Age- and Lesion-Related Comorbidity Burden Among US Adults With Congenital Heart Disease: A Population-Based Study

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Background—As patients with congenital heart disease (CHD) are living longer, understanding the comorbidities they develop as they age is increasingly important. However, there are no published population-based estimates of the comorbidity burden among the US adult patients with CHD.

Methods and Results—Using the IBM MarketScan commercial claims database from 2010 to 2016, we identified adults aged ≥18 years with CHD and 2 full years of continuous enrollment. These were frequency matched with adults without CHD within categories jointly defined by age, sex, and dates of enrollment in the database. A total of 40 127 patients with CHD met the inclusion criteria (mean [SD] age, 36.8 [14.6] years; and 48.2% were women). Adults with CHD were nearly twice as likely to have any comorbidity than those without CHD ($P<0.001$). After adjusting for covariates, patients with CHD had a higher prevalence risk ratio for "previously recognized to be common in CHD" (risk ratio, 9.41; 95% CI, 7.99–11.1), "other cardiovascular" (risk ratio, 1.73; 95% CI, 1.66–1.80), and "noncardiovascular" (risk ratio, 1.47; 95% CI, 1.41–1.52) comorbidities. After adjusting for covariates and considering interaction with age, patients with severe CHD had higher risks of previously recognized to be common in CHD and lower risks of other cardiovascular comorbidities than age-stratified patients with nonsevere CHD. For noncardiovascular comorbidities, the risk was higher among patients with severe than nonsevere CHD before, but not after, the age of 40 years.

Conclusions—Our data underscore the unique clinical needs of adults with CHD compared with their peers. Clinicians caring for CHD may want to use a multidisciplinary approach, including building close collaborations with internists and specialists, to help provide appropriate care for the highly prevalent noncardiovascular comorbidities. (*J Am Heart Assoc*. 2019;8:e013450. DOI: 10.1161/JAHA.119.013450.)

Key Words: cohort study • comorbidities heart failure • congenital cardiac defect

Congenital heart disease (CHD) is the most common birth defect.[1] It is estimated that two thirds of the estimated 2.4 million patients with CHD in the United States are now adults.[2–4] The physicians of aging patients with CHD not only face the challenge of managing long-term sequelae related to CHD lesions (like heart failure and arrhythmias) but may also

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be asked to manage comorbidities these patients acquire as they age (like coronary artery disease [CAD] and hyperlipidemia) and those that affect organs other than the heart (like renal failure and liver failure).[5–7]

Prior studies in the United States from single centers[8–10] or inpatient databases[11,12] have reported comorbidity rates among patients with CHD. However, single-center studies have small samples and may be affected by referral bias, whereas inpatient databases only include the sickest patients, so provide biased estimates of population-level comorbidity prevalence. Recently, population-based estimates of rates of comorbidities in adolescents with CHD from 3 US sites were reported,[13] but similar data about adults are not available. Although some non–US-based population estimates of the comorbidity burden have been published,[6,14] extrapolating these to the diverse US population is suboptimal.

To understand the burden of comorbidities among US patients with CHD, we used a large national cohort of patients with commercial insurance (1) to provide population-based estimates of the rates of "previously recognized to be common in CHD," "other cardiovascular," and "noncardiovascular"

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Clinical Perspective

What Is New?

- The present study is the largest population-based study of congenital heart disease (CHD) and provides novel estimates of prevalence rates of comorbidities among adults with CHD in the United States.
- In this ambulatory population, patients with CHD had higher prevalence of comorbidities "previously recognized to be common in CHD," "other cardiovascular," and "noncardiovascular" comorbidities when compared with patients without CHD, even before the age of 40 years.
- We found that patients with Eisenmenger syndrome and common ventricle had among the highest rates of comorbidities; after adjusting for covariates and considering interaction with age, patients with severe CHD of any age had higher risks of comorbidities previously recognized to be common in CHD and lower risks of other cardiovascular comorbidities than patients with nonsevere CHD, whereas the risk of noncardiovascular comorbidities was higher among patients with severe CHD than nonsevere CHD aged <40 years but not different after the age of 40 years.

What Are the Clinical Implications?

- These estimates of comorbidity prevalence could be used to plan for the clinical resources patients with CHD are likely to need.
- Our data suggest that preventive measures for cardiovascular comorbidities should be one of the important areas of focus in patients with CHD; targeted CHD-specific screening and treatment protocols need to be developed to address the high burden of comorbidities among patients with CHD.
- Centers that specialize in CHD care may want to adopt a multidisciplinary approach, including building close partnerships with primary care physicians and specialists, to address the noncardiovascular comorbidities we found to be prevalent among patients with CHD.

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comorbidities in the population with CHD and (2) to compare these rates with the rates observed in age-, sex-, and dates of enrollment–matched non-CHD controls.

Methods

All the data used for this study belong to the IBM MarketScan Commercial Database, and they should be contacted directly for any data requests.

Setting and Data Sources

We used Health Insurance Portability and Accountability Act–compliant deidentified patient-level inpatient and outpatient claims data from the IBM MarketScan Commercial Database, representing the claims of employees and dependents on large employer health benefit programs between January 1, 2010, and December 31, 2016. The plans include a variety of fee-for-service, preferred provider organization, and capitated health plans. Claims from Medicare, Medicaid, and Workers Compensation were not included.

