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The prevalence of premenstrual dysphoric disorder: Systematic review and meta-analysis

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ABSTRACT

Background: Premenstrual dysphoric disorder is characterised by symptoms confined to the premenstrual phase of the menstrual cycle. Confirmed diagnosis requires prospective monitoring of symptoms over two cycles, otherwise the diagnosis is provisional. We aimed to measure the point prevalence of premenstrual dysphoric disorder.

Methods: We searched for studies of prevalence using MEDLINE, EMBASE, PsycINFO and PubMed. For each study, the total sample size and number of cases were extracted. The prevalence across studies was calculated using random effects meta-analysis with a generalised linear mixed model. Potential sources of heterogeneity were explored by meta-regression and subgroup analyses. Pre-registration was with PROSPERO (CRD42021249249).

Results: 44 studies with 48 independent samples met inclusion criteria, consisting of 50,659 participants. The pooled prevalence was 3.2 % (95 % confidence intervals: 1.7 %–5.9 %) for confirmed and 7.7 % (95 % confidence intervals: 5.3 %–11.0 %) for provisional diagnosis. There was high heterogeneity across all studies (I^2 = 99 %). Sources of heterogeneity identified by meta-regression were continent of sample ($p < 0.0001$), type of sample (community-based, university, high school) ($p = 0.007$), risk of bias ($p = 0.009$), and method of diagnosis ($p = 0.017$). Restricting the analysis to community-based samples using confirmed diagnosis resulted in a prevalence of 1.6 % (95 % confidence intervals: 1.0 %–2.5 %), with low heterogeneity (I^2 = 26 %).

Limitations: A small number of included studies used full DSM criteria in community settings.

Conclusions: The point prevalence of premenstrual dysphoric disorder using confirmed diagnosis is lower compared with provisional diagnosis. Studies relying on provisional diagnosis are likely to produce artificially high prevalence rates.

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1. Introduction

Premenstrual dysphoric disorder (PMDD) has recently been incorporated as a disorder in DSM-5 (American Psychiatric Association, 2013), and ICD-11 (Reed et al., 2019), having previously been a condition for further study in DSM-III-R (American Psychiatric Association, 1980), DSM-IV (American Psychiatric Association, 1994), and DSM-IV-TR (American Psychiatric Association, 2010). PMDD is strongly associated with suicidality (Prasad et al., 2021) and has a similar impact on quality of life as other chronic health conditions (Yang et al., 2008). Diagnosis can reliably be determined using prospective daily ratings; requiring symptoms to be present in the week before menstruation and minimal or absent in the following week. Determining the prevalence of this disorder is crucial to for service provision.

Both DSM-5 and ICD-11 require luteal phase confinement of at least one of the following core emotional symptoms: (i) affective lability; (ii) irritability or anger; (iii) depressed mood; or (iv) anxiety. Supporting symptoms in both classification systems include poor concentration, lethargy, overeating, hypersomnia, and physical symptoms such as breast tenderness, swelling and joint pain. DSM-5 additionally includes supporting symptoms of decreased interest in activities and a sense of being overwhelmed, while ICD-11 includes the additional cognitive symptom of forgetfulness. A total of five or more symptoms are needed for DSM-5 diagnosis. Both require either significant distress or impairment in various spheres of functioning, as well as exclusion of other medical or drug-related causes or exacerbation of another mental disorder. DSM-III-R, DSM-IV, and DSM-IV-R requires interference with functioning (social life, education, occupation or relationships). For both DSM-5 and ICD-11, this was changed to either significant distress or interference with functioning.

Due to the importance of timing of symptoms in relation to the menstrual cycle, DSM-5 requires prospective ratings of symptoms over two menstrual cycles for a confirmed diagnosis; when this is not possible, a diagnosis based on retrospective (single-time-point) symptom report is labeled 'provisional'. ICD-11 advises that prospective symptom ratings should be done but does not stipulate this as a diagnostic requirement. The importance of prospective rating is emphasised by a lack of agreement between retrospective and prospectively diagnosed premenstrual mood disorders, with retrospective reporting of symptoms tending to lead to false positives (Eisenlohr-Moul et al., 2017; Gehlert et al., 2009; Rubinow et al., 1984). Prospective ratings may also differentiate between PMDD and premenstrual exacerbation of mental disorders (Hartlage, 2001).

