



Association Between Preconception Maternal Mental Health-Related Hospitalisation (MHRH) and Outcomes During Pregnancy: A Population-Based Cohort Study in the Northern Territory, Australia

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Abstract

Comprehensive studies investigating the link between maternal hospitalisation for mental health conditions prior to pregnancy and adverse outcomes in pregnancy are scarce in Australia. We aimed to fill this gap by using 18 years of administratively linked data to inform early interventions. We linked the perinatal data from the year 1999 to 2017 to the hospital hospitalisation data to create a cohort of pregnant women aged 15 to 44 years who gave birth in the Northern Territory (NT). We used the International Classification of Disease 10th revision (ICD-AM-10) codes to locate women with mental health-related hospitalisation (MHRH) (exposure of interest) and the perinatal data to access pregnancy outcomes. We used the modified Poisson regression with robust standard error to estimate the risk of pregnancy outcomes associated with maternal MHRH in the 5 years prior to pregnancy. We calculated the adjusted population attributable fraction (aPAF) for valid associations. We used the *E*-value to assess the effect of potential confounding bias. Out of 69,890 pregnancies, ~67,518 were eligible and included in the analysis. We found a significant variation in the incidence of substance use and complications between Aboriginal and non-Aboriginal women and women with and without MHRH in the 5 years prior to pregnancy. After adjusting, 5 years of preconception hospitalisation for substance misuse was associated with a 31% (95%CI, 1.05, 1.63) increased risk of Intrauterine Growth Restriction (IUGR), a 60% (CI, 1.37, 1.86) increased risk of smoking and a 2.21 (CI, 1.98, 2.47) times increased risk of drinking during pregnancy in Aboriginal women; and a 17% increased risk of drinking (CI, 1.11, 1.23) in pregnancy in non-Aboriginal women. A significant proportion of smoking (aPAF=14.7 to 37.4%), alcohol consumption (aPAF=46.0 to 66.7%), and IUGR (aPAF=23.6 to 38.5%) are attributed to maternal MHRH 5 years prior to pregnancy. Our findings are a ‘wake-up’ call for strengthening preconception care to reduce adverse outcomes of maternal MHRH prior to pregnancy.

Keywords Mental health related hospitalisation · Pregnancy complication · Smoking · Alcohol consumption · Australia

Abbreviations

CYDRP Child and Youth Development Research Partnership
IRSD Index of Relative Socio-economic Disadvantage
MHRH Mental health-related hospitalisation

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Pregnancy complications and substance use during pregnancy affect a significant portion of pregnancies and are reported to be correlated with maternal mental health conditions prior to pregnancy (Racine et al., 2021). Pregnancy complications have been associated with birth and neonatal complications such as preterm birth (PTB), low birth weight (LBW), hypoglycaemia, impaired immune function, respiratory distress, haemorrhage, and mortality (Martins et al., 2022; Tairy et al., 2021; Tanner et al., 2022). Neonates who experience adverse pregnancy and birth outcomes are more likely to develop long-term complications including restricted physical and mental growth, coronary artery disease, hypertension, and chronic kidney disease (Barker, 1999; Carmody & Charlton, 2013). The use of substances such as alcohol and tobacco during pregnancy has been associated with an increased risk of miscarriage, foetal malformation, placental abruption, LBW, PTB, congenital anomalies, perinatal death, and different forms of offspring mental health (Gibberd et al., 2019; Pereira et al., 2021).

A significant number of Australians reported alcohol use and smoking during pregnancy (Symons et al., 2020) despite the National Health and Medical Research Council (NHMRC) guideline recommendation to abstain when pregnant or trying to become pregnant (NHMRC, 2020). The Northern Territory (NT) is a large, remote, and sparsely populated area in Australia with the smallest total population and a greater proportion of Aboriginal people (an estimated total population of 232,605 with just over one-quarter (of 26.3%) being Aboriginal people) (ABS, 2021). About 22% of NT mothers experienced pregnancy complications (22.8% gestational diabetes and 1.6% pre-eclampsia) in 2020—a prevalence that is higher than the national estimates (AIHW, 2019). Around 6.2% of non-Aboriginal and 12.5% of Aboriginal women reported consuming alcohol, and 19% of non-Aboriginal and 48% of Aboriginal women reported smoking during pregnancy (Chondur & Wang, 2010; Chondur et al., 2014).

Previous complications, high body mass index, age, and substance use in pregnancy are reported to increase pregnancy complications where the effect of preconception maternal mental conditions is unknown (Lee et al., 2018; Maple-Brown et al., 2018; Yang et al., 2019). Low awareness, societal pressure, unwanted pregnancy, peer experience, and substance dependence are reported to predict substance use in pregnancy (Popova et al., 2022). Australian studies that investigated the link between maternal preconception mental health conditions and adverse outcomes during pregnancy are nil. We used administratively linked data spanning 18 years to explore the association between maternal MHRH in the 5 years prior to pregnancy and substance use (smoking and drinking) and complications during pregnancy in NT. This knowledge is crucial to advocate the need for screening and intervention of psychosocial risk factors in women planning pregnancy.

