

Neonatal and Maternal Outcomes in Pregnant Women With Cardiac Disease

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Background—Pregnant women with underlying heart disease (HD) are at increased risk for adverse maternal, obstetric, and neonatal outcomes.

Methods and Results—Inpatient maternal delivery admissions and linked neonatal stays for women with cardiomyopathy, adult congenital HD, pulmonary hypertension (PH), and valvular HD were explored utilizing the Statewide Planning and Research Cooperative System (New York), January 1, 2000, through December 31, 2014, with the *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)*. Maternal major adverse cardiac events, neonatal adverse clinical events (NACE), and obstetric complications were recorded. Outcomes were compared using multiple logistic regression modeling. Among 2 284 044 delivery admissions, 3871 women had HD; 676 (17%) had cardiomyopathy, 1528 (40%) had valvular HD, 1367 (35%) had adult congenital HD, and 300 (8%) had PH. Major adverse cardiac events occurred in 16.1% of women with HD, with most in the cardiomyopathy (45.9%) and PH (25%) groups. NACE was more common in offspring of women with HD (18.4% versus 7.1%), with most in the cardiomyopathy (30.0%) and PH (25.0%) groups. Increased risk of NACE was noted for women with HD (odds ratio [OR]: 2.8; 95% confidence interval [CI], 2.5–3.0), with the highest risk for those with cardiomyopathy (OR: 5.9; 95% CI, 5.0–7.0) and PH (OR: 4.5; 95% CI, 3.4–5.9). Preeclampsia (OR: 5.1; 95% CI, 3.0–8.6), major adverse cardiac events (OR: 2.3; 95% CI, 1.8–2.9), preexisting diabetes mellitus (OR: 4.3; 95% CI, 1.5–12.3), and obstetric complications (OR: 2.9; 95% CI, 1.7–5.2) were independently associated with higher NACE risk.

Conclusions—Neonatal complications were higher in offspring of pregnant women with HD, particularly cardiomyopathy and PH. Preeclampsia, major adverse cardiac events, obstetric complications, and preexisting diabetes mellitus were independently associated with a higher risk of NACE. (*J Am Heart Assoc.* 2018;7:e009395. DOI: 10.1161/JAHA.118.009395.)

Key Words: adult congenital heart disease • cardiomyopathy • pregnancy • pulmonary hypertension • valve

Heart disease (HD) is a leading cause of maternal deaths in the United States and other developed countries.^{1–3} HD in pregnancy represents a spectrum of etiologies, inclusive of cardiomyopathies, valvular HD (VHD), pulmonary hypertension (PH), and adult congenital HD (ACHD). Recent epidemiological data suggest that the prevalence of maternal HD during pregnancy is rising,^{4–6} not only for those with ACHD but for those with acquired HD such as cardiomyopathy and PH.⁷ Both acquired and ACHD predispose

pregnant women and their offspring to a heightened risk of adverse events, particularly during labor and delivery.^{8–10} However, an overwhelming majority of the data in the arena of fetal or neonatal outcomes in women with HD are centered on the outcomes of women with ACHD^{11–19} and not on those with acquired HD such as cardiomyopathy, VHD, or PH, although these forms of HD are collectively more common. Comparative research in these areas is also lacking.

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Accompanying Tables S1 and S2 are available at <https://www.ahajournals.org/doi/suppl/10.1161/JAHA.118.009395>

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Clinical Perspective

What Is New?

- In this study of delivery admissions in New York State over a 15-year period, pregnant women with multiple forms of cardiac disease including cardiomyopathy, valvular heart disease, adult congenital heart disease, and pulmonary hypertension experienced an increased risk of adverse maternal cardiac, obstetric, and fetal/neonatal events.
- Women with cardiomyopathy and pulmonary hypertension and their offspring had the worst overall outcomes.

What Are the Clinical Implications?

- This study highlights the neonatal risks for offspring in women with cardiac disease.
- These findings may guide risk assessment and monitoring decisions for pregnant women with cardiac disease and their offspring.

In this study, we sought to evaluate the maternal, obstetric, and neonatal outcomes of pregnant women with and without multiple forms of HD (cardiomyopathy, VHD, PH, ACHD) in a contemporary cohort of women admitted for delivery in New York State. Furthermore, we sought to identify the risk factors and predictors of adverse fetal/neonatal events in the offspring of women with all major forms of HD affecting women of childbearing potential.

Methods

Data Source and Study Population

The Statewide Planning And Research Cooperative System (SPARCS) database from the New York State Department of Health was used to characterize maternal and fetal/neonatal outcomes from January 1, 2000, through December 31, 2014 (Figure 1). The SPARCS data set allows for linking of maternal and fetal records through birth certificate data. Only singleton records with a linked baby's discharge number and observation number were used in our analysis because multiple births and women with >1 delivery during the study period could not be accurately linked. In addition, only women's earliest singleton deliveries during the study period were used in the analysis to avoid the possible confounding effect of multiple deliveries. *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* codes to identify pregnancy, forms of HD, and complications were obtained (Table S1). Records containing predetermined diagnosis or procedure codes (Table S1) were treated as delivery records. Patients aged <18 years and those with missing information including unique patient identifiers were

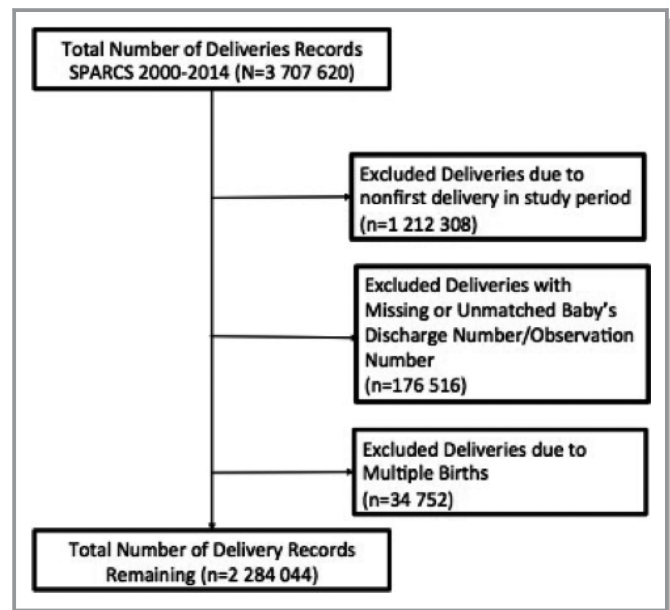


Figure 1. Study population creation. Inclusion and exclusion of study records utilized from the Statewide Planning And Research Cooperative System (SPARCS).

excluded. Records with the same unique patient identifier, date of birth, admission date, discharge date, and facility name were considered as pure duplications, and only one of such records was kept. Records showing multiple subtypes of cardiomyopathy (peripartum, hypertrophic, dilated) simultaneously were excluded (n=184). Institutional review board approval from Stony Brook University was obtained before obtaining the data and proceeding with analysis. The data set was analyzed retrospectively, and the informed consent requirement was waived.

Outcome Measures

Maternal major adverse cardiac events (MACE) were defined by *ICD-9-CM* codes as a composite of in-hospital death, cardiac arrest, acute myocardial infarction, heart failure, arrhythmia, cerebrovascular events, pulmonary embolism, arterial embolism, obstetric pulmonary embolism, and cardiac complications of anesthesia or other sedation in labor and delivery, cardiorespiratory failure or shock, dissection of the aorta, dissection of another artery, and respiratory failure (Table S1).^{6,8,20} Cardiac procedural and non-cardiac-associated procedural covariates were also recorded for patients with and without HD but not included in MACE. Non-MACE maternal outcomes included 30-day readmission rate, acute renal failure, length of stay, and total hospital charges. Obstetric outcomes included gestational diabetes mellitus, polyhydramnios, premature rupture of membranes, placental insufficiency, transient hypertension of pregnancy,

preeclampsia/eclampsia (all types), postpartum hemorrhage or infection, laceration, and antepartum hemorrhage. Neonatal adverse clinical events (NACE) were a composite of fetal death (in utero), neonate death (within 30 days of birth), prematurity (<37 weeks), small-for-gestational-age birth weight (<10th percentile), intrauterine growth restriction, respiratory distress syndrome, intracranial/intraventricular hemorrhage, and congenital HD (CHD) in the newborn. Other neonatal outcomes such as length of stay and birth weight category were included.

Statistical Analysis

ANOVA under the assumption of unequal variance was used to examine existence of significant differences of continuous variables such as length of stay and total hospital charges between women with and without HDs and among 4 HD populations. The Pearson χ^2 test with *P* values from Monte Carlo simulation when appropriate and the Fisher exact test were used to compare categorical variables. A multivariable logistic regression model was used to explore risk factors for NACE among the offspring of women with HD. Factors that were significantly associated with NACE based on the Pearson χ^2 test at a significance level of 0.05 were simultaneously investigated in the multivariable logistic regression model. Odds ratios and 95% confidence intervals were reported. An odds ratio >1 indicated that one category had more risk of having NACE than the reference category, and odds ratio <1 indicated that one category had less risk of having NACE than the reference category. Risk factors for NACE were modeled because those for MACE have been previously explored.^{6–8} Statistical significance was set at 0.05, and analysis was done using SAS 9.3 (SAS Institute).

