

Lifetime Prevalence and Risk Factors for Perinatal Depression in a Large Cohort of Women with Depression

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Abstract

Objectives

Amongst women with a history of depression, this study sought to identify risk factors associated with reporting perinatal depression (PND)). Lifetime prevalence, length and severity of PND were evaluated, as well as the effect of PND onset either after previous depression episodes, or as the first episode of depression.

Setting

The Australian Genetics of Depression Study (AGDS), an online case cohort study of the etiology of depression.

Participants

In a large sample of parous women who met DSM criteria for major depressive disorder (MDD) (n=7,182), we identified two subgroups of PND cases (Edinburgh Postnatal Depression Scale score ≥ 13) with and without prior depression history (n=2,261; n=878 respectively). For a range of risk factors, both subgroups were compared to women with MDD who did not report depressive symptoms in the perinatal period (non-perinatal depression (NPD) cases). PND cases with prior depression history were compared to NPD cases with depression onset before their first pregnancy (n=672). PND cases without prior depression history were compared to all NPD cases (n=2,124).

Primary and secondary outcome measures

Descriptive measures reported lifetime prevalence, length, and severity of PND. Logistic regression compared a range of characteristics of PND cases to those of the comparison group of NPD cases.

Results

Of women who experienced depression prior to first pregnancy, PND cases were significantly more likely to report more episodes of depression (OR=1.1 per additional depression episode, CI=[1.1-1.1], $P=1.9e-13$), non-European ancestry (OR=1.5, CI=[1.0-2.1], $P=3.4e-02$), severe nausea during pregnancy (OR=1.3, CI=[1.1-1.6], $P=6.6e-03$) and emotional abuse (OR=1.4, CI=[1.1-1.7], $P=5.3e-03$). Women without any depression before their first perinatal episode were significantly more likely to report emotional abuse (OR=1.3, CI=[1.1-1.6], $P=1.0e-02$) than women with NPD.

Conclusions

The majority of parous women in this study experienced PND, associated with more complex, severe depression. Results highlight the importance of perinatal assessments of depressive symptoms, particularly for women with a history of depression or childhood adverse experiences.

Strengths And Limitations Of This Study

- Largest study of its kind, comparing characteristics of women with perinatal depression to those of women with non-perinatal depression.
- Reports detailed characteristics of women with PND but with different psychiatric histories.
- An online questionnaire, with no personalized interviews or clinical reports to provide supporting evidence for self-reported data.
- Reliance on self-report information years after experiencing PND could lead to recall bias.
- The AGDS cohort is mostly young and well-educated and may not generalize to the entire population.

Introduction

Background

Perinatal depression (PND), including both antenatal and postpartum depression, commonly classified as a subtype of major depressive disorder (MDD)¹, carries serious risk for both mother and infant. An estimated 53% of women with postpartum depression have “high suicidality”², whilst the rate of self-harming thoughts is three times that of the postpartum community population³. Estimated economic costs of PND in the UK, of which 72% are for ongoing care of the child⁴ reflect findings that children of women with persistent and severe PND are at increased risk of adverse outcomes^{1,5}.

The diagnostic criteria for MDD and PND are the same⁶, but the strongest known PND risk factor is a previous diagnosis of any psychiatric disorder^{1,7-10}, not only MDD¹¹. Other risk factors may also increase PND vulnerability. Possible psychosocial factors include stress and history of abuse¹² whilst biological factors include changes that accompany pregnancy, such as hormonal fluctuations and increased inflammation^{13,14}.

The complexity of these risk factors contribute to ongoing debate about the heterogeneous nature of PND in relation to MDD; in particular, whether it is simply another episode of MDD that happens to coincide with the perinatal period¹⁵; or a subset of MDD, termed “reproductive depression”, stimulated at times of hormone fluctuation such as pre-menstruation, peripartum and menopause^{16,17}; or a distinct disorder, stimulated by changes occurring during pregnancy and confined to the perinatal period¹³. One suggestion is that PND is itself heterogeneous^{10,18}, with clinical subtypes differentiated by timing and severity of symptoms, perinatal complications, and history of psychiatric disorders. Silverman et al.⁷ examined PND heterogeneity according to previous psychiatric disorders, and suggested two PND pathways: as a further episode of MDD occurring peripartum; or, alternatively, through perinatal complications leading to disengagement from the infant. However, a comprehensive investigation of the characteristics of women with PND, with and without a prior psychiatric history, has not been attempted.

Objectives

Using the Australian Genetics of Depression Study (AGDS), a large cohort study with over 20,000 participants self-reporting a depression diagnosis¹⁹, we examined PND heterogeneity, based on the presence or absence of previous major depression history. We sought to address two questions:

1) What are the differences in clinical and psychosocial characteristics between women with and without PND after a depressive episode prior to their first pregnancy?

2) What are the differences in clinical and psychosocial characteristics between women whose first episode of depression was during the perinatal period and parous women who have also experienced depression, but never during any perinatal period?

Method

Study Design

Within a case cohort study of the etiology of depression, two groups of PND cases and two comparison groups of NPD cases were identified according to their history of prior depression. For both PND groups, the length and severity of their “worst case” of PND was measured. To investigate risk factors associated with PND after a previous history of psychiatric disorders, or as first onset depression, both PND groups were compared with their comparison group of NPD cases, across a range of variables.

Setting: The Australian Genetics of Depression Study

The AGDS is a large ongoing case cohort study of the etiology of depression that recruited 20,689 participants (aged between 28 and 58 years; 75% female) during 2016-2018. The analyses conducted here are from participants enrolled prior to the initial data freeze in September 2018. Recruitment was primarily through a media campaign (86%) as well as specific invitations to women who had responded to a mobile phone app focused on PND, originally developed in the USA²⁰, and also ascertainment through the Pharmaceutical Benefits Scheme prescription records for antidepressants, which requested participation from anyone with a depression diagnosis from a health professional. For further details of the recruitment strategy, see Byrne, et al. ¹⁹.

