Research Article

MENTAL HEALTH TREATMENT AND METABOLIC DISORDERS IN PREGNANCY: A LONGITUDINAL STUDY

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Abstract

Objective: This study aimed to measure sequential rates of obesity, gestational diabetes, polycystic ovary syndrome, and anxiety, depression and antidepressant treatment in pregnant women in Australia between 2008 and 2022.

Materials and Methods: BMI ≥ 30 (obesity), BMI ≥ 35 (severe obesity/obesity class II and III), gestational diabetes, Type II diabetes, polycystic ovary syndrome, clinical diagnoses of anxiety and depression, antidepressant treatment.

Results: Women taking antidepressants in pregnancy were substantially more vulnerable to obesity (BMI ≥ 30) with rates of 43.59% *vs* 26.00%. Women taking antidepressants in pregnancy also had higher rates of severe obesity (BMI ≥ 35) at 25.63% *vs* 12.98%. A small minority of these women were also nearly 6 times more likely to drink alcohol in pregnancy (2.7% *vs* 0.47%) and to use other drugs in pregnancy such as amphetamines (0.35% *vs* .07%) and cannabis (3.4% *vs* 0.73%). When compared with peers matched for diagnosis of depression and anxiety, women taking antidepressants were still more likely to be obese (25.63% *vs* 20.17%) though this difference was not so marked. Rates of obesity have increased in the cohort studied from 26.86% to 31.27%; of gestational diabetes from 3.98% to 21.77%; of polycystic ovary syndrome from 1.47% to 5.47%; of anxiety from 1.11% to 5.77%; of depression from 2.17% to 4.31%, and antidepressant treatment from 1.45% to 2.16%.

Conclusions: Obesity, gestational diabetes and polycystic ovary syndrome rates have substantially increased between 2008 and 2022 in Australia. Rates of anxiety in pregnant women have increased substantially over this period, as have rates of depression. Women living with depression and anxiety in pregnancy are increasing to suffer obesity and related metabolic conditions. Antidepressant treatment may also increase these women's vulnerability to obesity and severe obesity. *ASEAN Journal of Psychiatry, Vol. 25 (7) July, 2024; 1-10.*

Keywords: Obesity; Gestational Diabetes; Type II Diabetes; Polycystic Ovary Syndrome; Pregnancy; Depression; Anxiety; Antidepressant

Introduction

A social change makes an indelible imprint on individuals' mental and physical health and wellbeing. Our data provides a section of pregnant women's mental and physical health over the 15

years between 2008 and 2022. Considering the trends we observed over time in these women frames our thinking about how to structure and provide integrated mental and physical health services now and into the future, presuming that the trends we observed continue. In particular, our team was concerned with the physical wellbeing of women living with mental illness and the impact that their physical and mental ill-health in pregnancy may have on them and their babies in pregnancy, at birth, and in the months and years to come.

Contextualising this data: Obesity and metabolic syndromes over time in Australia

Rates of Gestational Diabetes (GDM) have soared over the past decades in Australia, from an incidence of 5.4% in 2008-2009 to 19.3% in 2021-2022, the duration of our dataset [1,2]. The jump in this period relates in part to changed parameters for diagnosis of GDM widely adopted between 2011-2016, a change in the ethnic and demographic background of women giving birth in Australia, as well as a marked underlying increase in rates of GDM in the broader population associated with an increase in rates of obesity, as shown in this paper [3-5].

By contrast with the rapid increase in rates of GDM, rates of Type II diabetes have not escalated to the same degree in Australia in the past two decades, consistent with other wealthy nations worldwide: Among women who gave birth in 2009-11 in Australia, 0.7% had pre-existing diabetes [6,7]. In 2021, rates of Type II Diabetes ranged between 1.4% and 2.1% in women aged 25-44 [8].