Results

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

Prevalence of HD

Among the 2 284 044 women composing the study population, 3871 (0.2%) women had HD and 2 280 173 (99.8%) did not. Of the women with HD, 676 (17%) had cardiomyopathy, 1528 (40%) had VHD, 1367 had ACHD (35%), and 300 (8%) had PH (Figure 2).

Patient Characteristics

Patient characteristics and demographics are described in Table 1. Mothers with HD had greater tobacco dependence, obesity, and preexisting hypertension than mothers without

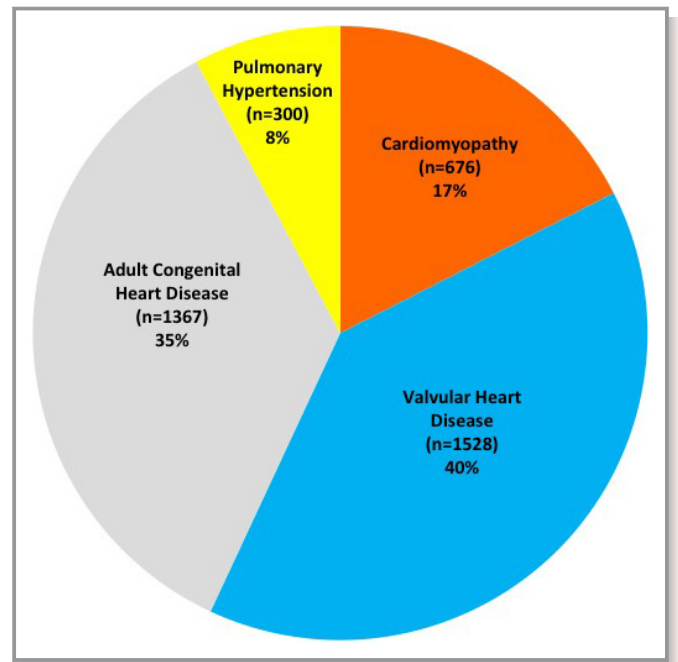


Figure 2. Prevalence of pregnancy and heart disease of various etiologies in New York State, 2000–2014.

HD. Women with HD were more likely to be delivered by a cesarean approach compared with the no-HD group, with most in the cardiomyopathy and PH groups. Assisted delivery was also more common in patients with versus without HD, particularly those with VHD or ACHD compared with cardiomyopathy or PH. Analysis of the small group of women excluded because of multiple deliveries (2.8% of total patient population analyzed) showed that the excluded patients were more likely to be older and more medically complicated (more likely to be obese, to use anticoagulants, to have diabetes mellitus and chronic hypertension)—factors that have previously been shown to be associated with MACE⁸ and would have confounded our data were they included.

Maternal Cardiac Outcomes

Adverse maternal cardiac events during the hospitalization for delivery are listed in Table 2 and Figure 3A. Compared with women without HD, MACE was more common in women with HD, predominantly because of higher rates of arrhythmia, heart failure, and respiratory failure. MACE rates were highest in the cardiomyopathy and PH groups and lowest among women with ACHD.

Both cardiac procedural interventions and non-cardiac-associated procedural covariates were more common in women with HD than No HD. Women with HD experienced longer length of stay, higher total hospital charges, higher rate of 30-day readmission, and higher rate of acute renal failure

Table 1. Patient Characteristics of Pregnant Women With and Without HD in New York State, 2000–2014

	HD (n=3871)	No HD (n=2 280 173)	P Value	Cardiomyopathy (n=676)	VHD (n=1528)	ACHD (n=1367)	PH (n=300)	P Value
Age, y, mean±SD	29.3±6.3	28.6±6.1	<0.0001	30.3±6.4	29.6±6.2	28.2±6.0	29.8±6.7	<0.0001
Age group								
18–25	1184 (30.6)	769 239 (33.7)	<0.0001	177 (26.2)	434 (28.4)	484 (35.4)	89 (29.7)	<0.0001
26–35	2009 (51.9)	1 191 106 (52.2)		344 (50.9)	805 (52.7)	709 (51.9)	151 (50.3)	
>35	678 (17.5)	319 828 (14.0)		155 (22.9)	289 (18.9)	174 (12.7)	60 (20.0)	
Race								
White	1770 (45.7)	962 861 (42.2)	<0.0001	232 (34.3)	675 (44.2)	773 (56.6)	90 (30.0)	<0.0001
Black	651 (16.8)	334 658 (14.7)		180 (26.6)	252 (16.5)	138 (10.1)	81 (27.0)	
Hispanic	40 (1.0)	20 253 (0.9)		7 (1.0)	13 (0.9)	18 (1.3)	2 (0.7)	
Asian	151 (3.9)	163 886 (7.2)		25 (3.7)	62 (4.1)	44 (3.2)	20 (6.7)	
Other	1259 (32.5)	798 515 (35.0)		232 (34.3)	526 (34.4)	394 (28.8)	107 (35.7)	
Insurance status								
Commercial	3005 (77.6)	1 710 573 (75.0)	<0.0001	503 (74.4)	1175 (76.9)	1112 (81.4)	215 (71.7)	<0.0001
Medicaid	785 (20.3)	536 607 (23.5)		155 (22.9)	328 (21.5)	226 (16.5)	76 (25.3)	
Medicare	50 (1.3)	8014 (0.4)		15 (2.2)	11 (0.7)	17 (1.2)	7 (2.3)	
Other	31 (0.8)	24 979 (1.1)		3 (0.4)	14 (0.9)	12 (0.9)	2 (0.7)	
Hospital region*								
North of NYC	320 (8.3)	236 602 (10.4)	<0.0001	57 (8.4)	134 (8.8)	102 (7.5)	27 (9.0)	<0.0001
Western NYS	528 (13.6)	274 178 (12.0)		91 (13.5)	184 (12.0)	227 (16.6)	26 (8.7)	
Long Island	563 (14.5)	305 292 (13.4)		89 (13.2)	243 (15.9)	184 (13.5)	47 (15.7)	
Mid-/North NYS	630 (16.3)	311 247 (13.7)		87 (12.9)	229 (15.0)	285 (20.9)	29 (9.7)	
NYC	1830 (47.3)	1 152 854 (50.6)		352 (52.1)	738 (48.3)	569 (41.62)	171 (57.00)	
Tobacco dependence	58 (1.5)	17 947 (0.8)	<0.0001	5 (0.7)	21 (1.4)	29 (2.1)	3 (1.0)	0.0753
Alcohol dependence	4 (0.1)	363 (0.0)	0.0031	0 (0.0)	2 (0.1)	2 (0.2)	0 (0.0)	0.7841
Drug dependence	17 (0.4)	4409 (0.2)	0.0005	8 (1.2)	8 (0.5)	1 (0.1)	0 (0.0)	0.0043
Obesity	167 (4.3)	40 336 (1.8)	<0.0001	44 (6.5)	46 (3.0)	43 (3.2)	34 (11.3)	<0.0001
Anticoagulant use (long term)	33 (0.9)	1484 (0.1)	<0.0001	3 (0.4)	23 (1.5)	6 (0.4)	1 (0.3)	0.0052
Diabetes mellitus (complicated)	20 (0.5)	1914 (0.1)	<0.0001	6 (0.9)	2 (0.1)	7 (0.5)	5 (1.7)	0.0059
Diabetes mellitus (uncomplicated)	59 (1.5)	10 874 (0.5)	<0.0001	19 (2.8)	23 (1.5)	10 (0.7)	7 (2.3)	0.0023
Transient hypertension	113 (2.9)	55 172 (2.4)	0.0433	25 (3.7)	45 (3.0)	32 (2.3)	11 (3.7)	0.3011
Preexisting hypertension	64 (1.7)	1801 (0.1)	<0.0001	15 (2.2)	15 (1.0)	8 (0.6)	26 (8.7)	<0.0001
Chronic hypertension	54 (1.4)	9617 (0.4)	<0.0001	18 (2.7)	21 (1.4)	9 (0.7)	6 (2.0)	0.0028
Delivery type								
Cesarean delivery	1747 (45.1)	705 935 (31.0)	<0.0001	420 (62.1)	645 (42.2)	505 (36.9)	177 (59.0)	<0.0001
Assisted delivery	340 (8.8)	112 064 (4.9)		53 (7.8)	139 (9.1)	125 (9.1)	23 (7.7)	
Vaginal delivery	1784 (46.1)	1 462 174 (64.1)		203 (30.0)	744 (48.7)	737 (53.9)	100 (33.3)	

Data are shown as n (%) except as noted. *P* values were based on ANOVA for continuous outcomes and Pearson χ^2 test or Fisher exact test for categorical outcomes. ACHD indicates adult congenital heart disease; HD, heart disease; NYC, New York City; NYS, New York State; PH, pulmonary hypertension; VHD, valvular heart disease. *Hospital regions in NYS: North of NYC: Westchester, Putnam, Rockland, Orange, Sullivan, Ulster, and Dutchess counties; Western NYS: Chautaugua, Cattaraugus, Allegany, Erie, Wyoming, Genesee, Niagara, Orleans, Steuben, Livingston, Monroe, Wayne, Ontario, Yates, Seneca, Schuyler and Chemung counties; Long Island: Nassau and Suffolk counties; Mid-/North NYS: Cayuga, Tompkins, Tioga, Cortland, Onondaga, Broome, Chenango, Madison, Oswego, Oneida, Lewis, Jefferson, St Lawrence, Herkimer, Hamilton, Franklin, Clinton, Essex, Warren, Saratoga, Warren, Fulton, Washington, Albany, Rensselaer, Montgomery, Schoharie, Otsego, Delaware, Greene, Columbia and Schenectady counties; NYC: Bronx, New York, Richmond, Kings, and Queens counties.

