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

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Abstract

Background

History of psychiatric disorders, particularly depression, is the strongest risk factor for perinatal depression (PND). Yet many women without such history experience their first depression episode perinatally, whilst other women with depression history do not experience any episodes during the perinatal period. PND may itself be heterogenous, according to differences in psychiatric history. However, a comprehensive investigation of characteristics of women with PND, with and without a prior psychiatric history, has not been attempted.

Methods

In a large sample of parous women with depression, we sought to identify risk factors associated with PND after previous depression episodes, or as first-onset depression. Using data from the Australian Genetics of Depression Study, we identified two subgroups of PND cases (Edinburgh Postnatal Depression Scale score >= 13) with and without prior depression history. For both subgroups, we investigated lifetime prevalence, length and severity of PND. Logistic regression compared a range of characteristics of cases to those of a comparison group with major depression without any perinatal episodes.

Results

Criteria for PND was met by 5,058 (70%) of 7,182 parous women who met criteria for major depression. Of women reporting depression onset before first pregnancy, 2,261 (77%) PND cases were compared to 672 (23%) without PND. Among women reporting their first depression episode during or after their first pregnancy, 878 women for whom this first episode was PND were compared to 2,124 parous women who had experienced depression but never perinatally.

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=1.3E-13), non-European ancestry (OR=1.8, CI=[1.3-2.5], P=1.2E-03), 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=2.0E-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=1.1E-02) than women with depression without PND.

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.

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 population (3). Estimated economic costs of PND in the UK, of which 72% are for ongoing care of the child (4) reflect findings (5) that children of women with persistent and severe PND are at increased risk of adverse outcomes.

The diagnostic criteria for MDD and PND are the same (6), but the strongest known PND risk factor is a previous diagnosis of any psychiatric disorder (1, 7–10), not only MDD (11). Other risk factors may also increase PND vulnerability. Possible psychosocial factors include stress and history of abuse (12) whilst biological factors include changes that accompany pregnancy, such as hormonal fluctuations and increased inflammation (13).

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 period (14); or a subset of MDD, termed “reproductive depression”, stimulated at times of hormone fluctuation such as pre-menstruation, peripartum and menopause (15, 16); or a distinct disorder, stimulated by changes occurring during pregnancy and confined to the perinatal period (13). One suggestion is that PND is itself heterogenous (10), 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.

Using the Australian Genetics of Depression Study (AGDS), a large cohort study with over 20,000 participants self-reporting a depression diagnosis (17), 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

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 (n = 20,395; 99%) which requested participation from anyone with a depression diagnosis from a health professional. For details of the recruitment strategy, see Byrne (19).

AGDS participants were invited to complete an online questionnaire. A core module assessed self-reported psychiatric history, the Composite Interview Diagnostic Interview Short Form (CIDI-SF) which asseses the Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-V) criteria for MDD (6), 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) (20), an adaptation of the standard EPDS (21) 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 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.

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 (priorDep_PND) were compared with parous participants who reported an episode of depression before their first pregnancy, but did not experience any depression associated with childbirth (priorDep_NoPND). The second group comprised participants whose first episode of depression occurred during the perinatal period (PNDfirst), compared to participants with depression onset at other times, but never during any peripartum period (Dep_NoPND). The priorDep_noPND that forms the comparison group for the priorDep sample is a subset of the Dep_NoPND comparison group. It was expected that, given the early onset of major depression (before first pregnancy) the priorDep_noPND would have more severe depression than the full Dep_NoPND comparison group and might more closely match the priorDep_PND cases. Figure 1 and Supplementary Table S1 illustrate sample selection. Further details are provided in Supplementary Methods.

For both samples, a sensitivity analysis was conducted to investigate the effect of time of onset of PND (both during and after pregnancy).

Measures

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. Severity of the worst PND episode was measured using the level of interference with functioning.

