

Appendix 1 (as supplied by the authors): Supplemental material

Supplemental Table S1. Description and purpose of each data source utilized in the study

Database	Description	Information collected
MOMBABY Database	Contains inpatient admission records of delivering mothers and their respective newborns (including stillbirths), which are linked by a unique matching identifier on each hospitalization record. This administrative dataset, maintained and annually updated at ICES, links approximately 98% of maternal-infant records for in-hospital deliveries in Ontario.	This database was used to assemble the cohort of live births, as well as collect maternal and newborn information such as gestational age at birth, maternal age, birth weight, baby's sex, parity and plurality.
Registered Persons Database (RPDB)	Demographic repository containing information on all Ontario residents eligible for publicly funded health care in the province.	Was used to establish the duration for which each participant was eligible to receive health care services, as well as obtain demographic information regarding neighbourhood income quintiles and region of residence.
Canadian Institute for Health Information Discharge Abstract Database (CIHI-DAD)	Captures demographic and clinical information regarding hospital admissions from all acute care institutions throughout Canada.	<p>We used this database to obtain information from both the mothers and newborns regarding medical diagnoses (e.g., gestational diabetes), interventions (e.g., neonatal ventilatory support), number of previous preterm deliveries, as well as admissions and discharges to any special care units (e.g., neonatal intensive care unit).</p> <p>We also used ICD-10-CA codes O36.4, Z37.1, Z37.3, Z37.4, Z37.6, and Z37.7 to identify maternal hospital admissions for stillbirth.</p>
Ontario Health Insurance Plan (OHIP) Database	Contains health care billing information made by physicians, or other health care providers,	Specific OHIP fee codes are used when a vaccine is administered, which provided

	for service reimbursement. This database includes information on the diagnosis (i.e., reason for the visit), type of service received, and the associated billing code.	the information to identify our exposure group. In addition, we identified prenatal care visits (via OHIP fee codes) and health care provider specialties (via SPEC variable) through from this database.
Ontario Marginalization Index (ON-Marg)	Data tool that quantifies the level of marginalization occurring in Ontario. This multifaceted index uses data from Statistics Canada's Census and consists of four dimensions that indicate marginalization: residential instability, material deprivation, dependency and ethnic concentration. Scores corresponding to each of these four dimensions were previously divided into quintiles, where quintile 1 represents areas that are the least marginalized and quintile 5 represents the most marginalized areas.	Provided information regarding the four indices of marginalization.
Permanent Resident Database (PRD) from Immigration, Refugee and Citizenship Canada (IRCC)	Contains records of permanent residents that immigrated to Canada.	Used to obtain information regarding maternal country of birth.

Supplemental Table S2. Definitions and diagnostic/procedural codes used to define study variables

Study Variable	Patient record	Definition	Data source, ICD10 diagnostic code, OHIP fee code, and/or CCI procedure code
Study outcomes			
Gestational hypertension	Mother	Hypertension in pregnant women (blood pressure >140/90mmHg) after 20 weeks of gestation without presence of proteinuria or preeclampsia.	O13, O16
Chorioamnionitis	Mother	Acute inflammation of the chorion and membranes of the placenta due to bacterial infection.	O41.12, O41.13, O41.19
Postpartum hemorrhage	Mother	Blood loss of ≥ 500 mL following vaginal delivery or ≥ 1000 mL following Caesarean section, or diagnosis as noted by a health care provider.	O720-O723
Severe postpartum hemorrhage	Mother	Postpartum hemorrhage in conjunction with one of the following procedures to control bleeding: blood transfusion, hysterectomy, and other procedures to control bleeding.	-
-Hysterectomy			5MD60KE; 5MD60RC; 5MD60CB; 5MD60RD; 1RM87LAGX; (1RM89LA without 1PL74;1RS80; 1RS74)
-Other procedures to control bleeding			5PC91LA, 1RM13, 1KT51;5PC91HT
-Blood transfusion			Measured using DAD variable "BTANY".
Small-for-gestational-age birth	Fetal/infant	Birth weight <10th percentile for gestational age and sex.	Measured using infant sex, gestational age, and birth weight variables in MOMBABY.
NICU Admission >24 hours	Fetal/infant	Intensive care unit admission lasting >24 hours	Measured using DAD variables (special care unit admission and discharge dates) from infant records.

Neonatal morbidity composite outcome	Fetal/infant	The Neonatal Adverse Outcome Indicator is a validated composite outcome that will be utilized to identify neonatal morbidity. It combined ICD-based codes relating to treatments of severe events.	Refer to eTable 3 for a complete list of the diagnostic and procedural codes included.
Preterm birth	Fetal/infant	Live birth prior to 37 weeks of gestation.	Measured using gestational age variable in MOMBABY.
Very preterm birth	Fetal/infant	Live birth prior to 32 weeks of gestation.	Measured using gestational age variable in MOMBABY.
Stillbirth	Fetal/infant	Fetal death occurring at or after 20 weeks of gestation.	O36.4; Z37.1; Z37.3; Z37.4; Z37.6; Z37.7
Study exposures			
Tdap vaccine	Mother	Adult tetanus, diphtheria and acellular pertussis (Tdap) vaccine.	OHIP fee codes: G847
Tdap <i>possible</i> vaccine (sensitivity analysis #1)	Mother	General immunization with or without physician consultation.	OHIP fee codes: G538; G539 *OHIP codes billed between October 1 to January 31 were excluded as these were assumed to be influenza vaccinations
Baseline variables included in propensity score model			
Parity	Mother	Total number of previous pregnancies (live births and stillbirths) that reached a viable gestational age.	Measured using MOMBABY variable.
Multiple birth	Mother	Total number of fetuses in the current pregnancy.	Z372, Z373, Z374, Z375, Z376, Z377, Z3790, O31, and O30
Maternal age	Mother	Age of the mother at the time of giving birth.	Measured using MOMBABY variable.
Baby's sex	Fetal/infant	Infant's sex.	Measured using MOMBABY variable.

