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The Effects of Neighborhood Socioeconomic Status on Survival Outcomes Post-Congenital Heart Surgery in Infants

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By

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B.S. in Public Health with an Emphasis in Health Services
University of Georgia
2019

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An abstract of
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Abstract

The Effects of Neighborhood Socioeconomic Status on Survival Outcomes Post-Congenital Heart Surgery in Infants

By Shreya Tailor

Background: Infants with serious congenital heart disease (CHD) require frequently cardiac surgery or other invasive interventions and close follow-up. Low socioeconomic status (SES) can be associated with adverse exposures or compromise access to quality care thus, placing these children at risk for poor survival outcomes.

Methods and Results: Data from the PCCC (Pediatric Cardiac Care Consortium) data set were matched with state birth registry information in Arkansas, Missouri, and Ohio to examine the relationship between neighborhood SES with one year mortality or cardiac transplant among infants who had a congenital heart surgery (n=3,536). Neighborhood SES score was developed by matching available U.S Census data to create a six-component Z score including the log of the median household income, log of the median value of housing units and the percentages of households receiving interest, dividend or net rental income, among adults 25 years of age or older, the percentage who had completed high school and the percentage who had completed college, and the percentage of employed people 16 years of age or older in executive, managerial or professional specialty occupations. Overall, survival across neighborhood SES tertiles was considered to be high [Survival Probability: 95.7%; 95% Confidence Interval (CI) 94.3, 96.7%]. The survival outcomes of patients in high tertile of the neighborhood SES score were different than the survival outcomes of patients in the low tertile. At one year, patients in the lowest SES tertile had a 50% higher hazard of death than patients in the highest SES tertile [hazard ratio (HR) of high vs low tertile 1.50, 95% CI: 1.05, 2.14)) and a 13% higher hazard of death than patients in the middle tertile (HR 1.13; 95% CI, 0.78, 1.64). There was no significant effect modification between neighborhood SES score and covariates included in the model.

Conclusion: Survival outcomes after infantile congenital heart surgery are adversely affected by low neighborhood SES, suggesting that socioeconomic and environmental factors may be important modifiers to target if we want to improve outcomes. Future studies should further evaluate aspects of SES and environment in regard to post hospital care.

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Table of Contents

Literature Review

Congenital heart disease (CHD), defined as "a gross structural abnormality of the heart or intrathoracic great vessels that is actually or potentially of functional significance," is the most common birth defect in the United States[1-2]. In 2010, nearly 1% of infants (approximately 400,000) were born with some form of CHD[3].

While all CHDs impact the structure and the function of the heart, there are several types, each with varying severity. The severity of the CHD determines how the defect is diagnosed. Overall, tests for diagnosing CHD in children or adults include taking blood pressure measurements and an electrocardiogram (ECG) or X-ray of the heart[4]. Minor defects, also known as non-critical CHDs, are often diagnosed during a routine medical check-up, either during pregnancy or at the time of birth, and have limited presenting symptoms. Like minor defects, critical CHDs may be diagnosed during pregnancy; however, infants may only show indications of a critical CHD after birth. A critical CHD diagnosis indicates the need for surgery or other procedures within the first year of life[3]. About 1 out of 4 babies born with a CHD are diagnosed with a critical CHD[3]. By utilizing a pulse oximetry screening within the first 24 hours after birth, medical professionals can confirm the amount of oxygen in the infant's blood. Pulse oximetry screening is most likely to detect seven out of over 18 of critical CHD diagnoses; this includes: hypoplastic left heart syndrome, pulmonary atresia, tetralogy of Fallot, total anomalous pulmonary venous return, transposition of the great arteries, tricuspid atresia, and truncus arteriosus[5].

The severity of a CHD also influences available options for surgical intervention as well as the survival of the infant. Some CHDs are managed without any intervention. This is common among certain defects, such as patent ductus arteriosus (PDA) or atrial septal defect (ASD), where the minor defect may be resolved on its own. While waiting for a hole to close, often a child may be required to take medication to ensure the heart continues to beat properly and there is appropriate blood circulation[4]. About 97% of infants with a non-critical CHD are expected to survive to one year of age. When looking into long term outcomes, about 95% of infants with a non-critical CHD are expected to survive to 18 years of age. This percentage continues to increase with further medical advancements[5].

The second option for CHD treatment includes receiving a CHD-related intervention via a CHD-related catherization procedure. CHD-related catherization, which involves inserting a thin flexible tube into a vein or artery to strategically plug the intended hole, is commonly used to avoid open-heart surgery to repair the heart defect. It is most used to repair heart defects such as ASD and pulmonary valve stenosis. However, a catherization procedure is only feasible in certain cases, as in more severe cases, a repair may require stitches or a patch in the inner wall and valves of the heart[4]. Overall, 99.1% of infants who underwent a CHD related catherization, adjusting for differences in CHD severity, survived up to 30 days post catherization. This rate falls to a 98.1% survival rate at 1 year post catherization for infants[6].