AGDS participants were invited to complete an online questionnaire. A compulsory core module assessed self-reported psychiatric history, the Composite Interview Diagnostic Interview Short Form (CIDI-SF) which assesses the Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-V) criteria for MDD⁶, and experiences of using commonly prescribed antidepressants. Women reporting symptoms of

depression during pregnancy or up to 6 months following childbirth were asked to complete the lifetime Edinburgh Postnatal Depression Scale (EPDS)²¹, an adaptation of the standard EPDS²² that assesses lifetime PND episodes. They were also asked whether symptoms of depression occurred during pregnancy, after giving birth, or both, the age at which they experienced their worst episode of PND, its severity and duration. For all AGDS participants, further voluntary modules assessed history of psychiatric health conditions and stressful life events. The AGDS protocol was approved by the Human Research Ethics Committee of QIMR Berghofer Institute for Medical Research.

Participants: PND cases and comparison groups

Participants with major depression either met DSM-V criteria for MDD, or had been previously diagnosed with depression by a health professional. PND cases were defined as women reporting at least one live birth who had been previously diagnosed with PND by a health professional, or who scored ≥ 13 on the lifetime EPDS, or who met criteria for major depression and reported at least one perinatal episode.

We identified two groups of cases, based on whether they had a history of MDD prior to their first PND episode. Parous participants who reported an episode of depression before their first pregnancy and met PND criteria (PND_priorDep) were compared with parous participants who reported an episode of depression before their first pregnancy, but did not experience any depression associated with childbirth (NPD_priorDep). The second group comprised participants whose first episode of depression occurred during the perinatal period (PND_firstDep), compared to participants with depression onset at other times, but never during any peripartum period (NPD_all). The NPD_priorDep that forms the comparison group for the PND_priorDep sample is a subset of the NPD_all comparison group. It was expected that, given the early onset of major depression (before first pregnancy) the NPD_priorDep would have more severe depression than the full NPD_all comparison group and might more closely match the PND_priorDep cases. Fig. 1 and Supplementary Table S1 illustrate sample selection. Further details are provided in Supplementary Methods.

Figure 1 about here

Variables

The outcome of interest was a PND episode for women with either a history of previous depressive episode(s), or no previous depression history. An exposure to a PND episode is defined as the period of time from conception up to six months postpartum, so that the number of reported live births represents

the number of exposures. The cross-sectional nature of our study meant that no direction of causality could be assessed, but we investigated risk factors for PND using variables that have previously been associated with PND^{1,23,24}, including severity of depression; ancestry; comorbidity with other psychiatric disorders; adverse childhood experiences; reproductive traits and response to antidepressants.

We investigated previous history of depression as a modifier of the effect of each variable, by conducting two separate analyses of PND cases categorized as PND_priorDep or PND_firstDep, for both descriptive and comparative measures. For comparative measures each of the two PND groups was compared to an appropriate comparison group. A further effect modifier is the time of onset of PND: during pregnancy, after delivery, or both. For both samples, a sensitivity analysis was conducted to investigate the effect of PND onset both during and after pregnancy.

Descriptive measures for cases

Clinical characteristics of PND cases included the length and severity of the worst PND episode. For both groups, the length of the PND worst episode was calculated, according to detailed occurrence before or after delivery. Length of the worst PND episode was measured using a 5 point scale: "Up to two weeks", "2-4 weeks", "1-3 months", "3-6 months", "More than 6 months". Details of occurrence included trimester of pregnancy or length of time after delivery.

Severity of the worst PND episode was measured using the level of interference with functioning, defined as the need for any of the following: professional help, medication, and hospitalisation. More than one of the three measures could be chosen.

Comparative measures

Case and comparison groups were compared on a range of variables that have previously been identified to be associated with PND^{1,23}. Demographic measures included current age, marital status, education and ancestry. A list of geographical regions from which ancestry is identified is provided in Table S2. More details are provided in Supplementary Methods. Clinical measures included the number and severity of episodes of major depression, history of childhood trauma and sexual or other physical assault, and previous diagnoses of psychiatric disorders. Eighteen psychiatric disorders were listed, of which twelve, identified by more than 3% of participants, were used in this study (Table S3). Reproductive measures included age at menarche, parity, age at first birth, presence and severity of nausea and vomiting during pregnancy (NVP), and previous diagnosis of gestational diabetes, endometriosis or polycystic ovarian syndrome. Antidepressant measures included the number of antidepressants that had been tried, their efficacy and any side-effects. More details of these measures are provided in Supplementary Methods, which also lists the questions used to assess each characteristic.

Potential sources of bias

Two variables, number of births and age, significantly associated with PND, were identified as exposure and confounder respectively. Each birth represents an additional exposure to PND, whilst the negative association of PND with increasing age may reflect increasing awareness and diagnosis of the disorder, or imprecise memory of past events. Reliance on self-report information years after experiencing PND could lead to recall bias, although the inclusion of age as a covariate in regression analyses may alleviate this trend and participants who provided contradictory evidence were excluded from analysis. The lifetime EPDS used to assess PND is a screening, rather than diagnostic tool and may result in overestimation of PND case status²⁵, although O'Connor et.al.²⁶ reported a sensitivity of 0.8 for the EPDS in identifying MDD with a cut-off score ≥ 13 , and a specificity of 0.9. The lifetime EPDS is a modification of this scale which has demonstrated internal consistency²¹.

Statistical Analysis

For both priorDep and firstDep groups, length and severity of the worst reported episode of PND was calculated, and logistic regression measured the association of depression length with early onset of PND (first trimester of pregnancy or within 4 weeks of delivery). Associations between variables and PND were assessed using logistic regression, with PND the dependent variable, separately for both priorDep and firstDep groups, including age at survey time and number of births as covariates.

