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# Familiality of psychiatric disorders and risk of postpartum psychiatric episodes: A population-based cohort study

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## Abstract

**Objective—**Postpartum psychiatric disorders are common and morbid complications of pregnancy. We sought to evaluate how family history of psychiatric disorders is associated with postpartum psychiatric disorders in proband mothers with and without a prior psychiatric history by assessing degree of relationship, type of disorder, and sex of family members.

**Method—**We linked Danish birth and psychiatric treatment registers to evaluate familial risk of postpartum psychiatric episodes in a national, population-based cohort. Probands were first-time mothers who gave birth after age 15 years and before December 31, 2012 who were born in Denmark in 1970 or later (n=362,462). The primary exposure was a diagnosed psychiatric disorder in a relative. We used Cox regression models to estimate the hazard ratio (HR) of postpartum psychiatric disorders in proband mothers.

**Results—**Relative risk of psychiatric disorders in the postpartum period was elevated when first-degree family members had a psychiatric disorder (HR 1.45; 95% CI 1.28–1.65) and highest when proband mothers had a first-degree family member with bipolar disorder (HR 2.86; 95% CI, 1.88–4.35). Associations were stronger among proband mothers with no previous psychiatric history. There were no notable differences by sex of the family member.

**Conclusions—**Family history of psychiatric disorders, especially bipolar disorder, is an important risk factor for postpartum psychiatric disorders. To assist identification of women at-risk for postpartum psychiatric disorders, questions related to female and male first-degree relatives with bipolar disorder is of the highest importance, and should be added to routine clinical screening guidelines to improve prediction of risk.

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## Introduction

The postpartum period is a vulnerable time for onset of psychiatric disorders, being one of the few identified periods of heightened risk throughout the life course (1–3). Prior history of a psychiatric disorder, occurring either within or outside of the perinatal period, increases risk of experiencing a postpartum psychiatric disorder (3–8). Although personal psychiatric history is a highly predictive risk factor for postpartum psychiatric disorders, predicting who will experience a new-onset psychiatric disorder in the postpartum period remains a significant challenge.

Family psychiatric history is a strong and consistent risk factor for psychiatric disorders outside of the perinatal period (8, 9). Perinatal mood disorders may be more heritable than other mood disorders, as the heritability for perinatal depression is estimated to be 44% (11) compared with 37% for major depressive disorder (11, 12). Heritability of other types of perinatal psychiatric disorders is unknown. Family history of a postpartum mood disorder in a mother or sister doubles or triples risk of experiencing a postpartum mood disorder (14–16), and postpartum psychosis in a mother or sister increases risk of postpartum psychosis five-fold (14). Family history of non-postpartum mood disorders is also associated with postpartum mood disorders, especially for bipolar disorder and the most severe postpartum episodes like postpartum psychosis (14,16–19). These prior studies, however, have primarily been conducted in high-risk populations of women and their families with previously diagnosed psychiatric disorders. There is much less known about how familiality of psychiatric disorders outside of the perinatal period influence postpartum psychiatric disorders for the broader spectrum of psychiatric disorders, particularly in women without a personal psychiatric history. The few existing population-based studies examining the association between family history of non-postpartum mood disorders with postpartum mood disorders have not investigated specific types of psychiatric disorders among different degrees of familial relationships (3, 19).

Prior work has not explored whether the familial associations of postpartum psychiatric disorders are related to a specific female vulnerability (e.g. mother to daughter). Because previous studies of familiality of postpartum psychiatric disorders have primarily evaluated the relationship between postpartum mood disorders in proband mothers and postpartum mood disorders in first-degree relatives, most have exclusively evaluated pairs of female relatives (e.g., mother-daughter or sister-sister pairs) (11,14–16,21,22). Among studies including both male and female relatives with psychiatric disorders outside of the perinatal period, none have evaluated the difference in recurrence risk among female relatives compared to male relatives (11,17). Understanding the degree to which familial history of psychiatric disorders predicts risk for postpartum psychiatric disorders would substantially aid our ability to identify those at greatest risk for postpartum psychiatric disorders and intervene early.

We aimed to address this gap in the literature by evaluating how family history of psychiatric disorders influences risk for postpartum psychiatric episodes. We wanted to evaluate whether familial risk of postpartum psychiatric disorders differs by degree of relationship and sex of the family members in both women with and without a prior personal psychiatric

history. To address these aims, we conducted a population-based study of recurrence risk (the likelihood a trait in one family member will occur again in another family member) (23–25), a study design frequently applied in psychiatric genetics (10,14,16,25,26). Recurrence risk studies typically evaluate the same disorder in family members (e.g. postpartum depression in both a proband mother and her sister). In our study, we sought to determine the unique familial contributions of psychiatric disorders outside of the perinatal period to psychiatric events within the postpartum period; thus, we consider the recurrent event (a psychiatric diagnosis within the postpartum period) to be different than the familial event (a psychiatric diagnosis at any time point). We refer to this specific type of recurrence risk as 'familial risk' from this point forward.

## Methods

### Study population

We conducted a population-based cohort study within the Danish Civil Registration System (27). A unique personal identifier of all people living in Denmark enables comprehensive linkages with multiple health-related national registers as well as linkages to family members. Probands (hereafter referred to as proband mothers) were selected from all women born in Denmark from 1970 onward with non-missing links to both parents (n=1,336,419). Proband mothers were all first-time mothers who gave birth to a live-born child when at least 15 years of age and before the end of follow-up on December 31, 2012. A total of 362,462 proband mothers were included in our study (Figure 1).

