

## ORIGINAL RESEARCH

# Cardiovascular Disease Among Women and Birthing Individuals After Delivering a Child With Congenital Heart Disease



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## ABSTRACT

**BACKGROUND** Individuals have a higher risk of cardiovascular disease later in life if they give birth to a child with congenital heart disease (CHD). The mechanism of this association has not been well documented.

**OBJECTIVES** The authors aimed to describe the prevalence of cardiovascular disease and risk factors in women and birthing individuals 18 to 23 years after delivery of a child with CHD compared to normative data.

**METHODS** A cross-sectional survey was distributed to mothers whose infants with CHD had undergone cardiac surgery in 1998 to 2003 and previously enrolled in a prospective observational study. We compared rates of cardiovascular disease and risk factors to age- and sex-matched parous women and birthing individuals from National Health and Nutrition Examination Survey.

**RESULTS** An attempt was made to contact 533 mothers; 222 (42%) completed the survey. The mean age was 52 years, 86% were White, and 69% completed college. Common cardiovascular risk factors were high cholesterol (32%), hypertension (27%), preterm delivery (32%), and hypertensive disorder of pregnancy (13%). Overall, 15.3% reported presence of cardiovascular disease as defined by atherosclerotic cardiovascular disease, heart failure, valvular disease, or arrhythmia. A higher severity of child's CHD was significantly associated with self-reported maternal cardiovascular disease ( $P = 0.03$ ). Compared to National Health and Nutrition Examination Survey participants, rates of atherosclerotic cardiovascular disease and cardiovascular risk factors were similar.

**CONCLUSIONS** Women and birthing individuals whose children had CHD had similar rates of cardiovascular risk factors and disease at 18 to 23 years after delivery, compared to age- and sex-matched parous controls. Higher severity of child's CHD was associated with increased risk of maternal cardiovascular disease, an association that should be evaluated in future studies. (JACC Adv. 2025;4:101434) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the [Author Center](#).

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**ABBREVIATIONS  
AND ACRONYMS****ASCVD** = atherosclerotic  
cardiovascular disease**CHD** = congenital heart disease**CHOP** = Children's Hospital of  
Philadelphia**M-CHOP** = Maternal-Children's  
Hospital of Philadelphia**NHANES** = National Health and  
Nutrition Examination Survey**STAT** = Society of Thoracic  
Surgeons-European Association  
for Cardio-Thoracic Surgery

**C**ardiovascular disease is the leading cause of death among women.<sup>1</sup> Hypertension continues to be the leading cardiovascular risk factor in women; however, sex-specific risk factors have been increasingly reported in the literature.<sup>1</sup> Women and birthing individuals who give birth to an infant with congenital heart disease (CHD) have been shown to have a higher risk of developing cardiovascular disease later in life, as well as a higher risk of all-cause and cardiovascular disease-specific mortality.<sup>2,3</sup> This association persists after controlling for traditional cardiovascular

risk factors and preeclampsia, an adverse pregnancy outcome that occurs more commonly among women and birthing individuals who deliver an infant with CHD compared to those whose infants do not have CHD.<sup>4,5</sup>

The mechanisms linking infant CHD with maternal acquired cardiovascular disease are not well understood. One proposed mechanism is angiogenic imbalance, which occurs when antiangiogenic factors in the maternal circulation lead to vascular damage. Other potential mechanisms include shared risk factors (such as hypertension or diabetes), genetic risk, increased psychosocial and financial stress of caring for a medically complex child, or a combination of multiple factors.<sup>6-8</sup>

The purpose of this study is to estimate the prevalence of cardiovascular disease and risk factors among a cohort of mothers who gave birth to an infant with CHD requiring surgical repair and to compare rates of cardiovascular disease to age-matched parous women and birthing individuals from a national sample. A unique feature of this study is access to details of the child's medical history and CHD; we were therefore particularly interested to see if there was an association between features of the infant's medical history, including severity of the infant's CHD, and later development of maternal cardiovascular disease.

**METHODS**

**STUDY POPULATION.** We recruited mothers of children enrolled in a prospective study of neurodevelopmental who required surgical repair of CHD as neonates or infants between 1998 and 2003. Surgical interventions involved cardiopulmonary bypass, with or without deep hypothermic circulatory arrest. Exclusion criteria included: 1) multiple congenital abnormalities; 2) recognizable genetic/phenotypic

syndrome other than chromosome 22q11.2 microdeletion syndrome; and 3) language other than English spoken in the home.<sup>9</sup> The participants in this cohort are contacted annually to complete surveys on medical, behavioral, and developmental outcomes, which have informed multiple studies investigating growth and neurodevelopmental outcomes in this patient population.<sup>9-12</sup> Ours is the first study from this cohort to focus primarily on a nonpatient member of these families. The participants in this study will be referred to as the Maternal-Children's Hospital of Philadelphia (CHOP) (M-CHOP) cohort. The protocol for our study was approved by the Institutional Review Board at the CHOP. Written informed consent was obtained from all of the participants. Individual requests for access to deidentified data will be considered and require a data use agreement.