Study Population

We limited analyses to enrollees, aged 18 to 64 years, who had at least 2 full years of continuous enrollment. Patients were identified as having CHD if they had a diagnosis code for a CHD lesion. The diagnosis codes used were the *International Classification of Diseases, Ninth Revision* (*ICD-9*), and the *International Classification of Diseases, Tenth Revision* (*ICD-10*), codes (see Table 1 in online appendix) that were used by prior investigators.[15–17] Because studies on adult CHD using *ICD-10* codes do not yet exist, we used forward-backward mapping to determine the *ICD-10* codes for patients with CHD.[18] If an *ICD-9* or *ICD-10* code for CHD was present on any inpatient or outpatient claim at any billing position during the period of enrollment, these patients were then considered to have CHD. For patients with codes for >1 CHD diagnosis, we used the hierarchical algorithm, proposed by Broberg et al,[17] to designate one condition per patient as his/her principal CHD diagnosis. As described by Broberg et al[17] and like Burchill et al,[19] we excluded *ICD-9* and *ICD-10* codes that have lower specificity for CHD, including atrial septal defect, bicuspid aortic valve, aortic stenosis, and unspecified congenital anomalies. We also excluded any patients who had pregnancy- or delivery-related claims during the study period to avoid inclusion of pregnant women with fetuses affected by CHD.[20] The remaining patients with CHD were categorized on the basis of their anatomic subgroups into[16]:

1. *Severe CHD:* Eisenmenger syndrome (ES),[17] hypoplastic left heart syndrome, common ventricle, transposition of great arteries, tetralogy of Fallot, truncus arteriosus, and endocardial cushion defect; and
2. *Nonsevere CHD:* Ebstein anomaly, coarctation of aorta, anomalies of the pulmonary artery, anomalies of pulmonary valve, except pulmonary atresia, anomalies of the tricuspid valve, ventricular septal defect, patent ductus arteriosus, unspecified septal defects, anomalies of veins, subaortic stenosis, and aortic anomalies.

Adult CHD cases were frequency matched to adults without CHD within categories jointly defined by age, sex, and starting and ending year of enrollment in the IBM MarketScan database.

Table 1. Types of CHD Lesions and Their *ICD-9* and *ICD-10* Codes

Type of Lesion	*ICD-9* Codes	*ICD-10* Codes
Severe lesions		
Eisenmenger syndrome (CHD code AND cyanosis)	782.5 PLUS other congenital code (782.5+745–747)	I27.83 PLUS other congenital code (I27.83+Q20–Q28)
Hypoplastic left heart syndrome	746.7	Q23.4
Common ventricle	745.3	Q20.4
Transposition complex	745.10, 745.11, 745.12, 745.19	Q20.1, Q20.3, Q20.5, Q20.8
Tetralogy of Fallot	745.2	Q21.3
Truncus arteriosus	745.0	Q20.0
Endocardial cushion defect	745.60, 745.61, 745.69	Q21.2
Nonsevere lesions		
Ebstein anomaly	746.2	Q22.5
Aortic coarctation	747.10	Q25.1
Anomalies of the pulmonary artery (except pulmonary atresia)	747.31, 747.39	Q25.6, Q25.79, Q25.5, Q25.71
Anomalies of the pulmonary valve	746.0, 746.02, 746.09	Q22.1, Q22.2, Q22.3
Anomalies of the tricuspid valve	746.1	Q22.4, Q22.8, Q22.9
Ventricular septal defect	745.4	Q21.0
Patent ductus arteriosus	747.0	Q25.0
Anomalies of veins	747.4, 747.41, 747.42	Q26.2, Q26.3, Q26.9
Unspecified defect of septal closure	745.9	Q21.9
Subaortic stenosis	746.81	Q24.4
Aortic anomalies	747.29	Q25.41, Q25.42, Q25.43, Q25.44, Q25.48, Q25.49

CHD indicates congenital heart disease; *ICD-9*, *International Classification of Diseases, Ninth Revision*; *ICD-10*, *International Classification of Diseases, Tenth Revision*.

Comorbidities

Several tools are available to identify comorbidities in administrative data.[21] To estimate comorbidity rates, we modified the types of comorbidities listed in the Agency for Healthcare Research and Quality Elixhauser comorbidity measures.[22] We made this modification because the Agency for Healthcare Research and Quality measure does not include some conditions that are important in CHD care (eg, arrhythmias) and to combine some conditions for ease of presentation (eg, combining diabetes mellitus with and without complications). First, the revised version of the Elixhauser comorbidities was modified to obtain 21 conditions. These modifications included the following: excluding valvular disorders (because patients with CHD often have valvular problems as their inherent structural abnormality); combining 2 types of diabetes mellitus (diabetes mellitus with complication and diabetes mellitus without complication) into 1 condition (diabetes mellitus); combining 2 types of anemia (blood loss anemia and deficiency anemia) into 1 condition (anemia); combining neurodegenerative disorders and paralysis into 1 condition (neurologic disorder); combining

psychosis and depression into 1 condition (psychiatric disorder); combining alcohol and drug use into 1 condition (substance abuse); and combining all types of tumors, like lymphoma, metastasis, and solid tumors, into one condition (any tumor). Finally, 4 conditions were added: CAD (codes 410.x, 414.0x, 414.2x, 414.3x, 414.8x, 414.9x, I21.XX, I22.X, and I25); stroke (codes 431, 434, 436, 438, I61, I63, I64, and I69); atrial or ventricular arrhythmias (codes 427.31, 427.32, I48.0, I48.1, 427.41, 427.42, 427.5, I46.9, I49.01, and I49.02); and hypercholesterolemia (codes 272.0, 272.2, 272.4, E78.0, E78.2, and E78.4).[23,24]