Pre-existing chronic hypertension	Mother	Identified through ICD-10 codes in the DAD on the mother's delivery abstract.	I10, I15, O10.0
Pre-existing asthma	Mother	Identified through ICD-10 codes in the DAD on the mother's delivery abstract.	J45-46
Pre-existing diabetes	Mother	Identified through ICD-10 codes in the DAD on the mother's delivery abstract.	O24.0, O24.1 O24.3, O24.5, O24.6, O24.7, E10, E11, E13, E14
Pre-existing heart disease	Mother	Identified through ICD-10 codes in the DAD on the mother's delivery abstract.	O10.1, I05-I09, I34-I39, I150.0, I20, I25, Q20-26, O99.4
Fiscal year of conception	Mother and infant	Refers to the fiscal year that the infant was conceived.	Estimated by subtracting gestational age from date of birth.
Maternal world region of birth	Mother	Refers to the region of the world the mother was born in (North America, Asia, Europe, Africa, Caribbean, Yugoslavia/USSR, South America, Central America, Oceania).	Measured using country of birth variable within CIC database.
Residential instability	Mother	Refers to area-level concentrations of people who experience high rates of family or housing instability.	Measured using "residential instability factor score" variable within the ON-Marg database.
Material deprivation	Mother	Refers to inability for individuals and communities to access and attain basic material needs. This dimension is closely connected to poverty.	Measured using "material deprivation factor score" variable within the ON-Marg database.
Dependency	Mother	Refers to area-level concentrations of people who don't have income from employment.	Measured using "dependency factor score" variable within the ON-Marg database.
Ethnic concentration	Mother	Refers to high area-level concentrations of recent	Measured using "ethnic concentration factor score" variable within the ON-Marg database.

		immigrants and people belonging to a 'visible minority' group.	
Maternal obesity	Mother	Identified through ICD-10 codes in the DAD on the mother's delivery abstract.	E66
Tobacco/substance abuse	Mother	Identified through ICD-10 codes in the DAD on the mother's delivery abstract.	F10-F19; G312
Income quintile	Mother	Nearest Census Based Neighbourhood Income Quintile.	Measured using "INCQUINT" variable within RPDB.
Rural residence	Mother	Rurality determined using second digit of postal code from Canada Post Corporation.	Measured using rural flag variable from postal code conversion file (PCCF).
Local Health Integration Network (LHIN) Group	Mother	Local Health Integration Networks (LHINs) are not-for-profit corporations that are responsible for planning, integrating and funding local health services in 14 different geographic areas of the province. In collaboration with the Ontario Ministry of Health, ICES developed the geographic building blocks for LHINs by defining areas within which residents received most of their hospital care from local hospitals.	Using the LHIN database, the 14 LHIN corporations were grouped into 5 regions according to the Ontario's Ministry of Health website: http://www.health.gov.on.ca/en/news/connectedcare/2019/CC_20191113.aspx
Other variables included in propensity score model			
Revised Graduated Prenatal Care Index (R-GINDEX)	Mother	Categorizes adequacy of prenatal care into 6 groups: inadequate, intermediate, adequate, intensive, no care, and missing.	Derived from a combination of gestational age of the infant at birth (GEST), trimester when prenatal care began (TCPB), and total number of prenatal care visits (PCV). The index is based on work from Alexander and Kotelchuck. ¹ The codes associated with prenatal care visits are shown in eTable 4.

Outpatient visits within 6 months before the index pregnancy (sensitivity analysis #2)	Mother	Total number of outpatient visits in the 6 months prior to index pregnancy. This sub-cohort was drawn from women who were eligible for OHIP at least 6 months before their pregnancy.	Measured using CIHI-DAD and OHIP databases.
Non-obstetric hospital admissions within 2 years before the index pregnancy (sensitivity analysis #2)	Mother	Total number of non-obstetric hospital admissions in the 2 years prior to index pregnancy. This sub-cohort was drawn from women who were eligible for OHIP at least 2 years before their pregnancy.	Measured using the CIHI-DAD, excluding hospitalizations related to obstetrics (ICD10: Z37, O).

Supplemental Table S3. Components of the Neonatal Adverse Outcome Indicator (NAOI) composite outcome

Components of Variable	MOMBABY Variable	DAD Variable	Diagnostic Code (ICD-10)
Gestational age <32 weeks	B_GESTWKS_DEL (or M_GESTWKS_DEL)		
Birth weight <1500grams	B_WEIGHT		
Respiratory distress syndrome			P22.0
Seizures			P90, R56
Intraventricular hemorrhage (grades 2,3, or 4)			P52.1, P52.2
Cerebral infarction			I63
Periventricular leukomalacia			P91.2
Birth trauma (intracranial hemorrhage paralysis due to brachial plexus injury, skull or long bone fracture)			P10.0 to P10.3, P13.0, P13.2, P13.3, P14.0, P14.1
Hypoxic ischemic encephalopathy			P91.5, P91.81, P91.6
Necrotizing enterocolitis			P77
Bronchopulmonary dysplasia			P27.1
Sepsis/septicemia			P36, A40, A41.5, A41.9, B95.1, B96.2
Pneumonia			P23, J12 to J18

Primary atelectasis			P28.0
Respiratory failure			P28.5
	MOMBABY Variable	DAD Variable	Procedural code (CCI)
Resuscitation			1.GZ.30
Ventilatory support (mechanical ventilation and/or CPAP)			1.GZ.31
Central venous or arterial catheter			1.IS.53, 1.KV.53
Transfusion of blood or blood products		BTANY, BTOTHER	
Pneumothorax requiring an intercostal catheter			1.GT.33

Supplemental Table S4. OHIP fee codes associated with a prenatal visit

OHIP fee code	Description
A920	Medical management of early pregnancy, initial visit
A921	Medical management of early pregnancy, subsequent visit
A005	Consultation
A006	Re-consultation
A665	Prenatal consult
Q606	Prenatal care - gen. Assess - major prenatal visit
Q607	Prenatal care - min. Assess - subsequent prenatal visit
P002	High risk prenatal assessment
P003	Obs.-prenatal care-general assess - major prenatal visit
P004	Obs.-prenatal care-minor prenatal assess - subsequent prenatal visit
P005	Antenatal health screen

* Prenatal visits were defined by limiting to one record per person per type of doctor per day. Only visits with an associated OHIP fee code related to prenatal care were included in this definition.

