

Effects of timing and duration of gestational exposure to serotonin reuptake inhibitor antidepressants: population-based study

Tim F. Oberlander, William Warburton, Shaila Misri, Jaafar Aghajanian and Clyde Hertzman

Background

Late-gestational serotonin reuptake inhibitor (SRI) exposure has been linked to adverse neonatal outcomes; however, the impact of timing and duration of exposure is unknown.

Aims

To determine whether late-gestational exposure to an SRI is associated with increased risk of adverse neonatal outcome relative to early exposure.

Method

Population-based maternal and neonatal health records were linked to prenatal maternal prescription records for an SRI medication ($n=3500$).

Results

After controlling for maternal illness and duration of exposure, using propensity score matching, neonatal

outcomes did not differ between late and early exposure ($P>0.05$). After controlling for maternal illness, longer prenatal exposure increased the risks of lower birth weight, respiratory distress and reduced gestational age ($P<0.05$).

Conclusions

Using population health data, length of gestational SRI exposure, rather than timing, increased the risk for neonatal respiratory distress, lower birth weight and reduced gestational age, even when controlling for maternal illness and medication dose. These findings highlight the importance of distinguishing the specific impact of medication exposure from exposure to maternal illness itself.

Declaration of interest

None.

Exposure to serotonin reuptake inhibitor (SRI) antidepressant medication during the late gestational period has been associated with an increased risk of lower birth weight, respiratory distress, seizures, jitteriness and irritability in up to 30% of exposed infants, compared with early prenatal exposure.^{1–4} However, the effects of the SRI medication on neonatal outcomes are confounded by prenatal exposure to depressed maternal mood, and distinguishing this influence from the effects of SRI antidepressants has been challenging.⁵ The study reported here was undertaken to examine the impact of the timing and duration of gestational SRI exposure using population health data linking records of maternal prescriptions for an SRI medication dispensed during pregnancy with records of maternal mental health and neonatal outcomes, accounting for maternal illness severity. We expected that late (prolonged exposure including the third trimester) gestational SRI exposure would be associated with increased neonatal risks compared with early (first and second trimester)² gestational exposure, even when controlling for characteristics of maternal illness severity.

Method

This study was undertaken with approval from the University of British Columbia Research Ethics Board, the Children's and Women's Health Centre of British Columbia Research Review Committee, the British Columbia Ministry of Health, and the British Columbia College of Pharmacists.

Data-set compilation

Data used in this study came from five administrative sources housed in the British Columbia Linked Health Database (registry of births, hospital separation records, physician billing records and the registry of Medical Services Plan subscribers),⁶ linked to

PharmaNet, a province-wide network record of all prescriptions dispensed by British Columbia pharmacists. Individuals on all files are identified with an encrypted personal health number (PHN). The data were processed and linked by the Centre for Health Services and Policy Research (CHSPR) at the University of British Columbia, as described in an earlier paper.⁵ The CHSPR replaced the encrypted PHN with an anonymised study ID. Diagnosis of maternal mood was obtained from Ministry of Health Medical Services Plan (MSP) ICD–9 diagnostic codes that referred to depression.⁷ A total of 203 520 registered live births in British Columbia occurred between 1 April 1997 and 31 March 2002. Of these, 200 291 (98.4%) had a valid study ID that was linked to the mother's study ID and 192 725 (96.2%) of these records unambiguously matched hospital birth records. Of these records, 1259 were dropped because they did not report a gestational age. Another 13 records (less than 0.01%) were dropped because they reported estimated gestational ages less than 22 weeks on the hospital separation record. Eight records (again less than 0.01%) with reported gestational ages greater than 43 weeks were top-coded at 43 weeks. Hospital separation records also contain up to 16 diagnostic/procedure codes that are provided by the physician attending during the neonatal period. Physicians entered at least one ICD–9 diagnostic code for 40 733 (34%) and at least two diagnostic codes for 27 192 (23%) of the births.