Methods

Study Setting and Cohort Selection

We conducted a population-based retrospective cohort study in NT, Australia. The research cohort comprised pregnancies involving women residing in the NT, ranging in age from 15 to 44 years, during the period spanning from January 1, 1999, to December 30, 2017. We omitted a limited number of pregnancies involving women under the age of 15 and those over the age of 44 years as adverse outcomes for this group might relate to biological age

(rather than the social risk factors), and these age-related risk factors are less amenable to intervention.

Outcomes

The outcomes of the study were pregnancy complications (pre-eclampsia, gestational diabetes, IUGR) and substance use during pregnancy (smoking and alcohol indication at the first antenatal care visit) all recorded as 'Yes' or 'No'. These variables were accessed from the NT Perinatal Data Register, which was established in 1986 as a statutory collection of maternal and perinatal information for all births in the NT.

Exposure

The exposures of the study were admissions from mental health conditions in the 5 years prior to pregnancy. We used the NT Inpatient Activity Collection (IA) data, an administrative dataset containing detailed information for all admissions to all public hospitals in the NT, between 1 July 1993 and 31 December 2017. The IA collection data contained a clinical diagnosis coded using the International Statistical Classification of Disease and Related Health Problems 10th Revision (ICD-10) allowing up to 50 fields of clinical diagnosis. Women were considered exposed if the IA data indicated that they were hospitalised for mental health conditions, as indicated by ICD-10 codes (Dean et al., 2018; Harron et al., 2021; Lima et al., 2019), listed as primary or within the first ten diagnosis codes. The ICD codes used are presented in Table 1 (supplementary information). We first created the following six mutually exclusive broad psychiatric diagnostic categories of maternal MHRH: (i) severe mental illness; (ii) common mental disorders; (iii) personality disorders; (iv) substance misuse; (v) all other adulthood-onset illness; and (vi) all other childhood-onset illness. We then formed three relatively homogeneous psychiatric categories because of small observations in some of the categories: Mental illnesses (merging categories i, ii, iii, v, and vi); substance misuse (category iv); and both conditions (concomitant occurrence).

To see the effect of exposure on the outcomes at two different exposure times, we created a group of births to women hospitalised for MHRH 5 years prior to pregnancy. We used a 5-year look-back as this period prior to pregnancy is reported to be correlated with adverse pregnancy and birth outcomes (Dadi et al., 2020). We also further assessed the risk of the outcomes in the 3- and 2-year lookback period to evaluate if the risks vary based on the proximity of the exposure to the outcomes.

Covariates

We considered a pre-specified covariate based on the guideline for antenatal care for women with complex social needs (Australian Government Department of Health, 2020). These include preexisting diabetes, pre-existing pre-eclampsia, maternal morbidity during pregnancy (such as anaemia, urinary tract infection, renal disease) all recorded as 'Yes' or 'No', maternal age (five categories: 15–19, 20–24, 25–29, 30–34, 35–45), parity (0, 1, 2, ≥ 3), Aboriginal status, and history of adversity-related admissions (violence and self-harm) recorded as 'Yes' or 'No'. We accessed the perinatal, Aboriginal status, and health district variables from the NT Perinatal Data Register. We

Table 1 Multivariable modified Poisson regression to assess the association between maternal MHH up to 5 years prior to pregnancy and obstetric complications during pregnancy (1999–2017), (N= 67,518)

