Supplemental appendix

Supplement to: Jorgensen SCJ, Hernandez A, Fell DB, *et al.* Maternal mRNA covid-19 vaccination during pregnancy and delta or omicron infection or hospital admission in infants: test negative design study.

Contents

Table S1: Linked databases

Database	Description
Linked Delivering Mother and Newborns (MOMBABY)	Deterministically linked maternal-newborn hospital delivery records and information on maternal and newborn characteristics (e.g., gestational age, birthweight), diagnoses for pre-existing health conditions (mothers) and complications that arise around the time of the delivery (mothers and newborns)
Registered Persons Database (RPDB)	Date of birth, sex, postal code, and death date (if applicable) for Ontario residents
Canadian Institute for Health Information Discharge Abstract Database (CIHI-DAD)	Information related to acute care hospitalizations in Ontario (e.g., sociodemographic, diagnoses, procedures, treatments, transfers, deaths)
Ontario Health Insurance Plan (OHIP)	Diagnostic and procedure information from inpatient and outpatient claims submitted by Ontario physicians for Ontario residents
Ontario Drug Benefit (ODB)	Claims for prescription drugs and vaccines (influenza) received under the ODB program
National Ambulatory Care Reporting System (NACRS)	Information related to emergency department visits in Ontario
Same Day Surgery Database (SDS)	Information related to day surgeries in Ontario
Ontario Asthma Dataset (ASTHMA)	Information related to asthma diagnoses
Ontario Hypertension Dataset (HYPER)	Information related to hypertension diagnoses
Ontario Diabetes Dataset (ODD)	Information related to diabetes diagnoses
Canadian Organ Replacement Registry (CORR)	Canadian information system with information on patients who received dialysis or transplantation
Ontario Cancer Registry (OCR)	Information on Ontario residents with newly diagnosed cancer or who have died of cancer
Ontario HIV database (HIV)	Information on Ontario residents with HIV infection
Ontario Rheumatoid Arthritis Database (ORAD)	Information on Ontario residents with rheumatoid arthritis
Ontario Crohn's and Colitis Cohort Dataset (OCCC)	Information on Ontario residents with Crohn's disease or colitis
Public Health Case and Contact Management (CCM) solution	Central data repository for COVID-19 reporting and case and contact management in Ontario
COVID-19 Integrated Testing Data (C19INTGR)	Comprehensive dataset of all COVID-19 laboratory diagnostic testing results in Ontario
Ontario COVID-19 Vaccine Data (COVaxON)	A centralized COVID-19 vaccine information system which contains comprehensive documentation (e.g., administration date, brand, dose) of all COVID-19 vaccination events in Ontario
Ontario Census Area Profiles (CENSUS)	Data from the 2016 Canadian Census
Postal Code Conversion File (PCCF)	Links six-character postal codes to standard geographic areas such as dissemination area and census tracts

Table S2: Number of Delta and Omicron cases by laboratory testing categorization, May 2021 to September 2022, Ontario, Canada[a]

Classification criteria	Delta May 31, 2021 to January 2, 2022 N = 99	Omicron November 22, 2021 to September 5, 2022 N = 1501
Delta confirmed via WGS[b] or SGTF[c]	58	-
Delta classified if date < December 3, 2021 and no or inconclusive WGS[b] and SGTF[c] results	41	-
Omicron confirmed via WGS[b] or SGTF[c]	-	290
Omicron classified if date ≥ December 21, 2021 and no or inconclusive WGS[b] and SGTF[c] results	-	1211

a. 55 SARS-CoV-2 positive specimens could not be classified as Delta or Omicron and were excluded from the study.
b. WGS: whole genome sequencing.
c. SGTF: s-gene target failure.

Table S3: Vaccine effectiveness of the primary mRNA COVID-19 vaccine series[a] during pregnancy against Omicron infection in infants younger than six months of age, by trimester of pregnancy of the second vaccine dose and infant age at the time of SARS-CoV-2 testing, November 22, 2021 to September 5, 2022, Ontario, Canada

|	Case infants	Control infants	Effectiveness of maternal vaccination[b]
	no. vaccinated mothers/total no. (%)		*% (95% confidence interval)*
Trimester of pregnancy of the second vaccine dose			
First	130/730 (17.8)	427/1814 (23.5)	47 (31 to 59)
Second	395/995 (39.7)	1280/2667 (48.0)	37 (24 to 47)
Third	265/865 (30.6)	1173/2560 (45.8)	53 (42 to 62)
Infant age when tested for SARS-CoV-2			
0-8 weeks	206/428 (48.1)	1360/2111 (64.4)	57 (44 to 66)
9-16 weeks	310/515 (60.2)	803/1105 (72.7)	47 (31 to 60)
>16 weeks	274/447 (61.3)	717/1051 (68.2)	40 (21 to 54)

a. Primary COVID-19 vaccine series defined as two doses up to 14 days before delivery with at least one dose after conception.
b. Vaccine effectiveness estimated as one minus the adjusted odds ratio of maternal vaccination in cases versus controls times 100%. Multivariable logistic regression adjusted for the following variables: calendar week of testing, infant age in weeks when tested (continuous), infant sex, mother's age at birth in years (continuous), parity, maternal SARS-CoV-2 infection preconception or during pregnancy, maternal influenza vaccination during the 2019/ 2020 or 2020/2021 influenza season, maternal pre-pregnancy comorbidities (diabetes mellitus, hypertension, heart disease, asthma, autoimmune disease), maternal immunosuppression, adequacy of prenatal care (Revised Graduated Prenatal Care Index), four census dissemination area-level variables (income quintile, proportion of the population who self-identify as a visible minority, proportion of the population employed in a high-risk non-health occupation, and average number of people in each dwelling), and public health unit region.