All modules apart from the first were optional, and some categories applied only to a limited number of participants (for example, those who had used at least one antidepressant). For these reasons, the number of participants who completed each category or variable varied. For each variable, the number of respondents is reported. Within each category, analysis employed Bonferroni correction for multiple testing (N=number of tests within each category).

Finally, to evaluate whether effect sizes were influenced by time of PND onset, we conducted a sensitivity analysis that included only women who reported experiencing PND both before and after delivery. We conducted this analysis separately for both PND_priorDep and PND_firstDep samples.

All analyses were conducted using R (version 3.6.0). Figures were generated using ggplot2²⁷ and Gliffy software²⁸.

Results

Lifetime prevalence of depression during the peripartum period

Just over 97% of AGDS participants (n= 20,191) reported previous diagnosis of depression by a health professional, of whom 88% met DSM-V criteria for MDD. The remaining 12% either did not complete the CIDI-SF, or did not meet DSM criteria. Of these participants with major depression, 75% (n=15,198) were female with median age of 39. Among female participants, 7,182 (47%) reported at least one live birth, and, of these, 5,058 (70%) met criteria for PND.

Of the 7,182 parous women, 2,933 reported a history of major depression prior to first pregnancy. At least one episode of PND (PND_priorDep) was reported by 2,261 (77%) of these 2,933 women, whilst the remaining 672 women with no PND episodes (23%) formed their comparison group (NPD_priorDep). A total of 878 women reported that their first episode of depression occurred during pregnancy or within the first 6 months after delivery (PND_firstDep), whilst all women who met criteria for major depression, had given birth to at least one child but did not satisfy criteria for PND (NPD_all, n=2,124) formed its comparison group. Of women who met criteria for PND, 1,919 were unable to be categorized as PND_priorDep or PND_firstDep and were lost to further analysis. Fig. 1 and Supplementary Table S1 provide details of the sample selection process. Table 1 shows the reported time of onset of symptoms (for any PND episode) for both case groups (only during pregnancy, only after delivery, or both before and after delivery).

Table 1. Reported timing of symptoms of perinatal depression among women with PND. Results are shown for all those meeting PND criteria and separately for those with a prior history of major depression (PND_priorDep) and those whose first onset of major depression was perinatal (PND_firstDep).

	During pregnancy only	After delivery only	Both during pregnancy and after delivery	Missing
All PND cases (N=5,058)	295 (6%)	1,627 (32%)	3,073 (61%)	63 (1%)
PND_priorDep (N=2,261)	144 (6%)	592 (26%)	1,507 (67%)	18 (1%)
PND_firstDep (N=878)	28 (3%)	325 (37%)	510 (58%)	15 (2%)

The reported length of the worst episode of PND is shown in Fig.2 for PND_priorDep and in Fig.3 for PND_firstDep. Full details are provided in Table S4. For both groups of cases, PND was most commonly reported to have lasted for more than six months. The most commonly reported time of PND onset for

women whose episode began during pregnancy was during the first trimester, and for those whose episode began after delivery was within 0-4 weeks. Both PND_priorDep and PND_firstDep were more likely to report that their worst episode began after delivery (66% and 79% respectively), including 60% of PND_priorDep cases and 72% of PND_firstDep cases who had reported that they experienced PND both before and after delivery. This difference between the groups is significant, with PND_firstDep having 2.0 times the odds of reporting postpartum onset of worst case symptoms (CI=[1.7-2.4], P=4.6e-13) compared to the odds of PND_priorDep. For both groups, symptom onset in the first trimester or 0-4 weeks postpartum was associated with longer duration of symptoms, significantly so for PND_priorDep (Table S4).

Figure 2 about here

Figure 3 about here

For both groups, more than 60% required some sort of professional help, although less than 45% of women reported using medication to deal with this worst episode (Fig.4, Table S4).

Figure 4 about here

Clinical and psychosocial risk factors for PND in parous women

Table S5 provides the number and percentage of participants that completed each of the risk factor variables, for both priorDep and firstDep groups.

Clinical and psychosocial risk factors for PND in parous women with a history of depression.

We investigated which risk factors are associated with PND in women with a previous history of depression. Age at enrolment (OR [PND case status]=0.97 per additional year of age, CI=[0.96-0.98], P=2.3e-17), and number of births (OR [PND case status]=1.3 per additional birth, CI=[1.2-1.4], P=4.7e-07) were significantly associated with PND. Both age and number of births were included as covariates in subsequent analyses, which were also adjusted for multiple testing. Fig. 5 illustrates nominally significant results after the inclusion of covariates, with details of all results provided in Table S6.

Figure 5 about here

Ancestry (both non-European and Australian Indigenous) was significantly associated with PND (non-European: OR=1.5, CI=[1.0-2.1], P=2.8e-02; Australian Indigenous: OR=2.3, CI=[1.2-4.8], P=2.4e-02), although after correction for multiple testing, only Australian Indigenous remained significant. There was no association between marital status or level of education and PND. On all measures, PND_priorDep reported more severe depression than NPD_priorDep (Fig. 5), although as expected, the NPD_priorDep comparison group also experienced significantly more severe depression than the NPD_all comparison group on all measures (Table S7).

Five of twelve psychiatric disorders (premenstrual dysphoric disorder (PMDD), attention deficit hyperactive disorder (ADHD), anxiety disorder, post-traumatic stress disorder (PTSD), and social anxiety disorder) were significantly associated with PND, although none survived Bonferroni correction. There was a significant association between PND and a history of self-reported childhood emotional abuse (OR=1.4, CI=[1.1-1.7], P=5.5e-03) and neglect (OR=1.3, CI=1.0-1.6], P=3.1e-02) and physical neglect (OR=1.4, CI=[1.1-1.9], p=2.3e-02), although only emotional abuse survived Bonferroni correction.