### Identification of postpartum psychiatric episodes

Our outcome of interest was a psychiatric episode diagnosis during the postpartum period in proband mothers. Information on psychiatric episodes was obtained from the Psychiatric Central Register (28), which provides information on inpatient treatment since 1969 and outpatient treatment since 1995. Outpatient diagnoses come from specialty psychiatric clinics and do not include diagnoses from primary care settings. Diagnoses are recorded using International Classification of Disease (ICD) codes (ICD-8 prior to 1994 and ICD-10 codes 1994 and later). We defined a postpartum psychiatric disorder as a treated psychiatric episode (290–315 in ICD-8 codes and F00–F99 in ICD-10 codes), excluding organic mental disorders (290.09, 290.10, 290.11,290.18, 290.19, 292.X9, 293.X9, 294.X9, and 309.X9 in ICD-8 codes; F00–F09 in ICD-10 codes), substance abuse (291.X9, 294.39, 303.X9, 303.20,303.28, 303.90 and 304.X9 in ICD-8 codes and F10–19 in ICD-10 codes), and mental retardation (310–315 in ICD-8 codes; F70–F79 in ICD-10 codes), which have been well-validated in these registries (28,29). For our primary analysis, we considered the postpartum period to be 0 to 6 months after childbirth. Prior work in our data have indicated increasing vulnerability for depressive episodes up to 6 months after childbirth (2) and we wanted to ensure we accounted for a potential delay between symptom onset and recorded diagnosis. In sensitivity analyses, we also examined two other time periods separately: 1) 0 to 3 months postpartum, a more narrowly defined and possibly more etiologically similar phenotype (30–32), and 2) 0 to 12 months postpartum, an increasingly applied clinical definition for the postpartum period (30,33,34).

### Identification of relatives of proband mothers and family history of psychiatric episodes

To identify relatives, proband mothers were linked to their parents by unique identifier and subsequent family relationships were identified through these linkages. The degree of relationship of family members was defined as follows: First-degree relatives included mother, father, and full sibling; Second-degree relatives included grandparents, half-siblings, uncles, and aunts; Third-degree relatives included cousins. Because the register was established in 1970, we were unable to identify people born before this date, and thus, second- and third-degree relationships are less complete.

Among the proband mothers included in our study population, we considered the association between a postpartum psychiatric disorder and any psychiatric disorder in our categorized relatives. Furthermore, we investigated specifically five hierarchical diagnostic groups of psychiatric disorders in the relatives: 1) schizophrenia and related disorders (highest in hierarchy; ICD-10 codes F20–F29); 2) bipolar disorder (ICD-10 codes F30–31; 3) unipolar disorder (ICD-10 codes F32–33; 4) other mood disorders except for bipolar and unipolar disorders (ICD-10 codes F34–39); 5) other psychiatric disorders (lowest in hierarchy; ICD-10 codes F40–F69 and F80–F99). This hierarchical system is built into the ICD diagnostic system and accounts for individuals with more than one recorded diagnoses.

### Statistical analysis

We started follow-up at the date of childbirth for each proband mother and followed her until a postpartum psychiatric episode, 3, 6 or 12 months postpartum, death, emigration, or December 31, 2012, whichever came first. We restricted proband mothers to first-time mothers for several reasons: 1) history of PPD increases risk in subsequent pregnancies, 2) prior birth outcome may influence later reproductive behavior, and 3) environmental factors during the postpartum period are different after first and subsequent births. To ensure that detection of a psychiatric diagnosis in a relative occurred before the postpartum psychiatric diagnosis and was not dependent on the proband mother's age at childbirth, we assessed whether the relatives had a diagnosis of psychiatric disorder on or prior to the proband mother's $15^{th}$ birthday, going back to 1970. We adjusted for the calendar year and the proband mother's age at birth.

We evaluated the association by determining familial risk, a register-based estimate of the risk of experiencing a postpartum psychiatric disorder when a relative of a proband mother had a psychiatric disorder. We further examined the association of postpartum psychiatric disorders with each of the five hierarchical psychiatric disorders. We used Cox regression analysis to calculate hazard ratios (HR). Given postpartum psychiatric disorders among proband mothers with a psychiatric history prior to childbirth may be a distinct psychiatric phenotype, we examined the associations in proband mothers with and without previous psychiatric history separately.

To estimate whether the associations between family history of psychiatric disorders and postpartum psychiatric disorders were due to a genetic contribution or shared environmental factors, we repeated the analyses by first-, second-, and third-degree relatives and sex of the relatives with a psychiatric disorder. If an increased risk is due to familial factors attributable

to non-genetic factors shared by nuclear families, we would expect to see excess risk only among first-degree relatives. Conversely, if the increased risk is due to a genetic contribution in some extent, we would expect to see excess among both close and distant relatives in line with their coefficient of relationship.

Statistical analyses were performed using the statistical software package Stata 13.1.

## Results

The final population-based cohort consisted of 362,462 proband mothers who gave birth to their first child in Denmark between 1985 and 2012. Mean (SD) age of proband mothers was 27.0 (4.3) years at the time of delivery. Of these mothers, 2,603 (0.7%) experienced a psychiatric disorder within 6 months postpartum and 4,085 (1.1%) within 12 months postpartum (Table 1).

