Trends in Preterm Delivery among Singleton Gestations with Critical Congenital Heart Disease

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Objective To examine state-wide population trends in preterm delivery of children with critical congenital heart disease (CHD) over an 18-year period. We hypothesized that, coincident with early advancements in prenatal diagnosis, preterm delivery initially increased compared with the general population, and more recently has decreased.

Study design Data from the Texas Public Use Data File 1999-2016 was used to evaluate annual percent preterm delivery (<37 weeks) in critical CHD (diagnoses requiring intervention at <1 year of age). We first evaluated for pattern change over time using joinpoint segmented regression. Trends in preterm delivery were then compared with all Texas livebirths. We then compared trends examining sociodemographic covariates including race/ethnicity, sex, and neighborhood poverty levels.

Results Of 7146 births with critical CHD, 1339 (18.7%) were delivered preterm. The rate of preterm birth increased from 1999 to 2004 (a mean increase of 1.69% per year) then decreased between 2005 and 2016 (a mean decrease of −0.41% per year). This represented a faster increase and then a similar decrease to that noted in the general population. Although the greatest proportion of preterm births occurred in newborns of Hispanic ethnicity and non-Hispanic black race, newborns with higher neighborhood poverty level had the most rapidly increasing rate of preterm delivery in the first era, and only a plateau rather than decrease in the latter era.

Conclusions Rates of preterm birth for newborns with critical CHD in Texas first were increasing rapidly, then have been decreasing since 2005. *(J Pediatr 2020;222:28-34)*.

Aprenatal diagnosis of congenital heart disease (CHD) has been associated with improved preoperative clinical status, neurodevelopmental outcomes, and decreased mortality.[1-8] This likely results from coordination of resources and in utero transport of the fetus with CHD to appropriate care facilities with rapid delivery of postnatal therapy.[9] Although the benefits of prenatal diagnosis of CHD have been reported, many studies show no benefit and some studies suggest that infants with a prenatal diagnosis have increased mortality.[2,4,5,9-18]

One possible contributor to the apparent lack of benefit of prenatal diagnosis is that infants with a prenatal diagnosis of CHD are more likely to be delivered at earlier gestational ages than those without a prenatal diagnosis.[1,5,19-21] Earlier delivery may result from institutions performing induction of labor or a planned cesarean delivery before natural labor occurs. This strategy may decrease the beneficial impact of prenatal diagnosis, because preterm infants with CHD have worse outcomes than those born at term.[22-26] A study in Utah demonstrated that even early term birth (37-38 weeks) is associated with increased mortality compared with later term birth.[27] A-single center study identified that preterm and early term birth in infants with critical CHD (CCHD; defined as lesions that require intervention early in life) were associated with worse outcomes than later term birth.[28] Since then, multicenter studies have supported these findings.[24,29,30] These studies emphasize that that every week in utero is important and advocate for efforts to extend the duration of pregnancy in situations where a prenatal diagnosis of CCHD is made with no clear indication for early delivery.[31] Such considerations hold true for the general population; the American College of Obstetricians and Gynecologists has advocated against elective deliveries at less than 39 weeks of gestation.[32,33]

We sought to determine if the proportion of preterm births in children diagnosed with CCHD changed between 1999 and 2016 in a large, diverse, population-based cohort. We hypothesized that the proportion of preterm

CCHD	Critical CHD
CHD	Congenital heart disease
HLHS	Hypoplastic left heart syndrome
ICD-CM	*International Classification of Diseases, Clinical Modification*
NCHS	National Center for Health Statistics
RR	Relative risk
TBDR	Texas Birth Defects Registry
TPUIDF	Texas Public Use Inpatient Data File

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CCHD births would increase initially, coinciding with improving rates of prenatal diagnosis in the 1990s and 2000s, but would then decrease, owing to changing medical management after publications about risks of preterm and early term birth in CCHD.[34,35] We also investigated the potential influence of race/ethnicity, sex, and neighborhood poverty level on trends.

Methods

We conducted a retrospective, population-based study using the 1999-2016 Texas Public Use Inpatient Data File (TPUIDF). The TPUIDF is a nonsampled, population-based, administrative database that includes all state licensed hospitals (except for a small proportion that are statutorily exempt from the reporting requirement before 2015, accounting for an estimated <3% of state birth hospitalizations).[36] The Texas Department of State Health Services validates the data through automated auditing and verification. Up to 25 discharge diagnoses and 25 procedures are coded with the use of the *International Classification of Diseases* (ICD), *Ninth Revision, Clinical Modification* (ICD-9-CM) through September 30, 2015, and ICD-10-CM codes from October 1, 2015, onwards. The Institutional Review Board of the Baylor College of Medicine determined that this activity did not constitute human subjects research, and therefore was exempt from review.

We included all birth hospitalizations with any diagnosis code indicative of CCHD. A birth hospitalization was defined as a discharge with either a diagnostic code for live-born infant or a source of admission coded as a newborn from inside the hospital. We defined CCHD as a CHD likely to require a cardiac intervention within the first year of life (**Table I**; available at www.jpeds.com). Given the heterogeneity in presentation and diagnosis of aortic arch obstruction, only infants with codes for both arch obstruction and arch intervention during birth hospitalization were included (**Table II**; available at www.jpeds.com). Exclusion criteria included a diagnosis of multiple gestation birth, unknown sex, genetic syndrome, or extracardiac birth defects (**Table III**; available at www.jpeds.com).

