Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Pregnancy, fetal, and neonatal outcomes following a first booster dose of COVID-19 vaccine during pregnancy in Ontario, Canada: a population-based retrospective cohort study

Table of Contents

Supplementary Table 1. Description of data sources

BORN Information System	Details about the BORN Information System (BIS) are available elsewhere.[1] Briefly, the BIS captures information on all Ontario births ≥20 weeks' gestation or ≥500 grams (all hospital births and the ~2.8% of home births with a midwife [2]) from over 250 hospitals, birth centres, midwifery practice groups, and prenatal screening labs. Prenatal and maternity care are publicly funded in the province. Records for pregnant individuals who undergo prenatal screening (about 70% in Ontario [3]) are uploaded weekly to the BIS from hospital- and community-based labs and ultrasound clinics. Thus, screened pregnancies are identifiable in the BIS as early as 10 weeks' gestation; 97% of prenatal screening records are linked with other health care encounters pertaining to birth. Unscreened pregnancies typically become identifiable in the BIS only at the time of the birth. When a pregnant individual presents to care around the time of birth, the birthing site generates a "Labour and birth encounter" in the BIS that captures information about labour and birth through to the first hour postpartum, regardless of birth setting (hospital, home, or birth centre). A separate "Birth-child encounter" documents information about each newborn (live births and stillbirths) through to the first hour postpartum. Postpartum encounters then capture clinical information about the mother and newborn(s) from the immediate postpartum period until discharge from hospital/birth centre. Unique identifiers (mother and newborn), assigned upon first record entry into the BIS, are used by the system to deterministically link all encounters through a robust automated algorithm. A system-generated signal indicates when each encounter record is complete. The BIS has a comprehensive data quality framework. Submitting sites are required to perform monthly automated data validation checks that flag records with missing encounters or data errors so that corrections can be made; every month, each site must report that it has reviewed and resolved flagged errors.[1] A formal validation study has been conducted, in which the accuracy of 29 core variables in the BORN registry was assessed by comparing data entered into the registry with original clinical data extracted from patient health records in a sample of hospitals. The study found good agreement between the two sources, with 76% of the variables (22 of 29) having greater than 90% agreement, and 12 of the categorical elements having almost perfect (kappa 0.81–0.99) or substantial (kappa 0.61–0.80) agreement.[4]
Canadian Census	To obtain information on rural/urban residence and dissemination-area based neighbourhood income quintile, we linked the study population to Statistics Canada's 2016 Census, based on postal code of maternal residence using Statistics Canada's Postal Code Conversion File Plus (PCCF+).
Ontario Marginalization Index	The Ontario Marginalization Index, which is derived from data from Statistics Canada's Census, quantifies the level of marginalization across the province. [5] The Index consists of four dimensions: residential instability, material deprivation, dependency, and ethnic concentration. Area-based quintile scores are available for each dimension, with quintile one representing the least marginalized areas, and quintile five representing the most marginalized. The Ontario Marginalization Index is linked with the BIS using postal code of maternal residence.

COVaxON	COVaxON, Ontario's COVID-19 immunization database, contains records for all COVID-19 vaccines administered in the province. Data are reported into COVaxON at the time of immunization, regardless of type of provider or delivery location (mass immunization clinic, pharmacy, etc.). Information includes vaccine product, dose number, and date(s) of vaccination. On a monthly basis, an extract of all immunization events in females aged 15-45 years is transferred to BORN Ontario, where they are deterministically linked using health card number to the BIS to identify individuals who received COVID-19 vaccination during pregnancy.
CCM	Ontario's Case and Contact Management System (CCM) is a centralized repository for COVID-19 case and contact management.[6] Each public health unit in the province collects information on COVID-19-positive cases and reports it to the Ministry of Health. On a monthly basis, an extract of all PCR-confirmed positive cases in females aged 15-45 years is transferred to BORN Ontario, where they are deterministically linked using health card number with the BIS to identify individuals who had laboratory-confirmed COVID-19 during pregnancy. A rapid increase in COVID-19 cases, due to the highly transmissible Omicron variant, starting in December 2021 led to changes in COVID-19 testing policies in the province (e.g., high-risk individuals, and individuals who work in high-risk settings were prioritized for testing) and delays in data entry. Consequently, COVID-19 case counts may be greatly underestimated since late 2021.

Supplementary Table 2. Description of study variables

Variable	Description
Exposure	
Third COVID-19 vaccine dose during pregnancy	Individuals who received a third dose any time between the LMP date up to one day before delivery (or before the end of the outcome-specific follow-up window for preterm birth outcomes) were considered 'exposed'. Those who did not receive a third COVID-19 vaccine dose before the end of pregnancy (or before the end of the outcome-specific follow-up window for preterm birth outcomes) were considered 'unexposed'. [NOTE: this study only included individuals who had already received their primary COVID-19 vaccine series prior to their LMP date, and became eligible to receive a third dose any time between their LMP date and the end of pregnancy, defined as 6 months after dose 2 (i.e., dose 2 date + 168 days)]
Pregnancy outcomes	
Hypertensive disorders of pregnancy	Gestational hypertension is hypertension that develops for the first time at ≥20 weeks of gestation without evidence of preeclampsia. Hypertension is defined as an office (or in-hospital) systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg, based on the average of at least 2 measurements, taken after 5 minutes' rest, at least 15 minutes apart, using the same arm. Pre-eclampsia is gestational hypertension with new-onset proteinuria or one/more adverse conditions (defined as a maternal end-organ complication or evidence of uteroplacental dysfunction). Eclampsia is a severe complication of preeclampsia. It is a rare but serious condition where high blood pressure results in seizures during pregnancy. HELLP is an acronym for another severe condition associated with hypertensive disorders in pregnancy. It stands for Hemolysis, Elevated Liver Enzymes and Low Platelets.
Placental abruption	Defined as the early separation of the placenta from the lining of the uterus before the completion of the second stage of labour.
Chorioamnionitis	Acute inflammation of the chorion and membranes of the placenta due to bacterial infection.
Postpartum haemorrhage	Postpartum haemorrhage is defined as excessive bleeding that occurs within the first 24 hours after delivery. It is usually defined as >500 ml of blood loss for a vaginal delivery and >1000 ml for an abdominal delivery. Now, any blood loss that produces hemodynamic instability should be called postpartum haemorrhage and this will vary with the pre-existing condition of the woman.
Cesarean delivery	Delivery by cesarean section, including those for non-emergent indications (e.g., maternal request; elective; planned due to previous cesarean section) and emergent indications (see below).
Emergency cesarean delivery	Emergency cesarean is a subset of all cesarean births. Indication for emergent cesarean delivery: VBAC - Failed attempt; Uterine rupture; Placental abruption; Hypertensive disorders of pregnancy – Eclampsia; Hypertensive disorders of pregnancy – HELLP; Failed Induction; Failed forceps / vacuum; Prelabour Rupture of Membranes (PROM) in women with planned C-Section; Preterm prelabour rupture of membranes (PPROM) in women with planned C-Section; Nonprogressive second stage of labour; Nonprogressive labour/descent/dystocia; Suspected Chorioamnionitis; Other Obstetrical Complication; Nonprogressive first stage of labour; Hypertensive disorders of pregnancy – Preeclampsia; Placenta Previa

