

Maternal, perinatal and post-neonatal outcomes in women with chronic heart disease in  
Washington State

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**Abstract**

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**Objective:** European and British reports suggest that the prevalence of maternal heart disease is increasing. The consequences of maternal congenital heart disease, ischemic heart disease, heart failure and pulmonary hypertension on the health of offspring are understudied. We explored the association between the presence of maternal heart disease and maternal, perinatal and infant outcomes.

**Methods:** We conducted a population-based retrospective cohort study using Washington State birth certificates linked with hospital discharge records of mothers for whom the presence of maternal congenital heart disease, ischemic heart disease, heart failure or pulmonary hypertension was noted. Women who gave birth between 1987 and 2009 (n=2,171) were compared to a sample of mothers without these conditions (n=21,710), frequency matched by calendar year. We described the characteristics of pregnant women with heart disease over time. Logistic regression was used to describe the association between reported chronic maternal heart disease and small for gestational age (SGA) birth, as well as perinatal, post-neonatal and maternal death.

**Results:** The proportion of births to women with reported heart disease increased 224% between the 1987-1994 and 2002-2009 calendar periods. Chronic maternal heart disease was associated with increased risk of SGA birth (OR 1.7, 95% CI 1.5-1.9), perinatal death (OR 2.5, 95% CI 1.8-3.5), post-neonatal death (OR 4.6, 95% CI 2.4-8.9) and maternal death (OR 55, 95% CI 12-249). Associations were similar among types of cardiac disease.

**Conclusion:** The presence of chronic maternal heart disease is associated with elevated risk for poor maternal, perinatal and post-neonatal outcomes.

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## **Introduction**

Pregnancy is accompanied by physiologic changes that stress the heart. Normal pregnancy leads to increased blood volume, heart rate and cardiac output(1). These changes appear to support normal fetal growth(2), but can lead to cardiac hypertrophy, dilation and increased cardiac oxygen requirements in the mother(3). Although these changes are well tolerated in healthy women, women with underlying heart disease may suffer adverse consequences from the additional burden(4,5).

Experience in the United Kingdom suggests that heart disease in pregnancy is an increasing public health concern and now represents the leading cause of death in pregnant women(6). The increase in prevalence is thought to be a manifestation of greater longevity in congenital heart disease patients, a trend toward older mothers with more prevalent diabetes and hypertension, and newer guidelines regarding pregnancy risk(6-8). Epidemiologic studies of maternal heart disease in the United States (U.S.) are sparse. A sole U.S. report suggests that the number of mothers with heart disease and the fraction of these mothers who experience complications have increased over time. This report did not address perinatal outcomes and no reports address post-neonatal outcomes(9).

In a population of mothers giving birth in Washington State between 1987 and 2009, we sought to describe pregnant women with heart disease and examine the associations between maternal heart disease and poor outcomes in mothers and children.

## **Methods**

### ***Study Design and Subject Eligibility***

We conducted a population-based retrospective cohort study using hospital discharge records linked with birth certificate data from all nonfederal hospitals in the Comprehensive Hospital Abstract Reporting System (CHARS) in Washington State. Routine linkage of birth records to hospital discharge records, using a combination of sequential probabilistic and deterministic linkages, has been conducted in Washington State for decades with increased accuracy over either modality alone when compared to chart review(10,11). The study was reviewed by the Human Subjects Division at the University of Washington and was determined to be exempt from full IRB review as the authors only had access to de-identified data (Exempt #41371). The primary research question focused on the following types of *chronic* heart disease: (a) congenital heart disease; (b) heart failure; (c) ischemic heart disease; and (d) pulmonary hypertension. Pulmonary hypertension was included as it is increasingly recognized as a combined disease of the heart and pulmonary vasculature(12). Mothers with isolated valvular heart disease, peripartum cardiomyopathy, infectious heart disease (e.g., endocarditis or myocarditis), diseases of the electrical system or unspecified heart disease who did not also meet our criteria for *chronic* heart disease were not included, as we believed these could represent isolated, late and/or acute events. We identified mothers with presumed chronic heart disease as those whose discharge records contained ICD-9 codes for specified conditions during the birth or antecedent hospitalizations between 1987 and 2009 (Appendix 1). Births to mothers with chronic heart disease were stratified by birth year and the distribution of birth years was used to select births to mothers without heart disease. Within each birth year, the selection of births to mothers without heart disease was performed at random. We utilized a sampling ratio of ten to one (births to mothers without chronic heart disease : births to mothers with chronic heart disease) to provide 80% power to detect a 20% increase in the odds of SGA birth,