There was no association between age at menarche and PND and no significant difference in the incidence of gestational diabetes, polycystic ovarian syndrome or endometriosis. Although there was no significant difference in the incidence of NVP for PND compared to NPD cases (P = 0.11), there was a significant difference in the severity of NVP between PND_priorDep and NPD_priorDep. For PND_priorDep, the odds that a woman with PND had experienced disruptive nausea during pregnancy, compared to NPD_priorDep, is 1.3 (CI=[1.1-1.6], P=6.6e-03), significant after Bonferroni correction.

PND_priorDep were significantly more likely to have tried more than three antidepressants than its comparison group (OR=1.4, CI=[1.1-1.8], P=1.4e-03), were less likely to report high efficacy of any antidepressant (OR=0.7, CI=[0.5-0.8], P=5.5e-04), and were 1.5 times more likely (CI=[1.2-1.8], P=3.0e-04) to report at least one side effect for antidepressants, compared with women with NPD_priorDep (including age, number of births and the number of antidepressants tried as covariates in the model) (Fig. 4). All of the 23 side effects were more commonly reported by PND_priorDep, 15 of them significantly so, although only 2 survived Bonferroni correction.

Clinical and psychosocial risk factors associated with PND as first episode of depression.

As there may be unique risk factors associated with onset of depression perinatally, we conducted further analyses to evaluate differences between women who report their first episode occurring perinatally (PND_firstDep) and all NPD cases. Similar to priorDep findings, we found that age at enrolment and number of births were associated with increased risk of PND (Fig S2 and Table S6). After both these variables were included as covariates, PND_firstDep was associated with emotional abuse during childhood, increased likelihood of trying at least 3 antidepressants compared with controls, and increased odds of reporting 13 of the 23 side effects, 5 of which were significant, although no side effects survived Bonferroni correction. No associations were found with other variables. FirstDep results (for variables that

were nominally significant for priorDep) are illustrated in Fig.5 and full details of all results are provided in Supplementary Table S6.

Effect of PND onset on clinical and psychosocial risk factors associated with PND.

Symptoms of PND were experienced both during pregnancy and after delivery by 67% of PND_priorDep and 58% of PND_firstDep. A sensitivity analysis using only these cases found that the odds ratios of variables already significantly associated with these groups increased. For priorDep, association of PND with three comorbidities: anxiety disorder, PTSD and social anxiety disorder remained significant after Bonferroni correction. Sexual abuse at any time became significantly associated with PND for priorDep as well as comorbidity with bipolar disorder, and PMDD became significantly associated with PND_firstDep, although none of these survived Bonferroni correction. Full details are provided in Supplementary Table S8.

Discussion

We investigated lifetime prevalence and correlates of perinatal depression in a large cross-sectional study of depression. This is to date one of the largest studies of perinatal depression among women with major depression. Although previous research highlighted heterogeneity of PND^{7,10}, until now detailed characteristics of women with PND but different psychiatric history have been lacking. Our study has enabled the identification of such characteristics through a comparison of two subsets of PND cases, with and without a prior history of major depression.

We found high lifetime prevalence of meeting criteria for probable PND in this sample, with the majority of women reporting symptoms both during and after pregnancy. Among those with prior history of major depression, PND was associated with more chronic, complicated depression, characterized by earlier onset, more reported episodes, more symptoms during the worst episode and increased likelihood of having a comorbid psychiatric disorder. They had significantly higher rates of reported emotional abuse and neglect and physical neglect during childhood, were more likely to report severe symptoms of NVP and suffer from more side effects to antidepressants. Women with no such prior history, whose first depressive episode occurred during the perinatal period, did not report more severe depression, were no more likely to be comorbid with other psychiatric disorders, apart from PMDD, and no more likely to report severe NVP than women who experienced depression outside the perinatal period. Like PND cases with a prior history of depression, women who experienced PND as their first depressive episode reported significantly more side effects to antidepressants than women with depression without a perinatal episode, and were also more likely to report childhood emotional abuse.

The main limitation of this study is that it is based on an online questionnaire, with no personalized interviews or clinical reports to provide supporting evidence for self-reported data. Answers were based on total life experience, including, but not exclusive to, the perinatal period. Furthermore, the AGDS is a cross-

sectional study. Its strength lies in its sample size, but, unlike a longitudinal study, it provides no information with respect to timing of variables significantly associated with PND (with the exception of childhood adverse experiences), so no inference can be made pertaining to cause and effect. The results of the study should also be considered in the context that the AGDS cohort is mostly young and well-educated, and may not generalize to the entire population.

Despite these limitations, the findings of this study are consistent with previous reports. PND for women with a previous history of depression seems to be more severe and complex than for women who experience PND as first depression onset, supporting the notion of PND heterogeneity according to previous psychiatric history. Prior history of psychiatric disorders, stress, and a history of abuse have emerged as strong predictive factors for PND^{1,7-10,12,29}. PMDD is the severe form of premenstrual syndrome, recently identified as a risk factor for PND³⁰, and NVP has been recognized as the strongest obstetric predictor of PND³¹. Previous studies have also found that women suffering from both MDD and PND had more severe depression and higher incidence of anxiety disorder and childhood trauma than women suffering from MDD alone²¹, and that most severe depression is suffered by women who experience PND both during pregnancy and after delivery¹⁰.

This study found high reported rates of non-response to antidepressants in women experiencing PND for both subgroups. Studies of the efficacy of antidepressants for the treatment of PND have been inconclusive³², and, to our knowledge, increased incidence of side effects amongst women with PND has not been previously reported. Further clinical studies of antidepressant efficacy in PND are warranted, as well as efficacy of alternative treatments.