Table 2. Maternal Outcomes of Women With and Without HD in New York State, 2000–2014

Outcome	HD (n=3871)	No HD (n=2 280 173)	P Value	Cardiomyopathy (n=676)	VHD (n=1528)	ACHD (n=1367)	PH (n=300)	P Value
MACE	624 (16.1)	9390 (0.4)	<0.0001	310 (45.9)	155 (10.1)	84 (6.1)	75 (25.0)	<0.0001
Acute myocardial infarction	19 (0.5)	67 (0.0)	<0.0001	13 (1.9)	5 (0.3)	0 (0.0)	1 (0.3)	<0.0001
Arrhythmia	278 (7.2)	7134 (0.3)	<0.0001	103 (15.2)	97 (6.4)	50 (3.7)	28 (9.3)	<0.0001
Arterial embolism	1 (0.0)	18 (0.0)	0.0322	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1.0000
Cardiac arrest	11 (0.3)	97 (0.0)	<0.0001	9 (1.3)	2 (0.1)	0 (0.0)	0 (0.0)	<0.0001
Cardiac complications of anesthesia or other sedation in labor and delivery	13 (0.3)	309 (0.0)	<0.0001	8 (1.2)	4 (0.3)	1 (0.1)	0 (0.0)	0.0006
Cardiorespiratory failure or shock	13 (0.3)	16 (0.0)	<0.0001	10 (1.5)	1 (0.1)	2 (0.2)	0 (0.0)	<0.0001
Cerebrovascular events	11 (0.3)	316 (0.0)	<0.0001	4 (0.6)	4 (0.3)	2 (0.2)	1 (0.3)	0.3447
Dissection of another artery	0 (0.0)	7 (0.0)	1.0000	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	.
Dissection of the aorta	10 (0.3)	12 (0.0)	<0.0001	0 (0.0)	4 (0.3)	4 (0.3)	2 (0.7)	0.2925
Heart failure	278 (7.2)	343 (0.0)	<0.0001	197 (29.14)	42 (2.8)	14 (1.0)	25 (8.3)	<0.0001
In-hospital death	23 (0.6)	157 (0.0)	<0.0001	13 (1.9)	2 (0.1)	3 (0.2)	5 (1.7)	<0.0001
Obstetric pulmonary embolism	30 (0.8)	465 (0.0)	<0.0001	11 (1.6)	5 (0.3)	4 (0.3)	10 (3.3)	<0.0001
Pulmonary embolism	4 (0.1)	46 (0.0)	<0.0001	4 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0.0025
Respiratory failure	125 (3.2)	720 (0.0)	<0.0001	80 (11.8)	14 (0.9)	11 (0.8)	20 (6.7)	<0.0001
Cardiac procedural interventions	75 (1.9)	200 (0.0)	<0.0001	43 (6.4)	11 (0.7)	9 (0.7)	12 (4.0)	<0.0001
Implantation of pulsation balloon	1 (0.0)	6 (0.0)	0.0099	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0.2537
Implantation ICD or ICD-CR	4 (0.1)	2 (0.0)	<0.0001	3 (0.4)	0 (0.0)	1 (0.1)	0 (0.0)	0.0424
LVAD, RVAD, or biventricular system*	0 (0.0)	2 (0.0)	1.0000	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	.
Open chest cardiac massage	1 (0.0)	2 (0.0)	0.0053	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0.0727
Right and left heart cardiac catheterization	25 (0.7)	17 (0.0)	<0.0001	17 (2.5)	3 (0.2)	2 (0.2)	3 (1.0)	<0.0001
Central venous pressure monitoring	6 (0.2)	82 (0.0)	<0.0001	3 (0.4)	1 (0.1)	1 (0.1)	1 (0.3)	0.1341
Pulmonary artery pressure monitoring	1 (0.0)	0 (0.0)	0.0018	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0.2551
Pulmonary artery wedge monitoring	37 (1.0)	56 (0.0)	<0.0001	21 (3.1)	6 (0.4)	5 (0.4)	5 (1.7)	<0.0001
Systemic arterial pressure monitoring	7 (0.2)	47 (0.0)	<0.0001	4 (0.6)	1 (0.1)	0 (0.0)	2 (0.7)	0.0059
Non-cardiac-associated procedural covariates†	77 (2.0)	2094 (0.1)	<0.0001	42 (6.2)	14 (0.9)	7 (0.5)	14 (4.7)	<0.0001
Measurement of systemic arterial blood gases	8 (0.2)	1509 (0.1)	0.0052	3 (0.4)	3 (0.2)	1 (0.1)	1 (0.3)	0.3217
Mechanical ventilation	31 (0.8)	245 (0.0)	<0.0001	18 (2.7)	4 (0.3)	2 (0.2)	7 (2.3)	<0.0001
Noninvasive positive pressure ventilation	44 (1.1)	377 (0.0)	<0.0001	26 (3.9)	7 (0.5)	4 (0.3)	7 (2.3)	<0.0001
Non-MACE outcomes								
30-d readmission	163 (4.2)	26 215 (1.2)	<0.0001	65 (9.62)	51 (3.34)	27 (1.98)	20 (6.67)	<0.0001
Acute renal failure	24 (0.6)	514 (0.0)	<0.0001	18 (2.7)	0 (0.0)	2 (0.2)	4 (1.3)	<0.0001
Length of stay, d, mean±SD	4.8±7.3	2.9±2.2	<0.0001	7.6±11.1	4.3±5.8	3.7±5.6	6.7±8.1	<0.0001
Total hospital charge, \$, mean±SD	21 384.8±47 037.5	10 175.1±9698.1	<0.0001	36 838.9±54 793.4	17 079.3±25 677.6	16 604.0±58 735.1	30 276.0±43 736.4	<0.0001

Continued

Table 2. Continued

Outcome	HD (n=3871)	No HD (n=2 280 173)	P Value	Cardiomyopathy (n=676)	VHD (n=1528)	ACHD (n=1367)	PH (n=300)	P Value
Hypertensive disorders of pregnancy (all types)	426 (11.0)	94 667 (4.2)	<0.0001	171 (25.3)	113 (7.4)	72 (5.3)	70 (23.3)	<0.0001
Eclampsia complicating pregnancy/childbirth	6 (0.2)	1421 (0.1)		4 (0.6)	0 (0.0)	2 (0.2)	0 (0.0)	
Severe preeclampsia	180 (4.7)	27 598 (1.2)		88 (13.0)	42 (2.8)	27 (2.0)	23 (7.7)	
Mild preeclampsia	149 (3.9)	56 910 (2.5)		47 (7.0)	46 (3.0)	38 (2.8)	18 (6.0)	
Preeclampsia/eclampsia with preexisting hypertension	91 (2.4)	8738 (0.4)		32 (4.7)	25 (1.6)	5 (0.4)	29 (9.7)	

Data are shown as n (%) except as noted. P values were based on the Pearson chi-squared test or Fisher exact test. ACHD indicates adult congenital heart disease; HD, heart disease; ICD, implantable cardioverter-defibrillator; ICD-CR, implantable cardioverter-defibrillator with cardiac resynchronization; LVAD, left ventricular assist device; MACE, major adverse cardiac event; PH, pulmonary hypertension; RVAD, right ventricular assist device; VHD, valvular heart disease.

*Implantation or replacement, repair, or removal of an LVAD or RVAD, heart replacement, or assist systems such as a total internal single or biventricular system.

†No patients had continuous intra-arterial blood gas monitoring (*International Classification of Diseases, Ninth Revision [ICD-9-CM] code 89.60*).

compared with women without HD. Women with cardiomyopathy and PH experienced the longest length of stay, the highest total hospital charges, and the highest 30-day readmission rate compared with other groups. Eclampsia/preeclampsia or hypertensive complications were significantly more common in women with HD compared with those without HD. Mothers with cardiomyopathy and PH had the highest rates of eclampsia/preeclampsia among women with subtypes of HD.

Obstetric Complications

Obstetric complications were higher among women with versus without HD, with similar distributions among HD subtypes (Table S2). Placental insufficiency, postpartum hemorrhage, postpartum infection, and venous complications were more common in mothers with HD.

Neonatal/Fetal Outcomes

Neonatal/fetal outcomes in the offspring of women with and without HD and 4 subtypes of HD are listed in Table 3 and Figure 3B and 3C. NACE was more common in offspring of women with than without HD and most common in offspring of women with cardiomyopathy and PH compared with those with VHD and ACHD. This was primarily due to increased rates of prematurity and small-for-gestational-age birth weight. Offspring of mothers with HD had an increased rate of fetal death, in-hospital death, intrauterine growth restriction, respiratory distress syndrome, intracranial or cerebral intraventricular hemorrhage, and CHD. Among women with HD, those with cardiomyopathy and PH had the highest rates of prematurity and small-for-gestational-age birth weight. Mothers with ACHD had the highest rate of

CHD in their infants. Newborns of mothers with HD had longer length of stay, particularly the newborns of mothers with cardiomyopathy or PH. Normal birth weight >2500 g was less likely in newborns of mothers with HD (86.6% versus 94.2%). Very low birth weights of <1500 g occurred at highest rates in newborns of mothers with PH or cardiomyopathy.