which is comparable to other identified risk factors for SGA birth(13). For women with multiple births in Washington State, the first recorded birth was used.

Isolated valvular heart disease is a form of chronic heart disease, but we chose not to focus on valvular disease because we were concerned that these mothers would be heterogeneous and include many mothers with benign valvular diseases of pregnancy (e.g., mitral valve prolapse), which have no meaningful systemic effects.

## **Outcomes**

The primary outcome was SGA birth, defined as a birth weight of less than the 10<sup>th</sup> percentile by week of gestational age for all births in Washington State from 1987-2009(14,15). Gestational age and birth weight were collected from the birth certificate and coded centrally using this Washington based standard as SGA. Secondary outcomes, including perinatal and post-neonatal mortality, were collected from linked death certificates. Perinatal mortality included stillbirth (>20 weeks gestation) and neonatal deaths prior to 28 days of life, excluding elective terminations(16). Post-neonatal mortality included death up to one year of age excluding the perinatal period. Combined perinatal and post-neonatal mortality was also assessed. Maternal mortality was estimated from the CHARS database for mothers who died in any nonfederal Washington State Hospital within 90 days of the birth hospitalization.

## **Clinical Characteristics**

Clinical characteristics potentially associated with heart disease and maternal, perinatal and post-neonatal outcomes were selected from birth certificate data, including maternal age, race, body mass index (BMI), smoking status, diabetes, and hypertension. Maternal age and BMI were modeled continuously and other covariables were modeled categorically. Three birth cohorts of 92 months each (January 1987 to August 1994, September 1994 to April 2002, May 2002 to December 2009) were created to describe temporal changes over the study period.

Hospital charges for the mother and baby and maternal length of stay for the birth hospitalization were available in CHARS and used descriptively.

### **Statistical Analyses**

Women with and without heart disease were compared descriptively. This included descriptions of maternal heart disease as a proportion of total births in Washington State using published state-wide birth rates(17). Logistic regression estimated the relationship between maternal heart disease, SGA, perinatal, post-neonatal and maternal mortality (unadjusted model). The odds ratio (OR) was felt to be a reasonable proxy for relative risk given the rarity of all outcomes except SGA where the OR may overestimate the relative risk(18). Model 1 was adjusted for cardiac risk factors including maternal age, race, BMI, smoking status, diabetes and hypertension. For the outcomes of perinatal and post-neonatal mortality, model 2 was further adjusted for birth weight and gestational age in addition to the terms included in model 1. Twenty datasets with multiple imputation for missing data from chained equations were used in adjusted models(19). Unadjusted rates of SGA, maternal, perinatal and post-neonatal death per 1,000 births and attributable risk (incidence in the exposed cohort – incidence in the unexposed cohort) were reported. Analyses were performed using STATA 11.0 (StataCorp, College Station, TX, USA).

## **Results**

### **Demographic characteristics of mothers**

There were 1,871,770 births between 1987 and 2009 in Washington State. Among these, 2,171 births were to women who met our definition of chronic heart disease and 21,710 births, frequency matched by year, were sampled from women without known chronic heart disease. Of mothers with heart disease, 1,262 had congenital heart disease (58.2%), 532 had heart failure (24.5%), 186 had ischemic heart disease (8.6%), 91 had pulmonary hypertension (4.2%) and 100 women had more than one condition (4.6%).