The primary outcome was preterm birth, defined as birth at less than 37 weeks of gestation using ICD-9-CM and ICD-10-CM codes (**Table IV**; available at www.jpeds.com). ICD-9-CM codes do not distinguish between early and late term births, so this variable could not be investigated. We examined covariates to define the population and evaluate for confounders, including sex, race/ethnicity, and insurance. Public insurance included federal programs apart from military insurance. To account for socioeconomic status, percent of the population living in poverty in the discharge home zip code was determined using publicly available US Census data (2000 Census data for 1999-2006, 2010 Census data for 2007-2011, American Community Survey for 2012-2016).[37] Poverty levels were dichotomized between less than 20% of a zip code living in poverty and 20% or greater, because 20% or greater define the poverty area by the US Census.[38]

Statistical Analyses

For validation of the dataset, we first compared the number of annual live births in our dataset to those published for Texas by the National Center for Health Statistics (NCHS).[39] Of note, some difference was expected because the NCHS dataset includes information on home births. For further validation, we then compared the total live births in our dataset with those in the Texas Birth Defects Registry (TBDR) for a sample of lesions: hypoplastic left heart syndrome (HLHS), truncus arteriosus, and tetralogy of Fallot. Some difference was also expected, because our dataset only included hospitalizations during which a diagnosis was made before the end of the newborn hospitalization, whereas the TBDR captures diagnoses made through the first year of life. Then, after applying inclusion and exclusion criteria, discharge characteristics and diagnoses were compared between infants with and without preterm birth using generalized estimating equations accounting for clustering by hospital using log-binomial regression to estimate relative risk (RR).

To evaluate change in percent of preterm births over time, joinpoint segmented regression was performed to identify any temporal changes in the data. This process delineated a significant change after 2004. First, crude rates and rates of change of preterm delivery before and after 2004 were reported in the group with CCHD and compared with the NCHS data for all Texas births using linear regression, stratified by the 2 eras. Then analyses were performed using generalized estimating equations with log-binomial regression employing autoregression and hierarchical modeling accounting for clustering by hospital to calculate RR per year in the two eras. Models were created (model 1) for the entire cohort, accounting only for time (using year, a binary division <2004 and >2004, and an interaction of the two to allow for separate slopes) and delivery hospital. Then multivariable analysis was performed accounting for time, hospital, and demographics (model 2). The analysis was stratified by race/ethnicity and then by poverty in secondary models to allow better estimates of changes in preterm birth within subgroups (models 3 and 4, respectively).

A subanalysis was then performed limiting the study population to CCHD lesions likely to be prenatally diagnosed: tricuspid atresia, HLHS, pulmonary atresia, other single ventricle lesions, and combinations of these lesions.[40] We performed the same analyses with this subpopulation as the entire cohort. Statistical analysis was performed on SAS version 9.4 (SAS Institute, Cary, North Carolina).

Results

Annual live births in the TPUIDF ranged from a minimum of 326 348 in 1999 to a maximum of 400 443 in 2015. There were 3.4% fewer live births in TPUIDF relative to live births

reported by the NCHS (6 707 262 vs 6 945 023, respectively). When comparing live births with selected CCHD in the TPUIDF with that of the TBDR, the case counts were as follows: HLHS, 1248 vs 1336; truncus arteriosus, 454 vs 519; and tetralogy of Fallot, 2220 vs 2298 in the TPUIDF vs the TBDR, respectively.

A total of 7146 total births fulfilled CCHD inclusion criteria (**Figure 1**; available at www.jpeds.com), of which 1339 (18.7%) were born preterm (**Table V**). Variables associated with higher percentage of preterm birth included Hispanic ethnicity, non-Hispanic black race, living in a high poverty neighborhood, and having public health insurance. We observed considerable variation in preterm prevalence by type of CCHD, from 11.2% to 31.6%. Transposition of the great arteries was used as the reference owing to having the lowest defect-specific percentage of premature births and owing to its historically poor rates of prenatal diagnosis.[41]

Table V. Univariable analysis of characteristics associated with preterm delivery among infants with CCHD

Characteristics	All, n	Preterm, n (%)	RR (95% CI)	*P* value
CCHD	7146	1339 (18.7)		
Sex				.077
Male	4188	756 (18.1)	Reference	
Female	2958	583 (19.7)	1.09 (0.99-1.20)	
Race/ethnicity				
Non-Hispanic white	2568	434 (16.9)	Reference	
Hispanic	3072	593 (19.3)	1.14 (1.02-1.28)	.020
Non-Hispanic black	667	162 (24.3)	1.44 (1.23-1.68)	<.001
Other/missing	839	150 (17.9)	1.06 (0.89-1.25)	.513
Poverty level of zip code				
<20%	4668	821 (17.6)	Reference	<.001
≥20%	2233	475 (21.3)	1.21 (1.09-1.34)	
Insurance				
Private	2685	477 (17.8)	Reference	
Medicare/other federal	3534	699 (19.8)	1.11 (1.00-1.24)	.045
Self-pay	284	46 (16.2)	0.91 (0.69-1.20)	.513
VA/CHAMPUS	114	13 (11.4)	0.64 (0.38-1.08)	.094
Other	99	21 (21.2)	1.19 (0.81-1.76)	.371
CCHD lesion				
Transposition of the great arteries	961	108 (11.2)	Reference	
Arch obstruction and VSD	164	21 (12.8)	1.14 (0.74-1.76)	.558
HLHS	899	121 (13.5)	1.20 (0.94-1.53)	.146
Total anomalous venous return	380	58 (15.3)	1.36 (1.01-1.83)	.043
Combination	540	87 (16.1)	1.43 (1.10-1.86)	.007
Other single ventricle	143	24 (16.8)	1.49 (1.00-2.24)	.053
CCTGA	29	5 (17.2)	1.53 (0.68-3.47)	.305
Arch obstruction, isolated	174	31 (17.8)	1.59 (1.10-2.28)	.013
Tricuspid atresia	428	81 (18.9)	1.68 (1.29-2.19)	<.001
Double outlet right ventricle	382	75 (19.6)	1.75 (1.33-2.29)	<.001
Pulmonary atresia-VSD	175	36 (20.6)	1.83 (1.30-2.57)	<.001
Congenital aortic stenosis	487	103 (21.1)	1.88 (1.47-2.41)	<.001
Ebstein anomaly	303	66 (21.8)	1.94 (1.47-2.56)	<.001
Tetralogy of Fallot	1268	298 (23.5)	2.09 (1.71-2.56)	<.001
Pulmonary atresia-IVS	286	69 (24.1)	2.15 (1.64-2.82)	<.001
Truncus arteriosus	233	63 (27.0)	2.41 (1.83-3.17)	<.001
Atrioventricular septal defect	294	93 (31.6)	2.81 (2.20-3.59)	<.001