To match maternal prescription records in the PharmaNet database, we restricted our analysis to records of neonates with an estimated date of conception between 1 January 1998 and 26 March 2001, reducing our sample to 120 702. To ensure that babies with long hospital stays were not underreported in our sample, we restricted our analysis to those with dates of conception before 26 March 2001, allowing 90 days between the last expected birth date and the last hospital separation date of 31 March 2002. After removing 87 records with data entry errors and 1068 records for multiple births, the study population

comprised records related to 119 547 live births. To these records we linked information about maternal prescriptions for all records for SRI antidepressants, other antidepressants, benzodiazepines and antipsychotic medications dispensed between 1 January 1998 and 31 March 2002. This was derived from 363 641 records with 915 distinct drug identity numbers; 98% of these records had a unique combination of date, drug identification number and study ID, leaving 356 727 prescriptions. The file identified the drug by brand name and generic name, the date that the drug was dispensed and the number of days supplied, together with the unique study number for the mother. From the total 356 727 prescriptions we identified 75 456 prescriptions for SRIs, specifically citalopram (2.7%), fluoxetine (24.6%), fluvoxamine (4.5%), paroxetine (38.9%), sertraline (22.7%) and venlafaxine (6.6%). Prenatal exposure occurred if the period from the date the drug was dispensed until that date plus the number of days for which the drug was supplied overlapped with the pregnancy. We excluded the date of birth from the pregnancy to eliminate drugs dispensed after the infants' birth.

Information on medical histories, including diagnosis of maternal mood both during pregnancy and in the 12 months before conception, was obtained from the Ministry of Health Medical Services Plan billing records. Infant birth date and length of gestation from the hospital discharge record enabled us to calculate the dates of pregnancy. In the construction of the variable for the number of days on which an SRI was taken during pregnancy, double counting was eliminated by first identifying the days covered by any prescription for an SRI and then summing the days. The implicit assumption was that when prescriptions overlapped it was because physicians had prescribed a different SRI to replace one that had not been suitable for that patient.

Study group identification

The date of conception was estimated using the date of birth and gestational age provided in the hospital record. The first trimester was from the estimated date of conception to day 92 of the pregnancy. The second trimester was from day 93 to day 185 (or birth, whichever came first) and the third trimester was from day 186 to birth. Using Chambers' definition of exposure,² we assigned to the early exposure group infants of mothers who discontinued the drug in the first and/or second trimester and never resumed taking it. A late exposure (i.e. prolonged late-gestational exposure) group included infants of mothers who had received a prescription for an SRI during the first and/or second trimester and continued to take the drug into the third trimester (at least 185 days of gestation).

Neonatal outcome

On the basis of previous work,² four key neonatal outcomes were identified: birth weight (in grams, and incidence of birth weight less than the 10th percentile for gestational age); percentage born with a gestational age below 37 weeks; length of stay in hospital greater than 3 days; and incidence of adverse neonatal symptoms (respiratory distress, jaundice, convulsions, feeding difficulties).

Data analysis

Two approaches to data analysis were used. Propensity score matching was used to control for potential confounding variables such as duration of exposure and maternal characteristics that might reflect the severity of mental illness in our analysis of the effects of early and late exposure on these outcomes. Logistic regression was used to estimate the relationship between duration of exposure and the same outcomes, again controlling for possible

confounding variables. For both techniques the following maternal characteristics (pre-pregnancy and prenatal) were controlled for:

- Pre-pregnancy characteristics (the year before becoming pregnant): number of visits to a psychiatrist; number of times diagnosed as depressed; number of times receiving a three-digit ICD-9 code that included reference to a depression-related diagnosis; number of times diagnosed as having a mental health disorder other than depression; number of times provided counselling by a general practitioner; number of visits to a physician; income decile; and drugs subsidised.
- Prenatal characteristics (during pregnancy): maternal age during pregnancy; number of prenatal visits; diagnosed as depressed; diagnosed with a three-digit ICD-9 code that included reference to a depression-related diagnosis; number of times diagnosed as depressed; number of treatments by a psychiatrist; filled a prescription for an antipsychotic drug; and filled a prescription for a tricyclic antidepressant.

Propensity score matching

To account for the potential confounding influences of these differences in maternal characteristics (see 'Data analysis'), propensity score matching^{8,9} was undertaken to identify a subgroup of women in the early exposure group who were matched for characteristics with women in the late exposure group. Propensity score matching was carried out in three stages. First, the parameters of a model predicting SRI exposure were estimated using maximum likelihood probit analysis. Second, these parameters were used to calculate the propensity score for each individual in our sample. Third, for each late-exposed mother, an early-exposed mother with a similar propensity score was selected for comparison purposes, without replacement. We used Stata SE version 9 for Windows for the first two steps and FoxPro version 9 for the third step. In this way each infant with late exposure was compared with an infant with early exposure with a mother with similar characteristics.

