

Contemporary pregnancy outcomes for women with moderate and severe congenital heart disease

**Short title:** Pregnancy in congenital heart disease

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**Guarantor:** MDS

**Contributorship:** SAK, DDS and MDS researched literature and conceived the study. JAG, SEK and MDS devised the methodology. MDS performed formal analyses. SAK wrote the first draft of the manuscript. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

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**Abstract**

*Background:* Women with congenital heart disease (CHD) are surviving into adulthood, with more undergoing pregnancy.

*Methods:* Retrospective review of the Vizient database from 2017-2019 for women 15-44 years old with moderate, severe or no CHD and vaginal delivery or caesarian section. Demographics, hospital outcomes and costs were compared.

*Results:* There were 2,469,117 admissions: 2,467,589 with no CHD, 1,277 with moderate and 251 with severe CHD. Both CHD groups were younger than no CHD, there were fewer white race/ethnicity in the no CHD group and more women with Medicare in both CHD groups compared to no CHD. With increasing CHD severity there was an increase in length of stay, ICU admission rates and costs. There were also higher rates of complications, mortality and caesarian section in the CHD groups.

*Conclusion:* Pregnant women with CHD have more problematic pregnancies and understanding this impact is important to improve management and decrease healthcare utilization.

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## **Background**

The number of adults living with congenital heart disease (CHD) has increased as a result of advances in medical and surgical management. This has led to an increase in the prevalence of women with CHD from 6.4 to 9.0 per 10 000 delivery hospitalizations from 2000-2010.(1) During pregnancy, there are increased demands on the cardiovascular system due to increased cardiac output, elevated resting heart rate and decreased systemic vascular resistance, putting women with CHD, who may have little reserve, at risk throughout pregnancy and delivery. Studies of pregnancy in women with CHD have found higher rates of maternal cardiac comorbidities and pregnancy-related adverse events including heart failure, dysrhythmias, pulmonary edema, pulmonary hypertension, thromboembolic events and pre-eclampsia.(1-11) The fetuses and neonates are also at increased risk with higher rates of adverse events including preterm delivery, intrauterine growth restriction (IUGR) and fetal and neonatal demise.(4-10, 12-14)

These data have been enlightening, but the most recent reports have only analyzed data through 2013, while the population of women of child-bearing age with CHD, particularly complex CHD such as those with single ventricle physiology post-Fontan palliation, has continued to increase, making an update on current pregnancy outcomes imperative. In addition, new guidelines for the care of patients with Adult CHD were published in 2018, which include more physiologic categorization of the severity of CHD, and there have not been new studies of pregnancy in CHD since this publication.(15) Accordingly, prior studies have included all forms of CHD, including women with small

intracardiac shunts which are considered Simple CHD in the new guidelines, and these women would physiologically be essentially the same as women without CHD and should be expected to have the same pregnancy outcomes. We hypothesize that the increasing complexity of CHD in pregnant women leads to worse outcomes compared to women without CHD. The purpose of the present study is to report the most contemporary cardiac and pregnancy-related comorbidities and hospital outcomes for pregnant women with moderate and severe CHD and to compare these outcomes to pregnant women without CHD.

## **Methods**

The Vizient Clinical Data Base/Resource Manager™ is an analytic platform for performance improvement populated by hundreds of health systems and community hospitals nationwide in the United States, including nearly all academic medical centers. The database includes data such as demographics, length of stay (LOS), complication rates, mortality, readmission rates, resource utilization and other information. We performed a retrospective review of the Vizient Clinical Data Base/Resource Manager™. The database was queried from January 2017 through December 2019 for women between 15 and 44 years of age; further extremes of age were excluded to limit the additional confounding effect of maternal age on comorbidities and outcomes. Based on the 2018 Adult Congenital Heart Disease guidelines,<sup>(15)</sup> groups were defined using ICD-10 codes as Moderate CHD, Severe CHD or No CHD (Table S1 for ICD-10 codes). Admissions with isolated atrial septal defects (ASD, Q21.1) and isolated ventricular septal defects (VSD, Q21.0) were excluded from all groups as the size of the defect could not be quantified to distinguish between mild or moderate CHD, as were codes for non-specific congenital heart disease

(Table S1). By excluding these codes from all groups, we expected to more appropriately categorize patients whose CHD physiology would be more likely to increase their risks during pregnancy. Similar to prior studies of pregnant women,(2) we utilized the same codes as Clowse and colleagues,(16) however, we chose to limit the query to only admissions with a procedure code for vaginal delivery or caesarian section to limit the study population to women who completed a pregnancy (Table S2 for ICD-10 codes). The database was only queried for inpatient admissions, so outcomes such as spontaneous abortions that did not require hospitalization would not be captured and were therefore inappropriate to include in the analysis.