CCTGA, congenitally corrected transposition of the great arteries; *CHAMPUS*, Civilian Health and Medical Program of the Uniformed Services; *IVS*, intact ventricular septum; *VA*, US Department of Veterans Affairs; *VSD*, ventricular septal defect.
For CCHD lesions, categories are mutually exclusive. When >1 CCHD was present, lesion is listed as combination.

Based on the yearly percentage of preterm birth, joinpoint segmented regression models identified a change in trend after 2003 for infants overall in Texas, and after 2004 for infants with CCHD (**Figure 2**). In both populations, the annual percent of preterm births initially increased, with mean change of +1.69% per year (95% CI, +0.95 to +2.44) for the CCHD cohort and +0.31% per year (95% CI, +0.25 to +0.38) for the total population (CCHD vs population change; $P < .001$). After 2004, the annual percent of preterm births for infants with CCHD and the general population decreased, with a mean change of −0.41% per year (95% CI, −0.73 to −0.09) in CCHD, and −0.16% per year (95% CI, −0.18 to −0.14) in the general population (CCHD vs population; $P = .123$).

When accounting for hospital clustering, we observed an increasing RR of preterm births with CCHD from 1999 to 2004 (era 1; RR per year, 1.10; **Table VI**, model 1) followed by a decreasing RR in the period after 2004 (era 2; RR, 0.98; *P* value comparing both eras ≤ .001). These findings were consistent after additional adjustment for sociodemographic variables (**Table VI**, model 2). In the third model (**Table VI**, model 3), to account for observed interactions between race/ethnicity and with time, multivariable analysis was performed while stratifying by race/ethnicity. The overall pattern of an increase in the first era and decrease in the second era were present across all race/ethnicities. When comparing race/ethnicity within each era, there were no significant differences in rate of change of preterm delivery. In the fourth model (**Table VI**, model 4, and **Figure 3**), to account for observed

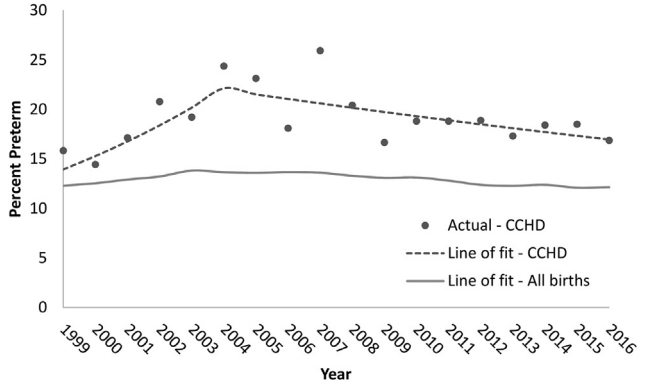

Figure 2. Annual percentage of infants born preterm in Texas with CCHD, 1999-2016. The *dotted line* represents joinpoint segmented regression for newborns born with CCHD and the *solid line* represents the percentage preterm births for all newborns. A point in which there is a change in the slope of the data for the population with CCHD is noted in 2004, with the slope of the earlier era being +1.69% per year and the slope of the later era being −0.41% per year.

Table VI. Multivariable models of RR per year of preterm delivery among infants with CCHD in era 1 and era 2

Models	RR per year (95% CI), 1999-2004 (era 1)	RR per year (95% CI), 2005-2016 (era 2)	Interaction *P* value*
Model 1: Adjusted only for hospital	1.10 (1.04-1.16)	0.98 (0.96-0.99)	<.001
Model 2: Adjusting for hospital, poverty, race/ethnicity, and sex	1.10 (1.04-1.16)	0.98 (0.96-0.99)	<.001
Model 3: Adjusting for hospital, poverty, and significant interactions, stratified by race/ethnicity†			
Non-Hispanic white	1.07 (0.98-1.16)	0.98 (0.94-1.01)	.070
Hispanic	1.09 (1.01-1.19)	0.98 (0.96-1.01)	.009
Non-Hispanic black	1.14 (0.99-1.31)	0.96 (0.93-1.00)	.026
Other	1.15 (0.93-1.42)	0.98 (0.92-1.04)	.125
Model 4: Adjusting for hospital, race/ethnicity, and significant interactions, stratified by poverty†			
Low poverty	1.06 (0.99-1.13)‡	0.97 (0.95-0.99)	.018
High poverty	1.23 (1.08-1.39)	1.00 (0.93-1.53)	<.001

*Compares the RR per year of eras 1 and 2.
†Interaction noted between race/ethnicity and era and poverty and era.
‡Denotes significant differences by poverty within the era.

interactions between neighborhood poverty level and time, multivariable analysis was performed while stratifying by poverty level. This calculation demonstrated that those living in a high poverty area had a faster increase in risk of preterm delivery in the first era and a plateau in the second era.