Probit regression

Multivariate regression models were used to study relationships between risk of adverse neonatal outcome and intensity of prenatal exposure in terms of days of exposure and dosage. To account for the possible impact of maternal illness severity a number of key maternal variables reflecting illness severity were added to the model. A major challenge in studying the relationship between risk of adverse neonatal outcome and length of prenatal exposure arises because each are highly interrelated – the length of gestation can affect the duration of exposure, and duration of exposure can affect the length of gestation. To isolate the effect of exposure on length of gestation we restricted our sample to the 97% of mothers with gestation lasting more than 244 days and limited our analysis to exposure that occurred at some point during the first 244 days of gestation. Although this method could introduce bias (i.e. if babies with longer exposure had shorter gestations, resulting in neonates with longer exposures being disproportionately withdrawn from the sample) we believe that the bias would be small because few babies in our sample were born at less than 35 weeks gestation.

We also used regression analysis to explore the effect of maternal dosage. We developed indicators of whether the dosage was low, medium or high in two steps. First, because of differences in dose range for each SRI medication, for each medication we converted dosage to a *z* score based on the distribution of

dispensed doses. Second, we classified the dosage as low if the *z* score was less than -0.5 , medium if the *z* score was between -0.5 and 0.5 and high if the *z* score was greater than 0.5 . For example, paroxetine was prescribed in doses of 10 mg, 20 mg and 30 mg, so the 10 mg dose was classified as low, the 20 mg dose as medium and the 30 mg dose as high. We then summed the number of days of exposure for low, medium and high doses and entered these separately into the regression equations. We performed Wald tests for equality of the three coefficients.

Regression analyses were undertaken using probit, Stata SE version 9. We estimated parameters of eight models, one for each of the outcomes reported and another eight models were used to study risk and maternal dosage.

Results

Impact of late v. early exposure

Late exposure (i.e. exposure after 185 days of gestation, including the third trimester) to SRI medication ($n=1925$) was associated with lower birth weights, shorter gestations, an increased proportion of neonates with a birth weight less than the 10th percentile and higher rates of respiratory distress, compared with neonates with early exposure alone ($n=1575$). The differences in birth weight, gestational age and respiratory distress remained significant: $z=4.37$; $z=4.90$; Fisher's exact test (two-sided) 95% CI 1.18–1.81; all $P<0.01$ – after a Bonferroni correction for ten comparisons. The proportion of infants born by caesarean section was higher among the late group (24.6% v. 21.9%; OR=1.16, $P=0.06$). A total of six infants with convulsions was reported; although five were in the late group and one in the early group, group differences were not statistically significant.

Propensity score matching

Importantly, characteristics of the mothers during pregnancy differed substantially between the late exposure and early exposure groups (Table 1). Although the women in the two groups were similar in the year before pregnancy, during pregnancy women in the late exposure group were diagnosed as depressed about 1.7 times more frequently, visited a psychiatrist about 2.5 times more frequently and had 3.6 times more days of SRI exposure than those in the early group, clearly suggesting that women who took SRIs during their late pregnancy substantially differed from the early exposure group in duration of exposure and in ways that might have reflected differences in depression severity. Propensity score matching as described above was used to ensure that a subgroup of infants with late exposure ($n=429$) were comparable with those in the early exposure group in terms of maternal characteristics.¹⁰ In contrast to the increased risk of lower birth weight, reduced gestational age and increased incidence of respiratory distress observed using unmatched comparison between the late and early exposure groups (Table 2), using propensity-matched subgroups neonatal outcomes were similar between the late and early exposure groups, with the exception of lower birth weights persisting in the late exposure group. However, this difference did not remain statistically significant after a Bonferroni correction for multiple comparisons ($P>0.05$).

Effects of duration of gestational exposure

After controlling for characteristics reflecting maternal illness severity, increased duration of exposure (days) was significantly associated with reduced gestational age ($z=4.59$), decreased birth weight ($z=2.61$), increased risk of respiratory distress ($z=4.24$),

