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Association between maternal serious mental illness and adverse birth outcomes

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Abstract

Objective: To evaluate the contribution of serious mental illness (SMI), and specific risk factors (comorbidities and substance use) to the risk of adverse birth outcomes.

Study design: This cross-sectional study uses maternal delivery records in the Healthcare Cost and Utilization Project Nationwide/National Inpatient Sample (HCUP-NIS) to estimate risk factor prevalence and relative risk of adverse birth outcomes (e.g. preeclampsia, preterm birth, and fetal distress) in women with SMI.

Results: The relative risk of adverse gestational (1.15, 95% CI: 1.13-1.17), obstetric (1.07, 1.06-1.08) and fetal (1.24, 1.21-1.26) outcomes is increased for women with SMI. After adjusting for risk factors the risk is significantly reduced, but remains elevated for all three adverse outcome categories (gestational: 1.08, 1.06-1.09; obstetric: 1.03, 1.02-1.05; fetal: 1.12, 1.09-1.14).

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Supplementary information is available at JPER's website.

Conclusions: Maternal serious mental illness is independently associated with increased risk for adverse birth outcomes. However, approximately half of the excess risk is attributable to comorbidities and substance use.

Introduction

Research shows that serious mental illness (SMI) is associated with an increased risk of a variety of adverse maternal and fetal outcomes.[1–13] Most of these studies however, focus on a single adverse outcome, or do not adjust for other comorbid medical conditions. It is known that patients with SMI have a higher prevalence of obesity,[14] diabetes,[14] thyroid dysfunction,[15] epilepsy,[16] anemia,[2] substance use disorders,[17] and viral,[18] parasitic, and bacterial infections.[19] When present during pregnancy, these comorbid conditions may be independently associated with adverse maternal and fetal outcomes.[20–31] Thus, there is a need for a comprehensive estimate of the risk of adverse birth outcomes associated with SMI, while controlling for these potentially modifiable conditions.

In this study, we provide an estimate of the association between serious mental illness (major depressive disorder (MDD), bipolar disorder (BD), and/or schizophrenia) and a broad range of adverse gestational, obstetric and fetal outcomes on maternal records in a national database of U.S. hospital discharges. We add to the existing literature by additionally providing an estimate of how much of any elevated risk is attributable to medical comorbidity or substance use. Finally, we explore the association between hospital charges, length of stay and the presence of maternal SMI.

Methods

Study data

For this cross-sectional study, we used data from the Healthcare Cost and Utilization Project - Nationwide and National Inpatient Sample (HCUP-NIS), from 2008 to 2014. The HCUP-NIS is a nationally-representative sample of all inpatient hospitalizations in community hospitals in the United States. Patient records are included regardless of payer, making the HCUP-NIS the largest all-payer database publicly available in the United States. Prior to 2012, the HCUP-NIS dataset contained all discharge records from approximately 20% of participating hospitals, whereas beginning in 2012, it contains approximately 20% of discharge records from all participating hospitals. The HCUP-NIS is based on data collected by state partners (listed at https://www.hcup-us.ahrq.gov/partners.jsp) and overseen by the Agency for Healthcare Research and Quality, a division of the U.S. Department of Health and Human Services. Each record in this database represents a unique admission and includes information on diagnoses, procedures, patient characteristics (age, insurance type, income quartile of zip code, hospital admission via emergency department, elective admission, weekend admission) and hospital characteristics (urban/rural location, U.S. region).

The HCUP-NIS captures the vast majority of births in the United States, as only 1.5% of births in 2014 were out-of-hospital births.[32] Note that the design of the HCUP-NIS is such

that there is no method to link maternal and child records. Thus, we focused on diagnoses recorded on the maternal record only.

Following previous publications,[33] hospital stays with a childbirth event were identified using International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) diagnostic codes related to delivery (650, V27), ICD-9-CM procedure codes (72, 73.22, 73.59, 73.6, 74.0, 74.1, 74.2, 74.4, 74.99) and Diagnosis Related Group codes, version 24 (370-375). ICD-9-CM diagnostic codes for ectopic pregnancy (633, 761.4), hydatidiform mole (630), other abnormal product of conception (631), postnatal visit (V24), or abortion (632, 634, 635, 636, 637, 638, 639, or ICD-9-CM procedure codes 69.01, 69.51, 74.91, 75.0) were excluded. Only deliveries by women ten years and older were included for analysis.

Several states did not supply information on race (10.7% of values were missing); these cases were therefore included in the “others/unknown” race category. Other control variables were missing in 1.8% (income), 0.8% (urban/rural location), 0.4% (elective admission), 0.2% (payer), and 0% (U.S. region, weekend admission, emergency department admission, admission year) of the subpopulation of women (ten years and older) with a hospital delivery. Maternal age was missing for 0.1% of all women with a hospital stay for a delivery; these deliveries were excluded from the analyses.

Serious mental illness diagnosis

Mothers with SMI were identified using ICD-9-CM diagnosis codes indicating schizophrenia (295), BD (296.0-296.1, 296.4-296.9), or MDD (296.2, 296.3). The term “any SMI” in our study indicates a diagnosis of schizophrenia, BD and/or MDD. Sensitivity analyses consisted of defining a broader definition of SMI by including psychosis diagnoses (ICD-9-CM diagnosis codes 297, 298, in addition to 295), as well as a more stringent definition by excluding SMI in partial or full remission (xxx.x5 and xxx.x6 for MDD and BD, and xxx.x5 for schizophrenia).

Adverse outcomes and risk factors

Adverse outcomes were divided into three composite categories: gestational outcomes (e.g. preeclampsia), obstetric outcomes (e.g. preterm labor), and fetal outcomes (e.g. poor fetal growth). Cesarean deliveries were considered separately from obstetric outcomes as the prevalence is affected by voluntary or involuntary decision-making processes that could be affected by SMI status. From these three composite categories, several outcomes were selected *a priori* to analyze and present in more detail. All specific ICD-9-CM diagnostic codes that were used to identify hospital discharges with these diagnoses are listed in Appendix Tables 1–3.