There were 2349 live births and 401 (17.1%) preterm births in the subpopulation of CCHD most commonly prenatally diagnosed (**Table VII**; available at www.jpeds.com). Variables associated with higher percentage of preterm birth included Hispanic ethnicity, non-Hispanic Black race, and living in a high poverty neighborhood. The percent of preterm births over time for this population is shown in **Figure 4** (available at www.jpeds.com) and compared with overall live births. Joinpoint segmented regression identified a change in trend after 2004. The annual percent of preterm births initially increased with a mean change of +1.95% per year (95% CI, 0.71-3.19), which was similar to the overall change rate in CHD (P = .729), and faster than the general population (P = .010). After 2004, the annual percent of preterm births had a similar change to that noted in the overall CHD and population groups (P = .845 and P = .535 respectively), with a mean change of −0.48% per year (95% CI, −1.00 to 0.03).

When accounting for hospital clustering, there was an increase in proportion of preterm births with CCHD most likely to be diagnosed from 1999 to 2004 (RR per year, 1.14; **Table VIII**; model 1; available at www.jpeds.com) followed by a plateau in the period after 2004 (RR per year, 0.97; P value comparing the RR of both eras = .002). This pattern was consistent in the second multivariable model that adjusted for demographics (**Table VIII**, model 2). When stratifying by race/ethnicity (**Table VIII**, model 3), the overall patterns of an increase in the first era and plateau in the second era were similar between race/ethnicities, but no significant difference in the RRs per year between eras noted for any race/ethnicity. Stratifying by poverty level (**Table VIII**, model 4), demonstrated that those living in a high poverty area only had a plateau in the later era, whereas those in a lower poverty area noted a decrease in preterm delivery rates.

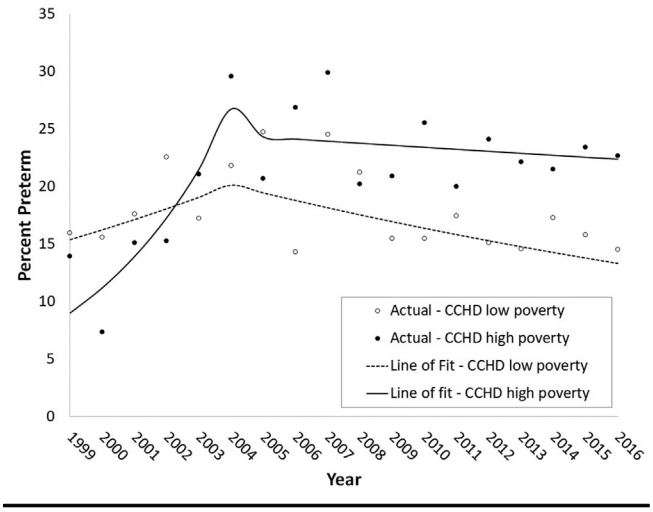

Figure 3. Annual percentage of infants born preterm in Texas with CCHD stratified by poverty level, 1999-2016. The *dashed line* represents joinpoint segmented regression for infants born with CCHD in low poverty areas. The *solid line* represents joinpoint segmented regression for infants born with CCHD in high poverty areas. Those living in a low poverty area had an increase in preterm delivery in the first era and decrease in the second. Those living in a high poverty area had a faster increase in preterm delivery in the first era, and only a plateau, but not a decline in the second era.

Discussion

Although a prenatal diagnosis of CCHD is associated with improvements in preoperative clinical status and neurodevelopmental outcomes, it has also been associated with earlier gestational age at birth, which is associated with worse outcomes.[1,2,5,19-23,28-30] The dilemma involves the interplay between the benefits of prenatal diagnosis and the earlier gestational age at birth. Although we cannot directly evaluate the reasons for the change of trend in the rate of preterm

births, we hypothesize that the earlier increase was due to increasing prenatal CCHD diagnosis.[9] Later, a change in practice may have occurred in response to the growing body of literature associating earlier gestational age at birth with worse outcomes.[22,23,28-30] Other factors that may have influenced the gestational age at birth during the time period of our study include literature describing that progestogens in select populations will decrease the rate of preterm delivery in at-risk women.[42-45] Adoption of this agent over the time period could have further influenced gestational age at birth.

This study noted that Hispanic ethnicity and non-Hispanic black race were associated with a higher percentage of preterm birth of newborns with CCHD, a finding previously noted in the general population when comparing non-Hispanic blacks with non-Hispanic whites.[46-50] Although maternal risk factors were not a part of our assessment, studies have noted racial disparities persist even when accounting for maternal risk factors for preterm birth.[46] Despite the association of Hispanic ethnicity and non-Hispanic black race with a higher percentage of preterm birth, the decreasing rate of premature birth in the recent era suggests improvement in preterm delivery in these populations.

Our ability to speculate on why trends in preterm delivery are modified by poverty level are limited. However, published data demonstrate that large city and urban areas showed a decrease in preterm births after 2005, whereas rural areas that were more socioeconomically isolated only exhibited a plateau in preterm delivery rates.[51] It is possible that changes to public policy and clinical practice have had less impact on populations in poverty.

There were inherent limitations in our analysis. The specific type of CCHD was not included in our statistical models for 2 reasons. First, the rates of prenatal diagnosis of CCHD vary by lesion.[52] As prenatal diagnosis has improved, the changes have been discrepant by lesion, with lesions that were more challenging to detect in the past now being recognized more often. Therefore, adjusting for lesion potentially would have adjusted for a factor in the mechanistic pathway. Second, our overall aim was to evaluate preterm delivery rates in the Texas population with CCHD. Accounting for individual types of CCHD and potential interactions would significantly limit statistical power and fail to answer the primary question.