Comparative measures

Case and comparison groups were compared on a range of variables that have previously been identified to be associated with PND (1, 22), including severity of depression; ancestry; comorbidity with other psychiatric disorders; adverse childhood experiences; reproductive traits and response to antidepressants. 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, previous diagnoses of psychiatric disorders, and history of childhood trauma and sexual or other physical assault. 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. Answers were based on total life experience, including, but not exclusive to, the perinatal period.

Statistical Analysis

For both groups, length and severity of the worst reported episode of 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).

For both priorDep and PNDfirst groups, associations between variables and PND were assessed using logistic regression, with PND the independent variable. Exceptions were depression severity and age at survey time, for which PND is the dependent variable. All analysis also included age at survey time as a covariate, given the significant age difference between women who had experienced PND and women who had not. 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 onset of PND, 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 PriorDep and PNDfirst samples.

All analyses were conducted using R (version 3.6.0). Figures were generated using ggplot2 (23) and Gliffy software (24).

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. Of these participants with major depression, 75% (n = 15,198) were female with median age of 39. Among female participants, 7,182 (47%) reported having given 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 (priorDep_PND) 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 (priorDep_noPND). A total of 878 women reported that their first episode of depression occurred during pregnancy or within the first 6 months after delivery (PNDfirst), whilst all women who met criteria for major depression, had given birth to at least one child but did not satisfy criteria for PND (Dep_noPND, n = 2124) formed its comparison group. Fig. 1 and Supplementary Table S1 provide details of the sample selection process. Table 1 shows the reported time of onset of symptoms 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 (priorDep) and those whose first onset of major depression was perinatal (PNDfirst).

	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%)
PriorDep (N = 2,261)	144 (6%)	592 (26%)	1,507 (67%)	18 (1%)
PNDfirst (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 priorDep_PND and in Fig. 3 for PNDfirst. Full details are provided in Table S5. For both groups of cases, PND was most commonly reported to have lasted for more than six months. The most commonly reported time of 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. PriorDep were more likely to report their worst episode to begin during pregnancy (33%), whereas PNDfirst overwhelmingly reported symptoms after delivery (80%). For both groups, symptom onset in the first trimester or 0–4 weeks postpartum was associated with longer duration of symptoms, significantly so for priorDep_PND (Table S5).

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).

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. Figure 5 illustrates nominally significant results and all results are provided in Supplementary Table S6.

Among demographic variables, age at enrolment was significantly associated with PND. Each additional year of age at enrolment was associated with a 0.07 decrease in EPDS score. There was no association between marital status or level of education and PND. Ancestry (both non-European and Australian Indigenous) was significantly associated with PND (non-European: OR = 1.5, CI=[1.1–2.2], P = 2.0E-02; Australian Indigenous: OR = 2.3, CI=[1.2–5.1], P = 1.7E-02).

Five of thirteen 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. PriorDep_PND also reported more severe depression than PriorDep_noPND (Fig. 4).

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 = 2.0E-03) and neglect (OR = 1.3, CI = 1.1–1.6], P = 1.5E-02) and physical neglect (OR = 1.5, CI=[1.1-2.0], p = 1.2E-02), although only emotional abuse survived Bonferroni correction.

PND was significantly associated with the number of births, with the average number of live births being 2.1 for priorDep_PND compared to 1.9 for priorDep_noPND. 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 all cases (P = 0.11), there was a significant difference in the severity of NVP between PriorDep_PND and PriorDep_NoPND. For PriorDep_PND, the odds that a woman with PND had experienced disruptive nausea during pregnancy, compared to PriorDep_NoPND, is 1.3 (CI=[1.1–1.6], P = 6.6E-03), significant after Bonferroni correction.