Data collected included age, race/ethnicity (white, black, Hispanic or Asian/Pacific Islander), insurance type (Private, Medicaid, Medicare or Self-pay/uninsured), hospital outcomes (LOS, ICU admission rate, rate of the presence of complications listed in the Vizient Clinical Data Base,(17) in-hospital mortality) and costs. In addition, rates of non-pregnancy associated comorbidities (non-gestational hypertension, dysrhythmia, heart failure, pulmonary hypertension, non-gestational diabetes, hypothyroidism, hemorrhage, mental illness and drug abuse) and obstetric complications (caesarian section rate, pre-eclampsia, embolic events, acute respiratory distress syndrome/pulmonary edema) and neonatal complications (preterm delivery, IUGR, non-cardiac birth defects and fetal demise) were identified and compared (Tables S2 and S3 for ICD-10 codes). Comparisons were made with one-way ANOVA with Tukey HSD for post-hoc analysis for continuous data and  $\chi^2$  with Bonferroni adjustment for post-hoc analysis for categorical data. Odds ratios were also calculated for categorical variables with significant differences for No CHD vs Moderate CHD, No CHD vs Severe CHD and Moderate vs Severe CHD.

Statistical analysis was performed using SPSS v26 (IBM Corporation, Armonk, New York, USA).

### *Ethical approval*

The University of Arizona Institutional Review Board reviewed this study (Protocol #2101393130, January 22, 2021) and waived the need for informed consent for this review of deidentified data.

## **Results**

There were 4 448 875 total admissions during the study period, with 4 425 424 (99.5%) with No CHD, 5591 (0.13%) with Moderate CHD and 2217 (0.05%) with Severe CHD; the remaining had either an ASD, VSD or non-specific CHD and were not included in the analysis. There was a decreasing proportion of admissions for deliveries with increasing severity of CHD: No CHD 2 467 589 (55.8%), Moderate CHD 1277 (22.8%) and Severe CHD 251 (11.3%) ( $p < 0.001$  each for No CHD vs Moderate, No CHD vs Severe and Moderate CHD vs Severe CHD); these admissions made up the study population.

Demographics, insurance status and hospital outcomes are shown in Table 1. Both CHD groups were younger than No CHD, with no difference between the CHD severities. There were fewer white race/ethnicity and more black race/ethnicity in the No CHD group. There were more women with private insurance and fewer with Medicaid in No CHD compared to the Moderate CHD group. There were more women with Medicare in both CHD groups compared to No CHD and fewer Self-pay/uninsured in the Moderate compared to No CHD group.

There were increases in LOS, ICU admission rates and costs with increasing CHD severity. There was a higher presence of complications listed in the Vizient Clinical Data Base and mortality rate in the CHD groups compared to No CHD with no difference between CHD severities (Table 1). The in-hospital mortality rate was 0.16% for the Moderate CHD group with an odds ratio of 17.9 (95% CI 4.4 – 72.2) compared to the No CHD group and 0.8% for the Severe CHD group with an odds ratio of 91.8 (95% CI 22.7 – 371.3) compared to the No CHD group (Table 1).

The rates of non-pregnancy related comorbidities are shown in Table 2. There was more hypertension and mental illness in both CHD groups than No CHD with no difference between CHD severities. There were increasing rates of dysrhythmia, heart failure, pulmonary hypertension and hypothyroidism with increasing rates of CHD severity. There was a higher rate of hemorrhage in the Severe CHD group compared to No CHD. There were no differences in the rates of diabetes or drug abuse.