The prevalence of PMDD has been reported as between 1.8 % and 5.8 % of menstruating females (American Psychiatric Association, 2013). However, a synthesis of studies across countries has not previously been performed to estimate a pooled prevalence. Previous meta-analyses in single countries, India (Dutta and Sharma, 2021) and Ethiopia (Duko et al., 2021), have not specified whether diagnosis was confirmed by prospective ratings. It is crucial to have an accurate prevalence of PMDD, as both overestimation (overdiagnosis, unnecessary treatment) and underestimation (lack of recognition and resources) have consequences for patients. We conducted a systematic review and meta-analysis of the point prevalence of PMDD, using provisional or confirmed diagnosis (the gold standard). We explored potential sources of heterogeneity with meta-regression and subgroup analyses.

2. Methods

2.1. Search strategy and selection criteria

We included observational studies assessing the prevalence of PMDD in female participants between menarche and menopause. Included studies could use either DSM or ICD diagnostic criteria. We excluded studies solely using a self-diagnosis of PMDD, as this is known to be unreliable (Bosman et al., 2018). We excluded studies of participants presenting to health services (such as those attending gynaecological clinics) as these are likely to have inflated prevalence compared with the general population. When multiple studies were reported from the same sample, we used the study with the largest sample size. We did not place restrictions based on language and used Google Translate for reports that were not in English.

The following databases were searched from inception to March 2021: MEDLINE, Embase, PsycINFO and PubMed. Two authors screened study abstracts and retrieved potentially relevant full-texts for further examination.

We searched for PMDD and related terms to ensure broad coverage of the literature. Examples of search keyword terms (adapted for different databases, as shown in the Supplementary materials) are given below:

- Premenstrual Syndrome OR Premenstrual Dysphoric Disorder OR Late Luteal Phase Dysphoric Disorder OR PMS OR PMDD OR LLPDD.
- Diagnos* OR Community OR Preval* OR Inciden* OR Epidemiol*.

2.2. Data analysis

Two authors (SP, IU) extracted study level data in duplicate with disagreement discussed with a third author (TJR). The following variables of interest were extracted from each study: study setting, sample size, mean age, method of diagnosis, number of cases of PMDD identified. The risk of bias tool for prevalence studies (Hoy et al., 2012) was applied in duplicate to each study by two researchers (SP, IU), with disagreement resolved by a third author (TJR). This includes questions on the study population, target population, sampling frame, participant selection, data collection, case definition, reliable measurement, mode of data collection, length of prevalence period and whether correct numerator and denominator were used to calculate the prevalence. Studies could score a maximum of ten points, with higher score indicating lower risk of bias.

All statistical analyses were carried out using R Statistical Software version 3.6.3 (R Core Team, 2021) using the 'meta' and 'metafor' packages, with the 'dmetar' package for Egger's tests. We used a random-effects model to pool results across studies, as we assumed the true effect estimated in each sample varied due to the differences in sample characteristics and study methodology. The proportions were logit-transformed using the 'metaprop' function of the 'meta' package. We used a generalised linear mixed model, fitted by maximum likelihood, as has been advocated for meta-analysis of single proportions (Schwarzer et al., 2019). This method avoids the need for a continuity correction for studies with zero counts.

Heterogeneity was assessed using the I^2 statistic. Potential sources of heterogeneity were explored using subgroup analysis and meta-regression. We pre-specified the following subgroup analyses if three or more studies were found: sample type (community-based, workplace or place of education), setting (continent of sample), diagnosis (confirmed or provisional). We grouped Australia with Europe, as there was only a single Australian study. We used meta-regression to assess the effect of study factors (provisional/confirmed diagnosis, continent, sample type, risk of bias) on heterogeneity. For diagnostic method, confirmed diagnosis was considered the gold standard and used as the reference category. For continent, North America was specified as the reference, as this contained the most prospectively diagnosed samples. We specified community-based samples as the reference category for sample type. Small sample bias (publication bias) was assessed visually using funnel plots, with asymmetry quantified using Egger's test. p values < 0.05 were considered statistically significant.