Finally, complications of pregnancy and birth were not assessed in this study apart from NVP and gestational diabetes, so it was not possible to fully assess whether perinatal complications may contribute to PND vulnerability⁷.

Conclusions

PND is a leading cause of disease for women who give birth, adding to the overall family disease burden and potential cognitive and emotional problems for affected children. This sample of parous women with lifetime major depression found a high rate of PND, particularly for women who experienced an episode of depression before their first pregnancy. There is a compelling literature demonstrating that screening for PND should begin during pregnancy^{26,33}, particularly for women with prior history of depression, which is supported by the finding that the majority of cases in this study experienced PND both before and after delivery. Although women who have been previously diagnosed with major depression are, presumably, under clinical care, it is possible that women may have withdrawn from care if treatment has been ineffective. Standard prenatal care that adopts frequent assessment of depression status provides an opportunity to identify women who might otherwise “slip through the cracks” and ensure that they continue to receive support in finding a successful treatment or in the prevention of relapse²⁶. Our results

also support the screening of childhood adverse experiences and PMDD in pregnancy, given that all women with PND in this study had increased odds of a history of emotional abuse and neglect, as well as increased odds of PMDD. Cases were also more likely to have treatment resistant depression, with increased odds of side effects, supporting further clinical investigation of antidepressant efficacy in PND.

Declarations

Funding Statement

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Competing interests

No conflict of interest has been reported

Availability of data and material

Data used in this analysis and described in this article are available to all interested researchers through collaboration. Please contact NGM.

Ethics approval and consent to participate

All study protocols were approved by the QIMR Berghofer Medical Research Institute Human Research Ethics Committee. The protocol for approaching participants through the DHS, enrolling them in the study, and consenting for all phases of the study (including invitation to future related studies) and accessing MBS and PBS records was approved by the Ethics Department of the Department of Human Services.

Patient consent for participation in the study was obtained.

Authors' Contributions

EMB, SEM, NRW, IBH and NGM designed the AGDS study. JK and EMB analysed the data. JK and EMB drafted the manuscript. SM-B, JM, EB, TM, IBH, LC-C, SEM, NGM and NRW revised the article for intellectual content. All authors have read and approve of the final version.

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Figures

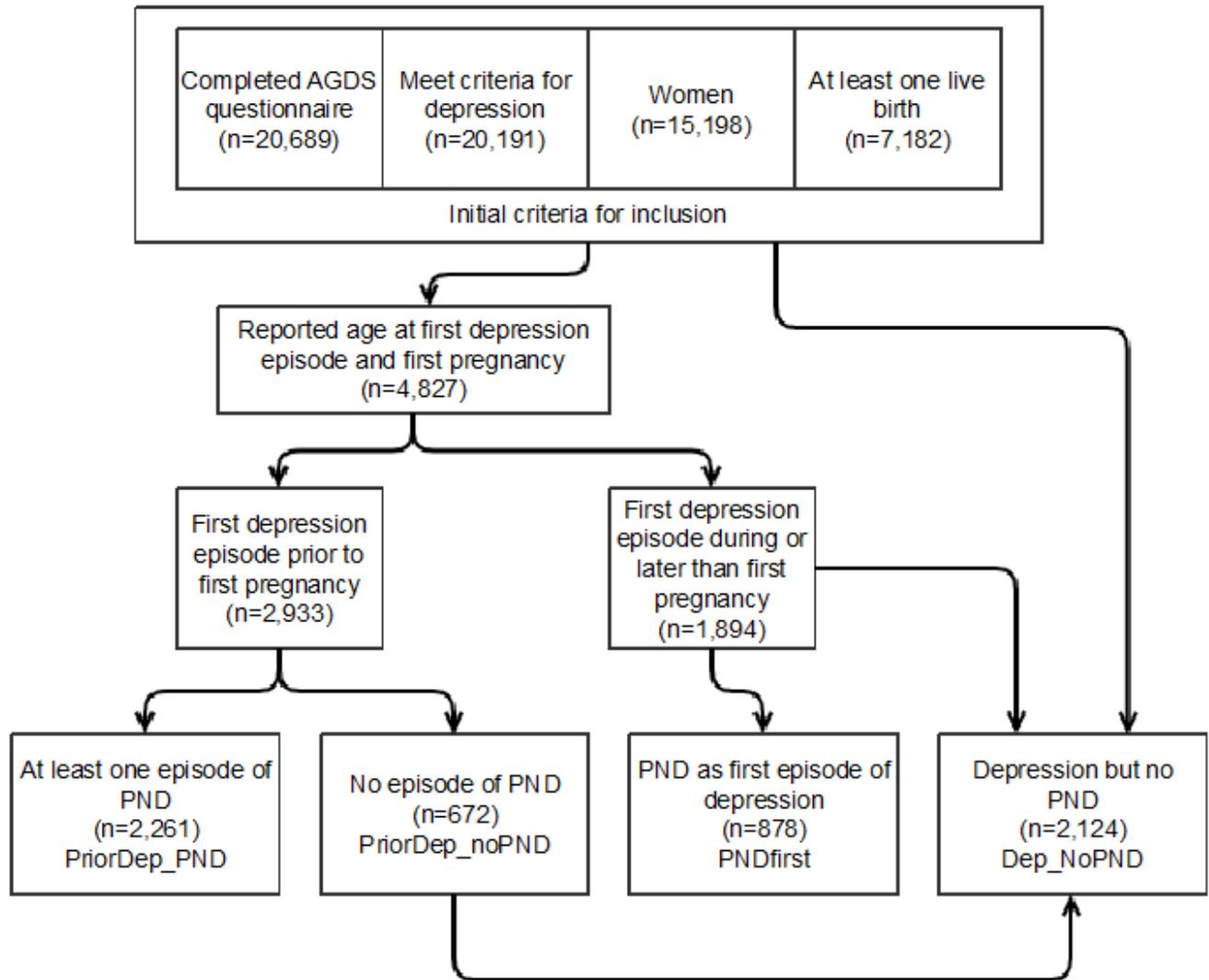


Figure 1

Flow chart: Selection of cases and associated comparative group for first analysis (prior history of major depression) and second analysis (PND is first experience of major depression). Cases met criteria for major depression and had at least one live birth, plus any of: EPDS score ≥ 13 ; a previous diagnosis of PND; or major depression during the perinatal period. Of the comparison groups, NPD_priorDep is a subset of NPD_all. NPD_priorDep was considered to be a more appropriate comparison group for PND_priorDep since members of both these groups experienced an episode of major depression before first pregnancy.