The rates of obstetric and neonatal complications are shown in Table 3. There were higher rates of caesarian sections in both CHD groups than No CHD with no difference between CHD severities. There were higher rates of pre-eclampsia and acute respiratory distress syndrome/pulmonary edema in the Moderate CHD group than No CHD. There were increasing rates of preterm delivery, IUGR and non-cardiac birth defects with increasing CHD severity. There was a higher rate of fetal demise in the severe CHD group compared to No CHD. There were too few embolic events for comparison.

## **Discussion**

Using a national administrative database, we were able to present the most contemporary U.S. data for pregnancy outcomes for women with moderate and severe congenital heart disease, and also the first to use the new physiologic classifications of CHD severity as defined by the 2018 Adult CHD guidelines. As the care for these women continues to evolve and improve, more of these challenging women will survive to childbearing age, making an understanding of their risk factors and outcomes imperative.

There are conflicting data regarding the influence of maternal age on pregnancy outcomes in maternal heart disease, with a small single center study showing no effect from maternal age over 35 years and a large international study finding higher maternal age as a predictor of adverse pregnancy outcomes.(12, 18) In our study, women with any degree of CHD were younger at delivery than women without CHD. Prior reviews of other U.S. national databases did not find a difference in age for women with and without CHD,(1-3) however these studies all looked at the total population of women with CHD, including ASD and VSD. It may be that women with more severe CHD have increased difficulty completing a successful pregnancy due to cardiac-related challenges and are unable to complete pregnancy at an older age. The inclusion in prior studies of women with truly mild disease (tiny patent foramen ovale, repaired ASD or VSD), who would be expected to be physiologically more similar to women with no CHD than those with moderate or severe CHD, likely explains the differences in age identified in the current study.

Similar to prior studies, we found that women with CHD had longer LOS and higher hospital costs.(1-3) We also found increasing rates of ICU admission with increasing CHD severity. This combination of longer LOS and higher ICU admission rates likely accounts for much of the higher costs, but one has to presume there may also be additional medications given and procedures performed for these women, further adding to the cost of

their hospitalizations. While we were not able to obtain that level of detail from the database, this would be expected when caring for more complicated women. In agreement with prior studies, we also found higher maternal mortality for women with moderate or severe CHD.

There is limited prior work looking specifically at the insurance status of pregnant women with CHD. While prior studies report issues of insurability for adults with CHD, including self-reported gaps in coverage,(19, 20) the current study as well as other reviews of national databases have shown very low rates of self-pay/uninsured status.(2, 3) It may be that pregnancy becomes a motivating factor for women with CHD to maintain or re-establish insurance coverage. An interesting multinational study specifically looking at the effect of socioeconomic status, as measured by the status of the country of origin, found minimal effect from factors such as income inequality, healthcare spending and gross domestic product on pregnancy outcomes and that most negative effects were related to patient specific factors, such as maternal age and CHD severity.(18)

We identified an occurrence rate of 23.6% of any cardiovascular comorbidities during pregnancy for women with CHD, similar to published reports. While there is some variability in the outcome definitions for each study, this has varied little in reports from the past 20 years (7.6 – 31%).(4-9, 12, 13, 21-23) Looking specifically at the severity of CHD, we found increased pregnancy related dysrhythmia, heart failure and pulmonary hypertension complications with increasing severity of CHD, as would be expected. The higher rate of hemorrhage is likely related to antiplatelet/anticoagulation medications and possibly platelet dysfunction associated with chronic cyanosis in the women with severe CHD. The increasing rates of hypothyroidism with increasing CHD severity may be due to the thyrotoxic effects of some medications, particularly anti-arrhythmics. The higher rate of

mental illness in women with any severity of CHD has also been reported by Schlichting,(3) and in particular, adults with CHD have higher rates of depression and anxiety.(19, 24) Recognition of this important comorbidity in the adult CHD population is becoming increasingly important.(25) While not all of these comorbidities are modifiable, some are, and diagnosis and intervention of mental illness has the potential to positively impact the outcomes for pregnant women with CHD and their children.