PriorDep_PND 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), and were 1.5 times more likely (CI=[1.2–1.8], P = 4.6E-04) to report at least one side effect for antidepressants, compared with women with PriorDep_NoPND (including age and the number of antidepressants tried as covariates in the model) (Fig. 4). All of the 23 side effects were more commonly reported by PriorDep_PND, 16 of them significantly so, although only 4 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 (PNDfirst) and those who did not experience PND. Similar to priorDep findings, we found that age at enrolment, age at first birth, number of births, and emotional trauma in childhood were associated with increased risk of PND (Fig. 4). PNDfirst also reported increased likelihood of trying at least 3

antidepressants, and experiencing 17 of the 23 side effects compared with controls, 4 of which were significant, although none survived Bonferroni correction. No associations were found with other variables. Full details of all results are provided in Supplementary Table S6.

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

Symptoms of PND were experienced both during pregnancy and after delivery by 67% of priorDep_PND and 58% of PNDfirst. For these cases, the odds ratios of variables already significantly associated with these groups increased. For priorDep, association of PND with three comorbidities: ADHD, PTSD and social anxiety disorder remained significant after Bonferoni 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 PNDfirst, although none of these survived Bonferroni correction. Full details are provided in Supplementary Table S7.

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. 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. An important limitation is that those reporting symptoms during pregnancy may have been experiencing a depressive episode at the time that they became pregnant, and it is also possible that younger women reporting no PND may experience a future episode .

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.

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 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 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.

These findings 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). PMDD is the severe form of premenstrual syndrome, recently identified as a risk factor for PND (25), and NVP has been recognized as the strongest obstetric predictor of PND (26). 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 alone (20), and that most severe depression is suffered by women who experience PND both during pregnancy and after delivery (10).

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 inconclusive (27), 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.

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. The lifetime EPDS used to assess PND is a screening, rather than diagnostic tool and may result in overestimation of PND case status (28). 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. Also, reliance on self-report information years after experiencing PND could lead to recall bias. 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.

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 vulnerability (7).

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 (29, 30), 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 relapse (29). 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.

Abbreviations

ADHD
Attention Deficit Hyperactive Disorder
AGDS
Australian Genetics of Depression Study
CI
Confidence Interval (95%)
CIDI-SF
Composite Interview Diagnostic Interview Short Form
DSM-V
Diagnostic and Statistical Manual of Mental Disorders Fifth Edition
Dep_NoPND
Depression cases who have never experienced PND
EPDS
Edinburgh Postnatal Depression Scale
MDD
Major Depressive Disorder
NVP
Nausea and vomiting during pregnancy
OR
Odds Ratio
P
P-value
PMDD
Premenstrual Dysphoric Disorder
PND
Perinatal Depression
PNDfirst
PND cases whose first PND episode was also their first episode of depression
priorDep_PND
PND cases with a prior history of depression

priorDep_NoPND
Depression cases with a history of depression before their first pregnancy, but no PND episodes
PTSD
Post-traumatic Stress Disorder

Declarations

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.

Written patient consent for participation in the study was obtained.

Consent for publication

Not applicable

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 (Nick.Martin@qimrberghofer.edu.au) for data and JK (j.kiewa@uq.edu.au for code)

Competing Interests

No conflict of interest has been reported

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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