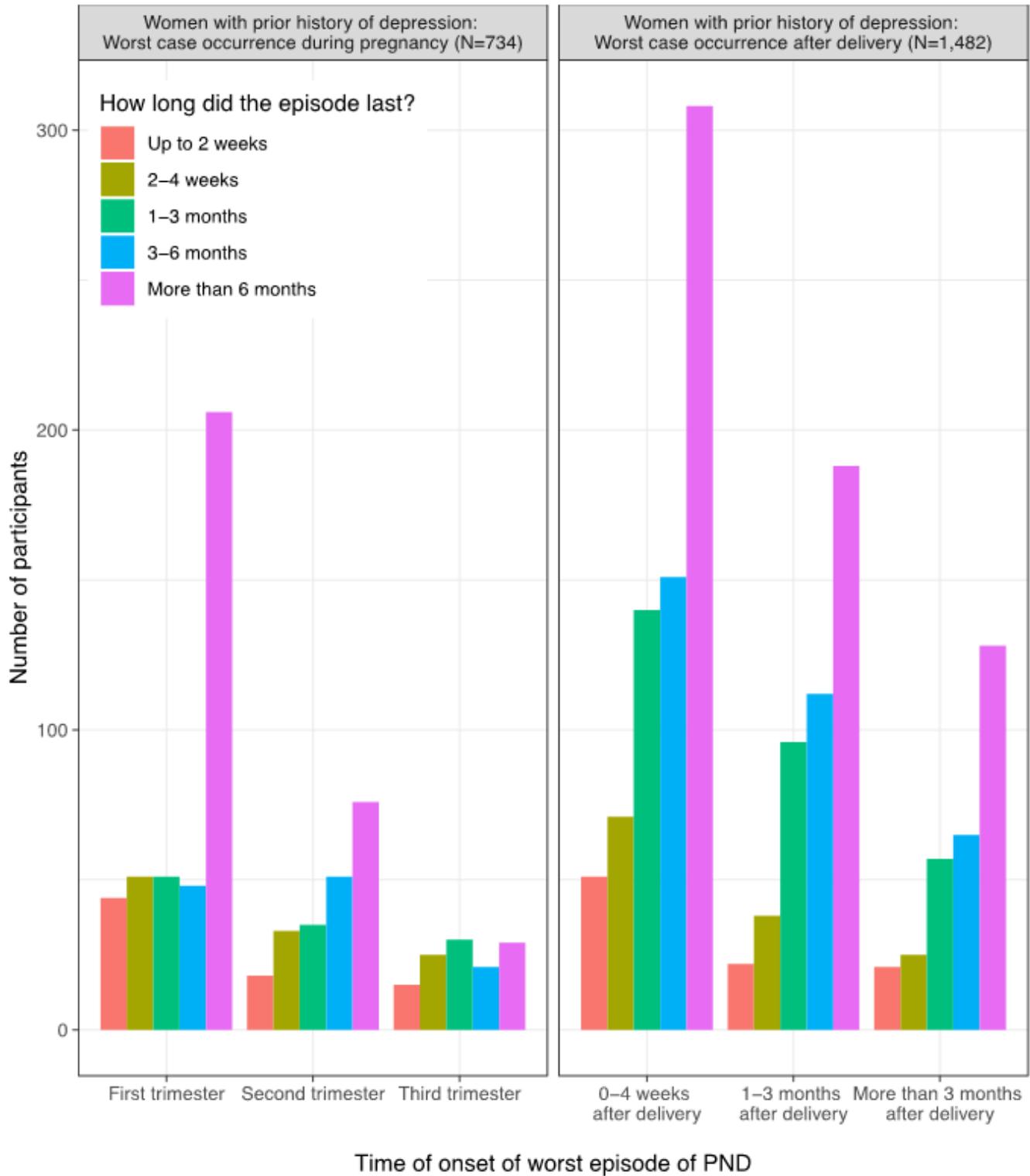


Figure 2

Length of worst episode of symptomatic PND for priorDep cases, for onset either during pregnancy or after delivery. Episode length is divided into 5 categories, and the Y-axis provides the number of women reporting each category, according to the timing of onset.

