenatal depression: systematic reviews and meta-analyses. Clin Psychol Rev. 2021;83:101932. doi:10.1016/j.cpr.2020.101932
- [5] Letourneau NL, Dennis C-L, Cosic N, et al. The effect of perinatal depression treatment for mothers on parenting and child development: a systematic review. Depress Anxiety. 2017;34(10):928-966. doi:10.1002/ da.22687
- [6] Thiel F, Pittelkow M-M, Wittchen H-U, et al. The relationship between paternal and maternal depression during the perinatal period: a systematic review and meta-analysis. Front Psychiatry. 2020;11:563287. doi:10.3389/fpsyt.2020.563287
- [7] Zhang T, Luo Z-C, Ji Y, et al. The impact of maternal depression, anxiety, and stress on early neurodevelopment in boys and girls. J Affect Disord. 2023;321:74-82. doi:10.1016/j.jad.2022.10.030
- [8] Bauer A, Gregoire A, Tinelli M, et al. Costs and benefits of scaling psychosocial interventions during the perinatal period in England: a simulation modelling study. Int J Nurs Stud. 2024;154:104733. doi:10.1016/j.ijnurstu.2024.104733
- [9] Knapp M, Wong G. Economics and mental health: the current scenario. World Psychiatry. 2020;19(1):3-14. doi:10.1002/wps.20692
- [10] Camoni L, Mirabella F, Gigantesco A, et al. The Impact of the COVID-19 Pandemic on Women's Perinatal Mental Health: preliminary Data on the Risk of Perinatal Depression/Anxiety from a National Survey in Italy. IJERPH. 2022;19(22):14822. doi:10.3390/ijerph192214822
- [11] Smorti M, Mirabella F, Calamandrei G, et al. Prevalence of anxiety and depression risk during the prepartum period in the different groups of women and responses from the Italian National Health Service, Minerva Pediatr. 2023. doi:10.23736/S2724-5276.23.07410-4
- [12] Cena L, Mirabella F, Palumbo G, et al. Prevalence of maternal antenatal and postnatal depression and their association with sociodemographic and socioeconomic factors: A multicentre study in Italy. J Affect Disord. 2021;279:217-221. doi:10.1016/j.jad.2020.09.136
- [13] Ankerstjerne LBS, Laizer SN, Andreasen K, et al. Landscaping the evidence of intimate partner violence and postpartum depression: a systematic review. BMJ

- Open. 2022;12(5):e051426. doi:10.1136/bmjopen-2021-051426
- [14] Wittkowski A, Patel S, Fox JR. The experience of postnatal depression in immigrant mothers living in western countries: a meta-synthesis. Clin Psychol Psychother. 2017;24(2):411-427. doi:10.1002/cpp.2010
- [15] Sampson M, Torres MIM, Duron J, et al. Latina immigrants' cultural beliefs about postpartum depression. Affilia. 2018;33(2):208-220. doi:10.1177/0886109917738745
- [16] Pebryatie E, Paek SC, Sherer P, et al. Associations between spousal relationship, husband involvement, and postpartum depression among postpartum mothers in West Java, Indonesia. Prim Care Community 2022;21501319221088355. doi:10.1177/21501319221088355
- [17] Faisal-Cury A, Tabb K, Matijasevich A. Partner relationship quality predicts later postpartum depression independently of the chronicity of depressive symptoms. Braz J Psychiatry. 2020;43(1):12-21. doi:10.1590/1516-4446-2019-0764
- [18] Kızılırmak A, Calpbinici P, Tabakan G, et al. Correlation between postpartum depression and spousal support and factors affecting postpartum depression. Health Care Women Int. 2021;42(12):1325-1339. doi:10.1080/07 399332.2020.1764562
- [19] Cena L, Palumbo G, Mirabella F, et al. Perspectives on early screening and prompt intervention to identify and treat maternal perinatal mental health. Protocol for a prospective multicenter study in Italy. Front Psychol. 2020;11:365. doi:10.3389/fpsyg.2020.00365
- [20] Cena L, Biban P, Janos J, et al. The collateral impact of COVID-19 emergency on neonatal intensive care units and family-centered care: challenges and opportunities. Front Psychol. 2021;12:630594. doi:10.3389/fpsyg.2021. 630594