Exposure variable	IUGR		Pre-eclampsia		Gestational DM	
	cIRR	aIRR	cIRR	aIRR	cIRR	aIRR
Hospitalisation five years prior to pregnancy (ref: No)						
Mental illness only	1.54 (1.13, 2.10)	1.28 (0.93, 1.76)	0.97 (0.69, 1.35)	1.04 (0.75, 1.45)	0.98 (0.77, 1.23)	0.90 (0.72, 1.14)
Substance misuse only	2.47 (2.05, 2.99)	1.31 (1.05, 1.63)*	1.17 (0.92, 1.48)	1.09 (0.84, 1.41)	1.29 (1.10, 1.50)	0.86 (0.72, 1.02)
Both reasons	2.68 (1.88, 3.82)	1.63 (1.11, 2.38)*	0.69 (0.37, 1.27)	0.67 (0.36, 1.25)	1.55 (1.18, 2.03)	1.16 (0.87, 1.55)
cPAF; aPAF, %						
Substance misuse only	59.6 (51.2, 66.5)	23.6 (4.6, 38.8)				
Both reasons	62.7 (46.9, 73.8)	38.5 (9.7, 58.1)				
Three years prior to pregnancy (ref: No)						
Mental illness only	1.30 (0.87, 1.95)	1.09 (0.73, 1.63)	1.24 (0.87, 1.77)	1.35 (0.95, 1.92)	1.00 (0.76, 1.31)	0.93 (0.71, 1.22)
Substance misuse only	2.68 (2.19, 3.28)	1.44 (1.14, 1.81)*	1.22 (0.94, 1.58)	1.10 (0.83, 1.46)	1.26 (1.06, 1.50)	0.85 (0.69, 1.03)
Both reasons	2.71 (1.79, 4.09)	1.64 (1.05, 2.56)*	0.87 (0.46, 1.66)	0.82 (0.43, 1.58)	1.70 (1.25, 2.31)	1.33 (0.96, 1.83)
Two years prior to pregnancy (ref: No)						
Mental illness only	1.22 (0.75, 1.98)	0.96 (0.59, 1.58)	1.21 (0.80, 1.85)	1.28 (0.85, 1.91)	1.01 (0.74, 1.39)	0.91 (0.66, 1.25)
Substance misuse only	2.78 (2.24, 3.46)	1.45 (1.13, 1.85)*	1.22 (0.91, 1.62)	1.09 (0.79, 1.49)	1.17 (0.96, 1.43)	0.80 (0.64, 1.01)
Both reasons	2.66 (1.63, 4.34)	1.46 (0.86, 2.47)	0.94 (0.45, 1.95)	0.88 (0.42, 1.85)	1.83 (1.30, 2.58)	1.43 (1.01, 2.05)*

The model has been adjusted for the age of the mother at pregnancy, epidemiological districts (a proxy for social disadvantages), maternal adversities (history of self-harm, violence, and assault), maternal smoking and drinking in the first 20 weeks of pregnancy, and other prenatal complications

cIRR crude incidence rate ratio, aIRR adjusted incidence rate ratio, cPAF crude population attributable fraction, aPAF adjusted population attributable fraction

*Significant at p-value < 0.05

identified a history of adversity-related hospitalisations (violence and self-harm) from the IA data (1993 to 2017) on the bases of published lists of ICD-10 diagnosis codes (Harron et al., 2021; Herbert et al., 2015) (Table 2 in supplementary information).

Data Source and Linkage

The datasets used in this study were sourced from an extensive repository of linked administrative datasets maintained by the Child and Youth Development Research Partnership (CYDRP), a collaborative work between Menzies School of Health Research and NT Government agencies. Data are routinely collected as part of the health service delivery. The first stage data linkage process was carried out by the SA NT Data-Link using a probabilistic linkage method with a clerical review of uncertain matches (Christen, 2012). The detailed data linkage process has been described and published elsewhere (Schneider et al., 2019). The final stage of linking de-identified data files and preparing a dataset for this analysis was done by a research team.

Statistical Analysis

We prepared the analysis dataset by linking perinatal data to the hospital hospitalisation where we combined the exposure, outcome, and potential covariates. We checked for data completeness, missingness, multicollinearity, and potential misclassification of exposure variable and made appropriate corrections prior to analysis. The exposure, maternal MHRH, was assessed for the first 5 years prior to pregnancy. We checked the potential risk of women's different exposure times on the outcome variables through a stratified analysis of years prior to pregnancy (0 to <2, 2 to <3, 3 to <5, and ≥ 5 years) adjusting for other covariates. We calculated prevalence rates of types of maternal MHRHs and complications with their 95% confidence intervals. We calculated the number and proportion of women with each risk factor and their univariate association with the outcome variables. We used tables to present the findings.

We estimated the prevalence rate ratio of substance use (smoking and alcohol consumption during pregnancy) and risk ratio of pregnancy complications using a Modified Poisson regression comparing women with and without MHRH in the 5 years prior to pregnancy adjusting for confounders (Yelland et al., 2011). All models used robust standard errors to allow for clustering of pregnancies and births within a single woman. We did a separate analysis for estimating the risk of maternal MHRH on substance misuse during pregnancy for Aboriginal and non-Aboriginal women as the risks differ across the two populations. We calculated the adjusted population attributable fraction (aPAF) using `punaf` command in Stata 17 by comparing the exposure-free scenario (zero counterfactual) to the real-world scenario (as observed in our adjusted model) (Newson, 2015). The PAF estimates a fraction of substance and pregnancy complications that are attributed to maternal MHRH that can then be avoided if public health and clinical interventions are designed to eliminate MHRH. We evaluated the robustness of the rate ratios to potential unmeasured confounding by calculating an *E*-value (VanderWeele & Ding, 2017). We used Stata 17 for analysis (StataCorp, 2021).