The third option for CHD treatment is a CHD-related intervention via congenital heart surgery. In this case, an open-heart surgery is performed to close holes in the heart, repair or replace heart valves, widen arteries or openings to heart valves, and repair complex defects. The average

age an infant undergoes their first congenital heart surgery is solely based on the severity of their CHD. If the CHD is more severe, specifically if it is one of the seven critical CHDs mentioned previously, the surgery will occur earlier, with the median age at first surgery ranging from 26 days to 1.7 years after birth[7-20]. Among non-critical CHD diagnoses identified during infancy, most will require a congenital heart surgery within the first 6 years of life[7-20]. Overall, 94.1% of infants who underwent a congenital heart surgery, adjusting for differences in CHD severity, survived up to 30-day post-surgery. This rate falls to 91.2% at 1 year post surgery for infants[6,32].

Lastly, in the case that the infant is born with multiple defects that are too complex to repair, the infant can have a heart transplant. When a heart transplant is needed, a heart transplant surgery is performed using the healthy heart of an infant of the same age and blood type[4]. Currently, 90% of infants who undergo a heart transplant survive up to 1 year post transplant[21].

Role of Socioeconomic Status

While the underlying CHD severity and associated comorbidities and genetic contributions are the main determinants of prognosis in infants with CHD, other factors, such as socioeconomic status (SES), are also known to influence health outcomes[22]. SES is defined as "an individual's or group's position within a hierarchical social structure," but remains a difficult concept to measure. SES is commonly conceptualized as the combination of economic, sociologic, and racial factors that influence and represent a position of an individual or group. Often these factors include income, education status, and occupation[23].

Socioeconomic variables that have previously been associated with CHD diagnosis include maternal age at childbirth, race/ethnicity of the mother, and mother's education level at childbirth[24]. A recent study evaluating one-year survival of infants with CHD who did not have surgical intervention, found a strong association between survival and SES[24]. This was especially true among non-critical CHD patients when looking at the effects of maternal race/ethnicity, education, and marital status on survival outcomes[24]. This is consistent with other research, which has found socioeconomic disadvantage to be adversely associated with survival among infants with CHD[25]. As mentioned previously, infants with critical CHD diagnoses require early healthcare interventions, which are highly specialized, and often continue throughout the first years of life[7-20]. Access to these lifesaving procedures can be limited for those with a lower SES, especially among individuals who live in medically underserved areas, lack reliable transportation, or do not have adequate health insurance[26]. Little is known about the association between race/ethnicity, parental education levels, insurance status, income, and survival, specifically after a congenital heart surgery[27].

Influence of Maternal Age at Childbirth

Maternal age at birth has been predicted to increase complications at pregnancy and increase neonatal and infant mortality[28]. While overall evidence suggests that mothers who give birth at an older age have an increased risk of pregnancy complications, some studies also suggest there is a relationship with survival after a congenital heart surgery. However, there have been inconsistent findings on the specifics of the association between maternal age and congenital heart disease. Some studies report a linear relationship with maternal age and ventricular septal defect (VSD), ASD, and hypoplastic left heart syndrome – indicating as maternal age at

childbirth increases, so does the rate of infants born with a critical CHD[29]. Other studies report there is little evidence to support increased maternal age at childbirth as a risk-factor for CHD[30]. While this study did not evaluate the direct association of maternal age at childbirth on CHD, maternal age remains strongly associated with socioeconomic status. In fact, multiple studies support the hypothesis that maternal age at birth may be an important proxy variable to indicate a supportive, resourceful family environment for a young child[28]. This is particularly important when evaluating outcomes of high-risk children – specifically children with a critical CHD who undergo a congenital heart surgery.

Influence of Race and Ethnicity of Mother

The influence of race and ethnicity of the mother requires a multifactorial approach, since certain populations experience systematic and cyclic health inequity. Overall, when evaluating the relationship between race and infant mortality, maternal race is a significant risk factor especially among Black individuals. Mothers who identify as Black have the highest rates of infant mortality compared to other groups[31]. When specifically looking at the influence of race among patients who have had a previous congenital heart disease related surgery, studies show non-white patients have a higher risk of dying, after adjusting for baseline clinical differences, compared to white patients[26]. In fact, among Black patients who have a CHD and undergone a congenital heart surgery there is an approximate two times higher hazard of a 15-year mortality compared to white patients[32].

It is also important to recognize the relationship between race/ethnicity and access to insurance, especially when discussing survival outcomes of CHD patients. Black mothers and infants with

Medicaid insurance experience worse survival outcomes compared to white mothers with private insurance. In particular, uninsured infants with critical CHDs had a three times greater mortality rate than that of privately insured infants with critical CHDs[26]. Because individuals with a critical CHD require specialized surgical and medical care, regular and affordable access to care and service utilization are also vital indicators of survival. Unexplained racial/ethnic disparities remain a major health equity concern and are currently thought to be contributing factors that need further action via public health program implementation and further research[26].

Influence of Maternal Education Level at the Time of Birth

Maternal education plays a significant role in children's health outcomes. Educational status can influence social characteristics, such as general and health-related knowledge, health literacy, and problem-solving skills. In addition to the highest level of education achieved, an individual's quality of education and access to material resources also influences health outcomes. In a pediatric population, parental education levels heavily influence a child's future earnings, occupation and overall health[27]. Maternal education has been repeatedly shown to be associated with neurodevelopmental outcomes in premature infants and children with complex CHDs[27]. In a recent study evaluating the role of socioeconomic mediators with congenital heart disease outcomes in California, researchers found maternal education directly explained the large percentage difference in poor survival outcomes when comparing survival outcomes of Hispanic patients to non-Hispanic patients with the same CHD diagnosis[27].