In sum, we assessed for the presence of a total of 25 comorbidities. We classified these into 3 categories:

1. *Previously recognized to be common in CHD:* congestive heart failure (CHF), arrhythmias, and pulmonary circulation disorders;
2. *Other cardiovascular:* hypertension, hypercholesterolemia, CAD, peripheral vascular disorders, and stroke; and
3. *Noncardiovascular*: diabetes mellitus, obesity, neurologic disorder, hypothyroidism, liver disease, peptic ulcer, AIDS, any tumor, rheumatoid arthritis/collagen vascular disease,

coagulopathy, weight loss, fluid and electrolyte disorders, anemia, renal disease, substance abuse, psychiatric disorder, and chronic pulmonary disease.

(employee, spouse, child/other, or dependent relation unknown). We determined whether the patient was the primary beneficiary (employee).

Basic Demographics

Demographic characteristics assessed included age, sex, and US region. The MarketScan database includes information on the relationship of the patient to the primary beneficiary

Statistical Analysis

Continuous variables are summarized by mean±SD, and categorical variables are summarized by percentages. Student t and Pearson χ^2 tests were used as appropriate
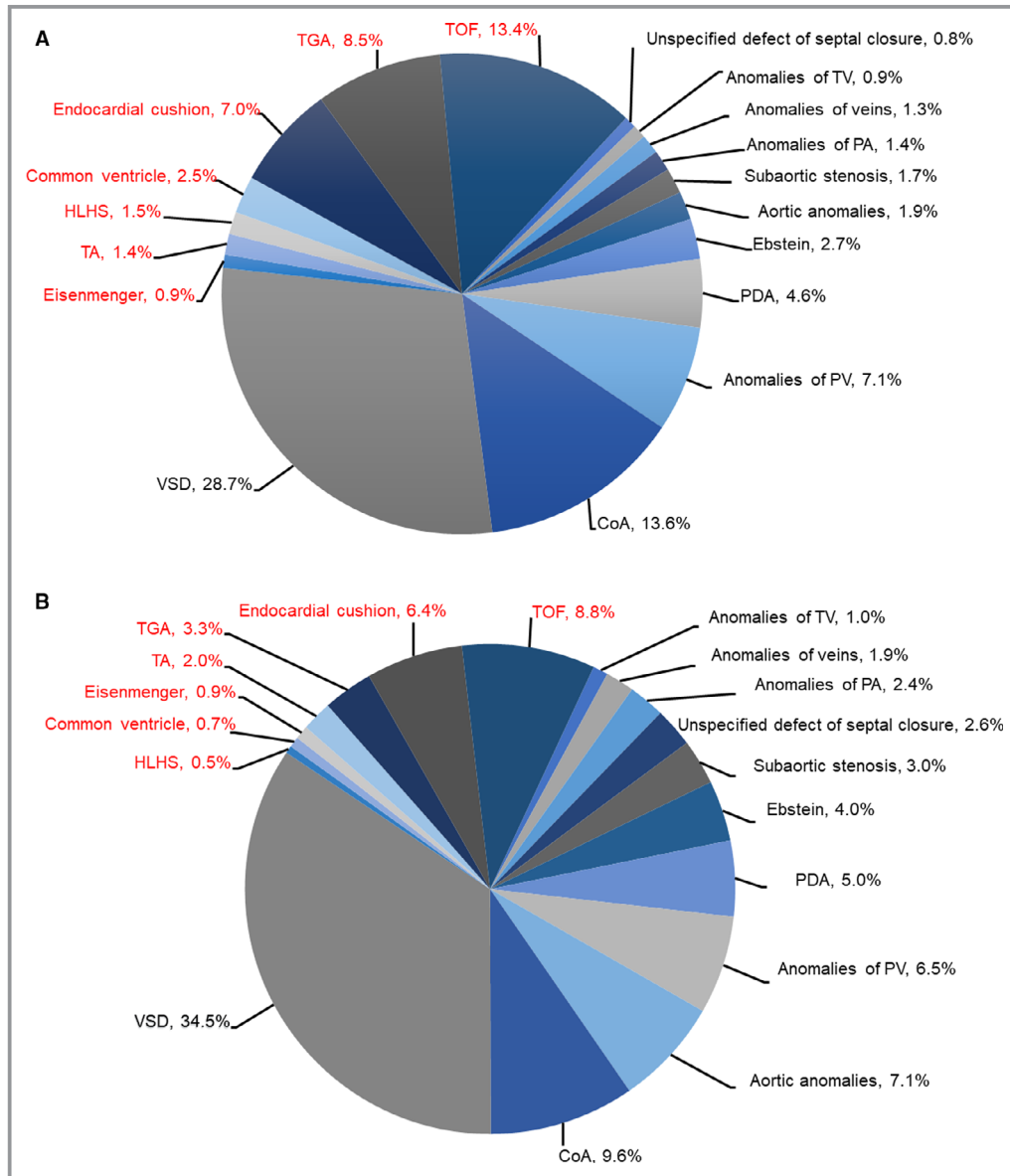
Figure 1. Anatomical subgroup distribution of the cohort with congenital heart disease, stratified by age categories into those aged 18 to 40 years (n=32 605; **A**) and those aged ≥40 years (n=17 642; **B**). Source: IBM MarketScan database, 2010 to 2016. *Severe lesions are represented in red.* CoA indicates coarctation of aorta; HLHS, hypoplastic left heart syndrome; PA, pulmonary artery; PDA, patent ductus arteriosus; PV, pulmonary valve; TA, truncus arteriosus; TGA, transposition of great arteries; TOF, tetralogy of Fallot; TV, tricuspid valve; VSD, ventricular septal defect.
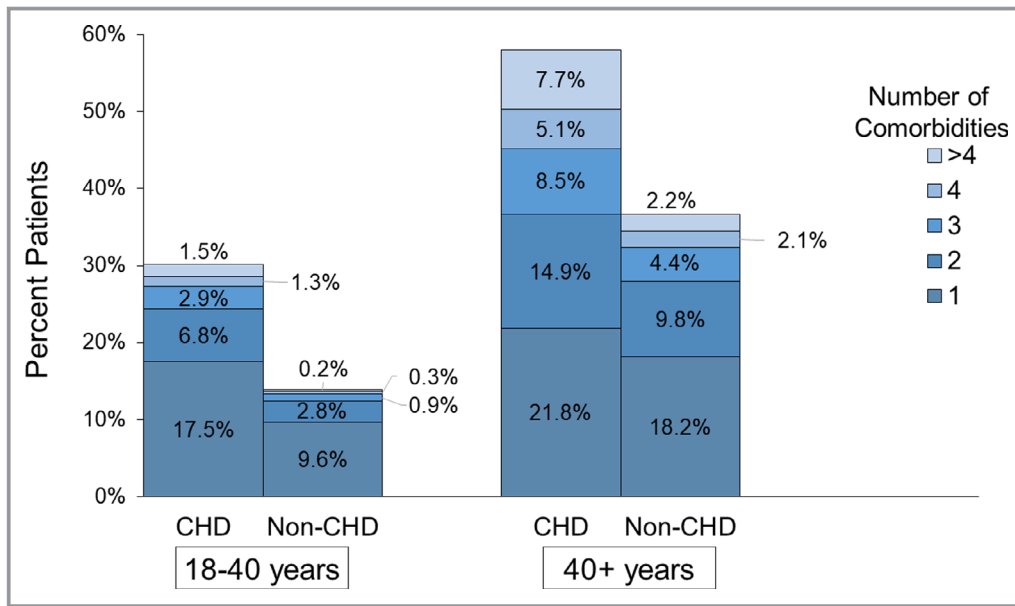
Figure 2. Number of comorbidities among patients with congenital heart disease (CHD) and patients without CHD, stratified by age groups ($P<0.001$ for all comparisons between patients with CHD and patients without CHD). Source: IBM MarketScan database, 2010 to 2016.