SGA status was available for 2,106 of 2,171 infants of women with heart disease (97%) and 21,349 of 21,710 infants of women without heart disease (98%). Perinatal and neonatal mortality was obtained from death certificates and was likely completely ascertained. Age, race, smoking status, birth weight, gestational age, diabetes and hypertension were missing in less than 10% of instances; however, BMI was missing for 30.2% of women.

Annual births in Washington increased from 70,409 in 1987 to 89,242 in 2009(17). The proportion of births to mothers with chronic heart disease increased 224% over the study period (56 to 179 per 100,000 births)(Figure 1). The proportion of births to mothers with congenital heart disease increased 218% (33 to 105 per 100,000 births), heart failure increased 173% (15 to 41 per 100,000 births), ischemic heart disease increased 240% (4.7 to 16 per 100,000 births) and pulmonary hypertension increased 727% (1.6 to 8.8 per 100,000 births).

Figure 1. Proportion of births to mothers with heart disease per 100,000 births, by calendar period, Washington State, 1987-2009. (A) Increase in proportion of births to mothers with heart disease (B) Increase in proportion of births to mothers by type of heart disease

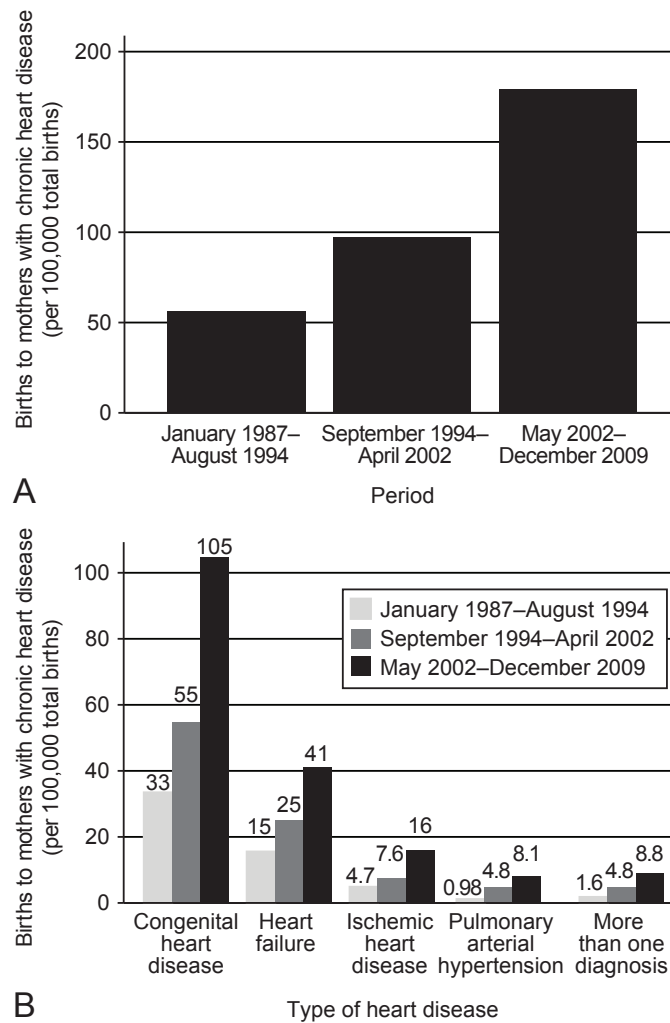


Table 1 describes the cohorts. Mothers with chronic heart disease tended to have a higher prevalence of smoking, diabetes and hypertension. Hospital charges were higher and hospitalization longer for mothers with chronic heart disease. Characteristics were similar among the four types of chronic heart disease (data not shown) with the exception that mothers with ischemic heart disease tended to be older (30.4 years old) with a higher prevalence of diabetes (12.6%) and smoking (18.7%). Table 2 describes changes in maternal characteristics over time.