Polycystic Ovary Syndrome (PCOS) has been less well characterized in international and local population data to date [9]. This may relate to reduced recognition of this condition even by health providers, with low rates of diagnosis and lengthy time to diagnosis recorded for this condition [10]. However, rates of PCOS have been described at between 5%-15% in middle-income nations, with a substantial environmental vulnerability relating to poor quality nutrition and socioeconomic stress [11,12]. Existing data suggests a global increase in incidence of 4.47% over the years 2007-2017, with a large proportion of this increase occurring in low to middle income countries and in regions including Oceania, South Asia, and Southern and Eastern Africa [13].

Materials and Methods

Characterizing our cohort

This sample was taken from an outer suburban, lower socioeconomic area in a major capital city of Australia. Women were birthing in the public (government-funded) maternity service over the past 15 years. This rapidly growing local government area has a high proportion of culturally and linguistically diverse residents, many of whom have migrated from overseas (54.1% of those living in the southern region served by the hospital have migrated to Australia) [14]. The nations contributing most substantially to this migration include India, the Philippines, New Zealand and Vietnam. Refugees from Syria and Sri Lanka have settled locally, as has a population from Horn of Africa countries.

Formal unemployment levels range between 6.7%-7.9% at present in this region, though in addition there is a substantial population classed as "away from work" (6.7%-6.9%). Household incomes are below the state and national average, by up to 25% in the southern region. Consistent with the socioeconomic deprivation experienced in this region with to Socioeconomic Indices for Areas (SEIFA) of 921 and 994, rates of obesity and smoking are higher than the average across Australia at the present time (2022 data): 14%-21% smoking rates *vs* 10.9% state-wide; 29%-31% obesity rates *vs* 19% state-wide average [15,16].

International changes in antidepressant medication prescribing patterns over time

Throughout the world, in tandem with an increase in the recognition of the incidence, severity, risks and sequelae of peripartum depression and anxiety symptoms in women, prescribing of antidepressants in pregnancy has increased over time. English authors noted a four-fold increase in antidepressant prescribing rates in pregnancy from 0.8% in 1992 to 3.3% in 2006 [17]. Use of antidepressants in France in 2014, at 2.57% of singleton pregnancies, contrasted with use of antidepressants in Japan over the period 2005-2016 of 133/10,000 [18,19]. North American patterns of prescribing, meanwhile, have continued to climb in all published data; 4.5% in Quebecois women between 1998 and 2009; an increase from 2.5% in 1998 to 8.1% in 2005 in 4 American states; rates of up to 13.4% in Tennessee were found in 2003 [20,21]. In Australia, prevalence of antidepressant

use has increased by 7% for women between 2015 and 2019 (159.3/1,000 to 170.4/1,000) [22].

This data was drawn from a clinical database used to enter information at each antenatal visit for women birthing at a local, publicly funded metropolitan maternity hospital. Of a total of 78,482 births, data was trimmed to ensure that relevant parameters were within acceptable limits, example BMI between 15 and 60. After this process 75,308 births remained for examination in the dataset (Figure 1).

Ethics approval

Ethics approval was provided by Western Health Ethics, approval number QA2017.80 and Monash University.

Statistical analysis

The dataset was transformed for analysis using R version 4.1.1 [23]. Subsequent analysis including derivation of descriptive statistics was performed using STATA version 17 [24] (Table 1).
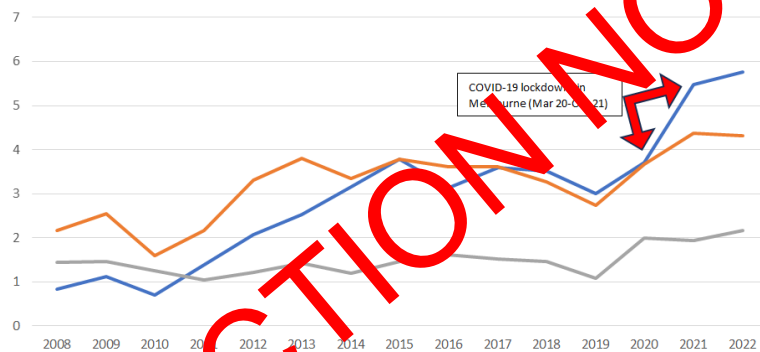
Figure 1. Anxiety, depression, and anti-depressant medication treatment over time (%) overall cohort. Note: (━━━) Anxiety; (━━━) Depression; (━━━) Anti-depressant medication.