Table S4: Sensitivity analyses for effectiveness of the primary mRNA COVID-19 vaccine series[a] during pregnancy against Omicron infection in infants younger than six months of age, Ontario, Canada

	Case infants	Control infants	Effectiveness of maternal vaccination[b]
	no. vaccinated mothers/total no. (%)		% (95% confidence interval)
Infants tested between Nov. 22, 2021 and Dec. 30, 2021	101/179 (56.4)	1294/1854 (69.8)	52 (29 to 67)
Infants tested between Dec. 31, 2021 and Sep. 05, 2022	689/1211 (56.9)	1586/2413 (65.7)	45 (35 to 53)
Infants of mothers with a positive SARS-CoV-2 PCR test before the infant's birth excluded[c]	754/1302 (57.9)	2486/3556 (69.9)	44 (35 to 52)
Infants of mothers with immunosuppression[d] excluded[c]	773/1362 (43.3)	2810/4169 (67.4)	45 (37 to 53)
Infants of mothers who received vaccine dose 1 preconception excluded[c]	666/1266 (52.6)	2426/3813 (63.6)	44 (35 to 52)
Infants tested in the first week of life excluded[c]	774/1352 (57.3)	2394/3447 (69.5)	47 (38 to 54)

a. Primary COVID-19 vaccination series defined as two doses up to 14 days before delivery with at least one dose after conception.
b. Vaccine effectiveness estimated as one minus the adjusted odds ratio of maternal vaccination in cases versus controls times 100%. Multivariable logistic regression adjusted for the following variables: calendar week of testing, infant age in weeks when tested (continuous), infant sex, mother's age at birth in years (continuous), parity, maternal SARS-CoV-2 infection preconception or during pregnancy, maternal influenza vaccination during the 2019/ 2020 or 2020/2021 influenza season, maternal pre-pregnancy comorbidities (diabetes mellitus, hypertension, heart disease, asthma, autoimmune disease), maternal immunosuppression, adequacy of prenatal care (Revised Graduated Prenatal Care Index), four census dissemination area-level variables (income quintile, proportion of the population who self-identify as a visible minority, proportion of the population employed in a high-risk non-health occupation, and average number of people in each dwelling to account for transmission risk), and public health unit region.
c. Infants tested between November 22, 2021 and September 5, 2022.
d. Immunosuppression defined as solid organ or stem cell transplant, active cancer, sickle cell anaemia, HIV infection, immunosuppressing therapies, and other immune system disorders.

Figure S1: Percentage of COVID-19 cases by the most prevalent lineages and week, representative surveillance, Ontario, October 3, 2021 to October 1, 2022[1]
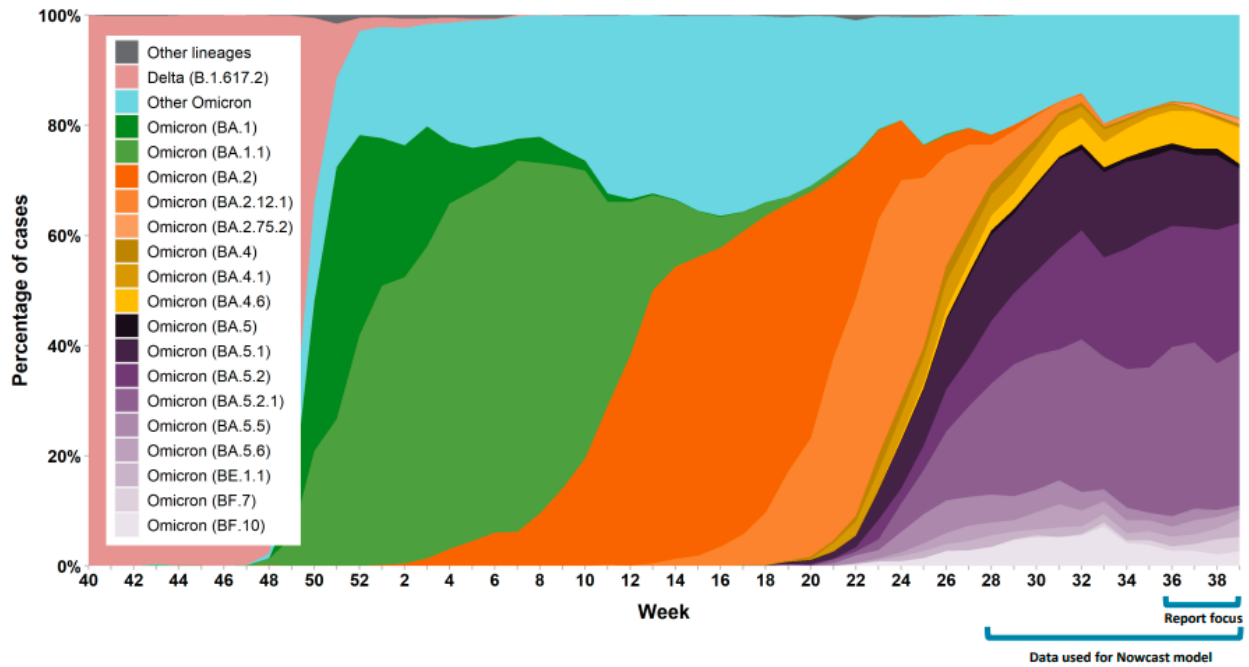

