Impact of Pre-Existing Ischemic Heart Disease on Severe Maternal Morbidity and Mortality During Delivery Hospitalizations

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Abstract

BACKGROUND—The impact of pre-existing ischemic heart disease (IHD) on pregnancy is incompletely described.

OBJECTIVES—The purpose of this study was to compare adverse pregnancy outcomes between those with IHD and those with a cardiac diagnosis categorized by the modified World Health Organization classification and those without a cardiac diagnosis.

METHODS—This retrospective study used the 2015 to 2018 Nationwide Readmissions Database. Delivery hospitalizations, comorbidities, and outcomes were identified using diagnosis and procedure codes. The exposure was isolated IHD. The primary outcome was severe maternal morbidity (SMM) or death during the delivery hospitalization, analyzed using adjusted relative risk (aRR) regression and weighted to account for the Nationwide Readmissions Database's complex survey methods.

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RESULTS—Of 11,556,136 delivery hospitalizations, 65,331 had another cardiac diagnosis, and 3,009 had IHD alone. Patients with IHD were older and had higher rates of diabetes and hypertension. In unadjusted analyses, adverse outcomes were more common among patients with IHD alone than among patients with no cardiac disease and modified World Health Organization class I-II disease. After adjustment, patients with IHD alone were associated with a higher risk of SMM or death (aRR: 1.51; 95% CI: 1.19–1.92) than those without a cardiac disease. In comparison, the aRR was 1.90 (95% CI: 1.76–2.06) for WHO class I-II diseases and 5.87 (95% CI: 5.49–6.27) for WHO II/III-IV diseases. Nontransfusion SMM or death (aRR: 1.60; 95% CI: 1.11–2.30) and cardiac SMM or death (aRR: 2.98; 95% CI: 1.75–5.08) were also higher for those with IHD.

CONCLUSIONS—Isolated IHD in pregnancy is associated with worse outcomes than no cardiac disease during delivery hospitalization and approximates the risk associated with WHO I-II diagnoses.

The leading causes of maternal mortality in the United States are attributed to cardiac diseases. Cardiac disease and cardiomyopathy account for over 26% of maternal deaths in the United States.[1] It is probable that with increasing maternal age in pregnancy, as well as the rise in accompanying comorbidities, such as obesity and hypertension, cardiovascular risk factors such as pre-existing ischemic heart disease (IHD) will also increase in prevalence in pregnant patients.[2] While maternal outcomes related to acute coronary syndromes in pregnancy, such as pregnancy-associated myocardial infarction[3–6] and spontaneous coronary artery dissection,[7,8] have been explored in the literature in recent years, maternal medical and obstetric complications, such as severe maternal morbidity (SMM), in individuals with pre-existing IHD have not been well characterized. To date, there have been 2 principal studies on this topic: a retrospective analysis of 50 pregnancies in 43 individuals[9] and a subsequent systematic review by the same group of 124 pregnancies in 116 individuals, including the 50 pregnancies in the previous retrospective analysis.[10] Both these analyses suggested that people entering pregnancy with pre-existing IHD had a risk (approximately 5%-10%) of ischemic cardiovascular complications. However, more comprehensive analyses of outcomes in this population are lacking.

Counseling of patients with pre-existing IHD prior to conception or during pregnancy is difficult for 2 reasons. First, as explained above, data regarding outcomes are lacking. Second, pre-existing IHD is not included in the modified World Health Organization (mWHO) classification of maternal cardiovascular risk, a classification schema that is widely used to aid in counseling individuals with a pre-existing cardiac disease considering or in pregnancy.[11,12]

The first aim, therefore, of the present study was to assess rates of SMM and mortality, as defined by the Centers for Disease Control and Prevention (CDC), in pregnant people with pre-existing IHD in a large nationwide database. The second aim was to compare rates of

SMM and mortality in pregnant women with pre-existing IHD to those of women with other cardiac lesions that are classified in the mWHO classification.

METHODS

This was a retrospective cohort study utilizing the Nationwide Readmissions Database (NRD), Healthcare Cost and Utilization Project, and Agency for Healthcare Research and Quality.[13] The NRD data set is a large administrative data set that, in 2018, contained all hospitalizations for 28 states, representing 59.7% of the U.S. population and 58.7% of all hospitalizations in the United States regardless of primary payer. Data available in each record include demographic information (eg, age, gender, primary payer), diagnosis and procedure codes, hospital characteristics, including location and academic affiliation, hospital length of stay, inpatient charges, and discharge disposition. Methods used for the purposes of this analysis are further described in detail elsewhere.[14]

INCLUSION AND EXCLUSION CRITERIA.

Subjects were included if they experienced a delivery hospitalization from October 1, 2015, to December 31, 2018, identified by International Classification of Diseases-10th Revision-Clinical Modification (ICD-10) code Z37.x, with subjects entering the study at the time of their delivery hospitalization. Subjects are not linked across years within the NRD; therefore, it is possible that 1 individual may have contributed multiple pregnancies. The final quarter of 2015 was selected as the start date for the study as this was the date of adoption of ICD-10 for billing in the United States. At the time of the analysis, December 2018 was the most recent time when NRD data were available for review. There were no exclusion criteria.

EXPOSURE OF INTEREST.