Risk Factors Associated With NACE

All forms of HD were associated with an increased risk of incident NACE, with the highest risk in those with cardiomyopathy or PH. Offspring of women with VHD and ACHD also remained at risk, albeit relatively lower. Particularly among offspring of women with HD, the risk factors associated with adverse fetal/neonatal outcomes are listed on Table 4. After multivariable adjustment, preeclampsia/eclampsia or severe preeclampsia, MACE, and obstetric complications were independently associated with NACE. Diabetes mellitus was associated with NACE in newborns.

Discussion

In this contemporary study of >2.2 million admissions for delivery in New York State during a 15-year period of time, women with HD including cardiomyopathy, ACHD, VHD, and PH experienced elevated rates of MACE, mainly related to arrhythmia and heart failure. Obstetric complications were more common in women with versus without HD. Women with HD experienced longer lengths of stay, higher total hospital charges, and a higher rate of 30-day readmission compared with those without HD. In this largest ever study of neonatal outcomes, neonatal complications were significantly increased in the offspring of pregnant women with

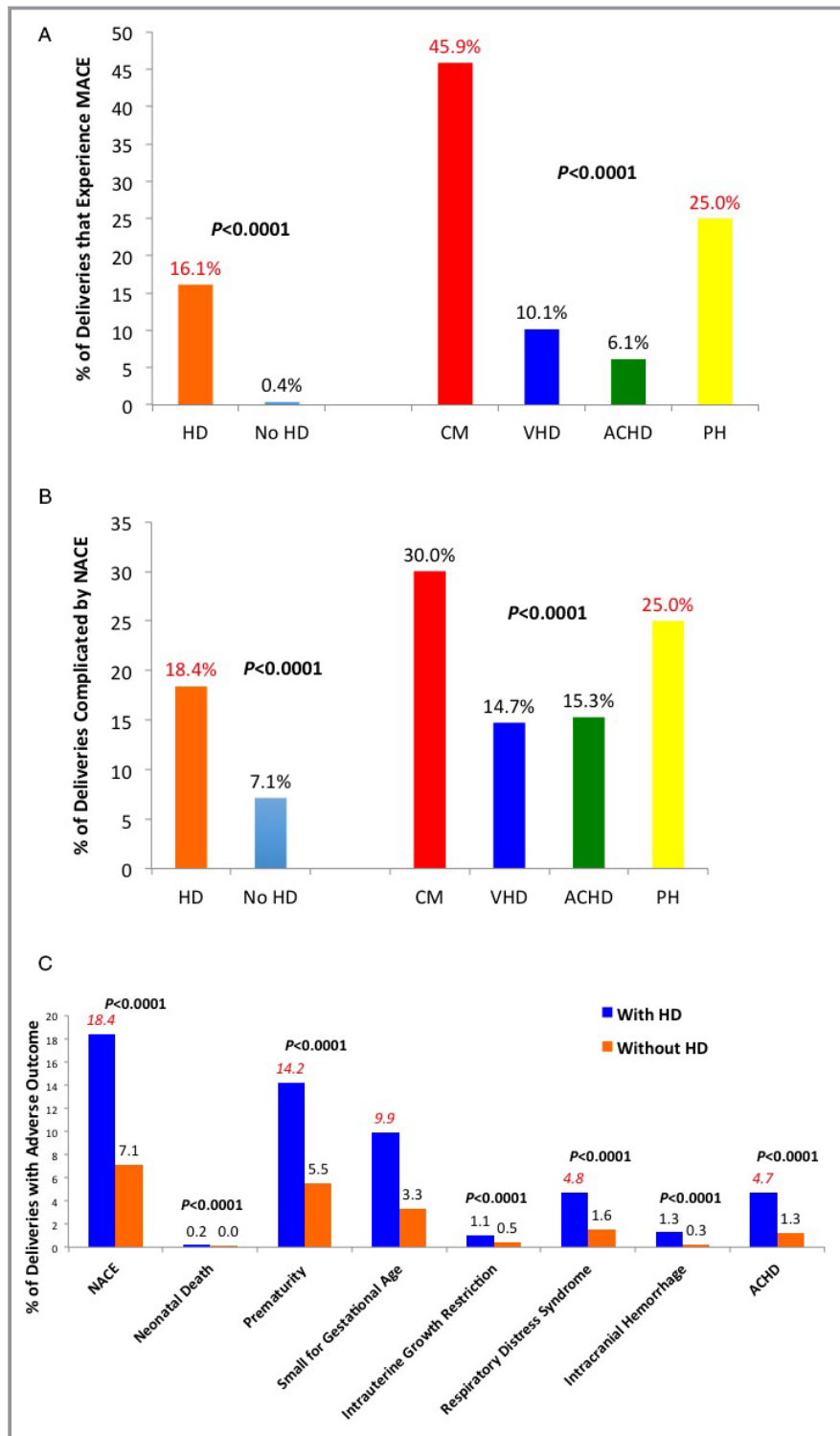


Figure 3. Maternal and neonatal adverse events. **A**, MACE in pregnant women with HD and by HD subtype. **B**, NACE in offspring of pregnant women with HD and by HD subtype. **C**, Neonatal complications in offspring of women with HD. ACHD indicates adult congenital heart disease; CM, cardiomyopathy; HD, heart disease; MACE, major adverse cardiac event; NACE, neonatal adverse clinical events; PH, pulmonary hypertension; VHD, valvular heart disease.

Table 3. Fetal/Neonatal Outcomes of Women With and Without HD in New York State, 2000–2014

Outcome	HD (n=3871)	No HD (n=2 280 173)	P Value	Cardiomyopathy (n=676)	VHD (n=1528)	ACHD (n=1367)	PH (n=300)	P Value
NACE	712 (18.4)	162 696 (7.1)	<0.0001	203 (30.0)	225 (14.7)	209 (15.3)	75 (25.0)	<0.0001
Fetal death	7 (0.2)	488 (0.0)	<0.0001	3 (0.4)	2 (0.1)	1 (0.1)	1 (0.3)	0.2673
In-hospital death	28 (0.7)	5248 (0.2)	<0.0001	10 (1.5)	6 (0.4)	10 (0.7)	2 (0.7)	0.0522
Prematurity (birth <37 wk gestation)	551 (14.2)	125 242 (5.5)	<0.0001	170 (25.2)	184 (12.0)	130 (9.5)	67 (22.3)	<0.0001
Small-for-gestational-age birth weight (<10th percentile for gestational age or weight <2500 g)	383 (9.9)	76 189 (3.3)	<0.0001	129 (19.1)	113 (7.4)	87 (6.4)	54 (18.0)	<0.0001
Intrauterine growth restriction	41 (1.7)	10 203 (0.5)	<0.0001	12 (1.8)	10 (0.7)	14 (1.0)	5 (1.7)	0.0797
Respiratory distress syndrome	184 (4.8)	35 538 (1.6)	<0.0001	76 (11.2)	52 (3.4)	26 (1.9)	30 (10.0)	<0.0001
Intracranial or cerebral intraventricular hemorrhage	50 (1.3)	6058 (0.3)	<0.0001	16 (2.4)	13 (0.9)	11 (0.8)	10 (3.3)	0.0001
CHD	182 (4.7)	28 754 (1.3)	<0.0001	27 (4.0)	45 (3.0)	96 (7.0)	14 (4.7)	<0.0001
Non-NACE variables								
Length of stay, d, mean±SD	6.0 (13.7)	3.32 (6.6)	<0.0001	10.7 (23.4)	4.7 (8.3)	4.4 (10.0)	9.4 (17.7)	<0.0001
Birth weight, g								
<1000	64 (1.7)	10 407 (0.5)	<0.0001	20 (3.0)	15 (1.0)	15 (1.1)	14 (4.7)	<0.0001
1000–1500	72 (1.9)	11 404 (0.5)		26 (3.9)	17 (1.1)	13 (1.0)	16 (5.3)	
1500–2500	381 (9.8)	110 044 (4.8)		118 (17.5)	122 (8.0)	110 (8.1)	31 (10.3)	
>2500	3354 (86.6)	2 148 318 (94.2)		512 (75.7)	1374 (89.9)	1229 (89.9)	239 (79.7)	

Data are shown as n (%) except as noted. P values were based on ANOVA for continuous outcomes and the Pearson chi-squared test or Fisher exact test for categorical outcomes. ACHD indicates adult congenital heart disease; CHD, congenital heart disease; HD, heart disease; NACE, neonatal adverse clinical events; PH, pulmonary hypertension; VHD, valvular heart disease.

HD, including fetal and in-hospital death, prematurity, small-for-gestational-age birth weight, respiratory distress syndrome, and CHD. Incident MACE and NACE were highest in women with cardiomyopathy and PH compared with those with VHD and ACHD. HD including cardiomyopathy, VHD, ACHD, and PH as well as eclampsia or preeclampsia, maternal MACE, obstetric complications, and diabetes mellitus were independently associated with a higher risk of incident NACE.