**SURVEY DEVELOPMENT AND ADMINISTRATION.** We developed a multifaceted survey designed to gather information regarding mothers' personal medical and pregnancy history, including pregnancy complications (eg, gestational hypertension, preeclampsia, gestational diabetes), cardiovascular risk factors (eg, hypertension, diabetes, high cholesterol, smoking history, and obesity), cardiovascular diagnoses (eg, coronary artery disease, stroke, heart failure or cardiomyopathy, valvular disease and arrhythmia), and family history of atherosclerotic cardiovascular disease (ASCVD) in first-degree relatives. Questions pertained to all pregnancies and were not limited to the pregnancy of the child with CHD. Survey questions were modeled after the Centers for Disease Control and Prevention (CDC)'s National Health and Nutrition Examination Survey (NHANES). NHANES is an annual survey of approximately 5,000 persons in the United States that requests information regarding demographic, socioeconomic, and health-related information.<sup>13</sup>

The mothers of 533 children enrolled in the original study were contacted via mail and email with information on enrolling in the study. There were 21 individuals who were not contacted for various reasons: the family withdrew from the original study (n = 5), the mothers were deceased (n = 11), the child was adopted as a newborn (n = 2), and there was no parent information available, or the parent/family specifically requested not to be contacted (n = 3). Potential participants with deceased children were contacted via mail and email to inquire initially about interest in participating in our study. If participants responded affirmatively, they were then given the information to enroll in the study. All participants received a link to a REDCAP questionnaire that

allowed their survey responses to be entered directly into a REDCAP database. Participants with incomplete responses were contacted by one of the study coordinators via phone or email to obtain complete and accurate data.

**COVARIATES.** Socioeconomic data were collected and participants' responses scored using the Hollingshead Four-Factor Index, which provides a family's composite socioeconomic status score incorporating education, occupation, sex, and marital status.<sup>14</sup> Hollingshead raw scores range from 8 to 66, with higher scores for higher levels of education and occupational prestige. The severity of CHD in the child was classified using previously described categories shown to predict perioperative mortality: class I, 2 ventricles with no aortic arch obstruction; class II, 2 ventricles with aortic arch obstruction; class III, single ventricle without arch obstruction; and class IV, single ventricle with arch obstruction.<sup>15</sup> D-transposition of the great arteries or tetralogy of Fallot are generally in class I, whereas hypoplastic left heart syndrome is class IV. CHD severity was also coded using a STAT score (Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery) of operative mortality, ranging from level 1 (lowest) to level 5 (highest).<sup>16</sup>

**OUTCOMES.** The primary outcomes were rates of self-reported cardiovascular disease and risk factors. Cardiovascular disease included ASCVD, structural heart disease, and arrhythmia. ASCVD was comprised of myocardial infarction, coronary artery disease, stroke, transient ischemic attack, or peripheral artery disease. Structural heart disease included valvular heart disease, cardiomyopathy, or heart failure. Lastly, arrhythmia was defined as supraventricular tachycardia, atrial fibrillation or flutter, ventricular tachycardia or fibrillation. The primary outcome differed according to the primary and secondary analysis. The primary analysis was conducted exclusively in the M-CHOP cohort, among mothers who gave birth to an infant with CHD. In this analysis, we examined the association of infant CHD and maternal cardiovascular risk factors with maternal cardiovascular disease, as defined as a composite of ASCVD or structural heart disease. These conditions were combined, given shared risk factors.<sup>17</sup> Self-reported arrhythmia may include patients with palpitations or benign arrhythmias, and therefore was excluded from the primary outcome. The secondary analysis focused on comparing self-reported cardiovascular disease among participants in the M-CHOP to NHANES cohorts. In this analysis, cardiovascular

disease included only ASCVD due to missing comparable variables for structural heart disease and arrhythmia in the NHANES data.