	(emergent if indication not known until time of delivery or uterine bleeding is present); Placenta Increta/Accreta/Percreta (emergent if indication not known until time of delivery or uterine bleeding is present); Cord prolapse; Cord prolapse \ Other; Atypical or Abnormal Fetal Surveillance; Malposition/Malpresentation; Intrauterine Growth Restriction (emergent if indication not known until time of delivery or fetal/atypical or abnormal surveillance observed); Congenital Anomalies (emergent if not planned C-section).
Fetal/neonatal outcomes	
Stillbirth	BORN Ontario uses the Ontario Vital Statistics Act's definition of stillbirth: "…..the complete expulsion or extraction from a person of a product of conception either after the 20th week of pregnancy or after the product of conception has attained a birth weight of 500g or more and shows no signs of life at birth." (**https://www.ontario.ca/laws/statute/90v04).** Stillbirth includes an antepartum or intrapartum fetal death at ≥20 weeks or ≥500 grams, with the gestational timing of the event based on the date of birth (information on the timing of fetal demise was not available).
Preterm birth	Live birth or stillbirth before 37 completed weeks of gestation.
Spontaneous preterm birth	Preterm birth was considered spontaneous if it occurred after spontaneous onset of labour or preterm premature rupture of membranes.
Clinician-initiated preterm birth	Preterm birth was considered spontaneous if it occurred after spontaneous onset of labour or preterm premature rupture of membranes, and considered clinician-initiated otherwise.
Very preterm birth	Live birth or stillbirth before 32 completed weeks of gestation.
NICU admission	Admission to neonatal intensive care unit (NICU) is related to prematurity, congenital anomalies requiring higher level of care (e.g., babies who are ill following birth). In the BIS, there is a flag on the file of any baby admitted to an NICU (Level 2 or Level 3).
5-minute Apgar score <7	The Apgar scoring system is a standardized method to assess the status of newborns immediately after birth (1, and 5 minutes). It comprises five components: 1) skin color, 2) heart rate, 3) reflexes, 4) muscle tone, and 5) respiration, each of which is given a score of 0, 1, or 2 (the highest score is 10).
Small for gestational age (SGA) at birth	Calculated field in the birth registry based on infant sex, gestational age, and birth weight. SGA at birth is defined as a singleton live birth below the 10th percentile of the sex-specific birth weight for gestational age distribution, based on a Canadian reference standard.[7]
Baseline variables included in propensity score model	
Maternal age	Calculated field indicating maternal age at time of live birth or stillbirth.
Estimated date of last menstrual period	Estimated date of last menstrual period was calculated from gestational age at birth. Gestational age in days is recorded in the birth registry and most pregnancy dating in Ontario is based on early ultrasound assessment.
Parity	The number of previous live births and stillbirths (term + preterm). This is automatically calculated by the birth registry at the time of data upload/entry.
Multiple birth	Number of fetuses in the current pregnancy.
Pre-existing medical condition	Maternal health conditions and/or complications including those pre-existing, diagnosed during pregnancy or active during pregnancy. Variable was derived as a composite of the following conditions: thyroid disease, asthma, diabetes, chronic hypertension, and heart disease.
Self-reported smoking during pregnancy	Self-reported amount of smoking per day closest to time of labour/admission or at time of first prenatal visit. Smoking status includes any self-reported cigarettes that were smoked at any time during the pregnancy. This does not include marijuana or vaping.

Self-reported substance use during pregnancy	Maternal self-reported drug and substance use during pregnancy. This refers to the use of street drugs and the inappropriate use of prescription and non-prescription drugs and includes cocaine, gas/glue, hallucinogens, opioids, and cannabis. Measure of substance use included maternal self-reported cannabis exposure (i.e., smoking, vaping, consumption of edibles and cannabis products, and topical application) at any point during this pregnancy as documented in the medical record.
Pre-pregnancy maternal BMI (kg/m^2)	Derived using maternal weight (kg) and height (cm). Maternal weight is reported as mother's self-reported weight closest to conception and no later than 12 weeks of gestation (metric or imperial units) and maternal height is reported in imperial or metric units.
Rural/urban residence	Rural or urban residence based on postal code of maternal residence.
Neighbourhood income quintile	Dissemination-area based neighbourhood income quintile.
Ontario Marginalization Index [5] – Residential instability	Residential instability identifies areas with high rates of family or housing instability. The Census indicators used to derive residential instability are: 1) percentage of population living alone; 2) percentage of population who are not youth aged 5-15 years; 3) average number of persons per dwelling; 4) percentage of dwellings that are in apartment buildings; 5) percentage of population who are single/divorced/widowed; 6) percentage of dwellings that are not owned; and 7) percentage of population who moved during the past five years.
Ontario Marginalization Index [5] – Material deprivation	Material deprivation, which is closely connected to poverty, identifies individuals and communities unable to access and attain basic material needs. The Census indicators used to derive material deprivation are: 1) percentage of population ≥20 years without a secondary diploma; 2) percentage of lone-parent families; 3) percentage of total income received from government transfer payments for population aged ≥15 years; 4) percentage of population aged ≥15 years who are unemployed; 5) percentage of population considered low-income; and 6) percentage of household dwellings in need of major repair.
Ontario Marginalization Index [5] – Dependency	Dependency identifies areas with high concentrations of residents who do not receive employment income. The Census indicators used to derive dependency are: 1) percentage of population who are aged ≥65 years; 2) dependency ratio (total population aged 0-14 years and ≥65 years / total population aged 15 to 64 years); and 3) percentage of population aged ≥15 years not participating in labour force.
Ontario Marginalization Index [5] – Ethnic concentration	Ethnic concentration identifies areas with high concentrations of recent immigrants and/or "visible minorities" (defined by Statistics Canada as "persons, other than Aboriginal peoples, who are non-Caucasian in race or non-white in colour"). Ethnic concentration is derived from two Census variables: 1) percentage of population who are recent immigrants (arrived in past five years); and 2) percentage of population who self-identify as a visible minority (Census respondents can indicate more than one race/ethnicity from a list, or can specify a group not listed on the Census questionnaire).
Public health unit region of residence	South West, Central West, Central East, Greater Toronto Area, Eastern, North West, North East
First prenatal visit during first trimester	Indication that mother had a prenatal care visit with a regulated health care provider during the first trimester (<14 weeks of gestation).

Supplementary Appendix 1. Multiple imputation and propensity score methods

Multiple imputation was used to address missing covariate values (16.6% of records had missing information for one or more covariates included in the propensity score models). Ten multiple imputation datasets were generated using a fully conditional specification ('MI' procedure in SAS Version 9.4, SAS Institute Inc, Cary, NC).

We used logistic regression to generate propensity scores (using each of the 10 imputed datasets) representing the predicted probability of receiving a third dose of COVID-19 vaccine during pregnancy (compared with not receiving a third dose of COVID-19 vaccine during pregnancy), conditional on the baseline variables listed in Supplementary table 2.