Identification of neonatal risk in women with HD has not been extensively studied but remains an important component of maternal prepregnancy assessment and decision making.^{12,19} Our study successfully identified novel predictors of adverse neonatal outcomes such as cardiac disease as a whole and specifically ACHD, cardiomyopathy, PH, and VHD, as well as comparative risk. MACE, in addition to previously known risk factors such as hypertensive syndromes and obstetric complications, was also identified. To date, neonatal complication risk stratification has been very limited, based predominantly on preexisting maternal risk scores and obstetric characteristics and mainly in

populations of ACHD. Beginning with the landmark prospective CARPREG (Cardiac Disease in Pregnancy) trial,¹¹ as well as earlier studies,²¹ in women with HD and concurrent obstetric risk factors, the risk of neonatal complications was notably higher. The ZAHARA (Zwangerschap bij Aangeboren HARTafwijkingen) study identified twin/multiple gestation, smoking during pregnancy, cyanotic HD (corrected and uncorrected), mechanical valve prosthesis, and other cardiac medication before pregnancy as risk factors for adverse neonatal events.¹⁹ Khairy and colleagues identified subaortic ventricular outflow tract gradient >30 mm Hg, oxygen saturation (per 1% decrease), smoking history, and symptomatic arrhythmia during pregnancy as predictors of neonatal events.¹⁶ The present analysis unifies prior study findings by demonstrating the risk of cardiac and obstetric characteristics and complications. Our study, in a large retrospective cohort, highlights the significance of individual forms of HD on neonatal and maternal outcomes and their relative risk compared with each other. Notably, patients with ACHD and their newborns appear to be at lower risk than those with PH or cardiomyopathy. A recent study of ACHD in an

Table 4. Risk of NACE in Offspring of Pregnant Women in New York State, 2000–2014

	OR (95% CI)	P Value
NACE risk among all pregnant women		
HD (reference: no HD)	2.8 (2.5–3.0)	
Cardiomyopathy (reference: no HD)	5.9 (5.0–7.0)	
ACHD (reference No HD)	1.8 (1.5–2.1)	
PH (reference No HD)	4.5 (3.4–5.9)	
VHD (reference No HD)	2.2 (1.9–2.6)	
NACE risk among pregnant women with HD		
Age (reference: 18–25 y)		0.1867
26–35 y	0.9 (0.8–1.2)	
>35 y	1.2 (0.9–1.5)	
Race (reference: white)		0.0758
Asian	1.0 (0.6–1.6)	
Black	1.4 (1.1–1.8)	
Hispanic	1.8 (0.8–3.8)	
Other	1.1 (0.9–1.3)	
Insurance (reference: commercial)		0.1116
Medicaid	1.2 (0.9–1.4)	
Medicare	2.1 (1.1–4.0)	
Other	0.6 (0.2–1.9)	
Eclampsia (reference normal)		<0.0001
Eclampsia	2.1 (0.4–12.1)	
Severe preeclampsia	6.5 (4.6–9.3)	
Mild preeclampsia	1.2 (0.7–1.8)	
Preeclampsia/eclampsia with preexisting hypertension	5.1 (3.0–8.6)	
Diabetes mellitus (uncomplicated)*	2.2 (1.2–4.8)	0.0269
Diabetes mellitus (complicated)*	4.3 (1.5–12.3)	0.0238
Obesity	1.0 (0.7–1.5)	0.9596
Tobacco dependence	1.8 (1.0–3.0)	0.0899
Preexisting hypertension	1.7 (1.0–3.1)	0.1115
Chronic hypertension	1.2 (0.6–2.5)	0.5906
MACE	2.3 (1.8–2.9)	<0.0001
Obstetric complications	2.9 (1.7–5.2)	<0.0001
Cardiac procedural interventions	1.6 (0.9–3.0)	0.1441
Non-cardiac-associated procedural covariates	1.6 (0.9–3.0)	0.1474

ACHD indicates adult congenital heart disease; CI, confidence interval; HD, heart disease; MACE, major adverse cardiac events; NACE, neonatal adverse clinical events; OR, odds ratio; PH, pulmonary hypertension; VHD, valvular heart disease.

*Refers to preexisting diabetes mellitus, not gestational diabetes mellitus.

administrative data set demonstrated that although maternal cardiac complications were uncommon in the overall population, they were higher in those with complex ACHD.¹⁵

Neonatal complications tended to follow a pattern similar to maternal and obstetric outcomes. They were highest in the offspring of cardiomyopathy and PH patients and lower in ACHD and VHD patients. NACE in the offspring of women with HD was slightly higher than past estimations of 5% to 7% in patients without any obstetric risk factors and lower than the previously reported projections of 27% to 33% in patients with obstetric risk factors.¹² CHD recurred in offspring of mothers with ACHD, with a prevalence similar to those in previous reports.²² Notably, however, other populations of women with HD (VHD, cardiomyopathy, and PH) also gave birth to offspring with CHD above the approximate risk of 1% in the general population, a finding that requires further study. Notably, age, chronic hypertension, and obesity were not found to be risk factors for neonatal adverse events in multivariable analysis in this cohort of women with HD, contrary to published reports for the general population.^{23–26} Nevertheless, both age and obesity could have contributed to obstetric complications, either directly or indirectly, which were significantly related to NACE.

The largest contributors to adverse neonatal outcomes were prematurity and small-for-gestational-age birth weight, common issues associated with prematurity. Although not captured in our study, prematurity and extremely low birth weight are known to pose increased risk for complications in early life through adulthood. Newborns and children can have respiratory issues, asthma, developmental delays, intestinal problems, infections, hearing loss, and retinopathy, among other issues.²⁷

We also found a significantly higher prevalence of preeclampsia/eclampsia or other hypertensive syndromes in women with HD compared with those without HD, a finding that we^{6,8,9} and others have observed previously in various study populations.^{15,28} Preeclampsia alone, without the presence of overlapping HD, is a life-threatening disorder that, once evident clinically, can be cured only by delivery. Coupled with HD, the combination can be extremely high risk. In developed countries, surveillance through prenatal visits allows for early identification and intervention, which has been shown to be effective in reducing maternal mortality in women without HD. Although not well elucidated, reduced placental perfusion may cause preeclampsia,²⁸ which could be more common in women with HD than those without. It has been shown previously that, in women with HD, a decline in maternal cardiac output during pregnancy occurs, as well as abnormal umbilical artery Doppler flows, and that these factors independently predict neonatal complications.²⁹ These types of changes may result in placental ischemia, particularly in women with cardiomyopathy.³⁰ Moreover, in a recent report, offspring CHD was strongly associated with maternal preterm preeclampsia.³¹ Women at high risk of

preeclampsia, regardless of a history of HD, including those with a history of preeclampsia, multifetal gestation, chronic hypertension, diabetes mellitus, renal disease, and autoimmune diseases, are recommended to use low-dose aspirin after 12 weeks of gestation to reduce the risk of preeclampsia, preterm birth, and intrauterine growth restriction.^{32,33} Whether or not aspirin can be recommended in women with HD remains to be determined by future investigation.

The effects of the complications of HD on the neonate make appropriate prenatal counseling critical for mothers with preexisting HD who are considering becoming pregnant. This type of counseling is complex and should be done by a comprehensive team of physicians, including primary care and specialists, to most effectively offer guidance and support to the patient. It requires expert advice on the assessment of maternal and fetal/neonatal risk of pregnancy, labor and delivery, timing of pregnancy, timing of pregnancy relative to future surgery or intervention, management during and after pregnancy, discontinuation of medications that may be teratogenic or continuation of medications that may prevent symptoms or complications during pregnancy, and proper knowledge of contraceptive choices appropriate for a patient's condition before the decision to become pregnant is made.

Study Limitations

Despite the large number of women with HD and their offspring captured in this study, these data should be interpreted within the context of several limitations. SPARCS is a New York State regional database, and although New York is a diverse state, these findings may not be generalizable to the entire United States. However, the data in this study appear to be similar to the findings from the National Inpatient Sample in terms of maternal risk.⁶ Our study delineates a low (0.2%) incidence of HD; however, the analytical cohort is a subsection of the overall patient population captured in the SPARCS database. Consequently, because of the exclusion criteria applied, it may be possible that HD patient representation was selected from the overall population. Our study utilizes administrative and procedural codes (*ICD-9-CM*) and birth certificate linkage, instead of medical chart review. *ICD-9* codes have imperfect sensitivity and specificity.³⁴ Under-coding or miscoding are possibilities, although this would be unlikely to bias the results, because even a small number of misclassifications would not have a sizable effect on summary estimates of >2.2 million women. Obstetric complication rates were high in our study population, even in the control group, potentially related to inclusion of multiple nonspecific codes. Moreover, the administrative nature of the data set does not allow verification of

diagnoses; certain aspects of patient history, imaging data, laboratory values, medications, and long-term follow-up were not available for analysis. Moreover, the SPARCS data set did not allow reliable linking of mothers to neonates in certain instances (multiple births and repeat pregnancies), and many records had to be eliminated from the analysis because of concern about reliability issues. In addition, the inpatient nature of this data set does not allow us to capture the intensity or quality of care before and after the delivery hospitalization for mothers or neonates. Deaths, events, or hospitalizations after the index delivery hospitalization would not be included.

Conclusions

In this study of >2.2 million admissions for delivery in New York State during a 15-year period of time, women with HD including cardiomyopathy, ACHD, VHD, and PH experienced elevated rates of MACE, mainly related to arrhythmia and heart failure. Obstetric complications were more common in women with HD compared with those without HD. Neonatal complications were significantly increased in the offspring of pregnant women with HD, including fetal and in-hospital neonatal death, prematurity, small-for-gestational-age birth weight, respiratory distress syndrome, and CHD. Incident MACE and NACE were highest in women with cardiomyopathy and PH compared with those with VHD and ACHD. Eclampsia, preeclampsia, maternal MACE, obstetric complications, and diabetes mellitus were independently associated with a higher risk of incident NACE among women with HD. These results may guide monitoring decisions and risk assessment for pregnant women with HD and their offspring at the time of delivery. Given the higher rate of cardiac, obstetric, and neonatal complications, pregnant women with HD should be treated in a center with expertise in this area, with a multidisciplinary approach to labor and delivery. Prenatal counseling of fetal risks is warranted in women with HD.