Considering only studies of provisionally diagnosed PMDD, these were further divided into two groups: those that used questionnaires (Premenstrual Symptoms Screening Tool, Steiner's self-rated premenstrual syndrome questionnaire, Premenstrual Symptoms Questionnaire, Calendar of Premenstrual Experiences, Composite International

Diagnostic Interview, Mini International Neuropsychiatric Interview) and those that either did not report which questionnaire was used, or who used their own author-developed questionnaire.

We followed PRISMA guidelines (Moher et al., 2009) (see checklist in Supplementary material) and pre-registered with PROSPERO (CRD42021249249).

3. Results

The search retrieved 12,340 records, of which 44 studies met the inclusion criteria (see Fig. 1), representing 48 independent samples and 50,659 participants. The sample size ranged from 62 to 8694, with a mean of 1151. The mean age of samples ranged between 14.3 and 38.6. Study characteristics are reported in Supplementary Table 1. Samples were obtained across the world: seven from Africa, 19 from Asia, one from Australia, nine from Europe, ten from North America and three from South America. All studies that sufficiently described diagnostic method, used DSM criteria, with none using ICD-11 (this is the first version of ICD to include the diagnosis of PMDD). Two studies used DSM III-R criteria, 34 used DSM-IV, four used DSM IV-TR, two used DSM-5 and two did not report the diagnostic classification. Of the 44 included studies, a minority ($n_{samples} = 10$) used prospective ratings of symptoms to make a confirmed diagnosis of PMDD. The mean sample size of studies with confirmed diagnosis was 798 and those with provisional diagnosis 1255. One study (Hardie, 1997) with sample size 83 found zero cases.

The pooled prevalence was 3.2 % (95 % Confidence Intervals (CI): 1.7 %–5.9 %) in samples with confirmed diagnosis and 7.7 % (95 % CI: 5.3 %–11.0 %) in samples that had provisional diagnosis, as shown in Fig. 2. There was significant heterogeneity, $I^2 = 99$ %. Risk of bias scores are shown in Supplementary Table 2, ranging from 3 to 9, with a median of 6 and interquartile range of 2. All studies scored low risk of bias for collecting data directly from participants and all scored low risk for using the same form of data collection for all participants. The highest scoring study was Gehlert et al., 2009 which utilised full diagnostic criteria in four samples taken from sites in the USA. The median score was 6 in studies using confirmed diagnosis and 5.5 in studies using provisional diagnosis. A funnel plot (Supplementary Fig. 1) did not find significant asymmetry, Egger's test $p = 0.52$.

As shown in Table 1, univariate meta-regression showed a significant effect of diagnosis (with a higher prevalence in provisional diagnosis than confirmed diagnosis) ($p = 0.017$). There was a significant effect of continent from which the sample was taken ($p < 0.001$), with highest prevalence in African samples and lowest in North American samples (see Supplementary Fig. 2). There was a significant effect of sample type ($p = 0.007$), with highest prevalence in university samples (see Supplementary Fig. 3). There was a significant effect of risk of bias ($p = 0.009$), with a bubble plot (Supplementary Fig. 4) illustrating that prevalence rates were negatively associated with risk of bias.

Of the studies reporting a provisional diagnosis of PMDD, 22 used a recognised questionnaire and 12 did not. The most commonly used questionnaire was the Premenstrual Symptoms Screening Tool (employed by eight studies), with the Premenstrual Symptoms Questionnaire used by four studies. As shown in Supplementary Fig. 5, those using a questionnaire had a pooled prevalence of 4.9 % (95 % CI: 3.5 %–6.9 %) $I^2 = 98$ %, while those that did not use a questionnaire had a prevalence of 16.6 % (95 % CI: 9.0 % −28.4 %) $I^2 = 99$ %.

Considering only confirmed diagnosis of PMDD, de la Gándara Martín and de Diego Herrero, 1996, was an outlier, with a prevalence of 30.5 %. This may be due to the study making the diagnosis only on PMDD symptoms, rather than fully applying DSM-III-R criteria which additionally requires symptoms to be severe enough to disrupt functioning. We therefore excluded this study from further analysis. The pooled prevalence with this exclusion was 2.7 % (95 % CI: 2.0 %–3.6 %) as shown in Supplementary Fig. 6, with heterogeneity reduced to $I^2 = 81$ %. There were significant differences ($p < 0.01$) in the prevalence from community-based samples (1.9 %, 95 % CI: 1.0 %−3.4 %) and other samples (recruited from educational, occupational, sporting