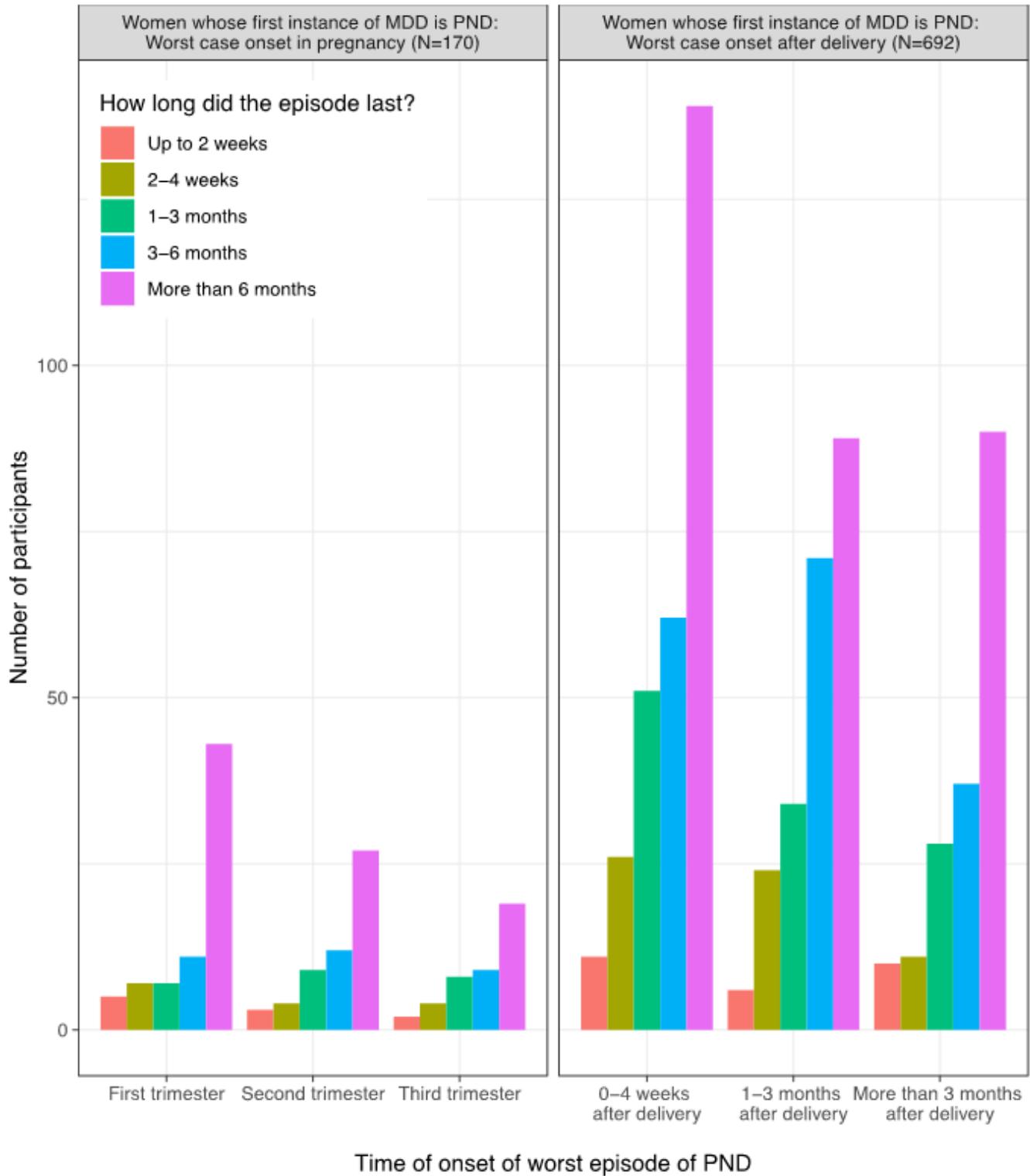


Figure 3

Length of worst episode of symptomatic PND for PND_firstDep cases, for onset either during pregnancy or after delivery. Episode length is divided into 5 categories, and the Y-axis provides the number of women reporting each category, according to the timing of onset.