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Disclosures

None.

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Supplemental Material

Table S1. Data Extraction. Codes Used for Variable Definition.

Codes Used for Variable Definition

1. Delivery records extraction

- 1.1.(DX): 650, 651.00, 651.01, 651.03, 651.10, 651.11, 651.13, 651.20, 651.21, 651.23, 651.30, 651.31, 651.33, 651.40, 651.41, 651.43, 651.50, 651.51, 651.53, 651.60, 651.61, 651.63, 651.70, 651.71, 651.73, 651.80, 651.81, 651.83, 651.90, 651.91, 651.93, 652.00, 652.01, 652.03, 652.10, 652.11, 652.13, 652.20, 652.21, 652.23, 652.30, 652.31, 652.33, 652.40, 652.41, 652.43, 652.50, 652.51, 652.53, 652.60, 652.61, 652.63, 652.70, 652.71, 652.73, 652.80, 652.81, 652.83, 652.90, 652.91, 652.93, 653.00, 653.01, 653.03, 653.10, 653.11, 653.13, 653.20, 653.21, 653.23, 653.30, 653.31, 653.33, 653.40, 653.41, 653.43, 653.50, 653.51, 653.53, 653.60, 653.61, 653.63, 653.70, 653.71, 653.73, 653.80, 653.81, 653.83, 653.90, 653.91, 653.93, 654.00, 654.01, 654.02, 654.03, 654.04, 654.10, 654.11, 654.12, 654.13, 654.14, 654.20, 654.21, 654.23, 654.30, 654.31, 654.32, 654.33, 654.34, 654.40, 654.41, 654.42, 654.43, 654.44, 654.50, 654.51, 654.52, 654.53, 654.54, 654.60, 654.61, 654.62, 654.63, 654.64, 654.70, 654.71, 654.72, 654.73, 654.74, 654.80, 654.81, 654.82, 654.83, 654.84, 654.90, 654.91, 654.92, 654.93, 654.94, 655.00, 655.01, 655.03, 655.10, 655.11, 655.13, 655.20, 655.21, 655.23, 655.30, 655.31, 655.33, 655.40, 655.41, 655.43, 655.50, 655.51, 655.53, 655.60, 655.61, 655.63, 655.70, 655.71, 655.73, 655.80, 655.81, 655.83, 655.90, 655.91, 655.93, 656.00, 656.01, 656.03, 656.10, 656.11, 656.13, 656.20, 656.21, 656.23, 656.30, 656.31, 656.33, 656.40, 656.41, 656.43, 656.50, 656.51, 656.53, 656.60, 656.61, 656.63, 656.70, 656.71, 656.73, 656.80, 656.81, 656.83, 656.90, 656.91, 656.93, 657.00, 657.01, 657.03, 658.00, 658.01, 658.03, 658.10, 658.11, 658.13, 658.20, 658.21, 658.23, 658.30, 658.31, 658.33, 658.40, 658.41, 658.43, 658.80, 658.81, 658.83, 658.90, 658.91, 658.93, 659.00, 659.01, 659.03, 659.10, 659.11, 659.13, 659.20, 659.21, 659.23, 659.30, 659.31, 659.33, 659.40, 659.41, 659.43, 659.50, 659.51, 659.53, 659.60, 659.61, 659.63, 659.70, 659.71, 659.73, 659.80, 659.81, 659.83, 659.90, 659.91, 659.93, V27.0, V27.1, V27.2, V27.3, V27.4, V27.5, V27.6, V27.7, V27.9
- 1.2.(PR): 72.0, 72.1, 72.21, 72.29, 72.31, 72.39, 72.4, 72.51, 72.52, 72.53, 72.54, 72.6, 72.71, 72.79, 72.8, 72.9, 73.01, 73.09, 73.1, 73.21, 73.22, 73.3, 73.4, 73.51, 73.59, 73.6, 73.8, 73.91, 73.92, 73.93, 73.94, 73.99, 74.0, 74.1, 74.2, 74.3, 74.4, 74.91, 74.99, 75.0, 75.1, 75.2, 75.31, 75.32, 75.33, 75.34, 75.35, 75.36, 75.37, 75.38, 75.4, 75.50, 75.51, 75.52, 75.61, 75.62, 75.69, 75.7, 75.8, 75.91, 75.92, 75.93, 75.94, 75.99

2. Maternal clinical information and characteristics

2.1 Delivery type

2.1.1 Vaginal: 650

2.1.2 Cesarean

2.1.2.1 Cesarean_PR: 74.0, 74.1, 74.2, 74.3, 74.4, 74.91, 74.99

2.1.2.2 Cesarean_DX: 669.70, 669.71, 763.4, 649.81, 649.82

2.1.3 Assisted (Forceps, Vacuum): 72.0, 72.1, 72.21, 72.29, 72.31, 72.39, 72.4, 72.6, 72.71, 72.79, 72.8, 72.9

2.1.4 Breech: 72.51, 72.52, 72.53, 72.54

2.1.5 Stillbirth: 656.40

2.1.6 Others_73_75: 73.01, 73.09, 73.1, 73.21, 73.22, 73.3, 73.4, 73.51, 73.59, 73.6, 73.8, 73.91, 73.92, 73.93, 73.94, 73.99, 75.0, 75.1, 75.2, 75.31, 75.32, 75.33, 75.34, 75.35, 75.36, 75.37, 75.38, 75.4, 75.50, 75.51, 75.52, 75.61, 75.62, 75.69, 75.7, 75.8, 75.91, 75.92, 75.93, 75.94, 75.99

2.2 Heart Disease (CDM > VHD > CHD > PH)

- 2.1.1 **Cardiomyopathy (CDM):** Multiple-CDM cases were removed because of the specific requirement “Patients with more than one cardiomyopathy (CDM) diagnosis will be excluded” in the file “Jie Analysis objectives and questions-20151223 KS 1-5-16” ;
 - 2.1.1.1 CDM_PPCM: 674.50, 674.51, 674.52, 674.53, 674.54
 - 2.1.1.2 CDM_Hypertrophic: 425.11, 425.18
 - 2.1.1.3 CDM_Other (Dilated, Restrictive and Other Secondary Cardiomyopathy): 425.0, 425.2, 425.3, 425.4, 425.5, 425.7, 425.8, 425.9
- 2.1.2 **Valvular Heart Disease (VHD):** 394.0, 394.1, 394.2, 394.9, 395.0, 395.1, 395.2, 395.9, 396.0, 396.1, 396.2, 396.3, 396.8, 396.9, 397.0, 397.1, 397.9, 424.1, 424.2, 424.3, 424.90, 424.91, 424.99, V42.2, V43.3
- 2.1.3 **Congenital Heart Disease (CHD):** 745.0, 745.10, 745.11, 745.12, 745.19, 745.2, 745.3, 745.4, 745.5, 745.60, 745.61, 745.69, 745.7, 745.8, 745.9, 746.00, 746.01, 746.02, 746.09, 746.1, 746.2, 746.3, 746.4, 746.5, 746.6, 746.7, 746.81, 746.82, 746.83, 746.84, 746.85, 746.86, 746.87, 746.89, 746.9, V13.65. Exclude 747.5, 747.60, 747.61, 747.62, 747.63, 747.64, 747.69, 747.81, 747.82, 747.83, 747.89
- 2.1.4 **Pulmonary Hypertension (PH):** 415.0, 416.0, 416.1, 416.8, 416.9, 417.0, 417.1, 417.8, 417.9

2.3 Age: 18-25, 26-35, >35

2.4 Race

2.5 Insurance Status

2.6 NY Region

2.7 Tobacco Dependence: 305.1

2.8 Alcohol Dependence: 303.00, 303.01, 303.02, 303.03, 303.90, 303.91, 303.92, 303.93

2.9 Drug Dependence: 304.00, 304.01, 304.02, 304.03, 304.10, 304.11, 304.12, 304.13, 304.20, 304.21, 304.22, 304.23, 304.30, 304.31, 304.32, 304.33, 304.40, 304.41, 304.42, 304.43, 304.50, 304.51, 304.52, 304.53, 304.60, 304.61, 304.62, 304.63, 304.70, 304.71, 304.72, 304.73, 304.80, 304.81, 304.82, 304.83, 304.90, 304.91, 304.92, 304.93

2.10 Obesity: 278.00, 278.01, 278.02, 278.03

2.11 Long Term Use of Anticoagulants: V58.61

2.12 Central Cyanosis: 782.5

2.13 Diabetes Mellitus (Uncomplicated): 249.00, 250.00, 250.01, 790.21, 790.22, 790.29, 791.5, 791.6, V45.85, V53.91, V65.46

2.14 Diabetes Mellitus (Complicated): 249.01, 249.10, 249.11, 249.20, 249.21, 249.30, 249.31, 249.40, 249.41, 249.50, 249.51, 249.60, 249.61, 249.70, 249.71, 249.80, 249.81, 249.90, 249.91, 250.02, 250.03, 250.10, 250.11, 250.12, 250.13, 250.20, 250.21, 250.22, 250.23, 250.30, 250.31, 250.32, 250.33, 250.40, 250.41, 250.42, 250.43, 250.50, 250.51, 250.52, 250.53, 250.60, 250.61, 250.62, 250.63, 250.70, 250.71, 250.72, 250.73, 250.80, 250.81, 250.82, 250.83, 250.90, 250.91, 250.92, 250.93