Table 2 Multivariable modified Poisson regression showing the association between maternal MHRH prior to pregnancy and smoking in the first 20 weeks of pregnancy and alcohol consumption at the first ANC visit in the NT, Australia (1999–2017)

Exposure variable	Aboriginal mothers (N=21,242)				Non-Aboriginal mothers (N=40,852)			
	Alcohol consumption		Smoking		Alcohol consumption		Smoking	
	cPRR	aPRR	cPRR	aPRR	cPRR	aPRR	cPRR	aPRR
Hospitalisation in the 5 years prior to pregnancy (ref: No)								
Mental illness	1.23 (0.95, 1.59)	0.99 (0.77, 1.29)	1.13 (1.04, 1.23)	0.96 (0.89, 1.04)	1.21 (0.81, 1.82)	0.94 (0.63, 1.41)	2.04 (1.74, 2.40)	1.10(0.93,1.28)
Substance misuse	3.78 (3.47, 4.11)	2.21 (1.98, 2.47)*	1.27 (1.21, 1.33)	1.17 (1.11, 1.23)*	1.98 (1.11, 3.21)	1.16 (0.71, 1.91)	4.32 (3.81, 4.90)	1.60 (1.37, 1.86)*
Both	3.19 (2.64, 3.84)	1.85 (1.51, 2.26)*	1.51 (1.41, 1.63)	1.19 (1.10, 1.29)*	5.16 (3.62, 7.37)	3.00 (1.96, 4.60)*	5.28 (4.68, 5.96)	1.54 (1.23, 1.91)*
cPAF; aPAF, %								
Substance misuse	73.5 (71.2, 75.7)	54.8 (49.5, 59.6)	21.2 (17.5, 24.8)	14.7 (10.2, 18.8)			76.8 (73.7, 79.6)	37.4 (27.1, 46.3)
Both	68.6 (62.2, 74.0)	46.0 (34.0, 55.8)	34.0 (28.9, 38.8)	16.3 (9.3, 22.7)	80.6 (72.4, 86.4)	66.7 (49.0, 78.2)	81.1 (78.6, 83.2)	35.0 (19.0, 47.8)
Three years prior to pregnancy (ref: No)								
Mental illness	1.17 (0.85, 1.60)	0.95 (0.69, 1.30)	1.13 (1.02, 1.25)	0.97 (0.89, 1.07)	1.22(0.75, 1.96)	0.98 (0.62, 1.56)	2.25 (1.89, 2.69)	1.23 (1.03, 1.45)*
Substance misuse	3.87(3.54, 4.22)	2.18 (1.94, 2.44)*	1.26 (1.19, 1.32)	1.15 (1.09, 1.22)*	2.49 (1.50, 4.16)	1.49 (0.89, 2.50)	4.53 (3.94, 5.21)	1.61 (1.36, 1.92)*
Both	2.71 (2.13, 3.45)	1.64 (1.28, 2.11)*	1.55 (1.42, 1.68)	1.22 (1.11, 1.34)*	4.89(3.23, 7.42)	2.60 (1.56, 4.33)*	5.21 (4.54, 5.99)	1.52 (1.20, 1.93)*
Two years prior to pregnancy (ref: No)								
Mental illness	1.12 (0.77, 1.62)	0.88 (0.61, 1.27)	1.15 (1.03, 1.29)	0.98 (0.89, 1.09)	1.25 (0.72, 2.16)	0.96 (0.57, 1.63)	2.36 (1.93, 2.87)	1.19(0.98, 1.44)
Substance misuse	3.95 (3.60, 4.33)	2.17 (1.93, 2.43)*	1.22 (1.16, 1.30)	1.12 (1.05, 1.19)*	2.38 (1.28, 4.40)	1.48 (0.79, 2.75)	4.70, 4.03, 5.48)	1.70 (1.40, 2.07)*
Both	2.93 (2.26, 3.81)	1.81 (1.40, 2.34)*	1.63 (1.49, 1.77)	1.28 (1.16, 1.41)*	4.82 (2.94, 7.91)	2.40 (1.34, 4.29)*	5.18 (4.39, 6.12)	1.42 (1.05, 1.92)*

The model has been adjusted for the age of the mother at pregnancy, epidemiological districts (a proxy for social disadvantages), maternal adversities (history of self-harm, violence, and assault), and other perinatal complications

cPRR crude prevalence rate ratio, aPRR adjusted prevalence rate ratio, cPAF crude population attributable fraction, aPAF adjusted population attributable fraction

*Significant at p-value < 0.05

Ethical Clearance and Role of Funding Source

The study was approved by the Human Research Ethics Committee of the NT Department of Health and the Menzies School of Health Research (HREC-2016–2708) and was supported by the First Nations Advisory Group for the Child and Youth Development Research Partnership which includes independent Aboriginal community members. The funder of the study had no role in the study design, data collection, analysis, interpretation, or writing of this report. The research team had full access to all the data in the study and final responsibility for the decision to submit for publication.

