Title

Impact of Socioeconomic Status, Race and Ethnicity, and Geography on Prenatal Detection of Hypoplastic Left Heart Syndrome and Transposition of the Great Arteries

Journal

Circulation, 143(21)

ISSN

0009-7322

Authors

Krishnan, Anita
Jacobs, Marni B
Morris, Shaine A
et al.

Publication Date

2021-05-25

DOI

10.1161/circulationaha.120.053062

Peer reviewed

HHS Public Access

Author manuscript

Circulation. Author manuscript; available in PMC 2022 May 25.

Published in final edited form as:

Circulation. 2021 May 25; 143(21): 2049–2060. doi:10.1161/CIRCULATIONAHA.120.053062.

The impact of socioeconomic status, race/ethnicity, and geography on prenatal detection of hypoplastic left heart syndrome and transposition of the great arteries

Anita Krishnan, MD[1], **Marni B. Jacobs, PhD**[2,3], **Shaine A. Morris, MD MPH**[4], **Shabnam Peyvandi, MD**[5], **Aarti H. Bhat, MD**[6], **Anjali Chelliah, MD**[7], **Joanne S. Chiu, MD**[8,9], **Bettina F. Cuneo, MD**[10], **Grace Freire, MD**[11], **Lisa K. Hornberger, MD**[12], **Lisa Howley, MD**[10,13], **Nazia Husain, MD**[14], **Catherine Ikemba, MD**[15], **Ann Kavanaugh-McHugh, MD**[16], **Shelby Kutty, MD PHD MHCM**[8,17], **Caroline Lee, MD**[18], **Keila N Lopez, MD MPH**[4], **Angela McBrien, MD**[12], **Erik C Michelfelder, MD**[19], **Nelangi M. Pinto, MD**[20], **Rachel Schwartz, MD**[21,22], **Kenan W.D. Stern, MD**[23,24], **Carolyn Taylor, MD**[25], **Varsha Thakur, MD**[26], **Wayne Tworetzky, MD**[21], **Carol Wittlieb-Weber, MD**[27,28], **Kris Woldu, MD**[15,29], **Mary T. Donofrio, MD**[1] **Fetal Heart Society**

[1]Division of Cardiology, Children's National Hospital, Washington, DC

[2]Division of Biostatistics, Children's National Hospital, Washington DC

[3]Department of Obstetrics, Gynecology, and Reproductive Sciences, University of California, San Diego, San Diego, CA

[4]Division of Pediatric Cardiology, Baylor College of Medicine, Houston, TX

[5]Division of Cardiology, Department of Pediatrics, University of California, San Francisco, San Francisco, CA

[6]Division of Cardiology, Seattle Children's Hospital, University of Washington, Seattle, WA.

[7]Division of Pediatric Cardiology, Columbia University Irving Medical Center, New York, NY

[8]Division of Pediatric Cardiology, Johns Hopkins University, Baltimore, MD

[9]Division of Cardiology, Department of Pediatrics, Massachusetts General Hospital, Boston, MA

[10]Division of Cardiology, Children's Hospital of Colorado/University of Colorado, Aurora, CO

[11]Division of Cardiology, Johns Hopkins University All Children's Hospital, St. Petersburg, FL

[12]Division of Pediatric Cardiology, University of Alberta, Edmonton, Canada

[13]Division of Cardiology, The Children's Heart Clinic/Children's Minnesota, Minneapolis, MN

[14]Division of Cardiology, Ann and Robert H Lurie Children's Hospital of Chicago, Chicago, IL

[15]Division of Cardiology, Department of Pediatrics, UT Southwestern Medical Center, Dallas, TX

Corresponding Author: Dr. Anita Krishnan, Children's National Medical Center, 3rd Floor, Cardiology, 111 North Michigan Avenue, NW, Washington, DC 20010, (p) 202-476-6552, (f) 202-476-5700, akrishna@childrensnational.org.

Conflict of Interest Disclosures:
None

[16]Division of Pediatric Cardiology, Monroe Carell Jr. Children's Hospital at Vanderbilt, Nashville, TN

[17]University of Nebraska Medical Center, Omaha, NE

[18]Division of Cardiology, Department of Pediatrics, Washington University School of Medicine, St. Louis, MO

[19]Emory University School of Medicine, Children's Healthcare of Atlanta/Sibley Heart Center, Atlanta, GA

[20]Division of Pediatric Cardiology, University of Utah, Salt Lake City, UT

[21]Division of Cardiology, Boston Children's Hospital, Boston MA

[22]The George Washington School of Medicine, Washington, DC

[23]Division of Pediatric Cardiology, Albert Einstein College of Medicine, Children's Hospital at Montefiore, New York, NY

[24]Division of Pediatric Cardiology, Icahn School of Medicine at Mount Sinai, Kravis Children's Hospital, New York, NY

[25]Division of Pediatric Cardiology, Medical University of South Carolina, Charleston, SC

[26]Division of Cardiology, University of Toronto, Toronto, Canada

[27]Division of Pediatric Cardiology, University of Rochester, Rochester NY

[28]Division of Cardiology, Children's Hospital of Philadelphia, Philadelphia, PA

[29]Division of Cardiology, Cook Children's Heart Center, Ft. Worth TX

Abstract

Background: Prenatal detection (PND) has benefits for infants with hypoplastic left heart syndrome (HLHS) and transposition of the great arteries (TGA), but associations between sociodemographic and geographic factors with PND have not been sufficiently explored. This study evaluated whether socioeconomic quartile (SEQ), public insurance, race/ethnicity, rural residence and distance of residence (distance and driving time from a cardiac surgical center, DOR) are associated with the PND or timing of PND, with secondary aim to analyze differences between the US and Canada.

Methods: In this retrospective cohort study, fetuses and infants <2 months of age with HLHS or TGA admitted between 2012 and 2016 to participating Fetal Heart Society Research Collaborative (FHSRC) institutions in the United States and Canada were included. SEQ, rural residence, and DOR were derived using maternal census tract from the maternal address at first visit. Subjects were assigned a SEQ z score using the neighborhood summary score or Canadian Chan index and separated in quartiles. Insurance type and self-reported race/ethnicity were obtained from medical records. We evaluated associations between SEQ, insurance type, race/ethnicity, rural residence, and DOR with PND of HLHS and TGA (aggregate and individually) using bivariate analysis with adjusted associations for confounding variables, and cluster analysis for centers.

Results: Data on 1862 subjects (HLHS n=1171, 92% PND, TGA n = 691, 58% PND) were submitted by 21 centers (19 US). In the US, lower SEQ was associated with lower PND in HLHS and TGA, with the largest effect in the lower SEQ of pregnancies with fetal TGA (Quartile 1: 0.78 (CI 0.64–0.85), 2: 0.77 (CI 0.64–0.93), 3: 0.83 (0.69–1), 4: reference). Hispanic ethnicity (RR 0.85 (CI 0.72–0.99)) and rural residence (RR 0.78 (CI 0.64–0.95)) were also associated with lower PND in TGA. Lower SEQ was associated with later PND overall; in the US, rural residence and public insurance were also associated with later PND.