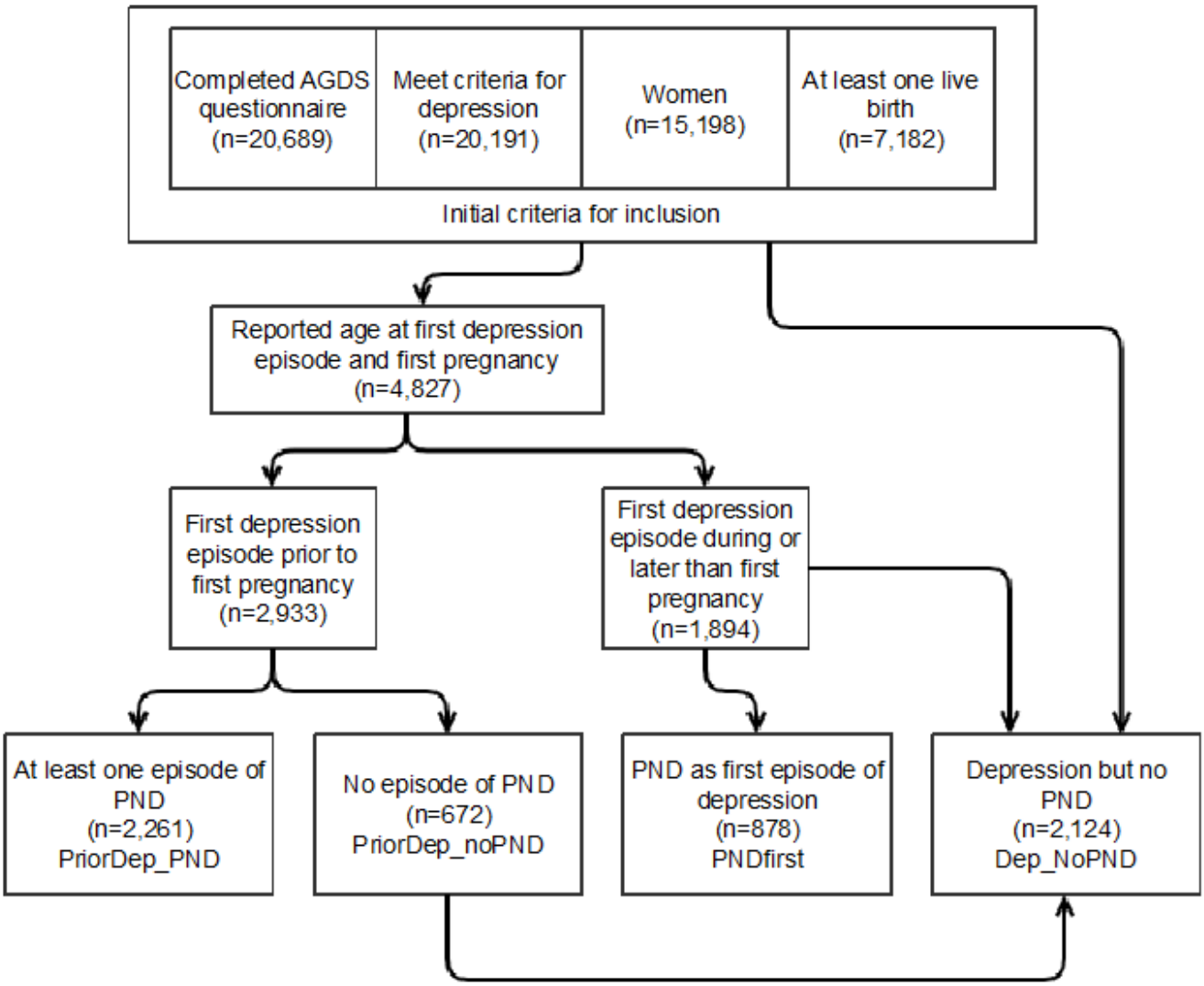

Figure 1

Flow chart: Selection of cases and associated comparison 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, PriorDep_noPND is a subset of Dep_NoPND. PriorDep_noPND was considered to be a more appropriate comparison group for

PriorDep_PND since members of both these groups experienced an episode of major depression before first pregnancy.