Risk factors were classified as medical comorbidities (anemia, malposition/malpresentation of the fetus, diabetes, viral/bacterial/parasitic infection, obesity, thyroid dysfunction, epilepsy), or substance use (illicit drug use, alcohol use, and tobacco use). These risk factors were selected based on clinical relevance and inclusion in prior studies that report on multiple adverse birth outcomes, though to our knowledge, no prior study has controlled for a comprehensive set of risk factors simultaneously.[2–13] The specific ICD-9-CM diagnostic

codes that were used to identify hospital discharges with these risk factors are listed in Appendix Table 4.

Total hospital charges and length of stay

To measure the impact of maternal SMI on hospital resource use, total charges and length of stay were compared between women with and without SMI. Total charges for each hospital visit from all years were normalized to 2014 U.S. dollars using the Consumer Price Index published by the U.S. Bureau of Labor Statistics. The length of stay was based on the difference between discharge date and admission date. Same-day discharges are assigned a value of one day, overnight stays equal two days or more. The total extra charges for maternal hospital stays associated with deliveries by women with SMI in the U.S. were calculated by multiplying the average extra charges ($3,104 in 2014 U.S.$) for women with any SMI by the total number of women with any SMI (208,879); dividing this outcome by seven years yields a yearly average of charges for years 2008 to 2014.

Statistical analyses

Two-tailed Student's *t*-tests were used to compare baseline differences in patient/hospital characteristics, and in prevalence of risk factors in women with and without SMI. We then analyzed differences in adverse birth outcomes between these two groups. To adjust for potentially confounding differences, we ran multivariable logistic regressions that adjust for covariates: race, maternal age, insurance coverage (private insurance, Medicaid, or other), urban/rural hospital location, U.S. region, weekend, emergency department, or elective admission, income, and admission year and other SMI diagnosis (MDD, BD, or schizophrenia). Year-fixed effects were included to adjust for time trends, and age was modeled as a quadratic term to allow for an increasing risk of adverse outcomes at older ages. The multivariable logistic regression results were used to calculate the adjusted relative risk (RR) to analyze the associations between maternal SMI and adverse gestational, obstetric and fetal outcomes. Ordinary least squares regression was used to analyze the association between maternal SMI and hospital charges and length of stay, using similar adjustments to control for covariates. Survey prefix commands were used in Stata (version 14.0; StataCorp LLC) to account for the survey weights in accordance with guidance provided by HCUP. To allow for analyzing data across years despite different HCUP sampling strategies, "trend weights" were used instead of "discharge weights" for records prior to 2012, both of which were supplied by HCUP. The primary sampling unit was the hospital ID; the strata consist of a combination of "NIS stratum" and year. To allow for accurate standard error analysis of subsets of the data, all non-delivery hospital records were removed from the dataset, and all unique strata from the HCUP hospital files were subsequently added back with zero-values for analytical variables, including weights, according to HCUP Methods Series protocols.

We tested our primary hypothesis, that rates of adverse outcomes are higher among pregnant women with SMI, all else equal, using logistic regression models. Our secondary hypothesis, that part of this elevated rate is attributable to medical comorbidity and substance use among women with SMI, was tested by adding these risk factors as covariates to our models, and testing the change in relative risk associated with SMI (using the technique Seemingly

Unrelated Estimation[34] implemented with the "suest" command in Stata). The association with SMI should be partially or fully mitigated in models with risk factors included if our secondary hypothesis is correct. Results were considered significant at $P < 0.05$.

The study was approved by the University of Southern California Institutional Review Board.

Results

Patient and hospital characteristics

Table 1 and Appendix Table 5 report the patient and hospital characteristics of our sample of hospital deliveries by women with any SMI and with a specific SMI diagnosis, respectively. After applying inclusion and exclusion criteria, our sample includes 5,518,766 women older than 10 years who gave birth at a hospital in the 20% sample, 43,027 (0.8%) of whom have a diagnosis of SMI. Among women with SMI, the majority have a diagnosis of BD (80.8%) (Table 1), consistent with past studies of SMI in pregnant women using administrative databases.[1] Over a third of women with schizophrenia in this sample also have a diagnosis of BD (35.6%); women diagnosed with BD or MDD are relatively less likely to have a concurrent diagnosis of another type of SMI (Appendix Table 5).

Women with a diagnosis of any SMI on their delivery record are more likely to be younger, white or black, be in the lowest two income quartiles, be admitted through the emergency department, have a longer length of stay, and have higher hospital charges than women without SMI. They are less likely to have an elective admission, or to be covered by private insurance (Table 1). The difference in the distribution of women with and without SMI by race or ethnicity is dependent on the specific SMI diagnosis. Most notably, white women are overrepresented in the sample with BD, and black women are overrepresented in the sample with schizophrenia relative to their distribution in the population with no SMI diagnosis (Appendix Table 5). These differences have been observed in the general population before, and are likely due to differential presentation of symptomology, access to and participation in mental health care, and bias in diagnostic procedures for people of different race or ethnicity.[35]

Risk factor prevalence

Medical comorbidities and substance use are more prevalent among women with SMI than women without SMI at the time of delivery (Figure 1 and Appendix Table 4). Tobacco use disorder (29.1%, 95% CI 28.4-29.8 vs. 5.2%, 95% CI 5.1-5.4, in women without SMI), anemia (18.8%, 95% CI 18.2-19.4 vs. 12.0%, 95% CI 11.6-12.3) and infection (13.7%, 95% CI 13.3-14.1 vs. 5.2%, 95% CI 5.1-5.3) are the three most prevalent medical conditions in women with SMI; in women without SMI, anemia is most prevalent, followed by malposition/presentation of the fetus (7.5%, 95% CI 7.4-7.5), and diabetes (7.2%, 95% CI 7.1-7.3). Additionally, the prevalence rates of all ten assessed medical and substance use risk factors are significantly increased in women with MDD and BD compared to women without any SMI. For women with schizophrenia however, the difference in prevalence of

malposition/presentation of the fetus and thyroid dysfunction is not statistically significant (Appendix Table 4).