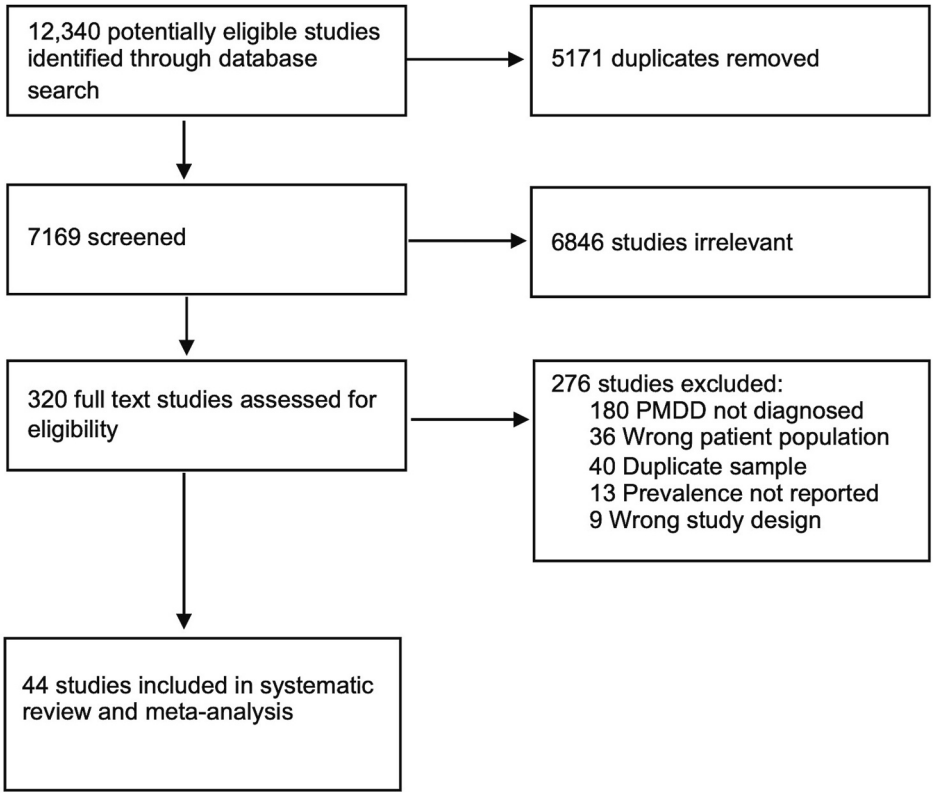

Fig. 1. PRISMA flow diagram of study selection.