Results

From 69,890 pregnancies initially assessed for eligibility, 67,518 pregnancies were included in maternal complication analysis; 60,982 pregnancies were included in alcohol consumption analysis; and 62,095 pregnancies were included in smoking analysis. Figure 1 summarises the number of excluded pregnancies and reasons of exclusion. About 713 (1.6%) of non-Aboriginal and 1079 (4.4%) Aboriginal women had mental illness-related hospitalisation and 280 (0.6%) of non-Aboriginal and 1691 (6.9%) Aboriginal women had substance misuse related hospitalisation in the complication cohort in the 5 years prior to pregnancy. (Table 3 in supplementary information).

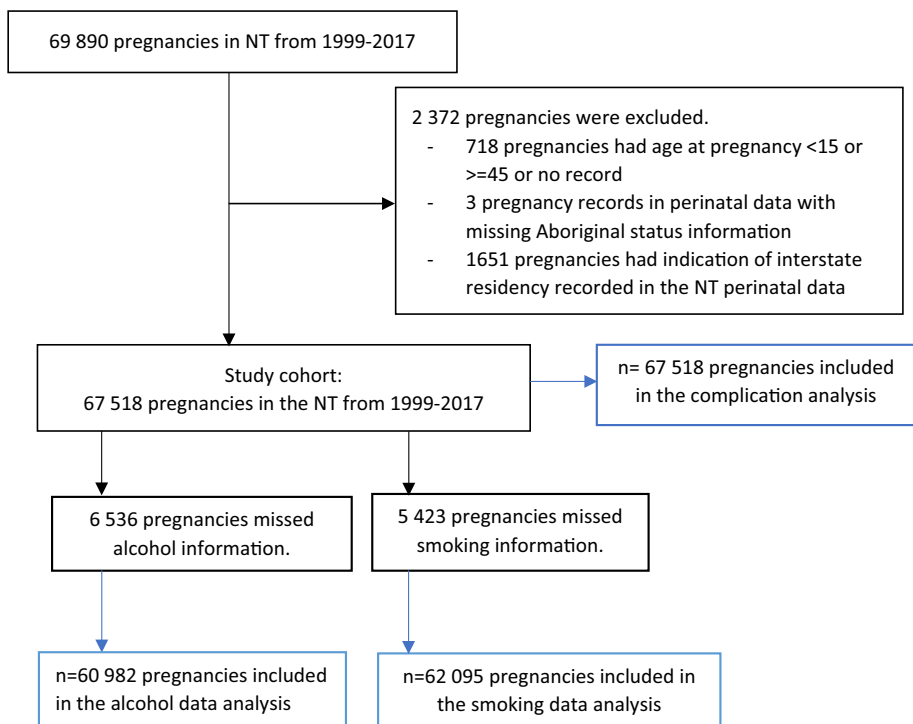


Fig. 1 Cohort selection in the study of pregnancy outcomes in the NT, Australia (1999–2017)

About 1118 (4.62%; 95%CI, 4.37, 4.89) non-Aboriginal and 1380 (3.19; 95%CI, 3.03, 3.36) Aboriginal pregnancies had pre-eclampsia. After adjustment, there was no evidence of association between pre-eclampsia and maternal mental illness (Adjusted Incidence Rate Ratio (aIRR), 1.04; 95%CI, 0.75, 1.45) or substance misuse-related hospitalisation (aIRR, 1.09; 95%CI, 0.84, 1.41) in the 5 years prior to pregnancy (Table 1). However, some variation existed in a stratified analysis by Aboriginal status where hospitalisation for mental illness increased the risk of pre-eclampsia in non-Aboriginal women but not in Aboriginal women. (Table 4 & 5 in supplementary information).

About 2983 (7.61%; 95%CI, 7.36, 7.87) non-Aboriginal and 2156 (10.22%; 95%CI, 9.84, 10.61) Aboriginal pregnancies had gestational diabetes. (Table 6 in supplementary information). Gestational diabetes was associated with most of the categories of maternal MHRH in unadjusted model but disappeared after adjustment for potential confounders except for a group of women concurrently hospitalised for mental illness and substance misuse in the 2 years prior to pregnancy in which the risk of developing gestational diabetes was found to be 43% (aIRR, 1.43; 95%CI, 1.01, 2.05). (Table 1).

IUGR was reported in 779 (1.8%; 95%CI, 1.68, 1.93) non-Aboriginal and 1169 (4.8%; 95%CI, 4.54, 5.08) Aboriginal pregnancies. (Table 7 in supplementary information). Women hospitalised for substance misuse and concurrently hospitalised for mental illness and substance misuse in the 5 years prior to pregnancy were 31% (aIRR, 1.31; 95%CI, 1.05, 1.63) and 63% (aIRR, 1.63; 95%CI, 1.11, 2.38) more likely to experience IUGR, respectively. About 23.6% (aPAF; 95%CI, 4.6, 38.8) and 38.5% (aPAF; 95%CI, 9.7, 58.1) of IUGR was attributed to maternal hospitalisation for substance misuse and concomitant hospitalisation for both mental illness and substance misuse 5 years prior to pregnancy, respectively, which could be avoided if mothers were prevented from these risk factors. The association remains in the 3 and 2 years prior to pregnancy (Table 1).