Adverse childbirth outcomes

After adjusting for hospital and patient characteristics, women with SMI have significantly higher relative risk for adverse gestational, obstetric, and fetal outcomes (collectively called 'adverse birth outcomes'). After additionally adjusting for medical comorbidities and substance use (collectively called 'risk factors'), women with SMI remain at elevated risk for adverse birth outcomes; however, the magnitude of the elevated risk is significantly reduced (Table 2 and Appendix Figure 1). The relative risk for adverse gestational outcomes in women with SMI falls from 1.15 (95% CI 1.13-1.17) to 1.08 (95% CI 1.06-1.09) (test of difference between models: $F_{1,16393} = 892.34$, $P < .001$). Similarly, the elevated risk is reduced from 1.24 (95% CI 1.21-1.26) to 1.12 (95% CI 1.09-1.14) for adverse fetal outcomes ($F_{1,16393} = 837.16$, $P < .001$), and from 1.07 (95% CI 1.06-1.08) to 1.03 (95% CI 1.02-1.05) for adverse obstetric outcomes ($F_{1,16393} = 1894.10$, $P < .001$). These findings were robust to alternate definitions of SMI (see Appendix Tables 6 and 7 for details). The pattern of a reduction of relative risk in the fully adjusted model is generally similar for most specific diagnoses embedded within these composite terms (e.g. preeclampsia, preterm birth, fetal distress) (Table 2). In contrast, the risk of umbilical cord complications is slightly but significantly decreased for women with SMI compared to women without SMI (0.98, 95% CI 0.96-1.00). However, the association with SMI disappears when additionally controlling for the increased rates of cesarean sections in this population (RR 0.99, 95% CI 0.97-1.01; data not shown in table).

Substance use appears to explain adverse fetal and obstetric outcomes more so than gestational outcomes (Table 3 and Appendix Table 8). Further analysis does not yield large differences between substances (tobacco, drugs, or alcohol) (data not shown).

Additional analyses of specific diagnoses of SMI show that for women with MDD and BD, the fully adjusted risk of gestational, obstetric and fetal outcomes is significantly higher, whereas schizophrenia is associated with a higher risk of adverse gestational outcomes only (Appendix Table 9).

Relative risk values after regression analyses for all three composite categories of adverse outcomes including the risk factors and other adjustments are listed in Appendix Table 10. Appendix Tables 1 through 4 contain the prevalence rates for adverse outcome and risk factor subcategories.

Length of stay and hospital charges

In addition to higher prevalence of risk factors and adverse birth outcomes, a maternal SMI diagnosis during delivery is also associated with increased hospital charges ($3,104, 95% CI 2,801-3,407) and length of stay (0.6 days, 95% CI 0.5-0.6; Table 4 and Appendix Table 11). Women with SMI have a hospital delivery stay of 4.2 days on average, compared to 3.6 days for women without SMI. Higher charges are mostly explained by length of stay, however, as the average charges *per day* are only slightly higher ($179, 95% CI 134-225)) for women

with SMI. Higher rates of cesarean sections among women with SMI did not substantially explain the increased charges or length of stay (data not shown).

Discussion

Women with a diagnosis of SMI have a 7%, 15% and 24% higher risk of adverse gestational, obstetric and fetal outcomes, respectively. Some of the elevated risk comes from the fact that medical comorbidities and substance use are more prevalent in women with SMI; adjusting for these risk factors reduces the elevated risk by approximately 50%. For a few specific adverse birth outcomes, the elevated risk among women with specific SMI diagnoses is completely negated after adjustment for medical comorbidities and substance use.

Our findings of associations between SMI and adverse birth outcomes are broadly consistent with results of previous studies,[1–3,6–9,11,12,36–38] although some of these reports show no association for combinations between specific disorders and adverse outcomes that are observed in our study. The associations between MDD and chorioamnionitis, and MDD and placental complications (antepartum hemorrhage, abruptio placentae and placenta previa), have not been reported before. Likewise, no associations have been indicated previously between BD and amniotic complications (oligo- and polyhydramnios), and BD and cervical complications (predominantly cervical shortening).

The elevated rate of adverse outcomes has lifelong implications for children of mothers with SMI. One of the most prevalent adverse outcomes, preterm birth, has been associated with long-term health issues, such as visual, hearing, speech, neuromotor, cognitive and behavioral impairments, and cerebral palsy.[39] Fetal distress during birth increases the risk of cardiovascular disorders, neurological deficits, limited mobility, and cerebral palsy.[40–42] Another adverse outcome, intrauterine growth restriction, has been associated with growth retardation, neurodevelopmental deficits, metabolic syndrome, and cardiovascular disease in later life.[43] Many other adverse outcomes assessed in this study (e.g. preeclampsia, placental complications, and cervical complications) could also indirectly lead to adverse outcomes due to increased risk of preterm birth and/or intrauterine growth restriction.[44–46]

We also found that a diagnosis of SMI is associated with increased length of stay and hospital charges. Increased length of stay and hospital charges have been demonstrated previously for women with a broader diagnosis of depression,[2,47] but not for SMI, which is defined in this study and previous studies as MDD, BD, or schizophrenia. When incremental costs were aggregated on a national level, the contribution of SMI to the extra maternal hospital charges amount to more than $92 million (in 2014 U.S.$) on average per year between 2008 and 2014. This is in addition to extra costs associated with antenatal care and long-term effects of adverse birth outcomes.