- [21] Souch AJ, Jones IR, Shelton KHM, et al. Maternal childhood maltreatment and perinatal outcomes: a systematic review. J Affect Disord. 2022;302:139-159. doi:10.1016/j.jad.2022.01.062
- [22] Pingeton BC, Nieser KJ, Cochran A, et al. Childhood maltreatment exposure is differentially associated with transdiagnostic perinatal depression symptoms. J Affect Disord. 2024;358:183-191. doi:10.1016/j.jad.2024.05.021
- [23] American College of Obstetricians and Gynecologists. Screening and diagnosis of mental health conditions during pregnancy and postpartum: ACOG Clinical Practice Guideline No. 4. Obstet Gynecol. 2023;141:1232-1261. doi:10.1097/AOG.0000000000005200
- [24] Siu AL, Bibbins-Domingo K, Grossman DC, et al. Screening for depression in adults: US Preventive Services Task Force recommendation statement. JAMA. 2016;315(4):380-387. doi:10.1001/jama.2015.18392
- [25] Thombs BD, Coyne JC, Cuijpers P, et al. Rethinking recommendations for screening for depression in primary care. CMAJ. 2012;184(4):413-418. doi:10.1503/cmaj.111035
- [26] Wagas A, Koukab A, Meraj H, et al. Screening programs for common maternal mental health disorders among perinatal women: report of the systematic review of evidence. BMC Psychiatry. 2022;22(1):54. doi:10.1186/ s12888-022-03694-9
- [27] Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. Br J Psychiatry. 1987; 150(6):782-786. doi:10.1192/bjp.150.6.782

- [28] Moraes GPdA, Lorenzo L, Pontes GAR, et al. Screening and diagnosing postpartum depression: when and how? Trends Psychiatry Psychother. 2017;39(1):54-61. doi:10.1590/2237-6089-2016-0034
- [29] Puyané M, Subirà S, Torres A, et al. Personality traits as a risk factor for postpartum depression: a systematic review and meta-analysis. J Affect Disord. 2022;298(Pt A):577-589. doi:10.1016/j.jad.2021.11.010
- [30] Levis B, Negeri Z, Sun Y, et al. Accuracy of the Edinburgh Postnatal Depression Scale (EPDS) for screening to detect major depression among pregnant and postpartum women: systematic review and meta-analysis of individual participant data. BMJ. 2020;371:m4022. doi:10.1136/bmi.m4022
- [31] Qiu X, Wu Y, Sun Y, et al. Individual participant data meta-analysis to compare EPDS accuracy to detect major depression with and without the self-harm item. Sci Rep. 2023;13(1):4026. doi:10.1038/s41598-023-29114-w
- [32] Cox J. Thirty years with the Edinburgh Postnatal Depression Scale: voices from the past and recommendations for the future. Br J Psychiatry. 2019;214(3):127-129. doi:10.1192/bjp.2018.245
- [33] Lee DTS, Yip SK, Chiu HFK, et al. Detecting postnatal depression in Chinese women: validation of the Chinese version of the Edinburgh Postnatal Depression Scale. Br J Psychiatry. 1998;172(5):433-437. doi:10.1192/bjp.172.5.433
- [34] Garcia-Esteve L, Ascaso C, Ojuel J, et al. Validation of the Edinburgh Postnatal Depression Scale (EPDS) in Spanish mothers. J Affect Disord. 2003;75(1):71-76. doi:10.1016/S0165-0327(02)00020-4
- [35] Joshi U, Lyngdoh T, Shidhaye R. Validation of Hindi version of Edinburgh postnatal depression scale as a screening tool for antenatal depression. Asian J Psychiatr. 2020;48:101919. doi:10.1016/j.ajp.2019.101919
- [36] Naja S, Al-Kubaisi N, Chehab M, et al. Psychometric properties of the Arabic version of EPDS and BDI-II as a screening tool for antenatal depression: evidence from Qatar. BMJ Open. 2019;9(9):e030365. doi:10.1136/ bmjopen-2019-030365
- [37] Benvenuti P, Ferrara M, Niccolai C, et al. The Edinburgh Postnatal Depression Scale: validation for an Italian sample. J Affect Disord. 1999;53(2):137-141. doi:10.1016/ S0165-0327(98)00102-5