Utilizing Neighborhood Socioeconomic Status

Multiple studies have confirmed where a person lives is not necessarily independent of an individual's health outcomes[33]. In fact, characteristics of an area where people live are strongly associated with mortality risk and other health related behaviors like smoking, dietary habits, and physical activity, while adjusting for any risk factors at the individual level[34]. As mentioned previously, socioeconomic status remains a limiting factor for many families in receiving appropriately scheduled surgical interventions[35]. By evaluating neighborhood socioeconomic status, we can understand the potential need for further resources and care among specific populations.

It is also important to note that obtaining population-based estimates of access to care remains difficult since individual-level information on health insurance and SES are not commonly available in population-based data in the United States. Thus, some researchers have identified community-level factors, that might be a suitable substitute[26].

When evaluating CHD, neighborhood socioeconomic status is often used as a composite community level variable in order to relate individual demographic information, while also appropriately adjusting for socioeconomic factors[33]. In a recent study evaluating children who underwent a Norwood procedure surgery (a common procedure for patients with single ventricle heart disease) and their related survival outcomes, low neighborhood socioeconomic status was associated with worse survival outcomes than compared to a higher neighborhood socioeconomic status (37% crude death rate among the lowest neighborhood SES score versus 31% and 23.6% among the middle and highest neighborhood SES score)[35]. This study utilized

a 6-point census-based score developed by Diez Rous et al. to develop the neighborhood SES score used as the exposure variable[33]. In the 6-point scale, each point corresponds to measures related to wealth and income (log of the median household income, log of the median value of housing units and the percentages of households receiving interest, dividend or net rental income), education (among adults 25 years of age or older, the percentage who had completed high school and the percentage who had completed college) and the occupation (the percentage of employed people 16 years of age or older in executive, managerial or professional specialty occupations). Z scores were then calculated for each census block group and summed to create the neighborhood summary score.

However, this is not the only score utilized to measure socioeconomic status. In a study evaluating survival of infants with critical CHDs and community-level factors influencing sociodemographic information, the study employed a 11-factor census-tract score. This score include census data across 4 states, and comprised of the proportion of the population aged 18 years or older who did not graduate from high school, proportion of people aged 16 years or older who were employed, proportion of the population aged 16 years or older who had an operator or laborer occupation, proportion of the noninstitutionalized population living below the federal level, proportion of all occupied housing units with more than 1 person per room, proportion of all occupied housing units that were renter occupied and the proportion speaking a language other than English at home[26].

Many studies utilize population-based birth defects surveillance programs and link with vital records, to provide the most complete ascertainment of infants born with major birth defects in a

specific population[26]. Currently, there are a limited number of studies that account for survival analyses in a neighborhood-based SES study, and there is an even more limited number that evaluate survival outcomes of CHD patients from a neighborhood based lense[26].

Purpose of this Study

Studies have suggested that maternal sociodemographic characteristics, such as maternal age at childbirth, race/ethnicity of the mother, and mother's education level at childbirth are related to congenital heart disease-related mortality. However, the extent
of how these sociodemographic variables interrelate to socioeconomic status, specifically at a neighborhood level, and to the survival of infants with CHDs has not been established. The primary aim of this study was to determine the relationship between composite neighborhood SES and survival outcomes of infants one year after receiving their first congenital heart surgery. Understanding the role of socioeconomic factors, through the use of a neighborhood composite score, on survival outcomes of CHD infants will be helpful for developing target intervention strategies for particularly vulnerable populations.

Methods

We conducted a registry-based cohort study utilizing the Pediatric Cardiac Care Consortium (PCCC), a large U.S. multi-institutional registry containing information on cardiac interventions performed from 1982-2011[32]. This registry includes reports on cardiac surgeries, diagnostic and interventional catheterizations, as well as electrophysiological procedures and their in-hospital outcomes for pediatric and congenital heart diseases[32]. The PCCC is linked to the National Death Index (NDI) and the Organ Procurement and Transplantation Network (OPTN), establishing a cohort describing the long-term mortality of patients with repaired CHD[32]. Individuals were then linked with birth certificates from state health departments in Missouri, Arkansas, and Ohio to obtain maternal sociodemographic characteristics at the time of patient's birth, which is very close to most patients' first congenital heart surgery. This study also utilizes the United States Decennial Census to obtain neighborhood socioeconomic data for cohort participants using the zip code reported at the time of birth.

Exposure Ascertainment

Pediatric Cardiac Care Consortium (PCCC) Registry

This study included PCCC patients who were U.S. residents and underwent a congenital heart surgery before the age of 6 in a PCCC designated center between January 1, 1982 and April 15, 2003. All patients were 5 years and under at the time of the first congenital heart surgery and underwent their first congenital heart disease related surgery at a PCCC center. To avoid immortal person-time bias, the cohort only included person from their first surgery in the PCCC.

Patient survival time was calculated from the time when patients were discharged from the hospital after their surgery to appropriate observe the effect of SES.

Birth Registry & Social Explorer

Birth registry information, including data on maternal race, maternal educational level, zip code at birth, maternal ethnicity, and maternal marital status, were obtained by linking state birth certificate information to the PCCC cohort.