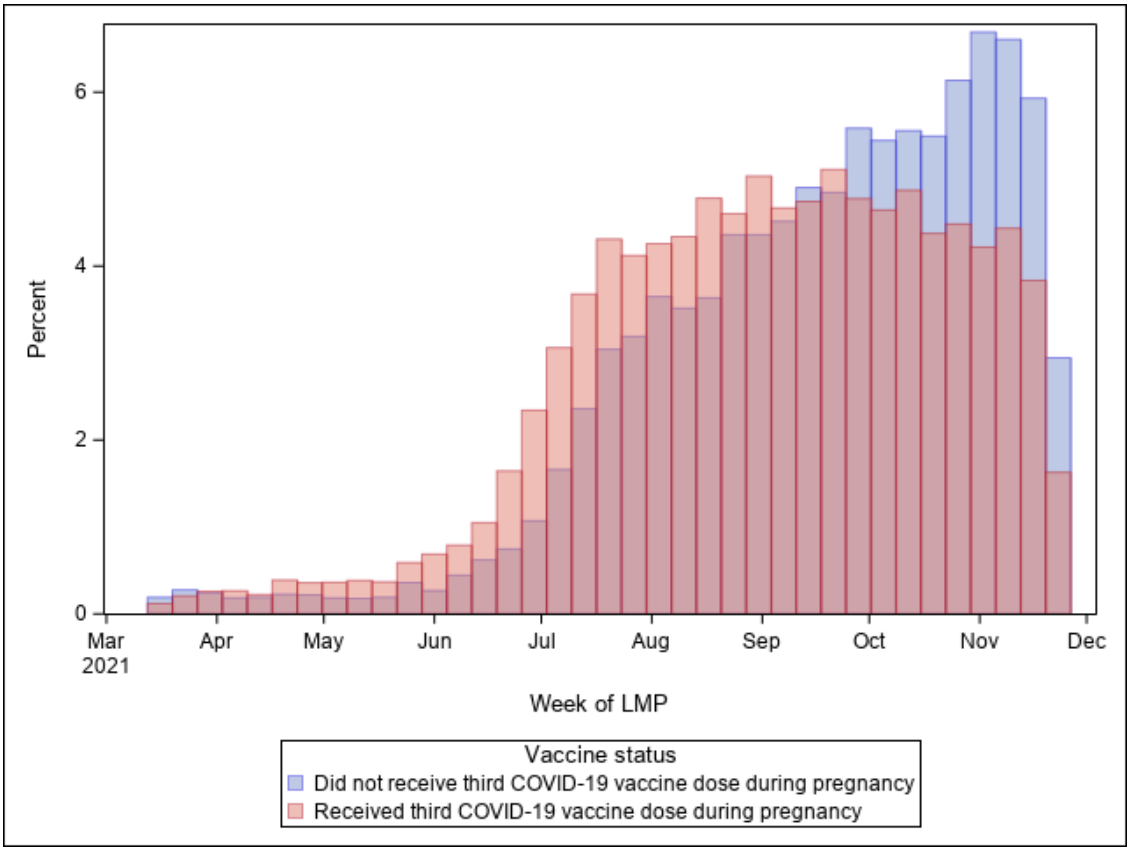
The propensity scores were then used to generate 10 sets of inverse probability of treatment weights using each of the 10 multiply-imputed datasets. Weight were computed as the inverse of the propensity score for exposed individuals and the inverse of 1 minus the propensity score for the comparison group.[8] We stabilized the weights by multiplying by the marginal propensity score [9,10] and applied trimming by reassigning any weights with a value below the 1st percentile or above the 99th percentile to the values at the 1st or 99th percentiles, respectively, to account for any large weights that could potentially influence the results and inflate variance.[11] We re-assessed the distribution of baseline variables by exposure group after applying propensity score weights (table 2 and Supplementary table 3).

Regression models incorporating stabilized weights from each of the 10 imputed datasets were used to generate adjusted coefficients and standard errors, which were combined using the 'MIANALYZE' procedure (SAS Version 9.4, SAS Institute Inc, Cary, NC) to produce adjusted estimates and 95% confidence intervals (CI).

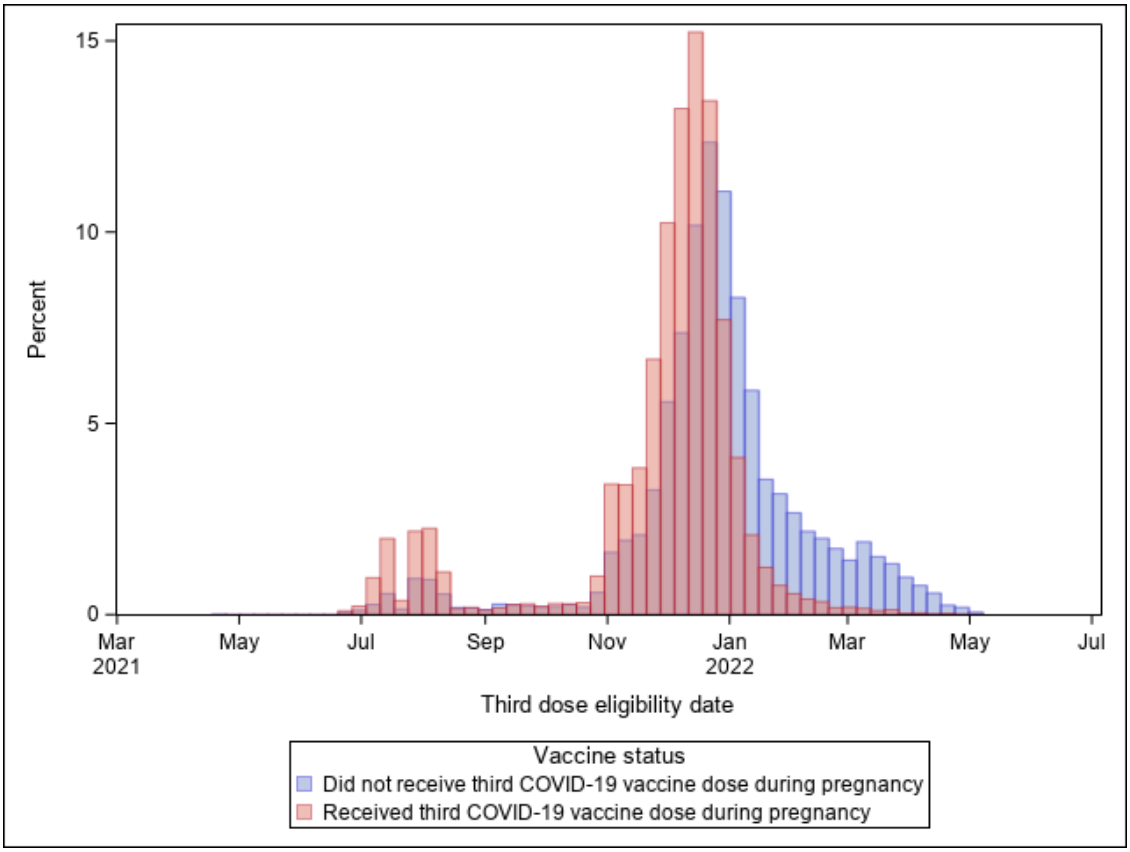
Supplementary Figure 1. Timing of COVID-19 primary series, relative to index pregnancy, among 53,905 individuals excluded from study

N=53,905 individuals who were excluded because they were not eligible, based on timing of primary series		BEFORE PREGNANCY			DURING PREGNANCY			AFTER PREGNANCY			Number
		Dose 1	Dose 2	Dose 3	Dose 1	Dose 2	Dose 3	Dose 1	Dose 2	Dose 3	
Never vaccinated	Excluded										21,530
Initiated vaccine series on or after date of delivery - received 1 dose	Excluded										585
Initiated vaccine series on or after date of delivery - received 2 doses	Excluded										1,325
Initiated vaccine series on or after date of delivery - received 3 doses	Excluded										56
Dose 1 before pregnancy, no further doses	Excluded										736
Dose 1 before pregnancy, dose 2 during pregnancy, no further doses	Excluded										5,475
Dose 1 before pregnancy, dose 2 after pregnancy, no further doses	Excluded										145
Dose 1 before pregnancy, dose 2 + 3 during pregnancy	Excluded										5,619
Dose 1 before pregnancy, dose 2 during pregnancy, dose 3 after pregnancy	Excluded										710
Dose 1 before pregnancy, dose 2 + 3 after pregnancy	Excluded										7
Dose 1 during pregnancy, no further doses	Excluded										1,290
Dose 1 + 2 during pregnancy, no further doses	Excluded										9,380
Dose 1 during pregnancy, dose 2 after pregnancy, no further doses	Excluded										540
Dose 1 + 2 + 3 during pregnancy	Excluded										3,669
Dose 1 + 2 during pregnancy, dose 3 after pregnancy	Excluded										2,811
Dose 1 during pregnancy, dose 2 + 3 after pregnancy	Excluded										27

Supplementary Figure 2. Distribution of last menstrual period (LMP) date among those who received a third COVID-19 dose during pregnancy (exposed) and those who did not (unexposed)