The current study design has several limitations. The chief limitation arises from using data limited to maternal hospital discharge records. Because women and newborn children cannot be followed longitudinally or linked together due to the lack of personal identifiers, no information is available on the course or timing of onset of maternal SMI, diagnostic codes present on the newborn record, or on prescription medication use for maternal SMI.

Psychotropic medication use is associated with adverse birth outcomes, although many studies have not sufficiently controlled for SMI symptom severity, medical comorbidities and/or substance use. The benefits of continuing medication during pregnancy to prevent relapse of symptoms is generally preferred over the potential negative effects of these drugs on the fetus, and there are types of psychotropic medication that are less harmful than others.[48,49] Thus, it is possible that women in our sample have used psychotropic or other medication during pregnancy, and estimates should be interpreted as reflecting differences in risk factors and adverse birth outcomes given the underlying average psychiatric medication use of SMI patients in our sample. Additional information on personal and family characteristics and prenatal care is also unavailable in our dataset. The quality of the data further differs by state; some states in the HCUP-NIS dataset do not disclose race/ethnicity and/or illicit drug use. Nevertheless, the size and comprehensive nature of this nationally-representative dataset make it uniquely suited to analyze adverse outcomes in a relatively rare study population (pregnant women with SMI).

Another limitation of the data is that apparent (i.e. more severe) cases of SMI are more likely to be coded, resulting in an overestimation of the impact of SMI on adverse outcomes. The prevalence of SMI diagnoses in our sample (MDD, 0.11%; BD, 0.63%; schizophrenia, 0.07%; any SMI, 0.78%) is low compared to national estimates of SMI prevalence among women of childbearing age, but consistent with other studies of maternal hospital records.[50] Although fertility rates are lower in women with mood disorders[51] and schizophrenia,[52] it is more likely due to clinicians not being aware of SMI symptoms, or placing little value on coding these mental health conditions in hospital records during a delivery. Under-coding may lead to underestimating prevalence of associated risks, and missing a well-defined patient group that would benefit from more intensive risk factor mitigation strategies, such as aggressive medical management, substance use counseling when appropriate, and enhanced prenatal monitoring.

In conclusion, our results show that a significant part of the association between SMI and adverse outcomes is explained by potentially modifiable conditions; managing these risk factors before and during pregnancy and delivery, as well as increasing awareness of maternal SMI, is instrumental in reducing the higher risk of adverse health outcomes with associated sequelae.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Funding sources and conflict of interest statement

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References

1. Baer RJ, Chambers CD, Bandoli G, Jelliffe-Pawlowski LL. Risk of preterm birth by subtype among Medi-Cal participants with mental illness. Am J Obstet Gynecol 2016;215(4):519.e511–519. [PubMed: 27329688]
2. Bansil P, Kuklina EV, Meikle SF, Posner SF, Kourtis AP, Ellington SR, et al. Maternal and fetal outcomes among women with depression. J Womens Health. 2010;19(2):329–334.
3. Bennedsen BE, Mortensen PB, Olesen AV, Henriksen TB. Congenital malformations, stillbirths, and infant deaths among children of women with schizophrenia. Arch Gen Psychiatry. 2001;58(7):674–679. [PubMed: 11448375]
4. Bodén R, Lundgren M, Brandt L, Reutfors J, Andersen M, Kieler H. Risks of adverse pregnancy and birth outcomes in women treated or not treated with mood stabilisers for bipolar disorder: population based cohort study. BMJ. 2012;345:e7085. [PubMed: 23137820]
5. Howard LM, Goss C, Leese M, Thornicroft G. Medical outcome of pregnancy in women with psychotic disorders and their infants in the first year after birth. Br J Psychiatry. 2003;182:63–67. [PubMed: 12509320]
6. Jablensky AV, Morgan V, Zubrick SR, Bower C, Yellachich L-A. Pregnancy, delivery, and neonatal complications in a population cohort of women with schizophrenia and major affective disorders. Am J Psychiatry. 2005;162(1):79–91. [PubMed: 15625205]
7. Kim DR, Sockol LE, Sammel MD, Kelly C, Moseley M, Epperson CN. Elevated risk of adverse obstetric outcomes in pregnant women with depression. Arch Womens Ment Health. 2013;16(6):475–482. [PubMed: 23934018]
8. Männistö T, Mendola P, Kiely M, O'Loughlin J, Werder E, Chen Z, et al. Maternal psychiatric disorders and risk of preterm birth. Ann Epidemiol 2016;26(1):14–20. [PubMed: 26586549]
9. Mei-Dan E, Ray JG, Vigod SN. Perinatal outcomes among women with bipolar disorder: a population-based cohort study. Am J Obstet Gynecol 2015;212(3):367.e361–368. [PubMed: 25446660]
10. Nylen KJ, O'Hara MW, Engeldinger J. Perceived social support interacts with prenatal depression to predict birth outcomes. J Behav Med 2013;36(4):427–440. [PubMed: 22710981]
11. Räisänen S, Lehto SM, Nielsen HS, Gissler M, Kramer MR, Heinonen S. Risk factors for and perinatal outcomes of major depression during pregnancy: a population-based analysis during 2002-2010 in Finland. BMJ Open. 2014;4(11):e004883.
12. Vigod SN, Kurdyak PA, Dennis CL, Gruneir A, Newman A, Seeman MV, et al. Maternal and newborn outcomes among women with schizophrenia: a retrospective population-based cohort study. BJOG. 2014;121(5):566–574. [PubMed: 24443970]
13. Wangel A-M, Molin J, Moghaddassi M, Stman M. Prior psychiatric inpatient care and risk of cesarean sections: a registry study. J Psychosom Obstet Gynaecol 2011;32(4):189–197. [PubMed: 22040006]
14. Nousen EK, Franco JG, Sullivan EL. Unraveling the mechanisms responsible for the comorbidity between metabolic syndrome and mental health disorders. Neuroendocrinology. 2013;98(4):254–266. [PubMed: 24080959]
15. Wysokinski A, Kloszewska I. Level of thyroid-stimulating hormone (TSH) in patients with acute schizophrenia, unipolar depression or bipolar disorder. Neurochem Res 2014;39(7):1245–1253. [PubMed: 24723220]
16. Gaitatzis A, Carroll K, Majeed A, J WS. The epidemiology of the comorbidity of epilepsy in the general population. Epilepsia. 2004;45(12):1613–1622. [PubMed: 15571520]
17. Regier DA, Farmer ME, Rae DS, Locke BZ, Keith SJ, Judd LL, et al. Comorbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiologic Catchment Area (ECA) Study. JAMA. 1990;264(19):2511–2518. [PubMed: 2232018]