to contrast the characteristics of CHD cases and controls. Poisson regression models with robust SEs were used to estimate prevalence ratios for comorbidities.[25] All regression analyses were adjusted for age, sex, whether the patient was the primary beneficiary, start and end year of enrollment, and region of the United States. Interaction of age on the association of the presence or absence of CHD or the type of CHD (severe versus nonsevere) with comorbidities was studied. Statistical analyses were performed using STATA/SE software, version 14 (Stata-Corp).

Certification to use deidentified MarketScan data was obtained from the University of California, San Francisco, Committee on Human Research; and the need for informed consent was waived.

Results

Study Cohort Characteristics

A total of 40 127 CHD cases met our inclusion criteria. Mean age of the study population was 36.8 ± 14.6 years, 57.2% were aged 18 to 40 years, and 48.2% were women. Of all the patients, 49.4% were primary beneficiaries and 48.9% were actively employed. Patients with severe CHD constituted 29.9% of the entire CHD population (38.1% for the 18- to 40-year-old population versus 26.5% of the ≥40-year-old CHD population; $P<0.001$). The distribution of patients with CHD within individual anatomical subgroups for the 2 age categories is shown in Figure 1.

Comorbidities

Adults with CHD were nearly twice as likely to have a comorbidity than those without CHD (30.1% versus 13.8% for 18- to 40-year-old patients; 58.1% versus 36.7% for ≥40-year-old patients; $P<0.001$). In addition, adults with CHD were also more likely to have a higher number of comorbidities than adults without CHD ($P<0.001$; Figure 2). Each type of comorbidity (whether previously recognized to be common in CHD, other cardiovascular, and non cardiovascular) was more common in patients with CHD than in patients without CHD (Table 2). After adjusting for age, sex, dates of enrollment, employment status, and the region of the United States, patients with CHD had significantly higher prevalence risk ratios for all individual comorbid diseases, except for substance abuse, AIDS, and peptic ulcer, compared with patients without CHD (Table 2). In an assessment of effect modification by age, risk ratios for the association of CHD versus non-CHD with comorbidities were significantly higher (interaction $P<0.05$) among younger patients for CHF, arrhythmias, CAD, hypertension, peripheral vascular disorder, renal failure, liver disorder, hypothyroidism, and psychiatric disorders but not for other comorbidities. After adjusting for the covariates and considering interaction with age, patients with severe CHD aged <40 years had higher risks of comorbidities previously recognized to be common in CHD and noncardiovascular ones but lower risks for cardiovascular comorbidities than patients with nonsevere CHD (Table 3). After the age of 40 years, there were higher risks of "comorbidities previously recognized to be common in CHD," lower risks of other cardiovascular comorbidities, and no