Conclusions: We demonstrate that lower SEQ, Hispanic ethnicity, and rural residence are associated with decreased PND for TGA, with lower SEQ also being associated with lower rates of PND for HLHS. Future work to increase PND should be considered in these specific populations.

Keywords

fetal echocardiogram; social determinants of health; congenital heart disease

BACKGROUND

Prenatal diagnosis (PND) reduces morbidity and mortality in hypoplastic left heart syndrome (HLHS) and transposition of the great arteries (TGA), two of the most common critical neonatal cardiac defects.[1,2] The benefits of PND include perinatal stabilization, coordination of timely interventions such as catheterization[3], and selection of a delivery center in proximity to the tertiary care center.[4] In HLHS, patients with PND are reported to have lower pre-and post-operative mortality, shorter hospital stay, and lower rates of acidosis and multi-organ dysfunction.[2] PND is also thought to positively impact longer-term outcomes including better neurodevelopmental outcomes[5], improvements in postnatal brain maturation and decreased risk of postnatal brain injury.[6] While the benefits of PND have been recognized for decades, it occurs in less than 60% of CHD cases in many regions of the United States.[7,8] Understanding barriers to PND is critical for identifying effective strategies to improve holistic care and outcomes for patients with CHD.

Limited data exist that specifically explore the impact of social determinants of health on PND of CHD. In particular, limited prior studies have demonstrated that Hispanic ethnicity, lower maternal education, lower population density, public/governmental insurance, and lower socioeconomic status have been associated with lower rate of prenatal detection.[9–11] However, these data have largely been derived from single center or regional investigations, making generalizability across multiple regions challenging.[9] Additionally, the largest study to date on this topic grouped all CHD together, not accounting for the clear variability in PND by lesion.[11]

The current study examined a large multicenter retrospective cohort from 21 North American cardiology centers. Our primary aim was to evaluate whether socioeconomic, demographic, or geographic factors are associated with lower rates of PND or delayed gestational age at time of PND of HLHS or TGA in the United States. A secondary aim was to examine whether impact (or lack thereof) of socioeconomic, demographic or geographic

factors is comparable between the US and Canada, which have divergent health care systems.

METHODS

Study Design:

The authors state that the findings from this study are available from the corresponding author upon reasonable request. We conducted a multicenter retrospective cohort study performed through the Fetal Heart Society Research Collaborative (FHSRC) to identify potential socioeconomic, demographic, and geographic barriers to PND of HLHS and TGA. Twenty-one sites in the United States (n=19) and Canada (n=2) participated. These sites represented all United States Department of Health and Human Services defined geographic regions within the United States. Institutional Review Board approval was obtained for each participating site with a waiver of consent, and a data use agreement was established between each site and the University of Utah. Data was submitted through an Open Clinica Database managed by the Data Collection Center at the University of Utah.

Study Population:

This study population included prenatally diagnosed fetuses with HLHS or TGA and postnatally diagnosed live born infants of <2 months of age with HLHS or TGA with at least one visit recorded in the institutional database of the participating FHSRC center with a first hospital encounter in the system between January 1, 2012 and December 31, 2016. These two specific CHD lesions were chosen because they represent two of the most common critical newborn CHDs. They also represent both single and biventricular forms of CHD that require urgent, and in some cases, emergent intervention. Furthermore, while HLHS is identifiable through four chamber imaging, detection of TGA requires additional fetal outflow tract views on prenatal ultrasound screening and may be more difficult to detect prenatally than HLHS.[10,11]

HLHS was defined as classic forms of this diagnosis (mitral and aortic stenosis, mitral stenosis and aortic atresia, mitral and aortic atresia) with an intact ventricular septum or double outlet right ventricle with mitral atresia and intact ventricular septum, amenable to a Stage I palliation or hybrid procedure. TGA was defined as D-transposed great arteries with D-looped ventricles and concordant ventricular size with intact ventricular septum or small muscular ventricular septal defect (VSD). When possible, the cardiac diagnosis was confirmed postnatally or at autopsy.

Exclusion criteria included any of the following: lack of confirmation regarding the diagnosis in liveborn patients, missing maternal address either due to lack of documentation or patient being homeless, or absent documentation of whether a case was diagnosed prenatally or postnatally. Subjects with anatomic variants of HLHS including critical aortic stenosis without evolution to HLHS or Shones complex, or TGA variants with tricuspid atresia, heterotaxy, double outlet right ventricle, Taussig-Bing anomaly, or hypoplasia of one ventricle or atrioventricular septal defect were also excluded, given that their presence may increase or decrease likelihood of PND. With respect to TGA, fetuses/newborns with a

ventricular septal defect larger than a small muscular ventricular septal defect, more than mild pulmonary stenosis, or coarctation of the aorta were not included.

Study Variables:

The primary independent variables were neighborhood SEQ, neighborhood poverty level >20%, neighborhood race/ethnicity distribution, rural residence, at risk geographic location (Mexican/American border, Native American reservation, or island home), driving distance to cardiac surgical center, driving time to cardiac surgical center, maternal insurance, and maternal race/ethnicity. Maternal age, maternal primary language, presence of extra-cardiac defects and multiple gestation pregnancy were treated as covariates.

SEQ calculation: For United States patients, the SEQ was determined using the neighborhood summary score derived from the maternal census tract as previously described by Diez Roux et al.[12] For each patient, z-scores of the neighborhood summary score were calculated. The neighborhood summary score was calculated by summing six elements extracted from each census tract: 1) log of median household income; 2) log of median housing value; 3) percentage of high school graduates (percent whose highest educational attainment was graduation from high school or equivalent for the population 25 years and over); 4) percentage of college graduates (percent whose highest educational attainment was a bachelor's degree or advanced degree for the population 25 years and over); 5) percentage of employed persons 16 years of age or older in executive, managerial, or professional specialty occupations; 6) percentage of households receiving interest, dividend, or net rental income for each patient census tract. A z-score was calculated for each of these elements based on distribution within the dataset and z-scores were then summed for each subject. Subjects were grouped into four quartiles based on total neighborhood SES score, with Quartile 4 being the wealthiest. The maternal census tract was determined using the first address available in the maternal or infant medical record. Relevant variables for each census tract were derived from the 2015 American Community Survey data using a CDX Zipstream software package (CDX Technologies, Randolph, NJ).

For the Canadian cohort, patients came from the two largest centralized fetal cardiology and surgical centers in 2 provinces, Alberta and Ontario. The postal code for the mother during pregnancy or the first postal code for the infant on record was recorded. The Chan index[13] was derived by investigators at the Canadian centers by extracting variables from the Canadian census. These included 22 variables related to cultural identities, environmental pollutants, environmental injustice studies, and the Pampalon deprivation index. Principal component analysis was performed on the 22 variables, and then the factor scores were averaged together to generate the score. These scores were then converted to z-scores and categorized into quartiles to be comparable to the United States data.

Additional neighborhood characteristics—Neighborhood poverty level, race/ethnic distribution, rural designation, and at risk geographic location were based on maternal census tract data derived from the 2015 American Community Survey and extracted using the CDX Zipstream software. A neighborhood in poverty was designated using a cutoff of ≥20%, in accordance with the U.S. Census Bureau.[14] Given that maternal race and ethnicity

data were not available for all subjects, the neighborhood variable of > 50% Hispanic, non-Hispanic Black, or Native American inhabitants was examined as an independent variable. Rural versus urban status was based on the United States Department of Agriculture (USDA) 1–9 classification.[15] Rural residence was defined as categories 4–9. These variables were not available for Canadian subjects.