About 645 (1.6%) of non-Aboriginal and 903 (4.4%) Aboriginal women in alcohol cohort and 650 (1.6%) of non-Aboriginal and 964 (4.5%) Aboriginal women in the smoking cohort had mental illness-related hospitalisation in the 5 years prior to pregnancy. About 243 (0.4%) of non-Aboriginal and 1459 (7.1%) Aboriginal women in alcohol cohort and 255 (0.6%) of non-Aboriginal and 1489 (7.0%) Aboriginal women in smoking cohort had substance misuse-related hospitalisation in the 5 years prior to pregnancy. (Table 8 and 9 in supplementary information).

About 2033 (5.0%; 95%CI, 4.8, 5.2) of non-Aboriginal and 2439 (11.9%; 95%CI, 11.4, 12.3) Aboriginal pregnancies had alcohol consumption at first ANC visit (Table 10 in supplementary information). In the adjusted model for Aboriginal women, alcohol consumption in pregnancy was significantly associated with maternal hospitalisation for substance misuse (aPRR, 2.21; 95%CI, 1.98, 2.47) and concurrent hospitalisation for mental illness and substance misuse (aPRR, 1.85; 95%CI, 1.51, 2.26) in the 5 years prior to pregnancy. About 54.8% (aPAF; 95%CI, 49.5, 59.6) and 46.0% (aPAF; 95%CI, 34.0, 55.8) of alcohol consumption in pregnancy in Aboriginal women were attributed to maternal hospitalisation for substance misuse and concomitant hospitalisation for mental illness and substance misuse in the 5 years prior to pregnancy, respectively (Table 2). The association also persisted for the 3- and 2-years prior to pregnancy. In adjusted model for non-Aboriginal women, the risk of alcohol consumption was 3.00 (95%CI, 1.96, 4.60) times higher in women concurrently hospitalised for substance misuse and mental illness in the 5 years prior to pregnancy. About 66.7% (aPAF; 95%CI, 49.0, 78.2) of alcohol consumption during pregnancy in non-Aboriginal women was attributed to maternal concomitant hospitalisation for substance misuse and mental illness (Table 2).

About 5942 (14.5%; 95%CI, 14.2, 14.9) of non-Aboriginal and 10,560 (49.7%; 95% CI, 49.0, 50.4) Aboriginal women were smoking in the first 20 weeks of pregnancy. (Table 11 in supplementary information). In the adjusted model for Aboriginal women, smoking was significantly associated with maternal hospitalisation for substance misuse (aPRR, 1.17; 95%CI, 1.11, 1.23) and concurrent hospitalisation for mental illness and substance misuse (aPRR, 1.19; 95%CI, 1.10, 1.29) in the 5 years prior to pregnancy. The PAF for smoking during pregnancy was 14.7% (aPAF; 95%CI, 10.2, 18.8) for substance misuse and 16.3% (aPAF; 95%CI, 9.3, 22.7) for concomitant hospitalisation for substance misuse and mental illness for Aboriginal women. The association also persists for 3- and 2-years prior to pregnancy (Table 2).

For non-Aboriginal women, the risk of smoking during pregnancy was 60% (aPRR, 1.60; 95%CI, 1.37, 1.86) and 54% (aPRR, 1.54; 95%CI, 1.23, 1.91) higher for women hospitalised for substance misuse and for those concurrently hospitalised for both substance misuse and mental illnesses respectively in the 5 years prior to pregnancy. The adjusted PAF for smoking in non-Aboriginal women was 37.4% (aPAF; 95%CI, 27.1, 46.3) for substance misuse and 35.0% (aPAF; 95%CI, 19.0, 47.8) for concomitant hospitalisation for substance misuse and mental illness (Table 2). The association also persisted for the 3- and 2-years prior to pregnancy. Associations were not found between mental illness-related hospitalisation and substance use during pregnancy except for smoking in non-Aboriginal women 2 years prior to pregnancy (Table 2) The reported *E*-values (upper 95%CI) for all associations arguably showed that it was unlikely for unmeasured or unknown confounders to explain away the reported association between all categories of maternal MHRH and adverse maternal outcomes during pregnancy for both non-Aboriginal and Aboriginal women (Table 12 & 13 in supplementary information). The outcomes did not significantly vary across different exposure times confirming no risk of potential exposure misclassification bias (Table 14 & 15 in supplementary information).

Discussion

Developmental origin of disease through foetal programming has explained the link between the stress process during pregnancy and foetal development (Keenan et al., 2018). However, from a developmental and life-course perspective, psychological disorders during pregnancy do not only occur following pregnancy, and there is a strong link with preconception maternal psychological health (Dadi et al., 2020). As such, preconception health is emerging as an important area of research when dealing with adverse pregnancy and birth outcomes linked to preconception maternal psychological disorders (Keenan et al., 2018). Our population-based study consisting of 18 years of pregnancy cohort investigated the association of maternal preconception MHRH with complications and substance use (smoking and alcohol consumption) during pregnancy. We believe the estimates from our study would best represent the state population and found the necessary knowledge for the induction of specific measures aimed at reducing this risk in a population; and would also be used as a baseline for further studies.

