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ASSOCIATION BETWEEN COMBINED ANATOMIC AND PHYSIOLOGIC CLASSIFICATION OF ADULTS WITH CONGENITAL HEART DISEASE AND SELECTED HEALTHCARE UTILIZATION AND CLINICAL OUTCOMES

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Bachelor of Science

University of Georgia

2016

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An abstract of

A thesis submitted to the Faculty of the

Rollins School of Public Health of Emory University

in partial fulfillment of the requirements for the degree of

Master of Public Health

in Epidemiology

2021

Abstract

ASSOCIATION BETWEEN COMBINED ANATOMIC AND PHYSIOLOGIC CLASSIFICATION OF ADULTS WITH CONGENITAL HEART DISEASE AND SELECTED HEALTHCARE UTILIZATION AND CLINICAL OUTCOMES

By David Rink

Background: Classifying complexity of congenital heart disease in adults (ACHD) through native anatomy alone based on ICD codes may not identify those at risk of adverse outcomes. Incorporating physiologic comorbidities into classification may improve the ability to predict adverse outcomes using administrative data. The objective of this study is to examine the association between combined anatomic and physiologic classification of congenital heart disease (CHD) complexity with healthcare utilization and adverse clinical outcomes among adults.

Methods: Data from Georgia Medicaid claims and Emory Healthcare electronic health records (eHR) were examined for adult patients aged 18-45 years with a CHD-related diagnosis with encounters from 2008 to 2013. Anatomic complexity was examined and categorized as complex anatomy or shunt and/or valve. ACHD guideline-based physiologic comorbidities captured at one year were used to determine physiologic classification, categorized as A/B or C/D. Healthcare utilization (i.e., hospitalizations and emergency department (ED) visits) and adverse clinical outcomes (i.e., transplantation and mortality) were examined for one year. Adjusted relative risks (aRR) and 95% confidence intervals (95% CI) were estimated using multivariable logistic regression.

Results: Among 2,384 eligible patients, 34.4% had complex anatomy and 41.6% had C/D physiology. Overall, 10.2% had at least one hospitalization and 8.3% had at least one ED visit. There were 22 deaths and one transplant with no significant group differences by combined anatomic and physiologic classification status. The risk of any hospitalization for those with complex ACHD and C/D physiology was 31.2 (aRR 31.2, 95% CI: 11.9, 81.6) times higher than those with shunt and/or valve anatomy and A/B physiology over 1-year of follow-up. The risk of having any ED visit for those with complex ACHD and C/D physiology was 10.6 (aRR 10.6, 95% CI: 3.4, 33.5) times higher than those with shunt and/or valve anatomy and A/B physiology over 1-year of follow-up.

Conclusions: Physiologic comorbidities provide additional information compared to native anatomy alone in assessing outcomes in adults using healthcare administrative databases. Future analyses should examine the associations noted in this study and apply alternative study designs that may better handle influential covariates and potential confounders that inform outcomes.

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List of Abbreviations

ACC	American College of Cardiology
ACHD	Adults with Congenital Heart Defects
ACS	American Community Survey
AHA	American Heart Association
AP	Anatomy and Physiology
aRR	Adjusted Relative Risk
ASD	Atrial Septal Defect
AV	Atrioventricular
CDC	Centers for Disease Control and Prevention
CHD	Congenital Heart Disease
CI	Confidence Interval
CMH	Cochran-Mantel-Haenszel Chi-Square Test of Homogeneity
cRR	Crude (or unadjusted) Relative Risk
DM	Diabetes Mellitus
ECDW	Emory Clinical Data Warehouse
ED	Emergency Department
FISMA	Federal Information Security Management Act
FPL	Federal Poverty Line
HF	Heart Failure
IT	Information Technology
PDA	Patent Ductus Arteriosus
PFO	Patent Foramen Ovale

PHI	Protected Health Information
P-HTN	Pulmonary Hypertension
RSPH	Rollins School of Public Health
RVH	Right Ventricular Hypertrophy
TGA	Transposition of the Great Arteries
TOF	Tetrology of Fallot
VSD	Ventricular Septal Defect
ZCTA	ZIP Code Tabulation Areas

CHAPTER I: BACKGROUND

Congenital heart disease (CHD) represents the most common type of birth defect in the U.S. [1]. Over the past several decades, improved therapeutic techniques and management have resulted in significant decreases in mortality from CHD, resulting in a larger population of adults with CHD than children [2]. However, CHD represents a heterogeneous disease with unique patient courses dependent on a number of factors, including the type and size of defect, time of diagnosis, and treatment plans and/or corrective repairs performed, each associated with its own unique physiologic sequelae [2-4]. Patients with CHD have increased morbidity and mortality compared to the general population [5, 6] and data suggests that the incidence of hospitalization and ED visits among ACHD patients are increasing [7-9]. The increasing prevalence and heterogeneity of adults with CHD, along with the associated adverse clinical outcomes and growing healthcare utilization needs makes this cohort an important population to study in order to understand risk factors and mitigation strategies for poor outcomes.

Until recently in the U.S., no population-based system was in place to estimate ACHD prevalence or to assess long-term outcomes and healthcare utilization [10]. Studies examining healthcare utilization and clinical outcomes of ACHD patients were focused on tertiary referral populations, rather than being based on the general population as a whole. ACHD represents a heterogeneous disease with differing anatomy and physiology that is often unique to only a handful of patients [4]. This heterogeneity poses challenges in studying and standardizing treatment protocols, as well as in predicting outcomes for individual patients, especially when study data from tertiary centers is not generalizable to all populations.

Congenital Heart Defects (CHDs)

CHDs constitute a spectrum of structural abnormalities which are present at birth and may affect the normal functioning of the heart. The heart is the first fully functioning organ in the human embryo, generally beginning to beat by 2 to 3 weeks of gestation and fully formed by 8 to 9 weeks [11]. CHDs result from anomalous development of the cardiovascular system within the first 8 to 9 weeks of gestation. While the cause of CHDs remains largely unknown, several teratogens are associated with CHD development, including drug exposures, viral infections, and maternal conditions like obesity and diabetes mellitus (DM) [12, 13]. In addition, certain genetic syndromes and individual genetic mutations have been associated with the development of CHDs [1].

While all CHDs are characterized by abnormal cardiac development, not all manifest with signs and symptoms at birth [3]. Findings suggestive of congenital heart disease at birth may include excessive sweating, poor feeding, rapid heartbeat, or cyanosis [14]. With increasing prevalence of fetal ultrasonography and newborn pulse oximetry, many cases of CHD are identified and treated early. However, they can also be diagnosed later in life, especially those that are less likely to manifest with early signs and symptoms. Improvements in prenatal diagnosis does raise important ethical considerations as studies have shown an association with elective termination [15]. Data is limited, particularly in the U.S., but studies from Europe in 1999 and 2001 indicated an elective termination rate of approximately 12% in prenatally diagnosed CHD [16, 17]. More recently, a large retrospective study from Denmark examining diagnosis and outcome trends in CHD from 1996-2013 showed the rate of prenatal CHD detection had increased significantly from 4.5% to 71% over the course of the study period, and elective termination of pregnancy in these cases had increased from 0.6% to 39.1% over the

same period [18]. In general, larger, more morphologically complex lesions such as univentricular hearts, transposition of the great arteries (TGA), and truncus arteriosus were more frequently identified in the prenatal period. However, relative rates of elective termination were not significantly different for specific lesions. Given the cultural differences in elective termination practices, it is difficult to know how the U.S. compares.

The overall mortality for CHD is decreasing largely due to improvements in care. This has resulted in a shift in the age distribution of patients with CHD favoring the adult population. The prevalence of CHD in the U.S. is estimated to be about 1.4 million adults and 1 million children [19]. Isolated atrial or ventricular septal defects (ASD or VSD) are the most common CHDs in adults and children, followed by more complex and severe lesions such as tetralogy of Fallot (TOF), truncus arteriosus, and atrioventricular (AV) canal defects [20].

The growing adult population brings new challenges, including a need for adult specialists in congenital heart disease, the development of specialty and multidisciplinary care centers, and the greater comorbidity burden and healthcare utilization needs resulting from longer life spans among individuals with CHD [21-23]. In addition to developing the appropriate resources and guidelines to care for adults with CHD (ACHD) patients, creating a system that ensures reliable transitions from pediatric to adult care is paramount. Barriers to care such as lack of or limited insurance, distance to referral centers, and the concern of rebuilding the close rapport currently in place with their pediatric provider with a new adult provider have been shown to negatively impact the transition to adult care, and many ACHD patients do not successfully make the transition at all, often leaving care altogether [24-27]. Nonetheless, ACHD patients represent an important growing demographic and represent the majority of all CHD patients.

Prevalence of CHD in the United States

CHDs represent the most common type of birth defect with a birth prevalence of 8 per 1000 in the U.S. [1]. In the 1950s, approximately 15% of children born with CHD survived, but over the past several decades, improved therapeutic techniques and management have resulted in significant decreases in mortality from CHD [2]. Nowadays, over 90% of those with simple to moderate anatomic CHD complexity and 60% of those with complex CHD are estimated to survive to adulthood [21]. This has resulted in a population of ACHD who is larger than the pediatric CHD population [19]. Further, epidemiologic trends suggest that the prevalence and percentage of ACHDs with complex anatomy are increasing at greater rates than that of non-complex ACHD [28].

CHD Phenotypes

CHDs may involve any of the intrinsic heart structures or associated vessels [29]. This includes the heart walls, chambers, and valves, in addition to the coronary and great vessels. Defects can be singular lesions or a constellation of multiple anomalies. Some examples of singular lesions include ASD and VSD, valvular regurgitation or stenosis, coarctation of the aorta, and patent ductus arteriosus (PDA). TOF is an example of a complex CHD consisting of a constellation of multiple lesions, including infundibular pulmonary stenosis, a VSD, right ventricular hypertrophy (RVH), and an overriding aorta.

Natural History of CHD

CHD patients tend to follow unique courses dependent on a number of factors, including the type and size of their defect, time it was identified, and any treatments or repairs performed, which are associated with their own unique physiologic sequelae [2, 3]. CHD care is a rapidly evolving field in which interventional approaches to treatment have expanded to include not only

new techniques in cardiovascular surgery, but also an entire field of transcatheter procedures [30, 31]. Medical management remains an important piece to CHD care in an effort to prevent the development of physiologic sequelae and manage comorbidities and exacerbations. However, limited evidence for traditional heart failure (HF) and other cardiovascular condition therapeutics exist in the CHD population, so medical management remains highly individualized to a specific patient and their underlying syndrome [32, 33]. Consequently, CHD represents a heterogeneous disease with anatomy and physiology that is often unique to a relatively small number of patients and may vary dramatically based on the techniques and therapies available early in and throughout a patient's life [4].