Our primary exposure of interest was isolated pre-existing IHD without another cardiac diagnosis. This was defined as ICD-10 codes I25.1x, I25.2x, I25.5x, I25.6x I25.7x, I25.8x, and I25.9x, which are all codes for pre-existing, rather than acute, IHD. Comparator populations included those without an apparent cardiac disease and those with cardiac lesions included in the mWHO classification. The latter were divided into 2 cohorts. The first will be referred to as "low-risk" cardiac disease and included those with diagnoses consistent with mWHO class I or II cardiac lesions (see Supplemental Table 1 for list of lesions and associated ICD-10 codes). The second cohort consisted of those with a "high-risk" cardiac disease and included those with an mWHO class II/III, III, or IV cardiac disease. These classes were combined due to the potential overlap in classes with the use of ICD-10 diagnosis codes, as opposed to clinical data. For example, a patient might have an ICD-10 diagnosis code I42.0 for dilated cardiomyopathy. However, without echocardiographic data, we were unable to further classify as mWHO II/III, III, or IV. The pre-existing IHD cohort and low- and high-risk cardiac disease cohorts were mutually exclusive, meaning that *those with pre-existing IHD did not have another cardiac diagnosis* that could be classified within the mWHO classification and those with a low-risk cardiac lesion did not also have a high-risk lesion.

OUTCOMES.

Our primary outcome was a composite of SMM and maternal mortality occurring *during the delivery hospitalization*, as defined by the CDC (see Supplemental Table 2 for included diagnoses).[15] The specific indicators included are listed in the Supplemental Table 1, and the associated ICD-10 codes are available on the CDC website, including both non-transfusion- and transfusion-related SMM indicators. Secondary outcomes included non-transfusion SMM and mortality (SMM excluding blood products' transfusion codes as provided by the CDC), cardiac SMM and mortality (acute myocardial infarction, aortic aneurysm, cardiac arrest/ventricular fibrillation, conversion of cardiac rhythm, heart failure/arrest during the surgery or procedure, and pulmonary edema/acute heart failure), and preterm birth. Data regarding other obstetric and neonatal complications, such as small for gestational age, low neonatal Apgar scores, and neonatal intensive care unit admission, are not available in this data set due to the lack of linked neonatal records.

COVARIATES.

Covariates of interest that were available in the NRD data set included age in years at admission, calendar year and quarter, primary expected payer, and hospital characteristics. Hospital characteristics are defined by a standard method in the NRD and include hospital bed size and location and teaching status. Medical comorbidities were included exactly as published in a previously validated obstetric-specific comorbidity index (comorbidities included in the analysis are listed in Table 1).[16] However, cardiac comorbidities (eg, aortic aneurysm), other than hypertension, were excluded due to crossover with cardiac outcomes. Medication use was not available. Comorbidities such as body mass index 40 kg/m^2 and advanced maternal age were defined by their associated ICD-10 codes.

STATISTICAL ANALYSIS.

Statistical methods, weighted to account for a complex survey design of the NRD, were used to assess associations between the baseline characteristics, pre-existing IHD, and the primary and secondary outcomes. Relative risk (RR) regression using a Poisson model, using robust standard error estimates and accounting for the complex design of the NRD, was used to assess associations between cardiac disease and the outcomes, adjusting for age, delivery type, year and quarter of delivery, and comorbid conditions.[17] Statistical analysis was completed in Stata Statistical Software, Version 16.1 (StataCorp LLC). A 2-sided alpha value of 0.05 was considered statistically significant. Given the retrospective nature of this analysis using an existing, limited data set, the Duke University School of Medicine Institutional Review Board deemed it exempt from review.

RESULTS

BASELINE CHARACTERISTICS.

There were 6,109,133 unweighted and 11,556,136 weighted delivery hospitalizations. Henceforth, weighted data will be presented. Of the total delivery hospitalizations, 3,009 had a history of pre-existing IHD without another cardiac diagnosis, for a prevalence of 26.0 per 100,000 delivery hospitalizations (Figure 1). There were 34,742 deliveries with mWHO

I-II cardiac disease, 27,579 with mWHO II/III-IV cardiac disease, and 11,490,806 with no cardiac disease. Demographic and clinical characteristics demonstrated that patients with pre-existing IHD were older, more likely to deliver at a metropolitan teaching hospital, and more likely to be in the lowest quartile of median household income by zip code. Those with pre-existing IHD had higher rates of medical comorbidities than those without a cardiac disease. More specifically, 12% of pregnant people with pre-existing IHD had diabetes vs 1.3% (*P* < 0.001) without a cardiac disease, 10.4% had body mass index 40 vs 4.3% (*P* < 0.001), 27.8% had chronic hypertension vs 3.2% (*P* < 0.001), and 40% were of advanced maternal age vs 17.2% (*P* < 0.001) (Table 1).

UNADJUSTED ANALYSIS.

In unadjusted analyses, the risk of SMM and mortality among those patients with pre-existing IHD was higher than that in patients with no cardiac disease or low-risk cardiac disease but significantly lower than that for those with a high-risk cardiac disease. Of those with pre-existing IHD, 6.6% experienced SMM or mortality compared to 1.5% of those without a cardiac disease (unadjusted RR compared to no cardiac disease 4.3; 95% CI 3.5–5.2), 4.2% of those with mWHO I-II cardiac diseases (RR compared to no cardiac disease 2.7; 95% CI 2.5–2.9), and 23.1% of those with mWHO II/III-IV cardiac diseases (RR 14.9; 95% CI 14.3–15.6) (Table 2, Figure 2). Similar differences were noted for nontransfusion SMM and mortality, cardiac SMM and mortality, and preterm birth, with the risks of adverse outcomes for pre-existing IHD falling between those of mWHO I-II and II/III-IV cardiac diseases.

ADJUSTED ANALYSIS.

After adjustment, having pre-existing IHD alone was associated with a higher risk of SMM and mortality (adjusted RR [aRR]: 1.51; 95% CI: 1.19–1.92), nontransfusion SMM and mortality (aRR: 1.60; 95% CI: 1.11–2.30), and cardiac SMM and mortality (aRR: 2.98; 95% CI: 1.75–5.08) than no cardiac disease (Central Illustration). There were no significant differences in preterm birth for those with pre-existing IHD compared to those with no cardiac disease after adjustment. The risk of SMM and mortality, nontransfusion SMM and mortality, and cardiac SMM and mortality for IHD alone most closely approximated that of mWHO class I or II cardiac diseases.