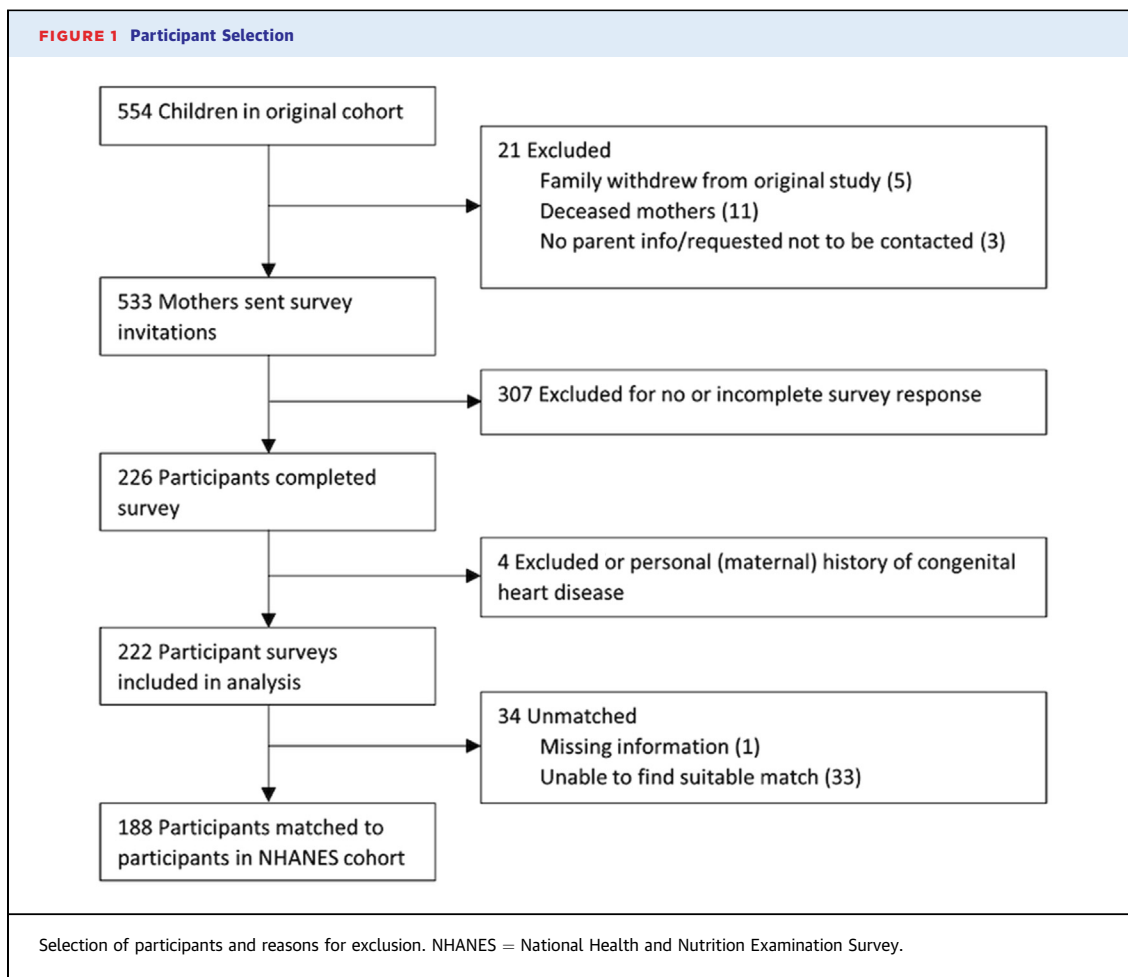
**ANALYSIS.** Baseline characteristics and rates of self-reported cardiovascular risk factors and disease among participants who completed the survey were summarized using counts and percentages for categorical variables and means (or medians) and standard deviations (or 25th and 75th percentiles) for continuous variables. Baseline characteristics of participants who completed the survey were compared to the characteristics of participants in the original cohort who did not respond to the survey.

Fisher exact tests were used to test the associations between maternal cardiovascular risk factors and child's CHD class with self-reported maternal cardiovascular disease. Given the small sample size of participants with this outcome ( $n = 18$ ), a limited number of traditional risk factors was identified a priori and tested using a Fisher exact test. These variables included high cholesterol, hypertension, diabetes, prediabetes, family history of ASCVD, smoking history, and elevated body mass index. The severity of the child's class of heart disease (class 1-4), as well as the associated mortality of the CHD surgical repair (STAT levels 1-5) were also examined. We also examined sex-specific risk factors including hypertensive disorders of pregnancy and gestational diabetes.