- [38] Dudeney E, Coates R, Ayers S, et al. Measures of suicidality in perinatal women: a systematic review. J Affect Disord. 2023;324:210-231. doi:10.1016/j.jad.2022.12.091
- [39] Chen C, Okubo R, Okawa S, et al. The prevalence and risk factors of suicidal ideation in women with and without postpartum depression. J Affect Disord. 2023;340:427-434. doi:10.1016/j.jad.2023.08.051
- [40] Xiao M, Hu Y, Huang S, et al. Prevalence of suicidal ideation in pregnancy and the postpartum: a systematic review and meta-analysis. J Affect Disord. 2022;296:322-336. doi:10.1016/j.jad.2021.09.083
- [41] Dudeney E, Coates R, Ayers S, et al. Acceptability and content validity of suicidality screening items: a qualitative study with perinatal women. Front Psychiatry. 2024;15:1359076. doi:10.3389/fpsyt.2024.1359076
- [42] Pope CJ, Xie B, Sharma V, et al. A prospective study of thoughts of self-harm and suicidal ideation during the postpartum period in women with mood disorders.

- Arch Womens Ment Health. 2013;16(6):483-488. doi:10.1007/s00737-013-0370-y
- [43] Howard LM, Flach C, Mehay A, et al. The prevalence of suicidal ideation identified by the Edinburgh Postnatal Depression Scale in postpartum women in primary care: findings from the RESPOND trial. BMC Pregnancy Childbirth. 2011;11(1):57. doi:10.1186/1471-2393-11-57
- [44] Lindahl V, Pearson JL, Colpe L. Prevalence of suicidality during pregnancy and the postpartum. Arch Womens Ment Health. 2005;8(2):77-87. doi:10.1007/s00737-005-0080-1
- [45] Sambrook Smith M, Cairns L, Pullen LSW, et al. Validated tools to identify common mental disorders in the perinatal period: a systematic review of systematic reviews. J Affect Disord. 2022;298(Pt A):634-643. doi:10.1016/j.jad.2021.11.011
- [46] Stefana A, Langfus JA, Palumbo G, et al. Comparing the factor structures and reliabilities of the EPDS and the PHQ-9 for screening antepartum and postpartum depression: a multigroup confirmatory factor analysis. Arch Womens Ment Health. 2023;26(5):659-668. doi:10. 1007/s00737-023-01337-w
- [47] Bhandari PM, Levis B, Neupane D, et al. Data-driven methods distort optimal cutoffs and accuracy estimates of depression screening tools: a simulation study using individual participant data. J Clin Epidemiol. 2021;137: 137-147. doi:10.1016/j.jclinepi.2021.03.031
- [48] Brehaut E, Neupane D, Levis B, et al. 'Optimal' cutoff selection in studies of depression screening tool accuracy using the PHQ-9, EPDS, or HADS-D: a meta-research study. Int J Methods Psych Res. 2023;32:e1956. doi:10.1002/mpr.1956
- [49] Mirabella F, Michielin P, Piacentini D, et al. Efficacia di un intervento psicologico rivolto a donne positive allo screening per depressione post partum. Rivista di Psichiatria. 2016;51(6):260–269. doi:10.1708/2596.26728
- [50] Spitzer RL, Kroenke K, Williams JBW, et al. A brief measure for assessing Generalized Anxiety Disorder: the GAD-7. Arch Intern Med. 2006;166(10):1092-1097. doi: 10.1001/archinte.166.10.1092
- [51] Power M, Fell G, Wright M. Principles for high-quality, high-value testing. Evid Based Med. 2013;18(1):5-10. doi:10.1136/eb-2012-100645
- [52] Stefana A, Cena L, Alice T, et al. The diagnostic accuracy of the Edinburgh Postnatal Depression Scale without the self-harm item: does culture matter? J Psychiatr Res. 2024;175:432-434. doi:10.1016/j.jpsychires.2024.05.018
- [53] Chen C, Okubo R, Okawa S, et al. The diagnostic accuracy of the Edinburgh Postnatal Depression Scale without the self-harm item. J Psychiatr Res. 2023;165:70-76. doi:10.1016/j.jpsychires.2023.07.015
- [54] Okano TMM, Masuji F, Tamaki R, et al. Validation and reliability of Japanese version of the EPDS. Arch Psychiatr Diagn Clin Eval. 1996;7:525-533.