The physiologic sequelae of CHD are varied [4]. The type, site, and size of lesion can all influence resulting hemodynamics and what physiologic consequences develop as a result of a specific CHD. Similarly, a patient's age, representing the length of time the lesion has existed and/or has been repaired, surgical era of repair, and access to regular or specialty healthcare play a role. Common sequelae can be classified as either cardiovascular or end-organ. Cardiovascular consequences of CHD may include HF, arrhythmias, new or worsening valvular disease, aortic aneurysm, and pulmonary hypertension (P-HTN). End-organ consequences include pulmonary, hepatic, and renal disease, along with their associated signs and symptoms. While high quality studies are lacking, there is evidence to suggest that many physiologic sequelae including HF, poor exercise tolerance, and renal dysfunction are associated with worse outcomes in ACHD patients [34-36]. In addition to these physiologic consequences of CHD, there is evidence that serum markers such as anemia, hyponatremia, and hypoalbuminemia are associated with relatively worse outcomes in ACHD patients [37-39]. Despite the broad associations with poorer

outcomes, it is not always clear which patients will develop these sequelae and how they can be used to independently risk stratify patients.

Cardiac Transplantation in ACHD

Cardiac transplantation has become a more prevalent treatment in patients with advanced HF over the past two decades, but it remains a relatively rare treatment among ACHD. It accounts for about 3% of all adult cardiac transplants, representing a relative increase of almost 40% since 1999, but an absolute increase of only about 1% [40, 41]. Perioperative morbidity and mortality are higher in ACHD-related transplants (17.4% vs. 7.4% in those transplanted for other reasons), which may explain some hesitancy towards performing the procedure on this population, but 10-year outcomes show a significant difference in survival favoring ACHD patients (40.7% vs. 49.0%) [40, 41].

Mortality in ACHD

Despite declining mortality over time among ACHD patients in all age groups, patients with CHD are known to have increased morbidity and mortality compared to the general population [5, 6]. Long-term outcomes in ACHD patients reveal high rates of arrhythmias, HF, and end-organ dysfunction [42]. HF and sudden cardiac death are the two most common causes of mortality in ACHD patients. HF, in particular, is estimated to cause between 26-42% of deaths among adults with CHD [6, 43].

Factors Associated with Adverse Clinical Outcomes in ACHD

A number of factors have been studied for their association with adverse clinical outcomes in ACHD. Clinical markers such as anemia, hyponatremia, and hypoalbuminemia have all been associated with approximately threefold higher mortality in ACHD patients [37-39]. Studies have also shown higher mortality associated with polypharmacy and comorbid

conditions such as diabetes mellitus (DM) and renal dysfunction in ACHD patients [35, 44, 45]. These factors represent markers of downstream sequelae resulting from CHD rather than intrinsic characteristics of the CHD itself. Studies focused on evaluating adverse clinical outcomes such as mortality in ACHD patients which use native anatomy as a predictor routinely fail to show significant differences in outcomes among different anatomic lesions [46-48]. This is likely because there is no good way to capture the heterogeneity and complexity of post-surgical anatomy in adults using population-based administrative data which is the type of data source most commonly available. This leads to a reliance on native anatomy as the predictor of anatomic CHD complexity, which has often been modified or corrected during childhood. Consequently, utilizing physiologic sequelae of CHD to predict adverse clinical outcomes in adult patients with CHD may be preferable as it may more accurately represent the severity of their present CHD.

Prevalence of Healthcare Utilization in ACHD

With advances in CHD care and the prolongation of life expectancy of individuals with CHD, the total population of ACHD patients continues to grow in the U.S. [19]. Similarly, the cost and complexity of CHD care is growing as access to multidisciplinary and specialty care is associated with better outcomes as well as higher costs [49-51]. Prevention of emergency department (ED) visits and hospitalization via routine outpatient management remains the goal of ACHD care. Despite that, data suggests that the incidence of ED visits and hospitalizations among ACHD patients is increasing.

Using data from the Nationwide Inpatient Sample (NIS), hospitalizations for ACHD patients from 1998 to 2005 showed a 101.9% increase from 35,992 in 1998 to 72,656 in 2005 [7]. The CHD sample examined in this study included adults who had an ICD-9-CM CHD-

related diagnosis code, who were at least 18 years of age and who were admitted to an acute care hospital for any reason. A more recent study which also used NIS data to examine trends of inpatient admissions between 2003-2012 showed an increase in the ACHD admissions from 63,950 in 2003 to 116,085 in 2012, corresponding to an 81.5% increase during the 10-year period [8]. The study sampled adults (>18 years of age) who were hospitalized with an ICD-9-CM diagnosis code of 745.0-747.49. After stratification for simple, complex, and unclassified CHD as categorized in the Bethesda classification system, all three groups had significant increases in hospitalization rates (101.4%, 52.8%, and 35.2% increases, respectively). This study also found a significant increase in hospital length of stay over the decade-long study period from 5.5 to 6.0 days for those with simple CHD and 6.1 to 6.9 days for those with a complex CHD.

Another study examining incidence trends of ACHD patients presenting to EDs between 2006 to 2012 used the Nationwide Emergency Department Sample (NEDS) database and showed an increase from 36,513 visits in 2006 to 52,765 in 2012, corresponding to a 44.5% increase during the 7-year period [9]. The study sample included adults with an ICD-9-CM diagnosis code of 745.0-747.49 (excluding 745.5). Notably, even after stratifying for simple, complex, and unclassified CHD as categorized in the Bethesda classification, all three categories had significant increases in ED visit rates (40.6%, 37.6%, and 62.8% increases, respectively). These studies indicate a significant increase in healthcare burden from ACHD, especially as the prevalence of ACHD and complexity of its care increase.

Factors Associated with Healthcare Utilization in ACHD

While increasing prevalence of ACHD does partially explain the increase in healthcare utilization, in order to reduce the burdens on the healthcare system, it is essential to understand

the factors associated with increased healthcare utilization and develop ways to predict and prevent them. Studies examining recent trends of healthcare utilization among ACHD patients show simple anatomic lesions associated with relatively greater increases in healthcare utilization than more complex anatomic lesions [8, 9]. These results suggest that native anatomic CHD classification in and of itself is not a sufficient predictor for healthcare utilization. A recent study examining clinic non-attendance and rates of ED visits showed that among ACHD patients, those with a non-attended clinic visit had a threefold increased odds of multiple ED visits compared to those who had not missed a clinic visit [52]. Access to care can be a risk factor for higher healthcare utilization, especially among the uninsured. An estimated 45% of ACHD patients in the U.S. live over an hour from the nearest ACHD center limiting their ability to regularly receive specialty care and placing them at higher risk for ED utilization [53].

Other factors associated with healthcare utilization include a greater burden of comorbid conditions and physiologic sequelae of CHD. The same study that examined hospitalization trends for ACHD patients from 2003 to 2012 also noted a 131% increase in concomitant P-HTN as well as increases in comorbid hypertension, DM, obesity, and chronic kidney disease [8]. Additionally, hospitalization among ACHD patients with HF have significantly increased compared to adult patients without CHD with HF [54]. These results indicate the sequelae of CHD, including HF, P-HTN, and other end-organ dysfunction may be useful in predicting future healthcare utilization among ACHD patients.

Anatomic CHD Complexity: Predicting Clinical Outcomes and Healthcare Utilization

Anatomic CHD complexity ranges dramatically from simple (anatomically non-complex) defects requiring no invasive treatments to more anatomically complex defects requiring complex, and often multiple surgical repairs and palliative procedures [23]. However, to date, no

reliable system of classifying patients based on anatomic complexity of disease and risk of adverse events has been developed. Previous attempts at classifying heart defects include the 2008 ACC/AHA Guidelines for the Management of ACHD, Marelli's five level anatomic complexity hierarchy which utilizes ICD-9 CHD-related diagnostic codes, and, more recently, modified efforts integrating hemodynamic severity and basic anatomy [10, 20, 55]. Marelli's classification focused on native anatomy, not accounting for previous surgical repairs or their physiologic sequelae, whereas the 2008 ACC/AHA does take into account post-surgical anatomy. As ACHD may or may not have had surgery in childhood, capturing anatomic complexity becomes complicated given the varied outcomes to the same surgical procedures across surgical eras and across individuals. Marelli's classification was not designed to predict outcomes later in life. Heart defects associated with cyanosis or need for surgery in the first year of life were assigned the severe category by Marelli, limiting extrapolation beyond its initial use. This classification was initially designed in part to understand and validate ICD codes for detecting CHDs, and not for predicting outcomes, although it is intuitive to think more complex anatomy would be associated with worse outcomes. Thus, the prognostic utility and accuracy of the Marelli system may not be predictive of outcomes outside of the first year of life. Indeed, grading systems like these have not consistently demonstrated anatomic complexity as an independent predictor for outcomes in ACHD patients [46-48]. Previous studies examined the effects that HF and other comorbidities have on outcomes with ACHD patients, but their comorbidity definitions relied on nonspecific diagnostic codes, some of which did not reflect individuals with true CHD [56]. Nevertheless, their results indicated a correlation of HF and other comorbidities with worse outcomes among ACHD patients that reinforce the need for further study.

In 2018, the ACC/AHA Task Force on Clinical Practice Guidelines published updated guidelines for managing ACHD [4]. They acknowledged that previous efforts to classify anatomic complexity inadequately accounted for the intrinsic heterogeneity of the ACHD population resulting from a rapidly evolving treatment landscape. In the guidelines, the task force developed the ACHD anatomic and physiological (AP) classification system which attempts to account for underlying anatomy, including possible repairs, and physiological comorbidities to classify the complexity of the disease. This system was developed primarily based on expert consensus and has not yet been studied for its validity in differentiating patients who are more likely to experience adverse outcomes.

At present, ACHD appears to exist at a crucial crossroads in which clinical outcomes are improving, resulting in an increase in prevalence, heterogeneity, and treatment complexity which places a growing burden on the healthcare system. These factors, coupled with the lack of validated risk stratification or complexity grading tools for this population, emphasize the importance of studying those factors associated with greater healthcare utilization and more adverse clinical outcomes. The present study will lay some groundwork in understanding these risk factors by examining both anatomic and physiologic characteristics of ACHD and their associations with these outcomes. First, the study will examine if patients with anatomically complex ACHD as defined by native anatomy requiring intervention in the first year of life is associated with greater 1-year healthcare utilization and worse 1-year clinical outcomes for ACHD compared to those with shunt and/or valve native anatomy. The study will also examine if a higher physiological stage as defined in the 2018 American Heart Association (AHA) / American College of Cardiology (ACC) Guideline for the Management of Adult Congenital Heart Disease is associated with greater 1-year healthcare utilization and worse 1-year clinical

outcomes in ACHD compared to a lower physiological stage. Finally, the study will assess whether incorporation of a collapsed 2-level physiologic stage classification in addition to a 2-level anatomic classification is more strongly associated with adverse 1-year clinical outcomes and greater 1-year healthcare utilization for ACHD than each factor individually.