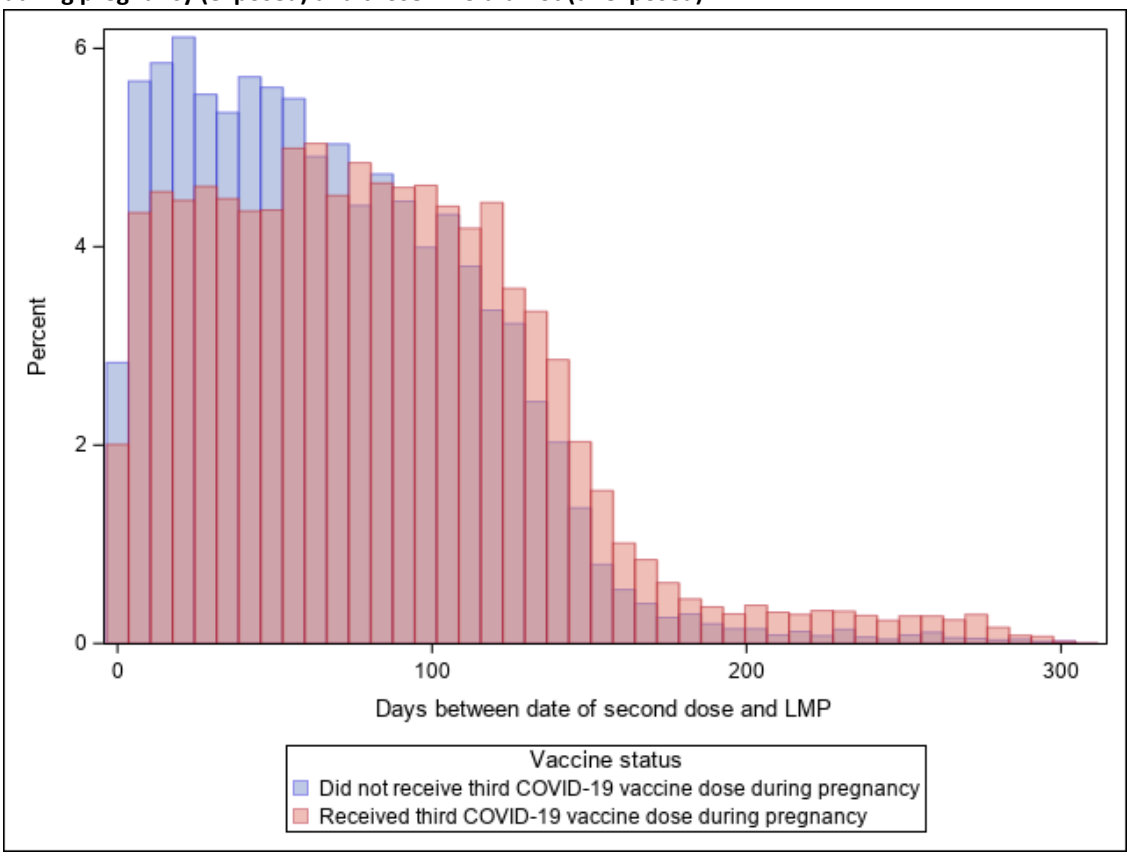


Supplementary Figure 3. Third dose eligibility date among those who received a third COVID-19 dose during pregnancy (exposed) and those who did not (unexposed) [a]

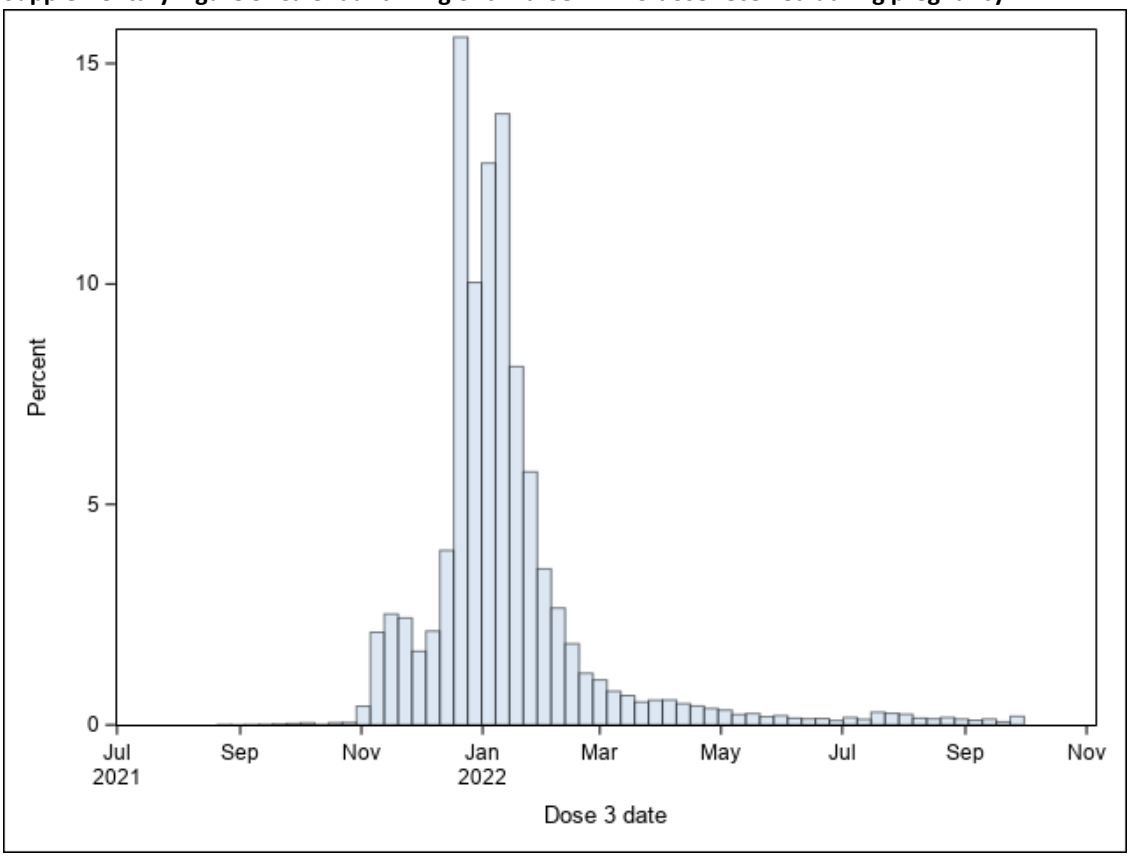


[a] Third dose eligibility date was calculated as 168 days (24 weeks) after the date of the second dose.