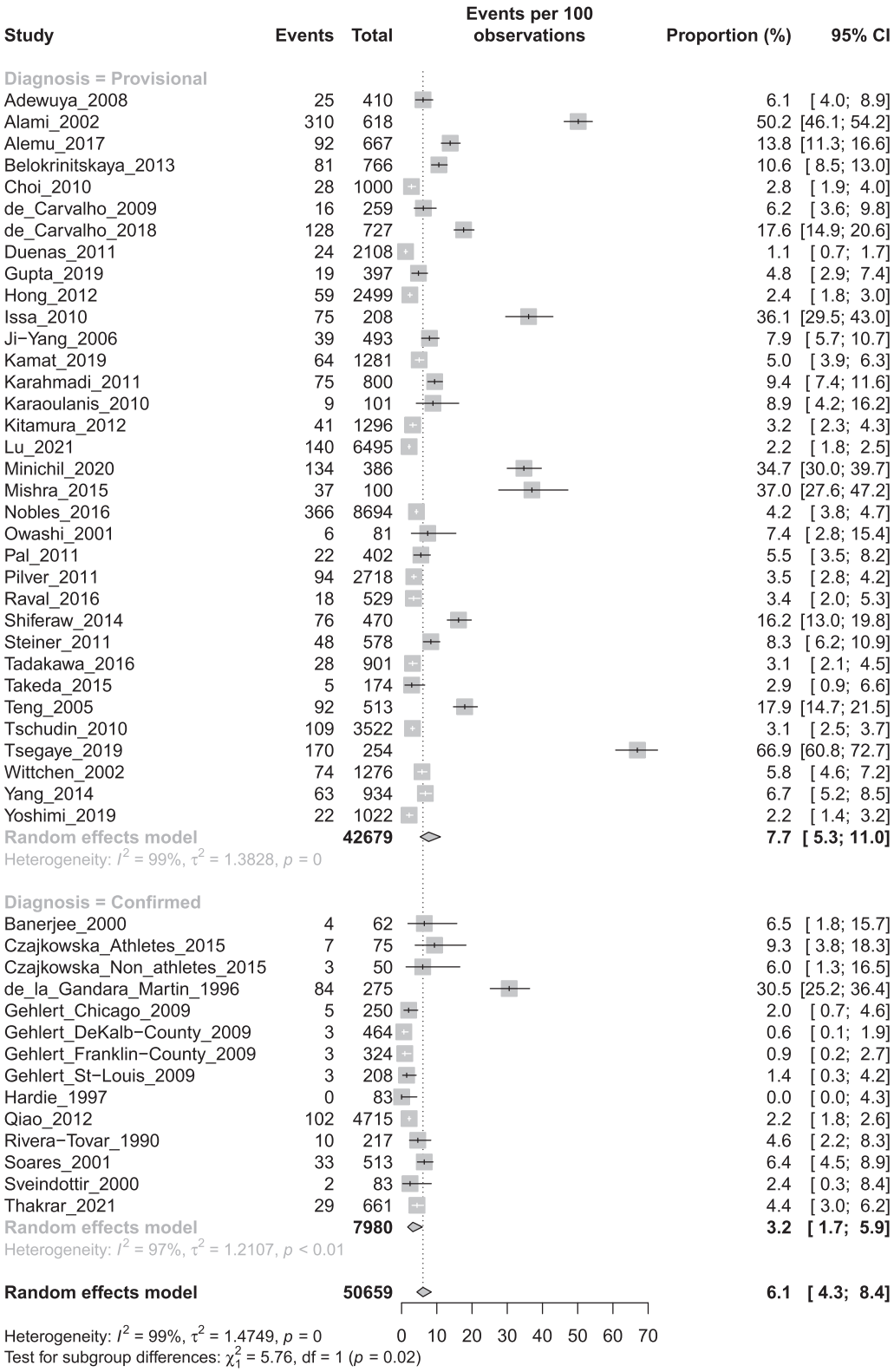

Fig. 2. Forest plot of pooled prevalence in provisional and confirmed diagnosed PMDD.

settings) (4.6 %, 95 % CI: 3.5 %−6.0 %), as shown in Supplementary Fig. 7.

Restricting the analysis to community-based samples, that strictly followed DSM diagnostic criteria of two cycles of symptom tracking (Soares et al., 2001 was therefore excluded for only tracking symptoms over one cycle), resulted in six samples. The pooled prevalence was 1.6 % (95 % CI: 1.0 %–2.5 %), with low heterogeneity ($I^2 = 26$ %), as shown in Fig. 3.

4. Discussion

This is the first meta-analysis of the PMDD prevalence across

Table 1
Univariate meta-regression of potential moderators, diagnosis (confirmed, provisional), continent (North America, Africa, Asia, Europe and Australia, South America), sample type (community-based, university, high school, other), risk of bias. τ is an estimate of between study variance, I^2 is variation in effect size due to heterogeneity.

		Beta-coefficient (95 % confidence interval)	*p* value	τ^2	I^2
Diagnosis	Provisional	0.93 (0.16–1.70)	0.017	1.34	98.44 %
Continent			<0.0001	0.75	96.93 %
	Africa	2.62 (1.75–3.48)	<0.0001		
	Asia	0.62 (−0.08–1.31)	0.084		
	Europe and Australia	0.57 (−0.27–1.41)	0.185		
	South America	1.65 (0.50–2.80)	0.005		
Sample type			0.007	1.17	98.13 %
	High school	0.073 (−0.94–1.08)	0.888		
	Mixed/other	−0.13 (−1.21–0.95)	0.811		
	University	1.15 (0.43–1.88)	0.002		
Risk of bias		−0.27 (−0.47 to −0.067)	0.009	1.29	98.38 %

countries and the first to use meta-regression to explore sources of heterogeneity. We identified many studies reporting the prevalence of PMDD; however, the majority did not use prospective symptom ratings and therefore would only be considered provisional diagnoses according to DSM criteria (American Psychiatric Association, 2013). When restricted to studies fully adhering to DSM diagnostic criteria for confirmed diagnosis, in community-based samples, the pooled prevalence was 1.6 % (95 % CI: 1.0 %–2.5 %). Our findings have clinical implications, in showing different prevalence based on diagnostic methodology, as well as being relevant for public health by estimating the pooled prevalence of PMDD in the general population.