18. Bauer-Staeb C, Jörgensen L, Lewis G, Dalman C, Osborn DPJ, Hayes JF. Prevalence and risk factors for HIV, hepatitis B, and hepatitis C in people with severe mental illness: a total population study of Sweden. Lancet Psychiatry. 2017.
19. King C, Feldman J, Waithaka Y, Aban I, Hu J, Zhang S, et al. Sexual risk behaviors and sexually transmitted infection prevalence in an outpatient psychiatry clinic. Sex Transm Dis 2008;35(10): 877–882. [PubMed: 18607313]
20. Annamraju H, Pavord S. Anaemia in pregnancy. Br J Hosp Med 2016;77(10):584–588.
21. Bruin JE, Gerstein HC, Holloway AC. Long-term consequences of fetal and neonatal nicotine exposure: a critical review. Toxicol Sci 2010;116(2):364–374. [PubMed: 20363831]
22. Cooper DS, Laurberg P. Hyperthyroidism in pregnancy. Lancet Diabetes Endocrinol 2013;1(3): 238–249. [PubMed: 24622372]
23. Desale M, Thinkhamrop J, Lumbiganon P, Qazi S, Anderson J. Ending preventable maternal and newborn deaths due to infection. Best Pract Res Clin Obstet Gynaecol 2016;36:116–130. [PubMed: 27450868]
24. Landon MB, Spong CY, Thom E, Carpenter MW, Ramin SM, Casey B, et al. A multicenter, randomized trial of treatment for mild gestational diabetes. N Engl J Med 2009;361(14):1339–1348. [PubMed: 19797280]
25. Lindsay MK, Burnett E. The Use of Narcotics and Street Drugs During Pregnancy. Clin Obstet Gynecol 2013;56(1):133–141. [PubMed: 23314719]
26. Metz TD, Stickrath EH. Marijuana use in pregnancy and lactation: a review of the evidence. Am J Obstet Gynecol 2015;213(6):761–778. [PubMed: 25986032]
27. Pruett D, Waterman EH, Caughey AB. Fetal alcohol exposure: consequences, diagnosis, and treatment. Obstet Gynecol Surv 2013;68(1):62–69. [PubMed: 23322082]
28. Razaz N, Tomson T, Wikström A-K, Cnattingius S. Association Between Pregnancy and Perinatal Outcomes Among Women With Epilepsy. JAMA Neurol 2017;74(8):983–991. [PubMed: 28672292]
29. Sharshiner R, Silver RM. Management of Fetal Malpresentation. Clin Obstet Gynecol 2015;58(2): 246–255. [PubMed: 25811125]
30. Teng W, Shan Z, Patil-Sisodia K, Cooper DS. Hypothyroidism in pregnancy. Lancet Diabetes Endocrinol 2013;1(3):228–237. [PubMed: 24622371]
31. Triunfo S, Lanzone A. Impact of overweight and obesity on obstetric outcomes. J Endocrinol Invest 2014;37(4):323–329. [PubMed: 24515300]
32. MacDorman MF, Declercq E. Trends and Characteristics of United States Out-of-Hospital Births 2004-2014: New Information on Risk Status and Access to Care. Birth. 2016;43(2):116–124. [PubMed: 26991514]
33. Kuklina EV, Whiteman MK, Hillis SD, Jamieson DJ, Meikle SF, Posner SF, et al. An enhanced method for identifying obstetric deliveries: implications for estimating maternal morbidity. Matern Child Health J. 2008;12(4):469–477. [PubMed: 17690963]
34. Zellner A An Efficient Method of Estimating Seemingly Unrelated Regressions and Tests for Aggregation Bias. J Am Stat Assoc 1962;57(298):348-&.
35. Haeri S, Williams J, Kopeykina I, Johnson J, Newmark A, Cohen L, et al. Disparities in Diagnosis of Bipolar Disorder in Individuals of African and European Descent: A Review. J Psychiatr Pract 2011;17(6):394–403. [PubMed: 22108396]
36. Bayrampour H, Salmon C, Vinturache A, Tough S. Effect of depressive and anxiety symptoms during pregnancy on risk of obstetric interventions. J Obstet Gynaecol Res 2015;41(7):1040–1048. [PubMed: 25772686]
37. Grote NK, Bridge JA, Gavin AR, Melville JL, Iyengar S, Katon WJ. A meta-analysis of depression during pregnancy and the risk of preterm birth, low birth weight, and intrauterine growth restriction. Arch Gen Psychiatry. 2010;67(10):1012–1024. [PubMed: 20921117]
38. Hu R, Li Y, Zhang Z, Yan W. Antenatal depressive symptoms and the risk of preeclampsia or operative deliveries: a meta-analysis. PLoS One. 2015;10(3):e0119018. [PubMed: 25789626]
39. Saigal S, Doyle LW. An overview of mortality and sequelae of preterm birth from infancy to adulthood. Lancet. 2008;371(9608):261–269. [PubMed: 18207020]