Table 1 Maternal characteristics: early v. late exposure groups

	Early exposure ($n=1575$)	Late exposure ($n=1925$)
Pre-pregnancy		
At least one visit to a psychiatrist in the year before becoming pregnant, %	16.5	20.9 ²
More than five visits to a psychiatrist in the year before becoming pregnant, %	5.4	7.3
At least one diagnosis of depression in the year before becoming pregnant, %	74.9	68.5 ^b
At least five diagnoses of depression in the year before becoming pregnant, %	18.0	17.5
At least one 3-digit ICD-9 code for depressive condition in year before becoming pregnant, %	31.9	29.5
At least five 3-digit ICD-9 codes for depressive condition in year before becoming pregnant, %	4.4	4.1
At least one diagnosis of a mental health disorder, excluding depression, in year before becoming pregnant, %	11.7	9.7
At least five diagnoses of a mental health disorder, excluding depression, in year before becoming pregnant, %	1.3	2.0
Counselled by GP at least once in previous year, %	56.6	50.9 ^b
Counselled by GP at least five times in previous year, %	1.1	0.8
Drugs subsidised through welfare programme in previous year, %	26.2	19.0 ^b
Income decile: median (IQR)	5 (3–7)	5 (3–8)
Pregnancy		
Number of days of SRI exposure during pregnancy: median (IQR)	30 (21–53)	1561 (81–215)
Age during pregnancy, years: median (IQR)	29 (25–33)	301 (26–34)
Number of prenatal visits during pregnancy: median (IQR)	12 (9–14)	111 (9–13)
Caesarean section, %	21.9	24.6
Diagnosed depressed at least once during pregnancy, %	52.8	65.7 ^b
Diagnosed depressed more than five times during pregnancy, %	4.0	9.5 ^b
Diagnosed with 3-digit ICD-9 code that might include depression during pregnancy, %	24.8	29.5 ^b
Treated by a psychiatrist at least once during pregnancy, %	13.3	26.8 ^b
Treated by a psychiatrist at least five times during pregnancy, %	2.7	6.9 ^b
Filled a prescription for an antipsychotic during pregnancy, %	2.0	1.9
Filled a prescription for a TCA during pregnancy, %	4.2	4.1
GP, general practitioner; IQR, interquartile range; SRI, serotonin reuptake inhibitor; TCA, tricyclic antidepressant. a. For differences between groups, $P<0.01$, two-sample <i>t</i> -test, d.f.=3498. b. For differences between groups, $P<0.01$, two-sided Fisher's exact test.		

Table 2 Neonatal outcomes: early v. late gestational exposure

	Non-matched sample		Matched sample	
	Early exposure (n=1575) Mean (s.d.)	Late exposure (n=1925) Mean (s.d.)	Early exposure (n=429) Mean (s.d.)	Late exposure (n=429) Mean (s.d.)
SRI exposure during pregnancy, days	40.4 (29)	146.8 (77)	62.8 (35)	61.7 (38)
Birth weight, g	3478 (594)	3392 (572) ^a	3443 (630)	3361 (512) ^b
Gestational age, weeks	39.0 (2.0)	38.7 (1.8) ^a	38.9 (2.1)	38.8 (1.7)
Gestational age <37 weeks, %	8.3 (28)	9.2 (29)	10.3 (30)	9.1 (29)
Length of stay in hospital, days	3.28 (6.2)	3.35 (5.3)	3.24 (7.8)	2.86 (3.2)
Birth weight <10th percentile for gestational age, %	6.2 (24)	8.1 (27) ^c	7.0 (26)	7.9 (27)
Caesarean section, %	21.9 (41)	24.6 (43) ^c	19.3 (40)	20.7 (41)
Respiratory distress, %	10.2 (30)	14.3 (35) ^c	9.3 (29)	10.3 (30)
Feeding problems, %	2.8 (16)	3.7 (19)	3.7 (19)	2.6 (16)

SRI, serotonin reuptake inhibitor.
a. For differences between early exposure and late exposure groups (non-matched) two-sample t-test, d.f.=3498, $P<0.01$.
b. For differences between early exposure and late exposure groups (matched) two-sample t-test, d.f.=856, $P=0.04$.
c. For differences between early exposure and late exposure groups (non-matched) two-sided Fisher's exact test $P<0.01$.

and low birth weight for gestational age ($z=2.34$); $P<0.01$ respectively (Table 3).

Effect of maternal dosage

Regression analysis was used to examine the impact of maternal SRI dosage. No adverse neonatal outcome was associated with either high or low dosage ($P>0.05$ for each outcome). Incidentally, high dosage was associated with an increased incidence of caesarean birth ($P=0.02$).