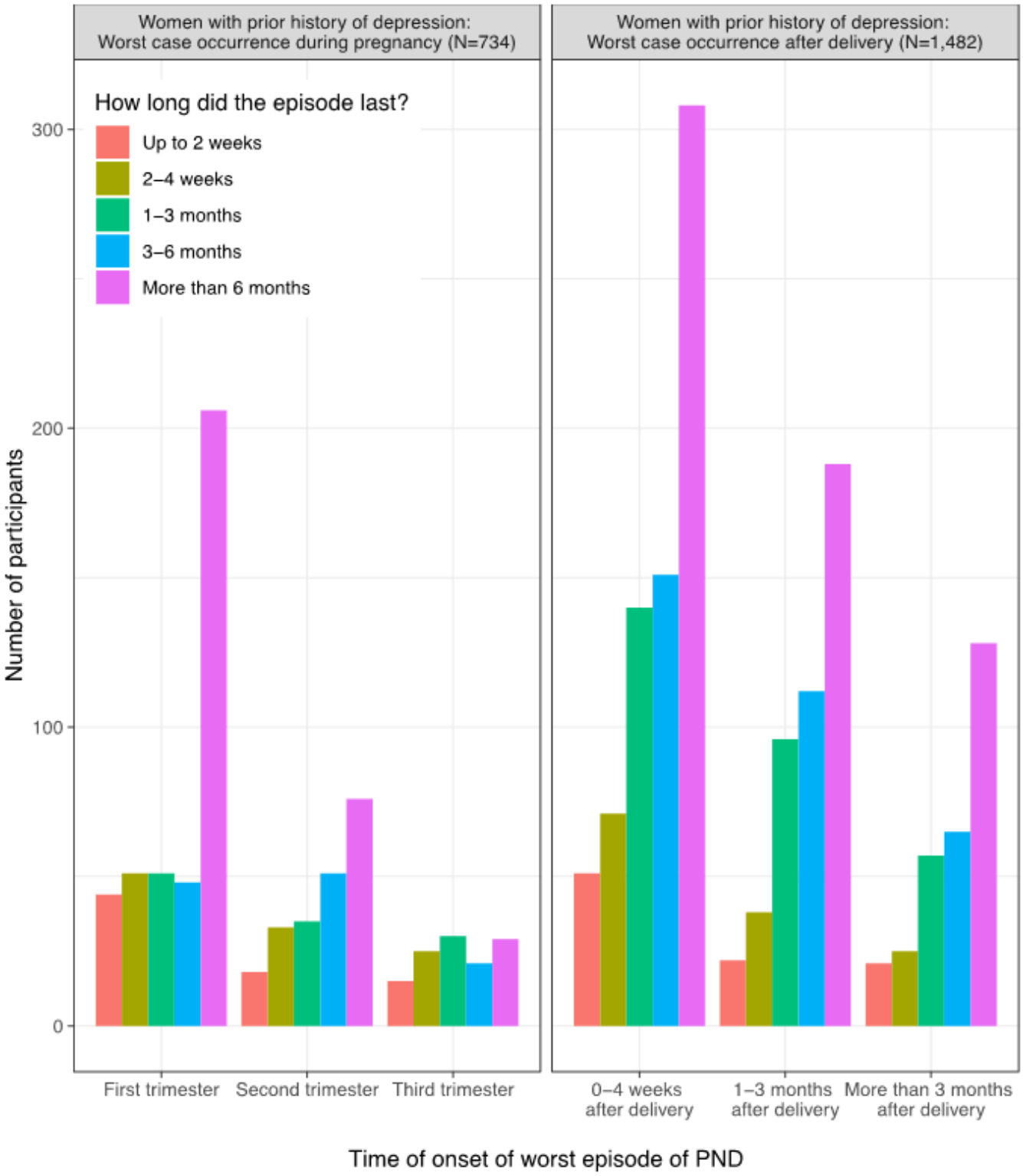

Figure 2

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 detailed timing of onset.