Geographic distance from maternal residence to care center—Distance from maternal address to the surgical center in minutes and miles for the US population was calculated using the CDX Zipstream software and was provided by the Canadian centers and expressed in quartiles. Cases where a patient was transferred from one surgical hospital near their home to another surgical center were not included in the distance analysis.

Determination of insurance status: Presence or absence of public insurance was used by the maternal or infant insurance type from the medical record, using the earliest available documentation for either the fetal or neonatal record. Public insurance was defined as Medicare, Medicaid, or military/government insurance plan. For the Canadian provinces of Alberta and Ontario, provincial government health services are publicly funded and available for the population. Therefore, insurance status was not examined in the Canadian sub-cohort and patients without insurance were not examined in the United States cohort. Self-pay patients in the United States were not included in the analysis. Patient with unknown or undocumented insurance in the chart, or missing insurance type in the chart were not included in the analysis.

Maternal and fetal/infant characteristics—Maternal age at delivery, race, ethnicity, and primary language, were derived from individual maternal and infant medical records. Maternal race/ethnicity was not reliably available for Canadian subjects. Presence of a multiple gestation pregnancy and extra-cardiac defects were also extracted from medical records.

Determination of Primary and Secondary Outcomes:

The primary outcome of interest was PND. This was defined by at least one fetal echocardiogram report or clinic visit (performed by a pediatric cardiologist) in the participating center carrying the fetal diagnosis of TGA or HLHS. When possible a PND was confirmed postnatally.

The secondary outcome studied was gestational age at PND (limited to prenatally diagnosed patients), as determined by the gestational age in weeks of the first fetal echocardiogram at the participating institution.

Statistical Analysis

Bivariate analyses were performed first overall and then stratified by country and diagnosis to determine whether there were associations between the primary independent variables, covariates, and the primary outcome using chi-square for categorical variables and t-test or Wilcoxon Rank Sum test for continuous variables, as appropriate. Adjusted analyses using log-binomial regression with robust standard errors were then performed for each

independent variable, stratified by country and diagnosis, adjusting for co-variates with $p \leq 0.1$ in bivariate analysis and clustering by site using generalized estimating equations. Sub-analyses were then performed evaluating associations between the primary independent variables and the secondary outcome of gestational age at PND, limiting to those with a PND. These analyses were performed for each variable, stratified by country and diagnosis, adjusting for covariates with $p \leq 0.1$ in bivariate analysis and clustering by site using generalized linear models. All analyses were performed using SAS software, version 9.4 (SAS Institute Inc, Cary, NC, USA)

RESULTS

The study included a total of 1862 patients, including 1171 patients with HLHS (91.8% prenatally diagnosed) and 691 with TGA (58% prenatally diagnosed). Of these, 1582 (85%) were from United States centers. Of the Canadian patients, there were 133 with HLHS (n= 120, 92% prenatally diagnosed) and 147 with TGA (n= 84, 57% prenatally diagnosed). Of the total cohort of 1862 patients, postnatal confirmation was not available for 209. This is because 138 did not survive to birth (1 miscarriage, 21 intrauterine fetal demise, and 114 termination of pregnancy). Thirty moved from the area prior to delivery and had unknown birth outcome. 41 were lost to follow up. PND was significantly more common among those with HLHS compared to TGA (91.8% vs. 58%; $p<0.0001$, Table 1).

Forty-three percent of maternal patients in the US cohort had public insurance. Three hundred fifty six patients were not included in the analysis (339 with unknown status (260 from one center without information in the database), 2 unable to be classified, 1 missing, and 14 self pay). The racial distribution of our cohort was similar to that of the US Census distribution.[16] Thirteen percent of US patients lived in a rural location as defined by USDA classifications 4–9.[15] The number of patients living in an at-risk geographic location was very small (n=7). Given this, this variable was not examined in stratified analyses.

Associations with PND

In unadjusted analyses evaluating the entire cohort, socioeconomic variables associated with a lack of prenatal diagnosis were lower SEQ, rural address, further distance in miles or time to a care center, and public insurance (Table 1). Younger maternal age was also associated with lack of PND, as was singleton pregnancy compared to multiple gestation pregnancy. When stratifying by country and lesion in unadjusted analyses, lower SEQ was only associated with lack of PND for TGA in the US (RR for SEQ 1 versus 4 0.69, 95%CI 0.57–0.84, Table 2). Further distance from a care center was associated with lack of PND of TGA in the US, which was most significant in the third quartile of distance (RR 0.71, 95% CI 0.58–0.88,Table 2). Although no association between further distance and lack of PND of HLHS was noted in the US cohort, an association was noted in the Canadian cohort however given small numbers further study is needed.

Adjusted analyses were then performed adjusting for maternal age and accounting for hospital clustering. Stratified analyses could not be stably adjusted for multiple gestation pregnancies given the infrequency overall, with only 3 patients in the no prenatal diagnosis group. Within the United States, adjusted analyses demonstrated that PND was 6% less

likely (RR = 0.94, 95% CI: 0.9–0.99) among HLHS subjects in the lowest SEQ compared to those in the highest SEQ and up to 22% less likely (RR= 0.78, 95% CI: 0.64–0.85) among TGA subjects in the lowest SEQ (1) compared to the highest SEQ (Table 3). This trend was not observed in the Canadian population. In the US, PND was less common among Hispanic mothers compared to non-Hispanic White mothers (HLHS: 0.97 95%CI 0.94–1.00; TGA: RR= 0.85, 95%CI: 0.72–0.99) and in those that lived in a rural location compared to an urban location (RR= 0.78, 95%CI: 0.64–0.95) in the TGA group. In the US, insurance, Black race, driving distance and time to surgical center were not associated with prenatal detection in the adjusted analysis. In the unadjusted analyses of the Canadian cohort, further distance from a care center was associated with lack of PND in HLHS in Quartile 3, but not in TGA. For Quartile 4, patients in the US and Canada may have traveled for second opinions after initial fetal diagnosis at a site in their region. We queried 5 US centers and of the 181 patients in quartile 4 in those centers 87.8% were second opinions.

Associations with Gestational Age at Time of PND:

When examining associations between independent variables and gestational age at prenatal diagnosis, lower SEQ was associated with later gestational age at PND for both HLHS and TGA in both the US and Canada (Table 4). In the US, public insurance, rural residence, and further DOR were all associated with a later gestational age at PND for both HLHS and TGA. In Quartile 4, this may reflect second opinions. In the United States, Hispanic ethnicity was associated with later gestational age at diagnosis for HLHS. In Canada, further DOR in Quartile 3 was associated with later gestational age at diagnosis for TGA.