DISCUSSION

Pre-existing IHD without another cardiac diagnosis was associated with a higher risk of SMM and mortality, nontransfusion, and cardiac SMM and mortality than no cardiac disease in both unadjusted and adjusted analyses. After adjustment for covariates, the risk of isolated pre-existing IHD, without additional evidence of cardiomyopathy, approximated that of low-risk, or mWHO class I or II, cardiac diseases. To our knowledge, this study provides the largest analysis to date examining the risk of severe morbidity and mortality among pregnant people with pre-existing IHD.

While, in unadjusted analyses, a pre-existing IHD appears to confer a risk of SMM and nontransfusion and cardiac SMM and mortality between that of low- and high-risk mWHO

cardiac disease, after adjustment for confounders, the risks of maternal morbidity and mortality approximated those of low-risk cardiac diseases. The differences in risk of SMM and mortality between the unadjusted and adjusted analyses may be due to the high rates of comorbidities in the pre-existing IHD group.

Existing literature on outcomes in individuals with pre-existing IHD in pregnancy is limited. Most studies focused on acute coronary events in pregnancy.[3–6] The largest study to date on pre-existing IHD in pregnancy is a systematic review of the literature that summarized 124 pregnancies among 116 individuals.[10] In this systematic review, 9% of cases experienced an ischemic cardiac event, and 34% experienced an obstetric complication. However, reporting of other cardiac and maternal outcomes was less comprehensive than the CDC's SMM indicators, and adverse event rates were not compared to those of other cardiac lesions. The second largest case series to date included 92 pregnancies to 79 women in Europe with an adverse cardiac event rate of 6.6% and with limitations similar to those of the study mentioned above.[18] To summarize, prior studies have concluded that people with a pre-existing cardiac disease during pregnancy have favorable outcomes in pregnancy from a cardiovascular standpoint but are at increased risk of other neonatal and obstetric complications.[10,18] Our findings corroborate these conclusions from previous, smaller studies of pre-existing IHD in pregnancy.

The RR of SMM and mortality in this study for patients with pre-existing IHD compared to patients with no cardiac disease was similar to that for cardiac lesions classified as mWHO class I or II, suggesting that this diagnosis should be considered for addition to mWHO class I or II. This knowledge will aid clinicians in their counseling of patients with pre-existing IHD preconceptually and during pregnancy. However, it should be remembered that the cohort with pre-existing IHD also had higher rates of comorbidities than the cohorts with no cardiac disease and with a mWHO class I-II disease. These comorbidities, and their potential interaction with or potentiation of cardiac disease, should be considered when assessing an individual's pregnancy-related risk.

This study was limited to evaluation of maternal outcomes occurring during the delivery hospitalization. Additional research examining rates of maternal adverse cardiac events and SMM occurring prior to or after the delivery hospitalization would be beneficial as the true rates of adverse events occurring during and after pregnancy in patients with pre-existing IHD may be higher than those described here. Future studies examining the potential gradation in risk associated with additional cardiac comorbidities in individuals with pre-existing IHD would also be worthwhile.

The strengths of this study included the use of a large, nationwide database, which provided the largest cohort to date with pre-existing IHD in pregnancy. Outcomes were not only reported for delivery hospitalizations for those with pre-existing IHD but were also compared to those with other low- and high-risk cardiac lesions. These data will aid clinicians in counseling patients with pre-existing IHD. Furthermore, in utilizing the CDC's definition of SMM and death, the primary outcome assessed a broader range of adverse outcomes than those typically included in studies of cardiac diseases in pregnancy.

Limitations included the reliance on diagnosis and procedure codes, which may underestimate the true incidence of pre-existing IHD and the outcomes. Additionally, as mentioned above, outcomes were limited to the delivery hospitalization, which likely underestimated the incidence of complications and may have introduced selection bias by only including those whose pregnancies ended in a delivery (ie, excluding those who may have experienced a spontaneous abortion or termination of pregnancy). Subjects included in the NRD are not linked across years, preventing adjustment for multiple pregnancies within the study period. A diagnosis of pre-existing IHD was, by necessity, mutually exclusive of other cardiac diagnoses. In other words, a patient with a diagnosis of pre-existing IHD only had a diagnosis code for IHD and did not have a code for one of the other cardiac lesions, such as cardiomyopathy or heart failure. This is a strength in the sense that it allowed direct comparisons between groups. However, it is also a limitation as patients with IHD may have co-existing conditions, such as ischemic cardiomyopathy, and rates of SMM in this population with multiple comorbid cardiac conditions could not be assessed. Therefore, the cohort of patients in this study with pre-existing IHD may represent a healthier group of patients with IHD than one might encounter clinically. Importantly, there are several clinical factors that might further stratify risk among patients with an IHD history, such as temporal relationship with pregnancy, disease severity, revascularization history and completeness of revascularization, and medication therapy that cannot be assessed in this study. Finally, the temporal relationships between the diagnoses of pre-existing IHD, SMM outcomes, and comorbidities could not be assessed using this administrative database.

CONCLUSIONS

Isolated pre-existing IHD is associated with worse outcomes at the time of delivery compared with no cardiac diagnosis. This risk approximates that of a patient with other low-risk cardiac diagnoses classified as either mWHO class I or II (Central Illustration). These data may be useful in counseling patients and could aid in efforts to further refine the mWHO classification of maternal cardiovascular risk.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ABBREVIATIONS AND ACRONYMS

CDC   Centers for Disease Control and Prevention

ICD-10	International Classification of Diseases-10th Revision-Clinical Modification
IHD	ischemic heart disease
mWHO	modified World Health Organization classification of maternal cardiovascular risk
NRD	Nationwide Readmissions Database
SMM	severe maternal morbidity and mortality

REFERENCES

1. Creanga AA, Syverson C, Seed K, Callaghan WM. Pregnancy-related mortality in the United States, 2011–2013. Obstet Gynecol. 2017;130:366. [PubMed: 28697109]

2. Martin JA, Hamilton BE, Osterman MJK, Driscoll AK. Births: final data for 2019. Natl Vital Stat Rep. 2021;70:1–51.

3. Jalnapurkar S, Xu KH, Zhang Z, Bairey Merz CN, Elkayam U, Pai RG. Changing incidence and mechanism of pregnancy-associated myocardial infarction in the state of California. J Am Heart Assoc. 2021;10:e021056.