Table 1. Characteristics of mothers with and without heart disease, Washington State, 1987-2009.

	Women with Heart Disease (n=2,171)	Women without Heart Disease (n=21,710)
<u>Demographics</u>		
Age, years	26.8 (6.8)	26.6 (6.2)
Race, %		
White	73.2%	71.9%
Black	6.7%	4.1%
Asian	7.6%	8.4%
Other	12.5%	15.6%
Married	58.6%	65.1%
Education, years	12.8 (2.7)	13.0 (3.0)
Income <sup>a</sup>	\$42,850	\$44,003
<u>Comorbidities</u>		
Body Mass Index, kg/m <sup>2</sup>	25.7 (6.4)	25.4 (5.9)
Smoking	13.7%	10.9%
Established or Gestational Diabetes	6.9%	4.8%
Chronic Hypertension	4.3%	1.3%
<u>Obstetric History</u>		
Number of prior pregnancies	1.3 (1.9)	1.1 (1.5)
Number of prenatal visits	11.5 (6.9)	11.1 (6.0)
<u>Birth Hospitalization</u>		
Caesarean-Section	37.1%	25.0%
Length of Stay, days	4.0 (7.6)	2.3 (1.9)
Hospital Charges	\$23,622	\$11,558

All values presented as mean (standard deviation), mean, or percentage

<sup>a</sup> Median income from census tract of residence

Table 2. Characteristics of mothers with and without heart disease, by calendar period (1-3)<sup>a</sup>, Washington State, 1987-2009.

	Women with heart disease			Women without heart disease		
	<i>Calendar Period</i>			<i>Calendar Period</i>		
	<i>One</i>	<i>Two</i>	<i>Three</i>	<i>One</i>	<i>Two</i>	<i>Three</i>
	n=345	n=611	n=1,215	n=3,427	n=6,191	n=12,089
<u>Demographics</u>						
Age, years	27.2(6.2)	27.6(6.8)	26.3(6.9)	26.5(5.9)	26.4(6.3)	26.8(6.2)
Race, %						
White	81.2%	73.8%	70.7%	81.6%	71.0%	69.6%
Non-white	18.8%	26.2%	29.3%	18.4%	29.0%	30.4%
Married	70.9%	63.5%	52.6%	72.2%	66.1%	62.6%
Education, years	13.1(2.8)	12.8(2.8)	12.8(2.6)	12.8(2.8)	12.9(2.9)	13.1(3.0)
Income <sup>b</sup>	\$34,686	\$43,371	\$44,838	\$34,712	\$43,628	\$46,693
<u>Comorbidity</u>						
Body Mass Index, kg/m <sup>2</sup>	23.8(6.5)	25.5(6.2)	25.9(6.5)	24.0(4.9)	24.4(5.2)	25.9(6.1)
Smoking	11.6%	15.0%	13.4%	17.7%	12.6%	8.7%
Established or Gestational Diabetes	5.9%	6.9%	7.1%	2.6%	3.5%	5.9%
Chronic Hypertension	1.6%	5.2%	4.6%	1.1%	1.2%	1.3%
<u>Obstetric History</u>						
Number of prior pregnancies	1.4(1.9)	1.3(1.8)	1.3(2.0)	1.2(1.6)	1.0(1.5)	1.0(1.6)
Number of prenatal visits	13.4(12.8)	11.7(4.4)	10.8(4.8)	12.7(11.4)	11.2(3.9)	10.6(4.0)
<u>Birth Hospitalization</u>						
Caesarean-Section	31.0%	37.2%	38.7%	20.0%	19.7%	29.2%
Length of Stay, days	4.6(9.4)	4.3(10.0)	3.7(5.4)	2.4(2.1)	2.1(1.6)	2.4(1.9)
Hospital Charges	\$9,034	\$32,547	\$31,470	\$4,281	\$16,127	\$16,033
<u>Offspring Outcomes</u>						
Perinatal & Post-neonatal death (# per 1,000 births)	26	30	29	12	9	9
Small for Gestational Age	18.9%	17.0%	15.6%	11.0%	10.5%	10.1%