Social Explorer, an online interactive platform for analyzing and understanding the demographics of the United States, was used to extract United States Decennial Census data. Variables abstracted included: education attainment for those aged 25 years and older, employment status for those aged 16 years and older, median household income (in dollars per year), and median housing unit. These variables correspond to those needed for the neighborhood SES score. All the variables were obtained from the nearest United States Decennial Census year (for example, 1992 corresponded with the 1990 report).

Data Linkage using ArcGIS

ArcGIS was used to link data from individual state birth registries and the United States Decennial Census. Birth registry information was first matched to eligible PCCC cohort individuals. Next, United States TIGER Line Shape Files were obtained from the United States Census Bureau for each patients' zip code. ArcGIS was utilized to geocode zip codes from the birth registry. Due to a lack of data available for the 1980's pertaining to median housing unit, we excluded all patients born in the 1980's (*Figure 1*).

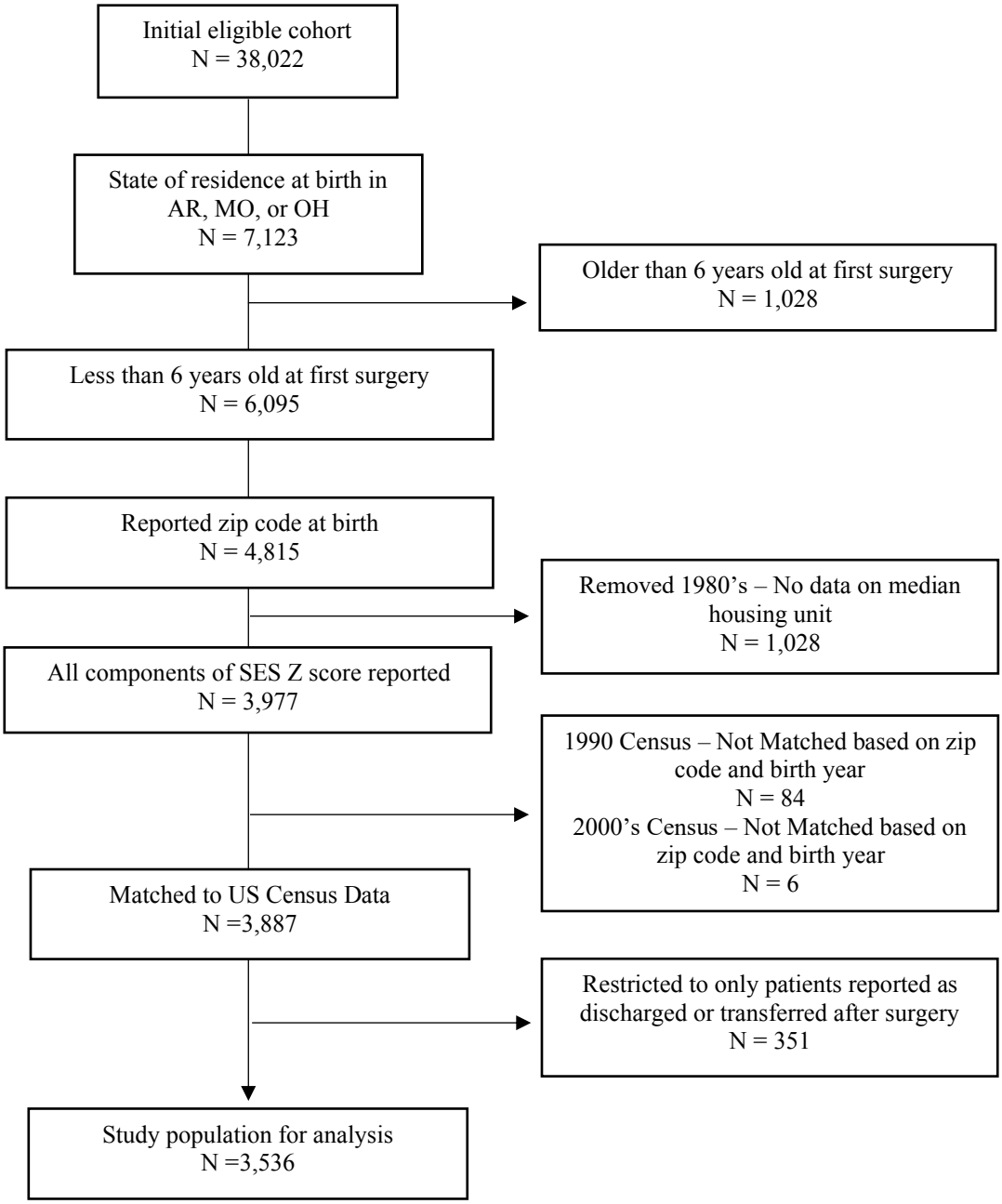
Neighborhood SES Score

Neighborhood SES was measured using a US census-based score previously developed by Diez Roux et al[33]**.** This score is composed of 6 measures related to wealth and income (log of the median household income, log of the median value of housing units, and the percentage of household receiving interest dividend or net rental income), education (among the adults 25 years of age or older, the percentage who had completed high school and the percentage who had completed college), and occupation (the percentage of employed people 16 years of age or older in executive, managerial or professional specialty occupations). Z-scores for each zip code were calculated for each variable and the neighborhood summary score was calculated as the sum of the z-scores, with a higher score indicating higher neighborhood SES.