Supplemental Table S5. Association between receipt of Tdap (main exposure + possible Tdap) vaccination during pregnancy and obstetrical and perinatal outcomes

Outcome	N (%)	N (%)	Crude Estimate (RR/HR [95% CI])	IPTW-Adjusted Estimate ^a (RR/HR [95% CI])
Cohort 1 (livebirth + stillbirth records)	Tdap Vaccinated (n=14,311)	Tdap Unvaccinated (n=600,902)	-	-
Chorioamnionitis ^b	179 (1.25)	6041 (1.01)	1.24 (1.07,1.44)	1.21 (1.04,1.41)
Gestational hypertension ^b	491 (3.43)	22984 (3.82)	0.90 (0.82,0.98)	0.89 (0.81,0.97)
Postpartum hemorrhage ^b	403 (2.82)	16837 (2.80)	1.01 (0.91,1.11)	1.01 (0.91,1.12)
Severe postpartum hemorrhage ^{b,c}	42 (0.29)	1991 (0.33)	0.89 (0.65,1.20)	0.88 (0.65,1.21)
Preterm birth, <37 weeks ^{d,e}	848 (6.36)	44751 (7.45)	0.99 (0.92,1.06)	0.98 (0.92,1.05)
Very preterm birth, <32 weeks ^{d,e}	91 (0.98)	7920 (1.32)	1.09 (0.88,1.34)	1.10 (0.89,1.36)
Stillbirth ^d	46 (0.32)	3239 (0.54)	0.97 (0.73,1.30)	1.14 (0.85,1.52)
Cohort 2 (livebirths records only)	Tdap Vaccinated (n=14,265)	Tdap Unvaccinated (n=597,663)	-	-
Small-for-gestational-age birth ^b	1339 (9.39)	56763 (9.50)	0.99 (0.94,1.04)	0.96 (0.90,1.02)
NICU admission >24 hours ^b	900 (6.31)	46084 (7.71)	0.82 (0.77,0.87)	0.82 (0.76,0.88)
Neonatal morbidity composite outcome ^b	821 (5.76)	41850 (7.00)	0.82 (0.77,0.88)	0.81 (0.75,0.87)

Abbreviations: CI, confidence interval; IPTW, inverse probability of treatment weights; RR, risk ratio; HR, hazard ratio; NICU, neonatal intensive care unit.

^a Stabilized inverse probability of treatment weights were used to adjust estimates.

^b Estimates represent risk ratios (RRs) that were computed using a log-binomial regression model.

^c Postpartum hemorrhage in conjunction with a procedure code for hysterectomy, blood transfusion, or other procedures to control bleeding.

^d Estimates represent hazard ratios (HR) that were computed using a Cox model, where Tdap vaccination was modelled as a time-varying exposure.

^e Women who received Tdap after 36 weeks' gestation or after 31 weeks' gestation were treated as unvaccinated in the analyses of preterm birth and very preterm birth, respectively.

Supplemental Table S6. Additional sensitivity analyses for association between Tdap vaccination during pregnancy and obstetrical and perinatal outcomes

	Original IPTW-Adjusted Results	Maternal Outpatient Visits (6 months before pregnancy)	Maternal Non-Obstetric Hospitalization (2 years before pregnancy)
	Adjusted estimate (RR/HR [95% CI]) ^a	Adjusted estimate (RR/HR [95% CI]) ^{a,b}	Adjusted estimate (RR/HR [95% CI]) ^{a,c}
Cohort 1 (livebirth + stillbirth records)	(n=615,213)	(n=603,289)	(n=573,348)
Chorioamnionitis ^d	1.17 (0.99,1.39)	1.17 (0.98,1.39)	1.18 (0.98,1.41)
Gestational hypertension ^d	0.87 (0.78,0.96)	0.87 (0.79,0.97)	0.88 (0.79,0.98)
Postpartum hemorrhage ^d	1.01 (0.91,1.13)	1.01 (0.90,1.13)	1.01 (0.90,1.14)
Severe postpartum hemorrhage ^{d,e}	0.79 (0.55,1.13)	0.76 (0.52,1.10)	0.76 (0.52,1.12)
Preterm birth, <37 weeks ^{f,g}	0.98 (0.91,1.06)	1.00 (0.92,1.08)	0.99 (0.91,1.07)
Very preterm birth, <32 weeks ^{f,g}	1.10 (0.86,1.41)	1.12 (0.87,1.44)	1.10 (0.84,1.42)
Stillbirth ^f	1.15 (0.82,1.60)	1.16 (0.84,1.62)	1.22 (0.87,1.69)
Cohort 2 (livebirths records only)	(n=611,928)	(n=600,061)	(n=570,267)
Small-for-gestational-age birth ^d	0.96 (0.90,1.02)	0.96 (0.91,1.02)	0.95 (0.89,1.01)
NICU admission >24 hours ^d	0.82 (0.76,0.88)	0.83 (0.77,0.89)	0.82 (0.76,0.89)
Neonatal morbidity composite outcome ^d	0.81 (0.75,0.87)	0.81 (0.75,0.88)	0.80 (0.74,0.87)

Abbreviations: CI, confidence interval; RR, risk ratio; HR, hazard ratio; IPTW, inverse probability of treatment weights; NICU, neonatal intensive care unit.

^a Adjusted using stabilized inverse probability of treatment weights.

^b Additionally adjusted for number of outpatient visits during the 6-month period prior to the index pregnancy. This sub-cohort was restricted to women with continuous Ontario insurance eligibility for the 6 months prior to pregnancy.

^c Additionally adjusted for number of non-obstetric hospitalization during the 2-year period prior to the index pregnancy. This sub-cohort was restricted to women with continuous Ontario insurance eligibility for the 2 years prior to pregnancy.