DISCUSSION

Our study evaluated a large, geographically diverse group of patients to determine associations between social determinants of health and rates of PND. We found that in the United States, lower SEQ was associated with lower PND of HLHS and TGA; for TGA, Hispanic ethnicity and rural location were also associated with decreased PND. Among Canadian patients, only further distance to a cardiac surgical center was associated with lower PND rates of HLHS, demonstrating differences between two countries with different healthcare systems. Our study adds more granular detail to earlier work showing that demographic and socioeconomic factors have a relationship with PND of CHD on a large scale with data from a large cohort of North American patients.

Prior studies in North America regarding the influences of race/ethnicity, insurance, and socioeconomic position on PND have been obtained from single center or regional studies and are conflicting or evaluate different parameters.[9,10,17] A study by Peiris et al. evaluated all critical CHD in Boston between 2003 and 2006 and found that higher socioeconomic position and private insurance were associated with increased rates of PND.[9] In contrast, in our United States cohort, public insurance (Medicare, Medicaid, or other government insurance such as military insurance) was not associated with decreased PND. This may be due to differences in eras or differences in regional influences versus national influences. Hill et al. studied children with critical CHD in Wisconsin and found that barriers to prenatal detection included need for outflow tract visualization, poverty, low population density area,

and absence of an extra-cardiac abnormality.[10] In our study, decreased PND was associated with Hispanic ethnicity among children with TGA, supporting prior studies.[18] Given the limitations of collecting self-reported race and ethnicity from retrospective data, we also used census tract data to assess the proportion of families in a given tract that were non-Hispanic Black, Hispanic, or Native American. For both the HLHS and TGA analyses, the effect estimates for those living in a census tract with >50% of those minorities mirrored those of Hispanic mothers, although not statistically significant. While the distribution of race and ethnicity in the United States cohort generally mirrors the country's racial/ethnic distribution, the conclusions may not be representative in individual areas with higher percentages of minority populations.

In the present study, we found overall prenatal detection rates of 92% for fetal HLHS and 58% for fetal TGA to be higher than previously reported, both before and after the publication of fetal echocardiography guidelines which include outflow tract evaluation.[11,19] After the initial publication of universal screening guidelines, nationwide PND rates were estimated to be around 67% for HLHS and 28% for TGA.[11] Following the most recent American Institute of Ultrasound in Medicine recommendations[19] for inclusion of outflow tract views in the evaluation of the fetal heart, diagnostic rates for DTGA have been reported at 30% - 41% in recent United States regional studies[20,21]although showing more of an improvement in Canadian studies.[22] Hence, while there has been a slow and steady trend towards increased PND, there continue to be clear discrepancies between detection rates of lesions such as HLHS that are readily identified on fetal four chamber views and TGA with intact ventricular septum that are frequently missed if outflow tract views are not systematically obtained.[11,17]There also continues to be regional variation in PND of both of these critical lesions. PND rates reported in different state-registry based studies have varied from 60–77% for HLHS and 17–36% for TGA.[7,11,17,23–25]Initial screening begins with obstetricians/radiologists who obtain cardiology or maternal fetal medicine consultation for screening indications or concerns of abnormality. Barriers to communication between these specialists may exist[26], so further effort is needed to study providers in the areas outlined in this manuscript.

Interestingly, despite universalized health care in Canada, the prenatal detection rates in the United States and Canada were almost identical in this study. There is regional variability of detection rates in Canada, and in this study only two centers, Alberta and Ontario, were studied. This may have been one reason for the lack of differences between the United States and Canada. The Canadian centers included were limited to those participating in the FHSRC, and had limitations in power to detect differences, but the authors felt it was important to include the positive findings which did highlight differences in the healthcare systems. Factors related to where and who performs the scan likely play a role and will require further investigation. Overall, the Canadian patients accounted for 20% of TGA patients and 10% of HLHS patients. While we cannot determine definitively why this is the case, it may reflect higher termination for HLHS; termination rates for prenatally diagnosed CHD in Canada are reported at 50% before 24 weeks,[27] and would reasonably be expected to be higher for single ventricle disease. Typically, at the Alberta/Calgary centers, the patients with HLHS would have still been included in the study because of a confirmatory fetal echocardiogram being done by a pediatric cardiologist. However, it is possible that

some patients in Toronto may have been seen by a pediatric cardiologist in the community and terminated before being seen by a provider at Hospital for Sick Children. This may have accounted for the lower overall percentage of Canadian patients with HLHS compared to the total.

Some factors associated with lack of PND (low SEQ, rural location) may have collinearity. The association of these factors with lack of PND could be related to access to specialized health care services which has been previously related to area deprivation.[28] The association of lower SEQ with lower PND was only seen in the United States, although patients with lower SEQ had later gestational age of diagnosis in both United States and Canadian subjects. While the total number of subjects was lower in the Canadian group, the inverse trend suggests that the differences are valid. This could suggest that universal healthcare may mitigate the effect of socioeconomic status on prenatal care and thus PND. There is precedent for this in neurodevelopmental outcomes after congenital heart disease surgery, which are more favorable in Canada than in the United States.[29]

In the final adjusted analyses, driving time and distance were not associated with lower PND in the United States, although effect estimates indicated a nominal association, and prior regional studies have shown otherwise.[4] However driving distance in the fourth quartile was associated with lower PND in Canada for HLHS and had lower effect estimates for quartile 3 in the small number of Canadian HLHS patients. Future directions include advanced geo-mapping studies to identify at risk locations, targeting outreach efforts on outflow tract screening to at-risk locations as well as assessment of the impact of strategies to mitigate the impact of distance to surgical center on PND, such as utilization of telehealth for remote fetal echocardiography assessments.

We hypothesize that the differences in findings between HLHS and TGA may identify a possibly etiology for the disparities in prenatal detection. HLHS can be diagnosed on a four chamber view, while TGA requires outflow tract screening and is potentially more likely to be detected by a subspecialist. The difference between the two diseases may point out a lack of presence of or access to subspecialist care for patients in lower SES quartiles, of Hispanic ethnicity, and in rural regions. Of further support to this hypothesis is that in twin pregnancies, which are typically referred to a sub-specialist and receive more frequent ultrasounds, detection rates were high for both HLHS and TGA. The high prenatal detection rates for HLHS suggest that complete lack of prenatal care is not the barrier to prenatal detection, since HLHS is detected at fairly high rates overall.

We also found that mothers of lower SEQ received later PND. Only those mothers in the highest SEQ had a mean GA at PND of less than 24 weeks. A stepwise effect was seen across quartiles. This is important as earlier time of diagnosis has implications for decision making and options regarding pregnancy termination, financial planning, coordination of care and arranging other testing. The average gestational age at PND in mothers of lower SEQ, for instance, was beyond the legal gestation for pregnancy termination in many North American jurisdictions, thus limiting choices for specific populations. There is also overlap of the rural regions with the lower SEQ regions, suggesting that further geo-mapping work may identify areas for targeted outreach. Improved access to the tertiary care sites for

pregnancies/fetuses who currently have disparate access is critical to improving cardiovascular health for infants with CHD. Further work will help identify the specific areas where patients are not being reached effectively by pediatric cardiac care centers and allow clinicians to develop efforts to reduce these disparities.