- [55] Kubota C, Inada T, Nakamura Y, et al. Stable factor structure of the Edinburgh Postnatal Depression Scale during the whole peripartum period: results from a prospective cohort study. Japanese Sci 2018;8(1):17659. doi:10.1038/s41598-018-36101-z
- [56] Kubota C, Okada T, Aleksic B, et al. Factor structure of the Japanese version of the Edinburgh Postnatal

- Depression Scale in the postpartum period. PLoS One. 2014;9(8):e103941. doi:10.1371/journal.pone.0103941
- [57] Stefana A, Cena L, Trainini A, et al. Screening for prenatal and post, natal maternal depression: comparative performance of the Edinburgh Postnatal Depression Scale and Patient Health Questionnaire- 9. Ann Ist Super Sanita. 2024;60(1):55-63. doi:10.4415/ANN_24_ 01_08
- [58] Chang MX, Jetten J, Cruwys T, et al. Cultural identity and the expression of depression: a social identity perspective. Community & Applied Soc Psy. 2017;27(1):16-34. doi:10.1002/casp.2291
- [59] Haroz EE, Ritchey M, Bass JK, et al. How is depression experienced around the world? A systematic review of qualitative literature. Soc Sci Med. 2017;183:151-162. doi:10.1016/j.socscimed.2016.12.030
- [60] Gopalkrishnan N. Cultural diversity and mental health: considerations for policy and practice. Front Public Health. 2018;6:179. [Internet]. [cited 2024 May 23. doi:10.3389/fpubh.2018.00179

- [61] Chu JP, Goldblum P, Floyd R, et al. The cultural theory and model of suicide. Applied and Preventive Psychology. 2010;14(1-4):25-40. doi:10.1016/j.appsy.2011.11.001
- [62] Yang LH, Kleinman A, Link BG, et al. Culture and stigma: adding moral experience to stigma theory. Soc Sci Med. 2007;64(7):1524–1535. doi:10.1016/j.socscimed.2006.11.013
- [63] Goff SL, Moran MJ, Szegda K, et al. Development and pilot testing of an adaptable protocol to address postpartum depression in pediatric practices serving lower-income and racial/ethnic minority families: contextual considerations. Implement Sci Commun. 2020; 1(1):66. doi:10.1186/s43058-020-00049-x
- [64] Yu H, Shen Q, Bränn E, et al. Perinatal depression and risk of suicidal behavior. JAMA Netw Open. 2024;7(1):e2350897. doi:10.1001/jamanetworkopen.2023.50897
- [65] O'Connor EA, Perdue LA, Coppola EL, et al. Depression and suicide risk screening: updated evidence report and systematic review for the US preventive services task force. JAMA. 2023;329(23):2068-2085. doi:10.1001/ jama.2023.7787