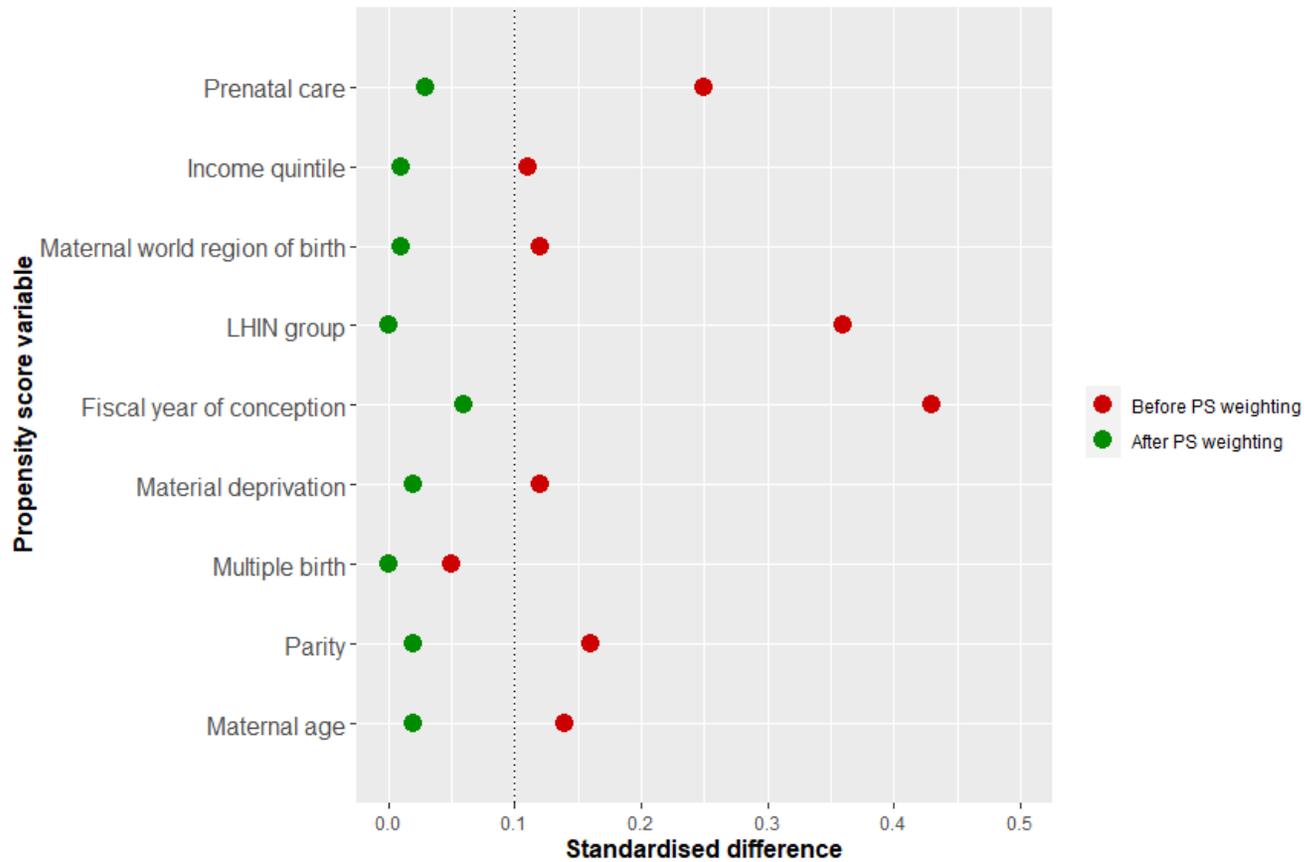
^d Estimates represent risk ratios (RRs) that were computed using a log-binomial regression model.

^e Postpartum hemorrhage in conjunction with a procedure code for hysterectomy, blood transfusion, or other procedures to control bleeding.

^f Estimates represent hazard ratios (HR) that were computed using a Cox model, where Tdap vaccination was modelled as a time-varying exposure.

^g Women who received Tdap after 36 weeks' gestation or after 31 weeks' gestation were treated as unvaccinated in the analyses of preterm birth and very preterm birth, respectively.

Supplemental Figure S1. Comparison of standardized difference scores before and after propensity score (PS) weighting*



* Data were weighted using stabilized inverse probability of treatment weights (IPTW) calculated based on propensity scores. Abbreviations: PS, propensity score; LHIN, local health integration network.

Coding algorithm for Revised Graduated Prenatal Care Utilization Index (R-GINDEX)

Key Variables:

GEST = Gestational Age (18-45 weeks based on LMP)

PCV = Number of Prenatal Care Visits (0 = None)

TPCB = Trimester Prenatal Care Began (0 = None, 1-3 trimesters) *

GINDEX = Graduated Prenatal Care Utilization Index

***NOTE:** Trimester 1 = (0-13 weeks or 1-91 days)
Trimester 2 = (14-27 weeks or 92-189 days)
Trimester 3 = (28+ weeks or 190+ days)

INTENSIVE PRENATAL CARE UTILIZATION;

IF (TPCB=1) &

((18<=GEST<=21) & (11=<PCV)) | ((22<=GEST<=25) & (13=<PCV))
| ((26<=GEST<=29) & (14=<PCV)) | ((30<=GEST<=31) & (15=<PCV))
| ((32<=GEST<=36) & (16=<PCV)) | ((37<=GEST<=40) & (17=<PCV))
| ((41<=GEST<=42) & (18=<PCV)) | ((43<=GEST<=45) & (19=<PCV))

THEN GINDEX = 'INTENSIVE (1st Trimester)';

IF (TPCB=2) &

((18<=GEST<=21) & (10=<PCV)) | ((22<=GEST<=25) & (11=<PCV))
| ((26<=GEST<=31) & (12=<PCV)) | ((32<=GEST<=35) & (13=<PCV))
| ((36<=GEST<=37) & (14=<PCV)) | ((38<=GEST<=40) & (15=<PCV))
| ((41<=GEST<=42) & (16=<PCV)) | ((43<=GEST<=45) & (17=<PCV))

THEN GINDEX = 'INTENSIVE (2nd Trimester)';

IF (TPCB=3) &

((GEST=25) & (9=<PCV)) | ((26<=GEST<=31) & (10=<PCV))
| ((32<=GEST<=35) & (11=<PCV)) | ((36<=GEST<=37) & (12=<PCV))
| ((38<=GEST<=40) & (13=<PCV)) | ((41<=GEST<=42) & (14=<PCV))
| ((43<=GEST<=45) & (15=<PCV))

THEN GINDEX = 'INTENSIVE (3rd Trimester)';

ADEQUATE PRENATAL CARE UTILIZATION CRITERIA:

IF (TPCB=1) &

((18<=GEST<=21) & (3=<PCV<=10)) | ((22<=GEST<=25) & (4=<PCV<=12))
| ((26<=GEST<=29) & (5=<PCV<=13)) | ((30<=GEST<=31) & (6=<PCV<=14))
| ((32<=GEST<=33) & (7=<PCV<=15)) | ((34<=GEST<=35) & (8=<PCV<=15))
| ((GEST=36) & (9=<PCV<=15)) | ((GEST=37) & (10=<PCV<=16))
| ((GEST=38) & (11=<PCV<=16)) | ((GEST=39) & (12=<PCV<=16))
| ((GEST=40) & (13=<PCV<=16)) | ((GEST=41) & (14=<PCV<=17))
| ((GEST=42) & (15=<PCV<=17)) | ((43<=GEST<=45) & (16=<PCV<=18)))

THEN GINDEX = 'ADEQUATE (1st Trimester)';

INTERMEDIATE PRENATAL CARE UTILIZATION CRITERIA:

IF (TPCB=1) &

((18<=GEST<=21) & (1=<PCV<=2)) | ((22<=GEST<=25) & (2=<PCV<=3))
| ((26<=GEST<=29) & (2=<PCV<=4)) | ((30<=GEST<=31) & (3=<PCV<=5))
| ((32<=GEST<=33) & (4=<PCV<=6)) | ((34<=GEST<=35) & (5=<PCV<=7))
| ((GEST=36) & (5=<PCV<=8)) | ((GEST=37) & (6=<PCV<=9))
| ((GEST=38) & (7=<PCV<=10)) | ((GEST=39) & (7=<PCV<=11))
| ((GEST=40) & (8=<PCV<=12)) | ((GEST=41) & (8=<PCV<=13))
| ((GEST=42) & (9=<PCV<=14)) | ((43<=GEST<=45) & (9=<PCV<=15)))

THEN GINDEX = 'INTERMEDIATE (1st Trimester)';

IF (TPCB=2) &

((18<=GEST<=21) & (1=<PCV<=9)) | ((22<=GEST<=25) & (2=<PCV<=10))
| ((26<=GEST<=29) & (2=<PCV<=11)) | ((30<=GEST<=31) & (3=<PCV<=11))
| ((32<=GEST<=33) & (4=<PCV<=12)) | ((34<=GEST<=35) & (5=<PCV<=12))
| ((36<=GEST<=37) & (6=<PCV<=13)) | ((38<=GEST<=39) & (7=<PCV<=14))
| ((GEST=40) & (8=<PCV<=14)) | ((GEST=41) & (8=<PCV<=15))
| ((GEST=42) & (9=<PCV<=15)) | ((43<=GEST<=45) & (9=<PCV<=16)))

THEN GINDEX = 'INTERMEDIATE (2nd Trimester)';

INADEQUATE PRENATAL CARE UTILIZATION CRITERIA:

IF (TPCB=1) &

((22<=GEST<=29) & (PCV=1)) | ((30<=GEST<=31) & (1<=PCV<=2))
| ((32<=GEST<=33) & (1<=PCV<=3)) | ((34<=GEST<=36) & (1<=PCV<=4))
| ((GEST=37) & (1<=PCV<=5)) | ((38<=GEST<=39) & (1<=PCV<=6))
| ((40<=GEST<=41) & (1<=PCV<=7)) | ((42<=GEST<=45) & (1<=PCV<=8)))

THEN GINDEX = 'INADEQUATE (1st Trimester)';

IF (TPCB=2) &

((22<=GEST<=29) & (PCV=1)) | ((30<=GEST<=31) & (1<=PCV<=2))
| ((32<=GEST<=33) & (1<=PCV<=3)) | ((34<=GEST<=35) & (1<=PCV<=4))
| ((36<=GEST<=37) & (1<=PCV<=5)) | ((38<=GEST<=39) & (1<=PCV<=6))
| ((40<=GEST<=41) & (1<=PCV<=7)) | ((42<=GEST<=45) & (1<=PCV<=8)))

THEN GINDEX = 'INADEQUATE (2nd Trimester)';

IF (TPCB=3) &

((GEST =25) & (1<=PCV<=8)) | ((26<=GEST<=31) & (1<=PCV<=9))
| ((32<=GEST<=35) & (1<=PCV<=10)) | ((36<=GEST<=37) & (1<=PCV<=11))
| ((38<=GEST<=40) & (1<=PCV<=12)) | ((41<=GEST<=42) & (1<=PCV<=13))
| ((43<=GEST<=45) & (1<=PCV<=14)))

THEN GINDEX = 'INADEQUATE (3rd Trimester)';

MISSING PRENATAL CARE CRITERIA:

IF (((PCV=.) & (TPCB^=0)) | ((TPCB=3) & (1<=GEST<=24))
| ((TPCB=2) & (1<=GEST<=11)) | ((GEST=.) & (PCV^=0))
| ((TPCB=.) & (PCV^=0)) | (TPCB=0 & (PCV>0)))
THEN GINDEX = 'MISSING';

NO PRENATAL CARE UTILIZATION:

IF (PCV=0) | (TPCB=0 & PCV=.)
THEN GINDEX = 'NOCARE';

Propensity score adjustment using stabilized inverse probability of treatment weights (IPTWs)

After fitting our propensity score model, we computed inverse probability of treatment weights (IPTW) based on our propensity scores to control for confounding. Theoretically, weighting individual study records with IPTWs forms a pseudo-population in which the distribution of baseline covariates is independent of the treatment assignment (i.e., the exposure).² Each subject was assigned a weight which represented the inverse of the predicted probability of exposure. For example, subjects that received an “expected” treatment based on the propensity score (i.e., high propensity score and received the vaccine) had a smaller weight, whereas subjects that received an “unexpected” treatment (i.e., low propensity score and received vaccine) had a larger weight.

To assist with extreme and influential weights, we calculated stabilized IPTWs. In this technique, the weights for exposed and unexposed subjects are separately multiplied by a constant, which is equal to the average predicted probability (i.e., average propensity score) in the entire study population. Stabilization does not influence the point estimate of the treatment effect; however, it does reduce the overall variance and helps to increase precision.³ In addition to stabilization, we trimmed observations with weights below the 1st or above the 99th percentiles of the propensity score distributions to minimize the influence of extreme weights concentrated in the tails of the distribution.⁴

Equations 1 and 2 shown below were used to calculate the stabilized IPTW for vaccinated and unvaccinated subjects, respectively. In these equations, *PS* signifies the propensity score, *i* is the vaccinated person, *j* is the unvaccinated person, *NT* is the total number of vaccinated subjects, and *NC* is the total number of unvaccinated subjects.