All values presented as mean (standard deviation), mean, or percentage

<sup>a</sup> Calendar period: One, December 1987 to August 1994; Two, September 1994 to April 2002; Three, May 2002 to December 2009, <sup>b</sup> Median income from census tract of residence

## Perinatal and post-neonatal outcomes

Compared to children of mothers without heart disease, those with chronic heart disease had lower mean birth weight (3148g versus 3378g) and shorter mean gestation ( $38 \frac{6}{7}$  versus  $39 \frac{1}{7}$  weeks). Premature delivery (less than 32 weeks) among women with heart disease occurred in 39 per 1,000 births (n=81) compared to 13 per 1,000 births to mothers without (n=277). SGA birth was more likely in children born to mothers with heart disease than in children born to mothers without heart disease (62 additional SGA births per 1,000 births, 95% CI 46-78, p-value <0.001)(Table 3). This association was little affected by adjustment for common cardiac risk factors (model 1) and was present within subtypes of chronic non-valvular heart disease.

Perinatal and post-neonatal deaths were elevated among children of mothers with chronic heart disease (Table 3). Perinatal deaths occurred in 22.1 per 1,000 births (n=48 deaths) to mothers with chronic heart disease compared to 8.1 per 1,000 births (n=176 deaths) to mothers without (14 additional deaths per 1,000 births, 95% CI 8-20, p<0.001). Of these, 17 per 1,000 births (n=37) and 5 per 1,000 births (n=103) were stillbirth in women with and without heart disease respectively. Post-neonatal deaths occurred in 6.4 per 1,000 births (n=14 deaths) to mothers with chronic heart disease compared to 1.3 per 1,000 births (n=29 deaths) to mothers without (5 additional deaths per 1,000 births, 95% CI 2-9, p<0.001). The associations between chronic heart disease, perinatal and post-neonatal mortality remained after adjustment for cardiac risk factors (model 1). With additional adjustment for gestational age and birth weight, chronic heart disease was but weakly associated with perinatal mortality (OR 1.3, 95% CI 0.9-2.0, p=0.16), but remained independently associated with post-neonatal mortality (OR 4.0, 95% CI 2.1-7.8, p<0.001). Risk estimates were similar among types of chronic heart disease. The cause-specific post-neonatal death rate to mothers with chronic heart disease appeared higher for sudden infant death syndrome, infection and congenital heart disease. There were no accidental infant deaths among mothers with chronic heart disease (Table 4).

Table 3. Association between maternal heart disease<sup>a</sup> and poor outcomes, Washington State, 1987-2009.