As described, we evaluated familial risk, a register-based estimate of the risk of experiencing a postpartum psychiatric disorder when a relative of a proband mother had a psychiatric disorder. Results are presented for familial risk of postpartum psychiatric episodes within 6 months postpartum, but results were similar for 0 to 3 months and 0 to 12 months postpartum (Table S1 and S2). Overall, the hazard of experiencing a psychiatric disorder within the first 6 months postpartum was higher among proband mothers with a first-degree relative who had experienced any psychiatric disorder compared with proband mothers whose relatives did not experience any psychiatric disorder (HR 1.45; 95% CI 1.28–1.65). The hazard ratio of experiencing a postpartum psychiatric episode was the highest when proband mothers had a first-degree relative with bipolar disorder (HR 2.86; 95% CI, 1.88–4.35). Familial risk was also elevated for those who had a first-degree relative with schizophrenia (HR 1.58; 95% CI 1.27–1.95), unipolar disorder (HR 1.52; 95% CI 1.24–1.87), or other mood disorder (HR 1.78; 95% CI 1.03–3.06), but not other psychiatric disorders (HR 0.90; 95% CI 0.70–1.16). The point estimates tended to be larger among proband mothers with no previous psychiatric history (Table 2, Figure 2). We found that prior psychiatric history was a strong risk factor for postpartum psychiatric disorders (HR 8.66; 95% CI 7.97–9.40, for postpartum disorders in women with prior psychiatric history compared to women with no psychiatric history, adjusted for psychiatric disorders in first, second, and third degree relatives).

Familial risk of postpartum psychiatric disorders was elevated when first-degree relatives experienced psychiatric disorders, as described above, and slightly elevated for familial psychiatric disorders among more distant relatives (for any psychiatric disorder, second-degree relatives: HR 1.16; 95% CI 1.02–1.31; third-degree relatives: HR 1.27; 95% CI 1.03–1.58). More distant relatives share both a reduced coefficient of relationship (Figure S1) and reduced shared family environment.

The familial risk of postpartum disorders in proband mothers born by mothers with psychiatric disorders (HR 1.50, 95% CI 1.27–1.77 for mothers) was similar to those born by fathers with psychiatric disorders (HR 1.54, 95% CI 1.27–1.87 for fathers). This pattern persisted for all five diagnostic groups of psychiatric disorders (Table 2). Likewise, when we

assessed familial risk separately in female and male relatives more generally, we did not observe differences by sex for either any psychiatric disorder or specific diagnostic groups of psychiatric disorders for any degree of relationship (Table 3, Figure 2).

## Discussion

We used linked Danish birth and psychiatric registry data to determine familial risk of postpartum psychiatric disorders associated with family history of psychiatric disorders within five hierarchical diagnostic groups. To our knowledge, this study is the first to use a large, population-based cohort to investigate familial risk of postpartum psychiatric disorders with psychiatric disorders outside of the perinatal period. Our analysis of first-ever postpartum psychiatric disorders provides evidence of the importance of psychiatric disorders in family members even among women with no personal history of mental illness.

Our study is the first to address whether familial risk of postpartum psychiatric disorders differs by sex of the family member. Since only women may experience the outcome of a postpartum psychiatric disorder, prior studies of recurrence risk of postpartum psychiatric disorders have exclusively studied female-relative pairs (e.g., mother-daughter, sisters) (11,14–16,21,22). However, both males and females experience non-postpartum psychiatric disorders, and it is unknown whether family history of non-postpartum psychiatric disorders experienced by male or female relatives differentially influences risk of postpartum psychiatric disorders. Studies of other psychiatric conditions (35) and small studies of mood disorders in selected populations (36,37) have shown some evidence of greater female heritability or transmission, but larger, population-based studies of psychiatric disorders have not found sex differences (10,38). Consistent with this, we found that despite postpartum psychiatric disorders being uniquely female events, family history of psychiatric disorders in male relatives was just as influential as their occurrence in female relatives. Thus, when assessing risk for postpartum episodes, clinicians should inquire about family history of psychiatric disorders broadly, and not limit discussion only to postpartum psychiatric disorders or psychiatric disorders in female relatives.

We found that familial risk for postpartum psychiatric disorders was higher for family history of bipolar disorder compared with family history of psychiatric disorders, which had previously only been identified for the most severe postpartum psychiatric episodes (14,17) or among women with a personal history of mood disorders (14–17). Outside of the perinatal period, familial risk for bipolar disorder is greater than that of unipolar depression (RR = 6.4 to 7.9 for bipolar disorder (10); RR = 2.8 for unipolar depression (12)). We found similar patterns in our study of psychiatric disorders within the postpartum period; familal risk was higher with family history of bipolar disorder than for family history of unipolar depression (HR= 2.86, 95% CI 1.88–4.35 for postpartum episodes with bipolar depression; HR=1.52, 95% CI 1.24–1.87 for postpartum episodes with unipolar depression). Our estimates, particularly for familial risk of postpartum disorders with familial bipolar disorder, were very similar to previous estimates for postpartum mood disorders overall (RR=2.3 to 3.9) (14–16). It should be noted that previous recurrence risk studies of postpartum psychiatric disorders have all been conducted in cohorts of women with a prior psychiatric history, whereas we evaluated familial risk separately in women with and

without prior psychiatric history. The link between bipolar disorder and postpartum psychosis is well established (6,39–42), and recent work in these same data have shown an increase in the risk of conversion to bipolar disorder with closer time to birth of psychiatric encounter (18). Taken together with our findings demonstrating that family history of bipolar disorder is more strongly associated with any postpartum psychiatric disorder and not only the most severe episodes, there is evidence for a genetic vulnerablity or other etiologically similar mechanisms linking bipolar disorder and psychiatric episodes specifically in the postpartum period and is supported by the literature (6,14,17,39–42).