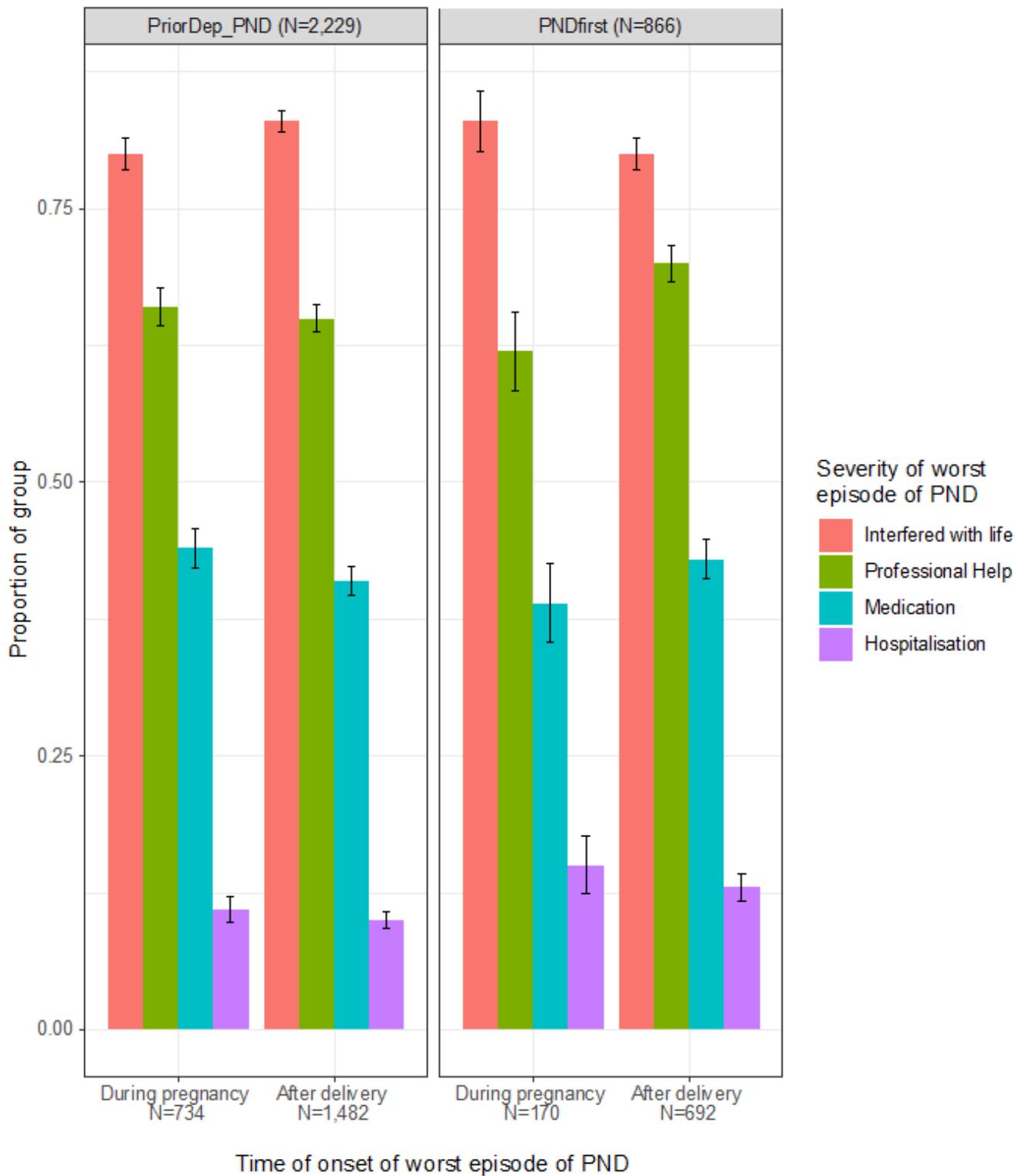


Figure 4

Severity of worst episode of PND for priorDep and PND_firstDep cases, according to the time of onset of the worst episode. Severity is characterised by interference in everyday life, need for professional help, need for medication, and need to be hospitalised. The Y-axis provides the proportion of each group reporting each variable. Standard errors are included.

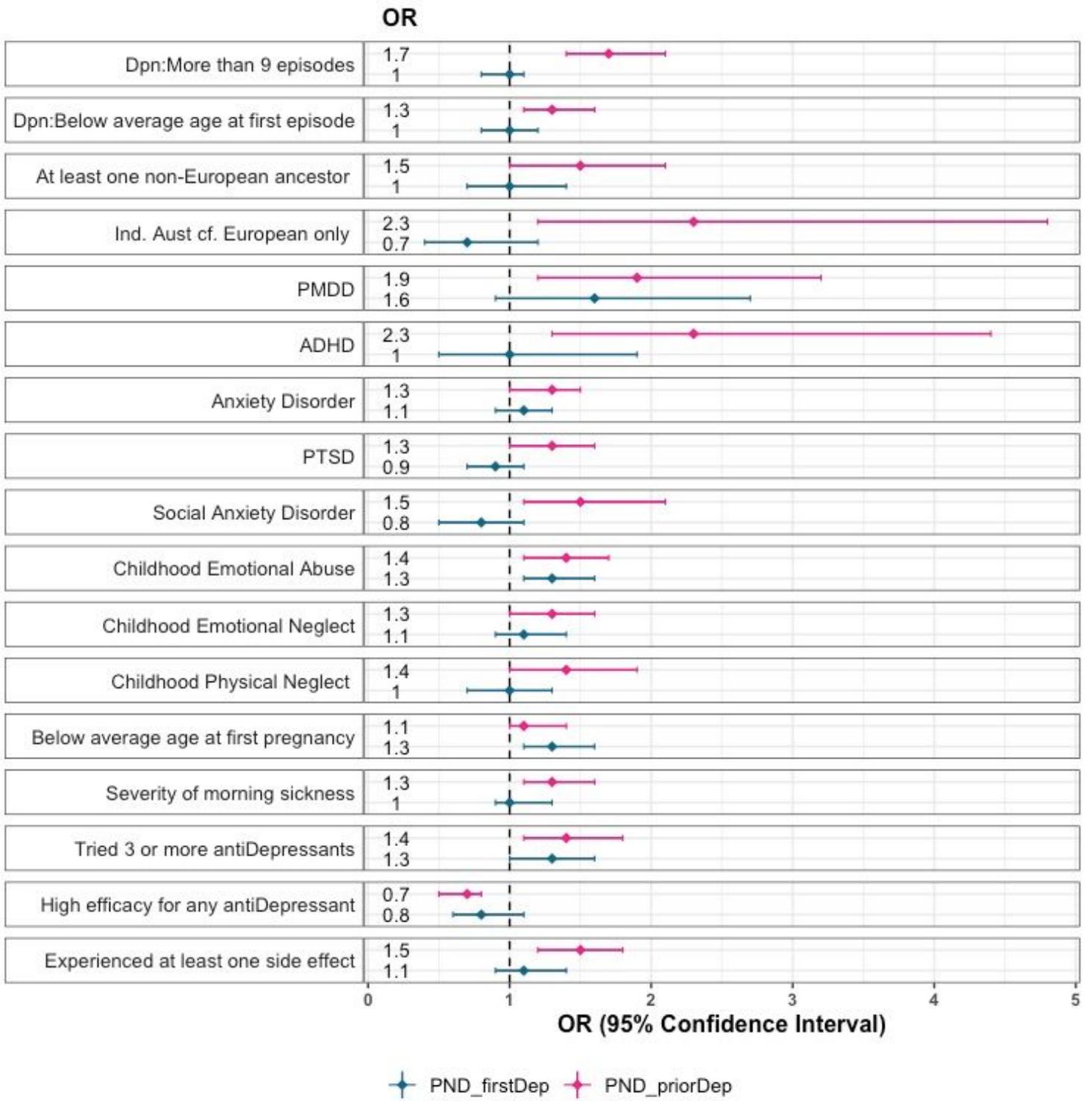


Figure 5

Forest plot of odds ratios with confidence intervals of all variables nominally significantly associated with PND_priorDep cases when compared with NPD_priorDep. Odds ratios for the association of these variables with PND_firstDep cases compared with NPD_all are also included for comparison. Logistic regression, including age and number of live births of participants as covariates, was used to calculate odds ratios.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SupplementaryMethods.docx](#)
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