differences in noncardiovascular comorbidities among patients with severe CHD than patients with nonsevere CHD (Table 3). The association of severe versus nonsevere CHD with cardiovascular comorbidities was similar in both age groups (interaction $P=0.27$) but differed across age groups for any ($P=0.003$), previously recognized in CHD ($P<0.001$), and noncardiovascular ($P=0.001$) comorbidities.

Among all CHD anatomic subgroups, patients with ES had the highest comorbidity rate of 65.4%. Among individual comorbidities, patients with ES had the highest rates of CHF (13.2%), pulmonary circulation disorders (15.1%), stroke (3.24%), anemia (8.65%), coagulopathy (7.40%), renal disease (2.43%), and liver disease (6.49%) (Tables 4 and 5). The rate of arrhythmia (11.8%) was highest in patients with a common ventricle. The rates of hypertension (31.9%), hyperlipidemia (13.2%), and peripheral vascular disorder (11.7%) were highest in patients with aortic anomalies, whereas those of CAD (6.62%) and diabetes mellitus (9.88%) were highest in patients with subaortic stenosis (Tables 4 and 5).

Table 2. RRs for Having Individual Comorbid Conditions Among Patients With CHD Versus Patients Without CHD

Comorbidities	% Prevalence		CHD vs Non-CHD	
	CHD	Non-CHD	Adjusted RR (95% CI)*	P Value
Any comorbidity	42.1	23.6	1.58 (1.54–1.63)	<0.001
Previously recognized to be common in CHD	8.34	0.66	9.41 (7.99–11.1)	<0.001
Congestive heart failure	3.93	0.26	11.9 (9.04–15.7)	<0.001
Arrhythmias	3.92	0.31	9.61 (7.61–12.1)	<0.001
Pulmonary circulation disorders	2.88	0.17	10.6 (7.82–14.2)	<0.001
Other cardiovascular	24.5	12.2	1.73 (1.66–1.80)	<0.001
Hypertension	19.0	10.0	1.67 (1.59–1.75)	<0.001
Hypercholesterolemia	7.49	3.95	1.61 (1.49–1.73)	<0.001
Coronary artery disease	3.13	0.76	3.43 (2.92–4.03)	<0.001
Peripheral vascular disease	3.51	0.51	5.35 (4.35–6.57)	<0.001
Stroke	1.09	0.15	5.60 (3.92–8.00)	<0.001
Noncardiovascular	29.3	17.9	1.47 (1.41–1.52)	<0.001
Chronic lung disease	6.52	3.35	1.77 (1.60–1.95)	<0.001
Hypothyroidism	6.00	3.23	1.59 (1.45–1.76)	<0.001
Obesity	5.64	3.66	1.43 (1.29–1.59)	<0.001
Psychiatric	5.59	3.75	1.49 (1.35–1.65)	<0.001
Diabetes mellitus	5.13	3.64	1.29 (1.18–1.42)	<0.001
Anemia	4.63	2.06	2.11 (1.86–2.38)	<0.001
Fluid and electrolyte disorders	3.46	1.25	2.32 (1.99–2.70)	<0.001
Neurologic disorders	3.08	0.96	2.62 (2.21–3.11)	<0.001
Coagulopathy	1.69	0.30	4.87 (3.64–6.53)	<0.001
Liver disorder	1.66	0.66	1.83 (1.48–2.27)	<0.001
Any tumor	1.58	0.96	1.41 (1.18–1.69)	<0.001
Rheumatoid arthritis	1.49	0.83	1.55 (1.27–1.88)	<0.001
Renal failure	1.20	0.36	2.35 (1.82–3.02)	<0.001
Weight loss	1.00	0.50	1.68 (1.30–2.18)	<0.001
Substance abuse	1.14	0.95	1.02 (0.81–1.27)	0.895
AIDS	0.09	0.04	2.09 (0.81–5.43)	0.126
Peptic ulcer	0.06	0.02	3.99 (0.49–32.4)	0.194

CHD indicates congenital heart disease; RR, risk ratio.
*Models were adjusted for age, sex, dates of enrollment, presence or absence of CHD, beneficiary status, and the US region.

Table 3. Age-Stratified RRs for Having Comorbid Diseases Among Patients With Severe CHD Versus Patients With Nonsevere CHD

Comorbidities	% Prevalence		Severe vs Nonsevere CHD	
	Severe CHD (n=8099)	Nonsevere CHD (n=14 837)	Adjusted RR (95% CI)*	P Value
Patients with CHD, aged 18–40 y				
Any comorbidity	32.4	28.8	1.16 (1.08–1.24)	<0.001
Previously recognized to be common in CHD	9.66	3.13	3.29 (2.75–3.93)	<0.001
Other cardiovascular	10.2	12.3	0.84 (0.74–0.96)	0.008
Noncardiovascular	24.2	21.2	1.19 (1.09–1.29)	<0.001
Patients with CHD, aged ≥40 y				
Any comorbidity	60.0	57.5	1.04 (0.99–1.08)	0.077
Previously recognized to be common in CHD	20.1	9.92	1.96 (1.76–2.19)	<0.001
Other cardiovascular	38.8	42.6	0.91 (0.86–0.96)	0.001
Noncardiovascular	39.6	38.6	1.00 (0.94–1.07)	0.939

CHD indicates congenital heart disease; RR, risk ratio.
*Models were adjusted for sex, dates of enrollment, type of CHD, beneficiary status, and the US region.