CHAPTER II: METHODS

Study Design

This study combined data from two larger U.S. Centers for Disease Control and Prevention (CDC) congenital heart disease (CHD) surveillance projects with Emory University, the "Surveillance of Congenital Heart Disease in Adolescents and Adults" (CDC-RFA-DD12-1207) (hereinto referred to as the "pilot project"), and the "Surveillance of Congenital Heart Disease Across the Lifespan" (CDC-RFA-DD15-1506) (hereinto referred to as the "lifespan project"). The aim of these projects was to design and expand population-based tracking of individuals with CHD. Objectives included acquiring a better understanding of the healthcare utilization, clinical outcomes, and mortality of individuals living with CHD. The current effort aims to address a critical gap in ACHD care by laying the groundwork for developing a validated clinical tool with prognostic value to grade the complexity of the full spectrum of ACHD. Emory IRB study approval (STUDY00001135) was received on 7/6/2020. Patient consent was waived by the IRB and confidentiality was maintained as this research is a secondary analysis of previously de-identified patient information.

In the current study, retrospective cohorts were extracted to directly compare the severity classification scheme developed in the CDC lifespan project with an expanded form of the classification scheme that accounts for physiologic comorbidities included in the 2018 AHA/ACC ACHD AP classification system. Instead of limiting the sample to a tertiary referral population, the current study uses a combination of Georgia Medicaid claims and Emory Healthcare data to determine if inclusion of current physiology in addition to native anatomy is more strongly associated with healthcare utilization and adverse clinical outcomes among the general ACHD patient population.

Data Sources

Georgia Medicaid MAX eligibility and claims files and Emory Clinical Data Warehouse (ECDW) data covering a six-year period from 2008-2013 were used to construct a de-identified, de-duplicated analytic dataset. To ensure data confidentiality, data were stored on a secure, private, Federal Information Security Management Act (FISMA)-compliant network storage device drive at the Emory University, Rollins School of Public Health (RSPH), Information Technology (IT) Department server system, maintained only by authorized IT personnel and study researchers. Protected Health Information (PHI) was excluded (de-identified) from this dataset to maintain confidentiality and replaced with a unique identifier for each patient.

Study Subjects

The study consisted of 2,384 ACHD patients between 18-45 years old as of the date of their first qualifying encounter (FQE; for pilot project data 1/1/2008-12/31/2010 and for lifespan project data 1/1/2011-12/31/2013) defined as the first encounter that at least one CHD-related ICD-9-CM code (Appendix B) appeared in the patient's clinical record between 1/1/2008 to 12/31/2011. Data from all encounters for a 1-year period were then analyzed to assess for presence of physiologic comorbidities and assigned a physiologic stage. Following the assignment of a physiologic stage, data were analyzed for one more year to assess for dependent variables.

Exclusions included anyone without a FQE (n = 33,703), which included those without encounters during the study period or those whose CHD-related ICD-9-CM diagnostic code(s) categorized them as having "other" CHD (Appendix B) and patients with diagnostic code 745.5 (secundum atrial septal defect (ASD) or patent foramen ovale (PFO)) in isolation or in combination with "other" CHD codes due to lack of specificity of these codes [57]. Of the

remaining 3,299 eligible participants with a FQE, 915 were excluded due to being pregnant or becoming pregnant over the course of the six-year surveillance period from 1/1/2008 to 12/31/2013 (see Figure 1).

Outcome Variables

Four outcome variables were examined, including two primary healthcare utilization outcomes and two secondary clinical outcomes. The primary healthcare utilization outcomes were the occurrence of any hospitalization or any ED visit within 1-year of physiologic categorization, each measured as Yes/No. Encounter type was used to operationalize inpatient and emergency department (ED) encounters. Any hospitalization was defined as at least one inpatient encounter within one year of the patient's physiologic staging (Yes/No). Any ED visit was defined as at least one ED encounter within one year of the patient's physiologic staging (Yes/No).

The clinical outcomes examined included mortality and cardiac transplant status. Mortality was defined as all-cause mortality in the year after the physiologic staging. In Georgia Medicaid, mortality was operationalized using the vital status variable, and, in the ECDW data source, patients were linked to Georgia vital record death certificate data to confirm mortality status. Cardiac transplantation was operationalized by the presence of either CPT code 33935 for heart-lung transplant with recipient cardiectomy-pneumonectomy or CPT code 33945 for cardiac transplant, with or without recipient cardiectomy in the year after the physiologic staging. Both mortality and cardiac transplant were measured using a dichotomous response (Yes/No).

Predictor Variables

Predictor variables included CHD anatomic complexity and physiologic staging. CHD anatomic complexity classification was operationalized by the native anatomic CHD grouping

scheme used in the lifespan project (Appendix B), based on CHD-related ICD-9-CM code(s) found on the patient's FQE. Physiologic stage was operationalized based on the presence of specific physiologic ICD-9-CM codes (Appendix D) corresponding to the physiologic comorbidities used in the 2018 AHA/ACC ACHD AP classification (Appendix C) occurring at any encounter within 1-year after the patient's FQE. Classification was either A/B corresponding to no/mild physiologic comorbidities or C/D corresponding to moderate/severe physiologic comorbidities. Collapsing from a 4-level A, B, C, and D classification scheme to a 2-level A/B and C/D scheme was done because the operationalization of physiology via ICD-9-CM codes was believed to lack the precision to distinguish between four unique levels. If the presence of any relevant physiology occurred within 1-year of the FQE, then the patient was classified with C/D. Classification as A/B reflected the absence of a physiology code in Appendix D within 1-year following the FQE.

All patients received a 2-level lifespan anatomic CHD complexity classification (complex vs. shunt and/or valve) and a collapsed 2-level AP physiology stage classification (A/B or C/D). Outcomes were evaluated in the 1 year following the physiologic staging.

Covariables

Age

Patients were between ages 18 and 45 years on the date of their first encounter for pilot project data 2008-2010 or their FQE for the lifespan project data 2011-2013. This variable was calculated by subtracting the patient's date of birth from the date of their first encounter or their FQE. Age was dichotomized and classified into two groups: '0' = 18-34 and '1' = 35-45 years of age. For all models, the youngest group served as the reference group.

Gender

Gender was coded ‘0’ for males and ‘1’ for female. For all models, males served as the reference group.

Race

Race was classified into the following three categories: ‘0’ for White, ‘1’ for Black, and ‘2’ for other. For all models, White served as the reference group.

Ethnicity

Ethnicity was classified into the following two categories: ‘0’ for non-Hispanic and ‘1’ for Hispanic. For all models, non-Hispanic served as the reference group.

Socio-Economic Status (SES)

Four metrics were considered as proxies for SES status, including neighborhood poverty, income, education, and renter occupancy levels. Data for each ZIP Code Tabulation Area (ZCTA) was obtained from the 2014 American Community Survey (ACS) 5-year estimates (2010-2014). For each SES proxy, cutoff values were determined and applied to each ZCTA to generate discrete categories. The ZCTA of residence of each patient in the study was then used to assign their respective discrete SES proxy level.

Neighborhood poverty was defined as the percent of households in that ZCTA below 100% of the federal poverty level (FPL) and was coded as ‘0’ for low poverty (<15%), ‘1’ for medium poverty (15-30%), and ‘2’ for high poverty (>30%). Low poverty served as the reference group.

Neighborhood income was defined by categorization of median income in that ZCTA and was coded as ‘0’ for low (<$40,000 per year), ‘1’ for medium ($40,000-$75,000 per year), and ‘2’ for high (>$75,000). Low income served as the reference group.

Neighborhood education was defined as the percent of people living in that ZCTA holding at least a bachelor's degree and was coded as '0' for low (<35%) and '1' for high (>=35%). Low education served as the reference group.

Neighborhood renter occupancy was defined as the percent of people living in that ZCTA who were renters and was coded as '0' for low (<35%), '1' for high (>=35%). Low renter occupancy served as the reference group.

Statistical Analysis

All analyses were conducted using the Statistical Analysis System (SAS) version 9.4 statistical software (SAS institute, Cary, NC). Descriptive analysis included frequencies and percentages for all categorical variables. The full sample consisted of 2384 patients. There were 303 (12.7%) missing variables for race and 751 (31.5%) missing variables for ethnicity. Bivariate analyses were conducted to describe and compare the two primary healthcare utilization outcomes (i.e., any hospitalization and any ED visits within 1-year of physiologic categorization) and two clinical secondary outcomes (i.e., mortality and cardiac transplant status) with the classification exposures and covariate predictors (i.e., age group, gender, race, ethnicity, SES proxies) using chi square tests.

Robust Poisson regression models, using the PROC GENMOD procedure with the LINK option, were conducted to generate crude relative risks (cRR) and 95% confidence intervals (CIs). Predictors with a statistically significant association for each outcome from the bivariate analyses were included in multivariable robust Poisson regression models to yield adjusted relative risks (aRRs) and 95% CIs.

Effect modification was examined through stratification, calculating stratum-specific risk estimates and 95% CIs, and the Cochran-Mantel-Haenszel (CMH) Chi-Square Test of

Homogeneity. *P* values <0.05 were considered significant. Confounding was assessed by comparing the cRR with aRR. A difference between the cRR and aRR of at least 10% was considered as evidence that confounding is present. Collinearity among the covariables was assessed for potential relationships with one another using a collinearity matrix. Variables which seemed to be collinear were examined to determine which should be included in the analysis. The final multivariate Poisson regression model included those predictors that met the 10% change in estimate rule when added to the model.

CHAPTER III: RESULTS

A total of 2,384 patients were included in the analytic sample. Overall, 244 (10.2%) had one or more hospitalization and 197 (8.3%) had one or more ED visits during the study period. There were 22 deaths and one case of cardiac transplantation during the study period. A majority of patients (65.6%) had shunt and/or valve native anatomy compared to 34.4% with complex anatomy. A majority of patients (58.4%) had A/B physiological stage compared to 41.6% with C/D stage. For the combined anatomic and physiological staging, shunt and/or valve native anatomy with A/B physiology was most common (43.5%), followed by shunt and/or valve native anatomy with C/D physiology (22.1%), then complex anatomy with C/D physiology (19.5%), and finally complex anatomy with A/B physiology (14.9%) (Table 1).

Approximately two-thirds of the patients were in the younger age group (68.8%) and patient gender was evenly distributed between male (51.2%) and female (48.7%). While most covariables had complete data, race data was missing for 303 patients (12.7%) and ethnicity data was missing for 751 patients (31.5%). Overall, the sample was majority White (6.15%) and non-Hispanic (66.7%), though there was a substantial Black population included (24.3%). Four different socioeconomic status (SES) proxies were studied, including neighborhood poverty level, median neighborhood income, neighborhood educational attainment, and neighborhood renter occupancy. Neighborhood was defined as the ZCTA (ZIP code tabulation areas) of residence for each patient. Each proxy had slightly different distributions which can be seen in Table 1.