Outcome	with heart disease # (#/1,000 births)	without heart disease # (#/1,000 births)	Attributable risk #/1,000 births (95% CI)	Unadjusted odds ratio (95% CI)	Model 1 <sup>e</sup> odds ratio (95% CI)	Model 2 <sup>f</sup> odds ratio (95% CI)
<b>Maternal Death<sup>b</sup></b>	<b>12 (6)</b>	<b>2 (0)</b>	<b>5 (2-9)</b>	<b>60 (14-269)</b>	<b>55 (12-249)</b>	
<b>Small for Gestational Age</b>	<b>348 (165)</b>	<b>2,204 (103)</b>	<b>62 (46-78)*</b>	<b>1.7 (1.5-1.9)*</b>	<b>1.7 (1.5-1.9)*</b>	
by pulmonary hypertension	29 (201)			2.0(1.3-3.1)*	1.8(1.2-2.8)*	
by heart failure	109 (205)			2.0(1.6-2.5)*	1.9(1.5-2.4)*	
by ischemic heart disease	47 (216)			2.1(1.5-3.0)*	2.0(1.4-2.9)*	
by congenital heart disease	201 (154)			1.5(1.3-1.8)*	1.5(1.3-1.7)*	
<b>Perinatal &amp; Post-neonatal Death</b>	<b>62 (29)</b>	<b>205 (9)</b>	<b>19 (12-26)*</b>	<b>3.1 (2.3-4.1)*</b>	<b>2.8 (2.1-3.8)*</b>	<b>1.7 (1.2-2.5)*</b>
by pulmonary hypertension	5 (35)			3.8 (1.5-9.3)*	3.2(1.3-7.9)*	0.9(0.3-2.9)
by heart failure	21 (40)			4.3 (2.7-6.8)*	3.7(2.3-6.0)*	1.5(0.9-2.7)
by ischemic heart disease	6 (28)			3.0 (1.3-6.8)*	2.4(1.0-5.7)*	1.1(0.4-3.1)
by congenital heart disease	34 (26)			2.8 (1.9-4.1)*	2.7(1.9-3.9)*	2.5(1.6-3.8)*
<b>Perinatal Death<sup>c</sup></b>	<b>48 (22)</b>	<b>176 (8)</b>	<b>14 (8-20)*</b>	<b>2.8 (2.0-3.8)*</b>	<b>2.5 (1.8-3.5)*</b>	<b>1.3 (0.9-2.0)</b>
by pulmonary hypertension	4 (28)			3.5(1.3-9.5)*	2.8(1.0-7.9)*	0.6(0.2-2.4)
by heart failure	14 (26)			3.3(1.9-5.7)*	2.7(1.5-4.9)*	0.9(0.4-1.8)
by ischemic heart disease	5 (23)			2.9(1.2-7.1)*	2.2(0.9-5.6)*	0.8(0.2-2.7)
by congenital heart disease	26 (20)			2.5(1.6-3.8)*	2.4(1.6-3.7)*	2.2(1.3-3.6)*
<b>Post-neonatal Death<sup>d</sup></b>	<b>14 (6)</b>	<b>29 (1)</b>	<b>5 (2-9)*</b>	<b>4.9 (2.6-9.2)*</b>	<b>4.6 (2.4-8.9)*</b>	<b>4.0 (2.1-7.8)*</b>
by pulmonary hypertension	1 (7)			5.2(0.7-38.6)*	5.0(0.7-38.2)*	4.1(0.5-32.3)*
by heart failure	7(13)			10.0(4.3-22.9)*	11.2(4.7-26.3)*	9.4(3.9-22.9)*
by ischemic heart disease	1 (5)			3.4(0.5-25.4)*	4.3(0.6-33.6)*	3.6(0.4-29.4)*
by congenital heart disease	8 (6)			4.6(2.1-10.1)*	4.0(1.8-8.8)*	3.7(1.7 - 8.2)*

p ≤ 0.05

<sup>a</sup> For the subtype analysis, Individuals with a combination of heart diseases were included in each component category (pulmonary hypertension, 144 women; heart failure, 532 women; ischemic heart disease, 218; congenital heart disease, 1302);

<sup>b</sup> maternal death included deaths between delivery and 90 days post-partum; <sup>c</sup> perinatal death included fetal death >20 weeks and neonatal death up to 28 days; <sup>d</sup> post-neonatal death included deaths between 28 and 365 days of life; <sup>e</sup> adjusted for education, age, race, body mass index, smoking status, diabetes, hypertension; <sup>f</sup> adjusted for Model 1 covariates plus gestational age and birth weight (model 2 not scientifically appropriate for SGA or maternal death)

Table 4. Post-neonatal mortality, Washington State, 1987-2009.