We identified several obstetric comorbidities in women with CHD. The rates of caesarian sections were higher for women with CHD, similar to prior reports.(2, 3, 13, 14) While some clinicians advocate elective caesarian sections for women with CHD to minimize the cardiovascular stress of delivery, Hidano and colleagues found higher rates of maternal and neonatal complications in women with CHD who had caesarian sections (13) and another recent study stressed that there is no evidence for elective caesarian sections in this population. (26) A higher rate of pre-eclampsia is consistent with prior reports; failure to reach a level of statistical significance for the severe CHD group in the current study is likely due to the relatively small number of women. Interestingly, we found a very low rate of pulmonary edema, though this was already noted to be decreasing in the CARPREG II study.(8) It is unclear why the rates of thromboembolic events were so low in the current study, but could be due to our specific exclusion of women with isolated ASDs who were the highest risk population for this complication in a recent report.(3)

We found a rate of any neonatal complication of 27.6% for pregnancies in women with CHD, consistent with prior reports.(4-7, 9, 12, 13, 21-23) There was an increasing rate of preterm delivery, IUGR and non-cardiac birth defects with increasing severity of maternal CHD. Recent studies have looked at the effect of maternal cardiac dysfunction on uterine arterial flow as a surrogate of placental health.(23, 27) Decreased maternal

ventricular systolic function, as well as elevated BNP as a surrogate biomarker, have been associated with worse uterine/placental function and a higher risk of IUGR.(23, 27, 28) Abnormal chronotropic response on cardiopulmonary exercise testing was also predictive for maternal and neonatal adverse events.(22) These data support an adverse impact on the developing fetal environment caused by impaired maternal cardiac output related to CHD-related functional limitations.

These pregnancy outcome data for women with CHD stress the importance of thorough pre-pregnancy counselling, even beginning as early as the adolescent transition period to adult care.(29) In addition, close monitoring for women with CHD, particularly those who are at the highest risk, such as those with single ventricle CHD, pulmonary hypertension or progressive severe aortic dilation, is vitally important.(30)

There are several limitations when utilizing data from an administrative database. There are limited details of ICD-10 codes and there is the risk for miscoding and erroneous data entry. Despite this concern, there is up to 85% sensitivity for CHD diagnosis in administrative databases.(31) The database, as queried, cannot track individual women across multiple admissions, but limiting the study population only to those with ICD-10 procedure codes for vaginal delivery or Caesarian section limits the possibility of the same woman being counted multiple times throughout the same pregnancy. We were unable to track other admissions that may have occurred during the pregnancies, but since the main interest of the current study was the outcome of the pregnancy, this would not be expected to affect our findings. Even with these limitations, utilizing a large national database provides a better understanding of hospital outcomes, resource utilization and complications than a single center study can to define the risks of pregnancy for women with CHD.

This study contributes to the growing body of literature with the most recent data, showing that pregnant women with moderate and severe CHD have longer hospital stays, higher costs and increased cardiac comorbidities as well as obstetric and neonatal complications. Continually reassessing these outcomes will be critical to provide the best counselling and care as this population continues to grow in size and complexity.

**Declaration of conflicting interests**

The authors declare that there are no conflicts of interest.

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### **Supplemental Table Legends**

**Table S1** – Congenital heart disease severity groups with corresponding ICD-10 codes. Admissions with only non-specific congenital heart disease diagnoses were excluded in the query.

**Table S2** – ICD-10 codes for vaginal delivery and caesarian sections and well as obstetric and neonatal complications.

**Table S3** – ICD-10 codes for cardiopulmonary and other system pregnancy complications.

**Table 1** – Comparisons of demographics, hospital outcomes and costs for admissions with completed pregnancies for the Moderate congenital heart disease (CHD), Severe CHD and No CHD groups. *P*-values are for comparison across all three groups with details of post-hoc analyses shown below the Table; \* =  $p \leq 0.05$  compared to No CHD, † =  $p \leq 0.05$  compared to Moderate CHD. Data are presented as n, %, mean ± standard deviation or odds ratio (95% confidence interval). Complications = higher presence of complications listed in the Vizient Clinical Data Base; ICU = intensive care unit; LOS = length of stay, OR = odds ratio. Data from the Vizient Clinical Data Base/Resource Manager used by permission of Vizient. All rights reserved.