Given the limited data on clinical outcomes, results are summarized here rather than in tabular form. The single case of cardiac transplantation occurred in a patient with complex anatomy and C/D physiology. The distribution of deaths by collapsed native anatomic

complexity was 14 (0.9%) in the shunt and/or valve group and 8 (1.0%) in the complex anatomy group (p-value ns). By AP physiological stage, there were 8 (0.6%) deaths in the A/B group and 14 (1.4%) in the C/D group ($p < 0.05$). Mortality by collapsed native anatomic CHD group with AP physiological stage over the study period showed 5 (0.5%) deaths for shunt and/or valve + A/B, 9 (1.7%) deaths for shunt and/or valve + C/D, 3 (0.8%) deaths for complex anatomy + A/B, and 5 (1.1%) deaths for complex anatomy + C/D (p-value ns).

When cardiac transplantation was combined with mortality into a single outcome (cardiac transplantation or death), the results of the bivariate analysis remained unchanged. Both native anatomic CHD group and combined collapsed native anatomic CHD group with AP physiological stage exposures were not significantly associated with this new combined outcome. However, the AP physiological stage exposure alone was significantly associated with the new combined outcome ($p < 0.05$).

Table 2 presents the association between collapsed native anatomic CHD group and AP physiological stage (exposures), covariables, and any hospitalization (outcome). Both native anatomic CHD group and physiological stage were associated with any hospitalization. Complex anatomy was associated with a higher percentage of hospitalization than shunt and/or valve (12.3% vs. 9.1%; $p < 0.05$). C/D physiological stage was associated with a higher percentage of hospitalization than A/B physiological stage (16.6% vs. 5.7%; $p < 0.0001$). Older age group and Black race were also associated with a higher percentage of hospitalization compared to the younger age group (12.5% vs. 9.2%; $p < 0.05$) or White race (14.3% vs. 9.9%; $p < 0.01$), respectively.

Table 3 presents the association between collapsed native anatomic CHD group and AP physiological stage (exposures), covariables, and any emergency department (ED) visit

(outcome). Both native anatomic CHD group and physiological stage were associated with any ED visit. Complex anatomy was associated with a higher percentage of ED visits than shunt and/or valve (11.8% vs. 6.4%; $p < 0.0001$) and C/D physiological stage was associated with a higher percentage of ED visits than A/B (11.7% vs. 5.8%; $p < 0.0001$). Younger age group was associated with a higher percentage of ED visits compared to older age (9.3% vs. 5.9%; $p < 0.01$). Additionally, lower neighborhood poverty level and higher neighborhood median income were associated with a higher percentage of ED visits compared to neighborhoods with higher poverty levels ($p < 0.05$) and lower median incomes ($p < 0.05$), respectively.

Table 4 presents the association between the covariables and the exposure of collapsed native anatomic CHD group. Younger age and male gender were both significantly associated with a greater percentage of complex anatomy compared to older age (39.0% vs. 24.2%; $p < 0.0001$) and female gender (36.9% vs. 31.7%; $p < 0.01$), respectively. White race was associated with a greater percentage of complex anatomy compared to Black race (36.8% vs. 29.4%; $p < 0.01$). Neighborhoods with a lower percentage of renters were associated with a greater percentage of complex anatomy compared to neighborhoods with a higher percentage of renters (36.3% vs. 31.4%, respectively).

Table 5 presents the association between the covariables and the exposure of collapsed AP physiological stage. Older age and male gender were both significantly associated with a greater percentage of C/D physiological stage compared to younger age (48.7% vs. 38.3%; $p < 0.0001$) and female gender (45.5% vs. 37.4%; $p < 0.0001$). Also, lower neighborhood education was significantly associated with a greater percentage of C/D physiological stage compared to higher levels (43.5% vs. 37.6%; $p < 0.01$).

Table 6 describes the unadjusted or crude relative risks (cRR) for the exposures and potential covariables with the healthcare utilization outcomes. The risk of having any hospitalizations for those with complex CHD anatomy was 1.35 (95% CI: 1.06, 1.71) times that for patients with shunt and/or valve CHD lesions. Those with a C/D physiological stage were associated with a 2.88-fold (95% CI: 2.23, 3.72) increase in risk for hospitalization compared to those with a A/B physiology stage. The risk of hospitalization for older patients and Black patients was 1.36 (95% CI: 1.07, 1.74) and 1.45 (95% CI: 1.13, 1.86) times that of younger and White patients, respectively. For ED visits, having a complex anatomy was associated with a 1.85-fold (95% CI: 1.42, 2.41) increase in the risk of having ED visits compared to those with shunt and/or valves. C/D physiological stage, relative to A/B physiological stage, was associated with a 2.01-fold (95% CI: 1.53, 2.64) increased risk for any ED visits. Older patients were at lower risk of having ED visits compared to younger patients (cRR 0.64; 95% CI: 0.46, 0.88) and residing in higher education level neighborhoods was associated with a 1.44-fold (95% CI: 1.10, 1.88) increase in risk for ED visits compared with those residing in neighborhoods of lower educational level.

Table 7 shows the unadjusted or crude relative risks (cRR) for the combined exposure of collapsed native anatomic CHD group with collapsed AP physiological stage and the two healthcare utilization outcomes. Compared to the baseline group of shunt and/or valve anatomy and A/B physiological stage, all three groups had significantly greater crude relative risk of any ED visit and two of the three had significantly greater crude relative risk of hospitalization. The shunt and/or valve and C/D physiological stage group was associated with a 3.15-fold (95% CI: 2.29, 4.34) increase in the risk of hospitalization and a 1.97-fold (95% CI: 1.35, 2.87) increase in risk of any ED visits than the baseline group. The complex anatomy and A/B physiological stage

group was at lower risk of any hospitalization compared to the baseline group, but did have a 1.81-fold (95% 1.17, 2.78) increased risk of any ED visits than the baseline group. The complex anatomy and C/D physiological stage group had a 3.09-fold (95% CI: 2.22, 4.29) increased risk of hospitalization and a 2.95-fold (95% CI: 2.08, 4.19) increased risk of any ED visit than the baseline group. These data were used to construct the final adjusted model and assess confounding.

Table 8 describes the multivariate regression models in which native anatomic CHD group and physiological stage were treated as separate exposures. The multivariate regression model for any hospitalization used only collapsed AP physiological stage as a predictor. Those with C/D physiology had an almost tripled risk (2.88, 95% CI: 2.23, 3.72) for hospitalization during the study period than those with A/B physiology. The multivariate regression model for any ED visits included both collapsed native anatomic CHD group and collapsed AP physiological stage in addition to age group, neighborhood poverty, and neighborhood education as associated covariables. Results revealed that those with complex anatomy had a 1.53-fold (95% CI: 1.15, 2.05) and those with C/D physiology had a 1.95-fold (95% CI: 1.46, 2.60) increased risk for ED visits compared to those with shunt and/or valve anatomy or A/B physiology, respectively. Older patients were at a lower risk for any ED visits (aRR 0.65, 95% CI: 0.46, 0.90) compared to younger patients and those residing in neighborhoods of higher poverty (where >30% of households below the FPL) or higher levels of education (where >= 35% had a bachelor's degree) were at increased risk for at least one ED visit during the study period (aRR 2.32, 95% CI: 1.27, 4.26 and aRR 1.65, 95% CI: 1.23, 2.21), respectively.

Table 9 describes the multivariate regression models in which native anatomic CHD group and physiologic stage are combined into a single exposure. The multivariate regression

model for any hospitalization included only that combined anatomic group and physiologic stage exposure variable. All combinations of anatomy and physiology above the baseline of shunt and/or valve + A/B were significantly associated with greater aRR for any hospitalization. In particular, the complex anatomy + C/D group had a 31.21-fold (95% CI: 11.94, 81.55) increased risk for any hospitalization compared to the baseline group. The multivariate regression model for any ED visits included the combined exposure variable of native anatomic CHD group and physiological stage in addition to age group, neighborhood poverty, and neighborhood education as associated covariables. Results revealed that younger patients (aRR 0.64, 95% CI: 0.46, 0.90), those residing in neighborhoods that were more impoverished (aRR 2.32, 95% CI: 1.26, 4.25) or had higher levels of neighborhood education (aRR 1.65, 95% CI: 1.23, 2.21) were at increased risk for a least one ED visit during the study period. Also, all combinations of anatomy and physiology above the baseline of shunt and/or valve + A/B were significantly associated with greater aRR for any emergency department visit. In particular, the complex anatomy + C/D group had a 10.60-fold (95% CI: 3.36, 33.48) increased risk for any ED visit compared to the baseline group.

CHAPTER IV: DISCUSSION

This study used a novel approach to operationalize the physiologic classes in the 2018 AHA/ACC ACHD AP classification system in order to study the risk associated with higher comorbidity burden and healthcare utilization and clinical outcomes. The results showed a significant association between combined native anatomic CHD group and AP physiological classification on risk of both healthcare utilization metrics. Those with complex anatomy and a higher burden of physiologic comorbidities were at greater risk of experiencing any hospitalization or having any ED visits in the following year. Importantly, the addition of physiology to the native anatomic complexity resulted in an even stronger association than either anatomy or physiology alone. Data for the clinical outcomes was too limited to construct models for risk assessment, but the crude data suggests that greater physiologic comorbidity burden is associated with cardiac transplantation and mortality.

Previous attempts at classifying complexity, including Marelli's five level severity hierarchy and the 2008 ACC/AHA Guidelines for the Management of ACHD, focused on native anatomy and, in the case of the ACC/AHA Guidelines, post-surgical anatomy, not accounting for the physiological sequelae of the anatomy [20, 55]. More recent efforts, including the 2018 AHA/ACC ACHD AP classification system, have focused on integrating hemodynamic severity and basic anatomy [4, 10]. However, since no studies, to our knowledge, have been performed to assess the validity of these classification systems, this study was conducted to assess the validity of the AP classification system. Results suggest that classification of ACHD patients may be a valid and useful clinical and public health tool for identifying those patients at higher risk for adverse outcomes and greater healthcare utilization.

Studies examining recent trends of healthcare utilization among ACHD patients show simple lesions associated with relatively greater increases in healthcare utilization than more complex lesions [8, 9]. Previous studies evaluating adverse clinical outcomes in ACHD patients, which have relied on using native anatomy as a predictor, have failed to show significant differences in outcomes among different anatomic lesions [46-48], and have left the relationship between native anatomic complexity and such outcomes unclear. Results of the current study suggest that native anatomic complexity alone is not associated with a greater risk of experiencing a hospitalization, but more complex native lesions have an associated higher risk of ED visits. While data was too limited for adjusted analyses, crude data showed no significant association between native anatomic complexity and cardiac transplantation or mortality. Only one of four outcome measures showed a significant association with the exposure of native anatomic complexity, which supports the results of previous studies indicating that native anatomic complexity alone may be an insufficient metric for classification of ACHD severity.