40. Cuneo BF, Strasburger JF, Wakai RT, Ovadia M. Conduction system disease in fetuses evaluated for irregular cardiac rhythm. Fetal Diagn Ther 2006;21(3):307–313. [PubMed: 16601344]
41. Malin GL, Morris RK, Khan KS. Strength of association between umbilical cord pH and perinatal and long term outcomes: systematic review and meta-analysis. BMJ. 2010;340:c1471. [PubMed: 20466789]
42. van Iersel PAM, Algra AM, Bakker SCM, Jonker AJH, Hadders-Algra M. Limitations in the Activity of Mobility at Age 6 Years After Difficult Birth at Term: Prospective Cohort Study. Phys Ther 2016;96(8):1225–1233. [PubMed: 26847013]
43. Miller SL, Huppi PS, Mallard C. The consequences of fetal growth restriction on brain structure and neurodevelopmental outcome. J Physiol 2016;594(4):807–823. [PubMed: 26607046]
44. Bokslag A, van Weissenbruch M, Mol BW, de Groot CJM. Preeclampsia; short and long-term consequences for mother and neonate. Early Hum Dev 2016;102:47–50. [PubMed: 27659865]
45. De Silva DA, Lisonkova S, von Dadelszen P, Synnes AR, Canadian Perinatal Network Collaborative G, Magee LA. Timing of delivery in a high-risk obstetric population: a clinical prediction model. BMC Pregnancy Childbirth. 2017;17(1):202. [PubMed: 28662632]
46. Vink J, Feltovich H. Cervical etiology of spontaneous preterm birth. Semin Fetal Neonatal Med 2016;21(2):106–112. [PubMed: 26776146]
47. Lancaster CA, Flynn HA, Johnson TRB, Marcus SM, Davis MM. Peripartum length of stay for women with depressive symptoms during pregnancy. J Womens Health. 2010;19(1):31–37.
48. Chisolm MS, Payne JL. Management of psychotropic drugs during pregnancy. BMJ. 2016;532:h5918. [PubMed: 26791406]
49. Ornoy A, Weinstein-Fudim L, Ergaz Z. Antidepressants, Antipsychotics, and Mood Stabilizers in Pregnancy: What Do We Know and How Should We Treat Pregnant Women with Depression. Birth Defects Res 2017;109(12):933–956. [PubMed: 28714604]
50. Kelly R, Zatzick D, Anders T. The detection and treatment of psychiatric disorders and substance use among pregnant women cared for in obstetrics. Am J Psychiatry. 2001;158(2):213–219. [PubMed: 11156803]
51. Williams KE, Marsh WK, Rasgon NL. Mood disorders and fertility in women: a critical review of the literature and implications for future research. Hum Reprod Update. 2007;13(6):607–616. [PubMed: 17895237]
52. Bundy H, Stahl D, MacCabe JH. A systematic review and meta-analysis of the fertility of patients with schizophrenia and their unaffected relatives. Acta Psychiatr Scand. 2011;123(2):98–106. [PubMed: 20958271]

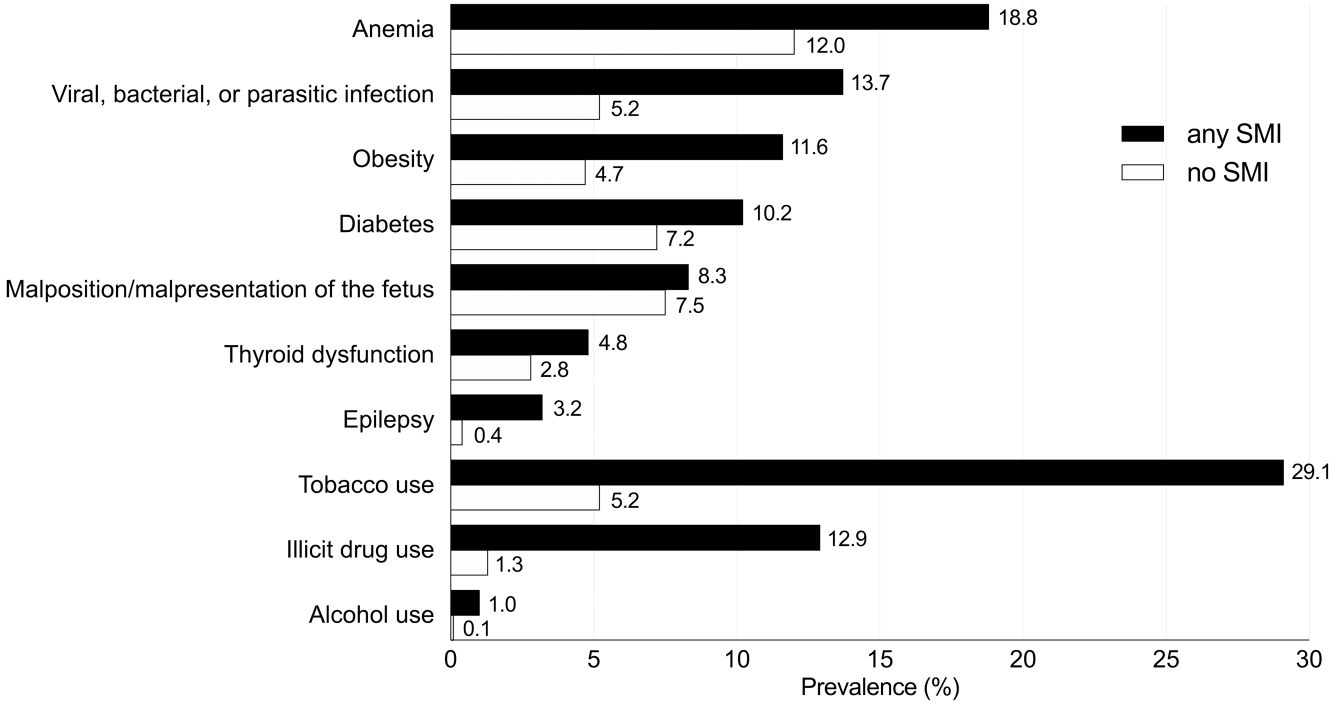

Figure 1.