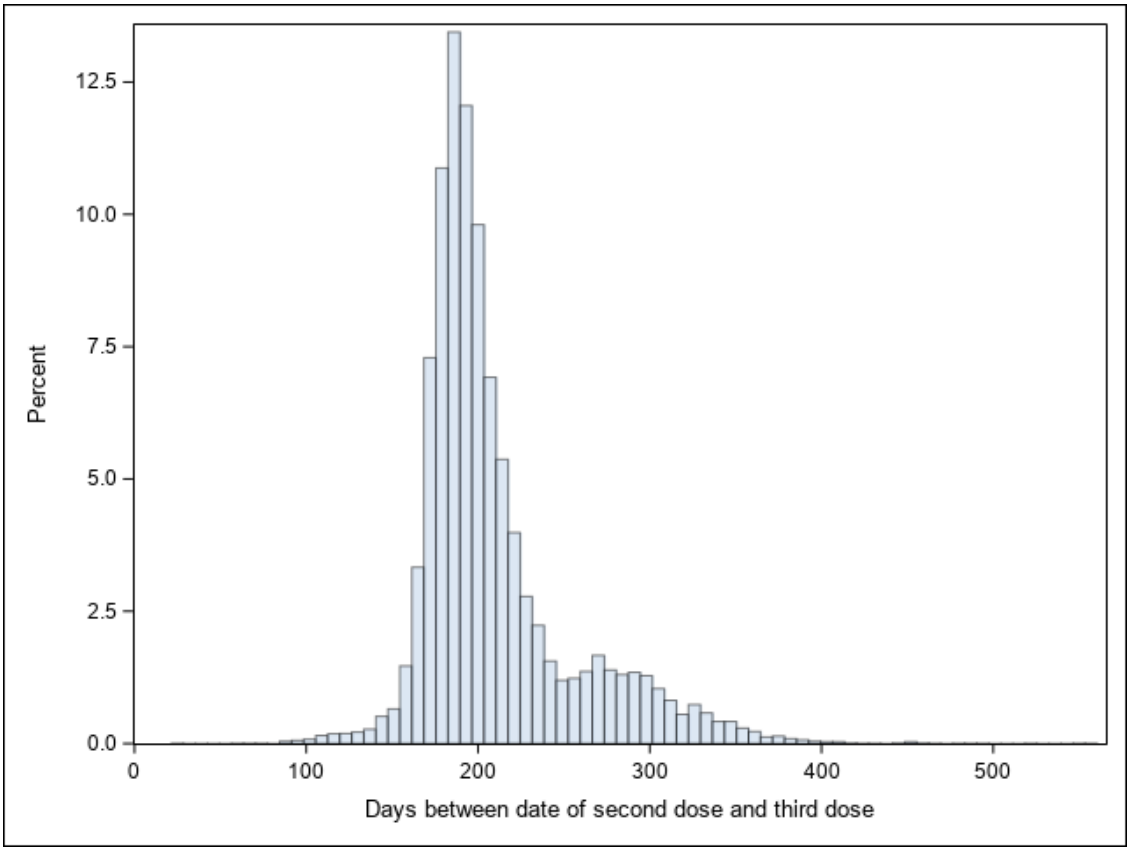
Supplementary Figure 4. Distribution of number of days between date that the second dose was received and the last menstrual period (LMP) date among those who received a third COVID-19 dose during pregnancy (exposed) and those who did not (unexposed)



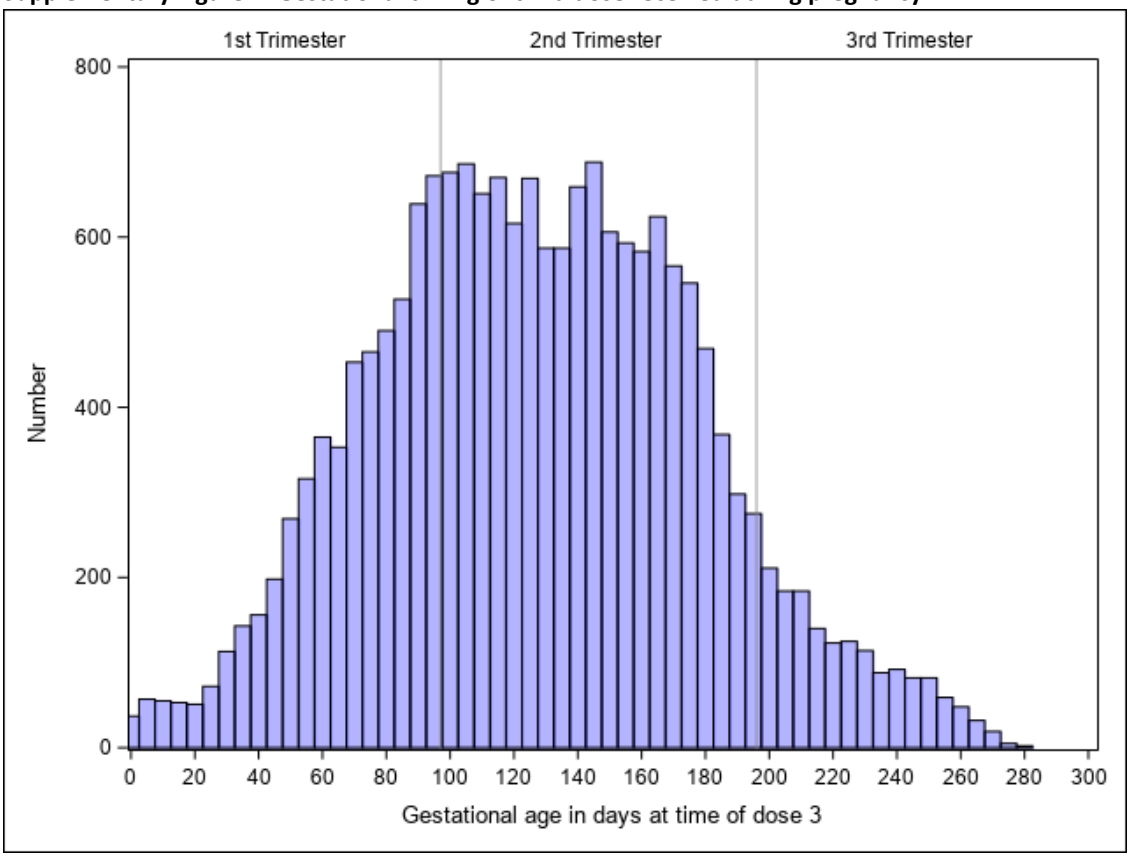
Supplementary Figure 5. Calendar timing of third COVID-19 dose received during pregnancy



Supplementary Figure 6. Distribution of number of days between the second and third COVID-19 dose, among those who received the third COVID-19 dose during pregnancy



Supplementary Figure 7. Gestational timing of third dose received during pregnancy



Supplementary Table 3. Additional characteristics of study population overall and by status of third COVID-19 vaccine dose received during pregnancy

Characteristics	Unweighted							Stabilized inverse probability of treatment weighted [a]		
	All live births and stillbirths (n =32,689)		Received third COVID-19 vaccine dose during pregnancy (n =18,491)		Did not receive third COVID-19 vaccine dose during pregnancy (n =14,198)		Standardized difference [b]	Received third COVID-19 vaccine dose during pregnancy	Did not receive third COVID-19 vaccine dose during pregnancy	Standardized difference [b]
	n	% [c]	n	% [c]	n	% [c]		% [c]	% [c]	
Last menstrual period date										
Before August 2021	7,087	21.7	4,757	25.7	2,330	16.4	0.23	21.7	21.9	0.00
August - September 2021	12,970	39.7	7,582	41.0	5,388	37.9	0.06	40.3	39.1	0.03
October - November 2021	12,632	38.6	6,152	33.3	6,480	45.6	0.26	37.9	39.0	0.02
Multiple birth										
No	31,565	96.6	17,876	96.7	13,689	96.4	0.01	96.6	96.5	0.01
Yes	1,124	3.4	615	3.3	509	3.6	0.01	3.4	3.5	0.01
Asthma										
No	31,375	96.0	17,674	95.6	13,701	96.5	0.05	95.8	96.3	0.02
Yes	1,314	4.0	817	4.4	497	3.5	0.05	4.2	3.7	0.02
Chronic hypertension										