We then examined the relationship between our participants who completed the survey with nationally representative data from NHANES survey database. To make the cohorts comparable, we selected participants from NHANES data that had previously given birth, and then matched participants who completed the survey with NHANES participants 1:1 based on age ( $\pm 5$  years), race (exact), and education (exact) using the Greedy algorithm. Descriptive statistics of each group after matching were examined along with any from the survey cohort that were unmatched. Fisher exact tests were used to compare the matched cohorts for prevalence of cardiovascular disease and risk factors. The criterion for statistical significance for all analyses was set at the nominal  $\alpha = 0.05$  level and all data were analyzed using SAS version 9.4 (SAS Institute Inc).

## RESULTS

**M-CHOP COHORT SURVEY RESULTS.** Of the 533 mothers invited to participate, 226 (42%) completed



the survey (**Figure 1**). A total of 4 of these 226 participants were excluded due to personal history of maternal CHD, leaving 222 participants who completed surveys and whose data were analyzed. Differences between responders and nonresponders are presented in **Supplemental Table 1**. Survey responders were more likely to be White, to have children with less severe CHD, and to have children who were less likely to be deceased.

Baseline characteristics of study participants and their children with CHD are presented in **Table 1**. Participants were predominantly White ( $n = 189$ , 85.5%) and married ( $n = 164$ , 74.2%) with a college degree ( $n = 152$ , 68.8%). The mean Hollingshead score was  $49 \pm 12$ , suggesting high socioeconomic status. Regarding pregnancy characteristics, a total of 70 (32.1%) participants reported preterm delivery, 16 (7.2%) had gestational hypertension, and 21 (9.5%) had preeclampsia. The most commonly reported cardiovascular risk factors were high cholesterol ( $n = 71$ , 32%) and hypertension ( $n = 59$ , 26.6%). A minority of

participants ( $n = 64$ , 29%) reported any smoking history, with 5% ( $n = 11$ ) reporting current cigarette use. The most common type of infant CHD was class I (2 ventricles with no obstruction) in 129 (58.1%) children. Class IV CHD (1 ventricle with obstruction) was the second most common in 60 (27.3%) children. A secondary analysis of CHD severity found that a higher STAT score correlated with more complex class of CHD ( $P < 0.001$ ). Ten (4.5%) children were deceased.

Prevalence of cardiovascular disease in the M-CHOP cohort is shown in the **Central Illustration**. Of 222 M-CHOP participants, 34 (15.3%) self-reported a history of any cardiovascular disease, including ASCVD (4.5%), structural heart disease (3.6%), and arrhythmia (8.6%). The distribution of CHD severity was significantly different among those with and without self-reported cardiovascular disease ( $P = 0.03$ ) (**Table 2**). Specifically, class I CHD was less prevalent in participants with self-reported cardiovascular disease compared to those without

**TABLE 1** Baseline Characteristics of Participants in the M-CHOP Cohort (N = 222)

<b>Maternal characteristics</b>	
Age, y	52.2 ± 5.8
<b>Race</b>	
White, non-Hispanic	189 (85.5)
Black, non-Hispanic	21 (9.5)
Other	11 (5.0)
Hispanic ethnicity	11 (5.0)
Married/domestic partner	164 (74.2)
<b>Highest attained education</b>	
<High school	2 (0.9)
High school or some college	67 (30.3)
College graduate or higher	152 (68.8)
<b>Income</b>	
<\$25 K	6 (2.7)
\$25-49.9 K	22 (10.0)
\$50-99.9 K	53 (24.0)
>\$100 K	120 (54.3)
Prefer no answer	20 (9.0)
Hollingshead score	49 ± 12
Hollingshead score, range	11-66
<b>Insurance</b>	
Private	199 (89.6)
Medicaid/Medicare	18 (8.1)
Uninsured	4 (1.8)
<b>CV risk factors</b>	
High cholesterol	71 (32.0)
HTN	59 (26.6)
Diabetes	26 (11.7)
Prediabetes (n = 196)	23 (11.7)
Family history of ASCVD (n = 221)	108 (48.6)
Family history of premature ASCVD (n = 107)	46 (42.6)
<b>Smoking history (n = 221)</b>	
Former smoker	53 (24.0)
Current smoker	11 (5.0)
BMI >30 kg/m <sup>2</sup>	82 ± 36.9
<b>Sex-specific CV risk factors</b>	
Preterm delivery (<37 wk)	70 (32.1)
Severe preterm delivery (<34 wk)	21 (9.7)
<b>Hypertensive disorders of pregnancy</b>	
Preeclampsia	21 (9.5)
Gestational hypertension	16 (7.2)
Gestational diabetes	29 (13.1)
Early menopause (<40 y) (n = 109)	12 (11.0)
<b>Child characteristics</b>	
Age in days at first surgery	8 (3-80)
<b>Sex of child</b>	
Female	95 (42.8)
Male	127 (57.2)
Child status is deceased	10 (4.5)
Birth weight	3.08 ± 0.66
<b>Class of heart disease</b>	
I. 2 ventricles, no obstruction	129 (58.1)
II. 2 ventricles, with obstruction	22 (9.9)
III. 1 ventricle, no obstruction	11 (5.0)
IV. 1 ventricle, with obstruction	60 (27.3)