Our analysis of a large, population-based cohort, provides the ability to investigate several types of psychiatric events and makes our results more generalizable to the broader population. Most prior studies of familiality of postpartum psychiatric disorders have been conducted in small cohorts or cohorts of high-risk women recruited specifically to study recurrent major depressive disorder and bipolar disorder. This study specifically captured psychiatric disorders in the postpartum period among proband mothers with and without prior psychiatric history. Prior studies typically have not distinguished between incident episodes and those that may reflect an ongoing psychiatric disorder that recurs during the postpartum period. Differentiating between new-onset episodes and recurrent episodes can have important implications for both screening and treatment. We also considered timing of onset of postpartum psychiatric episodes and separately analyzed three different time periods: 0 to 3 months postpartum, 0 to 6 months postpartum, and 0 to 12 months postpartum. There is evidence that etiology of postpartum psychiatric disorders may differ by time of symptom onset (2,31,32,43), and that the first few weeks after childbirth may be the most biologically vulnerable time point (30,31). However, because our data provide information about timing of diagnosis or treatment, but not the onset of symptoms, there is likely a potential lag between onset of symptoms and when a mother seeks care. This is an intrinsic limitation in nearly all studies of postpartum psychiatric disorders, and we sought to address this limitation by analyzing the 0 to 6 month time period. We also selected 0 to 12 months postpartum as a clinically relevant time period (30,33,34). External environmental factors change during the first year postpartum, which may influence each time period differently. Despite the potential for differences, we found results of how family psychiatric history affects postpartum psychiatric disorders to be similar across all three time periods.

Use of registry data improves generalizability to broader populations, but there are also limitations to the data available in the registers. Our data included inpatient hospital admissions and outpatient psychiatric clinic records, but not records from general practitioners. Rates of postpartum psychiatric disorders were lower compared to typically reported rates because cases were patients who obtained psychiatric care in a specialty clinic or hospital, which captured the most severe psychiatric episodes but not patients seeking care from their primary care provider. Therefore, these results are most generalizable to development of severe postpartum psychiatric disorders, and potentially not for postpartum psychiatric disorders overall. Additionally, because outpatient diagnoses were not included in the registers until 1995, psychiatric diagnoses prior to 1995 include only the most severe inpatient hospitalizations. To account for the secular trends, we adjusted for calender year of the proband mothers and age at first delivery in the models. Moreover, to assess how this differentially defined exposure may influence our results, we repeated our analyses in a

restricted cohort of only mothers who had children born after 1995. Similar trend was observed in this sub-analysis, although the interval estimates became wider and less precise due to small numbers of cases. We also acknowledge that our results are only generalizable to primiparous women. Finally, proband mothers were included only if they could be linked to their parents. The inability to identify many of the grandparents makes our groupings of second- and third-degree relatives incomplete. Despite our large sample size, there were not enough pairs of sisters or mothers and daughters that both experienced incident psychiatric disorders in the postpartum period following the birth of their first child to address recurrence risk of only postpartum psychiatric disorders. Our sample size also limited our ability to examine specific types of psychiatric disorders in the postpartum period as we did for the relatives. We also did not see an expected pattern of familial risk aligned with the coefficient of relationship and were underpowered to evaluate familial risk by type of disorder for third-degree relatives, both likely due to incomplete identification of third-degree relatives.

Predicting who will experience a postpartum psychiatric disorder is a challenge but also of great importance. The results of this study provide compelling evidence that assessment of risk for postpartum psychiatric illness, with a particular focus on history of bipolar disorder, should include inquiring about family history of psychiatric disorders in any male or female first-degree relative. Thus, inquiring about family history in fathers and brothers is as important as obtaining a history of postpartum psychiatric disorders in mothers or sisters. Further, as expected, we found personal psychiatric history to be a stronger independent predictor of postpartum psychiatric disorders than family history. However, we found associations of family history of psychiatric disorders to be stronger among women without a personal psychiatric history, indicating that family history may be particularly helpful in a risk-assessment tool for new-onset postpartum psychiatric episodes among women with no records of psychiatric disorders. Previously, a woman who has a brother with bipolar disorder but no personal history of mental illness would not necessarily be identified at higher risk for experiencing a postpartum psychiatric disorder. However, this research provides evidence that such characteristics may identify novel risk groups for which clinicians could direct additional screening efforts, earlier education about symptoms, or earlier referral to mental health resources. Few clinical practice guidelines include family history, but those that do suggest planning the timing of pregnancies in periods of stable mood (44) and increasing surveillance for symptoms of postpartum psychosis in the first two weeks after childbirth (45), which should also be considered for these novel risk groups.