Various factors likely influence the health outcomes of Hispanics in the US, including country of origin/cultural heritage and extent of acculturation to mainstream US culture.[53,54] Information regarding Hispanic ethnic subgroups and measures of acculturation were not available. In addition, the generalizability of this study may be limited. In 2016, Texas was the state with the lowest rate of first trimester initiation of prenatal care.[49] Additionally, Texas is a large state with many rural counties, and the percentage of hospitals in rural counties with obstetrical services has decreased during the time period of our study.[55] Issues with access to care in rural counties is associated with increased preterm birth.[56]

The database used in this study involves passive surveillance using administrative codes without active case validation. Also, the analysis assumes that newborns without ICD codes for prematurity are not preterm at birth. Only a subset of infants born preterm are coded as preterm by ICD.[57] Previous results have demonstrated that the sensitivity of ICD-9-CM codes is low, particularly for birth at 35 or 36 weeks of gestation.[58,59] Although the implication is that the incomplete sensitivity of ICD codes for preterm births would cause our study to underestimate preterm birth, we believe this factor does not bias our study, given that our primary outcome are changes in rates of preterm birth over time. Of note, when comparing 3 lesion-specific studies from the TBDR that include data on preterm delivery, the percent preterm in the TPUIDF for the same periods and lesions closely approximates those reported (Lupo et al reported 26% in Ebstein anomaly vs 24% in the TPUIDF; Morris et al reported 13% in nonsyndromic HLHS vs 14% in the TPUIDF; Lara et al reported 12% in nonsyndromic transposition of the great arteries vs 12% in the TPUIDF).[9,15,60] Additionally, the retrospective nature of the study does not allow the authors to draw conclusions on causality in the findings. Finally, we did not account for the clustering of births of the same mother (although multiples were excluded).

The rate of preterm birth in CCHD increased from 1999 to 2004, but decreased from 2005 to 2016. These patterns were similar in the population of CCHD most likely to be prenatally diagnosed. The change between these 2 periods may indicate a change in clinical practice in response to recommendations that infants with CCHD have worse outcomes when born preterm and early term. ■

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Data Statement

Data sharing statement available at www.jpeds.com.

References

1. 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;103:1269-73.
2. Kipps AK, Feuille C, Azakie A, Hoffman JI, Tabbutt S, Brook MM, et al. Prenatal diagnosis of hypoplastic left heart syndrome in current era. Am J Cardiol 2011;108:421-7.
3. Thakur V, Dutil N, Schwartz SM, Jaeggi E. Impact of prenatal diagnosis on the management and early outcome of critical duct-dependent cardiac lesions. Cardiol Young 2018;28:548-53.
4. Kumar RK, Newburger JW, Gauvreau K, Kamenir SA, Hornberger LK. Comparison of outcome when hypoplastic left heart syndrome and transposition of the great arteries are diagnosed prenatally versus when diagnosis of these two conditions is made only postnatally. Am J Cardiol 1999;83:1649-53.
5. Peyvandi S, De Santiago V, Chakkarapani E, Chau V, Campbell A, Poskitt KJ, et al. Association of prenatal diagnosis of critical congenital