This constitutes the largest study to date evaluating the associations between sociodemographic and geographic factors and PND of HLHS and TGA. This study powered by the FHSRC has created a unique registry of data variables that has not been possible using existing hospital databases which often do not include information about prenatal care because of absent linkages between maternal and pediatric records. There was, however, an inherent limitation to our data collection of not being able to account for cases where there was not a PND but the fetus had CHD and the pregnancy was terminated for other reasons or there was fetal demise.

This study was also limited by the use of a dataset biased towards fetal cardiology centers and lack of nationalized autopsy data on fetuses that may have died prior to a CHD diagnosis, or that had pregnancy termination without involvement of the participating fetal cardiology programs. We considered this limitation during the study design, however, due to the lack of a national registry for CHD, and to linkages between fetal and postnatal data, the FHSRC was the most feasible avenue to investigate this question. At the time the study was conducted, to the authors' knowledge, no existing national or cardiology databases contained the necessary variables to conduct this study.

Additionally, there were limitations in reporting of race and ethnicity data, and Affordable Care Act information may have been inconsistently recorded as public or private amongst centers. Lack of unifying SEQ scores also limited our ability to combine US and Canadian data.

CONCLUSIONS

Barriers to prenatal detection of CHD, specifically TGA, include lower SEQ, Hispanic ethnicity, and rural residence. Factors associated with increased antenatal surveillance, such as multiple gestation pregnancy, are associated with a protective effect. Lower socioeconomic status may have less of an effect on PND in socialized health care systems such as are available in Canada, however distance of residence may still remain a source of inadequate access to prenatal screening, and mothers with lower SEQ still received a later prenatal diagnosis than those of higher SEQs. Efforts surrounding education about congenital heart disease detection, as well as improving linkages between the tertiary care surgical centers and primary care physicians may decrease these disparities.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements:

We acknowledge Catherine Ingbar, Nora Cleary, and Sarah Litt for their assistance.

Funding Sources:

This study was supported by the National Institute on Minority Health and Health Disparities of the NIH under award number P20MD000198. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. It was also supported through a Children's National Heart Institute Cardiology Patient Research Fund and Gloria and Steven Seelig. This publication was developed with the support of the Fetal Heart Society sponsoring institutions including: Children's National Hospital, University of California, San Francisco Benioff Children's Hospitals, The Hospital for Sick Children, University of Utah, Stanford Children's Health, Texas Children's Hospital, Columbia University Medical Center, Phoenix Children's Hospital, Children's Hospital of Minnesota, Rainbow Babies Hospital, Mount Sinai Hospital, Children's Health Dallas, Ann & Robert H Lurie Children's Hospital of Chicago, Nemours Children's Hospital, Cincinnati Children's Hospital, UK Health Care Kentucky Children's Hospital, Arkansas Children's Hospital, Health University of Utah. Without their contributions, the evolution of the Fetal Heart Society and this research would not have been possible.

Non-standard Abbreviations and Acronyms:

DOR	distance of residence
FHSRC	Fetal Heart Society Research Collaborative
HLHS	hypoplastic left heart syndrome
PND	prenatal diagnosis
SEQ	socioeconomic quartile
TGA	transposition of the great arteries

REFERENCES

1. Bonnet D, Coltri A, Butera G, Fermont L, Le Bidois J, Aggoun Y, Acar P, Villain E, Kachaner J, Sidi D. [Prenatal diagnosis of transposition of great vessels reduces neonatal morbidity and mortality]. Arch Mal Coeur Vaiss 1999;92:637–640. [PubMed: 10367081]
2. Tworetzky W, McElhinney DB, Reddy VM, Brook MM, Hanley FL, Silverman NH. Improved surgical outcome after fetal diagnosis of hypoplastic left heart syndrome. Circulation 2001;103:1269–1273. doi:10.1161/01.cir.103.9.1269. [PubMed: 11238272]
3. Donofrio MT, Levy RJ, Schuette JJ, Skurow-Todd K, Sten M-B, Stallings C, Pike JI, Krishnan A, Ratnayaka K, Sinha P, et al. Specialized delivery room planning for fetuses with critical congenital heart disease. Am J Cardiol 2013;111:737–747. doi:10.1016/j.amjcard.2012.11.029. [PubMed: 23291087]
4. Morris SA, Ethen MK, Penny DJ, Canfield MA, Minard CG, Fixler DE, Nembhard WN. Prenatal diagnosis, birth location, surgical center, and neonatal mortality in infants with hypoplastic left heart syndrome. Circulation 2014;129:285–292. doi:10.1161/CIRCULATIONAHA.113.003711. [PubMed: 24135071]
5. Calderon J, Angeard N, Moutier S, Plumet M-H, Jambaqué I, Bonnet D. Impact of prenatal diagnosis on neurocognitive outcomes in children with transposition of the great arteries. J Pediatr 2012;161:94–98.e1. doi:10.1016/j.jpeds.2011.12.036. [PubMed: 22284567]
6. Peyvandi S, De Santiago V, Chakkarapani E, Chau V, Campbell A, Poskitt KJ, Xu D, Barkovich AJ, Miller S, McQuillen P. Association of Prenatal Diagnosis of Critical Congenital Heart Disease With Postnatal Brain Development and the Risk of Brain Injury. JAMA Pediatr 2016;170:e154450. doi:10.1001/jamapediatrics.2015.4450. [PubMed: 26902528]
7. Friedberg MK, Silverman NH, Moon-Grady AJ, Tong E, Nourse J, Sorenson B, Lee J, Hornberger LK. Prenatal detection of congenital heart disease. J Pediatr 2009;155:26–31, 31.e1. doi:10.1016/j.jpeds.2009.01.050. [PubMed: 19394031]

8. van Velzen CL, Ket JCF, van de Ven PM, Blom NA, Haak MC. Systematic review and meta-analysis of the performance of second-trimester screening for prenatal detection of congenital heart defects. Int J Gynaecol Obstet 2018;140:137–145. doi:10.1002/ijgo.12373. [PubMed: 29094357]

9. Peiris V, Singh TP, Tworetzky W, Chong EC, Gauvreau K, Brown DW. Association of socioeconomic position and medical insurance with fetal diagnosis of critical congenital heart disease. Circ Cardiovasc Qual Outcomes 2009;2:354–360. doi:10.1161/CIRCOUTCOMES.108.802868. [PubMed: 20031861]

10. Hill GD, Block JR, Tanem JB, Frommelt MA. Disparities in the prenatal detection of critical congenital heart disease. Prenat Diagn 2015;35:859–863. doi:10.1002/pd.4622. [PubMed: 25989740]

11. Quartermain MD, Pasquali SK, Hill KD, Goldberg DJ, Huhta JC, Jacobs JP, Jacobs ML, Kim S, Ungerleider RM. Variation in Prenatal Diagnosis of Congenital Heart Disease in Infants. Pediatrics 2015;136:e378–385. doi:10.1542/peds.2014-3783. [PubMed: 26216324]

12. Diez Roux AV, Merkin SS, Arnett D, Chambless L, Massing M, Nieto FJ, Sorlie P, Szklo M, Tyroler HA, Watson RL. Neighborhood of residence and incidence of coronary heart disease. N Engl J Med 2001;345:99–106. doi:10.1056/NEJM200107123450205. [PubMed: 11450679]