Restricting our analysis to studies that fully met DSM criteria substantially reduced the heterogeneity. Using prospective ratings allows for an accurate assessment of the number of participants in a given population who meet criteria for PMDD at a timepoint. However, it will not include those who may have a diagnosis of PMDD that is currently in remission, for example, due to pregnancy, suppression of the menstrual cycle or effective treatment with SSRIs. The lifetime prevalence of PMDD will therefore be higher. Furthermore, it was outside the scope of our review to consider other disorders associated with the menstrual cycle, such as premenstrual exacerbation of an underlying mental disorder or premenstrual syndrome, and whether or not participants were naturally cycling or using hormonal contraception. We are unable to identify whether there is a proportion of individuals not meeting strict diagnostic criteria for PMDD, who are nevertheless impaired by a premenstrual disorder or progestogen induced disorder. Since most studies did not explicitly exclude participants who were prescribed oral contraceptives or other ovulation-suppressing medication (which by inhibiting the natural menstrual cycle, precludes the diagnosis of PMDD), prevalence rates may be underestimated.

None of the studies of confirmed diagnosis used DSM-5. The main difference between this and previous DSM versions, is that interference with functioning is no longer required for diagnosis, provided the patient reports significant clinical distress. It is plausible that applying these new criteria would result in a higher prevalence estimate. Indeed, the largest prospective study (Gehlert et al., 2009) report that when the diagnosis was made solely by symptom change (irrespective of functioning or whether symptoms were better accounted by another disorder), the prevalence increased from 1.3 % to 5.5 %. Another subtle update in DSM-5 is requiring 'at least two symptomatic cycles' rather than 'at least two consecutive cycles'. In both versions, symptoms should be present in the majority of cycles. This slight relaxation could increase the prevalence slightly in clinical practice where a patient may monitor symptom changes over a longer-period than two months, but is unlikely to affect research studies, where tracking symptoms for even two cycles is logistically challenging. DSM-5 requires a total of five cyclical symptoms for a diagnosis but one study suggests a count of four symptoms would better predict clinically significant impairment (Schmalenberger et al., 2017). Reducing the required number of symptoms, may increase the number of individuals meeting diagnostic criteria.

Notably, the pooled prevalence was significantly higher for provisionally diagnosed PMDD 7.7 % (95 % CI: 5.3 %–11.0 %), suggesting that this method of diagnosis overestimates the true prevalence. It is in keeping with previous studies suggesting that a proportion of provisional diagnoses will not meet criteria when symptoms are confirmed prospectively. It is concerning that so many studies of prevalence, and many other research studies of PMDD, rely on this diagnostic method. A previous meta-analyses in India did not subgroup by diagnosis and found pooled prevalence of 8 % (95 % CI: 6 %–10 %) (Dutta and Sharma, 2021). A meta-analysis of adolescents in Ethiopia found a strikingly high pooled prevalence of 54.5 % (95 % CI: 40.8 %–67.6 %) (Duko et al., 2021). These estimations are likely inflated by a reliance on studies using provisional diagnoses. When studies were categorised according to type of measure used, the prevalence of PMDD was lower among those that used a recognised measure compared to those that did not (4.9 % vs 16.6 %, respectively); however, studies using recognised measures still showed high heterogeneity (I^2 = 98 %). Although the prevalence estimates obtained from studies employing validated measures are closer to that of the gold-standard of prospective symptom monitoring, the lack of agreement of retrospective reporting of symptoms with confirmed diagnosis of PMDD raises questions about the criterion validity of these questionnaires.