heart disease with postnatal brain development and the risk of brain injury. JAMA Pediatr 2016;170:e154450.
6. Fuchs IB, Müller H, Abdul-Khaliq H, Harder T, Dudenhausen JW, Henrich W. Immediate and long-term outcomes in children with prenatal diagnosis of selected isolated congenital heart defects. Ultrasound Obstet Gynecol 2007;29:38-43.
7. van Velzen CL, Haak MC, Reijnders G, Rijlaarsdam ME, Bax CJ, Pajkrt E, et al. Prenatal detection of transposition of the great arteries reduces mortality and morbidity. Ultrasound Obstet Gynecol 2015;45:320-5.
8. Bonnet D, Coltri A, Butera G, Fermont L, Le Bidois J, Kachaner J, et al. Detection of transposition of the great arteries in fetuses reduces neonatal morbidity and mortality. Circulation 1999;99:916-8.
9. Morris SA, Ethen MK, Penny DJ, Canfield MA, Minard CG, Fixler DE, et al. Prenatal diagnosis, birth location, surgical center, and neonatal mortality in infants with hypoplastic left heart syndrome. Circulation 2014;129:285-92.
10. Copel JA, Tan AS, Kleinman CS. Does a prenatal diagnosis of congenital heart disease alter short-term outcome? Ultrasound Obstet Gynecol 1997;10:237-41.
11. Mahle WT, Clancy RR, McGaurn SP, Goin JE, Clark BJ. Impact of prenatal diagnosis on survival and early neurologic morbidity in neonates with the hypoplastic left heart syndrome. Pediatrics 2001;107:1277-82.
12. Peake LK, Draper ES, Budd JLS, Field D. Outcomes when congenital heart disease is diagnosed antenatally versus postnatally in the UK: a retrospective population-based study. BMC Pediatr 2015;15:58.
13. Chakraborty A, Gorla SR, Swaminathan S. Impact of prenatal diagnosis of complex congenital heart disease on neonatal and infant morbidity and mortality. Prenat Diagn 2018;38:958-63.
14. Özer Bekmez B, Alyamaç Dizdar E, Okur N, Büyüktiryaki M, Uraş N, Oğuz SS. Does prenatal diagnosis of critical congenital heart diseases influence the prereferral mortality in a center without surgical intervention? J Matern Fetal Neonatal Med 2018:1-4.
15. Lara DA, Fixler DE, Ethen MK, Canfield MA, Nembhard WN, Morris SA. Prenatal diagnosis, hospital characteristics, and mortality in transposition of the great arteries. Birth Defects Res A Clin Mol Teratol 2016;106:739-48.
16. Wright LK, Ehrlich A, Stauffer N, Samai C, Kogon B, Oster ME. Relation of prenatal diagnosis with one-year survival rate for infants with congenital heart disease. Am J Cardiol 2014;113:1041-4.
17. Oster ME, Kim CH, Kusano AS, Cragan JD, Dressler P, Hales AR, et al. A population-based study of the association of prenatal diagnosis with survival rate for infants with congenital heart defects. Am J Cardiol 2014;113:1036-40.
18. Holland BJ, Myers JA, Woods CR. Prenatal diagnosis of critical congenital heart disease reduces risk of death from cardiovascular compromise prior to planned neonatal cardiac surgery: a meta-analysis. Ultrasound Obstet Gynecol 2015;45:631-8.
19. Levey A, Glickstein JS, Kleinman CS, Levasseur SM, Chen J, Gersony WM, et al. The impact of prenatal diagnosis of complex congenital heart disease on neonatal outcomes. Pediatr Cardiol 2010;31:587-97.
20. Peyvandi S, Nguyen TATT, Almeida-Jones M, Boe N, Rhee L, Anton T, et al. Timing and mode of delivery in prenatally diagnosed congenital heart disease- an analysis of practices within the University of California Fetal Consortium (UCfC). Pediatr Cardiol 2017;38:588-95.
21. Quartermain MD, Hill KD, Goldberg DJ, Jacobs JP, Jacobs ML, Pasquali SK, et al. Prenatal diagnosis influences preoperative status in neonates with congenital heart disease: an analysis of the Society of Thoracic Surgeons Congenital Heart Surgery Database. Pediatr Cardiol 2018;40:489-96.
22. Andrews RE, Simpson JM, Sharland GK, Sullivan ID, Yates RWM. Outcome after preterm delivery of infants antenatally diagnosed with congenital heart disease. J Pediatr 2006;148:213-6.
23. Dees E, Lin H, Cotton RB, Graham TP, Dodd DA. Outcome of preterm infants with congenital heart disease. J Pediatr 2000;137:653-9.
24. Steurer MA, Baer RJ, Keller RL, Oltman S, Chambers CD, Norton ME, et al. Gestational age and outcomes in critical congenital heart disease. Pediatrics 2017;140.
25. Miller TA, Ghanayem NS, Newburger JW, McCrindle BW, Hu C, DeWitt AG, et al. Gestational age, birth weight, and outcomes six years after the Norwood procedure. Pediatrics 2019;143.
26. Oppido G, Pace Napoleone C, Formigari R, Gabbieri D, Pacini D, Frascaroli G, et al. Outcome of cardiac surgery in low birth weight and premature infants. Eur J Cardiothorac Surg 2004;26:44-53.
27. Young PC, Glasgow TS, Li X, Guest-Warnick G, Stoddard G. Mortality of late-preterm (near-term) newborns in Utah. Pediatrics 2007;119:e659-65.
28. Costello JM, Polito A, Brown DW, McElrath TF, Graham DA, Thiagarajan RR, et al. Birth before 39 weeks' gestation is associated with worse outcomes in neonates with heart disease. Pediatrics 2010;126:277-84.
29. Costello JM, Pasquali SK, Jacobs JP, He X, Hill KD, Cooper DS, et al. Gestational age at birth and outcomes after neonatal cardiac surgery: an analysis of the Society of Thoracic Surgeons Congenital Heart Surgery database. Circulation 2014;129:2511-7.
30. Cnota JF, Gupta R, Michelfelder EC, Ittenbach RF. Congenital heart disease infant death rates decrease as gestational age advances from 34 to 40 weeks. J Pediatr 2011;159:761-5.
31. Donofrio MT, Moon-Grady AJ, Hornberger LK, Copel JA, Sklansky MS, Abuhamad A, et al. Diagnosis and treatment of fetal cardiac disease: a scientific statement from the American Heart Association. Circulation 2014;129:2183-242.
32. American College of Obstetricians and Gynecologists. ACOG committee opinion no. 561: nonmedically indicated early-term deliveries. Obstet Gynecol 2013;121:911-5.
33. Reddy UM, Ko C-W, Raju TNK, Willinger M. Delivery indications at late-preterm gestations and infant mortality rates in the United States. Pediatrics 2009;124:234-40.
34. Liberman RF, Getz KD, Lin AE, Higgins CA, Sekhavat S, Markenson GR, et al. Delayed diagnosis of critical congenital heart defects: trends and associated factors. Pediatrics 2014;134:e373-81.
35. Ailes EC, Gilboa SM, Riehle-Colarusso T, Johnson CY, Hobbs CA, Correa A, et al. Prenatal diagnosis of nonsyndromic congenital heart defects. Prenat Diagn 2014;34:214-22.
36. THCIC - inpatient PUDF. https://www.dshs.texas.gov/thcic/hospitals/Inpatientpudf.shtm. Accessed March 7, 2018.
37. American FactFinder. https://factfinder.census.gov/faces/nav/jsf/pages/index.xhtml. Accessed March 7, 2018.
38. Poverty Areas. https://www.census.gov/population/socdemo/statbriefs/povarea.html. Accessed November 28, 2018.
39. United States Department of Health and Human Services (US DHHS). Centers for Disease Control and Prevention (CDC), National Center for Health Statistics (NCHS), Division of Vital Statistics, Natality public-use data 1995-2017, on CDC, WONDER Online Database. https://wonder.cdc.gov/. Accessed October 1, 2018.
40. Quartermain MD, Pasquali SK, Hill KD, Goldberg DJ, Huhta JC, Jacobs JP, et al. Variation in prenatal diagnosis of congenital heart disease in infants. Pediatrics 2015;136:e378-85.
41. Escobar-Diaz MC, Freud LR, Bueno A, Brown DW, Friedman KG, Schidlow D, et al. Prenatal diagnosis of transposition of the great arteries over a 20-year period: improved but imperfect. Ultrasound Obstet Gynecol 2015;45:678-82.
42. Meis PJ, Klebanoff M, Thom E, Dombrowski MP, Sibai B, Moawad AH, et al. Prevention of recurrent preterm delivery by 17 alpha-hydroxyprogesterone caproate. N Engl J Med 2003;348:2379-85.
43. Fonseca EB, Celik E, Parra M, Singh M, Nicolaides KH, Fetal Medicine Foundation Second Trimester Screening Group. Progesterone and the risk of preterm birth among women with a short cervix. N Engl J Med 2007;357:462-9.
44. Hassan SS, Romero R, Vidyadhari D, Fusey S, Baxter JK, Khandelwal M, et al. Vaginal progesterone reduces the rate of preterm birth in women with a sonographic short cervix: a multicenter, randomized, double-blind, placebo-controlled trial. Ultrasound Obstet Gynecol 2011;38:18-31.