13. Chan E, Serrano J, Chen L, Stieb DM, Jerrett M, Osornio-Vargas A. Development of a Canadian socioeconomic status index for the study of health outcomes related to environmental pollution. BMC Public Health 2015;15:714. doi:10.1186/s12889-015-1992-y. [PubMed: 26215141]

14. United States Census Bureau; American Community Survey Reports 2010, Changes in Areas With Concentrated Poverty: 2000 to 2010, generated by Alemayehu Bishaw in June 2014. Retrieved from https://www.census.gov/library/publications/2014/acs/acs-27.html

15. United States Department of Agriculture (2013), Economic Research Service; Rural-Urban Continuum Codes. Updated 2020. Retrieved from https://www.ers.usda.gov/data-products/rural-urban-continuum-codes.aspx

16. United States Census Bureau (2015); American Community Survey 5-year Data Profiles, Table DP05 2015. Retrieved from https://data.census.gov/cedsci/table?q=DP05&tid=ACSDP5Y2015.DP05&hidePreview=false

17. Pinto NM, Keenan HT, Minich LL, Puchalski MD, Heywood M, Botto LD. Barriers to prenatal detection of congenital heart disease: a population-based study. Ultrasound Obstet Gynecol 2012;40:418–425. doi:10.1002/uog.10116. [PubMed: 21998002]

18. Ailes EC, Gilboa SM, Riehle-Colarusso T, Johnson CY, Hobbs CA, Correa A, Honein MA, National Birth Defects Prevention Study. Prenatal diagnosis of nonsyndromic congenital heart defects. Prenat Diagn 2014;34:214–222. doi:10.1002/pd.4282. [PubMed: 24222433]

19. American Institute of Ultrasound in Medicine. AIUM practice guideline for the performance of fetal echocardiography. J Ultrasound Med 2013;32:1067–1082. doi:10.7863/ultra.32.6.1067. [PubMed: 23716531]

20. Sun HY, Proudfoot JA, McCandless RT. Prenatal detection of critical cardiac outflow tract anomalies remains suboptimal despite revised obstetrical imaging guidelines. Congenit Heart Dis 2018;13:748–756. doi:10.1111/chd.12648. [PubMed: 30022603]

21. Escobar-Diaz MC, Freud LR, Bueno A, Brown DW, Friedman KG, Schidlow D, Emani S, Del Nido PJ, Tworetzky W. Prenatal diagnosis of transposition of the great arteries over a 20-year period: improved but imperfect. Ultrasound Obstet Gynecol 2015;45:678–682. doi:10.1002/uog.14751. [PubMed: 25484180]

22. Ravi P, Mills L, Fruitman D, Savard W, Colen T, Khoo N, Serrano-Lomelin J, Hornberger LK. Population trends in prenatal detection of transposition of great arteries: impact of obstetric screening ultrasound guidelines. Ultrasound Obstet Gynecol 2018;51:659–664. doi:10.1002/uog.17496. [PubMed: 28436133]

23. Acherman RJ, Evans WN, Luna CF, Rollins R, Kip KT, Collazos JC, Restrepo H, Adasheck J, Iriye BK, Roberts D, et al. Prenatal detection of congenital heart disease in southern Nevada: the need for universal fetal cardiac evaluation. J Ultrasound Med 2007;26:1715–1719; quiz 1720–1721. doi:10.7863/jum.2007.26.12.1715. [PubMed: 18029923]

24. Sekar P, Heydarian HC, Cnota JF, Hornberger LK, Michelfelder EC. Diagnosis of congenital heart disease in an era of universal prenatal ultrasound screening in southwest Ohio. Cardiol Young 2015;25:35–41. doi:10.1017/S1047951113001467. [PubMed: 24107431]

25. Sklansky MS, Berman DP, Pruetz JD, Chang R-KR. Prenatal screening for major congenital heart disease: superiority of outflow tracts over the 4-chamber view. J Ultrasound Med 2009;28:889–899. doi:10.7863/jum.2009.28.7.889. [PubMed: 19546331]

26. Pinto NM, Henry KA, Grobman WA, Ness A, Miller S, Ellestad S, Gotteiner N, Tacy T, Wei G, Minich LL, et al. Physician Barriers and Facilitators for Screening for Congenital Heart Disease With Routine Obstetric Ultrasound: A National United States Survey. J Ultrasound Med 2020;39:1143–1153. doi:10.1002/jum.15199. [PubMed: 31875341]

27. Trines J, Fruitman D, Zuo KJ, Smallhorn JF, Hornberger LK, Mackie AS. Effectiveness of prenatal screening for congenital heart disease: assessment in a jurisdiction with universal access to health care. Can J Cardiol 2013;29:879–885. doi:10.1016/j.cjca.2013.04.028. [PubMed: 23725863]

28. Vos AA, Posthumus AG, Bonsel GJ, Steegers EAP, Denktaş S. Deprived neighborhoods and adverse perinatal outcome: a systematic review and meta-analysis. Acta Obstet Gynecol Scand 2014;93:727–740. doi:10.1111/aogs.12430. [PubMed: 24834960]

29. Peyvandi S, Chau V, Guo T, Xu D, Glass HC, Synnes A, Poskitt K, Barkovich AJ, Miller SP, McQuillen PS. Neonatal Brain Injury and Timing of Neurodevelopmental Assessment in Patients With Congenital Heart Disease. J Am Coll Cardiol 2018;71:1986–1996. doi:10.1016/j.jacc.2018.02.068. [PubMed: 29724352]

CLINICAL PERSPECTIVE:

What is new?

- This is the largest multicenter study to our knowledge to identify socioeconomic, race/ethnic, and geographic barriers to the prenatal detection of critical congenital heart disease in North America
- This study finds that lower socioeconomic position, Hispanic ethnicity, and rural residence are associated with decreased prenatal detection rates of hypoplastic left heart syndrome and transposition of the great arteries.

What are the clinical implications?

- Clinicians can use the findings of this study to focus efforts on improving overall prenatal detection rates for congenital heart disease
- Clinicians can specifically improve health equity in prenatal detection of congenital heart disease and timing of prenatal detection by improving linkages between the tertiary care center and the populations and regions identified in this study

Table 1:

Socioeconomic, demographic and clinical characteristics of the cohort by prenatal diagnosis