Analysis of the addition of physiologic comorbidities outlined in the 2018 AHA/ACC ACHD AP classification system (Appendix D) revealed a significant association between a higher burden of physiologic comorbidities and risk of both hospitalization and ED visits. Additionally, while the data were too limited for adjusted analysis, the crude analysis showed a similar association for physiologic comorbidity burden and the adverse clinical outcomes of cardiac transplantation and mortality. There is previous evidence to suggest that many physiologic sequelae including HF, poor exercise tolerance, and renal dysfunction are associated with worse outcomes in ACHD patients [34-36]. In addition to these physiologic consequences of CHD, there is evidence that serum markers such as anemia, hyponatremia, and hypoalbuminemia are associated with relatively worse outcomes in ACHD patients [37-39].

However, to our knowledge, there are no studies which have directly studied the physiologic classification system utilized by the 2018 ACHD guidelines or demonstrated these associations between physiology and healthcare utilization.

Furthermore, no study to-date has examined risk of healthcare utilization and adverse clinical outcomes using such a classification scheme. The current data however were too sparse for adjusted analyses for the clinical outcomes, but the healthcare utilization data did indicate significant associations between complex anatomy, greater physiologic comorbidity burden, and greater healthcare utilization. The combination of the two exposures (anatomy and physiology) showed a stronger association than either did alone. This suggests that while native anatomic complexity alone does not have a significant association with these outcomes, it can be added into a classification scheme to provide a more robust picture of risk. Similarly, physiology alone was significantly associated with these outcomes of interest, but the addition of anatomy to the scheme also strengthened its association with the outcomes. These results represent an important first validation of the 2018 AHA/ACC ACHD AP classification system.

In the current study, information bias may have played a role. As the data were collected from administrative datasets utilizing an operationalized set of ICD and CPT codes to classify anatomy and physiology, it is possible to have some degree of misclassification and missing information. Attempts to rectify this included a comprehensive inclusion of codes thought to represent the relevant anatomy and physiology, as well as a year-long period of tracking and capturing codes representative of physiologic comorbidities; the aim in doing so was to reduce any amount of missed relevant anatomy and physiology. Similarly, since the data came from two primary sources (Emory Clinical Data Warehouse (ECDW) and Georgia Medicaid), it is possible that patients who sought care elsewhere, particularly those not on Medicaid who were captured

initially in the Emory dataset, would have incomplete data for this study. This was an unavoidable risk associated with this type of data capture and could only be partially mitigated by inclusion of the Medicaid dataset where Medicaid claims, no matter the facility, would be included. Additionally, Emory provides a highly specialized care team, thus there may be referral bias towards a sicker grouper of ACHD patients.

Strengths of the study include its novel approach to operationalizing physiologic comorbidities using ICD and CPT coding. This, in addition to the year-long period in which comorbidities were tracked and captured, allowed for the construction of a moderately large analytic sample that was more representative of the true comorbidity burden than a single instance would capture. Additionally, examining the associations of native anatomic complexity and physiologic classification independently as well as their combined association allowed for the exploration of the potential for interaction and compounding risk factors for more severe CHD complexity.

The primary limitation of this study was the use of administrative data. In particular, not all relevant diagnostic codes may be present in the datasets available for the study. Absence of codes does not necessarily mean absence of comorbidity. Further, diagnostic codes are an inexact way to measure comorbidity burden – their categorization may miss important comorbidities and not all physiology staging criteria was able to be categorized. Patients, particularly those from ECDW, may seek care elsewhere and their outcome measures may not be fully captured in the current study. Other limitations include the retrospective nature, short follow-up period (1-year), and small sample size of the current study. A longer follow-up period and a larger sample size would allow for more of the clinical outcomes (i.e., death, cardiac transplantation) to occur, and thus provide more useful information to assess. Additionally, a

prospective design would make it easier to reduce certain biases introduced through the retrospective nature of this study, particularly the information bias that may be present in using ICD and CPT coding to assess the anatomic and physiologic features of a patient's CHD. In addition, the data sources, ECDW and GA Medicaid claims, represent two unique patient populations, the first being those with access to subspecialty and tertiary care, and the second being those without access to commercial or private insurance due to limited finances or disability. This may limit the generalizability of study results. However, when these two data sources are combined, the study cohort does become much more generalizable than using either alone.

In conclusion, this study shows that physiologic comorbidity-based classification is a potentially significant predictor for healthcare utilization in ACHD patients. Additionally, while data were limited, it also suggests that physiologic comorbidity-based classification may be useful in predicting adverse clinical outcomes. Compared to classifying on the basis of native anatomic complexity alone, the addition of physiologic comorbidity-based classification provided additional information in assessing outcomes using healthcare administrative databases. Results provide support on the validity and continued use of the 2018 AHA/ACC ACHD AP classification system as a tool for risk stratifying ACHD patients. Future studies should examine the noted associations using other study designs, ideally a prospective one that does not rely on administrative data in order to more thoroughly examine covariables and potential confounders in ACHD classification.

CHAPTER V: PUBLIC HEALTH IMPLICATIONS AND FUTURE DIRECTIONS

While some tools have been developed and certain individual risk factors identified, accurate classification of ACHD complexity in order to risk stratify and predict clinical outcomes and healthcare utilization has not been accomplished to-date. Such a tool would have immense clinical utility considering the growing prevalence and complexity of ACHD care. This study begins to address this gap by operationalizing the American Heart Association (AHA) / American College of Cardiology (ACC) ACHD Anatomic and Physiologic (AP) classification system, assigning an associated class to patients based on their comorbidity burden, and examining selected clinical and healthcare utilization outcomes. In doing so, it is hoped that the current approach will begin to lay the groundwork for the development of a more robust, validated clinical complexity prediction tool for ACHD patients. The implications of such a tool to public health lie in first defining and understanding the scope of ACHD complexity in the population and then translating that understanding into prevention strategies that result in both decreasing the burden of utilization on the healthcare system and improving clinical outcomes for ACHD patients.

In understanding the scope of ACHD complexity across the population, many gaps remain. Population demographics have shifted such that adults with CHD now outnumber children with CHD, and modern treatment of CHD is leading to longer lifespans for all CHD phenotypes [19, 21, 28]. Traditionally, CHD has been understood through the lens of native anatomy, but it is becoming increasingly apparent that the sequelae of prior treatments and longer lifespans with CHD may represent a more relevant framework for defining and risk stratifying these diverse conditions as prior studies have been unable to reproducibly define severity by native anatomy alone [8, 9, 48, 58]. Our study used physiologic comorbidity burden

to capture these sequelae of prior treatments and longer lifespans with CHD, and our results suggest a stronger association with healthcare utilization than native anatomy. Applying this framework to the public health study of ACHD would allow for a new understanding of this heterogeneous population beyond simply counting the number of individuals with CHDs and/or characterizing those with CHD by their anatomic structural complexity. Integrating comorbid burden with anatomic complexity could lead to more accurate identification of population subsets of CHD at risk for increased healthcare utilization and adverse clinical outcomes.

This novel approach to understanding ACHD would allow for more targeted approaches to study risk factors associated with increased healthcare utilization and adverse clinical outcomes, how these risk factors develop, and eventually, how to intervene to prevent them. For instance, translation of this work into the clinical setting might look something like an ACHD risk rating scale where clinicians could input patient-specific risk factors including number and types of physiologic comorbidities along with the patient's confirmed anatomic complexity, demographics and biomarkers, and then, receive a grade or stage of ACHD for that individual that corresponds to a 1-, 5-, or 10- year risk score for hospitalization, ED visits, cardiac transplantation, death, or any other outcomes of interest. Such tools have been developed in other areas, such as the ASCVD Risk Calculator that calculates a 10-year risk of heart disease or stroke based on a handful of factors including basic demographics, behavioral indicators and bio measures like blood pressure, cholesterol, and blood sugar; the algorithm upon which the ASCVD Risk Calculator was designed was initially published in the 2013 ACC/AHA Guidelines on the Assessment of Cardiovascular Risk and has been further refined as new guidelines are published [62]. A risk calculator for CHD would provide an important clinical tool that could help further inform population-based treatment guidelines, and moreover, provide a framework

for patients to better understand the current status of their disease and its progression possibilities, and aid clinicians in delivering treatment plans that address both short-term outcomes and anticipate long-term ones with specific risk factors in mind [59-61]. Through further population studies and translation into a clinical environment with ACHD specialists, the risk factors driving healthcare utilization and adverse clinical outcomes in ACHD can be better understood and more appropriately addressed.

While this study does begin to address what factors influence healthcare utilization in ACHD patients, it raises further questions. Are specific comorbidities accounting for increased utilization? Are physiologic comorbidities also associated with adverse clinical outcomes? Is lack of access to routine and preventive healthcare a risk factor itself? Will better management of comorbid conditions translate into a significant decrease in risk for healthcare utilization or adverse outcomes for ACHD patients? Future directions should include analyses that examine the associations noted in this study, applying alternative study designs that may better uncover influential covariates and potential confounders influencing long-term outcomes.

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TABLES

Table 1. Descriptive Characteristics of Adult Congenital Heart Disease Patients (2008-2013)

	N=2384	%
Any Hospitalizations	244	10.2
Any Emergency Department Visits	197	8.3
***Collapsed Native Anatomic CHD Group**		
Shunt and/or Valve	1564	65.6
Complex Anatomy	820	34.4
****Collapsed AP Physiological Stage**		
A/B	1393	58.4
C/D	991	41.6
Combined Anatomic Complexity and Physiological Stage		
Shunt and/or Valve + A/B	1037	43.5
Shunt and/or Valve + C/D	527	22.1
Complex Anatomy + A/B	356	14.9
Complex Anatomy + C/D	464	19.5
Age group (in years)		
18-34	1641	68.8
35-45	743	31.2
Gender		
Male	1221	51.2
Female	1162	48.7
Race		
White	1466	61.5
Black	579	24.3
Other	36	1.5
Ethnicity		
Non-Hispanic	1589	66.7
Hispanic	44	1.9
Neighborhood^ Poverty		
< 15% households below FPL	1000	42.0
15-30% households below FPL	944	39.6
> 30% households below FPL	436	18.3
Median Neighborhood^ Income		
< $40,000 per year	588	24.8
$40,000 - $75,000 per year	1434	60.4
> $75,000 per year	351	14.8
Neighborhood^ Education		
< 35% with a bachelor's degree	1612	67.6
≥ 35% with a bachelor's degree	767	32.2
Neighborhood^ Renter Occupancy		
< 35% renters living in ZIP	1435	60.2
≥ 35% renters living in ZIP	945	39.6
	Mean	**SD**

Age 18-45 years	29.3	8.4
Age 18-34 years	24.5	5.0
Age 34-45 years	39.8	3.2

*refer to the algorithm (list of codes by group) in Appendix B
**refer to operationalization of 2018 AHA/ACC ACHD AP Physiologic Stages with ICD-9-CM codes in Appendix D
^neighborhood defined as the ZIP code of residence for the individual patient