Mental illnesses in non-Aboriginal women and substance misuse in Aboriginal women were found to be the primary reasons for maternal MHRH in the years 1999–2017 in the NT public hospitals. Maternal hospitalisations for substance misuse and mental illnesses up to 5 years prior to pregnancy increased the risk of IUGR, maternal smoking, and alcohol consumption during pregnancy. The risk of IUGR increased by 31% and 63% in pregnant

women who admitted for substance misuse and concurrently admitted for mental illness and substance misuse, respectively, where the risk also persists for the 3- and 2-year look-back period.

The risk of gestational diabetes accounting for 43% was estimated among women who were concurrently hospitalised for mental illnesses and substance misuse 2 years prior to pregnancy. There was no evidence of an independent association between hospitalisation for mental health in the 5 years prior to pregnancy and the risk of pre-eclampsia.

The estimated risks of substance use during pregnancy slightly differ across categories of admissions, exposure look-back period, and Aboriginal status. For Aboriginal women, the risk of alcohol consumption increased by 2.21 times and 85% and the risk of smoking increased by 17% and 19% among pregnant women who had 5-year preconception history of hospitalisation for substance misuse and concurrent hospitalisation for substance misuse and mental illnesses. For non-Aboriginal women, the risk of alcohol consumption was 3.00 times higher among women concurrently hospitalised for mental illnesses and substance misuse; and the risk of smoking was 60% and 54% higher for women hospitalised for substance misuse and concurrently hospitalised for substance misuse and mental illnesses in the 5 years prior to pregnancy. The associations did not change for the 3- and 2-year look-back period. The prevalence of maternal MHRH in the 5 years prior to pregnancy in the NT population looks arguably high and we found its significant contribution to an increased risk of IUGR, smoking and alcohol consumption during pregnancy that could potentially be averted.

Maternal health in pregnancy remains a major challenge for maternity services where the majority of maternal deaths occur in women with pre-existing maternal conditions (Knight et al., 2018). Adverse pregnancy outcomes, a leading cause of adverse neonatal health and developmental outcomes, were reported to be associated with preconception substance misuse in the current and previous studies (Bouquet et al., 2022). The current study confirms previous findings of high incidence of gestational diabetes among women with preconception history of substance misuse and mental illness (Beka et al., 2018). The association may be mediated through elevated norepinephrine (Fatima et al., 2017). The link between maternal mental health adversities prior to pregnancy and pregnancy complications could also be theoretically explained by chronic exposure to stress, a phenomenon known as the 'Weathering Effect' (Frazier et al., 2018). However, consistent with previous studies, pre-eclampsia was not associated with maternal MHRH prior to pregnancy (Thombre Kulkarni et al., 2019).

Substance use during pregnancy has been associated with plethora of adverse pregnancy, birth, childhood, and chronic health outcomes (Gibberd et al., 2019; Pereira et al., 2021). Consistent with a previous systematic review (Ward et al., 2021), we found that MHRH prior to pregnancy is a significant predictor of substance use during pregnancy for both Aboriginal and non-Aboriginal women in NT.

There is a high correlation and potential bi-directional association between mental health conditions and substance misuse during pregnancy. The results also show that women who have mental health and substance abuse problems prior to pregnancy are not able to abandon these habits during pregnancy. We could find some interesting hypotheses in this regard in theories about emotional regulation strategies (Gross, 2014). Alcohol abuse and tobacco consumption are regulation strategies to reduce negative emotions. Therefore, it is possible that these women who for a long time (5 or 3 years) have down-regulated their emotions with these strategies continue using them during pregnancy. On the other hand, the use of dysfunctional emotional regulation strategies may be the link between mental health problems and substance abuse in these women. The literature has

linked the use of avoidant emotional regulation strategies to mental health problems (Barlow et al., 2014). Substance abuse is a form of avoidant emotional regulation. Therefore, it could make sense that both cases correlate highly with pregnancy problems. In this sense, previous mental health problems, that is, the use of avoidant regulation strategies, can manifest in various ways such as smoking or drinking. Minor mental health disorders prior to pregnancy are less likely to be identified and treated, take a long time for remission, and a high risk of relapse after being treated leading the disorders to continuously manifest across perinatal period (Howard & Khalifeh, 2020).