Outcome Ascertainment

The primary outcome for this study was transplant-free survival up to one year post-first congenital heart surgery. Information on in-hospital deaths or transplants were available in the PCCC, and prospectively tracked by matching with the NDI and OPTN records through December 31, 2019**.** Records submitted to the NDI included first name, middle initial (when available), surname, date of birth, sex, state of last known residence, and state of birth. Patients without these identifiers could not be linked and were excluded from the analysis. The sensitivity of the NDI to the PCCC data linkage was 88.1% (95% CI: 87.1-89.0), and the specificity was 99.8% (95% CI: 99.7-99.8)[32].

Figure 1. Inclusion Criteria Flowchart



Covariates of Interest

Covariates considered for the potential to modify the association between the SES score and survival included sex, age at first surgery, era of first surgery, CHD severity, maternal ethnicity, maternal race, and maternal education at birth. Surgical era, determined by the year when the first CHD procedure occurred, was classified into three categories: 1990-1994, 1995-1998, 1999-2003. Maternal race and ethnicity were included as separate entities, with maternal race was classified as: Black, White, Asian, and unknown, and ethnicity classified as Hispanic or non-Hispanic. Additionally, to compare survival across different CHD diagnoses, patients were classified into mild, moderate, severe 2V, single ventricle and non-classifiable CHD severity categories. Because it is still important to account for measures of association between the exposure and outcome with another influence variable, all covariates were assumed to be effect modifiers until further confirmation from an interaction assessment. While evaluating existing associations a priori between each of these variables and neighborhood socioeconomic status, we determined each variable did not meet the criteria for consideration as a confounder. For example, in the case of CHD severity, while it is a risk factor for transplant-free survival, it likely has no effect on a person's neighborhood SES score – and, in fact, may be an intermediate variable.

Statistical Analysis

All analyses were performed using SAS version 9.4. Descriptive characteristics were compared across neighborhood SES score tertiles (a low SES score included a z score range of –11.65 to –1.67, a middle SES score included a z score range of –1.68 to 1.49, and a high SES included a z score range of 1.50 to 17.30) using Chi-square tests for categorical variables and ANOVA tests for continuous variables.

To evaluate the relationship between neighborhood SES and 1 year transplant-free survival, we used Kaplan-Meier curves and Cox proportional hazards models. Kaplan-Meier curves were generated for comparison across each SES score tertile. Survival time was calculated from the date of discharge following the first congenital heart surgery in the PCCC registry to the date of death, date of transplant or until one year after the date of discharge for patients who were not identified as deceased or transplanted in either the PCCC registry, NDI, and OPTN.

We evaluated whether the association between neighborhood SES and post-surgery survival was modified by any of the covariates of interest (sex, age at first surgery, era of first surgery, CHD severity, maternal ethnicity, maternal race, and maternal education at birth).

Results

Our sample includes 3,536 infants who underwent a congenital heart surgery. The neighborhood SES score ranged from -11.65 to 17.30 with a mean of 0 (by design) and a standard deviation of 3.92. *Table 1* presents sociodemographic and clinical characteristics of patients by their neighborhood SES score tertile. Compared with patients in the middle and highest SES tertiles, a greater percentage of patients in the lowest tertile were of Hispanic ethnicity and of non-White race. Additionally, there were more patients in the lowest tertile that reported having a high school diploma as their highest educational attainment. On average, patients in the lowest tertile were older at the time of their first surgery (median age in lowest tertile 149.0 days, IQR [27.0, 457.5]). Overall, there were differences in the distribution of neighborhood SES score by state of residence but not by CHD severity.

Neighborhood SES Score and One Year Transplant-Free Survival

The relationship between SES tertile and survival post-CHD surgery discharge is shown graphically in *Figure 2*. Overall, the one-year survival was relatively high, with over 93% of patients in all three SES groups having survived this time period; however, those with the lowest neighborhood SES scores had lower survival probabilities (Survival probability percentage 93.7, 95% Confidence Interval (CI): [92.1, 94.9]).