No	32,346	99.0	18,279	98.9	14,067	99.1	0.02	98.9	98.9	0.00
Yes	343	1.0	212	1.1	131	0.9	0.02	1.1	1.1	0.00
Diabetes										
No	32,274	98.7	18,242	98.7	14,032	98.8	0.02	98.7	98.7	0.00
Yes	415	1.3	249	1.3	166	1.2	0.02	1.3	1.3	0.00
Heart disease										
No	32,644	99.9	18,465	99.9	14,179	99.9	0.00	99.9	99.8	0.00
Yes	45	0.1	26	0.1	19	0.1	0.00	0.1	0.2	0.00
Thyroid disease										
No	30,466	93.2	17,178	92.9	13,288	93.6	0.03	93.4	92.8	0.02
Yes	2,223	6.8	1,313	7.1	910	6.4	0.03	6.6	7.2	0.02
Substance use during pregnancy [d]										
No	30,610	93.6	17,328	93.7	13,282	93.5	0.01	97.1	97.2	0.00
Yes	816	2.5	336	1.8	480	3.4	0.10	2.9	2.8	0.00
Missing	1,263	3.9	827	4.5	436	3.1	0.07			
PHU region of residence										
South West	3,501	10.7	1,900	10.3	1,601	11.3	0.03	10.9	10.9	0.00
Central West	6,217	19.0	3,567	19.3	2,650	18.7	0.02	19.0	19.1	0.00
Central East	9,702	29.7	4,812	26.0	4,890	34.4	0.18	29.8	29.8	0.00
Greater Toronto Region	6,914	21.2	4,396	23.8	2,518	17.7	0.15	21.2	21.2	0.00

Eastern	4,482	13.7	2,853	15.4	1,629	11.5	0.12	13.7	13.7	0.00
North West	666	2.0	346	1.9	320	2.3	0.03	2.2	2.1	0.00
North East	1,045	3.2	538	2.9	507	3.6	0.04	3.2	3.2	0.00
Missing	162	0.5	79	0.4	83	0.6	0.02			
Material deprivation quintile										
Quintile 1 - least deprived	8,377	25.6	5,407	29.2	2,970	20.9	0.19	25.8	26.0	0.00
Quintile 2	7,014	21.5	4,258	23.0	2,756	19.4	0.09	21.7	21.7	0.00
Quintile 3	6,163	18.9	3,382	18.3	2,781	19.6	0.03	19.0	18.8	0.00
Quintile 4	5,557	17.0	2,866	15.5	2,691	19.0	0.09	17.2	17.2	0.00
Quintile 5 - most deprived	5,076	15.5	2,340	12.7	2,736	19.3	0.18	16.4	16.3	0.00
Missing	502	1.5	238	1.3	264	1.9	0.05			
Residential instability quintile										
Quintile 1 – least unstable	6,603	20.2	3,532	19.1	3,071	21.6	0.06	20.3	20.3	0.00
Quintile 2	6,134	18.8	3,522	19.0	2,612	18.4	0.02	18.9	19.0	0.00
Quintile 3	5,982	18.3	3,422	18.5	2,560	18.0	0.01	18.6	18.5	0.00
Quintile 4	5,771	17.7	3,346	18.1	2,425	17.1	0.03	17.9	17.9	0.00
Quintile 5 – most unstable	7,697	23.5	4,431	24.0	3,266	23.0	0.02	24.2	24.3	0.00
Missing	502	1.5	238	1.3	264	1.9	0.05			

Dependency quintile										
Quintile 1 – least dependent	11,065	33.8	6,162	33.3	4,903	34.5	0.03	34.1	34.2	0.00
Quintile 2	6,791	20.8	3,875	21.0	2,916	20.5	0.01	21.0	21.0	0.00
Quintile 3	5,333	16.3	3,063	16.6	2,270	16.0	0.02	16.6	16.6	0.00
Quintile 4	4,767	14.6	2,754	14.9	2,013	14.2	0.02	14.9	14.9	0.00
Quintile 5 – most dependent	4,231	12.9	2,399	13.0	1,832	12.9	0.00	13.4	13.3	0.00
Missing	502	1.5	238	1.3	264	1.9	0.05			
Ethnic concentration quintile										
Quintile 1 – least concentration	4,282	13.1	2,484	13.4	1,798	12.7	0.02	13.9	13.9	0.00
Quintile 2	5,091	15.6	3,057	16.5	2,034	14.3	0.06	16.0	15.9	0.00
Quintile 3	6,011	18.4	3,735	20.2	2,276	16.0	0.11	18.6	18.5	0.00
Quintile 4	7,302	22.3	4,396	23.8	2,906	20.5	0.08	22.5	22.7	0.00
Quintile 5 – most concentration	9,501	29.1	4,581	24.8	4,920	34.7	0.22	29.1	29.0	0.00
Missing	502	1.5	238	1.3	264	1.9	0.05			
Birth location										
Home	510	1.6	312	1.7	198	1.4	0.02	1.7	1.4	0.02

Hospital	32,001	97.9	18,056	97.6	13,945	98.2	0.04	97.7	98.2	0.03
Birth centre, midwifery clinic, other Ontario location	178	0.5	123	0.7	55	0.4	0.04	0.6	0.4	0.03
Health care provider										
Midwives	3,449	10.6	2,116	11.4	1,333	9.4	0.07	11.5	9.4	0.07
CNS/NP, Registered nurse	179	0.5	98	0.5	81	0.6	0.01	0.6	0.5	0.01
Family physician	1,792	5.5	1,051	5.7	741	5.2	0.02	6.0	5.2	0.04
Obstetrician	24,063	73.6	13,288	71.9	10,775	75.9	0.09	72.7	75.9	0.07
Other Healthcare Provider, Resident, Surgeon	2,900	8.9	1,724	9.3	1,176	8.3	0.04	9.0	8.8	0.01
Unattended	58	0.2	31	0.2	27	0.2	0.01	0.2	0.2	0.00
Missing	248	0.8	183	1.0	65	0.5	0.06			

Abbreviations: PHU, Public Health Unit; CNS/NP, Clinical Nurse Specialist/Nurse Practitioner.

[a] Column percentages and weights for the weighted study population were based on imputation dataset 1.

[b] Absolute standardized difference comparing those who received a third dose of COVID-19 vaccine during pregnancy and those who did not; standardized difference >0.10 indicates an imbalance in the distribution of the baseline characteristic between these two exposure groups.

[c] Column percentages.

[d] Self-reported cannabis, opioid or alcohol use during pregnancy.

Supplementary Table 4. Third dose coverage of COVID-19 vaccine during pregnancy by baseline characteristics of the study population

	All		Received third COVID-19 vaccine dose during pregnancy		Unadjusted risk ratio (95% CI)
	n	% [a]	n	% [b]	
Overall	32,689		18,491		---
Maternal age at delivery (years)					
<25	1,441	4.4	453	31.4	0.53 (0.49 to 0.57)
25-29	6,932	21.2	3,130	45.2	0.76 (0.74 to 0.79)
30-34	14,107	43.2	8,351	59.2	1.00
35-39	8,333	25.5	5,414	65.0	1.10 (1.07 to 1.12)
≥40	1,876	5.7	1,143	60.9	1.03 (0.99 to 1.07)
Last menstrual period date					
Before August 2021	7,087	21.7	4,757	67.1	1.38 (1.35 to 1.41)
August – September 2021	12,970	39.7	7,582	58.5	1.20 (1.17 to 1.23)
October – November 2021	12,632	38.6	6,152	48.7	1.00
Parity					
0 (nulliparous)	15,519	47.5	9,047	58.3	1.00
≥1 (multiparous)	17,170	52.5	9,444	55.0	0.94 (0.93 to 0.96)
Multiple birth					
No	31,565	96.6	17,876	56.6	1.00
Yes	1,124	3.4	615	54.7	0.97 (0.92 to 1.02)
Pre-existing medical condition [c]					
No	28,615	87.5	16,041	56.1	1.00
Yes	4,074	12.5	2,450	60.1	1.07 (1.04 to 1.10)
Asthma					
No	31,375	96.0	17,674	56.3	1.00
Yes	1,314	4.0	817	62.2	1.10 (1.06 to 1.15)
Chronic hypertension					