Clinical practice guidelines in the United States have recently been updated to reflect a growing emphasis on the importance of perinatal mental health screening, but the current guidelines put forth by the US Preventive Services Task Force (46) and the American College of Obstetricians and Gynecologists (33) do not include family history as a consideration for postpartum psychiatric disorders. This is in contrast to other women's health conditions, such as breast cancer, in which family history of breast cancer in a first-degree relative is described extensively as an important screening consideration despite the magnitude of familial risk being similar to that of postpartum psychiatric disorders (47). Therefore, obtaining family history of psychiatric disorders is highly valuable information that should be acknowledged as an important factor in identifying at-risk women and

operationalized in clinical practice to improve prediction of risk for postpartum psychiatric illness.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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**Disclosures**

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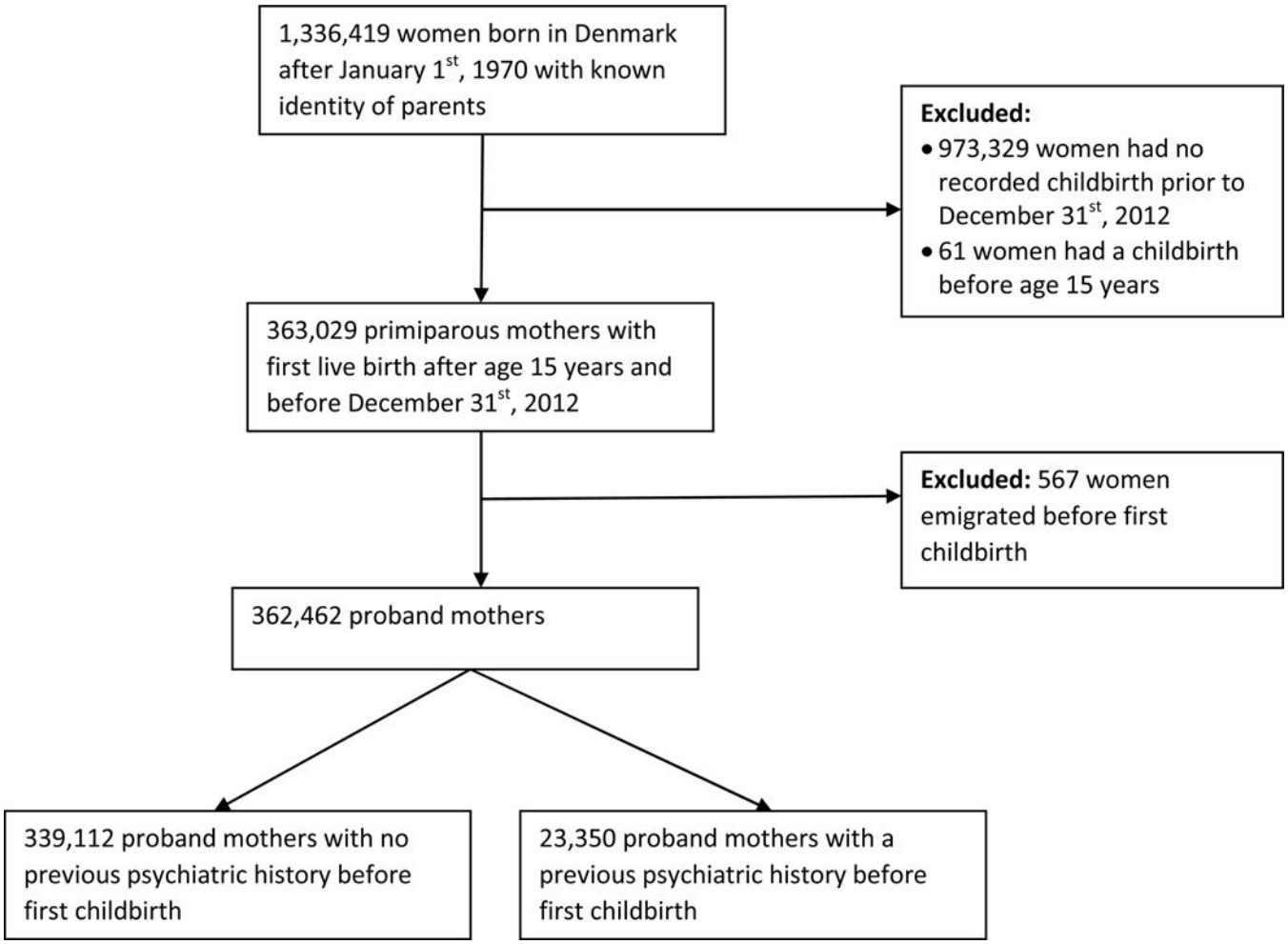