4. Smilowitz NR, Gupta N, Guo Y, et al. Acute myocardial infarction during pregnancy and the puerperium in the United States. Mayo Clin Proc. 2018;93:1404–1414. [PubMed: 30031555]

5. James AH, Jamison MG, Biswas MS, Brancazio LR, Swamy GK, Myers ER. Acute myocardial infarction in pregnancy: a United States population-based study. Circulation. 2006;113:1564–1571. [PubMed: 16534011]

6. Roth A, Elkayam U. Acute myocardial infarction associated with pregnancy. J Am Coll Cardiol. 2008;52:171–180. [PubMed: 18617065]

7. Chen S, Merchant M, Mahrer KN, Ambrosy AP, Lundstrom RJ, Naderi S. Pregnancy-associated spontaneous coronary artery dissection: clinical characteristics, outcomes, and risk during subsequent pregnancy. J Invasive Cardiol. 2021;33: E457–E466. [PubMed: 34001675]

8. Tweet MS, Hayes SN, Codsi E, Gulati R, Rose CH, Best PJM. Spontaneous coronary artery dissection associated with pregnancy. J Am Coll Cardiol. 2017;70:426–435. [PubMed: 28728686]

9. Burchill LJ, Lameijer H, Roos-Hesselink JW, et al. Pregnancy risks in women with pre-existing coronary artery disease, or following acute coronary syndrome. Heart. 2015;101:525–529. [PubMed: 25564557]

10. Lameijer H, Burchill LJ, Baris L, et al. Pregnancy in women with pre-existent ischaemic heart disease: a systematic review with individualised patient data. Heart. 2019;105:873–880. [PubMed: 30792240]

11. Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J, et al. 2018 ESC guidelines for the management of cardiovascular diseases during pregnancy. Eur Heart J. 2018;39:3165–3241. [PubMed: 30165544]

12. ACOG Practice Bulletin No. 212. Obstet Gynecol. 2019;133:e320–e356. [PubMed: 31022123]

13. HCUP Nationwide Readmissions Database (NRD). Healthcare Cost and Utilization Project (HCUP), 2015–2018. Agency for Healthcare Research and Quality, Rockville, MD. Accessed August 1, 2021. www.hcup-us.ahrq.gov/nrdoverview.jsp

14. Federspiel J, Suresh S, Darwin K, Szymanski L. Hospitalization duration following uncomplicated cesarean delivery: predictors, facility variation, and outcomes. Am J Perinatol Rep. 2020;10:e187–e197.

15. Division of Reproductive Health National Center for Chronic Disease Prevention and Health Promotion. How does CDC identify severe maternal morbidity? Accessed December 26, 2019. https://www.cdc.gov/reproductivehealth/maternalinfanthealth/smm/severe-morbidity-ICD.htm

16. Leonard SA, Kennedy CJ, Carmichael SL, Lyell DJ, Main EK. An expanded obstetric comorbidity scoring system for predicting severe maternal morbidity. Obstet Gynecol. 2020;136: 440–449. [PubMed: 32769656]

17. Chen W, Qian L, Shi J, Franklin M. Comparing performance between log-binomial and robust Poisson regression models for estimating risk ratios under model misspecification. BMC Med Res Methodol. 2018;18:63. [PubMed: 29929477]

18. Cauldwell M, Steer PJ, von Klemperer K, et al. Maternal and neonatal outcomes in women with history of coronary artery disease. Heart. 2020;106:380–386. [PubMed: 31533991]

PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE 1:

Pre-existing IHD is not currently included in the modified World Health Organization classification of maternal cardiovascular risk, which is widely used for preconception and pregnancy counseling.

COMPETENCY IN MEDICAL KNOWLEDGE 2:

The risk of severe maternal morbidity and death among patients with isolated pre-existing IHD in pregnancy approximates that of the lower-risk modified World Health Organization class I and II cardiac disease, suggesting that pregnancy can be safely considered in this population.

COMPETENCY IN INTERPERSONAL AND COMMUNICATION SKILLS:

It is important to communicate to patients that while pregnancy may be considered low risk in the setting of pre-existing IHD, 6.6% of patients with pre-existing IHD alone did experience severe maternal morbidity or death during the delivery hospitalization. Other medical comorbidities should be factored into discussions regarding the risks of pregnancy.

TRANSLATIONAL OUTLOOK 1:

Additional studies are needed to determine whether other factors, such as the time from the ischemic cardiac event to pregnancy, revascularization history and completeness of revascularization, and medication therapy may alter pregnancy-associated risks.
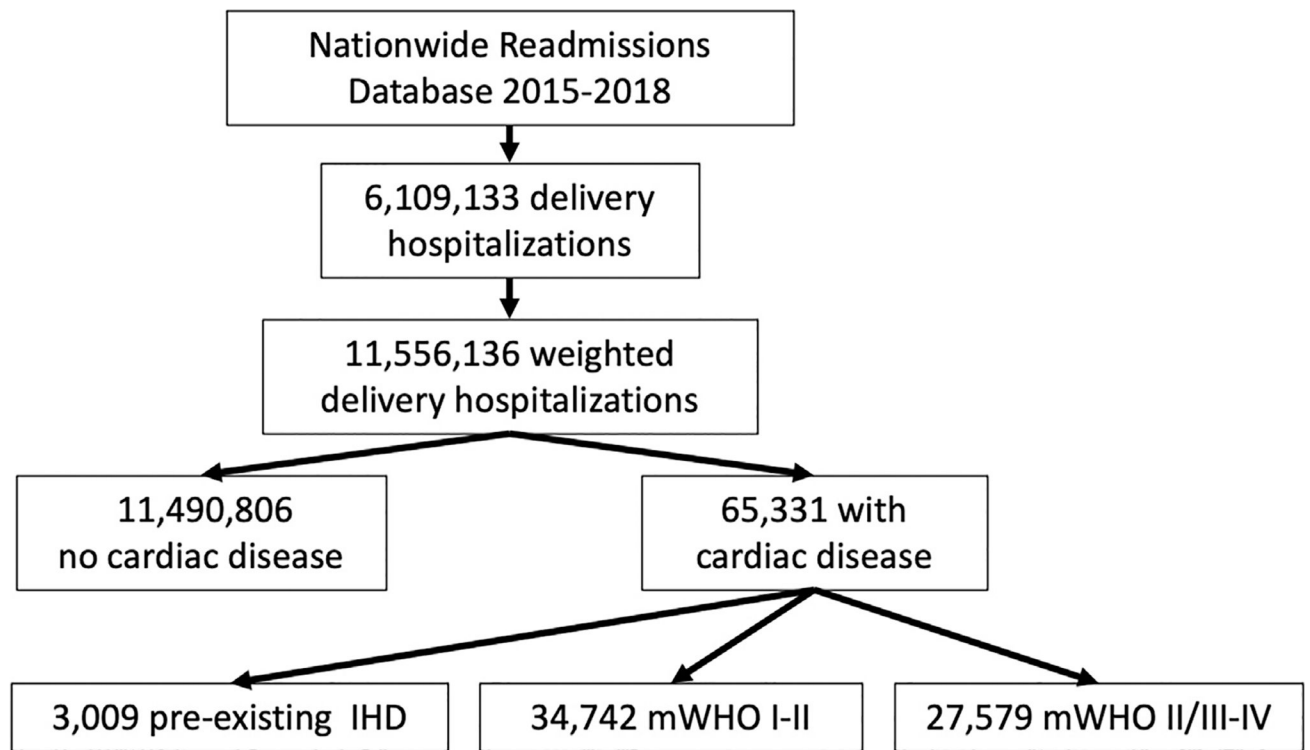
FIGURE 1.

Subject Inclusion Flow Chart

Delivery hospitalizations captured in the Nationwide Readmissions Database (NRD) from October 2015 to December 2018 were included in this study. A total of 6,109,133 delivery hospitalizations are included in the database. The sample was weighted as recommended by the data vendor to create a sample representative of the entire United States, including states not included in the NRD, yielding a total sample size of 11,556,136. Of the delivery hospitalizations, there were 65,331 with cardiac disease, of whom, 3,009 had pre-existing ischemic heart disease. IHD = ischemic heart disease; mWHO = modified World Health Organization Classification of Maternal Cardiovascular Risk.
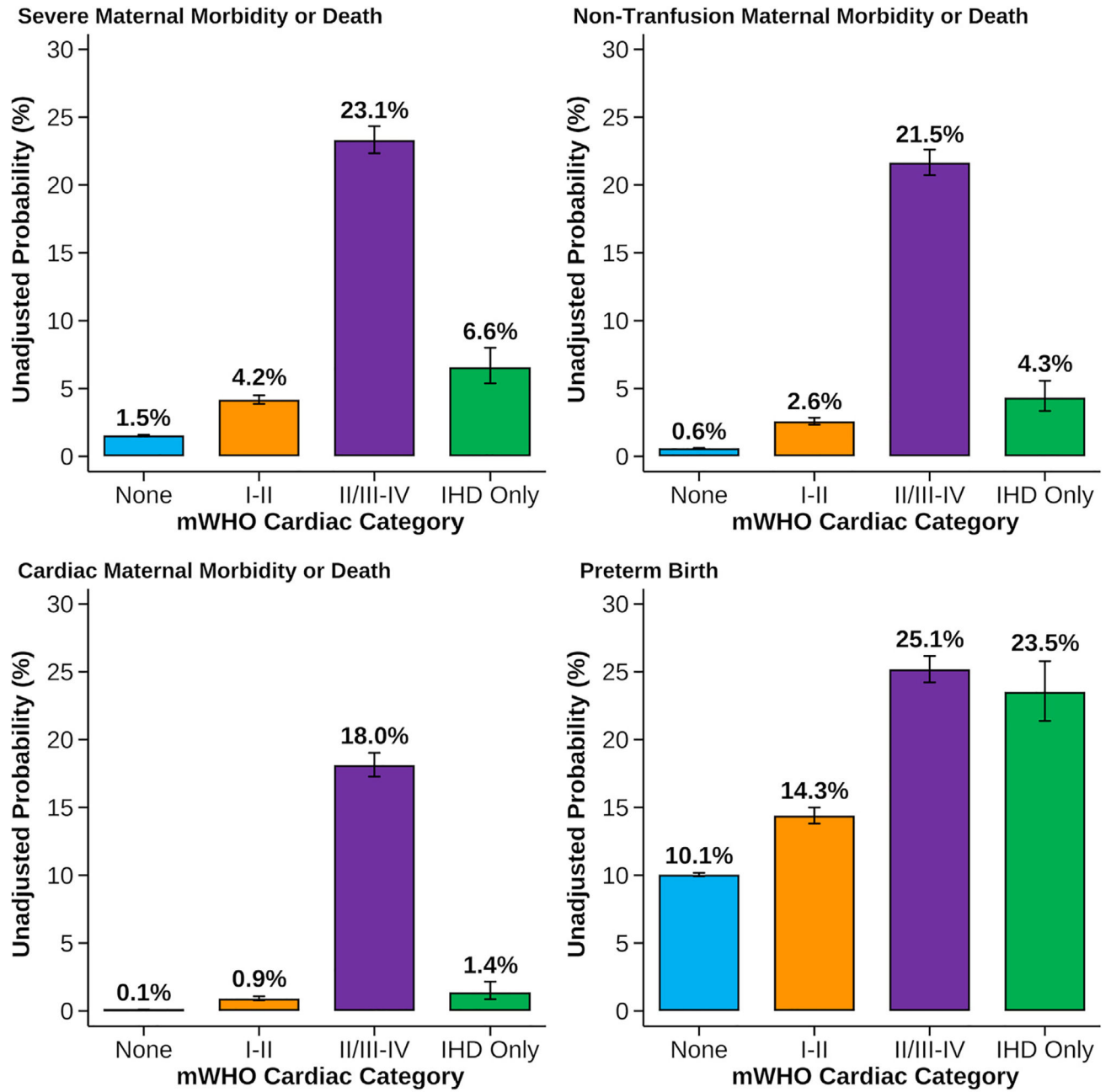
FIGURE 2.