Continued in the next column

**TABLE 1** Continued

<b>STAT score</b>	
Category 1 (lowest mortality risk)	82 (36.9)
Category 2	39 (17.6)
Category 3	19 (8.6)
Category 4	22 (9.9)
Category 5 (highest mortality risk)	60 (27.3)

Values are mean ± SD or n (%).

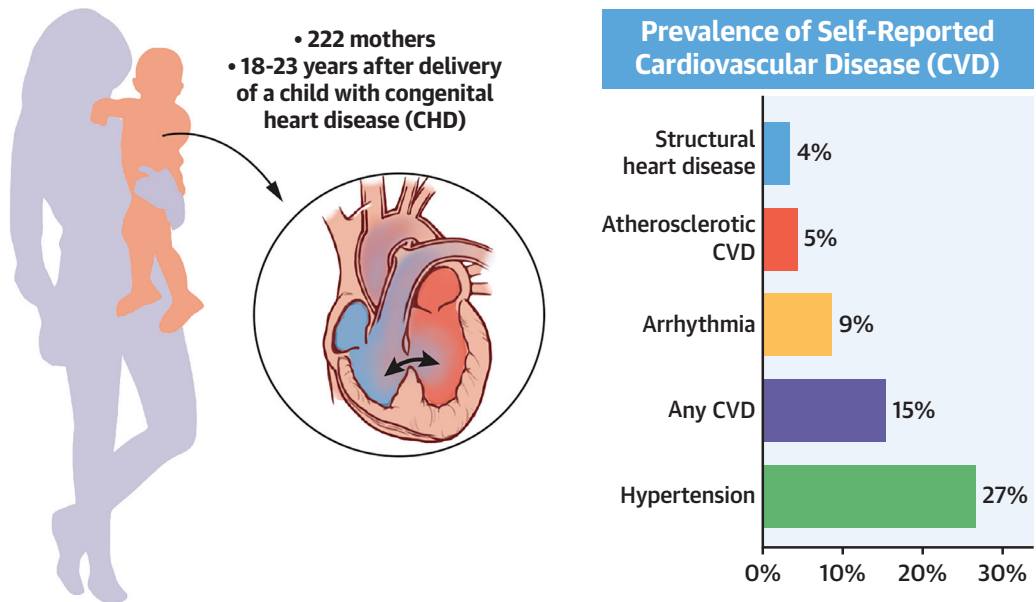
ASCVD = atherosclerotic cardiovascular disease; CV = cardiovascular; M-CHOP = Maternal-Children's Hospital of Philadelphia; HTN = hypertension; STAT = Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery.

cardiovascular disease (33.3% vs 60.3%). This correlation of maternal cardiovascular disease and severity of child's CHD was similarly found when using the STAT score to determine severity of the child's CHD.

Participants with self-reported cardiovascular disease comprised of either ASCVD and/or structural heart disease (n = 18) had higher rates of traditional and sex-specific cardiovascular risk factors (Table 2). A history of diabetes was more common in patients who reported cardiovascular disease (44.4% vs 8.8%,  $P < 0.001$ ). Hypertension was also more prevalent in participants with cardiovascular disease (61% vs 23.5%;  $P = 0.001$ ). Notably, participants with cardiovascular disease had significantly higher rates of preeclampsia compared to those without cardiovascular disease (27.8% vs 7.9%;  $P = 0.018$ ).

In order to examine the association between child's severity of CHD and maternal cardiovascular disease, we compared differences in cardiovascular risk factors among participants stratified by child's class of CHD (Supplemental Table 2). In this small cohort, there were no statistically significant differences in the rates of hypertension, diabetes mellitus, preeclampsia, gestational diabetes mellitus, and gestational hypertension between different classes of child's heart disease.