45. Keirse MJ. Progestogen administration in pregnancy may prevent preterm delivery. Br J Obstet Gynaecol 1990;97:149-54.
46. Lu MC, Halfon N. Racial and ethnic disparities in birth outcomes: a life-course perspective. Matern Child Health J 2003;7:13-30.
47. Alexander GR, Kogan MD, Nabukera S. Racial differences in prenatal care use in the United States: are disparities decreasing? Am J Public Health 2002;92:1970-5.
48. Shi L, Stevens GD, Wulu JT, Politzer RM, Xu J. America's health centers: reducing racial and ethnic disparities in perinatal care and birth outcomes. Health Serv Res 2004;39(6 Pt 1):1881-902.
49. Osterman MJK, Martin JA. Timing and adequacy of prenatal care in the United States, 2016. Natl Vital Stat Rep 2018;67:1-14.
50. Martin JA, Osterman MJK. Describing the increase in preterm births in the United States, 2014-2016. NCHS Data Brief 2018:1-8.
51. Kent ST, McClure LA, Zaitchik BF, Gohlke JM. Area-level risk factors for adverse birth outcomes: trends in urban and rural settings. BMC Pregnancy Childbirth 2013;13:129.
52. Chew C, Halliday JL, Riley MM, Penny DJ. Population-based study of antenatal detection of congenital heart disease by ultrasound examination. Ultrasound Obstet Gynecol 2007;29:619-24.
53. Lopez KN, Nembhard WN, Wang Y, Liu G, Kucik JE, Copeland G, et al. Birth defect survival for Hispanic subgroups. Birth Defects Res 2018;110:352-63.
54. Lara M, Gamboa C, Kahramanian MI, Morales LS, Hayes Bautista DE. Acculturation and Latino health in the United States: a review of the literature and its sociopolitical context. Annu Rev Public Health 2005;26:367-97.
55. State Variability in Access to Hospital-Based Obstetric Services in Rural U.S. Counties | The University of Minnesota Rural Health Research Center. http://rhrc.umn.edu/2017/04/state-variability-in-access-to-hospital-based-obstetric-services-in-rural-u-s-counties/. Accessed May 21, 2018.
56. Kozhimannil KB, Hung P, Henning-Smith C, Casey MM, Prasad S. Association between loss of hospital-based obstetric services and birth outcomes in rural counties in the United States. JAMA 2018;319:1239-47.
57. Andrade SE, Scott PE, Davis RL, Li DK, Getahun D, Cheetham TC, et al. Validity of health plan and birth certificate data for pregnancy research. Pharmacoepidemiol Drug Saf 2013;22:7-15.
58. Barrett JP, Sevick CJ, Conlin AMS, Gumbs GR, Lee S, Martin DP, et al. Validating the use of ICD-9-CM codes to evaluate gestational age and birth weight. J Registry Manag 2012;39:69-75.
59. Li Q, Andrade SE, Cooper WO, Davis RL, Dublin S, Hammad TA, et al. Validation of an algorithm to estimate gestational age in electronic health plan databases. Pharmacoepidemiol Drug Saf 2013;22:524-32.
60. Lupo PJ, Langlois PH, Mitchell LE. Epidemiology of Ebstein anomaly: prevalence and patterns in Texas, 1999-2005. Am J Med Genet A 2011;155A:1007-14.

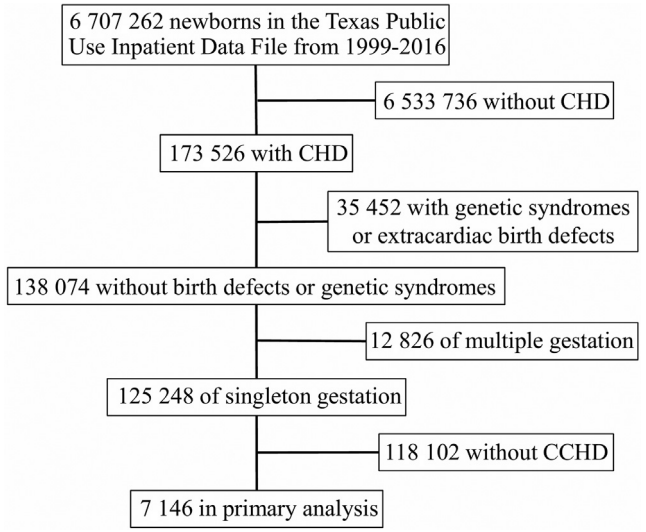

Figure 1. Study population. Of the newborns in the TPUIDF from 1999 to 2016, births of multiple gestation, those without CCHD, and those with birth defects or genetic syndromes were excluded. A total of 7146 newborns were included in the primary analysis.