Our finding that the vast majority of participants sampled prospectively do not meet diagnostic criteria for PMDD, is strong evidence that the diagnosis is not simply a medicalisation of normal female physiology, as some have argued (Offman and Kleinplatz, 2004). It is in keeping with the conceptualisation of a small proportion of females experiencing abnormal reaction to the hormonal fluctuations associated with the menstrual cycle (di Scalea and Pearlstein, 2019). Similarly, our finding that prevalence rates are higher in the African continent than in Europe or North America does not support the idea that PMDD is a

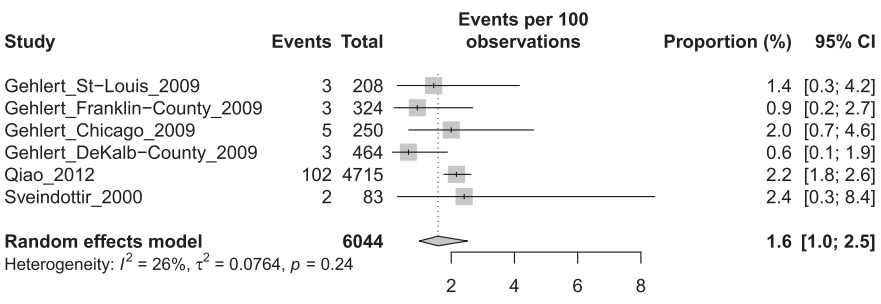

Fig. 3. Forest plot of studies from community-based samples with confirmed diagnosis of PMDD.

Western culture-bound syndrome, as others have suggested (Browne, 2015). Though it should be noted that all samples from Africa used provisional diagnosis, so may be an overestimation of the true prevalence.

There was very high heterogeneity ($I^2 = 99$ %) when all studies were included. Univariate meta-regression suggested that continent of sample, sample type, method of diagnosis, and risk of bias contributed to this heterogeneity. A major limitation of this study is that only a small number of samples ($n_{samples} = 6$), from three studies, could be included in the meta-analysis of PMDD meeting full DSM criteria in community settings. Although our pooled prevalence of these studies is precise with low heterogeneity, it is based on a relatively small number of participants ($n_{participants} = 6044$). A further limitation is that four of the six samples were derived from a single study (Gehlert et al., 2009), potentially violating the independence assumption. However, as these four samples were recruited from distinct geographical regions and varied in terms of sample demographics, it is appropriate to consider these samples independent.

Future studies of PMDD should adhere to current DSM guidelines and use prospective ratings over two menstrual cycles to confirm a diagnosis. This is necessary to assess the presence or absence of the disorder and thus to have accurate prevalence rates. Whether applying DSM-5 criteria or ICD-11 criteria (neither of which requires impairment of functioning if significant clinical distress is present) affects the prevalence rate of PMDD should be answered by future prospective studies. While the prospective method is considered the gold-standard for accurate diagnosis and is part of DSM criteria, it should be noted that not all patients are able to complete symptom-ratings. This could be due to the severity of their symptoms, co-morbid psychiatric disorders, lack of motivation, or lack of literacy. Large studies of prospectively diagnosed PMDD have also shown that more than a quarter of participants dropped-out before providing symptom-ratings over two menstrual cycles or had data that was not useable (Gehlert et al., 2009). This high dropout rate threatens the ecological validity of prospective ratings. Therefore, developing a diagnostic method that provides both a reliable diagnosis while minimising burden to participants is sorely needed.

In conclusion, studies using DSM criteria for a confirmed diagnosis of PMDD in community-based samples have a pooled point prevalence of 1.6 % of menstruating females. This is lower than has previously been reported. It is likely an underestimation of the lifetime prevalence of PMDD, but emphasises that at a given timepoint there is a minority of women with symptomatic PMDD who would benefit from effective, evidence-based treatment (RCOG, 2017).

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CRediT authorship contribution statement

Thomas J. Reilly: Conceptualization, Data curation, Formal analysis, Project administration, Writing – original draft, Writing – review & editing. **Siya Patel:** Data curation, Formal analysis, Methodology, Project administration, Writing – original draft. **Ijeoma Unachukwu:** Data curation, Methodology, Project administration. **Clare-Louise Knox:** Writing – review & editing. **Claire A. Wilson:** Methodology, Writing – review & editing. **Michael C. Craig:** Supervision, Writing – review & editing. **Katja M. Schmalenberger:** Supervision, Writing – review & editing. **Tory A. Eisenlohr-Moul:** Supervision, Writing – review & editing. **Alexis E. Cullen:** Methodology, Supervision, Writing – review & editing.

Declaration of competing interest

We declare no competing interests.

Data availability

The collected study-level data and R scripts for analyses are available on request to the corresponding author.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jad.2024.01.066.

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