**COMPARISON OF M-CHOP TO MATCHED NHANES PARTICIPANTS.** A total of 188 M-CHOP participants were matched to individuals in the NHANES cohort (Figure 2). One participant was not matched due to missing demographic data and 33 were unmatched due to NHANES not having sufficient participants to match on baseline characteristics. The unmatched participants were non-Hispanic white, college graduates or higher, and ages 50 to 57 years. There were no significant differences between the matched M-CHOP and NHANES groups with regard to marital

**CENTRAL ILLUSTRATION** Prevalence of Self-Reported Cardiovascular Disease Among 222 Participants in the Maternal-Children's Hospital of Philadelphia Cohort**Differences in Risk Factor Prevalence According to Self-Reported CVD History**

Risk Factor	No CVD (n = 204)	CVD (n = 18)	P Value
HTN	48 (23.5)	11 (51.1)	0.001
Diabetes	18 (8.5)	8 (44.4)	<0.001
<b>Pregnancy and fetal factors</b>			
Hypertensive disorder	33 (16.3)	10 (55.6)	<0.001
Gestational diabetes	21 (10.3)	8 (44.4)	0.001
<b>Child's class of CHD</b>			
I: 2 ventricles, no obstruction	123 (60.5)	6 (33.3)	0.030
II: 2 ventricles with obstruction	19 (9.3)	3 (16.7)	
III: 1 ventricle, no obstruction	8 (3.9)	3 (16.7)	
IV: 1 ventricle with obstruction	54 (26.5)	6 (33.3)	

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Any CVD indicates any atherosclerotic CVD, structural heart disease, or arrhythmia. CHD = congenital heart disease; CVD = cardiovascular disease; HTN = hypertension.

status or education (Supplemental Table 3). Data on several traditional cardiovascular risk factors were able to be obtained from the NHANES cohort and compared to the M-CHOP group. Overall, rates of traditional cardiovascular risk factors were similar between the groups, aside from a higher rate of family

history seen among M-CHOP compared to NHANES participants (46.7% vs 11.4%,  $P < 0.001$ ) (Table 3). There were no statistically significant differences in rates of ASCVD between the M-CHOP and the NHANES cohorts (4.8% vs 4.3%,  $P = 1.00$ ). While there were no statistically significant differences in

rates of hypertension in our group compared to the matched NHANES cohort (27.2% vs 28.2%,  $P = 1.00$ ), participants with a diagnosis of hypertension were much more likely to be taking antihypertensive medication in the M-CHOP group compared to those with hypertension in the NHANES group (90.4% compared to 73.5%,  $P = 0.037$ ); overall 25% of the matched M-CHOP cohort reported use of antihypertensive meds compared to 19% of the NHANES group.

## DISCUSSION

In our cross-sectional survey study of mothers who delivered a child with CHD 18 years prior, we identified a statistically significant relationship between child’s severity of CHD and diagnosis of maternal cardiovascular disease, despite finding similar rates of traditional cardiovascular risk factors between the 2 groups of participants with and without CVD in the M-CHOP cohort. This finding is hypothesis-generating given the size of our cohort, but may suggest an association between risk of maternal cardiovascular disease and complexity of CHD in their infant.

Previous studies have described increased risk of cardiovascular disease and mortality in women and birthing individuals who delivered a child with any type of congenital anomaly.<sup>3,18</sup> As congenital heart defects are the most common congenital anomaly, with an estimated prevalence of 7.7 per 1,000 births worldwide, it is possible a significant portion of this risk is mediated through congenital heart defects.<sup>19</sup> A longitudinal cohort analysis of over 1 million women and birthing individuals who had delivered infants in Quebec, Canada, between 1989 and 2013 found that the rates of cardiovascular disease-related hospitalizations were higher in individuals whose infants had any severity of congenital heart defects compared to those whose infants had no heart defects.<sup>2</sup> This large population-based study also found higher hazard ratios for cardiovascular disease-related hospitalization in individuals whose infants had critical heart defects compared to those with noncritical defects, although these were not statistically significant differences.

In contrast to this larger study, our smaller cross-sectional study did not find that mothers who delivered an infant with CHD had a higher overall prevalence of maternal cardiovascular disease. Our study results may differ for several reasons. First, we assessed self-reported cardiovascular disease outcomes in contrast to those identified through administrative data. Second, our sample size was small in comparison to the large cohort analysis of