Factor	Moderate CHD (n = 1,277)	OR for Moderate CHD vs No CHD (95% CI)	Severe CHD (n = 251)	OR for Severe CHD vs No CHD (95% CI)	OR for Moderate CHD vs Severe CHD (95% CI)	No CHD (n = 2,467,589)	<i>P</i>
Age (y)	28.2±5.8*		28.3±5.5*			29.6±5.8	<0.001
Age categories (n, %)							
15-19	80 (6.3)		9 (3.6)			105,302 (4.3)	<0.001
20-24	283 (22.2)		57 (22.7)			412,738 (16.7)	
25-29	404 (31.6)		85 (33.9)			673,756 (27.3)	
30-34	302 (23.6)		66 (26.3)			761,722 (30.9)	
35-39	178 (13.9)		27 (10.8)			421,455 (17.1)	
40-44	30 (2.3)		7 (2.8)			92,616 (3.8)	
Race/Ethnicity (n, %)							
White	836 (65.5)*		177 (70.5)*			1,431,615 (58)	<0.001
Black	177 (13.9)*		25 (10)*			456,767 (18.5)	
Hispanic	210 (16.4)		30 (12)			442,597 (17.9)	
Asian/Pacific Islander	37 (2.9)*		8 (3.2)			146,993 (6)	
Insurance (n, %)							
Private	611 (47.8)*		121 (48.2)			1,322,340 (53.6)	<0.001
Medicaid	602 (47.1)*		105 (41.8)			1,022,174 (41.4)	
Medicare	28 (2.2)*		8 (3.2)*			14,336 (0.6)	
Self-pay	6 (0.5)*		3 (1.2)			30,115 (1.2)	
LOS (d)	4.4±5.9*		6.6±10.0*,†			3.0±2.8	<0.001
ICU admission (%)	8.9*	16.2 (13.4 – 19.7)	19.1*,†	39.2 (28.6 – 53.7)	2.4 (1.7 – 3.5)	0.6	<0.001
Complications (n, %)	141 (11)*	1.3 (1.1 – 1.6)	37 (14.7)*	1.8 (1.3 – 2.6)	1.4 (0.9 – 2.1)	212,942 (8.6)	<0.001
In-hospital mortality (n, %)	2 (0.16)*	17.9 (4.4 – 72.2)	2 (0.8)*	91.8 (22.7 – 371.3)	5.1 (0.7 – 36.5)	216 (0.01)	<0.001
Total costs (\$)	\$6,391±15,430*		\$10,929±35,143*,†			\$3,672±3,196	<0.001

Post-hoc analyses: Age: Moderate CHD vs Severe CHD  $p=0.9662$ , Moderate CHD vs No CHD  $p<0.001$ , Severe CHD vs No CHD  $p=0.001$ . Race: White race/ethnicity – No CHD vs Moderate CHD  $p<0.001$  and No CHD vs Severe CHD  $p<0.001$ . Black race/ethnicity – No CHD vs Moderate CHD  $p<0.001$ , No CHD vs. Severe CHD  $p=0.004$ . Asian race/ethnicity – No CHD vs Moderate CHD  $p<0.001$ . Insurance: Private – No CHD vs Moderate CHD  $p<0.001$ . Medicaid – No CHD vs Moderate CHD  $p<0.001$ . Medicare – No CHD vs Moderate CHD  $p<0.001$ , No CHD vs Severe CHD  $p<0.001$ . Self-pay – No CHD vs Moderate CHD  $p=0.041$ . LOS:  $p<0.001$  for No CHD vs Moderate CHD, No CHD vs Severe CHD and Moderate CHD vs Severe CHD. ICU: No CHD vs Moderate CHD  $p<0.001$ , No CHD vs Severe CHD  $p<0.001$ , Moderate CHD vs Severe CHD  $p<0.001$ . Complications: No CHD vs Moderate CHD  $p=0.006$ , No CHD vs Severe CHD  $p=0.002$ . In-hospital mortality: No CHD vs Moderate CHD  $p<0.001$ , No CHD vs Severe CHD  $p<0.001$ . Total costs:  $p<0.001$  for No CHD vs Moderate CHD, No CHD vs Severe CHD and Moderate CHD vs Severe CHD.