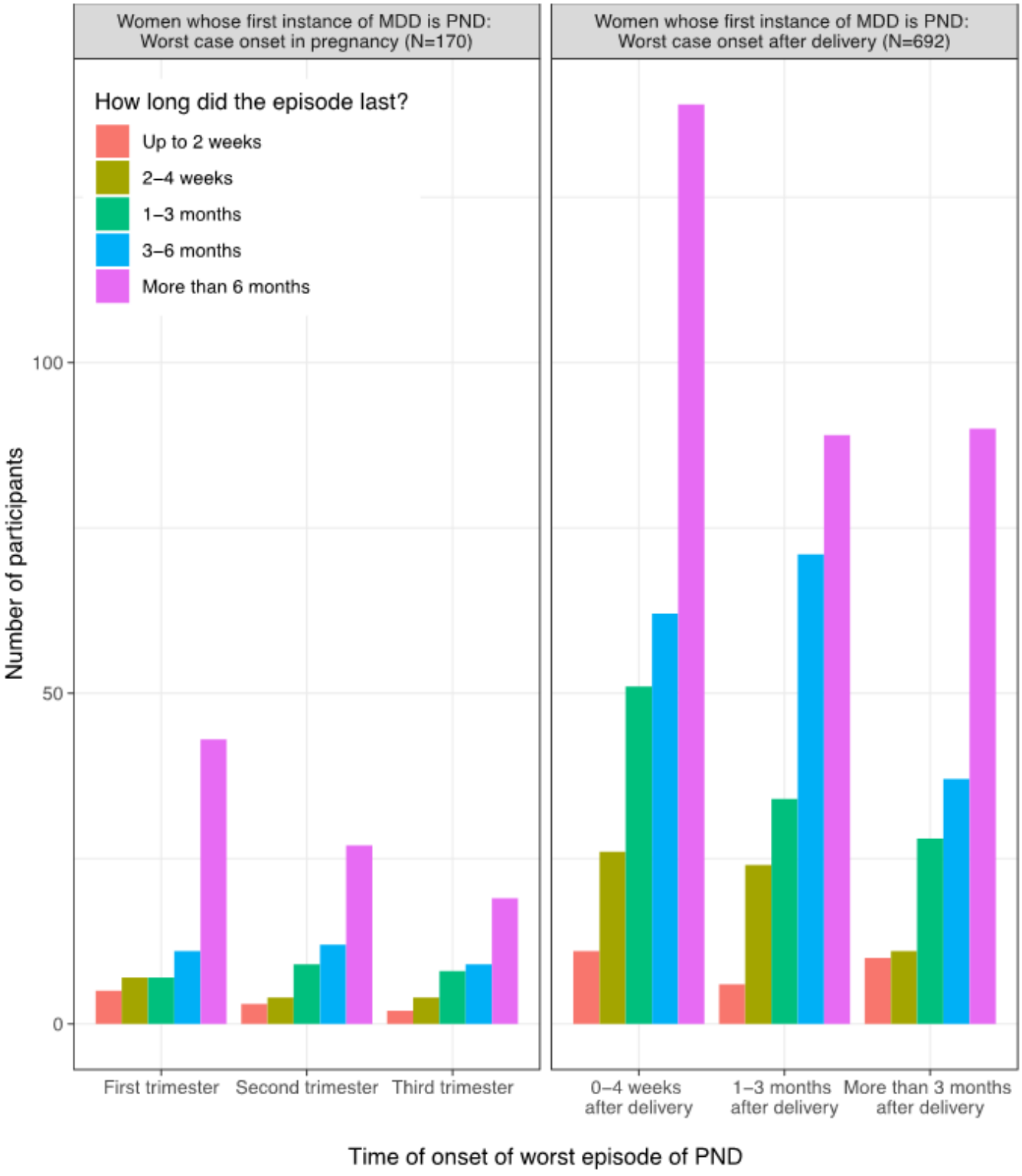

Figure 3

Length of worst episode of symptomatic PND for PNDfirst 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 detailed timing of onset.