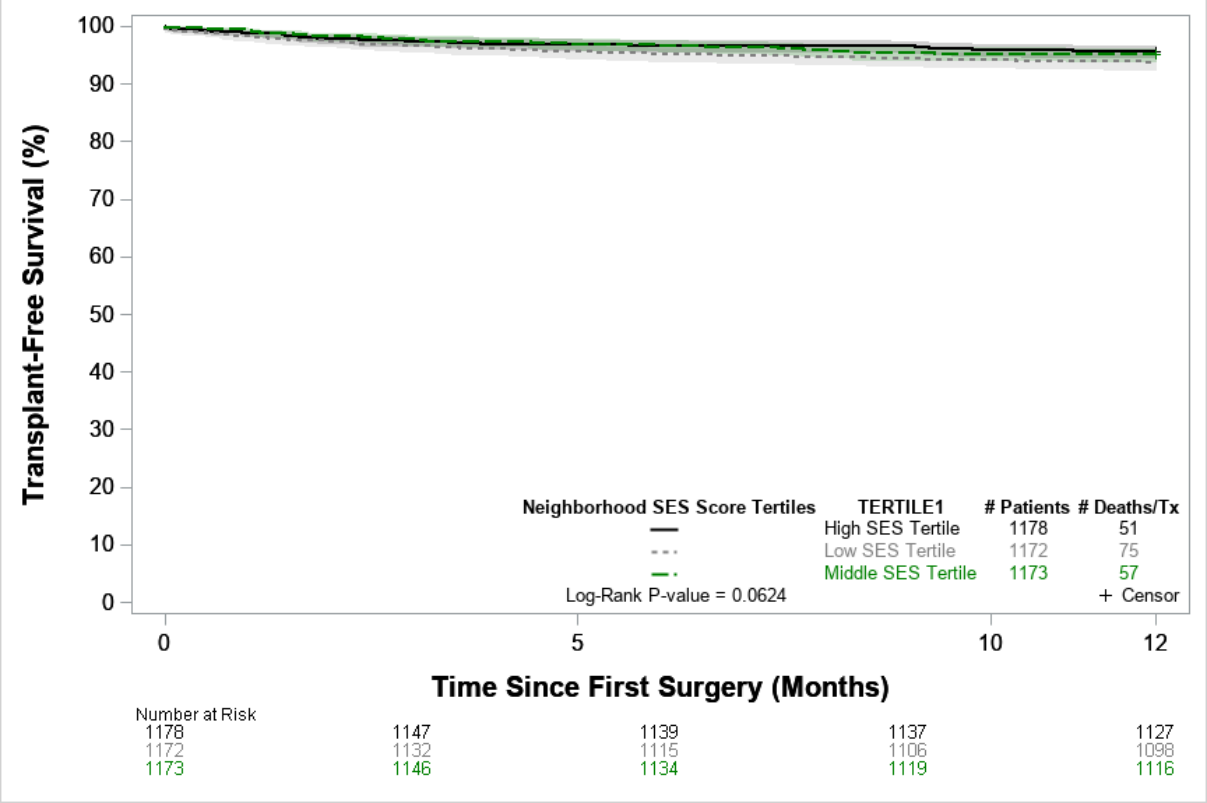
Table 1. Demographic and Clinical Characteristics by Neighborhood SES Tertiles

Variable	Level	Overall N=3536	High SES Score* N=1181	Middle SES Score* N=1179	Low SES Score* N=1176
SEX	Female	1671 (47.3%)	559 (47.3%)	584 (49.5%)	528 (44.9%)
	Male	1865 (52.7%)	622 (52.7%)	595 (50.5%)	648 (55.1%)
ETHNICITY	Hispanic	78 (2.2%)	22 (1.9%)	21 (1.8%)	35 (3.0%)
	Non-Hispanic	3424 (96.8%)	1135 (96.1%)	1151 (97.6%)	1138 (96.8%)
	Unknown	34 (1.0%)	24 (2.0%)	7 (0.6%)	3 (0.3%)
MATERNAL RACE	Asian	56 (1.6%)	24 (2.0%)	21 (1.8%)	11 (0.9%)
	Black	497 (14.1%)	78 (6.6%)	146 (12.4%)	273 (23.2%)
	White	2961 (83.7%)	1070 (90.6%)	1008 (85.5%)	883 (75.1%)
	Unknown	22 (0.6%)	9 (0.8%)	4 (0.3%)	9 (0.8%)
ERA AT FIRST SURGERY	1990-1994	1090 (30.8%)	274 (23.2%)	347 (29.4%)	469 (39.9%)
	1995-1998	1246 (35.2%)	392 (33.2%)	432 (36.6%)	422 (35.9%)
	1999-2003	1200 (33.9%)	515 (43.6%)	400 (33.9%)	285 (24.2%)
MATERNAL EDUCATION AT BIRTH	High School Diploma	2053 (58.1%)	475 (40.2%)	708 (60.1%)	870 (74.0%)
	Some College	772 (21.8%)	315 (26.7%)	260 (22.1%)	197 (16.8%)
	College Diploma	687 (19.4%)	387 (32.8%)	200 (17.0%)	100 (8.5%)
	Unknown	24 (0.7%)	4 (0.3%)	11 (0.9%)	9 (0.8%)
STATE OF RESIDENCE AT BIRTH	Arkansas	884 (25.0%)	103 (8.7%)	291 (24.7%)	490 (41.7%)
	Missouri	1864 (52.7%)	736 (62.3%)	585 (49.6%)	543 (46.2%)
	Ohio	788 (22.3%)	342 (29.0%)	303 (25.7%)	143 (12.2%)
CHD SEVERITY	Mild	1071 (30.3%)	331 (28.0%)	353 (29.9%)	387 (32.9%)
	Moderate	1410 (39.9%)	484 (41.0%)	474 (40.2%)	452 (38.4%)
	Severe 2V	575 (16.3%)	203 (17.2%)	199 (16.9%)	173 (14.7%)
	Single Ventricle	333 (9.4%)	111 (9.4%)	110 (9.3%)	112 (9.5%)
	Non-classifiable	147 (4.2%)	52 (4.4%)	43 (3.6%)	52 (4.4%)
MEDIAN AGE AT FIRST SURGERY IN DAYS (IQR)		137 (21, 384)	133.0 (17.0, 325.0)	130.0 (22.0, 379.0)	149.0 (27.0, 457.5)