Discussion

We used a large database containing claims for commercially insured enrollees to generate population-based estimates of comorbidity rates among adult patients with CHD within the United States. When compared with patients without CHD, we observed that patients with CHD had significantly higher comorbidity rates than age-, sex-, and dates of enrollment–matched controls without CHD. After multivariate adjustment, patients with CHD had 9.41-, 1.73-, and 1.47-fold higher risks of comorbidities that are previously recognized to be common in CHD, other cardiovascular, and noncardiovascular comorbidities, respectively, than controls without CHD. Among CHD patients, those with ES had the highest rate of having at least one comorbid disease and had high rates of CHF, pulmonary circulation disorders, stroke, anemia, coagulopathy, renal disorder, liver disorder, and most other noncardiovascular comorbidities. The rate of arrhythmia was highest in patients with common ventricle. After adjusting for covariates and considering interaction with age, patients with severe CHD of any age had higher risks of comorbidities previously recognized to be common in CHD and lower risks of other cardiovascular comorbidities than patients with nonsevere CHD, whereas the risks of noncardiovascular comorbidities was higher among patients with severe CHD than patients with nonsevere aged <40 years but not different after the age of 40 years.

Overall, our estimates of the prevalence of individual comorbidities in <65-year-old adult patients with CHD were lower than those observed by Afilalo et al.[6] However, Afilalo et al[6] studied an older cohort (aged ≥65 years) of patients with CHD, which likely contributed to the differences in findings from our study. Not surprisingly, CHF, arrhythmias, and pulmonary circulation disorders were much more prevalent among patients with CHD than patients without CHD in our study. This is likely caused by the impact of the underlying congenital lesions in altering the molecular and structural properties of the heart and lung vasculature. Consequently, the prevalence of CHF was highest in conditions known to have significant alteration in their underlying cardiac structure from prior surgery and hemodynamics, such as ES, common ventricle, transposition of great arteries, and tetralogy of Fallot. Similarly, arrhythmia was most prevalent in patients with common ventricle, followed by ES, transposition of great arteries, and anomalies of veins. The structural and hemodynamic changes are also expected to be more pronounced among patients with severe CHD, which may contribute to the higher rates of these comorbidities we observed among patients with severe CHD than among patients with nonsevere CHD of any age.

We found the rate of CAD in patients with CHD was lower than the 9.2% reported by Giannakoulas et al in the United Kingdom[26] but higher than the 0.8% observed by Bokma et al in the Dutch population.[27] This may be because Giannakoulas et al[26] reported the CAD rate among hospitalized patients from a tertiary center in the United Kingdom and included in their definition of CAD any significant coronary angiography findings. On the other hand, Bokma et al[27] defined CAD as acute coronary syndrome or those needing revascularization and, thus, were likely restricted to more severe forms of CAD than our study. Also, we found that patients with CHD had a significantly higher prevalence of CAD than patients without CHD. Bokma et al[27] had shown that traditional atherosclerotic risk factors were associated with CAD in adult patients with CHD.[27] Further studies in this area might help to develop appropriate screening and risk factor modification protocols.

Table 4. Lesion-Specific Prevalence Risks (%) for Having All Cardiovascular Comorbid Conditions

Variable	Previously Recognized to Be Common in CHD			Other Cardiovascular				
	CHF	Arrhythmias	Pulm Circ	Hypertension	Hyperlipidemia	CAD	PVD	Stroke
Severe CHD	6.69	6.27	4.32	13.5	5.81	2.79	2.72	1.49
Eisenmenger syndrome	13.2	10.3	15.7	22.2	8.92	6.49	7.84	3.24
HLHS	8.47	6.18	3.20	15.1	6.64	2.75	2.52	1.60
Common ventricle	9.70	11.8	3.28	7.85	3.00	2.43	2.14	1.57
TGA	8.64	7.29	3.25	12.6	4.32	2.22	1.98	1.07
TOF	6.61	5.34	4.30	12.6	5.10	2.49	3.14	0.72
Truncus arteriosus	3.18	4.54	4.08	17.9	8.17	3.78	3.63	2.87
Endocardial cushion defect	3.89	5.34	4.30	15.0	8.00	3.19	1.96	2.59
Nonsevere CHD	2.75	2.92	2.27	21.4	8.21	3.27	3.85	0.92
Ebstein anomaly	3.82	5.12	2.37	17.5	6.42	2.75	1.68	0.46
Aortic coarctation	2.27	2.31	1.13	27.1	7.05	2.87	7.01	0.44
Anomalies of the pulmonary artery	3.12	3.40	4.62	23.2	8.83	2.72	2.99	0.54
Anomalies of the pulmonary valve	1.97	1.35	2.16	17.1	6.94	3.07	2.59	0.44
Anomalies of the tricuspid valve	2.64	4.49	2.11	20.6	8.44	2.64	1.85	0.79
Ventricular septal defect	2.94	2.87	2.68	18.6	7.90	2.94	2.49	1.02
Patent ductus arteriosus	1.83	1.78	2.25	17.9	8.06	3.04	2.83	2.04
Anomalies of veins	2.53	6.96	3.16	21.0	8.54	3.32	2.69	1.58
Unspecified defect of septal closure	2.37	3.48	1.74	29.3	12.9	5.85	2.69	1.58
Subaortic stenosis	5.72	5.27	3.03	30.1	11.9	6.62	4.04	1.23
Aortic anomalies	2.78	3.69	0.97	31.9	13.2	5.50	11.7	0.91
Non-CHD	0.26	0.31	0.17	10.0	3.95	0.76	0.51	0.15