$$\frac{\sum_{i=1}^{N_T} PS_i}{N_T} * \frac{1}{PS_i}$$

Equation 1: IPTW calculation for vaccinated subjects

$$\frac{\sum_{j=1}^{N_C} (1 - PS_j)}{N_C} * \frac{1}{(1 - PS_j)}$$

Equation 2: IPTW calculation for unvaccinated subjects

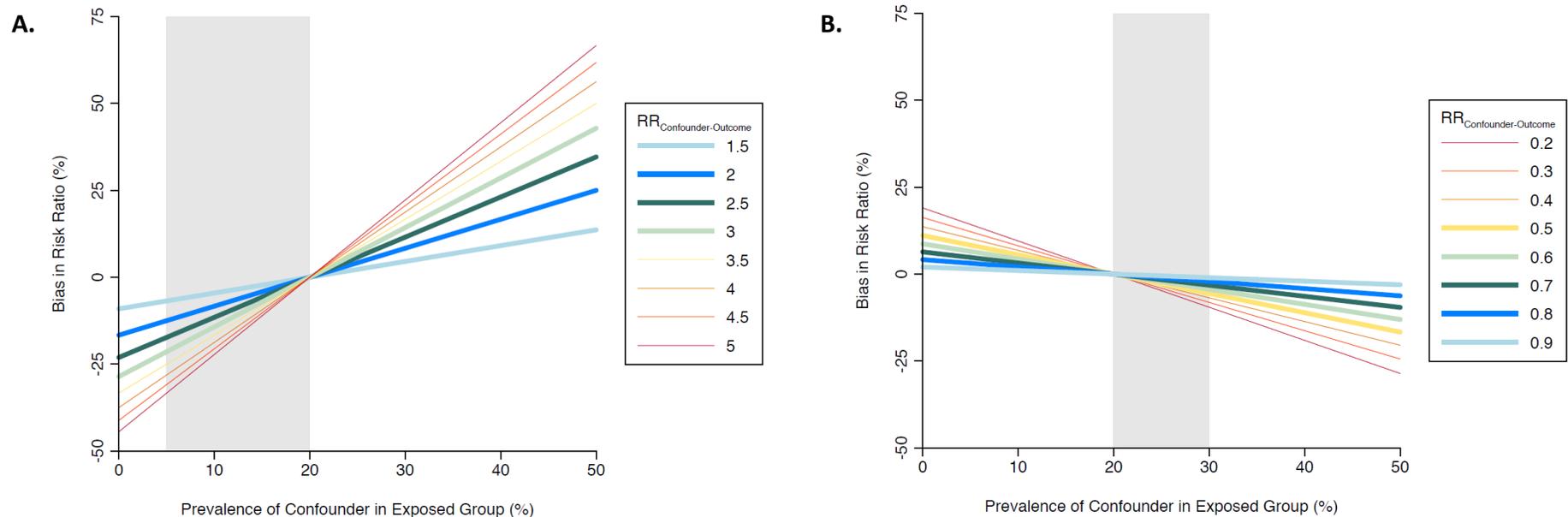
Bias analyses to estimate impact of residual confounding on outcome results

Background: Although we adjusted for numerous potential confounders in our propensity score model, we were limited by the availability of information captured within the databases. As such, unmeasured variables associated with both the exposure and outcome can result in residual confounding. With respect to the direction of any residual confounding bias, variables that could have obscured or attenuated any increased risk of an adverse outcome associated with Tdap vaccination during pregnancy would be of particular concern. For such a scenario to occur, there would have to be a higher prevalence of a protective unmeasured confounder (i.e., confounder associated with a lower risk of the outcome) or a lower prevalence of a harmful unmeasured confounder (i.e., confounder associated with a higher risk of the outcome) among the Tdap-vaccinated women, relative to unvaccinated women. This type of “healthy vaccinee” bias has been described in previous observational studies of influenza vaccination during pregnancy^{5,6} and has a predictable impact of biasing effect estimates downward (i.e., making vaccination appear less harmful for risk ratios [RR]>1, or making them appear more beneficial for RR<1).

Methods: A post-hoc sensitivity analyses was performed to estimate the effect of an unmeasured confounder on our study results. Using the array approach described by Schneeweiss,⁷ we modelled two scenarios for each outcome: A) non-vaccinated mothers with a higher prevalence of a hypothetical confounder that increases the risk of an outcome (i.e., harmful confounder); B) vaccinated mothers with a higher prevalence of a hypothetical confounder that decreases the risk of an outcome (i.e., protective confounder). Both scenarios assumed a common unmeasured confounder (20% in the unvaccinated group). For each study outcome and hypothetical scenario, the degree of potential bias was expressed as a percentage difference by comparing the observed estimate from our study to the bias-corrected estimate. For completeness of this assessment, we considered a range of input parameters (i.e., prevalence of unmeasured confounder in Tdap vaccinated women from 0 to 50%, relative risk for confounder-disease of 1.5 to 5 for harmful confounder and from 0.2 to 0.9 for protective confounder). However, some combinations of parameter values were considered highly unlikely, particularly when multiple extreme parameters occurred simultaneously.

Results: Among the more likely combinations of parameters for Scenario A, the percent bias ranged from a low of -2.27% (when the confounder-outcome association was 1.5 and the confounder prevalence differed by only 5 percentage points between exposure groups [i.e., 15% in vaccinated women and 20% in unvaccinated women]) to a high of -21.4% (when the confounder-outcome association was 3 and the confounder prevalence differed by 15 percentage points between exposure groups (i.e., 5% in vaccinated women and 20% in unvaccinated women). For a confounder-outcome association of 2 and a confounder prevalence of 10% in vaccinated women and 20% in unvaccinated women, an 8% underestimate in the hazard ratios/risk ratios means they could have been as high as RR=1.28 for chorioamnionitis (we estimated 1.17), RR=1.10 for post-partum hemorrhage (we estimated 1.01), HR=1.20 for very preterm birth (we estimated 1.10) and HR=1.25 for stillbirth (we estimated 1.15).

Among the more likely combinations of parameters for Scenario B, the percent bias was low, ranging from -1.02 to -5.56 and indicating that we were unlikely to have obscured an increased risk of any of the outcomes from residual confounding by a protective unmeasured confounder.



Notes: Prevalence of confounder in unexposed group set to 20%. Bolded lines and shaded areas represent most likely scenario.

Notes: Prevalence of confounder in unexposed group set to 20%. Bolded lines and shaded areas represent most likely scenario.

Supplemental Figure S2. Percent bias as a function of the prevalence of the confounder in the exposed group (Note: prevalence of confounder in unexposed group was held constant at 20%). The relationship between the confounder and outcome are presented in two hypothetical scenarios, with the bolded and shaded areas representing the more likely scenarios in each. Panel A presents a hypothetical harmful confounder with a higher prevalence among unvaccinated mothers (Scenario A). Panel B presents a hypothetical protective confounder with a higher prevalence among vaccinated mothers (Scenario B).

Tables. Array approach sensitivity analysis for unmeasured confounder. Two hypothetical scenarios are modelled for each outcome (explained below), with the prevalence of the confounder in the unvaccinated group held constant at 20%. Only scenarios deemed most likely are presented (i.e., corresponding to the bolded lines and shaded areas of the figures above).

Scenario A: demonstrates a hypothetical harmful confounder with a higher prevalence among unvaccinated mothers.

Scenario B: demonstrates a hypothetical protective confounder with a higher prevalence among vaccinated mothers.