Table 1. Descriptive statistics comparing women taking antidepressants in pregnancy with the overall birthing cohort.

Variable	Total sunshine birthing cohort 2008-2022	% of overall sample (75,308)	Women taking antidepressants in pregnancy	% of all women taking antidepressants in pregnancy (1,147)
BMI <30	55726	74	647	56.41
BMI ≥ 30	19582	26	500	43.59
BMI ≥ 35	9775	12.98	294	25.63
Age 35+	2426	3.22	58	5.06
Tobacco use in pregnancy	6402	8.5	269	23.45
Type II diabetes	511	0.68	4	0.35
Current depression in pregnancy	2538	3.37	712	62.07
Current anxiety symptoms in pregnancy	2433	3.23	416	36.27
Schizophrenia	67	0.09	16	1.39
Bipolar disorder	213	0.28	45	3.92
Benzodiazepines	40	0.05	3	0.26
Antipsychotic medication	112	0.15	17	1.48
Early (1st January 2008-30th June 2016)	36,195	48.06	474	41.33
Late (1st July 2016-31st December 2022)	39,113	51.94	673	58.67

Social issues in pregnancy	715	0.95	60	5.23
Anticonvulsants	137	0.18	4	0.35
Sedatives	15	0.02	3	0.26
Alcohol use	357	0.47	31	2.7
Poor/no attendance	979	1.3	20	1.74
Gestational diabetes	11576	15.37	167	14.56
Amphetamine use in pregnancy	54	0.07	4	0.35
Cannabis	550	0.73	39	3.4
Methadone/buprenorphine	-	-	19	1.66
Opiates	98	0.13	6	0.52
Antihypertensives	1099	1.46	46	4.01
Essential hypertension	333	0.44	13	1.13
Pre-eclampsia	1002	1.33	42	3.66
Eclampsia	1021	1.36	42	3.66

Results

Characterizing the cohort

In this data set, women taking antidepressants in pregnancy were much more vulnerable to obesity (BMI ≥ 30) and more severe obesity (class II and III, BMI ≥ 35) than women not taking antidepressants and birthing during the same period. Rates increased from 26% of women in the overall cohort to nearly half of women taking antidepressants, at 43.59%. Women taking antidepressants were more likely to use alcohol and other drugs in pregnancy; particularly these women were three times more likely to smoke than their peers who were not taking antidepressants in pregnancy, consistent with existing research [25].

Considering un-medicated depressed/anxious peers as a comparator group

Our study found that women taking antidepressants in pregnancy were far more similar to their depressed/anxious peers not taking antidepressant medication than the wider cohort. In particular, both groups shared very similar rates of smoking and other drug use, as well as similar rates of social issues and non-attendance at antenatal clinic. There were some areas in which the two groups diverged, notably alcohol use, current rates of diagnosis of bipolar affective disorder, schizophrenia and depression, and concurrent use of other psychotropic medications in pregnancy, including antipsychotics and sedatives. Rates of obesity diverged between those treated with antidepressant medication and those who were not, consistent with differences between the treated group and the overall comparator group though the difference was not quite so marked (Figure 2).

Considering the impact of time and societal events on rates of mental ill-health and antidepressant medication treatment

During this time period, diagnoses of anxiety and depression increased noticeably from rates of 2.17% (depression) and 1.11% (anxiety) in 2008, to 4.31% (depression) and 5.77% (anxiety) in 2022. The increase in reporting rates between 2010 and 2012/13 may relate in particular to standardization of the use of the Edinburgh Postnatal Depression Scale (EPDS) as routine in both pregnancy and postpartum care in Victoria and across Australia since 2013 as part of the National Perinatal Depression Initiative (NPDI) [25,26]. In particular, the midwives at this maternity centre were trained to use the EPDS as a screening tool for all women being provided antenatal care after 2012 [27].