**Figure 1.**
Study population

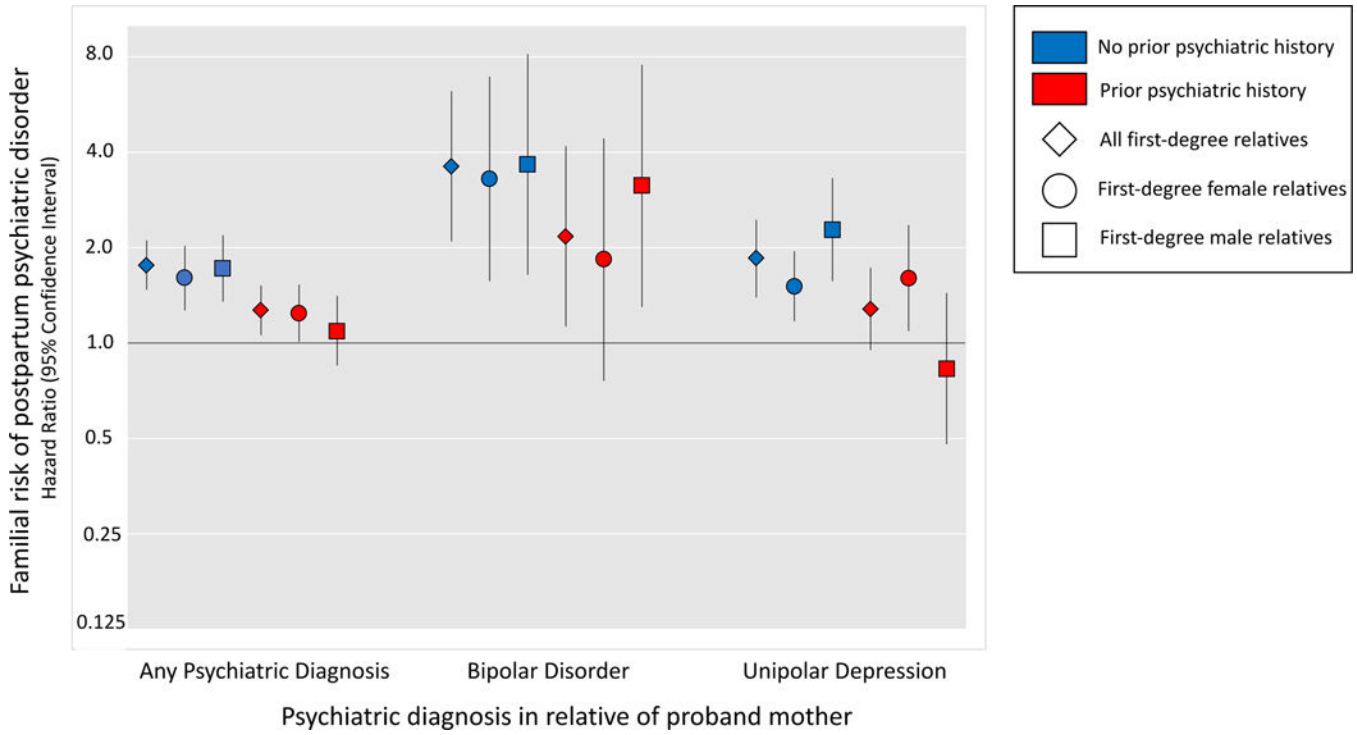


**Figure 2.**

Familial risk of psychiatric episodes within 6 months postpartum in proband mothers with and without personal psychiatric history, by type of disorder and sex in relatives.

**Table 1**

Characteristics of the study population for women with psychiatric episodes within 6 months and 12 months postpartum.

| Total proband mothers (N=362,462) | Probands with no prior psychiatric history (N=339,112) | | | | Probands with prior psychiatric history (N=23,350) | | | |
|---|---|---|---|---|---|---|---|---|
| | Postpartum episodes within | | | | Postpartum episodes within | | | |
| | 6 months | | 12 months | | 6 months | | 12 months | |
| | N | % | N | % | N | % | N | % |
| **N** | 1,585 | | 2,421 | | 1,018 | | 1,664 | |
| **Age at first childbirth** | | | | | | | | |
| Mean (SD) (years) | 27.0 | 4.3 | 26.5 | 4.6 | 26.7 | 4.7 | 26.3 | 4.7 |
| **Birth year of proband mother** | | | | | | | | |
| 1985–1994 | 35 | 2.2 | 73 | 3.0 | 12 | 1.2 | 16 | 1.0 |
| 1995–1999 | 254 | 16.0 | 391 | 16.2 | 99 | 9.7 | 151 | 9.1 |
| 2000–2004 | 392 | 24.7 | 619 | 25.6 | 203 | 19.9 | 343 | 20.6 |
| 2005–2009 | 588 | 37.1 | 902 | 37.3 | 438 | 43.0 | 709 | 42.6 |
| 2010–2012 | 316 | 19.9 | 436 | 18.0 | 266 | 26.1 | 445 | 26.7 |
| **Previous psychiatric history among parents** | | | | | | | | |
| Any psychiatric diagnosis, mother | 70 | 4.4 | 109 | 4.5 | 84 | 8.3 | 145 | 8.7 |
| Any psychiatric diagnosis, father | 57 | 3.6 | 85 | 3.5 | 51 | 5.0 | 88 | 5.3 |
| Any psychiatric diagnosis, first-degree | 132 | 8.3 | 203 | 8.4 | 141 | 13.9 | 244 | 14.7 |
| Any psychiatric diagnosis, second-degree | 173 | 10.9 | 281 | 11.6 | 163 | 16.0 | 294 | 17.7 |
| Any psychiatric diagnosis, third-degree | 47 | 3.0 | 76 | 3.1 | 49 | 4.8 | 97 | 5.8 |
| Schizophrenia, first-degree | 43 | 2.7 | 60 | 2.5 | 46 | 4.5 | 65 | 3.9 |
| Schizophrenia, second-degree | 58 | 3.7 | 91 | 3.8 | 45 | 4.4 | 78 | 4.7 |
| Schizophrenia, third-degree | 8 | 0.5 | 11 | 0.5 | 7 | 0.7 | 11 | 0.7 |
| Bipolar disorder, first-degree | 13 | 0.8 | 18 | 0.7 | 9 | 0.9 | 14 | 0.8 |
| Bipolar disorder, second-degree | 7 | 0.4 | 13 | 0.5 | 8 | 0.8 | 10 | 0.6 |
| Bipolar disorder, third-degree | 0 | 0 | <4 | | 0 | 0 | 0 | 0 |
| Unipolar disorder, first-degree | 50 | 3.2 | 81 | 3.3 | 46 | 4.5 | 83 | 5.0 |
| Unipolar disorder, second-degree | 73 | 4.6 | 118 | 4.9 | 66 | 6.5 | 125 | 7.5 |
| Unipolar disorder, third-degree | <4 | | 5 | 0.2 | 6 | 0.6 | 12 | 0.7 |
| Other mood disorders, first-degree | 9 | 0.6 | 12 | 0.5 | 4 | 0.4 | 14 | 0.8 |