Bar Plot of Unadjusted Probability of Primary and Secondary Outcomes

Bar plot demonstrating unadjusted probabilities of subjects with no cardiac disease, mWHO I-II cardiac disease, mWHO II/III-IV cardiac disease, and pre-existing ischemic heart disease (IHD only) experiencing severe maternal morbidity and death, nontransfusion severe maternal morbidity and death, cardiac severe maternal morbidity and death, or preterm birth. The unadjusted probabilities of the primary and secondary outcomes were significantly higher for IHD only compared to no cardiac disease. IHD = ischemic heart disease; mWHO = modified World Health Organization Classification of Maternal Cardiovascular Risk.

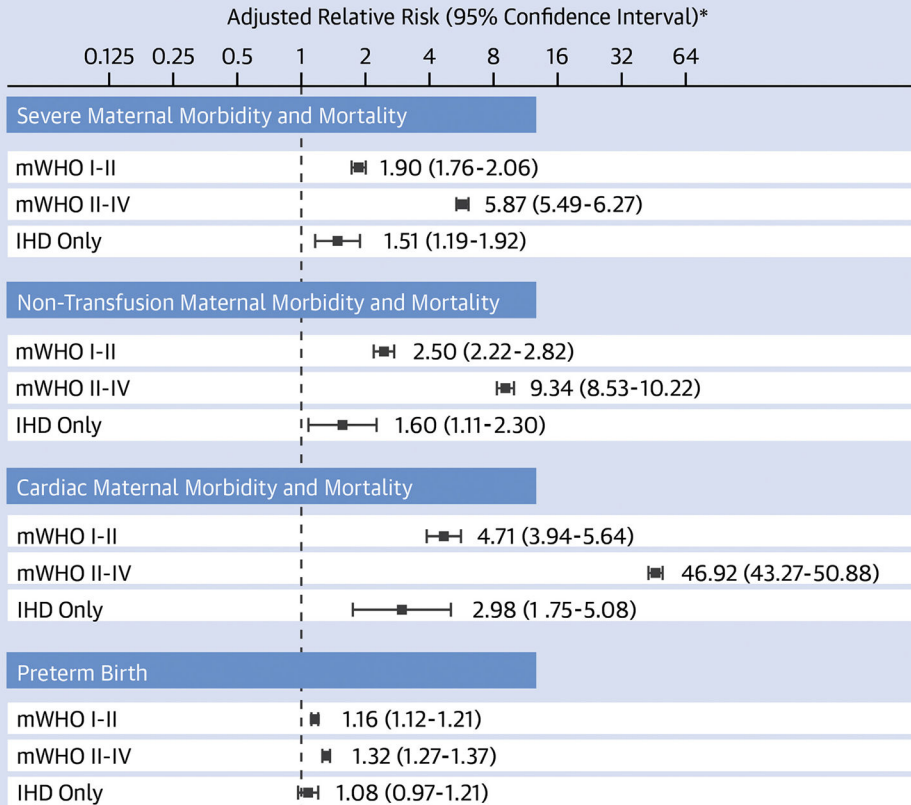## Pregnancy and Pre-Existing Ischemic Heart Disease

Study Population

11,556,136 delivery hospitalizations in the United States

3,009 (0.03%) with isolated pre-existing ischemic heart disease (IHD)

6.6% of women with IHD experienced SMM or death during delivery hospitalization

Risk of SMM in women with IHD similar to those in the modied WHO I or II risk class

Adjusted Relative Risk (95% Confidence Interval)*

0.125 0.25 0.5 1 2 4 8 16 32 64

Severe Maternal Morbidity and Mortality

mWHO I-II	1.90 (1.76-2.06)
mWHO II-IV	5.87 (5.49-6.27)
IHD Only	1.51 (1.19-1.92)

Non-Transfusion Maternal Morbidity and Mortality

mWHO I-II	2.50 (2.22-2.82)
mWHO II-IV	9.34 (8.53-10.22)
IHD Only	1.60 (1.11-2.30)

Cardiac Maternal Morbidity and Mortality

mWHO I-II	4.71 (3.94-5.64)
mWHO II-IV	46.92 (43.27-50.88)
IHD Only	2.98 (1.75-5.08)

Preterm Birth

mWHO I-II	1.16 (1.12-1.21)
mWHO II-IV	1.32 (1.27-1.37)
IHD Only	1.08 (0.97-1.21)

* All comparisons relative to cardiac disease and adjusted for age, delivery type, comorbid conditions, calendar year, and quarter

CENTRAL ILLUSTRATION.