Rates of anxiety increased particularly in the period 2020-2021, during the COVID-19 pandemic. Interestingly, this relatively high rate of anxiety in particular appears to have been sustained over the subsequent year. Rates of antidepressant use in pregnancy seem to have remained relatively low over the time period described despite an increase in reported rates of anxiety and depression (Figure 3).
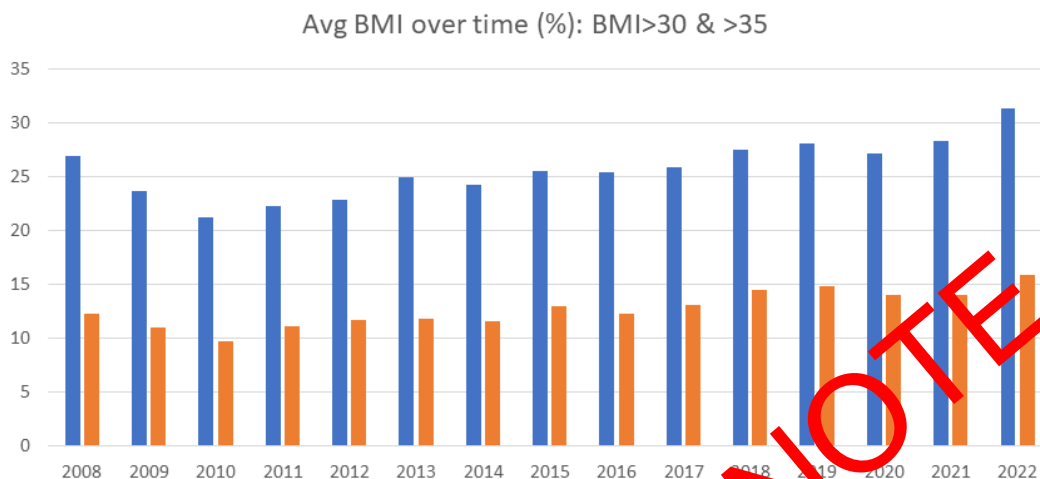
Figure 2. Obesity over time, overall cohort. Note: (■) BMI 30+; (■) BMI 35+.

Figure 3. Rates of gestational diabetes over time, overall cohort. Note: (———) Gestational diabetes.

Considering the effect of time and societal factors on rates of obesity and related metabolic and hormonal disorders

Aside from the first 2 years of this time period, it is notable that rates of obesity, and also of severe obesity (classes II and III, BMI $\geq$ 35) climbed rapidly over the course of the subsequent 12 years to a high point in 2022 of 31.27% for BMI $\geq$ 30, of whom women with BMI $\geq$ 35 made up just over half (15.82%).

Rates of metabolic disorders such as gestational diabetes appear to have increased over the course of this period as well, from 3.98% in 2008 to 21.77% in 2022. Note that the definition of gestational

diabetes in Australia was altered in around 2014-2016 to a more inclusive one, in line with guidelines published by the World Health Organization. These changed guidelines led to an increase in reported rates of GDM in Australian women.

Similarly, rates of Diabetes Type II have also increased over this period, though from a relatively low base rate of 0.24% in 2008 to a high of 1.01% in 2022.