Demographic and clinical Characteristics	Prenatal diagnosis			p-value
	Overall 1862	No 386 (20.8%)	Yes 1473 (79.2%)	
	n (%)	n (%)	n (%)	
Diagnosis				**< 0.0001**
HLHS	1171 (62.9)	96 (8.2)	1072 (91.8)	
TGA	691 (37.1)	290 (42.0)	401 (58.0)	
Socioeconomic characteristics				
SES quartile (1 is lowest)				**0.03**
1	454 (25.0)	98 (21.6)	355 (78.4)	
2	454 (25.0)	102 (22.5)	352 (77.5)	
3	450 (25.0)	99 (22.1)	349 (77.9)	
4	459 (25.0)	72 (15.7)	387 (84.3)	
Poverty (>20% of census block) *				0.89
No	1226 (77.8)	243 (19.8)	983 (80.2)	
Yes	349 (22.2)	68 (19.5)	281 (80.5)	
Neighborhood population >50% Black or Hispanic *				0.34
No	1226 (77.9)	236 (19.3)	990 (80.7)	
Yes	348 (22.1)	75 (21.5)	273 (78.5)	
Rural location (4–9) *				**0.02**
No	1368 (86.8)	257 (18.8)	1111 (81.2)	
Yes	208 (13.2)	54 (26.0)	154 (74.0)	
At risk geographic location *				1.00
No	1226 (99.4)	258 (21.0)	968 (79.0)	
Yes	7 (0.6)	1 (14.3)	6 (85.7)	
Driving distance to care center				**0.002**
1 (< 20 miles)	479 (25.9)	80 (16.7)	398 (83.3)	
2 (20 – 49 miles)	448 (24.3)	98 (22.0)	348 (78.0)	
3 (50 – 134 miles)	458 (24.8)	120 (26.2)	338 (73.8)	
4 (≥ 135 miles)	462 (25.0)	86 (18.6)	376 (81.4)	
Driving time to care center				**0.004**
1 (< 30 minutes)	422 (24.4)	66 (15.6)	356 (84.4)	
2 (30 – 59 minutes)	466 (26.9)	94 (20.2)	371 (79.8)	
3 (60 – 119 minutes)	362 (20.9)	95 (26.2)	267 (73.8)	
4 (≥ 120 minutes)	481 (27.8)	100 (20.8)	381 (79.2)	

Demographic and clinical Characteristics	Prenatal diagnosis			p-value
	Overall 1862	No 386 (20.8%)	Yes 1473 (79.2%)	
	n (%)	n (%)	n (%)	
Maternal insurance *				**0.01**
Private	702 (57.3)	121 (17.2)	581(82.8)	
Public †	524(42.7)	106 (20.2)	418 (79.8)	
Maternal Characteristics				
Maternal race/ethnicity				0.33
White, non-Hispanic	986 (68.0)	149 (16.1)	776 (83.9)	
Black, non-Hispanic	165 (11.8)	30 (18.7)	130 (81.3)	
Hispanic/Latino	210 (15.3)	43 (20.7)	165 (79.3)	
Asian	58 (3.7)	11 (22.0)	39 (78.0)	
Native American/Alaskan/PI	25 (1.3)	5 (27.8)	13 (72.2)	
Maternal age (mean, SD)	29.1 (5.9)	28.2 (5.7)	29.3 (5.9)	**0.008**
English as primary language				0.33
No	139 (8.0)	30 (21.6)	109 (78.4)	
Yes	1597 (92.0)	291 (18.2)	1305 (81.8)	
Fetal/Infant Characteristics				
Extracardiac birth defect				0.29
No	1594 (89.8)	318 (19.9)	1276 (80.1)	
Yes	180 (10.2)	30 (16.7)	150 (83.3)	
Multiple gestation pregnancy				**0.0002**
No	1765 (95.3)	378 (21.4)	1386 (78.6)	
Yes	87 (4.7)	4 (4.6)	83 (95.4)	

* US only

† All Canadian records except 3 are publicly insured

p-value based on t-test (continuous) or chi-square (categorical); numbers in bold significant at $p < 0.05$

Table 2:

Unadjusted associations between socioeconomic variables and prenatal diagnosis by diagnosis and country

Socioeconomic risk characteristics	United States*		Canada†	
	HLHS	TGA	HLHS	TGA
	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
SES quartile (1 is lowest)				
1	0.95 (0.81 – 1.00)	**0.69 (0.57 – 0.84)**	1.08 (0.97 – 1.19)	1.05 (0.72 – 1.53)
2	0.98 (0.93 – 1.02)	**0.71 (0.59 – 0.86)**	0.97 (0.82 – 1.13)	0.88 (0.59 – 1.32)
3	0.96 (0.92 – 1.01)	**0.75 (0.63 – 0.91)**	0.99 (0.83 – 1.16)	0.80 (0.52 – 1.23)
4	Ref.	Ref.	Ref.	Ref.
Poverty (>20% of census block)				
No	Ref.	Ref.	--	--
Yes	1.00 (0.96 – 1.04)	0.87 (0.71 – 1.07)		
Neighborhood population >50% Black or Hispanic				
No	Ref.	Ref.	--	--
Yes	0.98 (0.93 – 1.02)	0.81 (0.66 – 1.01)		
Rural location (4–9)				
No	Ref.	Ref.	--	--
Yes	0.96 (0.90 – 1.02)	0.77 (0.60 – 1.00)		
Driving distance to care center				
1 (< 20 miles)	Ref.	Ref.	Ref.	Ref.
2 (20 – 49 miles)	0.99 (0.94 – 1.04)	0.84 (0.70 – 1.00)	1.02 (0.98 – 1.07)	1.09 (0.74 – 1.59)
3 (50 – 134 miles)	0.97 (0.92 – 1.02)	**0.71 (0.58 – 0.88)**	**0.80 (0.66 – 0.97)**	0.70 (0.43 – 1.13)
4 (≥ 135 miles)	0.98 (0.94 – 1.03)	0.87 (0.71 – 1.04)	0.95 (0.84 – 1.06)	1.16 (0.82 – 1.64)
Driving time to care center				
1 (< 30 minutes)	Ref.	Ref.	Ref.	Ref.
2 (30 – 59 minutes)	0.99 (0.94 – 1.04)	0.91 (0.77 – 1.08)	0.95 (0.86 – 1.05)	1.07 (0.67 – 1.70)
3 (60 – 119 minutes)	0.97 (0.92 – 1.02)	**0.66 (0.53 – 0.83)**	0.88 (0.73 – 1.05)	0.65 (0.34 – 1.26)
4 (≥ 120 minutes)	0.98 (0.94 – 1.03)	0.87 (0.72 – 1.05)	0.80 (0.62 – 1.03)	0.78 (0.44 – 1.39)
Maternal insurance				
Private	Ref.	Ref.	--	--
Public	0.97 (0.93 – 1.01)	0.88 (0.75–1.04)		
Maternal race/ethnicity				
White, non-Hispanic	Ref.	Ref.		
Black, non-Hispanic	0.98 (0.93 – 1.04)	0.75 (0.54 – 1.03)		
Hispanic/Latino	0.97 (0.92 – 1.03)	0.78 (0.60 – 1.01)	--	--
Asian	0.95 (0.83 – 1.08)	1.00 (0.73 – 1.36)		

Socioeconomic risk characteristics	United States*		Canada†	
	HLHS	TGA	HLHS	TGA
	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
Native American/Alaskan/PI	0.89 (0.69 – 1.14)	0.77 (0.34 – 1.71)		

*Estimates based on log-binomial regression

†Estimates based on log-binomial regression or log-Poisson regression with robust standard errors

Numbers in bold significant at $p < 0.05$

Table 3:

Adjusted associations between socioeconomic variables and prenatal diagnosis by diagnosis and country