Note: Results may not be representative of Ontario overall, particularly in earlier weeks. Details on the proportion of eligible samples sequenced by the OCGN can be found in the technical notes. Week was assigned based on earliest date available for a sample. If more than one sample was sequenced for a case, the most recent sample was included. Results for recent weeks are incomplete as not all sequencing and bioinformatics analyses were complete at the time of data extraction and will be included in subsequent reports.

Data sources: PHO, Hospital for Sick Children, Kingston Health Sciences Centre, Shared Hospital Laboratory, Hamilton Regional Laboratory Medicine Program
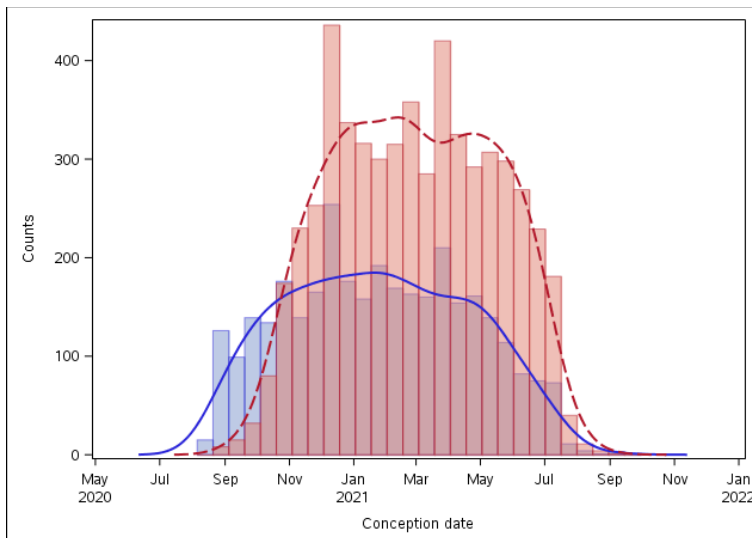
Figure S2: Distribution of conception dates among 8809 infants in Ontario, Canada

   A. Infant cases (red) versus controls (blue)
   B. Vaccinated (red) versus unvaccinated (blue) mothers

Figure S2-A
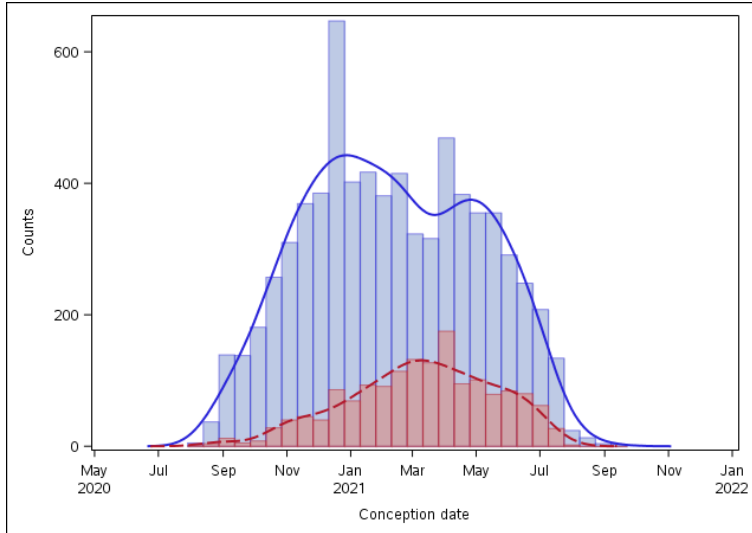
Figure S2-B

Reference

1. Ontario Agency for Health Protection and Promotion (Public Health Ontario). *SARS-CoV-2 Whole Genome Sequencing in Ontario, October 21, 2022*. Queen's Printer for Ontario; 2022. https://www.publichealthontario.ca/-/media/documents/ncov/epi/covid-19-sars-cov2-whole-genome-sequencing-epi-summary.pdf?sc_lang=en Accessed December 21, 2022.