Polycystic Ovary Syndrome (PCOS) rates have also escalated over this time period in the population studied, from 1.47% in 2008 to 5.47% in 2022, with associated implications for women's physical and mental health and fertility (Figure 4).
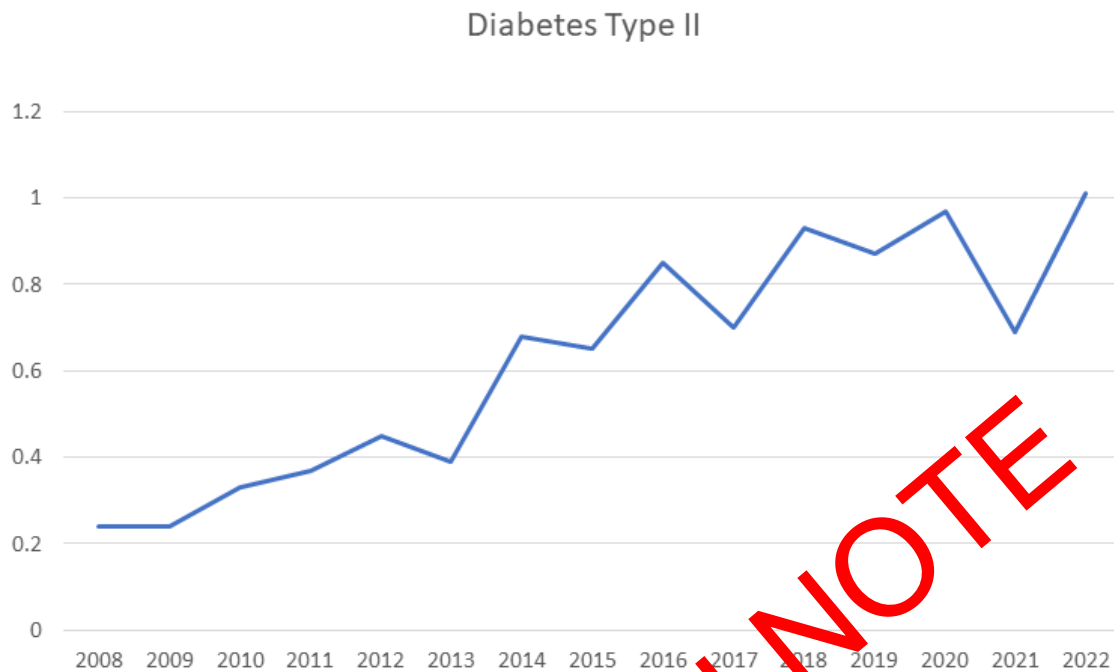
Figure 4. Diabetes type II over time, overall cohort.

Discussion

Considering the cohort

As described in the Introduction, our cohort represented a multiethnic group of women living in a lower socioeconomic area and attending public maternity care for the duration of their pregnancy. These women's vulnerability to conditions associated with poverty and disadvantage such as obesity was commensurately high. Also notable were relatively high rates of cigarette smoking, given that in Australia overall rates of smoking are low compared with many other OECD nations, and have declined steeply over the time period examined [28].

*Considering an appropriate peer comparator group*

Perinatal psychiatric research has been dogged by criticism of insufficiently close comparator groups to women actually taking medications of interest in pregnancy given that depression, schizophrenia, bipolar affective disorder and other mental health conditions themselves seem to correlate with higher rates of adverse outcomes for mothers and babies [29]. Accordingly, our team considered a peer cohort of women with current or past diagnoses of anxiety and depression in an attempt

to incorporate genetic and lifestyle vulnerabilities which could also contribute to adverse outcomes for women and babies. This peer comparator group seemed, on the basis of the descriptive statistics obtained, to more closely mirror the women treated with antidepressants on most known covariates including gestational diabetes, Type II diabetes and PCOS. Rates of obesity, and in particular severe obesity, were higher for women treated with antidepressants during pregnancy than their otherwise closely matched peers. This suggests that antidepressants may confer an increased risk of weight gain in pregnancy, and increase the risk of both obesity and severe obesity in pregnant women. Rates of polypharmacy with other psychotropic medications such as antipsychotics and sedatives were higher in the group currently taking antidepressants than in the untreated comparator group. This suggests the presence of several risks complicating the prior outcome: firstly a risk of confounding by severity, in that women taking antidepressants may have required multiple classes of psychotropic to manage the severity of their symptoms, and secondly a risk of confounding through the impact of polypharmacy itself. Each of these considerations tempers the suggestion of a link between antidepressant uses per se and increased risk of obesity (Table 2) (Figure 5).

Table 2. Descriptive statistics comparing women taking antidepressants in pregnancy with their anxious/depressed peers.