Table 2. Bivariate Analyses of Native Anatomy, AP Physiological Stage, and Covariates by Hospitalizations for Adults with Congenital Heart Disease (N=2384)

	Any Hospitalization n=244 (10.2%)		**No Hospitalizations n=2140 (89.2%)**		**X^2 *P* value**
	n	**%**	**n=2140**	**89.8%**	
***Collapsed Native Anatomic CHD Group**					
Shunt and/or Valve	143	9.1	1421	90.9	0.0152
Complex Anatomy	101	12.3	719	87.7	
****Collapsed AP Physiological Stage**					
A/B	80	5.7	1313	94.3	<0.0001
C/D	164	16.6	827	83.5	
Age Group (in years)					
18-34	151	9.2	1490	90.8	0.0134
35-45	93	12.5	650	87.5	
Gender					
Male	128	10.5	1093	89.5	0.6871
Female	116	10.0	1046	90.0	
Race					
White	145	9.9	1321	90.1	0.0016
Black	83	14.3	496	85.7	
Other	0	0	36	100.0	
Ethnicity					
Non-Hispanic	205	12.9	1384	87.1	0.2325
Hispanic	3	6.8	41	93.2	
Neighborhood^ Poverty					
< 15% households below FPL	95	9.5	905	90.5	0.5763
15-30% households below FPL	103	10.9	841	89.1	
> 30% households below FPL	46	10.6	390	89.5	
Median Neighborhood^ Income					
< $40,000 per year	55	9.4	533	90.7	0.1927
$40,000 - $75,000 per year	160	11.2	1274	88.8	
> $75,000 per year	29	8.3	322	91.7	
Neighborhood^ Education					
<35% with a bachelor's degree	164	10.2	1448	89.8	0.8471
≥35% with a bachelor's degree	80	10.4	687	89.6	
Neighborhood^ Renter Occupancy					
< 35% renters living in ZIP	139	9.7	1296	90.3	0.2622
≥ 35% renters living in ZIP	105	11.1	840	88.9	

*refer to the algorithm (list of codes by group) in Appendix B

**refer to operationalization of 2018 AHA/ACC ACHD AP Physiologic Stages with ICD-9-CM codes in Appendix D

^neighborhood defined as the ZIP code of residence for the individual patient

Table 3. Bivariate Analyses of Native Anatomy, AP Physiological Stage, and Covariates by Emergency Department Visits for Adults with Congenital Heart Disease (N=2384)

	Any Emergency Department Visits n=197 (8.3%)		No Emergency Department Visits n=2187 (91.7%)		X^2 *P* value
	n	%	n	%	
***Collapsed Native Anatomic CHD Group**					
Shunt and/or Valve	100	6.4	1464	93.6	<0.0001
Complex Anatomy	97	11.8	723	88.2	
****Collapsed AP Physiological Stage**					
A/B	81	5.8	1312	94.2	<0.0001
C/D	116	11.7	875	88.3	
Age Group (in years)					
18-34	153	9.3	1488	90.7	0.0052
35-45	44	5.9	699	94.1	
Gender					
Male	108	8.9	1113	91.2	0.2586
Female	88	7.6	1074	92.4	
Race					
White	132	9.0	1334	91.0	0.8119
Black	47	8.1	532	91.9	
Other	3	8.3	33	91.7	
Ethnicity					
Non-Hispanic	148	9.3	1441	90.7	0.5729
Hispanic	3	6.8	41	93.2	
Neighborhood^ Poverty					
< 15% households below FPL	80	8.0	920	92.0	0.0151
15-30% households below FPL	93	9.9	851	90.2	
> 30% households below FPL	23	5.3	413	94.7	
Median Neighborhood^ Income					
< $40,000 per year	36	6.1	552	93.9	0.0463
$40,000 - $75,000 per year	123	8.6	1311	91.4	
> $75,000 per year	37	10.5	314	89.5	
Neighborhood^ Education					
< 35% with a bachelor's degree	117	7.3	1495	92.7	0.0087
≥ 35% with a bachelor's degree	80	10.4	687	89.6	
Neighborhood^ Renter Occupancy					
< 35% renters living in ZIP	123	8.6	1312	91.4	0.4623
≥ 35% renters living in ZIP	73	7.7	872	92.3	

*refer to the algorithm (list of codes by group) in Appendix B
**refer to operationalization of 2018 AHA/ACC ACHD AP Physiologic Stages with ICD-9-CM codes in Appendix D
^neighborhood defined as the ZIP code of residence for the individual patient

Table 4. Bivariate Analyses of Covariates by Native Anatomy for Adults with Congenital Heart Disease (N=2384)

	Shunt and/or Valve n=1564 (65.6%)		**Complex Anatomy n=820 (34.4%)**		**X^2 *P* value**
	n	**%**	**n**	**%**	
Age Group (in years)					
18-34	1001	61.0	640	39.0	<0.0001
35-45	563	75.8	180	24.2	
Gender					
Male	770	63.1	451	36.9	0.0068
Female	794	68.3	368	31.7	
Race					
White	927	63.2	539	36.8	0.0057
Black	409	70.6	170	29.4	
Other	22	61.1	14	38.9	
Ethnicity					
Non-Hispanic	1037	65.3	552	34.7	0.4750
Hispanic	31	70.5	13	29.6	
Neighborhood^ Poverty					
< 15% households below FPL	633	63.3	367	36.7	0.1146
15-30% households below FPL	632	67.0	312	33.1	
> 30% households below FPL	297	68.1	139	31.9	
Median Neighborhood^ Income					
< $40,000 per year	402	68.4	186	31.6	0.1430
$40,000 - $75,000 per year	920	64.2	514	35.8	
> $75,000 per year	237	67.5	114	32.5	
Neighborhood^ Education					
< 35% with a bachelor's degree	1056	65.5	556	34.5	0.7758
≥ 35% with a bachelor's degree	507	66.1	260	33.9	
Neighborhood^ Renter Occupancy					
< 35% renters living in ZIP	914	63.7	521	36.3	0.0142
≥ 35% renters living in ZIP	648	68.6	297	31.4	

^neighborhood defined as the ZIP code of residence for the individual patient

Table 5. Bivariate Analyses of Covariates by AP Physiological Stage for Adults with Congenital Heart Disease (N=2384)

	A/B n=1393 (58.4%)		C/D n=991 (41.6%)		X^2 *P* value
	n	%	n	%	
Age Group (in years)					
18-34	1012	61.7	629	38.3	<0.0001
35-45	381	51.3	362	48.7	
Gender					
Male	665	54.5	556	45.5	<0.0001
Female	728	62.7	434	37.4	
Race					
White	800	54.6	666	45.4	0.2957
Black	338	58.4	241	41.6	
Other	20	55.6	16	44.4	
Ethnicity					
Non-Hispanic	894	56.3	695	43.7	0.9415
Hispanic	25	56.8	19	43.2	
Neighborhood^ Poverty					
< 15% households below FPL	589	58.9	411	41.1	0.7747
15-30% households below FPL	543	57.5	401	42.5	
> 30% households below FPL	258	59.2	178	40.8	
Median Neighborhood^ Income					
< $40,000 per year	338	57.5	250	42.5	0.5454
$40,000 - $75,000 per year	833	58.1	601	41.9	
> $75,000 per year	214	70.0	137	39.0	
Neighborhood^ Education					
< 35% with a bachelor's degree	911	56.5	701	43.5	0.0060
≥ 35% with a bachelor's degree	479	62.5	288	37.6	
Neighborhood^ Renter Occupancy					
< 35% renters living in ZIP	819	57.1	616	42.9	0.1047
≥ 35% renters living in ZIP	571	60.4	374	39.6	

^neighborhood defined as the ZIP code of residence for the individual patient

Table 6. Unadjusted Analysis – Association of Native Anatomy, AP Physiologic Stage, and Other Covariates with Any Hospitalization and Any Emergency Department Visits for Adults with Congenital Heart Disease

	Any Hospitalizations cRR (95% CI)	**Any Emergency Department Visits cRR (95% CI)**
[*]Collapsed Native Anatomic CHD Group		
Shunt and/or Valve	1.00	1.00
Complex Anatomy	1.35 (1.06, 1.71)	1.85 (1.42, 2.41)
[**]Collapsed AP Physiological Stage		
A/B	1.00	1.00
C/D	2.88 (2.23, 3.72)	2.01 (1.53, 2.64)
Age Group (in years)		
18-34	1.00	1.00
35-45	1.36 (1.07, 1.74)	0.64 (0.46, 0.88)
Gender		
Male	1.00	1.00
Female	0.95 (0.75, 1.21)	0.86 (0.65, 1.12)
Race		
White	1.00	1.00
Black	1.45 (1.13, 1.86)	0.90 (0.66, 1.24)
Other	---	0.93 (0.31, 2.77)
Ethnicity		
Non-Hispanic	1.00	1.00
Hispanic	0.53 (0.18, 1.59)	0.73 (0.24, 2.21)
Neighborhood[^] Poverty		
< 15% households below FPL	1.00	1.00
15-30% households below FPL	1.15 (0.88, 1.50)	1.23 (0.93, 1.64)
> 30% households below FPL	1.11 (0.80, 1.55)	0.66 (0.42, 1.03)
Median Neighborhood[^] Income		
< $40,000 per year	1.00	1.00
$40,000 - $75,000 per year	1.19 (0.89, 1.60)	1.40 (0.98, 2.01)
> $75,000 per year	0.88 (0.57, 1.36)	1.72 (1.11, 2.67)
Neighborhood[^] Education		
< 35% with a bachelor's degree	1.00	1.00
≥ 35% with a bachelor's degree	1.03 (0.80, 1.32)	1.44 (1.10, 1.88)
Neighborhood[^] Renter Occupancy		
< 35% renters living in ZIP	1.00	1.00
≥ 35% renters living in ZIP	1.15 (0.90, 1.46)	0.90 (0.68, 1.19)

[*]refer to the algorithm (list of codes by group) in Appendix B
[**]refer to operationalization of 2018 AHA/ACC ACHD AP Physiologic Stages with ICD-9-CM codes in Appendix D
[^]neighborhood defined as the ZIP code of residence for the individual patient

Table 7. Unadjusted Analysis - Association of Combined Native Anatomy and AP Physiologic Stages with Any Hospitalization and Any Emergency Department Visits for Adults with Congenital Heart Disease

	Any Hospitalizations cRR (95% CI)	**Any Emergency Department Visits cRR (95% CI)**
***Combined Collapsed Native Anatomic CHD Group and Collapsed AP Physiological Stage**		
Shunt and/or Valve + A/B	1.00	1.00
Shunt and/or Valve + C/D	3.15 (2.29, 4.34)	1.97 (1.35, 2.87)
Complex Anatomy + A/B	1.32 (0.84, 2.09)	1.81 (1.17, 2.78)
Complex Anatomy + C/D	3.09 (2.22, 4.29)	2.95 (2.08, 4.19)