CAD indicates coronary artery disease; CHD, congenital heart disease; CHF, congestive heart failure; HLHS, hypoplastic left heart syndrome; Pulm Circ, pulmonary circulation disorders; PVD, peripheral vascular disease; TGA, transposition of great arteries; TOF, tetralogy of Fallot.

Lanz et al found the cumulative risk over 12 years of ischemic stroke in patients with CHD up to the age of 64 years to be 6.1% in women and 7.7% in men, with another 0.8% of women and 1.3% of men having hemorrhagic strokes.[24] We found a prevalence rate of all types of stroke to be only 0.92% in our study, but we calculated annual estimates and did not have 12-year data. Although it is not clear what the stroke rate would have been had we been able to follow our population for 12 years, the annual rate we found is only a little higher than that observed by Lanz et al.[24] Prior investigators from the Netherlands have shown that the risk factors of ischemic stroke in patients with CHD are less likely to be traditional atherosclerotic risk factors and more likely to be factors related to their underlying congenital lesions.[27] This is further supported by the fact that the highest risk of stroke was found among patients with ES, endocardial cushion, truncus, and common ventricle, in whom hyperviscosity, shunts, valvular disease, and passive blood flow are known pathophysiological risk factors for thromboembolism and stroke.

The rates of hypertension within the adult population with CHD found in our study was lower than the rates reported in prior studies, which ranged from 24% to 38.7%.[8–10] Similarly, we found lower rates of hyperlipidemia, obesity, and diabetes mellitus than observed in these studies. It is possible that the higher rates of these comorbidities reported in prior studies reflects referral bias and sicker patients because each of those studies involved patients from a single tertiary center, whereas our study sample was drawn from a commercially insured population. In addition, those studies had much smaller sample sizes than the present study. However, similar to a prior UK study, the risks of the comorbidities related to atherosclerotic risks were higher in patients with CHD than in patients without CHD.[14] Also, among the CHD lesions, these comorbidities were much more prevalent in the patients with nonsevere CHD (like those with aortic anomalies and subaortic stenosis), who were older. The risks of the cardiovascular comorbidities remained higher for patients with nonsevere CHD than patients with severe CHD, aged <40 or ≥40 years, which suggests that preventive measures for

Table 5. Lesion-Specific Prevalence Risks (%) for Having Selected Noncardiovascular Comorbid Conditions (10 Most Frequent Conditions and Renal Failure)

Variable	Chronic Lung Disease	Hypothyroidism	Obesity	Psychiatric Disease	DM	Anemia	Lytes	Neurologic Disease	Coagulopathy	Liver Disease	Renal Disease
Severe CHD	6.07	6.49	4.91	5.52	4.32	4.40	3.80	4.14	2.45	2.20	1.34
Eisenmenger syndrome	13.5	10.0	5.14	8.92	7.03	8.65	12.70	10.3	7.30	6.49	2.43
HLHS	5.26	4.35	3.43	7.09	3.66	4.81	6.64	5.03	2.75	4.35	3.43
Common ventricle	4.42	6.42	2.85	4.42	3.00	3.85	4.99	4.85	3.99	5.71	1.71
TGA	4.79	3.80	4.24	4.83	3.41	2.85	3.13	3.17	1.70	1.70	1.19
TOF	5.82	5.69	4.43	5.13	4.30	3.84	3.56	3.60	2.44	1.83	1.33
Truncus arteriosus	7.87	7.26	6.81	8.17	5.45	5.90	2.72	5.30	3.18	3.18	1.51
Endocardial cushion defect	6.78	10.0	6.63	5.74	5.00	5.93	3.11	4.52	1.85	1.22	0.89
Nonsevere CHD	6.71	5.80	5.96	5.63	5.48	4.73	3.31	2.62	1.37	1.43	1.14
Ebstein anomaly	5.20	8.49	6.04	7.65	4.13	4.97	2.91	2.29	1.15	1.30	1.22
Aortic coarctation	5.77	3.94	4.72	4.57	3.50	3.27	2.79	2.01	1.01	0.86	0.80
Anomalies of the pulmonary artery	12.9	8.15	10.2	6.79	6.93	6.11	4.35	3.53	2.31	2.17	1.77
Anomalies of the pulmonary valve	7.09	5.33	5.96	5.85	4.93	5.15	3.43	2.19	0.91	1.46	0.95
Anomalies of the tricuspid valve	6.60	6.07	4.22	5.28	6.07	6.33	3.17	3.17	1.06	2.64	1.58
Ventricular septal defect	6.44	5.93	5.48	5.20	5.47	4.66	3.17	2.58	1.42	1.18	1.04
Patent ductus arteriosus	6.81	5.34	5.65	6.34	5.76	5.03	2.88	2.58	1.41	1.88	1.26
Anomalies of veins	7.91	5.70	6.96	6.80	6.49	5.85	5.06	4.59	2.69	4.27	1.11
Unspecified defect of septal closure	9.02	10.28	8.23	8.70	9.49	6.01	6.17	3.48	0.79	1.58	1.11
Subaortic stenosis	8.75	7.97	11.1	8.08	9.88	6.29	4.38	3.37	1.68	2.13	1.91
Aortic anomalies	6.71	5.38	7.92	5.74	7.85	5.50	3.75	2.72	2.11	2.30	2.30
Non-CHD	3.35	3.24	3.66	3.75	3.64	2.06	1.25	0.96	0.30	0.66	0.36