2.15 Transient Hypertension of Pregnancy: 642.30, 642.31, 642.32, 642.33, 642.34

2.16 Eclampsia (Eclampsia Complicating Pregnancy/Childbirth > Severe Preeclampsia > Mild Preeclampsia > Pre-eclampsia/Eclampsia with Pre-existing HTN)

- 2.16.1 Eclampsia Complicating Pregnancy/Childbirth: 642.60, 642.61, 642.62, 642.63, 642.64
- 2.16.2 Severe Preeclampsia: 642.50, 642.51, 642.52, 642.53, 642.54
- 2.16.3 Mild Preeclampsia: 642.40, 642.41, 642.42, 642.43, 642.44
- 2.16.4 Pre-eclampsia/Eclampsia with Pre-existing HTN: 642.70, 642.71, 642.72, 642.73, 642.74
- 2.17 Pre-existing Hypertension:** 642.20, 642.21, 642.23
- 2.18 Chronic Hypertension:** 401.9
- 2.19 Length of Stay:** Discharge Date – Admission Date
- 2.20 Total hospital charge**

3. Maternal outcomes

3.1. Major Adverse Cardiac Events (MACE)

- 3.1.1. In-hospital Death: SPARCS variable “DISP”=”20”, “40”, “41”, or “42”
- 3.1.2. Cardiac Arrest: 427.5
- 3.1.3. Acute Myocardial Infarction: 410.00, 410.01, 410.02, 410.10, 410.11, 410.12, 410.20, 410.21, 410.22, 410.30, 410.31, 410.32, 410.40, 410.41, 410.42, 410.50, 410.51, 410.52, 410.60, 410.61, 410.62, 410.70, 410.71, 410.72, 410.80, 410.81, 410.82, 410.90, 410.91, 410.92, 411.0, 411.1, 411.81, 411.89
- 3.1.4. Heart Failure: 428.0, 428.1, 428.20, 428.21, 428.22, 428.23, 428.30, 428.31, 428.32, 428.33, 428.40, 428.41, 428.42, 428.43, 428.9, 402.91
- 3.1.5. Arrhythmia: 426.0, 426.10, 426.11, 426.12, 426.13, 426.2, 426.3, 426.4, 426.50, 426.51, 426.52, 426.53, 426.54, 426.6, 426.7, 426.81, 426.82, 426.89, 426.9, 427.0, 427.1, 427.2, 427.31, 427.32, 427.41, 427.42, 427.5, 427.60, 427.61, 427.69, 427.81, 427.89, 427.9
- 3.1.6. Cerebrovascular Events: 430, 431, 432.0, 432.1, 432.9, 433.00, 433.01, 433.10, 433.11, 433.20, 433.21, 433.30, 433.31, 433.80, 433.81, 433.90, 433.91, 434.00, 434.01, 434.10, 434.11, 434.90, 434.91, 435.0, 435.1, 435.2, 435.3, 435.8, 435.9, 436, 437.0, 437.1, 437.2, 437.3, 437.4, 437.5, 437.6, 437.7, 437.8, 437.9
- 3.1.7. Pulmonary Embolism: 415.11, 415.12, 415.13, 415.19
- 3.1.8. Arterial Embolism: 444.01, 444.09, 444.1, 444.21, 444.22, 444.81, 444.89, 444.9
- 3.1.9. Atheroembolism: 445.01, 445.02, 445.81, 445.89
- 3.1.10. Obstetrical Pulmonary Embolism: 673.00, 673.01, 673.02, 673.03, 673.04, 673.10, 673.11, 673.12, 673.13, 673.14, 673.20, 673.21, 673.22, 673.23, 673.24, 673.30, 673.31, 673.32, 673.33, 673.34, 673.80, 673.81, 673.82, 673.83, 673.84
- 3.1.11. Cardiac Complications of Anesthesia or other Sedation in Labor and Delivery: 668.10, 668.11, 668.12, 668.13, 668.14
- 3.1.12. Cardiorespiratory Failure or Shock: 785.50, 785.51
- 3.1.13. Respiratory Failure: 517.3, 518.51, 518.52, 518.53, 518.81, 518.82, 518.83, 518.84, 799.1, V46.11, V46.12, V46.13, V46.14, V46.2
- 3.1.14. Dissection of the Aorta: 441.00, 441.01, 441.02, 441.03, 441.1, 441.2, 441.3, 441.6
- 3.1.15. Dissection of another Artery: 443.21, 443.22, 443.23, 443.24, 443.29

3.2. Non- MACE Outcomes

3.2.1. 30-Day Readmission

3.2.2. Acute Renal Failure: 584.5, 584.6, 584.7, 584.8, 584.9, 586

3.3.Procedural Interventions

- 3.3.1. Heart Transplantation: 37.51
- 3.3.2. Implantation or Replacement/Repair/Removal of Heart Replacement or Assist Systems such as Total Internal Single or Biventricular System: 37.52, 37.53, 37.54, 37.55, 37.60, 37.63, 37.64, 37.65, 37.66
- 3.3.3. Implantation of Pulsation Balloon: 37.61
- 3.3.4. Insertion of Temporary Non-implantable Extracorporeal Circulatory Assist Device: 37.62
- 3.3.5. Open Chest Cardiac Massage: 37.91
- 3.3.6. Implantation or Replacement of Automatic Cardioverter or Resynchronization Defibrillator Systems: 37.94, 00.51
- 3.3.7. Implantation or Replacement AICD Lead(s) or Pulse Generator: 37.95, 37.96, 37.97, 37.98
- 3.3.8. Implantation or Replacement of CRT-D Pulse Generator: 00.53, 00.54
- 3.3.9. Implantation or Replacement of Transvenous Lead [Electrode] into Left Ventricular Coronary venous system: 00.52
- 3.3.10. Rates of Right and Left Heart Cardiac Catheterization: 37.21, 37.22, 37.23

3.4.Non-cardiac Associated Procedural Covariates

- 3.4.1. Mechanical Ventilation: 96.70, 96.72
- 3.4.2. Non-invasive Positive Pressure Ventilation: 93.90
- 3.4.3. Continuous Intra-arterial Blood Gas Monitoring: 89.60
- 3.4.4. Systemic Arterial Pressure Monitoring: 89.61
- 3.4.5. Central Venous Pressure Monitoring: 89.62
- 3.4.6. Pulmonary Artery Pressure Monitoring 89.63
- 3.4.7. Pulmonary Artery Wedge Monitoring: 89.64
- 3.4.8. Measurement of Systemic Arterial Blood Gases: 89.65

4. Obstetric Complications

- 4.1.1. Gestational Diabetes Mellitus: 648.00, 648.01, 648.02, 648.03, 648.04, 648.80, 648.81, 648.82, 648.83, 648.84
- 4.1.2. Postpartum Infection: 670.00, 670.02, 670.04, 670.10, 670.12, 670.14, 670.20, 670.22, 670.24, 670.30, 670.32, 670.34, 670.80, 670.82, 670.84
- 4.1.3. Laceration (Third/Fourth Degree): 664.20, 664.21, 664.24, 664.30, 664.31, 664.34, 664.40, 664.41, 664.44, 664.50, 664.51, 664.54, 664.60, 664.61, 664.64
- 4.1.4. Antepartum Hemorrhage Abruptio Placentae and Placenta Previa: 641.00, 641.01, 641.03, 641.10, 641.11, 641.13, 641.20, 641.21, 641.23, 641.30, 641.31, 641.33, 641.80, 641.81, 641.83, 641.90, 641.91, 641.93
- 4.1.5. Known or Suspected Fetal Abnormality Affecting Management of Mother: 655.00, 655.01, 655.03, 655.10, 655.11, 655.13, 655.20, 655.21, 655.23, 655.30, 655.31, 655.33, 655.40, 655.41, 655.43, 655.50, 655.51, 655.53, 655.60, 655.61, 655.63, 655.70, 655.71, 655.73, 655.80, 655.81, 655.83, 655.90, 655.91, 655.93