*refer to the algorithm (list of codes by group) in Appendix B combined with operationalization of 2018 AHA/ACC ACHD AP Physiologic Stages with ICD-9-CM codes in Appendix D

Table 8. Adjusted Analysis - Association of Native Anatomy, AP Physiologic Stage, and Other Covariates with Any Hospitalization and Any Emergency Department Visits for Adults with Congenital Heart Defects

	Any Hospitalizations RR (95% CI)	**Any Emergency Department Visits aRR# (95% CI)**
[*]Collapsed Native Anatomic CHD Group		
Shunt and/or Valve	---	1.00
Complex Anatomy	---	1.53 (1.15, 2.05)
[**]Collapsed AP Physiological Stage		
A/B	1.00	1.00
C/D	2.88 (2.23, 3.72)	1.95 (1.46, 2.60)
Age Group (in years)		
18-34	---	1.00
35-45	---	0.65 (0.46, 0.90)
Neighborhood[^] Poverty		
< 15% households below FPL	---	1.00
15-30% households below FPL	---	1.52 (1.13, 2.06)
> 30% households below FPL	---	2.32 (1.27, 4.26)
Neighborhood[^] Education		
< 35%with a bachelor's degree	---	1.00
≥ 35% with a bachelor's degree	---	1.65 (1.23, 2.21)

[#]Each variable was adjusted for all other variables in the table
[*]refer to the algorithm (list of codes by group) in Appendix B
[**]refer to operationalization of 2018 AHA/ACC ACHD AP Physiologic Stages with ICD-9-CM codes in Appendix D
[^]neighborhood defined as the ZIP code of residence for the individual patient

Table 9. Adjusted Analysis – Association of Combined Native Anatomy and AP Physiologic Stages with Any Hospitalization and Any Emergency Department Visits for Adults with Congenital Heart Disease

	Any Hospitalizations RR (95% CI)	**Any Emergency Department Visits aRR[#] (95% CI)**
[*] Combined Collapsed Native Anatomic CHD Group and Collapsed AP Physiological Stage		
Shunt and/or Valve + A/B	1.00	1.00
Shunt and/or Valve + C/D	3.15 (2.29, 4.34)	2.20 (1.50, 3.22)
Complex Anatomy + A/B	9.91 (5.23, 18.80)	4.83 (2.24, 10.39)
Complex Anatomy + C/D	31.21 (11.94, 81.55)	10.60 (3.36, 33.48)
Age Group (in years)		
18-34	---	1.00
35-45	---	0.64 (0.46, 0.90)
Neighborhood[^] Poverty		
< 15% households below FPL	---	1.00
15-30% households below FPL	---	1.52 (1.12, 2.06)
> 30% households below FPL	---	2.32 (1.26, 4.25)
Neighborhood[^] Education		
< 35% with a bachelor's degree	---	1.00
≥ 35% with a bachelor's degree	---	1.65 (1.23, 2.21)

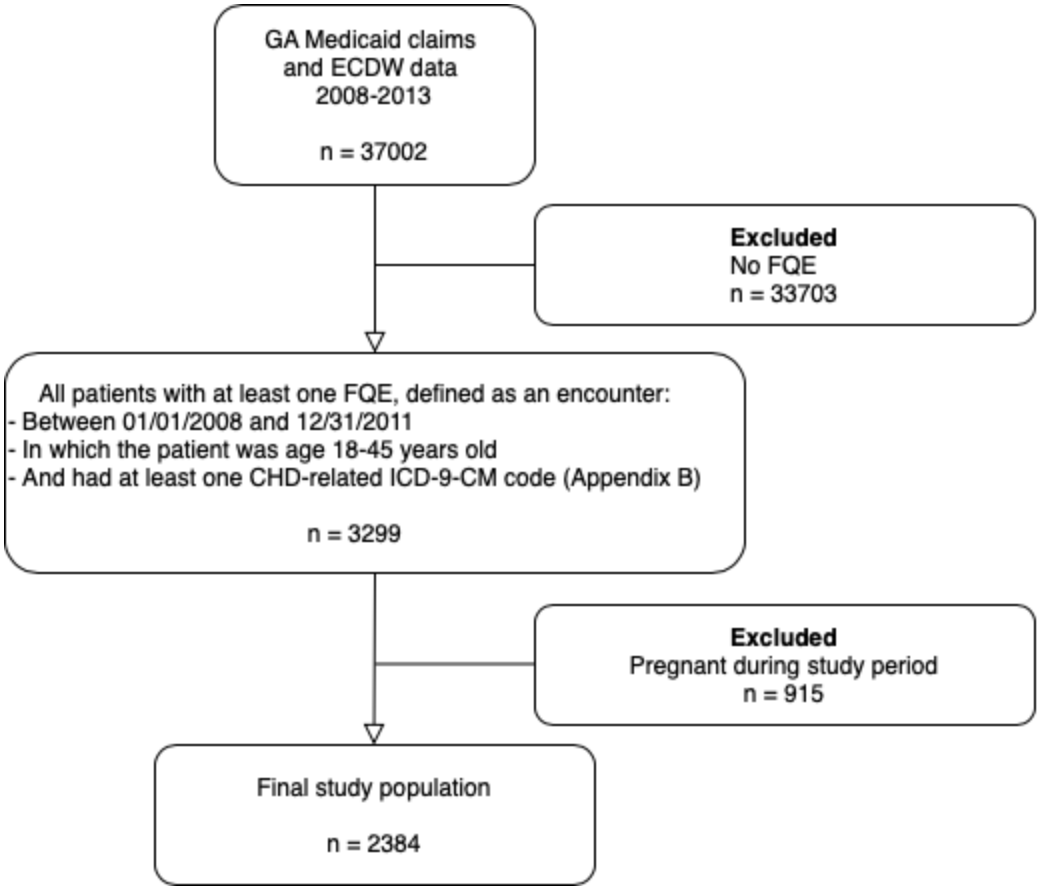
[#]Each variable was adjusted for all other variables in the table

*refer to the algorithm (list of codes by group) in Appendix B combined with operationalization of 2018 AHA/ACC ACHD AP Physiologic Stages with ICD-9-CM codes in Appendix D

^neighborhood defined as the ZIP code of residence for the individual patient

FIGURES

Figure 1. Analytic Dataset Construction: Inclusions and Exclusions



APPENDICES

Appendix A. Data Sources

DATA SOURCE	DESCRIPTION
Georgia Medicaid Claims	Georgia Medicaid administrative claims data for individuals with a CHD diagnosis were obtained from the Centers for Medicare and Medicaid Services (CMS) via Research Data Assistance Center (ResDAC), a CMS contractor which assists academic, government, non-profits and for-profits. Medicaid is a social health care program for families and individuals with low income and resources. The state and federal governments jointly fund the program, with each state having its own criteria for determining eligibility into the program based on state demographics and geography.
ECDW (Emory Clinical Data Warehouse)	EHC is the largest health care system in Georgia, encompassing many hospitals, clinics, local practices, and community-based specialty associates. EHC houses Georgia's only comprehensive adult CHD center, the Emory Adult Congenital Heart Center (EACHC), physically located in DeKalb County. EACHC serves a diverse population (10% uninsured, 27% Government insurance, 25% over age 44). Data will be collected through direct querying of Emory Clinical Data Warehouse and electronic data capture tools.
GA DPH Vital Statistics	Georgia birth and death certificates obtained directly from Georgia Department of Public Health.

Appendix B. ICD-9-CM Codes for Anatomic Complexity Classification* of Congenital Hearts Defects

Classification	ICD-9-CM Code	ICD-9-CM Description
Complex (contains at least one complex code) 16 codes	745.0	Common truncus
	745.1	Transposition of great vessels
	745.10	Transposition of great vessels: Complete transposit. great vessels
	745.11	Transposition of great vessels: Double outlet right ventricle
	745.12	Transposition of great vessels: Corrected transposit. great vessels
	745.19	Transposition of great vessels: Other
	745.2	Tetralogy of Fallot
	745.3	Common ventricle
	745.6	Endocardial cushion defects
	745.60	Endocardial cushion defects: Endocard cushion defect, unsp. type
	745.69	Endocardial cushion defects: Other
	746.01	Anomalies of pulmonary valve: Atresia, congenital
	746.1	Tricuspid atresia and stenosis, congenital
	746.7	Hypoplastic left heart syndrome
	747.11	Coarctation of aorta: Interruption of aortic arch
	747.41	Anomalies great veins: Tot anomalous pulm. venous connection
Shunt (contains at least one shunt code and no complex or valve codes) 7 codes	745.4	Ventricular septal defect
	745.5**	Ostium secundum type atrial septal defect**
	745.61	Endocardial cushion defects: Ostium primum defect
	745.8	Bulbus cordis anomalies & anomalies of card septal closure: Other
	745.9	Unspecified defect of septal closure
	747.0	Patent ductus arteriosus
	747.42	Anomalies great veins: Partial anomal. Pulm. venous connection
Valve (contains at least one valve code and no complex or shunt codes) 17 codes	746.0	Anomalies of pulmonary valve
	746.00	Anomalies of pulm valve: Pulmvalve anomaly, unspec
	746.02	Anomalies of pulmonary valve: Stenosis, congenital
	746.09	Anomalies of pulmonary valve: Other
	746.2	Ebstein's anomaly
	746.3	Congenital stenosis of aortic valve
	746.4	Congenital insufficiency of aortic valve
	746.5	Congenital mitral stenosis
	746.6	Congenital mitral insufficiency
	746.81	Other specified anomalies of heart: Subaortic stenosis
	746.83	Other specified anomalies of heart: Infundibular pulmonic stenosis
	747.1	Coarctation of aorta
	747.10	Coarctation of aorta: Coarctation of aorta (preductal) (postductal)
	747.22	Other anomalies of aorta: Atresia and stenosis of aorta