	Decedents among children of mothers with heart disease (n=14)	Decedents among children of mothers without heart disease (n=29)
<b>All post-neonatal deaths</b>		
<u>Cause of Death</u>	<u>Post-neonatal deaths per 1,000 births (% of deaths)</u>	
Congenital Anomaly	2.3 (36%)	0.5 (38%)
Infection	1.4 (21%)	0.05 (3%)
Sudden Infant Death Syndrome	1.8 (29%)	0.4 (28%)
Accidental Death	0 (0%)	0.2 (17%)
Miscellaneous	0.9 (14%)	0.2 (14%)
<u>Birth Characteristics of the deceased</u>		
Mean birth weight, grams (SD)	2803 (1040)	3090 (896)
Mean gestational age, days (SD)	263 (26)	275 (25)
<b>Post-neonatal deaths Excluding Extremely Low Birth Weight Births<sup>a</sup></b>		
<u>Cause of Death</u>	<u>Post-neonatal deaths per 1,000 births (% of deaths)</u>	
Congenital Anomaly	2.3 (42%)	0.5 (36%)
Infection	0.5 (8.3%)	0.05 (4%)
Sudden Infant Death Syndrome	1.8 (33%)	0.4 (29%)
Accidental Death	0 (0%)	0.2 (18%)
Miscellaneous	0.9 (17%)	0.2 (14%)
<u>Birth Characteristics of the deceased</u>		
Mean birth weight, grams (SD)	3151 (584)	3181 (770)
Mean gestational age, weeks (SD)	38 <sup>3</sup> / <sub>7</sub> (2 <sup>1</sup> / <sub>7</sub> )	38 <sup>6</sup> / <sub>7</sub> (2 <sup>6</sup> / <sub>7</sub> )

<sup>a</sup> 2 infants to mothers with heart disease excluded (birth weight 491 grams & 936 grams) and one infant to a mother without cardiac disease excluded (birth weight 637 grams)

Two exploratory analyses of the association between chronic heart disease and post-neonatal mortality were performed. Exclusion of extremely low birth weight infants (ELBW)( $<1,000\text{g}$ ) did not impact the relationship (unadjusted OR 4.3, 95% CI 2.2-9.5; model 1 OR 4.3, 95% CI 2.2-8.5, all  $p<0.001$ ). Similarly, analysis restricted to full term births ( $>37$  weeks gestation) did not alter the relationship between maternal heart disease and post-neonatal death (unadjusted OR 4.4, 95% CI 2.0-9.6; model 1 OR 4.3, 95% CI 2.0-9.2, all  $p<0.001$ ).

Twelve mothers of 2,171 mothers with chronic heart disease died within 90 days of a birth hospitalization (5.5 per 1,000 mothers). One of these women had congenital heart disease and pulmonary hypertension, two had pulmonary hypertension, seven had heart failure and two had ischemic heart disease. Two mothers without chronic heart disease died within 90 days of delivery (0.1 deaths per 1,000 mothers). Maternal deaths in Washington State over the study period averaged 0.1 deaths per 1,000 mothers(17).

## **Discussion**

In this population-based retrospective cohort study in Washington State, the proportion of mothers with chronic heart disease dramatically increased over the 22 years of study. Maternal deaths were more likely in women with chronic heart disease as were SGA birth, perinatal and post-neonatal deaths.

This study has several limitations. Unmeasured or residual confounding is possible. Misclassification is present, which would be expected to bias results toward the null(10,11). Missing data was present. We used imputation to account for this and reduce bias from complete case analysis; however, if the data was not missing at random this might bias the adjustment, particularly for obesity. Differential misclassification, in which adverse events lead to ICD-9 coding of chronic heart disease, could also lead to overestimation the negative ramifications of chronic heart disease. Our approach to try to limit this bias was focus on specific chronic heart diseases, excluding the use of ICD-9 codes for “unspecified heart disease” and diseases with both acute and chronic underpinnings such as sudden cardiac death. This may have led to missed cases and an underestimation of risk.