Discussion

Four main findings emerged from this study. First, using the accepted definitions of early and late gestational exposure may not be appropriate for assessing the effects of the timing of gestational SRI exposure. Maternal mental health characteristics differed substantially between the early and late exposure groups in ways that could potentially have influenced infant outcomes beyond SRI exposure alone (i.e. differences in maternal illness severity that lead to altered neonatal outcomes independent of the effects of the medication itself). Second, in contrast to our expectation, after using propensity score matching to account for characteristics of maternal mental illness severity, risk of poor neonatal outcomes did not significantly differ between the early and late exposure groups. Importantly, without controlling for maternal illness characteristics, late exposure was associated

with increased risk of adverse neonatal outcomes compared with early-gestational exposure – findings that are consistent with previous reports.¹ Although late-gestational SRI exposure was associated with a prolonged hospital stay, a reduction in birth weight, birth weight less than the 10th percentile, shorter gestational age, increased risk of respiratory distress and feeding difficulties at birth, such differences disappeared when propensity score matching was used to compare the groups. Third, with increasing length of prenatal SRI use, neonatal risk increased regardless of the timing of that exposure. Although the rate of caesarean section was higher in the SRI exposure group and this could have influenced neonatal outcomes as well as length of stay, using a propensity score-matched group to account for this confounding influence this factor no longer accounted for differences in outcomes. Fourth, maternal dosage was not associated with increased risk of adverse neonatal outcomes. Using population-based data linking maternal health and medication data with neonatal health outcome, greater length of gestational exposure rather than the timing of exposure was associated with a significantly increased risk of adverse outcomes after controlling for maternal characteristics.

Impact of maternal illness

Increased risk of neonatal behavioural disturbances following late exposure has been widely reported using cohort studies;¹

Table 3 Length of gestational exposure and neonatal outcome

	Change per day of exposure	Z score	Change due to additional 90 days of exposure
Gestational age, weeks	-0.00159	-4.59*	-0.14
Birth weight, g	-0.33110	-2.61*	-30
Length of stay in hospital, days	0.00039	0.55	0.03
Birth weight for gestational age <10th percentile, %	0.00014	2.34**	1.3
Respiratory distress, %	0.00031	4.24*	2.8
Jaundice, %	-0.00003	-0.50	-0.3
Feeding difficulties, %	0.00005	1.51	0.5
Caesarean section, %	0.00019	1.85	1.7

* $P<0.001$; ** $P=0.02$.

however, none of these studies controlled for the impact of maternal depression during pregnancy. Population-based studies using birth registries have also reported a variety of similar effects,^{11–13} but outcomes have been inconsistent. Using linked population health data, comparing first and third trimester exposure, accounting for some maternal characteristics (e.g. smoking), Malm reported an increased rate of admission to special care nurseries with third-trimester exposure,¹¹ but failed to demonstrate a difference in gestational age or birth weight between trimesters. Similarly, Simon, using linked health data reported an association between SRI exposure and lower gestational age and birth weight that was not limited to late-gestational exposure.¹² Comparison between studies has been challenged by a number of methodological limitations, including the lack of comparable control groups, cohort selection bias, failure to account for concurrent exposure to other psychotropic medication (e.g. benzodiazepines) and limited knowledge of the exact timing of gestational exposure. Importantly, failure to account for the impact of maternal illness has been recently cited as a critical methodological limitation in studies examining the impact of early *v.* late SRI exposure.¹ Exposure to maternal depression itself is associated with increased irritability, decreased motor tone and poor feeding in the neonate.¹⁴ For logistical, ethical and medical reasons, however, it is not possible to undertake masked randomised controlled studies of the effects of SRI exposure limited to specific trimesters.

Previously, controlling for the concurrent impact of maternal depression in cohort studies has been challenging because of ethical, medical and logistical factors. In this study propensity score matching was specifically used to account for measured maternal characteristics that could have influenced neonatal outcomes, but could not be directly controlled for using administrative population health data. Additionally, these factors had not been accounted for in previous population health data research in this field.^{11–13} One of the strengths of propensity score matching is that it identifies the part of the treated group for which there is an appropriate comparison. It is possible that the women taking SRIs in our sample who used these medications for more than 90 days were likely to have been treated for considerably longer times, and this too could have influenced neonatal outcomes. We controlled for this possibility by matching for length of exposure in our propensity-matched groups. The advantages of the use of propensity score matching include avoidance of functional form assumptions that underlie regression methods and the ability to identify the part of the untreated population that can be compared with the treated population without extrapolation. In their analysis of selection bias, Heckman *et al* concluded that the largest part of selection bias arises from ‘differences in the support’ and ‘differences in densities over the region of common support’.¹⁰ Moreover, inaccurate functional form and violations of the support condition – separately and in combination – introduce bias in regression methods, as illustrated in recent empirical work.¹⁵ Propensity score matching is a transparent method for eliminating bias due to measured confounders because the reader can verify that matching has produced a comparison group with similar characteristics to the treatment group.