Abbreviations: ARR, observed risk ratio in main analyses; AHR, observed hazard ratio in main analyses; RR_{cd}, association between confounder and outcome; P_{c1}, prevalence of confounder in exposed; P_{c0}, prevalence of confounder in unexposed; RR_{adjusted}, relative risk when adjusted for unmeasured confounder; % Bias, percent bias introduced by not adjusting for confounder (i.e., [(ARR-RR_{adjusted})/RR_{adjusted}]*100)

Supplemental Table S7. Gestational hypertension

ARR 0.87	RR _{cd}	P _{c1}	P _{c0}	RR _{adjusted}	% Bias
Scenario A					
	1.5	5%	20%	0.93	-6.82
	2	5%	20%	0.99	-12.50
	2.5	5%	20%	1.05	-17.31
	3	5%	20%	1.11	-21.43
	1.5	10%	20%	0.91	-4.55
	2	10%	20%	0.95	-8.33
	2.5	10%	20%	0.98	-11.54
	3	10%	20%	1.02	-14.29
	1.5	15%	20%	0.89	-2.27
	2	15%	20%	0.91	-4.17
	2.5	15%	20%	0.92	-5.77
	3	15%	20%	0.94	-7.14
Scenario B	0.5	25%	20%	0.89	-2.78
	0.6	25%	20%	0.89	-2.17
	0.7	25%	20%	0.88	-1.60
	0.8	25%	20%	0.88	-1.04
	0.9	25%	20%	0.87	-0.51
	0.5	30%	20%	0.92	-5.56

	0.6	30%	20%	0.91	-4.35
	0.7	30%	20%	0.90	-3.19
	0.8	30%	20%	0.89	-2.08
	0.9	30%	20%	0.88	-1.02

Supplemental Table S8. Chorioamnionitis

ARR: 1.17	RR_{cd}	P_{c1}	P_{c0}	RR_{adjusted}	% Bias
Scenario A					
	1.5	5%	20%	1.26	-6.82
	2	5%	20%	1.34	-12.5
	2.5	5%	20%	1.41	-17.3
	3	5%	20%	1.49	-21.4
	1.5	10%	20%	1.23	-4.55
	2	10%	20%	1.28	-8.33
	2.5	10%	20%	1.32	-11.5
	3	10%	20%	1.37	-14.3
	1.5	15%	20%	1.20	-2.27
	2	15%	20%	1.22	-4.17
	2.5	15%	20%	1.24	-5.77
	3	15%	20%	1.26	-7.14
Scenario B	0.5	25%	20%	1.20	-2.78
	0.6	25%	20%	1.20	-2.17
	0.7	25%	20%	1.19	-1.60
	0.8	25%	20%	1.18	-1.04
	0.9	25%	20%	1.18	-0.51
	0.5	30%	20%	1.24	-5.56
	0.6	30%	20%	1.22	-4.35
	0.7	30%	20%	1.21	-3.17
	0.8	30%	20%	1.19	-2.08
	0.9	30%	20%	1.18	-1.02

Supplemental Table S9. Postpartum hemorrhage

ARR 1.01	RR_{cd}	P_{c1}	P_{c0}	RR_{adjusted}	% Bias
Scenario A					
	1.5	5%	20%	1.08	-6.82
	2	5%	20%	1.15	-12.50
	2.5	5%	20%	1.22	-17.31
	3	5%	20%	1.29	-21.43
	1.5	10%	20%	1.06	-4.55
	2	10%	20%	1.10	-8.33
	2.5	10%	20%	1.14	-11.54
	3	10%	20%	1.18	-14.29
	1.5	15%	20%	1.03	-2.27
	2	15%	20%	1.05	-4.17
	2.5	15%	20%	1.07	-5.77
	3	15%	20%	1.09	-7.14
Scenario B	0.5	25%	20%	1.04	-2.78
	0.6	25%	20%	1.03	-2.17
	0.7	25%	20%	1.03	-1.60
	0.8	25%	20%	1.02	-1.04
	0.9	25%	20%	1.02	-0.51
	0.5	30%	20%	1.07	-5.56
	0.6	30%	20%	1.06	-4.35
	0.7	30%	20%	1.04	-3.19
	0.8	30%	20%	1.03	-2.08
	0.9	30%	20%	1.02	-1.02

Supplemental Table S10. Severe postpartum hemorrhage

ARR 0.79	RR_{cd}	P_{c1}	P_{c0}	RR_{adjusted}	% Bias
Scenario A					
	1.5	5%	20%	0.85	-6.82
	2	5%	20%	0.90	-12.50
	2.5	5%	20%	0.96	-17.31
	3	5%	20%	1.01	-21.43
	1.5	10%	20%	0.83	-4.55
	2	10%	20%	0.86	-8.33
	2.5	10%	20%	0.89	-11.54
	3	10%	20%	0.92	-14.29
	1.5	15%	20%	0.81	-2.27
	2	15%	20%	0.82	-4.17
	2.5	15%	20%	0.84	-5.77
	3	15%	20%	0.85	-7.14
Scenario B	0.5	25%	20%	0.81	-2.78
	0.6	25%	20%	0.81	-2.17
	0.7	25%	20%	0.80	-1.60
	0.8	25%	20%	0.80	-1.04
	0.9	25%	20%	0.79	-0.51
	0.5	30%	20%	0.84	-5.56
	0.6	30%	20%	0.83	-4.35
	0.7	30%	20%	0.82	-3.19
	0.8	30%	20%	0.81	-2.08
	0.9	30%	20%	0.80	-1.02

Supplemental Table S11. Small-for-gestational-age birth

ARR 0.96	RR_{cd}	P_{c1}	P_{c0}	RR_{adjusted}	% Bias
Scenario A					
	1.5	5%	20%	1.03	-6.82
	2	5%	20%	1.10	-12.50
	2.5	5%	20%	1.16	-17.31
	3	5%	20%	1.22	-21.43
	1.5	10%	20%	1.01	-4.55
	2	10%	20%	1.05	-8.33
	2.5	10%	20%	1.09	-11.54
	3	10%	20%	1.12	-14.29
	1.5	15%	20%	0.98	-2.27
	2	15%	20%	1.00	-4.17
	2.5	15%	20%	1.02	-5.77
	3	15%	20%	1.03	-7.14
Scenario B	0.5	25%	20%	0.99	-2.78
	0.6	25%	20%	0.98	-2.17
	0.7	25%	20%	0.98	-1.60
	0.8	25%	20%	0.97	-1.04
	0.9	25%	20%	0.96	-0.51
	0.5	30%	20%	1.02	-5.56
	0.6	30%	20%	1.00	-4.35
	0.7	30%	20%	0.99	-3.19
	0.8	30%	20%	0.98	-2.08
	0.9	30%	20%	0.97	-1.02