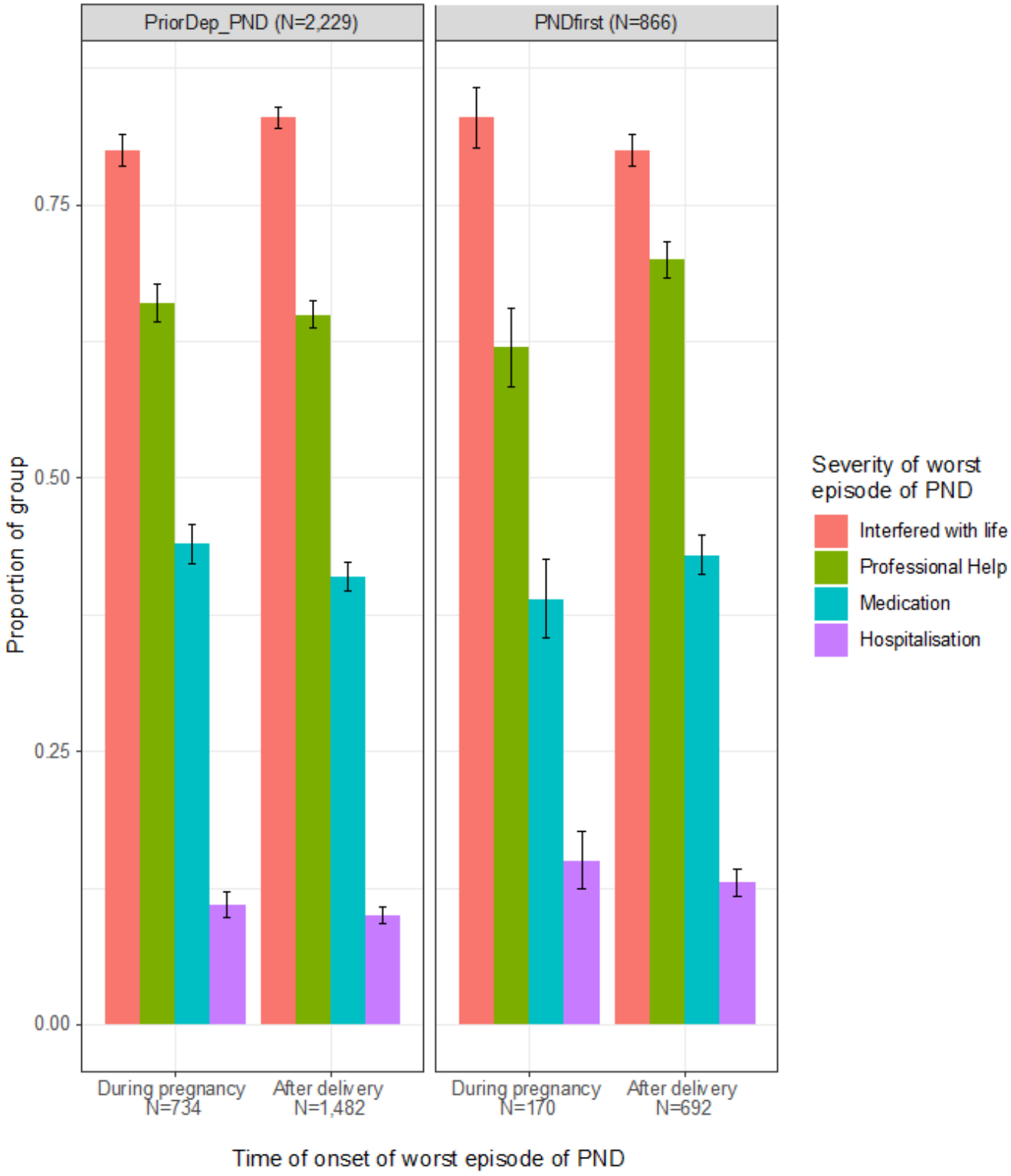

Figure 4

Severity of worst episode of PND for priorDep and PNDfirst 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.