**TABLE 2 Risk Factors Associated With Cardiovascular Disease Among Participants in the M-CHOP Cohort<sup>a</sup>**

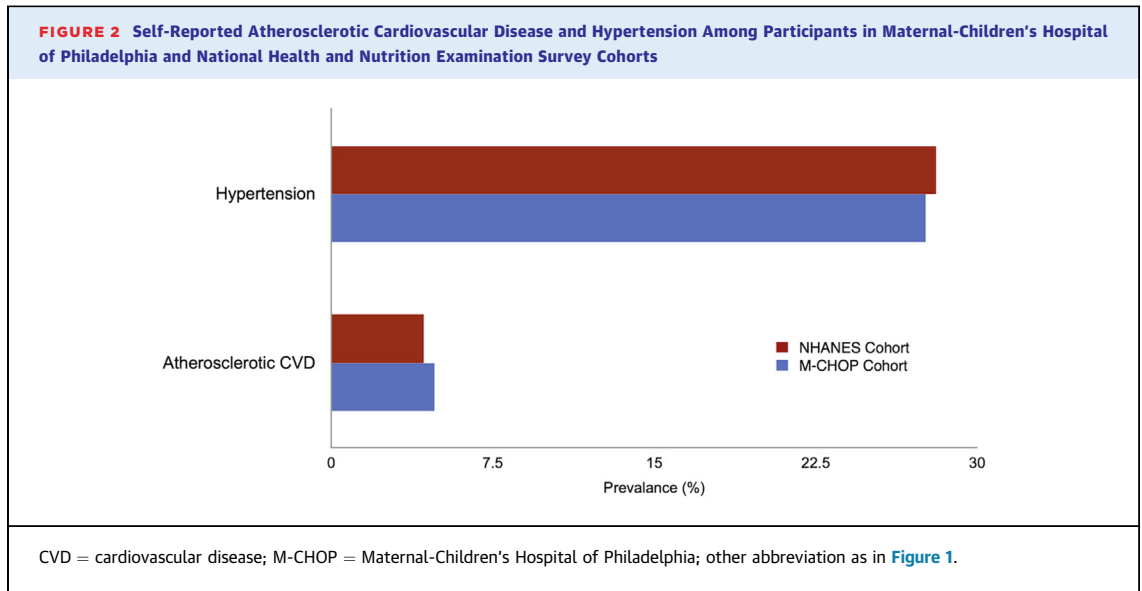
	No CVD (n = 204)	CVD (n = 18)	P Value
HTN	48 (23.5)	11 (61.1)	0.001
Any HDP <sup>b</sup>	33 (16.3)	10 (55.6)	<0.001
Preeclampsia	16 (7.9)	5 (27.8)	0.018
Gestational DM	21 (10.3)	8 (44.4)	0.001
Diabetes	18 (8.8)	8 (44.4)	<0.001
Female sex of child	88 (43.1)	7 (38.9)	0.807
Child's class of CHD			0.030
2 ventricles no obstruction (I)	123 (60.3)	6 (33.3)	
2 ventricles with obstruction (II)	19 (9.3)	3 (16.7)	
1 ventricle no obstruction (III)	8 (3.9)	3 (16.7)	
1 ventricle with obstruction (IV)	54 (26.5)	6 (33.3)	
STAT score of CHD			0.058
Category 1	75 (36.8)	7 (38.9)	
Category 2	39 (19.1)	0 (0.0)	
Category 3	15 (7.4)	4 (22.2)	
Category 4	21 (10.3)	1 (5.6)	
Category 5	54 (26.5)	6 (33.3)	

Values are n (%). <sup>a</sup>Cardiovascular disease as defined by presence of atherosclerotic cardiovascular disease and/or structural heart disease. <sup>b</sup>Hypertensive disease of pregnancy, including gestational hypertension and pre-eclampsia.  
 CHD = congenital heart disease; CVD = cardiovascular disease; DM = diabetes mellitus; HDP = hypertensive disorder of pregnancy; other abbreviations as in Table 1.

over 1 million individuals, which may limit our ability to detect uncommon outcomes. Our cohort study, however, focuses on collecting granular medical and sociodemographic factors that may link their child’s CHD with the maternal development of cardiovascular disease.

While we were not able to directly compare rates of sex-specific risk factors between participants in the M-CHOP and NHANES cohorts, we did note high rates sex-specific risk factors among M-CHOP participants. Specifically, 32% of participants reported at least one preterm birth before 37 weeks, with 9.7% of the cohort reporting preterm delivery <34 weeks. Rates of preterm birth have been increasing over the past several decades, however recent estimates of the incidence of late preterm birth (34-36 weeks gestation) were around 7% nationally.<sup>20</sup> This number includes only incident births and does not compare to our survey which included any history of preterm delivery in any pregnancy.