Covariate	No antidepressant treatment in pregnancy: 6412 births (% of untreated cohort)	Antidepressant treatment in pregnancy: 1147 births (% of treated cohort)	Total: 7,559 births (% of overall cohort)
Age 35+	218 (3.40%)	58 (5.06%)	276 (3.65%)
BMI ≥ 35	1293 (20.17%)	294 (25.63%)	1587 (20.99%)
BMI ≥ 30	2299 (35.85%)	500 (43.59%)	2799 (37.03%)
Type II diabetes diagnosed prior to pregnancy	21 (0.33%)	4 (0.35%)	25 (0.33%)
Gestational diabetes	1029 (16.05%)	167 (14.56%)	1196 (15.82%)
Social issues in pregnancy*	254 (3.96%)	60 (5.23%)	314 (4.15%)
Poor/no attendance at antenatal appointments	101 (1.58%)	20 (1.74%)	121 (1.6%)
Current diagnosis bipolar disorder	94 (1.47%)	45 (3.92%)	139 (1.84%)
Current diagnosis schizophrenia	19 (0.30%)	16 (1.39%)	35 (0.46%)
Current diagnosis depression	1826 (28.48%)	712 (62.07%)	2538 (33.58%)
Current diagnosis anxiety	2017 (31.46%)	416 (36.27%)	2433 (32.19%)
Antipsychotic use in pregnancy	18 (0.28%)	17 (1.48%)	35 (0.46%)
Benzodiazepine use in pregnancy	12 (0.19%)	3 (0.26%)	15 (0.20%)
Sedative use in pregnancy	5 (0.08%)	3 (0.26%)	8 (0.11%)
Anticonvulsant use in pregnancy	15 (0.23%)	4 (0.35%)	19 (0.25%)
Alcohol use in pregnancy	79 (1.23%)	31 (2.70%)	110 (1.46%)
Tobacco smoking in pregnancy	1273 (19.85%)	269 (23.45%)	1542 (20.40%)
Amphetamine use in pregnancy	16 (0.25%)	4 (0.35%)	20 (0.26%)
Cannabis use in pregnancy	193 (3.01%)	39 (3.40%)	232 (3.07%)
Opioid use in pregnancy	35 (0.55%)	6 (0.52%)	41 (0.54%)
Methadone/ buprenorphine treatment in pregnancy	69 (1.08%)	19 (1.66%)	88 (1.16%)
Total	6412 (100%)	1147 (100%)	7559 (100%)

Note: * "social issues" in this dataset primarily included homelessness or risk of homelessness, family violence, child protection involvement with the family, or imprisonment of one or both parents during the pregnancy period.
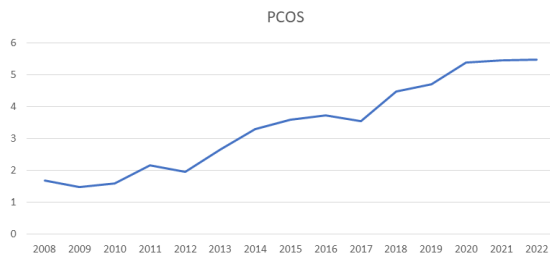
Figure 5. PCOS rates over time, overall cohort.

Considering the effect of time on reported rates of mental illness and related treatments, including antidepressant use

As noted, reported rates of anxiety and depression increased over the time period studied, with an especial increase during and after the COVID-19 pandemic. The social effect of attempts to manage the impact of the COVID-19 pandemic was felt particularly severely in Melbourne, as has been noted in other research [30,31]. During this period the population was affected by 6 total lockdowns, the longest of which lasted 111 days [2]. Restrictions on access to hospital for partners and support people for pregnant women during these periods were almost complete. At these times, most women were unable to have a birth partner attend to support them in appointments or during their baby's birth. There appear to have been correspondingly high rates of clinically significant anxiety symptoms reported during this period [32]. As previously noted, these high rates of anxiety do not seem to have settled after pandemic restrictions were eased: it remains to be seen whether this increased trend will continue. Rates of treatment with antidepressant medication for both anxiety and depression increased over the period studied, though these treatment rates did not rise to match the level of reported symptomatology.