Pregnancy in the Setting of Pre-existing Ischemic Heart Disease May Be Considered Safe But Is Not Without Risk

Pre-existing IHD is associated with worse outcomes at the time of delivery than no cardiac diagnosis. This risk approximates that of a patient with other low-risk cardiac diagnoses classified as either mWHO class I or II. Pregnancy in the setting of pre-existing ischemic heart disease is likely safe, but patients should be counseled that pregnancy is not without risk entirely. Forest plot of adjusted relative risk for severe maternal morbidity (SMM) and death, nontransfusion SMM and death, cardiac SMM and death, and preterm birth for

those with IHD only, mWHO class I-II cardiac disease, and mWHO class II/III-IV cardiac disease compared to no cardiac disease. The adjusted relative risk of SMM and death, nontransfusion SMM and death, and cardiac SMM and death were significantly higher for those with IHD only than for those with no cardiac disease and most closely approximates the risk posed by lesions included in mWHO class I-II. mWHO = modified World Health Organization Classification of Maternal Cardiovascular Risk.

TABLE 1

Baseline Characteristics Compared Between Groups

	Overall (N = 6,109,133) (Wt. N = 11,556,136)	No Cardiac Disease (N = 6,074,785) (Wt. N = 11,490,806)	mWHO I-II (N = 18,449) (Wt. N = 34,742)	mWHO II/III-IV (N = 14,334) (Wt. N = 27,579)	IHD Only (N = 1,565) (Wt. N = 3,009)	P Value[a]
Demographics						
Age in y at admission	28.7 ± 5.8	28.7 ± 5.8	30.2 ± 5.9	29.7 ± 5.9	32.2 ± 6.2	<0.001
Primary expected payer						<0.001
Medicare	91,879 (0.8)	90,492 (0.8)	466 (1.3)	790 (2.9)	131 (4.4)	
Medicaid	4,888,339 (42.4)	4,862,979 (42.4)	11,740 (33.8)	11,996 (43.6)	1,625 (54.1)	
Private	6,068,687 (52.6)	6,032,770 (52.6)	21,121 (60.9)	13,658 (49.6)	1,138 (37.9)	
Self-pay	161,004 (1.4)	160,369 (1.4)	304 (0.9)	305 (1.1)	27 (0.9)	
No charge	5,333 (0.0)	5,306 (0.0)	11 (0.0)	15 (0.1)	-	
Other	327,245 (2.8)	325,339 (2.8)	1,051 (3.0)	775 (2.8)	80 (2.7)	
Zip code median household income						<0.001
Quartile 1 (lowest)	3,181,513 (27.7)	3,164,018 (27.7)	8,324 (24.1)	8,153 (29.8)	1,017 (34.2)	
Quartile 2	3,018,578 (26.3)	3,002,227 (26.3)	8,395 (24.3)	7,197 (26.3)	759 (25.5)	
Quartile 3	2,888,005 (25.2)	2,871,394 (25.2)	9,201 (26.7)	6,669 (24.3)	741 (24.9)	
Quartile 4 (highest)	2,391,643 (20.8)	2,377,221 (20.8)	8,592 (24.9)	5,371 (19.6)	460 (15.4)	
Hospital bed size						<0.001
Small	1,901,888 (16.5)	1,893,633 (16.5)	4,655 (13.4)	3,254 (11.8)	347 (11.5)	
Medium	3,340,629 (28.9)	3,324,948 (28.9)	9,011 (25.9)	5,901 (21.4)	768 (25.5)	
Large	6,313,619 (54.6)	6,272,225 (54.6)	21,077 (60.7)	18,423 (66.8)	1,894 (62.9)	
Hospital location/teaching status						<0.001
Metropolitan nonteaching	2,587,302 (22.4)	2,576,632 (22.4)	6,118 (17.6)	4,059 (14.7)	494 (16.4)	
Metropolitan teaching	7,885,890 (68.2)	7,835,052 (68.2)	26,323 (75.8)	22,117 (80.2)	2,399 (79.7)	
Nonmetropolitan hospital	1,082,944 (9.4)	1,079,122 (9.4)	2,302 (6.6)	1,403 (5.1)	116 (3.9)	
Comorbidities						
Gestational diabetes mellitus	865,973 (7.5)	860,246 (7.5)	2,912 (8.4)	2,498 (9.1)	318 (10.6)	<0.001
HIV/AIDS	10,507 (0.1)	10,408 (0.1)	38 (0.1)	56 (0.2)	-	<0.001
Pre-existing diabetes mellitus	152,953 (1.3)	150,742 (1.3)	692 (2.0)	1,156 (4.2)	364 (12.1)	<0.001
Prior cesarean birth	2,024,423 (17.5)	2,009,682 (17.5)	7,379 (21.2)	6,521 (23.6)	841 (28.0)	<0.001