Socioeconomic risk characteristics	United States*		Canada†	
	HLHS	TGA	HLHS	TGA
	aRR (95% CI)	aRR (95% CI)	aRR (95% CI)	aRR (95% CI)
SES quartile (1 is lowest)				
1	**0.94 (0.90 – 0.99)**	**0.78 (0.64 – 0.85)**	1.00 (1.00 – 1.00)	1.17 (0.95 – 1.44)
2	0.97 (0.91 – 1.02)	**0.77 (0.64 – 0.93)**	0.96 (0.89 – 1.04)	0.90 (0.69 – 1.18)
3	0.96 (0.91 – 1.01)	0.83 (0.69 – 1.00)	0.95 (0.86 – 1.05)	**0.86 (0.76 – 0.97)**
4	Ref.	Ref.	Ref.	Ref.
Poverty (>20% of census block)				
No	Ref.	Ref.	--	--
Yes	1.00 (0.97 – 1.03)	0.97 (0.83 – 1.13)		
Neighborhood population >50% Black or Hispanic			--	--
No	Ref.	Ref.		
Yes	0.97 (0.94 – 1.00)	0.85 (0.70 – 1.04)		
Rural location (4–9)				
No	Ref.	Ref.	--	--
Yes	0.97 (0.92 – 1.02)	**0.78 (0.64 – 0.95)**		
Driving distance to care center				
1 (< 20 miles)	Ref.	Ref.	Ref.	**Ref.**
2 (20 – 49 miles)	1.00 (0.95 – 1.05)	0.88 (0.76 – 1.02)	1.00 (1.00 – 1.00)	**1.09 (1.04 – 1.15)**
3 (50 – 134 miles)	0.99 (0.95 – 1.02)	0.82 (0.67 – 1.01)	0.96 (0.89 – 1.04)	0.91 (0.67 – 1.24)
4 (≥ 135 miles)	1.00 (0.96 – 1.03)	0.94 (0.75 – 1.17)	0.96 (0.93 – 1.00)	**1.24 (1.03 – 1.51)**
Driving time to care center				
1 (< 30 minutes)	Ref.	Ref.		
2 (30 – 59 minutes)	1.00 (0.95 – 1.04)	0.93 (0.83 – 1.04)	--	--
3 (60 – 119 minutes)	1.00 (0.96 – 1.04)	0.83 (0.65 – 1.06)		
4 (≥ 120 minutes)	0.99 (0.95 – 1.03)	0.88 (0.71 – 1.09)		
Maternal insurance				
Private	Ref.	Ref.	--	--
Public	0.98 (0.94 – 1.02)	0.95 (0.81–1.13)		
Maternal race/ethnicity				
White, non-Hispanic	Ref.	Ref.		
Black, non-Hispanic	0.98 (0.94 – 1.01)	0.87 (0.66 – 1.16)		
Hispanic/Latino	0.97 (0.94 – 1.00)	**0.85 (0.72 – 0.99)**	--	--
Asian	0.97 (0.84 – 1.11)	0.97 (0.72 – 1.29)		

Socioeconomic risk characteristics	United States*		Canada†	
	HLHS	TGA	HLHS	TGA
	aRR (95% CI)	aRR (95% CI)	aRR (95% CI)	aRR (95% CI)
Native American/Alaskan/PI	0.88 (0.69 – 1.12)	0.83 (0.34 – 2.03)		

*Estimates based on log-binomial regression with clustering by site, adjusted for maternal age

†Estimates based on log-Poisson regression with robust standard errors with clustering by site, adjusted for maternal age

Numbers in bold significant at $p < 0.05$

Table 4:

Association of sociodemographic variables with gestational age at time of prenatal diagnosis of hypoplastic left heart syndrome and D-transposition of the great arteries in the United States and Canada

Socioeconomic risk characteristics	United States		Canada	
	HLHS	TGA	HLHS	TGA
	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)
SES quartile (1 is lowest)				
1	**25.4 (23.7 – 27.0)**	**27.8 (26.7 – 29.0)**	**24.4 (22.6 – 26.1)**	**25.4 (23.0 – 27.8)**
2	**24.9 (24.0 – 25.9)**	**26.7 (25.8 – 27.7)**	**22.0 (21.0 – 23.0)**	**25.5 (25.4 – 25.6)**
3	**24.4 (23.3 – 25.4)**	**25.1 (24.2 – 26.0)**	22.7 (21.9 – 23.5)	**23.2 (22.4 – 24.0)**
4 (reference)	22.3 (21.5 – 23.2)	23.6 (22.7 – 24.6)	22.4 (21.1 – 23.7)	22.0 (20.4 – 23.7)
Neighborhood population >50% Black or Hispanic				
No	24.2 (23.2 – 25.1)	25.5 (23.9 – 27.1)		
Yes	24.7 (23.3 – 26.0)	25.5 (24.5 – 26.5)		
Rural location (4–9)				
No (reference)	24.2 (23.2 – 25.2)	25.3 (24.4 – 26.1)		
Yes	**25.0 (24.2 – 25.9)**	**27.4 (25.8 – 29.0)**		
Driving distance to care center				
1 (< 20 miles, reference)	23.5 (22.6 – 24.4)	24.8 (23.6 – 26.0)	22.8 (20.5 – 25.1)	24.4 (22.4 – 26.5)
2 (20 – 49 miles)	23.7 (22.6 – 24.8)	24.3 (22.9 – 25.7)	22.4 (22.0 – 22.9)	23.8 (22.3 – 25.4)
3 (50 – 134 miles)	24.0 (22.8 – 25.1)	25.0 (24.1 – 25.9)	23.9 (22.9 – 24.9)	**25.1 (22.6 – 27.6)**
4 (≥ 135 miles)	**26.2 (24.3 – 28.1)**	**28.3 (26.9 – 29.7)**	22.5 (21.2 – 23.9)	**23.3 (20.1 – 26.5)**
Driving time to care center *				
1 (< 30 minutes, reference)	23.3 (22.5 – 24.2)	24.5 (23.3 – 25.7)	24.4 (22.4 – 26.4)	25.2 (22.3 – 28.1)
2 (30 – 59 minutes)	23.9 (22.8 – 25.1)	24.6 (23.5 – 25.7)	22.3 (20.1 – 24.4)	22.9 (20.6 – 25.3)
3 (60 – 119 minutes)	23.8 (22.5 – 25.1)	24.9 (23.9 – 26.0)	21.9 (19.5 – 24.4)	26.1 (22.7 – 29.5)
4 (≥ 120 minutes)	**26.1 (24.2 – 27.9)**	**28.3 (26.9 – 29.6)**	25.6 (22.9 – 28.2)	27.2 (24.2 – 30.2)
Maternal insurance				
Private (reference)	24.0 (23.2 – 24.8)	25.2 (24.1 – 26.2)		
Public	**25.3 (24.2 – 26.4)**	**26.7 (25.8 – 27.7)**		
Maternal race/ethnicity				
White, non-Hispanic (reference)	24.0 (23.1 – 24.9)	25.2 (24.1 – 26.4)		
Black, non-Hispanic	25.0 (23.2 – 26.8)	26.1 (22.8 – 29.3)		
Hispanic/Latino	**25.3 (24.0 – 26.7)**	25.9 (24.3 – 27.6)		
Other	25.1 (23.2 – 27.0)	24.2 (23.2 – 25.2)		

Least squares means estimates from generalized linear models controlling for maternal age with clustering by site; numbers in bold significant at $p < 0.05$

* Unable to control for site and maternal age; information provided for one Canadian site only