Prevalence of risk factors (medical comorbidities and substance use) for adverse birth outcomes in women with serious mental illness (SMI) during delivery hospital stays.

Table 1.

Hospital and patient characteristics of women with SMI diagnosis on maternal record.

Hospital and patient characteristics		No SMI[a]	SMI[a]	*P* Value
Unweighted sample size, n		5,475,739	43,027	
100% weighted population estimate, n		26,451,782	208,879	
SMI diagnoses, % (95% CI)	MDD	-	14.1	
	BD	-	80.8	
	Schizophrenia	-	8.6	
Age in years, mean (95% CI)		27.9 (27.8-27.9)	26.8 (26.7-26.9)	<.001
Race/ethnicity, % (95% CI)	White	47.1 (46.1-48.1)	57.9 (56.6-59.2)	<.001
	Black	12.6 (12.1-13.0)	16.3 (15.4-17.1)	<.001
	Hispanic	19.7 (18.9-20.6)	9.2 (8.5-9.8)	<.001
	Asian/Pacific Islander	4.8 (4.5-5.1)	1.1 (1.0-1.3)	<.001
	Native American	0.7 (0.7-0.8)	0.7 (0.6-0.8)	0.13
	Other/unknown	15.1 (14.1-16.1)	14.9 (13.5-16.3)	0.67
Insurance, % (95% CI)	Private	50.3 (49.4-51.2)	26.5 (25.5-27.5)	<.001
	Medicaid	43.2 (42.4-44.0)	61.0 (60.0-62.0)	<.001
	Other[b]	6.5 (6.2-6.8)	12.5 (12.1-13.0)	<.001
Income, % (95% CI)	1st quartile (lowest)	27.2 (26.5-28.0)	34.8 (33.7-35.9)	<.001
	2nd quartile	25.4 (24.9-26.0)	27.3 (26.6-28.1)	<.001
	3rd quartile	24.9 (24.4-25.4)	22.5 (21.8-23.1)	<.001
	4th quartile (highest)	22.5 (21.5-23.5)	15.4 (14.6-16.2)	<.001
Urban location of hospital, % (95% CI)		89.0 (88.6-89.4)	88.9 (88.2-89.5)	0.70
Region, % (95% CI)	Northeast	15.9 (15.2-16.8)	19.5 (18.2-21.0)	<.001
	Midwest	21.4 (20.5-22.2)	25.4 (24.2-26.8)	<.001
	South	38.0 (36.9-39.2)	34.5 (33.0-36.1)	<.001
	West	24.7 (23.7-25.6)	20.5 (19.3-21.8)	<.001
Hospital admission characteristics, % (95% CI)	Emergency department	7.6 (6.8-8.4)	8.2 (7.3-9.2)	0.01
	Elective	49.5 (48.1-50.9)	45.9 (44.2-47.6)	<.001
	Weekend	19.4 (19.3-19.5)	19.3 (18.9-19.6)	0.55
Length of stay, days (95% CI)		3.6 (3.6-3.7)	4.2 (4.2-4.3)	<.001
Total hospital charges, 2014 U.S.$s (95% CI)		15,136 (14,881-15,390)	17,911 (17,473-18,350)	<.001

Abbreviations: SMI, serious mental illness; MDD, major depressive disorder; BD, bipolar disorder.

[a]Diagnosis of MDD, BD and/or schizophrenia on maternal delivery record.

[b]Medicare, uninsured, or other/unknown.

Table 2.

Risk of adverse birth outcomes among women with SMI diagnosis on maternal record

Adverse birth outcomes	Prevalence, %		Relative Risk (95% CI) for women with SMI[a]			Fully adjusted *P* Value
	No SMI[a]	SMI[a]	Unadjusted	Base model	Fully adjusted model	
Adverse gestational outcomes (all)[b]	25.9	30.7	1.18 (1.17-1.20)	1.15 (1.13-1.17)	1.08 (1.06-1.09)	<.001
Preeclampsia	9.9	14.9	1.51 (1.47-1.55)	1.46 (1.42-1.49)	1.24 (1.21-1.28)	<.001
Amniotic complications	3.6	4.7	1.29 (1.23-1.34)	1.28 (1.22-1.33)	1.11 (1.06-1.16)	<.001
Placental complications	2.2	3.3	1.53 (1.45-1.62)	1.47 (1.39-1.55)	1.11 (1.05-1.17)	<.001
Cervical complications	0.2	0.4	1.82 (1.57-2.12)	1.67 (1.43-1.96)	1.32 (1.13-1.53)	0.002
Adverse obstetric outcomes (all)[c]	43.0	46.3	1.08 (1.06-1.09)	1.07 (1.06-1.08)	1.03 (1.02-1.05)	<.001
Umbilical cord complications	22.0	21.5	0.98 (0.96-1.00)	0.97 (0.96-1.00)	0.98 (0.96-1.00)	0.03
Preterm birth	9.8	14.5	1.49 (1.45-1.52)	1.43 (1.39-1.46)	1.19 (1.16-1.22)	<.001
Chorioamnionitis	1.9	2.2	1.17 (1.10-1.25)	1.22 (1.14-1.30)	1.10 (1.03-1.17)	0.007
Cesarean section[d]	33.1	38.1	1.15 (1.14-1.17)	1.20 (1.18-1.22)	1.08 (1.06-1.09)	<.001
Adverse fetal outcomes (all)[e]	21.5	27.3	1.27 (1.25-1.29)	1.24 (1.21-1.26)	1.12 (1.09-1.14)	<.001
Fetal distress	16.4	20.2	1.24 (1.21-1.26)	1.20 (1.17-1.22)	1.10 (1.08-1.13)	<.001
Poor fetal growth	2.4	4.5	1.88 (1.79-1.97)	1.69 (1.61-1.77)	1.24 (1.18-1.31)	<.001
Fetal malformations	0.9	1.6	1.78 (1.65-1.93)	1.63 (1.51-1.77)	1.33 (1.23-1.44)	<.001
Single stillbirth	0.5	0.9	1.67 (1.51-1.84)	1.45 (1.30-1.61)	1.19 (1.07-1.32)	0.004
Adjusts for:						
Hospital & patient characteristics[f]				x	x	x
Risk factors[g]					x	x

Abbreviations: SMI, serious mental illness.