Variable	Level	Overall N=3536	High SES Score* N=1181	Middle SES Score* N=1179	Low SES Score* N=1176
MEDIAN FOLLOW UP TIME IN MONTHS (IQR)		268 (229.6, 303.7)	258.8 (225.0, 295.5)	267.1 (227.7, 301.6)	278.0 (239.7, 311.5)
TRANSPLANT DURING FOLLOW UP TIME	No Transplant	3489 (98.7%)	1170 (99.1%)	1158 (98.2%)	1161 (98.7%)
	Transplant Received	47 (1.3%)	11 (0.9%)	21 (1.8%)	15 (1.3%)
DEATH DURING FOLLOW UP TIME	Alive	3181 (90.0%)	1074 (90.9%)	1068 (90.6%)	1039 (88.4%)
	Death Reported	355 (10.0%)	107 (9.1%)	111 (9.4%)	137 (11.6%)

*High SES Score includes a neighborhood SES z score range of 1.50 to 17.30
Middle SES Score includes a neighborhood SES z score range of -1.68 to 1.49.
Low SES Score includes a neighborhood SES z score range of -11.65 to -1.67.

Figure 2. Kaplan-Meier curve for one year mortality or cardiac transplantation among transplant free survivors by neighborhood SES tertiles by month



When evaluating survival probabilities across the covariates of interest, most covariates follow the pattern where increasing neighborhood SES is associated with greater survival; however, there are some notable departures from this trend. There are discrepancies in the general trend of increasing survival probabilities with increasing neighborhood SES. Overall, there is no significant difference between survival across sex. Additionally, patients identified as White and patients with their education attainment indicated as high school diploma or some college followed the hypothesized survival trend (lower neighborhood SES score relating to a higher risk of post-surgery mortality). Survival probabilities across CHD severity per neighborhood SES tertile were similar in nature (*Table 2*).

Table 2. One-Year Survival Probabilities Post-Surgery, by SES Tertiles and Patient Characteristics

	Survival Probabilities, 95% Confidence Intervals		
	High SES Score	Middle SES Score	Low SES Score
Overall	95.7 (94.3, 96.7)	95.1 (93.7, 96.2)	93.7 (92.1, 94.9)
Sex			
Female	95.3 (93.2, 97.7)	95.2 (93.1, 96.7)	94.1 (91.7, 95.8)
Male	96.0 (94.1, 97.3)	95.1 (93.0, 96.6)	93.4 (91.1, 95.0)
Ethnicity			
Hispanic	95.5 (71.9, 99.3)	100 (100, 100)	91.4 (75.7, 97.2)
Non-Hispanic	95.6 (94.2. 96.6)	95.0 (93.6, 96.1)	93.7 (92.2, 95.0)
Unknown	100 (100, 100)	100 (100, 100)	100 (100, 100)
Maternal Race			
White	96.0 (94.6, 97.0)	95.3 (93.7, 96.4)	93.5 (91.7, 95.0)
Black	91.0 (82.1, 95.6)	94.4 (89.2, 97.2)	93.8 (90.1, 96.1)
Asian	95.8 (73.9, 99.4)	95.2 (70.7, 99.3)	100 (100, 100)
Unknown	100 (100, 100)	100 (100, 100)	100 (100, 100)
Era of First Surgery			
1990-1994	96.3 (93.3, 98.0)	95.6 (92.9, 97.3)	94.0 (91.4, 95.8)
1994-1998	95.7 (93.1 97.3)	94.2 (91.5, 96.0)	93.6 (90.8, 95.6)
1999-2003	95.2 (93.1, 96.8)	95.7 (93.2, 97.3)	93.3 (89.7, 95.7)
Maternal Education at Birth			
High School Diploma	95.1 (92.8, 96.7)	94.8 (92.8, 96.2)	93.6 (91.8, 95.1)
Some College	95.9 (93.0, 97.6)	95.0 (91.5, 97.0)	93.9 (89.5, 95.6)
College Diploma	96.1 (93.6, 97.6)	96.5 (92.8, 98.3)	93.0 (85.9, 96.6)
Unknown	100 (100, 100)	100 (100, 100)	100 (100, 100)
Disease Severity			
Mild	99.1 (97.2, 99.7)	99.4 (97.8, 99.9)	98.4 (96.6, 99.3)
Moderate	97.7 (95.9, 98.7)	97.9 (96.1, 98.9)	94.2 (91.7, 96.0)
Severe 2V	91.1. (86.3, 94.3)	91.4 (86.5, 94.5)	89.0 (83.2, 92.8)
Single Ventricle	85.5 (77.4, 90.8)	75.2 (66.0, 82.3)	80.0 (71.2, 86.3)
Non-classifiable	94.2 (83.2, 98.1)	97.7 (84.6, 99.7)	98.1 (87.1, 99.7)

Although there were no differences in survival for those in the middle tertile of neighborhood SES compared to those in the highest (Hazard Ratio (HR) 1.13, [95% CI, 0.78, 1.64]), there was a greater hazard for death or transplant among those in the lowest tertile compared to the highest (HR 1.50, [95% CI 1.05, 2.14]) (*Table 3*). At one year, patients in the highest SES tertile had a 1.50 times higher hazard of death than patients in the lowest SES tertile and 1.13 times higher hazard of death than patients in the middle SES tertile (*Table 3*).