- 4.1.6. Polyhydramnios: 657.00, 657.01, 657.03
- 4.1.7. Premature Rupture of Membranes: 658.13
- 4.1.8. Other Indications for Care or Intervention Related to Labor and Delivery not elsewhere Classified: 659.00, 659.01, 659.03, 659.10, 659.11, 659.13, 659.20, 659.21, 659.23, 659.30, 659.31, 659.33, 659.40, 659.41, 659.43, 659.50, 659.51, 659.53, 659.60, 659.61, 659.63, 659.70, 659.71, 659.73, 659.80, 659.81, 659.83, 659.90, 659.91, 659.93
- 4.1.9. Venous Complications in Pregnancy and the Puerperium: 671.00, 671.01, 671.02, 671.03, 671.04, 671.10, 671.11, 671.12, 671.13, 671.14, 671.20, 671.21, 671.22, 671.23, 671.24, 671.30, 671.31, 671.33, 671.40, 671.42, 671.44, 671.50, 671.51, 671.52, 671.53, 671.54, 671.80, 671.81, 671.82, 671.83, 671.84, 671.90, 671.91, 671.92, 671.93, 671.94
- 4.1.10. Breech Delivery (Assisted) (Spontaneous) NOS: 652.10, 652.11, 652.13, 652.20, 652.21, 652.23
- 4.1.11. Delivery by Vacuum Extractor, Forceps, Cesarean Section, or Breech Extraction, without Specified Complication: 669.50, 669.51, 669.60, 669.61, 669.70, 669.71
- 4.1.12. Placental Insufficiency: 656.50, 656.51, 656.53
- 4.1.13. (Planned) Occurring after 37 Completed Weeks of Gestation but before 39 Completed Weeks Gestation due to (Spontaneous) Onset of Labor: 649.81, 649.82
- 4.1.14. Hemorrhage in Early Pregnancy: 640.00, 640.01, 640.03, 640.80, 640.81, 640.83, 640.90, 640.91, 640.93
- 4.1.15. Early or Threatened Labor: 644.00, 644.03, 644.10, 644.13, 644.20, 644.21
- 4.1.16. Late Pregnancy: 645.10, 645.11, 645.13, 645.20, 645.21, 645.23
- 4.1.17. Obstructed Labor: 660.00, 660.01, 660.03, 660.10, 660.11, 660.13, 660.20, 660.21, 660.23, 660.30, 660.31, 660.33, 660.40, 660.41, 660.43, 660.50, 660.51, 660.53, 660.60, 660.61, 660.63, 660.70, 660.71, 660.73, 660.80, 660.81, 660.83, 660.90, 660.91, 660.93
- 4.1.18. Abnormality of Forces of Labor: 661.00, 661.01, 661.03, 661.10, 661.11, 661.13, 661.20, 661.21, 661.23, 661.30, 661.31, 661.33, 661.40, 661.41, 661.43, 661.90, 661.91, 661.93
- 4.1.19. Long Labor: 662.00, 662.01, 662.03, 662.10, 662.11, 662.13, 662.20, 662.21, 662.23, 662.30, 662.31, 662.33
- 4.1.20. Postpartum Hemorrhage: 666.00, 666.02, 666.04, 666.10, 666.12, 666.14, 666.20, 666.22, 666.24, 666.30, 666.32, 666.34
- 4.1.21. Complications of the Administration of Anesthetic or other Sedation in Labor and Delivery: 668.00, 668.01, 668.02, 668.03, 668.04, 668.10, 668.11, 668.12, 668.13, 668.14, 668.20, 668.21, 668.22, 668.23, 668.24, 668.80, 668.81, 668.82, 668.83, 668.84, 668.90, 668.91, 668.92, 668.93, 668.94

5. Fetal/Neonatal Outcomes

5.1. Gender

5.2. LOS

5.3. Fetal Death: 768.0, 768.1, 768.2, 779.85, 656.40, 656.41, 656.43, 632

5.4. Neonatal Death: die after birth, in hospital within 30 days after birth

5.5. Prematurity [Birth < 37 Weeks Gestation]: 765.00-19, 765.21, 765.22, 765.23, 765.24, 765.25, 765.26, 765.27, 765.28

5.6. Small for Gestational Age Birth Weight [Birth Weight Less than < 10th Percentile for Gestational Age or Weight Less than 2500 g]: V21.30, V21.31, V21.32, V21.33, V21.34, V21.35, 765.01, 765.02, 765.03, 765.04, 765.05, 765.06, 765.07, 765.08, 765.10, 765.11, 765.12, 765.13, 765.14, 765.15, 765.16, 765.17, 765.18

- 5.7. Intrauterine Growth Restriction: 764.90, 764.91, 764.92, 764.93, 764.94, 764.95, 764.96, 764.97, 764.98, 764.99
- 5.8. Respiratory Distress Syndrome: 769
- 5.9. Intracranial Hemorrhage or Cerebral Intraventricular Hemorrhage: 772.10, 772.11, 772.12, 772.13, 772.14, 772.2, 767.0
- 5.10. Congenital Heart Disease: 745.0, 745.10, 745.11, 745.12, 745.19, 745.20, 745.30, 745.40, 745.50, 745.60, 745.61, 745.69, 745.70, 745.80, 745.90, 746.00, 746.01, 746.02, 746.09, 746.1, 746.2, 746.30, 746.40, 746.50, 746.60, 746.70, 746.80, 746.81, 746.82, 746.83, 746.84, 746.85, 746.86, 746.87, 746.89, 746.9
- 5.11. Birth Weight: (ELBW:"<1000", VLBW:"1000-1500", LBW:"1500-2500", NBW:">=2500")

Table S2. Obstetric Complications of Women with and without Heart Disease in New York State 2000-2014.

Outcome	Heart Disease (n=3871)	No Heart Disease (n=2280173)	p-value	CM (n=676)	VHD (n=1528)	CHD (n=1367)	PH (n=300)	p-value
Obstetric Complications	2595 (67.0%)	1332569 (58.4%)	<.0001	501 (74.1%)	974 (63.7%)	897 (65.6%)	223 (74.3%)	<.0001
(Planned) Occurring after 37 Completed Weeks of Gestation but before 39 Completed Weeks Gestation due to (Spontaneous) Onset of Labor	2 (0.1%)	1591 (0.1%)	0.7780	1 (0.2%)	0 (0.0%)	1 (0.1%)	0 (0.0%)	0.5849
Abnormality of Forces of Labor	454 (11.7%)	271255 (11.9%)	0.7470	82 (12.1%)	188 (12.3%)	145 (10.6%)	39 (13.0%)	0.4364
Antepartum Hemorrhage Abruptio Placentae and Placenta Previa	114 (2.9%)	34113 (1.5%)	<.0001	34 (5.0%)	40 (2.6%)	30 (2.2%)	10 (3.3%)	0.0033
Breech Delivery (Assisted) (Spontaneous) NOS	172 (4.4%)	75307 (3.3%)	<.0001	30 (4.4%)	60 (3.9%)	67 (4.9%)	15 (5.0%)	0.6031
Complications of the Administration of Anesthetic or other Sedation in Labor and Delivery	46 (1.2%)	8278 (0.4%)	<.0001	16 (2.4%)	20 (1.3%)	9 (0.7%)	1 (0.3%)	0.0040
Delivery by Vacuum Extractor, Forceps, Cesarean Section, or Breech Extraction, without Specified Complication	36 (0.9%)	24230 (1.1%)	0.4212	6 (0.9%)	14 (0.9%)	15 (1.1%)	1 (0.3%)	0.6615
Early or Threatened Labor	458 (11.8%)	128623 (5.6%)	<.0001	138 (20.4%)	158 (10.3%)	107 (7.8%)	55 (18.3%)	<.0001
Gestational Diabetes Mellitus	328 (8.5%)	134197 (5.9%)	<.0001	88 (13.0%)	115 (7.5%)	88 (6.4%)	37 (12.3%)	<.0001

Outcome	Heart Disease (n=3871)	No Heart Disease (n=2280173)	p-value	CM (n=676)	VHD (n=1528)	CHD (n=1367)	PH (n=300)	p-value
Hemorrhage in Early Pregnancy	4 (0.1%)	282 (0.0%)	0.0014	2 (0.3%)	2 (0.1%)	0 (0.0%)	0 (0.0%)	0.1962
Known or Suspected Fetal Abnormality Affecting Management of Mother	95 (2.5%)	23188 (1.0%)	<.0001	8 (1.2%)	31 (2.0%)	51 (3.7%)	5 (1.7%)	0.0012
Laceration (Third/Fourth Degree)	123 (3.2%)	77460 (3.4%)	0.4510	13 (1.9%)	56 (3.7%)	42 (3.1%)	12 (4.0%)	0.1481
Late Pregnancy	496 (12.8%)	374935 (16.4%)	<.0001	67 (9.9%)	185 (12.1%)	201 (14.7%)	43 (14.3%)	0.0130
Long Labor	32 (0.8%)	23501 (1.0%)	0.2092	5 (0.7%)	11 (0.7%)	12 (0.9%)	4 (1.3%)	0.7391
Obstructed Labor	148 (3.8%)	82792 (3.6%)	0.5227	22 (3.3%)	55 (3.6%)	62 (4.5%)	9 (3.0%)	0.3558
Placental Insufficiency	116 (3.0%)	37803 (1.7%)	<.0001	24 (3.6%)	33 (2.2%)	48 (3.5%)	11 (3.7%)	0.1067
Polyhydramnios	44 (1.1%)	16072 (0.7%)	0.0013	3 (0.4%)	17 (1.1%)	20 (1.5%)	4 (1.3%)	0.2313
Postpartum Hemorrhage	176 (4.6%)	55731 (2.4%)	<.0001	49 (7.3%)	59 (3.9%)	53 (3.9%)	15 (5.0%)	0.0022
Postpartum Infection	90 (2.3%)	16845 (0.7%)	<.0001	45 (6.7%)	17 (1.1%)	14 (1.0%)	14 (4.7%)	<.0001
Premature Rupture of Membranes	0 (0.0%)	34 (0.0%)	1.0000	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	.
Venous Complications in Pregnancy and the Puerperium	55 (1.4%)	18321 (0.8%)	<.0001	20 (3.0%)	16 (1.1%)	14 (1.0%)	5 (1.7%)	0.0022

CM = cardiomyopathy, VHD = valvular heart disease, CHD = congenital heart disease, PH = pulmonary hypertension, NOS = not otherwise specified
 *P-values were based on Pearson's chi-squared test or Fisher's exact test.