Our findings suggest that when accounting for factors reflecting the character of maternal mental illness in multiple comparisons, differences in neonatal outcomes between late and early exposure no longer remained significant. These findings raise the question of whether there is empiric evidence to support the suggestion to taper the dosage of antidepressants during the last trimester to ensure that there is no drug exposure in the last 7–10 days of gestation.¹⁶ Further, our failure to detect neonatal

differences between early- and late-gestational exposure when accounting for maternal illness characteristics also questions whether neonatal behavioural disturbances, such as respiratory distress, reflect a genuine pharmacological withdrawal phenomenon secondary to a sudden cessation of prenatal exposure or altered serotonin-related neurobehaviours. Instead, these findings might reflect the effects of prolonged prenatal exposure which could lead to a number of mechanisms, including neurotransmitter suppression,¹⁷ pharmacological toxicity,¹⁸ altered pulmonary vasculature,⁴ changes in serotonergic-related neurodevelopment^{19,20} or effects of maternal illness itself.⁵ The mechanisms that underlie our findings remain to be determined; however, there is emerging evidence from human studies suggesting that prenatal SRI exposure may be associated with changes in neonatal behaviours in ways that might reflect altered serotonin-dependent processes.¹⁹ Serotonin reuptake inhibitors block the reuptake of 5-hydroxytryptamine (5-HT), a monoamine neurotransmitter that has a key role in regulating neural growth and arousal regulation. Before it takes on its role as a neurotransmitter in the mature brain,²¹ 5-HT also acts as a trophic signal in the developing brain by directing neural ontogeny of the serotonergic and other systems.²² As a developmental signal, 5-HT regulates prenatal neural growth and physiological processes,²³ including foetal lung development. Using animal models, SRI exposure reduced central 5-HT levels and changes in serotonin transporter densities.²⁴ In human studies direct evidence of such alterations remain to be determined; however, changes in neonatal pulmonary blood flow,⁴ behavioural state regulation and pain reactivity^{19,20} have also been observed, possibly reflecting altered 5-HT-mediated processes.

Methodological limitations

The use of administrative health data to study the effects of prenatal SRI exposure poses a number of challenges. The concurrent use of tobacco and alcohol during pregnancy, maternal weight gain and parity could not be directly studied using such data. Although our sample was restricted to women with a diagnosis of depression treated with an SRI medication, dispensed during pregnancy, comorbid maternal conditions, which went unreported, could also not be accounted for in our study. The level, severity or course of prenatal depression as assessed by the woman’s clinician could not be directly determined, nor could the accuracy or way in which the physician made the mental health diagnosis be ascertained. Although we believed that because the medication was paid for and dispensed it was actually taken, this consumption could not be verified. Because SRI use occurred in the context of maternal depression, we were not able to study the effects of SRI exposure independent of exposure to depression alone or fluctuations in maternal mood that would not have been tabulated in administrative health data.

This study was undertaken to determine the effects of timing and duration of gestational medication exposure taking into account maternal illness severity and was not directed at assessing the safety of prenatal SRI use. Although the benefits of SRI treatment during pregnancy remain to be determined, it is important to emphasise that none of these findings should diminish the urgency of recognising and treating maternal depression during pregnancy in a timely fashion which may require pharmacological and non-pharmacological strategies. The decision to start or stop SRI treatment during pregnancy should be made by an informed patient with her physician on an individual basis.²⁵ Given that the neonatal

risks associated with both early and late gestational exposure do not appear to be substantially different, the need to taper or stop the use of an antidepressant during late gestation must be weighed against the risks of undertreated maternal illness and potential relapse.

Tim F. Oberlander, MD, Department of Pediatrics and Human Early Learning Partnership; **William Warburton**, PhD, Human Early Learning Partnership; **Shaila Misri**, MD, FRCPC, Department of Psychiatry; **Jaafar Aghajanian**, BSc; **Clyde Hertzman**, MD, Human Early Learning Partnership, University of British Columbia, Vancouver, British Columbia, Canada

Correspondence: Dr Tim F. Oberlander, Early Human Experience Unit, Centre for Community Child Health Research, Room L408, 4480 Oak Street, Vancouver, BC V6 3V4, Canada. E-mail: toberlander@cw.bc.ca

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