| Total proband mothers (N=362,462) | Probands with no prior psychiatric history (N=339,112) | | | | Probands with prior psychiatric history (N=23,350) | | | |
|---|---|---|---|---|---|---|---|---|
| | Postpartum episodes within | | | | Postpartum episodes within | | | |
| | 6 months | | 12 months | | 6 months | | 12 months | |
| | N | % | N | % | N | % | N | % |
| Other mood disorders, second-degree | 4 | 0.3 | 14 | 0.6 | 6 | 0.6 | 11 | 0.7 |
| Other mood disorders, third-degree | 0 | 0 | 0 | 0 | 0 | 0 | <4 | |
| Other psychiatric disorders, first-degree | 21 | 1.3 | 41 | 1.7 | 43 | 4.2 | 81 | 4.9 |
| Other psychiatric disorders, second-degree | 57 | 3.6 | 103 | 4.3 | 68 | 6.7 | 125 | 7.5 |
| Other psychiatric disorders, third-degree | 37 | 2.3 | 62 | 2.6 | 40 | 3.9 | 81 | 4.9 |

*Number of observations less than 4 cannot be presented due to possible identification of personal information

**Table 2**

Familial risk of psychiatric disorders within 6 months postpartum, by type of disorder of the proband mother's relative.

| Relationship to probandnew mother | Relatives with any psychiatric vs. no psychiatric disorders | | Relatives with schizophrenia vs. no schizophrenia | | Relatives with bipolar disorder vs. no bipolar disorder | | Relatives with unipolar disorder vs. no unipolar disorder | | Relatives with other mood disorder vs. no other mood disorder | | Relatives with other psychiatric disorders vs. no other psychiatric disorders | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | HR | 95% CI | HR | 95% CI | HR | 95% CI | HR | 95% CI | HR | 95% CI | HR | 95% CI |
| **All proband mothers**[a] | | | | | | | | | | | | |
| Mother | 1.50 | 1.27–1.77 | 1.58 | 1.19–2.10 | 2.43 | 1.34–4.39 | 1.58 | 1.21–2.05 | 1.82 | 0.81–4.05 | 1.02 | 0.71–1.46 |
| Father | 1.54 | 1.27–1.87 | 1.66 | 1.20–2.30 | 3.47 | 1.87–6.46 | 1.52 | 1.10–2.10 | 1.87 | 0.89–3.92 | 0.92 | 0.56–1.51 |
| Any first-degree relative | 1.45 | 1.28–1.65 | 1.58 | 1.27–1.95 | 2.86 | 1.88–4.35 | 1.52 | 1.24–1.87 | 1.78 | 1.03–3.06 | 0.90 | 0.70–1.16 |
| Any second-degree relative | 1.16 | 1.02–1.31 | 1.09 | 0.89–1.33 | 1.11 | 0.67–1.84 | 1.15 | 0.97–1.37 | 1.01 | 0.54–1.88 | 1.16 | 0.96–1.41 |
| Any third-degree relative | 1.27 | 1.03–1.58 | 2.15 | 1.29–3.58 | - | - | 1.39 | 0.72–2.68 | - | - | 1.16 | 0.92–1.47 |
| **Proband mothers with no prior psychiatric history**[b] | | | | | | | | | | | | |
| Mother | 1.78 | 1.40–2.27 | 1.96 | 1.31–2.93 | 3.53 | 1.68–7.42 | 1.56 | 1.04–2.34 | 3.33 | 1.27–8.88 | 1.19 | 0.65–2.16 |
| Father | 1.92 | 1.47–2.51 | 1.54 | 0.93–2.57 | 3.99 | 1.79–8.89 | 2.20 | 1.48–3.27 | 3.10 | 1.29–7.47 | 1.01 | 0.45–2.26 |
| Any first-degree relative | 1.76 | 1.47–2.11 | 1.82 | 1.34–2.47 | 3.61 | 2.09–6.23 | 1.85 | 1.39–2.45 | 3.10 | 1.61–5.97 | 0.90 | 0.58–1.40 |
| Any second-degree relative | 1.35 | 1.14–1.60 | 1.35 | 1.04–1.76 | 0.98 | 0.47–2.07 | 1.30 | 1.02–1.66 | 0.92 | 0.34–2.46 | 1.38 | 1.04–1.82 |
| Any third-degree relative | 1.46 | 1.08–1.98 | 2.68 | 1.33–5.39 | - | - | 1.10 | 0.35–3.43 | - | - | 1.31 | 0.94–1.84 |
| **Proband mothers with prior psychiatric history**[b] | | | | | | | | | | | | |
| Mother | 1.35 | 1.08–1.69 | 1.32 | 0.88–1.97 | 1.56 | 0.58–4.17 | 1.59 | 1.13–2.23 | 0.94 | 0.24–3.78 | 1.05 | 0.68–1.64 |
| Father | 1.28 | 0.97–1.70 | 1.74 | 1.14–2.65 | 2.79 | 1.04–7.45 | 0.97 | 0.56–1.67 | 0.90 | 0.22–3.60 | 0.96 | 0.51–1.80 |
| Any first-degree relative | 1.27 | 1.06–1.52 | 1.39 | 1.03–1.86 | 2.17 | 1.13–4.18 | 1.28 | 0.95–1.73 | 0.89 | 0.33–2.36 | 0.99 | 0.72–1.36 |
| Any second-degree relative | 1.03 | 0.86–1.24 | 0.88 | 0.65–1.19 | 1.28 | 0.64–2.57 | 1.05 | 0.81–1.36 | 1.12 | 0.50–2.50 | 1.11 | 0.85–1.44 |
| Any third-degree relative | 1.21 | 0.90–1.64 | 1.91 | 0.90–4.03 | - | - | 1.76 | 0.78–3.95 | - | - | 1.13 | 0.81–1.57 |