**Table 2** – Comparisons of rates of non-pregnancy related comorbidities for the Moderate congenital heart disease (CHD), Severe CHD and No CHD groups. *P*-values are for comparison across all three groups with details of post-hoc analyses shown below the Table; \* =  $p \leq 0.05$  compared to No CHD, † =  $p \leq 0.05$  compared to Moderate CHD. Data are presented as n, % or odds ratio (95% confidence interval). OR = odds ratio. Data from the Vizient Clinical Data Base/Resource Manager used by permission of Vizient. All rights reserved.

Factor	Moderate CHD (n = 1,277)	OR for Moderate CHD vs No CHD (95% CI)	Severe CHD (n = 251)	OR for Severe CHD vs No CHD (95% CI)	OR for Moderate CHD vs Severe CHD (95% CI)	No CHD (n = 2,467,589)	<i>p</i>
<b>Cardiopulmonary</b>							
<b>Hypertension (n, %)</b>	125 (9.8)*	2.4 (2.0 – 2.9)	23 (9.2)*	2.3 (1.5 – 3.5)	0.9 (0.6 – 1.5)	105,305 (4.3)	<0.001
<b>Dysrhythmia (n, %)</b>	68 (5.3)*	28.5 (22.3 – 36.4)	35 (13.9)*, †	82.0 (57.3 – 117.4)	2.9 (1.9 – 4.4)	4,865 (0.2)	<0.001
<b>Heart failure (n, %)</b>	47 (3.7)*	43.7 (32.5 – 58.6)	24 (9.6)*, †	126.4 (83.5 – 191.5)	2.9 (1.7 – 4.8)	2,157 (0.1)	<0.001
<b>Pulmonary hypertension (n, %)</b>	62 (4.9)*	127.0 (97.7 – 165.2)	22 (8.8)*, †	239.1 (153.7 – 372.0)	1.9 (1.1 – 3.1)	991 (0.04)	<0.001
<b>Other system</b>							
<b>Diabetes (n, %)</b>	54 (4.2)	1.2 (0.9 – 1.5)	6 (2.4)	0.6 (0.3 – 1.4)	0.6 (0.2 – 1.3)	90,569 (3.7)	0.318
<b>Hypothyroidism (n, %)</b>	158 (12.4)*	1.7 (1.5 – 2.0)	56 (22.3)*, †	3.5 (2.6 – 4.7)	2.0 (1.4 – 2.9)	187,873 (7.6)	<0.001
<b>Hemorrhage (n, %)</b>	48 (3.8)	1.4 (1.1 – 1.9)	13 (5.2)*	2.0 (1.1 – 3.4)	1.4 (0.8 – 2.6)	67,086 (2.7)	0.004
<b>Mental illness (n, %)</b>	238 (18.6)*	2.0 (1.7 – 2.3)	48 (19.1)*	2.0 (1.5 – 2.8)	1.0 (0.7 – 1.5)	255,849 (10.4)	<0.001
<b>Drug abuse (n, %)</b>	36 (2.8)	1.0 (0.7 – 1.4)	11 (4.4)	1.6 (0.9 – 3.0)	1.6 (0.8 – 3.1)	68,230 (2.8)	0.293

Post-hoc analyses: Hypertension: No CHD vs Moderate CHD  $p < 0.001$ , No CHD vs Severe CHD  $p < 0.001$ . Dysrhythmia: No CHD vs Moderate CHD  $p < 0.001$ , No CHD vs Severe CHD  $p < 0.001$ , Moderate CHD vs Severe CHD  $p < 0.001$ . Heart failure: No CHD vs Moderate CHD  $p < 0.001$ , No CHD vs Severe CHD  $p < 0.001$ , Moderate CHD vs Severe CHD  $p < 0.001$ . Pulmonary hypertension: No CHD vs Moderate CHD  $p < 0.001$ , No CHD vs Severe CHD  $p < 0.001$ , Moderate CHD vs Severe CHD  $p = 0.039$ . Hypothyroidism: No CHD vs Moderate CHD  $p < 0.001$ , No CHD vs Severe CHD  $p < 0.001$ , Moderate CHD vs Severe CHD  $p < 0.001$ . Hemorrhage: No CHD vs Severe CHD  $p = 0.050$ . Mental illness: No CHD vs Moderate CHD  $p < 0.001$ , No CHD vs Severe CHD  $p < 0.001$ .