[a]Diagnosis of major depressive disorder, bipolar disorder, and/or schizophrenia on maternal delivery record.

[b]Preeclampsia, cervical complications, placental complications, amniotic complications, maternal complication during in utero procedure, hemorrhage in early pregnancy (<20 weeks), spotting, uterine size date discrepancy, late pregnancy.

[c]Preterm birth, chorioamnionitis, failed mechanical or chemical induction, coagulation defects, forceps or vacuum extraction, complications with sedation, maternal distress, fetal-maternal hemorrhage, maternal hypotension, other indications for care or intervention, umbilical cord complications, long labor/ abnormality of forces, other obstetric complications, infection/fever.

[d]Not included in “adverse obstetric outcomes (all)”.

[e]Poor fetal growth, single stillbirth, fetal malformations, excessive fetal growth, fetal hematologic conditions, fetal complication from in utero procedure, maternal nutritional disorders affecting fetus or newborn, maternal injury affecting fetus or newborn, chronic maternal circulatory and respiratory diseases affecting fetus or newborn, fetal distress, multiple birth stillborn, maternal infection affecting fetus.

[f]Hospital and patient characteristics: race, age, payer, urban/rural location, U.S. region, weekend admission, emergency department admission, elective admission, income, admission year.

[g]Risk factors: anemia, malposition/malpresentation, diabetes mellitus, obesity, alcohol use, illicit drug use, tobacco use, thyroid dysfunction, viral/ bacterial/parasitic infection, epilepsy.

Table 3.

Risk of adverse birth outcomes, adjusted for specific covariates, among women with SMI diagnosis on maternal record

Adverse birth outcomes	Relative Risk (95% CI) for women with SMI[a]			
	Base model	Base model with adjustment for substance use	Base model with adjustment for medical comorbidities	Fully adjusted model
Adverse gestational outcomes[b]	1.15 (1.13-1.17)	1.14 (1.12-1.16)	1.08 (1.06-1.10)	1.08 (1.06-1.09)
Adverse obstetric outcomes[c]	1.07 (1.06-1.08)	1.05 (1.04-1.06)	1.05 (1.04-1.06)	1.03 (1.02-1.05)
Adverse fetal outcomes[d]	1.24 (1.21-1.26)	1.17 (1.15-1.19)	1.18 (1.16-1.20)	1.12 (1.10-1.14)
Adjusts for:				
Hospital & patient characteristics[e]	x	x	x	x
Substance use[f]		x		x
Medical comorbidities[g]			x	x

Abbreviations: SMI, serious mental illness.

[a]Diagnosis of major depressive disorder, bipolar disorder, and/or schizophrenia on maternal delivery record.

[b]Preeclampsia, cervical complications, placental complications, amniotic complications, maternal complication during in utero procedure, hemorrhage in early pregnancy (<20 weeks), spotting, uterine size date discrepancy, late pregnancy.

[c]Preterm birth, chorioamnionitis, failed mechanical or chemical induction, coagulation defects, forceps or vacuum extraction, complications with sedation, maternal distress, fetal-maternal hemorrhage, maternal hypotension, other indications for care or intervention, umbilical cord complications, long labor/ abnormality of forces, other obstetrical complications, infection/fever. Not including cesarean sections.

[d]Poor fetal growth, single stillbirth, fetal malformations, excessive fetal growth, fetal hematologic conditions, fetal complication from in utero procedure, maternal nutritional disorders affecting fetus or newborn, maternal injury affecting fetus or newborn, chronic maternal circulatory and respiratory diseases affecting fetus or newborn, fetal distress, multiple birth stillborn, maternal infection affecting fetus.

[e]Hospital and patient characteristics: race, age, payer, urban/rural location, U.S. region, weekend admission, emergency department admission, elective admission, income, admission year.

[f]Substance use: alcohol use, illicit drug use, tobacco use.

[g]Medical comorbidities: anemia, malposition/malpresentation, diabetes mellitus, obesity, thyroid dysfunction, viral/bacterial/parasitic infection, epilepsy.

Table 4.

Effect of maternal SMI on hospital charges and length of stay for child birth hospitalization

Hospitalization-related outcomes	No SMI[a]	β (95% CI) for women with SMI[a]		
		Unadjusted	Base model	Adjusted *P* Value
Total charges, 2014 U.S.$s (95% CI) n = 5,195,066	$15,136	2,776 (2,435-3,116)	3,104 (2,801-3,407)	<.001
Length of stay, days (95% CI) n = 5,323,493	3.6	0.6 (0.5-0.6)	0.6 (0.5-0.6)	<.001
Total charges per day, 2014 U.S.$s (95% CI) n = 5,195,058	$4,125	84 (22-146)	179 (134-225)	<.001
Adjusts for:				
Hospital & patient characteristics[b]			x	x

Abbreviations: SMI, serious mental illness.

[a]Diagnosis of MDD, BD and/or schizophrenia on maternal delivery record.

[b]Hospital and patient characteristics: race, age, payer, urban/rural location, U.S. region, weekend admission, emergency department admission, elective admission, income, admission year.