The increase in the proportion of pregnant women with chronic heart disease is similar to that observed in one report in the United States (9) and in several studies performed in the United Kingdom(6,20). The increased prevalence of maternal heart disease parallels population-wide increases in maternal diabetes, smoking, BMI and hypertension(6-8). The higher frequency of Caesarean section, perinatal death, post-neonatal death and SGA birth among mothers with heart disease was stable over time and mothers with chronic heart disease had longer hospital lengths of stay with higher charges. This reassures us that we accurately describe a similar group of ill mothers across the three birth cohorts with a truly increased prevalence of chronic heart disease rather than an artifact of changes in coding practice.

We included mothers with pulmonary hypertension because of the decreased cardiac output and right ventricular dysfunction that accompanies elevations in pulmonary arterial

pressure. Despite firm recommendations for contraception, births to women with pulmonary hypertension increased to a greater extent than births to women with other forms of chronic heart disease. This may be related to misclassification given the lack of normative values specific to gravid women where increased cardiac output from pregnancy may exaggerate pulmonary arterial pressures. Similarly, echocardiography was increasingly used during the study period and lacks precision to appropriately identify modest increases in pulmonary pressure without confirmation by right heart catheterization(21). These two factors may have compounded to increase the detection of mild cases with marginal impact in pregnancy.

The relationship of maternal heart disease with SGA birth, neonatal and fetal mortality has been described(22,23). We confirm these associations using a U.S. cohort. Furthermore, the magnitude of the association between perinatal death and maternal heart disease is similar to that seen in the United Kingdom(24).

The association between chronic heart disease and post-neonatal mortality has not been previously explored. The most common causes of post-neonatal death are sudden infant death syndrome, congenital abnormalities, accidents/assaults, infections and chronic respiratory disease from birth(25). We see increased post-neonatal death in every category but accidents. As the greatest difference was seen for infectious deaths, we speculated that these deaths might represent delayed death following prolonged hospitalization of sickly neonates. However, elevated risk was present even following restriction of the analysis to full-term pregnancies.

We lack a compelling explanation for the increase in post-neonatal deaths to mothers with chronic heart disease. This may reflect residual confounding from a factor such as smoking or suggest an unrecognized pathway linking subclinical fetal stress to childhood disease susceptibility(26). Alternatively, this association may implicate social factors such as a relatively low prevalence of breastfeeding in mothers with chronic heart disease or avoidance of medical care by mothers following a traumatic birth hospitalization. Further study is needed to reinforce the validity of this finding and then explore potential mechanisms.

Adjustment for diabetes, hypertension and smoking, which contribute to SGA birth (13,27), had little effect on associations with chronic heart disease. Heart disease may confer additional risk beyond a higher density of cardiac risk factors. In a subset of mothers with chronic heart disease this might include inflammation and derangements in hemodynamic and coagulation parameters(28).

Maternal mortality among mothers with chronic heart disease was approximately three times greater than that seen in the previous US study (553 versus 162 deaths per 100,000 women)(9). The previous study only accounted for maternal deaths during birth hospitalizations. When we apply this criterion we find similar maternal mortality (138 deaths per 100,000 women). This suggests that failure to account for maternal death following transfer or in the post-partum period may underestimate the burden of disease. Mortality among mothers with pulmonary hypertension (3%) is less than previously reported (17-50%)(7). When mothers with valvular disease were excluded, we saw death in three women of 43 with pulmonary hypertension (7.0%), which is similar to that seen in a recent case series(29). By comparison, we saw similar mortality among mothers with congenital heart disease (0.07%) to a recent report (0.09%)(8). Our data lacked disease severity metrics, so these numbers should be used cautiously in counseling women(22,23).

In conclusion, we found increasing prevalence of chronic heart disease among pregnant women in Washington State over the 22 years of study. Maternal heart disease was associated with poor outcomes including maternal death, SGA birth, perinatal mortality and post-neonatal mortality.

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