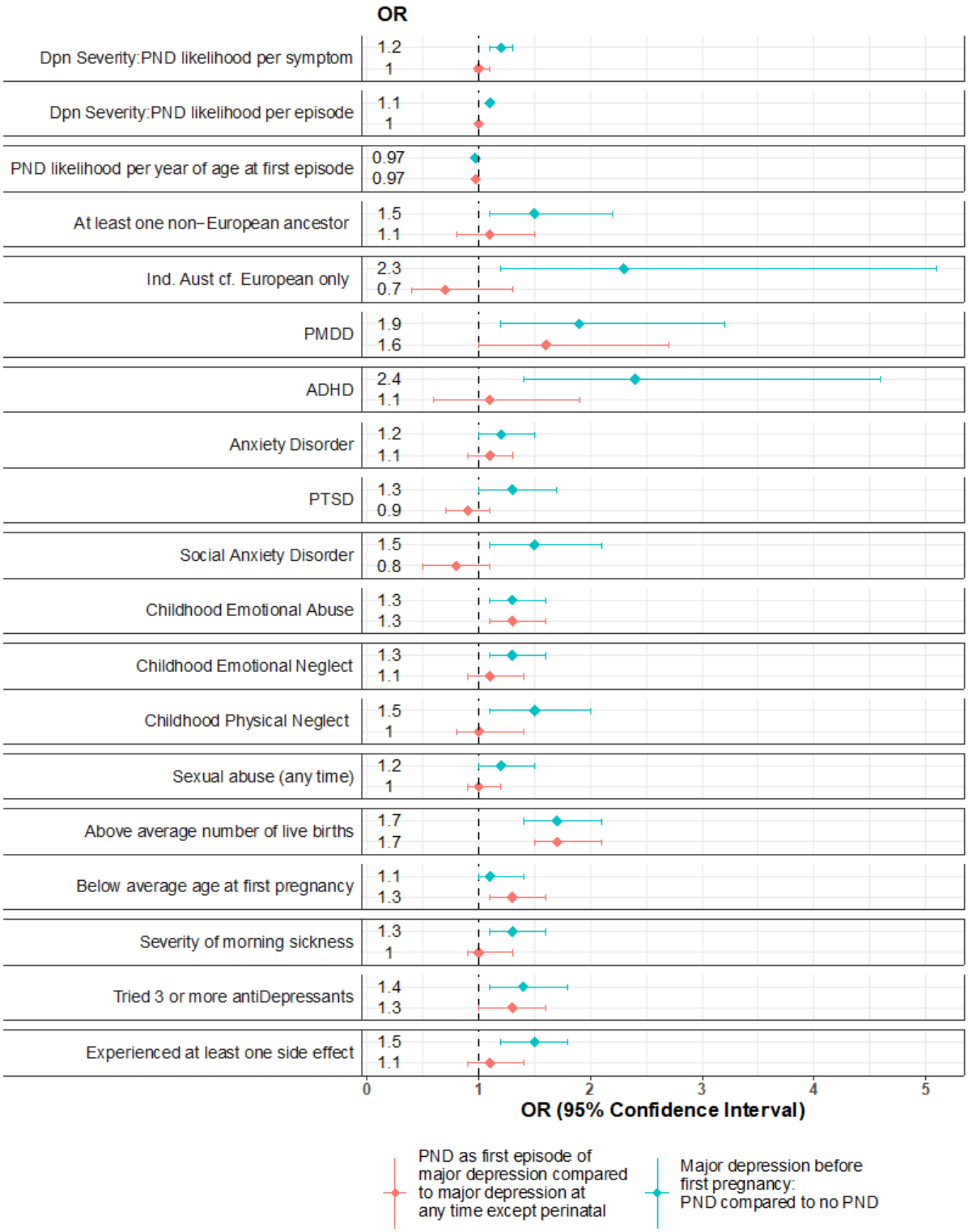

Figure 5

Forest plot of odds ratios with confidence intervals of all variables nominally significantly associated with priorDep_PND cases when compared with priorDep_noPND. Odds ratios for the association of these variables with PNDfirst cases compared with dep_noPND are also included for comparison. Logistic regression, including age of participants as a covariate, was used to calculate odds ratios.

Supplementary Files

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

- SupplementaryMethods.docx
- SupplementaryTables.xlsx