CHD indicates congenital heart disease; DM, diabetes mellitus; HLHS, hypoplastic left heart syndrome; Lytes, fluid and electrolyte abnormalities; TGA, transposition of great arteries; TOF, tetralogy of Fallot.

atherosclerotic disease could be an important area of focus in CHD clinics, especially for those with nonsevere lesions. It has been shown that eligible adults with CHD at large tertiary adult CHD centers in the United States are less likely to receive statin or primary cancer screening compared with adults without CHD.[10,28] This underscores that maybe CHD clinicians need to develop close partnerships with primary care physicians, including education of primary care providers of the need for screening.

Our rates of noncardiovascular conditions were lower than the 95% prevalence reported in a tertiary center cohort in Germany.[29] This is likely because different comorbidities were included within the noncardiovascular comorbidity category between the 2 studies, and our study was based on a commercially insured subset of the entire population rather than at a tertiary center. Within a national US inpatient data set, Rodriguez et al[30] found a much higher rate of renal failure in patients with CHD, ranging from 3.4% to 18.8%, depending on the chronicity of renal disease and presence or absence of heart failure, than our observations, but this again was a sample of hospitalized patients. The noncardiovascular comorbidities are the ones for which patients with CHD are more likely to be seen by internists or noncardiology specialists. A multicenter study from Germany found that 63% of inpatient adult CHD emergencies required management by a specialist other than a cardiologist.[31] Clinicians caring for CHD might thus consider using a multidisciplinary approach, including building close collaborations with internists and specialists to help provide appropriate care for the noncardiovascular comorbidities we found to be prevalent among patients with CHD. This could be similar to the prior efforts to bring together subspecialty experts from various

disciplines to initiate a formal evaluation of liver disease that is prevalent among single-ventricle patients after Fontan palliation.[32]

In summary, our overall estimates of the comorbidities were lower than expected from other publications, but our study sample was drawn from a commercially insured outpatient population and did not have tertiary center bias. Furthermore, there might be selection bias related to who is included in a commercially insured database, as these individuals generally are healthier and expected to have higher socioeconomic status than those without insurance or those insured by Medicaid. Thus, our estimates provide preliminary information about the care delivery model necessary to optimize care for patients with CHD but should be supplemented by analyses from the 51% of the US population who uses other types of insurance, including government programs. Nonetheless, these adult patients with CHD had significantly higher comorbidity burden than their peers, suggesting they have higher risks and thus need to be managed differently. The medical community at large need to recognize their unique healthcare needs, including the high burden of non–cardiovascular-related diagnoses that may mimic or be affected by coexisting CHD.

Limitations

This study has several limitations. First, *ICD 9* and *ICD 10* codes have imperfect sensitivity and specificity, and CHD may have been incorrectly coded. Where possible, however, we used the codes that have been previously validated and removed the ones that were nonspecific. Misclassification of comorbidities also can be a potential source of error, but that would be random and bias the results toward the null. Second, we did not use the recently published physiologic parameters to assign the severity of CHD lesions because most of those parameters are based on detailed clinical and/or imaging data,[33] which are not present in claims databases. Finally, patients carrying a diagnosis of CHD are expected to have more contact with the healthcare system and to be seen regularly by cardiovascular specialists; thus, they may be screened more frequently for some of the comorbidities.

Conclusions

The present study uses a large database containing claims for commercially insured enrollees to generate population-based estimates of comorbidity rates for ≈40 000 adults with CHD. Patients with CHD had 9.41-, 1.73-, and 1.47-fold higher risks of comorbidities previously recognized to be common in CHD, other cardiovascular, and noncardiovascular ones when compared with patients without CHD, after adjusting for the baseline characteristics. Among patients with CHD, those

with ES had the highest prevalence of comorbidities. After considering interaction with age, patients with severe CHD of any age had higher risks of comorbidities previously recognized to be common in CHD and lower risks of other cardiovascular conditions than patients with nonsevere CHD, whereas the risks of noncardiovascular comorbidities was higher among patients with severe CHD before the age of 40 years but similar after the age of 40 years than patients with nonsevere CHD. These data could be used to plan for the clinical resources patients with CHD are likely to need. Clinicians caring for CHD may want to use a multidisciplinary approach to the evaluation and management of these patients, including building close collaborations with internists and noncardiology specialists to help provide patients appropriate screening and preventive care.

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