The rise in risk factors of adverse perinatal outcomes among women of reproductive age has to be a ‘wake-up call’ to integrate and implement preconception care (Stephenson et al., 2021) as interventions designed to tackle these problems in pregnancy had limited impact (Howard & Khalifeh, 2020). Chronic mental health is reported to diminish mothers’ capacity of planning pregnancy and birth and needs to be considered for pre-screening (De Wolff et al., 2021). Preconception care provides an opportunity for early interventions of important public health problems that has proven to have an impact on pregnancy outcomes and intergenerational consequences (The Lancet, 2018). Clinical guidelines for preconception care that are used in different countries emphasised the need for preventive activities prior to pregnancy including education on ceasing potential risky practices and maintaining good mental and psychological health in couples expecting pregnancy (The Lancet, 2018).

Australia has no national guideline on preconception care (Dorney & Black, 2018) and the national clinical practice guideline only addressed pregnancy care (AGDH, 2020). The South Australia’s Preconception Advice Clinical Guideline (Government of South Australia Department of Health, 2015) and the Royal Australian College of General Practitioners (RACGP) Guideline for preventive activities (Edwina & Kirsten, 2018) are the only documents available online with limited national utility. The NT government has a strategy to tackle Foetal Alcohol Spectrum Disorder (FASD) that puts preventing drinking during pregnancy as a priority area for intervention (Policy, 2018) but has no smoking strategy. Proportionate universalism has been a key for public health interventions and preconception care is important to close the gap in the continuum of care and health risk gap between non-Aboriginal and Aboriginal women (Dennis et al., 2022). However, the key question is how preconception care guideline that could suggest ways of reaching the reproductive age group could be developed. The Canadian PreCHART, a digital preconception health risk assessment tool developed and tested has been offering a unique benefits to providers and clients planning pregnancy (Montanaro et al., 2023). As part of preconception care, investment should also be stretched to ensure that all women of childbearing age have access to specialist community perinatal mental health services and in mother and baby units. There is also new evidence calling pharmacists for better preconception care for women using drugs for mental health-related disorders with key roles including risk identification, counseling, and linking for needed services that could also be scaled up (Williamson et al., 2022). Community-led interventions for the prevention of prenatal alcohol exposure in regions with a high level of alcohol use have been a priority of the Australian government and reduction in reported alcohol use in pregnancy in Aboriginal communities has shown promising results (Symons et al., 2020).

The measurement error and incompleteness of data associated with secondary source would be a major limitation that users of this study should account. We could not access all the potential covariates and confounders of substance use and complications in pregnancy (such as pregnancy intention, having a smoking partner, partner support, body mass index prior to pregnancy and weight gain during pregnancy) from the data repository. As such, there would be a potential source of confounding bias though we were able to statistically

assess the effect. The exposure, maternal MHRH, was accessed from hospital record, which we only able to capture those with severe conditions and potentially underestimate the real effect in the general population. However, we tried to minimise the effect by including up to ten diagnostic codes which increase the chance of women with minor psychosocial problems being part of the study. Some of the mothers admitted for mental health disorders might be fully treated and could mask the real association between the exposure and outcomes. The mothers were asked about their smoking and drinking status face to face, and they might tend to respond no or prefer not to respond potentially due to social desirability and estimates are potentially an underestimate of the true burden of smoking and drinking in the community. The findings underscore the urgent need for further investigation to identify mediating variables that could clarify the observed outcomes. They also highlight a significant social issue, pointing to the necessity of psychological interventions for pregnant women struggling with substance abuse. Just as high-risk pregnancies receive medical attention, it's imperative to provide psychological support to improve the well-being of these women, suggesting a holistic approach to their care.

Conclusions

Substance misuse-related hospitalisation in the 5, 3, and 2 years prior to pregnancy increased the risk of IUGR in non-Aboriginal and smoking and alcohol consumption during pregnancy in both Aboriginal and non-Aboriginal women. Concurrent hospitalisation for mental illness and substance misuse 2 years prior to pregnancy also increased the risk of gestational diabetes. Maternal mental illness-related hospitalisation 3 years prior to pregnancy in non-Aboriginal women was associated with smoking during pregnancy. The study found strong evidence that women who used substances before pregnancy continued to do so during pregnancy. The findings highlight the need to investigate why pregnancy did not alter substance misuse trends and emphasise the importance of using maternal hospitalisation for psychosocial disorders as an entry point for preconception health interventions and linking mothers to community mental healthcare services. Universal preconception care is crucial for addressing women with psychosocial problems, while strengthening adolescent mental health services is pivotal to reducing preconception health risks, particularly among mid-and-late adolescent girls.

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Author Contribution AFD conceived the idea, designed and analysed the data, and prepared a draft of the manuscript. VH and SG actively participated in design, analysis, and data preparation and finally made a critical review of the manuscript. All authors critically reviewed the manuscript for content, methodological validity, and sound interpretation of the findings.

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Data Availability The study datasets contain potentially identifying or sensitive patient information and are held on a secure cloud-based server with restricted access. The data can be available upon request and approval of the ethics committee and data custodians.

Declarations

Informed Consent Not applicable.

Competing Interests The authors declare no competing interests.

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