	Overall (N = 6,109,133) (Wt. N = 11,556,136)	No Cardiac Disease (N = 6,074,785) (Wt. N = 11,490,806)	mWHO I-II (N = 18,449) (Wt. N = 34,742)	mWHO II/III-IV (N = 14,334) (Wt. N = 27,579)	IHD Only (N = 1,565) (Wt. N = 3,009)	P Value[a]
Pulmonary hypertension	2,615 (0.0)	67 (0.0)	<10 (0.0)	2,543 (9.2)	0 (0.0)	<0.001
Multiple gestation	209,450 (1.8)	207,634 (1.8)	877 (2.5)	884 (3.2)	55 (1.8)	<0.001
Asthma	571,759 (4.9)	562,958 (4.9)	3,666 (10.6)	4,617 (16.7)	517 (17.2)	<0.001
Bleeding disorder	250,009 (2.2)	246,872 (2.1)	1,481 (4.3)	1,501 (5.4)	156 (5.2)	<0.001
BMI 40 kg/m²	495,010 (4.3)	490,259 (4.3)	2,049 (5.9)	2,388 (8.7)	314 (10.4)	<0.001
Chronic hypertension	376,876 (3.3)	369,827 (3.2)	2,421 (7.0)	3,793 (13.8)	835 (27.8)	<0.001
Chronic renal disease	29,314 (0.3)	28,292 (0.2)	218 (0.6)	723 (2.6)	81 (2.7)	<0.001
Connective tissue or autoimmune disease	23,026 (0.2)	22,333 (0.2)	251 (0.7)	366 (1.3)	76 (2.5)	<0.001
Placenta previa	54,859 (0.5)	54,397 (0.5)	267 (0.8)	165 (0.6)	29 (1.0)	<0.001
Preeclampsia with severe features	362,283 (3.1)	356,771 (3.1)	1,715 (4.9)	3,418 (12.4)	379 (12.6)	<0.001
Gestational hypertension/preeclampsia without severe features	910,296 (7.9)	904,078 (7.9)	3,221 (9.3)	2,750 (10.0)	247 (8.2)	<0.001
Substance use disorder	746,072 (6.5)	739,814 (6.4)	2,480 (7.1)	3,150 (11.4)	628 (20.9)	<0.001
Advanced maternal age	1,989,716 (17.2)	1,974,002 (17.2)	8,350 (24.0)	6,161 (22.3)	1,203 (40.0)	<0.001
Pre-existing anemia	1,470,814 (12.7)	1,458,794 (12.7)	5,914 (17.0)	5,483 (19.9)	624 (20.7)	<0.001
Bariatric surgery	29,692 (0.3)	29,320 (0.3)	165 (0.5)	169 (0.6)	39 (1.3)	<0.001
Gastrointestinal disease	629,946 (5.5)	621,902 (5.4)	4,112 (11.8)	3,387 (12.3)	545 (18.1)	<0.001
Mental health disorder	819,175 (7.1)	808,775 (7.0)	5,551 (16.0)	4,178 (15.1)	672 (22.3)	<0.001
Neuromuscular disease	56,498 (0.5)	55,613 (0.5)	400 (1.2)	378 (1.4)	106 (3.5)	<0.001
Placental abruption	124,058 (1.1)	122,962 (1.1)	453 (1.3)	594 (2.2)	50 (1.7)	<0.001
Placenta accreta spectrum	12,933 (0.1)	12,765 (0.1)	75 (0.2)	77 (0.3)	16 (0.5)	<0.001
Thyrotoxicosis	29,714 (0.3)	29,219 (0.3)	276 (0.8)	200 (0.7)	19 (0.6)	<0.001
Calendar year						<0.001
2015	897,844 (7.8)	893,208 (7.8)	2,644 (7.6)	1,783 (6.5)	208 (6.9)	
2016	3,613,874 (31.3)	3,594,549 (31.3)	10,593 (30.5)	7,915 (28.7)	818 (27.2)	
2017	3,550,931 (30.7)	3,530,738 (30.7)	10,524 (30.3)	8,656 (31.4)	1,013 (33.7)	
2018	3,493,487 (30.2)	3,472,311 (30.2)	10,981 (31.6)	9,225 (33.4)	969 (32.2)	
Discharge quarter						0.13
1	2,573,113 (22.3)	2,558,699 (22.3)	7,693 (22.1)	6,056 (22.0)	664 (22.1)	
2	2,614,467 (22.6)	2,599,681 (22.6)	7,881 (22.7)	6,310 (22.9)	595 (19.8)	
3	2,824,332 (24.4)	2,808,163 (24.4)	8,433 (24.3)	6,979 (25.3)	756 (25.1)	

	Overall	No Cardiac Disease	mWHO I-II	mWHO II/III-IV	IHD Only	
	(N = 6,109,133) (Wt. N = 11,556,136)	(N = 6,074,785) (Wt. N = 11,490,806)	(N = 18,449) (Wt. N = 34,742)	(N = 14,334) (Wt. N = 27,579)	(N = 1,565) (Wt. N = 3,009)	P Value[a]
4	3,544,224 (30.7)	3,524,262 (30.7)	10,735 (30.9)	8,233 (29.9)	994 (33.0)	

Values are mean ± SD or n (%).

[a] P values by weighted chi-square test.

BMI = body mass index; IHD = pre-existing ischemic heart disease; mWHO = modified World Health Organization classification of maternal cardiovascular risk; Wt = weighted

TABLE 2

Primary and Secondary Outcomes Compared Between Groups

	Overall (N = 6,109,133) (Wt. N = 11,556,136)	No Cardiac Disease (N = 6,074,785) (Wt. N = 11,490,806)		WHO Cardiac Category				
				mWHO I-II (N = 18,449) (Wt. N = 34,742)		mWHO II/III-IV (N = 14,334) (Wt. N = 27,579)		IHD Only (N = 1,565) (Wt. N = 3,009)
Composite of SMM and death	185,981 (1.6)	177,953 (1.5)	ref	1,447 (4.2)	2.7 (2.5–2.9)	6,383 (23.1)	14.9 (14.3–15.6)	198 (6.6)	4.3 (3.5–5.2)
Any nontransfusion SMM during index admission	76,327 (0.7)	69,382 (0.6)	ref	888 (2.6)	4.2 (3.8–4.7)	5,926 (21.5)	35.6 (33.9–37.3)	130 (4.3)	7.2 (5.5–9.3)
Cardiac SMM during index event	17,467 (0.2)	12,159 (0.1)	ref	312 (0.9)	8.4 (7.2–10.0)	4,955 (18.0)	169.1 (159.9–178.8)	41 (1.4)	12.9 (8.2–20.3)
Preterm birth	1,168,105 (10.1)	1,155,484 (10.1)	ref	4,979 (14.3)	1.4 (1.4–1.5)	6,935 (25.1)	2.5 (2.4–2.6)	707 (23.5)	2.3 (2.1–2.6)

Values are n (%) or unadjusted RR (95% CI). Unadjusted relative risk by weighted Poisson regression; all comparisons relative to no cardiac disease.

IHD = pre-existing ischemic heart disease; mWHO = modified World Health Organization classification of maternal cardiovascular risk; SMM = severe maternal morbidity; Wt = weighted.