Preeclampsia is strongly associated with development of both acute cardiovascular dysfunction, as well as future maternal cardiovascular disease.<sup>21-23</sup> The association between preeclampsia and fetal congenital heart defects has been well described in the literature, noting both an increased risk of future preeclampsia in women and birthing individuals who



have a fetus with CHD, as well as increased risk of fetal CHD in those who have had prior preeclampsia.<sup>24</sup> The mechanism linking HDP to future cardiovascular disease is not well understood but may offer some insight in understanding the relationship between infant CHD and maternal cardiovascular disease. In our study, we found that preeclampsia was associated with maternal self-reported cardiovascular disease at 18 years after delivery. Preeclampsia did not appear to be associated with child's class of CHD (Supplemental Table 2), however this analysis is limited due to sample size.

The concept of shared angiogenic imbalance is promising as a possible mechanism for fetal CHD conferring maternal cardiovascular disease risk, given the known association of angiogenic imbalance

linking preeclampsia to future maternal vascular dysfunction and maternal cardiovascular disease.<sup>25</sup> Prior studies have noted abnormal levels of angiogenic growth factors such as vascular endothelial growth factor, soluble fms-like tyrosine kinase-1, and placental growth factor in maternal circulation of individuals with preeclampsia.<sup>26,27</sup> Abnormalities in these growth factors are also seen in maternal and cord blood samples from pregnancies with fetal CHD compared to controls.<sup>4</sup> Similar to the mechanism in preeclampsia, these abnormal levels of growth factors in pregnancies with CHD may affect the maternal systemic circulation during and after the pregnancy and could predispose to development future maternal cardiovascular disease. Although hypothesis generating due to small sample size, our study found an association with severity of fetal CHD and development of maternal cardiovascular disease. This effect could be driven by a greater degree of angiogenic imbalance, which may be found in more severe forms of CHD or in the setting of preeclampsia.

There were several limitations to our study. First, our study relied on self-reported diagnoses, which may lead to overreporting or underreporting of specific conditions. Second, responders and non-responders differed according to several important characteristics, including race, socioeconomic status, and severity of child's CHD, which contributes to selection bias; in particular, respondents to our survey had higher socioeconomic status compared to non-responders, which may be associated with lower cardiovascular risk. Additionally, non-English speaking households were excluded from the

**TABLE 3** Self-Reported Prevalence of Cardiovascular Disease Risk Factors and ASCVD Among Matched Participants in the M-CHOP Cohort Compared to Those in the NHANES Cohort

	M-CHOP Cohort (n = 188)	NHANES Cohort (n = 188)	P Value
Smoking history	54 (28.7)	72 (38.3)	0.063
Family history of ASCVD	42 (46.7)	21 (11.4)	<0.001
High cholesterol	55 (29.3)	51 (27.1)	0.731
Prediabetes	18 (11.0)	29 (16.9)	0.156
Diabetes	24 (12.8)	16 (8.5)	0.241
HTN	52 (27.7)	53 (28.2)	1.00
HTN meds	47 (90.4)	36 (73.5)	0.037
ASCVD	9 (4.8)	8 (4.3)	1.00

NHANES = National Health and Nutrition Examination Survey; other abbreviations as in Table 1.



prospective cohort. Third, our study was a cross-sectional study, and although intervals between pregnancy and development of disease were able to be estimated based on participants' responses, it is possible this data collection was obtained before a signal for higher rates of cardiovascular disease has occurred. Fourth, the original cohort of children was stratified by severity of their CHD—notably, this population only included those who underwent surgery in infancy, thus by definition excluding children with truly mild CHD. Fifth, although we compared our results to a matched cohort drawn from the U.S. population, it is possible that these cohorts differed on other unmatched characteristics that we could not measure. Finally, due to the low event rate of our primary outcomes, we were unable to control for confounding factors.

## CONCLUSIONS

In this cross-sectional study, mothers who delivered an infant with CHD did not have higher rates of age-adjusted cardiovascular risk factors or disease compared to normative data. Severity of fetal CHD was associated with maternal cardiovascular disease, and future studies should explore whether this association mediates increased maternal cardiovascular disease risk in larger cohorts.

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## PERSPECTIVES

**COMPETENCY IN MEDICAL KNOWLEDGE:** Pregnancy-specific factors can influence future maternal cardiovascular health. This study demonstrates that mothers who delivered an infant with CHD, and whose infants subsequently underwent surgery, did not have higher rates of age-adjusted cardiovascular disease. However, there may be an association between severity of CHD and maternal cardiovascular disease.

**TRANSLATIONAL OUTLOOK:** Larger cohort studies are needed to understand the association between severity of fetal CHD and future maternal cardiovascular risk.

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- KEY WORDS** congenital heart disease, pregnancy, women's health
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- APPENDIX** For supplemental tables, please see the online version of this paper.