	747.3	Anomalies of pulmonary artery
	747.31	Anomalies of pulmonary artery: Pulm. artery coarctation & atresia
	747.39	Anomalies pulmonary artery: Anomal. pulm. artery & pulm. Circ.
Shunt + Valve (contains at least one shunt code & at least one valve code and no complex codes)		
Other (contains one or more code listed in this grouping without any complex, shunt, or valve codes) This grouping is excluded from analyses in the current study	648.5	Other current conditions in mother classifiable elsewhere, but complicating preg., childbirth, or puerperium: Congen. cardio dis.
	648.50	Other current conditions in mother classifiable elsewhere, but complicating preg., childbirth, or puerperium: Congen. cardiovasc. dis.: unspecified as to episode of care or not applicable
	648.51	Other current conditions in mother classifiable elsewhere, but complicating preg., childbirth, or puerperium: Congen. cardiovasc. dis.: delivered, w/ or w/o mention of antepartum condition
	648.52	Other current conditions in mother classifiable elsewhere, but complicating preg., childbirth, or puerperium: Congen. cardiovasc. dis.: delivered, w/mention of postpartum complication
	648.53	Other current conditions in mother classifiable elsewhere, but complicating preg., childbirth, or puerperium: Congen. cardiovasc. dis.: antepartum condition or complication
	648.54	Other current conds. in mom classifiable elsewhere, but complic. preg., childbirth, or puerperium: congen. cardio. dis.: PP conds.
	745.7	Cor biloculare
	746.8	Other spec. anomalies of heart
	746.82	Other spec. anomalies of heart: Cor triatriatum
	746.84	Other spec. anomalies of heart: Obstructive anomalies, NEC
	746.85	Other spec. anomalies of heart: Coronary artery anomaly
	746.87	Other spec. anomalies of heart: Malposition of heart & cardi apex
	746.89	Other specified anomalies of heart: Other
	746.9	Unspecified anomaly of heart
	747.2	Other anomalies of aorta
	747.20	Other anomalies of aorta: Anomaly of aorta, unspecified
	747.21	Other anomalies of aorta: Anomalies of aortic arch
	747.29	Other anomalies of aorta: Other
	747.4	Anomalies of great veins
	747.40	Anomalies of great veins: Anomaly of great veins, unspecified
	747.49	Anomalies of great veins: Other anomalies of great veins
	747.9	Unspecified anomaly of circulatory system
	V13.65	Congenital (corrected) malformations: Personal hx of (corrected) congenital malformations of heart and circulatory system

*adopted from the Lifespan CHD surveillance project (unpublished manuscript: Glidewell, MJ, Farr, SL, Book, WM, et al. Prevalence of congenital heart defects among 1- to 64-year-olds receiving health care at five U.S. surveillance sites, 2011-2013)

**745.5 in isolation or with 'other' codes have been omitted from analyses due to lack specificity

Notes.

- Complex – case has a complex code, regardless of presence of shunt, valve, shunt+valve
- Shunt + Valve – case has shunt AND valve codes
- Shunt – case has at least one shunt code, no valve or complex codes
- Valve – case has at least one valve code, no shunt or complex codes
- Other – case has 1+ codes in this category; this category is omitted from analyses due to non-specificity

- 745.5 – case has only code 745.5 or code 745.5 in addition to only codes from “other” category; this category is omitted from analyses due to non-specificity

Appendix C. 2018 AHA/ACC ACHD AP Classification Physiological Stages

Stage	Criteria
A	NYHA FC I symptoms Normal exercise capacity No arrhythmias No hemodynamic or anatomic sequelae Normal renal/hepatic & pulmonary function
B	NYHA FC II symptoms Abnormal cardiac limitation to exercise Arrythmias (not requiring treatment) Mild hemodynamic sequelae (mild aortic enlargement, mild ventricular enlargement, mild ventricular dysfunction) Trivial or small shunt Mild valvular disease (not hemodynamically significant)
C	NYHA FC III symptoms ≥ Moderate valvular disease or ventricular dysfunction Moderate aortic enlargement Arrhythmias controlled with treatment Mild-moderate cyanosis Pulmonary hypertension End organ dysfunction (responsive to therapy) Arterial or venous stenosis Hemodynamically significant shunts
D	NYHA FC IV Symptoms Severe aortic enlargement Refractory arrhythmias Severe hypoxemia Severe pulmonary hypertension/Eisenmenger syndrome Refractory end organ dysfunction

Appendix D. Operationalization of 2018 AHA/ACC ACHD AP Classification Physiological Stages with ICD-9-CM codes

PHYSIOLOGY	DESCRIPTOR	ICD-9-CM CODE
Cyanosis	cyanosis	782.5
Pulmonary Hypertension	prim pulm hypertension	416.0
	chr pulmon heart dis nec	416.8
	chr pulmon heart dis nos	416.9
Aortic Enlargement (Severe)	thoracic aortic aneurysm	441.2
	thoracic aortic ectasia (begin 2010)	447.71
	dissecting thoracic aneurysm (begin 1994)	441.01
	ruptur thoracic aneurysm	441.1
Arrhythmias (treated, refractory)	atriovent block complete	426.0
	atriovent block nos	426.10
	atrioven block-mobitz ii	426.12
	av block-2nd degree nec	426.13
	bilat bb block nec	426.53
	cardiac pacemaker status (end 1994)	V45.0
	cardiac device nos in situ (begin 1994)	V45.00
	cardiac pacem in situ (begin 1994)	V45.01
	auto implant debril in situ (begin 1994)	V45.02
	oth cardiac device nec in situ (begin 1994)	V45.09
	adjust cardiac pacemaker (end 1994)	V53.3
	adjust cardiac pacemaker (begin 1994)	V53.31
	adjust auto implant debril (begin 1994)	V53.32
	adjust oth cardiac device (begin 1994)	V53.39
	parox atrial tachycardia	427.0
	parox ventric tachycard	427.1
	atrial fibrillation	427.31
	atrial flutter	427.32
	sinoatrial node dysfunct	427.81
	ventricular fibrillation	427.41
	ventricular flutter	427.42
	cardiac arrest	427.5
	hx sudden cardiac arrest (begin 2007)	V12.53
	congenital heart block	746.86
Ventricular Dysfunction (>= moderate)	congestive heart failure	428.0
	left heart failure	428.1
	unspecified systolic heart failure (begin 2002)	428.20
	acute systolic heart failure (begin 2002)	428.21
	chronic systolic heart failure (begin 2002)	428.22
	acute on chronic systolic heart failure (begin 2002)	428.23
	unspecified diastolic heart failure (begin 2002)	428.30
	acute diastolic heart failure (begin 2002)	428.31
	chronic diastolic heart failure (begin 2002)	428.32
	acute on chronic diastolic heart failr (begin 2002)	428.33
	unspec cmbined syst & dias heart failr (begin 2002)	428.40
	acute cmbined syst & dias heart failr (begin 2002)	428.41
	chronic cmbined syst & dias heart failr (begin 2002)	428.42
	acu chro combi syst & dias hrt failr (begin 2002)	428.43
	heart failure nos	428.9

	cardiogenic shock	785.51
End Organ Dysfunction (treated, refractory; renal, hepatic, pulmonary)	chronic renal failure (end 2005)	585
	chronic kidney dis stage iii (begin 2005)	585.3
	chronic kidney dis stage iv (begin 2005)	585.4
	chronic kidney dis stage v (begin 2005)	585.5
	end stage renal disease (begin 2005)	585.6
	chronic kidney dis nos (begin 2005)	585.9
	kidney transplant status	V42.0
	renal dialysis status (end 2008)	V45.1
	noncmplnt w renal dialys (begin 2008)	V45.12
	renal dialysis encounter	V56.0
	fit adjust periton dial cath (begin 1998)	V56.2
	dialysis encounter- nec	V56.8
	compl kidney transplant (begin 1987)	996.81
	esoph varices w/o bleed	456.1
	esoph varice oth dis nos	456.21
	cirrhosis of liver nos	571.5
	biliary cirrhosis	571.6
	portal hypertension	572.3
	hepatorenal syndrome	572.4
	chronic passiv congest liver	573.0
	hepatomegaly	789.1
	ascites (end 2007)	789.5
	ascites nec (begin 2007)	789.59
	esophag varices w bleed	456.0
	bleed esoph var oth dis	456.20
	acute lung edema nos	518.4
Valvular Disease (inclusion in study will require presence of congenital heart defect code, so presence of procedural code used as measure of severe) Consider evidence of severe valvular disease presence of congenital valve ICD code + valve replacement/ surgery/ procedure (ICD/CPT); will miss moderate disease that does not go to	heart valve transplant	V42.2
	heart valve replac nec	V43.3
	Procedure	**CPT Code**
	Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; transaortic approach (e.g., median sternotomy, mediastinotomy)	33365
	Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; transapical exposure (e.g., left thoracotomy)	33366
	Valvuloplasty, aortic valve, open, with cardiopulmonary bypass; simple (ie, valvotomy, debridement, debulking, and/or simple commissural resuspension)	33390
	Valvuloplasty, aortic valve, open, with cardiopulmonary bypass; complex (eg, leaflet extension, leaflet resection, leaflet reconstruction, or annuloplasty)	33391
	Replacement, aortic valve, open, with cardiopulmonary bypass; with prosthetic valve other than homograft or stentless valve	33405
	Replacement, aortic valve, with cardiopulmonary bypass; with allograft valve (freehand)	33406
	Replacement, aortic valve, open, with cardiopulmonary bypass; with stentless tissue valve	33410
	Replacement, aortic valve; with aortic annulus enlargement, noncoronary sinus	33411
	Replacement, aortic valve; with transventricular aortic annulus enlargement (Konno procedure)	33412
	Replacement, aortic valve; by translocation of autologous pulmonary valve with allograft replacement of pulmonary valve (Ross procedure)	33413
	Repair of left ventricular outflow tract obstruction by patch enlargement of the outflow tract	33414

surgery; will miss anyone not getting surgery during period of f/u	Resection or incision of subvalvular tissue for discrete subvalvular aortic stenosis	33415
	Aortoplasty (gusset) for supravalvular stenosis	33417
	Valvotomy, mitral valve; closed heart	33420
	Valvotomy, mitral valve; open heart, with cardiopulmonary bypass	33422
	Valvuloplasty, mitral valve, with cardiopulmonary bypass;	33425
	Valvuloplasty, mitral valve, with cardiopulmonary bypass; with prosthetic ring	33426
	Valvuloplasty, mitral valve, with cardiopulmonary bypass; radical reconstruction, with or without ring	33427
	Replacement, mitral valve, with cardiopulmonary bypass	33430
	Replacement of aortic valve by translocation of autologous pulmonary valve and transventricular aortic annulus enlargement of left ventricular outflow tract with valved conduit replacement of pulmonary valve	33440
	Valvectomy, tricuspid valve, with cardiopulmonary bypass	33460
	Valvuloplasty, tricuspid valve; without ring insertion	33463
	Valvuloplasty, tricuspid valve; with ring insertion	33464
	Replacement, tricuspid valve, with cardiopulmonary bypass	33465
	Tricuspid valve repositioning and plication for Ebstein anomaly	33468
	Valvotomy, pulmonary valve, closed heart; transventricular	33470
	Valvotomy, pulmonary valve, closed heart; via pulmonary artery	33471
	Valvotomy, pulmonary valve, open heart, with cardiopulmonary bypass	33474
	Replacement, pulmonary valve	33475

EXCLUDED:
Hemodynamically Significant Shunts – will have been surgically corrected or, if still present, captured w/cyanosis
Eisenmenger Syndrome – no specific code, but should be captured w/ cyanosis & pulmonary HTN
Arterial or Venous Stenosis – vague, nonspecific