Effect Modification of CHD Severity and State of Residence at Birth

There was no evidence of effect modification of the association between neighborhood SES score and survival by any of the covariates we considered (sex, ethnicity, maternal race, era of first surgery, maternal education at birth, and CHD severity).

Table 3. Hazard ratios for the association between SES score and survival

	Hazard Ratio	**95 % Confidence Interval**
Low SES Score	1.50	(1.05, 2.14)
Middle SES Score	1.13	(0.78, 1.64)
High SES Score	1.00 (ref)	--

Discussion

Using a comprehensive measure of neighborhood SES, we found that overall survival for CHD patients 1-year post CHD surgery discharge remained high across all neighborhood SES tertiles. However, there were differences in survival between those in the highest and lowest groups, with an approximately 50% increase in the hazard of death or transplant among those with the lowest neighborhood SES scores.

There are many possible explanations for the difference in survival observed in patients with low versus high neighborhood SES scores, especially for those who require early and continued medical interventions.

When discussing access to healthcare services, patients with CHD are regularly in need of high-quality specialty care and continued follow-up with medical specialists. Patients who are able access this care, and regularly attend appointments are more likely to have better survival post-CHD surgery. Unfortunately, barriers impact the ability of families of infants living in low SES neighborhoods to access these follow up appointments[36-38]. Some of these barriers include living farther away from a primary treatment center,[39] a lack of community social support, and unstable employment resulting in limited health benefits, paid vacation, or time off to care for their child[40].

Other factors that could influence the difference in mortality observed in patients with high versus low neighborhood SES score include environmental exposures, such as low birth weight, birth complications and maternal age at birth, that influence the relationship between high

mortality and chronic conditions[41]. Gestational age at birth and birth weight are also independently associated with mortality in individuals with CHD[30]. Additionally, for infants diagnosed with a CHD, delivered at full term, and classified as having a low birth weight, there is a 19.1% difference in five-year survival outcomes than compared to high-birth weight children[30]. The influence of low birth weight, birth complications and maternal age at birth were not individually assessed in this study; however, each of these covariates have been strongly related with socioeconomic status[41]. For the purposes of this study, we utilized the calculated neighborhood SES score for each patient as a proxy variable for these potential influences. In future studies, it would be beneficial to individually evaluate the role of low birth weight, birth complications and maternal age at birth, given the needed data is available.

We found no consistent association between CHD severity and survival, and also that CHD severity did not modify the association between neighborhood SES and survival. These results differ from previous studies that have observed disease severity influencing sustained access to care[35]. The reasoning behind the proposed hypothesis for a presence of effect modification across CHD severity is based on the set follow-up schedule patients with critical CHD's must comply to for treatment. This is not the same follow-up schedule for patients with a non-critical CHD. As mentioned previously, the more severe a CHD, the earlier a congenital heart surgery is expected to occur – with the median age at first surgery for critical CHD's ranging from 26 days to 1.7 years after birth[7-20]. This means that patients with more severe CHD will be inducted into a system to regularly monitor their condition] throughout their life. Additionally, clinical resources and further interventions are often focused on survival outcomes for patients with critical CHDs[44]. However, for patients with a non-critical CHD, the median age at first surgery is much

later, extending up to 6 years of age[7-20]. This alone would influence when patients with non-critical CHDs would be seen, therefore potentially influencing survival outcomes. Further, the time elapsed from a patient's congenital heart surgery to continued follow-up visits is more likely to be later among non-critical CHD patients. In return, they are more likely to be lost to follow up and their survival time may be influenced because of this.

This study is not without limitations. First, the availability of data for evaluation was limited to matching across three different platforms (the PCCC cohort, accessible state birth registry information, and the corresponding year of the United States Decennial Census). Individuals had to be dropped from the cohort due to limited data matching from the United States Decennial Census from selected eras. In particular, the data was restricted to only patients born in the 1990's and 2000's, due to the lack of data available on the median housing unit at the zip code level in the 1980s. Also, because the data used in this study was abstracted from interstate monitoring programs, the generalizability of the results to all patients is limited. It is also important to note that distance from treatment center was not included in our study due to the limited ability to calculate the distance between each families' residence and their associated treatment center. Previous studies have indicated a relationship between SES and distance from treatment center so it would be most likely be considered as an effect modifier in this study[39].

However, this study also extends that of prior studies by evaluating the effect of neighborhood SES across all CHD disease severities post-congenital heart surgery. Although previous studies have documented the relationship between neighborhood SES and CHD outcomes, they often examine a single classification of disease severity or focus on pre-operation effects. For example,

Tweddell et al evaluated the role of neighborhood SES as a preoperative risk factor for 1 year mortality. This study found that lower SES was associated with higher early mortality within the first year, but not with mortality beyond 3 years of follow up[43]. Additionally, Bucholz et al evaluated the role of neighborhood SES with transplant-free survival after the Norwood procedure (a common procedure for patients with a single ventricle physiology), finding that patients with SV physiology from low SES neighborhoods were at significantly higher risk of death or transplant within the first year of the Norwood procedure[35].

This study has important implications for understanding and addressing socioeconomic disparities in pediatric cardiac outcomes. Although survival was relatively high overall, the inequity in survival between those with the highest and lowest neighborhood SES scores warrants further investigation and investment in strategies to improve patient outcomes among those with lower neighborhood SES scores.

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