Supplemental Table S12. NICU admissions >24 hours

ARR 0.82	RR_{cd}	P_{c1}	P_{c0}	RR_{adjusted}	% Bias
Scenario A					
	1.5	5%	20%	0.88	-6.82
	2	5%	20%	0.94	-12.50
	2.5	5%	20%	0.99	-17.31
	3	5%	20%	1.04	-21.43
	1.5	10%	20%	0.86	-4.55
	2	10%	20%	0.89	-8.33
	2.5	10%	20%	0.93	-11.54
	3	10%	20%	0.96	-14.29
	1.5	15%	20%	0.84	-2.27
	2	15%	20%	0.86	-4.17
	2.5	15%	20%	0.87	-5.77
	3	15%	20%	0.88	-7.14
Scenario B	0.5	25%	20%	0.84	-2.78
	0.6	25%	20%	0.84	-2.17
	0.7	25%	20%	0.83	-1.60
	0.8	25%	20%	0.83	-1.04
	0.9	25%	20%	0.82	-0.51
	0.5	30%	20%	0.87	-5.56
	0.6	30%	20%	0.86	-4.35
	0.7	30%	20%	0.85	-3.19
	0.8	30%	20%	0.84	-2.08
	0.9	30%	20%	0.83	-1.02

Supplemental Table S13. Neonatal morbidity composite outcome

ARR 0.81	RR_{cd}	P_{c1}	P_{c0}	RR_{adjusted}	% Bias
Scenario A					
	1.5	5%	20%	0.87	-6.82
	2	5%	20%	0.93	-12.50
	2.5	5%	20%	0.98	-17.31
	3	5%	20%	1.03	-21.43
	1.5	10%	20%	0.85	-4.55
	2	10%	20%	0.88	-8.33
	2.5	10%	20%	0.92	-11.54
	3	10%	20%	0.95	-14.29
	1.5	15%	20%	0.83	-2.27
	2	15%	20%	0.85	-4.17
	2.5	15%	20%	0.86	-5.77
	3	15%	20%	0.87	-7.14
Scenario B	0.5	25%	20%	0.83	-2.78
	0.6	25%	20%	0.83	-2.17
	0.7	25%	20%	0.82	-1.60
	0.8	25%	20%	0.82	-1.04
	0.9	25%	20%	0.81	-0.51
	0.5	30%	20%	0.86	-5.56
	0.6	30%	20%	0.85	-4.35
	0.7	30%	20%	0.84	-3.19
	0.8	30%	20%	0.83	-2.08
	0.9	30%	20%	0.82	-1.02

Supplemental Table S14. Preterm birth

AHR 0.98	RR_{cd}	P_{c1}	P_{c0}	RR_{adjusted}	% Bias
Scenario A					
	1.5	5%	20%	1.05	-6.82
	2	5%	20%	1.12	-12.50
	2.5	5%	20%	1.19	-17.31
	3	5%	20%	1.25	-21.43
	1.5	10%	20%	1.03	-4.55
	2	10%	20%	1.07	-8.33
	2.5	10%	20%	1.11	-11.54
	3	10%	20%	1.14	-14.29
	1.5	15%	20%	1.00	-2.27
	2	15%	20%	1.02	-4.17
	2.5	15%	20%	1.04	-5.77
	3	15%	20%	1.06	-7.14
Scenario B	0.5	25%	20%	1.01	-2.78
	0.6	25%	20%	1.00	-2.17
	0.7	25%	20%	1.00	-1.60
	0.8	25%	20%	0.99	-1.04
	0.9	25%	20%	0.99	-0.51
	0.5	30%	20%	1.04	-5.56
	0.6	30%	20%	1.02	-4.35
	0.7	30%	20%	1.01	-3.19
	0.8	30%	20%	1.00	-2.08
	0.9	30%	20%	0.99	-1.02

Supplemental Table S15. Very preterm birth

AHR 1.10	RR_{cd}	P_{c1}	P_{c0}	RR_{adjusted}	% Bias
Scenario A					
	1.5	5%	20%	1.18	-6.82
	2	5%	20%	1.26	-12.50
	2.5	5%	20%	1.33	-17.31
	3	5%	20%	1.40	-21.43
	1.5	10%	20%	1.15	-4.55
	2	10%	20%	1.20	-8.33
	2.5	10%	20%	1.24	-11.54
	3	10%	20%	1.28	-14.29
	1.5	15%	20%	1.13	-2.27
	2	15%	20%	1.15	-4.17
	2.5	15%	20%	1.17	-5.77
	3	15%	20%	1.18	-7.14
Scenario B	0.5	25%	20%	1.13	-2.78
	0.6	25%	20%	1.12	-2.17
	0.7	25%	20%	1.12	-1.60
	0.8	25%	20%	1.11	-1.04
	0.9	25%	20%	1.11	-0.51
	0.5	30%	20%	1.16	-5.56
	0.6	30%	20%	1.15	-4.35
	0.7	30%	20%	1.14	-3.19
	0.8	30%	20%	1.12	-2.08
	0.9	30%	20%	1.11	-1.02

Supplemental Table S16. Stillbirth

AHR 1.15	RR_{cd}	P_{c1}	P_{c0}	RR_{adjusted}	% Bias
Scenario A					
	1.5	5%	20%	1.23	-6.82
	2	5%	20%	1.31	-12.50
	2.5	5%	20%	1.39	-17.31
	3	5%	20%	1.46	-21.43
	1.5	10%	20%	1.20	-4.55
	2	10%	20%	1.25	-8.33
	2.5	10%	20%	1.30	-11.54
	3	10%	20%	1.34	-14.29
	1.5	15%	20%	1.18	-2.27
	2	15%	20%	1.20	-4.17
	2.5	15%	20%	1.22	-5.77
	3	15%	20%	1.24	-7.14
Scenario B	0.5	25%	20%	1.18	-2.78
	0.6	25%	20%	1.18	-2.17
	0.7	25%	20%	1.17	-1.60
	0.8	25%	20%	1.16	-1.04
	0.9	25%	20%	1.16	-0.51
	0.5	30%	20%	1.22	-5.56
	0.6	30%	20%	1.20	-4.35
	0.7	30%	20%	1.19	-3.19
	0.8	30%	20%	1.17	-2.08
	0.9	30%	20%	1.16	-1.02

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