No	32,346	99.0	18,279	56.5	1.00
Yes	343	1.0	212	61.8	1.09 (1.01 to 1.19)
Diabetes					
No	32,274	98.7	18,242	56.5	1.00
Yes	415	1.3	249	60.0	1.06 (0.98 to 1.15)
Heart disease					
No	32,644	99.9	18,465	56.6	1.00
Yes	45	0.1	26	57.8	1.02 (0.80 to 1.31)
Thyroid disease					
No	30,466	93.2	17,178	56.4	1.00
Yes	2,223	6.8	1,313	59.1	1.05 (1.01 to 1.09)
Smoked during pregnancy					
No	31,674	96.9	18,133	57.2	1.00
Yes	1,015	3.1	358	35.3	0.62 (0.57 to 0.67)
Substance use during pregnancy [d]					
No	31,768	97.2	18,113	57.0	1.00
Yes	921	2.8	378	41.0	0.72 (0.67 to 0.78)
Maternal BMI (kg/m2)					
<30.0	25,845	79.1	14,713	56.9	1.00
≥30.0	6,844	20.9	3,778	55.2	0.97 (0.95 to 0.99)
First prenatal care visit in the first trimester					
Yes	31,267	95.6	17,791	56.9	1.00
No	1,422	4.4	700	49.2	0.86 (0.81 to 0.91)
Birth location					
Home	510	1.6	312	61.2	1.08 (1.01 to 1.16)
Hospital	32,001	97.9	18,056	56.4	1.00
Birth centre, midwifery clinic, other Ontario location	178	0.5	123	69.1	1.22 (1.11 to 1.35)

Health care provider					
Midwives	3,478	10.6	2,142	61.6	1.11 (1.08 to 1.14)
CNS/NP, Registered nurse	179	0.5	98	54.7	1.00 (0.88 to 1.14)
Family physician	1,821	5.6	1,071	58.8	1.07 (1.02 to 1.11)
Obstetrician	24,242	74.2	13,418	55.4	1.00
Other Healthcare Provider, Resident, Surgeon	2,911	8.9	1,731	59.5	1.07 (1.04 to 1.11)
Unattended	58	0.2	31	53.4	0.97 (0.76 to 1.23)
Neighbourhood median family income quintiles					
Quintile 1 – lowest	5,808	17.8	2,792	48.1	0.74 (0.72 to 0.76)
Quintile 2	6,373	19.5	3,404	53.4	0.82 (0.80 to 0.85)
Quintile 3	7,238	22.1	4,067	56.2	0.86 (0.84 to 0.89)
Quintile 4	7,287	22.3	4,338	59.5	0.92 (0.89 to 0.94)
Quintile 5 – highest	5,983	18.3	3,890	65.0	1.00
Rural residence					
No	28,672	87.7	16,228	56.6	1.00
Yes	4,017	12.3	2,263	56.3	1.00 (0.97 to 1.02)
PHU region of residence					
South West	3,522	10.8	1,911	54.3	0.85 (0.83 to 0.89)
Central West	6,249	19.1	3,579	57.3	0.90 (0.88 to 0.93)
Central East	9,751	29.8	4,841	49.6	0.78 (0.76 to 0.80)
Greater Toronto Region	6,942	21.2	4,406	63.5	1.00
Eastern	4,507	13.8	2,866	63.6	1.00 (0.97 to 1.03)
North West	671	2.1	349	52.0	0.82 (0.76 to 0.88)
North East	1,047	3.2	539	51.5	0.81 (0.76 to 0.86)
Residential instability quintile					

Quintile 1 – least unstable	6,681	20.4	3,572	53.5	1.00
Quintile 2	6,188	18.9	3,550	57.4	1.07 (1.04 to 1.11)
Quintile 3	6,064	18.6	3,459	57.0	1.07 (1.03 to 1.10)
Quintile 4	5,859	17.9	3,383	57.7	1.08 (1.05 to 1.11)
Quintile 5 – most unstable	7,897	24.2	4,527	57.3	1.07 (1.04 to 1.10)
Material deprivation quintile					
Quintile 1 – least deprived	8,442	25.8	5,441	64.5	1.00
Quintile 2	7,086	21.7	4,296	60.6	0.94 (0.92 to 0.96)
Quintile 3	6,226	19.0	3,416	54.9	0.85 (0.83 to 0.88)
Quintile 4	5,633	17.2	2,901	51.5	0.80 (0.78 to 0.82)
Quintile 5 – most deprived	5,302	16.2	2,437	46.0	0.71 (0.69 to 0.74)
Dependency quintile					
Quintile 1 – least dependent	11,159	34.1	6,204	55.6	1.00
Quintile 2	6,876	21.0	3,919	57.0	1.03 (1.00 to 1.05)
Quintile 3	5,420	16.6	3,095	57.1	1.03 (1.00 to 1.06)
Quintile 4	4,869	14.9	2,808	57.7	1.04 (1.01 to 1.07)
Quintile 5 – most dependent	4,365	13.4	2,465	56.5	1.02 (0.98 to 1.05)
Ethnic concentration quintile					
Quintile 1 – least concentration	4,489	13.7	2,585	57.6	1.00
Quintile 2	5,180	15.8	3,107	60.0	1.04 (1.01 to 1.08)
Quintile 3	6,096	18.6	3,772	61.9	1.07 (1.04 to 1.11)
Quintile 4	7,362	22.5	4,421	60.1	1.04 (1.01 to 1.08)
Quintile 5 – most concentration	9,562	29.3	4,606	48.2	0.84 (0.81 to 0.86)
Time in days between second dose and LMP					

<56 days (<8 weeks)	12,924	39.5	6,544	50.6	1.00
56-<84 days (8-<12 weeks)	6,319	19.3	3,555	56.3	1.11 (1.08 to 1.14)
84-<112 days (12-<16 weeks)	5,816	17.8	3,350	57.6	1.14 (1.11 to 1.17)
112-<140 days (16-<20 weeks)	4,485	13.7	2,770	61.8	1.22 (1.19 to 1.26)
140-<168 days (20-<24 weeks)	1,767	5.4	1,215	68.8	1.36 (1.31 to 1.41)
≥168 days (≥24 weeks)	1,378	4.2	1,057	76.7	1.51 (1.46 to 1.57)

Abbreviations: CI, confidence interval; BMI, body mass index; PHU, Public Health Unit; CNS/NP, Clinical Nurse Specialist/Nurse Practitioner; LMP: last menstrual period date

[a] Column percentages. Percentages were based on imputation dataset 1.

[b] Row percentages. Percentages were based on imputation dataset 1.

[c] Composite of: asthma, chronic hypertension, diabetes, heart disease, thyroid disease. Sum of individual conditions does not equal the total number of individuals with any individual condition, as categories were not mutually exclusive.

[d] Self-reported cannabis, opioid or alcohol use during pregnancy.