**Table 3** – Comparisons of rates of obstetric and delivery-related complications for the Moderate congenital heart disease (CHD), Severe CHD and No CHD groups. Note, birth defects are non-cardiac. *P*-values are for comparison across all three groups with details of post-hoc analyses shown below the Table; \* =  $p \leq 0.05$  compared to No CHD, † =  $p \leq 0.05$  compared to Moderate CHD. Data are presented as n, % or odds ratio (95% confidence interval). ARDS = acute respiratory distress syndrome, IUGR = intrauterine growth restriction, OR = odds ratio. Data from the Vizient Clinical Data Base/Resource Manager used by permission of Vizient. All rights reserved.

Factor	Moderate CHD (n = 1,277)	OR for Moderate CHD vs No CHD (95% CI)	Severe CHD (n = 251)	OR for Severe CHD vs No CHD (95% CI)	OR for Moderate CHD vs Severe CHD (95% CI)	No CHD (n = 2,467,589)	<i>p</i>
<b>Pregnancy-related</b>							
Caesarian section (n, %)	446 (34.9)*	1.3 (1.2 – 1.4)	92 (36.7)*	1.4 (1.1 – 1.8)	1.1 (0.8 – 1.4)	726,282 (29.4)	<0.001
Pre-eclampsia (n, %)	269 (21.1)*	1.5 (1.4 – 1.8)	46 (18.3)	1.3 (0.9 – 1.8)	0.8 (0.6 – 1.2)	363,566 (14.7)	<0.001
Thromboembolic (n, %)	0 (0)	–	0 (0)	–	–	109 (0.004)	0.967
ARDS/pulmonary edema (n, %)	7 (0.5)*	6.7 (3.2 – 14.0)	1 (0.4)	4.8 (0.7 – 34.5)	0.7 (0.1 – 5.9)	2,037 (0.1)	<0.001
<b>Delivery-related</b>							
Preterm delivery (n, %)	90 (7)*	1.6 (1.3 – 2.0)	35 (13.9)*,†	3.5 (2.4 – 4.9)	2.1 (1.4 – 3.2)	110,499 (4.5)	<0.001
IUGR (n, %)	101 (7.9)*	2.1 (1.7 – 2.6)	42 (16.7)*,†	4.9 (3.5 – 6.9)	2.3 (1.6 – 3.5)	96,532 (3.9)	<0.001
Non-cardiac birth defects (n, %)	92 (7.2)*	4.3 (3.5 – 5.3)	36 (14.3)*,†	9.2 (6.5 – 13.2)	2.2 (1.4 – 3.3)	43,896 (1.8)	<0.001
Fetal demise (n, %)	18 (1.4)	1.7 (1.1 – 2.7)	9 (3.6)*	4.4 (2.3 – 8.6)	2.6 (1.2 – 5.9)	20,675 (0.8)	<0.001

Post-hoc analyses: C-section: No CHD vs Moderate CHD  $p < 0.001$ , No CHD vs Severe CHD  $p = 0.036$ . Pre-eclampsia: No CHD vs Moderate CHD  $p < 0.001$ .

ARDS/pulmonary edema: No CHD vs Moderate CHD  $p < 0.001$ . Preterm delivery: No CHD vs Moderate CHD  $p < 0.001$ , No CHD vs Severe CHD  $p < 0.001$ ,

Moderate CHD vs Severe CHD  $p = 0.001$ . IUGR: No CHD vs Moderate CHD  $p < 0.001$ , No CHD vs Severe CHD  $p < 0.001$ , Moderate CHD vs Severe CHD

$p < 0.001$ . Non-cardiac birth defects: No CHD vs Moderate CHD  $p < 0.001$ , No CHD vs Severe CHD  $p < 0.001$ , Moderate CHD vs Severe CHD  $p = 0.001$ . Fetal

demise: No CHD vs Severe CHD  $p < 0.001$ .