Figures are hazard ratios (95% confidence intervals);

[a] adjusted for calendar year at delivery and age at delivery and stratified by previous psychiatric history of the proband mothers;

[b] adjusted for calendar year at delivery and age at delivery.

**Table 3**

Familial risk of psychiatric disorders within 6 months postpartum, by type of disorder and sex of first-degree relatives

| Relationship to proband new mother | Relatives with any psychiatric vs. no psychiatric disorders | | Relatives with schizophrenia vs. no schizophrenia | | Relatives with bipolar disorder vs. no bipolar disorder | | Relatives with unipolar disorder vs. no unipolar disorder | | Relatives with other mood disorder vs. no other mood disorder | | Relatives with other psychiatric disorders vs. no other psychiatric disorders | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | HR | 95% CI | HR | 95% CI | HR | 95% CI | HR | 95% CI | HR | 95% CI | HR | 95% CI |
| **All proband mothers**[a] | | | | | | | | | | | | |
| Any first-degree relative | 1.45 | 1.28–1.65 | 1.58 | 1.27–1.95 | 2.86 | 1.88–4.35 | 1.52 | 1.24–1.87 | 1.78 | 1.03–3.06 | 0.90 | 0.70–1.16 |
| Female relative | 1.36 | 1.16–1.59 | 1.48 | 1.13–1.95 | 2.48 | 1.40–4.37 | 1.51 | 1.17–1.95 | 1.68 | 0.75–3.74 | 0.92 | 0.70–1.22 |
| Male relative | 1.32 | 1.11–1.57 | 1.52 | 1.12–2.06 | 3.45 | 1.91–6.23 | 1.45 | 1.07–1.98 | 1.73 | 0.83–3.64 | 0.84 | 0.60–1.16 |
| **Proband mothers with no prior psychiatric history**[b] | | | | | | | | | | | | |
| Any first-degree relative | 1.76 | 1.47–2.11 | 1.82 | 1.34–2.47 | 3.61 | 2.09–6.23 | 1.85 | 1.39–2.45 | 3.10 | 1.61–5.97 | 0.90 | 0.58–1.40 |
| Female relative | 1.61 | 1.27–2.02 | 2.02 | 1.40–2.91 | 3.30 | 1.57–6.93 | 1.60 | 1.09–2.36 | 3.07 | 1.15–8.18 | 0.95 | 0.58–1.54 |
| Male relative | 1.72 | 1.35–2.19 | 1.60 | 1.02–2.51 | 3.66 | 1.64–8.16 | 2.28 | 1.57–3.32 | 2.91 | 1.21–7.00 | 0.81 | 0.46–1.44 |
| **Proband mothers with prior psychiatric history**[b] | | | | | | | | | | | | |
| Any first-degree relative | 1.27 | 1.06–1.52 | 1.39 | 1.03–1.86 | 2.17 | 1.13–4.18 | 1.28 | 0.95–1.73 | 0.89 | 0.33–2.36 | 0.99 | 0.72–1.36 |
| Female relative | 1.24 | 1.01–1.53 | 1.12 | 0.75–1.68 | 1.84 | 0.76–4.42 | 1.45 | 1.03–2.05 | 0.87 | 0.22–3.50 | 1.01 | 0.71–1.43 |
| Male relative | 1.09 | 0.85–1.41 | 1.45 | 0.96–2.19 | 3.14 | 1.30–7.56 | 0.83 | 0.48–1.44 | 0.83 | 0.21–3.34 | 0.93 | 0.62–1.40 |

Figures are relative risks (95% confidence intervals);

[a] adjusted for calendar year at delivery and age at delivery and stratified by previous psychiatric history of the proband mothers;

[b] adjusted for calendar year at delivery and age at delivery.