Considering the effect of time and societal factors on rates of obesity and related metabolic and hormonal disorders

Obesity, gestational diabetes and Type II diabetes have been linked to adverse outcomes in pregnancy for both mother and child. Risks for the mother include "miscarriage, gestational diabetes, pre-eclampsia, venous thromboembolism, induced labor, caesarean section, anaesthetic complications and wound infections, and they are less likely to initiate or maintain breastfeeding" [33]. Babies also risk adverse outcomes, including "stillbirth, congenital anomalies, prematurity, macrosomia and neonatal death" [34]. PCOS has been linked, in a bidirectional manner, to depression in pregnancy and the postpartum.

Obesity in pregnancy and gestational diabetes have also been increasingly linked to longer-term adverse outcomes for mothers and babies, including cardiovascular disease for women in later life and their babies' development of childhood obesity. On the basis of our results, these adverse outcomes are likely to become increasingly common, especially for the vulnerable cohort of women with depression and anxiety who are treated for these conditions with antidepressant medication (Figure 6).
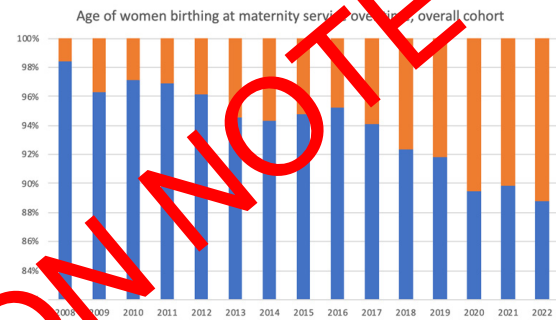
Figure 6. Age of women birthing over time at maternity service (total number 78,804). Note: (■) Women birthing aged under 35; (■) Women birthing aged under 35+.

Conclusion

Women birthing in the present time are increasingly vulnerable to physical health conditions such as obesity, gestational diabetes and polycystic ovary syndrome, as well as mental health concerns such as anxiety and depression. A confluence of these syndromes affects outcomes for mother and baby. We need to better understand treatment decisions in pregnancy, including both the need for treatment and the risks attendant on different modes of treatment for women and babies.

Throughout the study, it became evident that addressing mental health concerns in pregnant women not only positively impacts their emotional state but also potentially mitigates the risk of developing metabolic disorders. This highlights the interconnectedness of mental and physical health, especially during the vulnerable period of pregnancy.

Limitations

Our research data is limited by the mode of its collection. These datasets are designed for clinical care, and hence the use of structured instruments to diagnose and measure mental illness is not routinely included. Correlation with this data, including with clinical scales such as the Edinburgh Postnatal Depression Scale, routinely

administered in pregnancy and postpartum in Victorian maternity care services, would help to address concerns about diagnostic accuracy, as previously mentioned. Other limitations include the absence of details about antidepressant dosage or specific medication, which has been used in other research to provide practical guidance to clinicians. One consideration noted by existing literature that this comparator group did not include is severity, which may be picked up to some degree by the single covariate on which the two groups diverged in this case: Current diagnosis of depression, bipolar disorder or schizophrenia. One potential marker for severity might be high rates of polypharmacy with other psychotropic medications noted in the treatment group, including off-label use of antipsychotic medications such as quetiapine for insomnia in pregnancy associated with ongoing symptoms of anxiety or depression.

Future Directions

This data requires further evaluation to tease out the strength of different covariates' influence on the metabolic outcomes of interest. Given the detail available in terms of clinical and lifestyle factors in this data, it would be useful to undertake a logistic regression analysis to consider the contribution of these measured factors in more detail. This data also suggests that including a time specifier in this analysis would help to reduce the risk that time period itself contributes to the adverse outcome identified. Other future directions could include the use of machine learning techniques in analysis which may address the problems inherent in unconscious bias on the part of the researcher. It is notable that in this data set, around 25,000 women had multiple sequential births over the time period examined. This provides the opportunity to consider these women as their own controls, further reducing the potential effect of unmeasured confounders such as demographics or genetic factors.

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