Supplementary Table 5. Trimester-specific estimates for the third mRNA COVID-19 dose received during pregnancy

Outcome	Adjusted hazard ratio (95% CI) [a]
Pregnancy outcomes	
Hypertensive disorder during pregnancy [b]	
Dose 3 received in 1st trimester	1.07 (0.94 to 1.21)
Dose 3 received in 2nd trimester	1.06 (0.94 to 1.19)
Dose 3 received in 3rd trimester	NA
Placental abruption	
Dose 3 received in 1st trimester	0.66 (0.50 to 0.88)
Dose 3 received in 2nd trimester	0.93 (0.75 to 1.15)
Dose 3 received in 3rd trimester	1.11 (0.71 to 1.73)
Cesarean delivery	
Dose 3 received in 1st trimester	0.87 (0.82 to 0.92)
Dose 3 received in 2nd trimester	0.91 (0.87 to 0.96)
Dose 3 received in 3rd trimester	1.03 (0.93 to 1.13)
Emergency cesarean delivery	
Dose 3 received in 1st trimester	0.82 (0.75 to 0.90)
Dose 3 received in 2nd trimester	0.94 (0.87 to 1.01)
Dose 3 received in 3rd trimester	1.11 (0.96 to 1.28)
Chorioamnionitis	
Dose 3 received in 1st trimester	0.42 (0.25 to 0.70)
Dose 3 received in 2nd trimester	0.75 (0.54 to 1.05)
Dose 3 received in 3rd trimester	1.16 (0.60 to 2.21)
Postpartum hemorrhage	
Dose 3 received in 1st trimester	0.87 (0.72 to 1.05)
Dose 3 received in 2nd trimester	1.06 (0.92 to 1.23)
Dose 3 received in 3rd trimester	1.15 (0.87 to 1.53)
Fetal and neonatal outcomes	
Stillbirth [c]	
Dose 3 received in 1st trimester	0.73 (0.45 to 1.19)
Dose 3 received in 2nd trimester	0.61 (0.39 to 0.94)
Dose 3 received in 3rd trimester	0.26 (0.04 to 1.95)
Preterm birth <37 weeks [c]	
Dose 3 received in 1st trimester	0.92 (0.81 to 1.04)
Dose 3 received in 2nd trimester	0.94 (0.86 to 1.04)
Dose 3 received in 3rd trimester	0.89 (0.71 to 1.11)
NICU transfer [d]	
Dose 3 received in 1st trimester	0.90 (0.82 to 0.99)

Dose 3 received in 2nd trimester	0.98 (0.91 to 1.05)
Dose 3 received in 3rd trimester	1.01 (0.86 to 1.19)
5-minute Apgar score <7 [d]	
Dose 3 received in 1st trimester	0.89 (0.71 to 1.13)
Dose 3 received in 2nd trimester	0.99 (0.83 to 1.19)
Dose 3 received in 3rd trimester	0.95 (0.62 to 1.45)
Small-for-gestational-age (SGA) infant [e]	
Dose 3 received in 1st trimester	0.86 (0.76 to 0.97)
Dose 3 received in 2nd trimester	0.86 (0.79 to 0.95)
Dose 3 received in 3rd trimester	0.94 (0.78 to 1.14)

Abbreviations: CI, confidence interval

[a] Multivariable models were performed on ten multiple imputation datasets and adjusted for week of last menstrual period, maternal age, nulliparity, multifetal pregnancy, pre-existing maternal medical condition (composite of: asthma, chronic hypertension, diabetes, heart disease, thyroid disease), first prenatal care visit in the first trimester, smoking during pregnancy, self-reported substance use during pregnancy, maternal body mass index ≥30 kg/m2, neighbourhood median family income fifths, rural residence, public health region of residence, and four marginalization indices (residential instability, material deprivation, dependency, ethnic concentration).

[b] To ensure the correct temporal order of the exposure-outcome relationship, the model included only individuals who received a third COVID-19 vaccine dose before 20 weeks of gestation as gestational hypertensive disorders are diagnosed after 20 weeks of gestation. Individuals vaccinated on or after 20 weeks of gestation were excluded from the analysis.

[c] All live births and stillbirths.

[d] Live births.

[e] Singleton live births.

Supplementary Table 6. Product-specific estimates for the third mRNA COVID-19 dose received during pregnancy

Outcome	Adjusted hazard ratio (95% CI) [a]
Pregnancy outcomes	
Hypertensive disorder during pregnancy [b]	
Pfizer	1.14 (1.02 to 1.28)
Moderna (including bivalent)	0.95 (0.83 to 1.08)
Placental abruption	
Pfizer	0.88 (0.71 to 1.08)
Moderna (including bivalent)	0.80 (0.63 to 1.01)
Cesarean delivery	
Pfizer	0.92 (0.88 to 0.96)
Moderna (including bivalent)	0.88 (0.84 to 0.93)
Emergency cesarean delivery	
Pfizer	0.93 (0.87 to 1.00)
Moderna (including bivalent)	0.87 (0.80 to 0.95)
Chorioamnionitis	
Pfizer	0.62 (0.44 to 0.86)
Moderna (including bivalent)	0.71 (0.49 to 1.05)
Postpartum hemorrhage	
Pfizer	1.08 (0.94 to 1.24)
Moderna (including bivalent)	0.89 (0.75 to 1.05)
Fetal and neonatal outcomes	
Stillbirth [c]	
Pfizer	0.62 (0.41 to 0.94)
Moderna (including bivalent)	0.66 (0.41 to 1.06)
Preterm birth <37 weeks [c]	
Pfizer	1.00 (0.91 to 1.09)
Moderna (including bivalent)	0.84 (0.75 to 0.93)
NICU transfer [d]	
Pfizer	0.96 (0.89 to 1.04)
Moderna (including bivalent)	0.94 (0.86 to 1.02)
5-minute Apgar score <7 [d]	
Pfizer	0.94 (0.79 to 1.13)
Moderna (including bivalent)	0.97 (0.79 to 1.19)
Small-for-gestational-age (SGA) infant [e]	
Pfizer	0.87 (0.80 to 0.95)
Moderna (including bivalent)	0.86 (0.78 to 0.96)

Abbreviations: CI, confidence interval

[a] Multivariable models were performed on ten multiple imputation datasets and adjusted for week of last menstrual period, maternal age, nulliparity, multifetal pregnancy, pre-existing maternal medical condition (composite of: asthma, chronic hypertension, diabetes, heart disease, thyroid disease), first prenatal care visit in the first trimester, smoking during pregnancy, self-reported substance use during pregnancy, maternal body mass index ≥30 kg/m2, neighbourhood median family income fifths, rural residence, public health region of residence, and four marginalization indices (residential instability, material deprivation, dependency, ethnic concentration).
[b] To ensure the correct temporal order of the exposure-outcome relationship, the model included only individuals who received a third COVID-19 vaccine dose before 20 weeks of gestation as gestational hypertensive disorders are diagnosed after 20 weeks of gestation. Individuals vaccinated on or after 20 weeks of gestation were excluded from the analysis.
[c] All live births and stillbirths.
[d] Live births.
[e] Singleton live births.

Supplementary Table 7. Association between third COVID-19 vaccine dose received during pregnancy and adverse pregnancy, fetal, and neonatal outcomes following exclusion of individuals who had confirmed COVID-19 illness before or during pregnancy.

Outcome	Adjusted hazard ratio (95% CI) [a]
Pregnancy outcomes	
Hypertensive disorder during pregnancy [b]	1.02 (0.92 to 1.14)
Placental abruption	0.88 (0.72 to 1.08)
Cesarean delivery	0.91 (0.87 to 0.95)
Emergency cesarean delivery	0.93 (0.87 to 1.00)
Chorioamnionitis	0.76 (0.55 to 1.06)
Postpartum hemorrhage	1.02 (0.89 to 1.18)
Fetal and neonatal outcomes	
Stillbirth [c]	0.51 (0.34 to 0.76)
Preterm birth <37 weeks [c]	0.91 (0.84 to 1.00)
NICU transfer [d]	0.97 (0.90 to 1.04)
5-minute Apgar score <7 [d]	0.95 (0.80 to 1.14)
Small-for-gestational-age (SGA) infant [e]	0.87 (0.80 to 0.95)

Abbreviations: CI, confidence interval

[a] Models were performed on ten multiple imputation datasets and adjusted using stabilised inverse probability of treatment weights derived from a propensity score model including the variables listed in Supplementary table 2.

[b] To ensure the correct temporal order of the exposure-outcome relationship, the model included only individuals who received a third COVID-19 vaccine dose before 20 weeks of gestation as gestational hypertensive disorders are diagnosed after 20 weeks of gestation. Individuals vaccinated on or after 20 weeks of gestation were excluded from the analysis.

[c] All live births and stillbirths.

[d] Live births.

[e] Singleton live births.

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