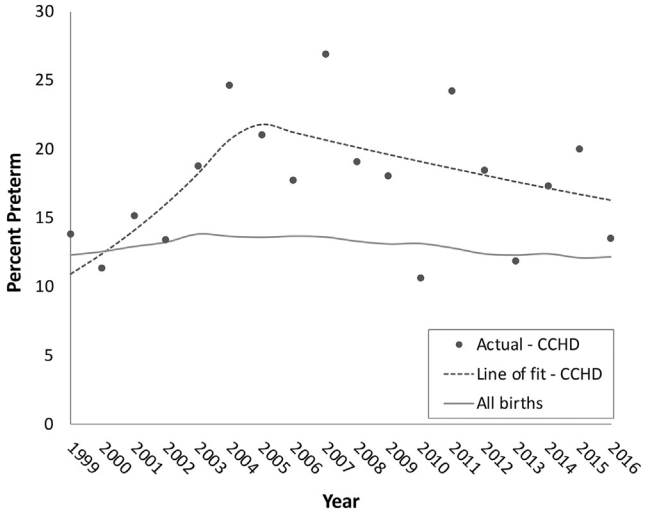

Figure 4. Annual percentage of infants born preterm in Texas with CCHD most likely to be prenatally diagnosed, 1999-2016. The *dotted line* represents joinpoint segmented regression for infants born with CCHD most likely to be prenatally diagnosed and the solid line represents the percentage preterm births for all infants. A point in which there is a change in the slope of the data for this subgroup of CCHD is noted in 2004, with the slope of the earlier era being +1.95% per year and the slope of the later era being −0.48% per year.

Table I. List of included diagnoses by ICD-9-CM and ICD-10-CM codes

Diagnoses	ICD-9-CM	ICD-10-CM
Atrioventricular septal defect	745.60, 745.61, 745.69	Q21.2
Coarctation/other arch obstruction	747.1, 747.10, 747.11, 747.21, 747.22	Q25.1, Q25.21, Q25.29, Q25.41, Q25.42
Congenital aortic stenosis	746.3	Q23.0, I35.0*
Double outlet left ventricle		Q20.2
Double outlet right ventricle	745.11	Q20.1
Ebstein anomaly	746.2	Q22.5
HLHS	746.7	Q23.4
Mitral stenosis	746.5	Q23.2, I34.2
Other single ventricle	745.3, 745.7	Q20.4, Q22.6
Pulmonary atresia	746.01	Q22.0, Q25.5
Tetralogy of Fallot	745.2	Q21.3
Total anomalous venous return	747.41	Q26.2
Transposition of the great arteries	745.10, 745.12	Q20.3, Q20.5
Tricuspid atresia	746.1	Q22.4
Truncus arteriosus	745.0	Q20.0

*Despite being a code for adult-onset aortic stenosis, I35.0 was included to account for common miscoding of this congenital lesion and no adults in this cohort.

Table II. Procedure codes used to define arch interventions

Procedures	Codes
Surgical	38.04, 38.05, 38.34, 38.35, 38.44, 38.45, 38.64, 38.65, 39.56, 39.57, 39.58, 39.59, 39.73, 02BX0ZX, 02BX0ZZ, 02QX0ZZ, 02QW0ZZ, 02RX0*, 02UW0*, 02UX0*, 02RW0*, 027X0*, 027W0*, 02BW0*, 02BX0*, 021W08B, 021W08D, 021W09B, 021W09D, 021W0AB, 021W0AD, 021W0JB, 021W0JD, 021W0KB, 021W0KD, 021W0ZB, 021W0ZD, 021X08B, 021X08D, 021X09B, 021X09D, 021X0AB, 021X0AD, 021X0JB, 021X0JD, 021X0KB, 021X0KD, 021X0ZB, 021X0ZD
Catheter-based	395.0, 399.0, 027W3*, 027W4*, 027X3*, 027X4*

*All billable codes under this stem.

Table III. List of excluded genetic syndromes and birth defects

ICD-9-CMs	ICD-10-CM
275.1, 279.11, 553.3, 747.81, 270.*, 271.*, 272.*, 277.*, 740.*, 741.*, 742.*, 743.*, 744.*, 748.*, 749.*, 750.1-750.9, 751.*, 752.*, 753.*, 754.*, 755.*, 756.*, 757.*, 758.*, 759.*	D82.1, K44.9, Q28.2, Q28.3, E70*, E71.*, E72.*, E74.*, E75.*, E76.*, E77.*, E78.*, E79.*, E84.*, E80.0, E80.1, E80.20, E80.21, E80.29, E80.3, E80.5, E83.01, Q0.*, Q1.*, Q3.*, Q4.*, Q5.*, Q6.*, Q7.*, Q8.*, Q9.*

*All billable codes under this stem.

Table IV. Lists of ICD-9-CM and ICD-10CM codes used to define preterm birth

ICD-9-CMs	ICD-10-CM
362.20-362.27, 765.0x, 765.1x, 765.20-765.28	H35.1x, P07.2x, P07.3x, 0.061x

An x indicates all billable codes under this stem.

Table VII. Univariable analysis of characteristics associated with preterm delivery among the subgroup of infants with CCHD most likely to be prenatally diagnosed

Characteristics	All (n)	Preterm, n (%)	RR (95% CI)	*P* value
CCHD subgroup	2349	401 (17.1)		
Sex				.123
Female	985	182 (18.5)	Reference	
Male	1364	219 (16.1)	1.15 (0.96-1.38)	
Race/ethnicity				
Non-Hispanic white	801	110 (13.7)	Reference	
Hispanic	1027	190 (18.5)	1.35 (1.09-1.67)	.007
Non-Hispanic black	254	56 (22.0)	1.61 (1.20-2.14)	.001
Other	267	45 (16.9)	1.23 (0.89-1.69)	.207
Poverty level of zip code				
<20%	1470	215 (14.6)	Reference	
≥20%	767	168 (21.9)	1.50 (1.25-1.80)	<.001
Insurance				
Private	822	125 (15.2)	Reference	
Medicare/other federal	1199	214 (17.8)	1.17 (0.96-1.44)	.120
Self-pay	93	18 (19.4)	1.27 (0.82-1.99)	.288
VA/CHAMPUS	100	64 (10.0)	0.66 (0.26-1.69)	.384
Other	40	10 (25.0)	1.64 (0.94-2.88)	.082
CCHD lesion				
HLHS	899	121 (13.5)		
Other single ventricle	143	24 (16.8)		
Complex combination	418	70 (16.7)		
Tricuspid atresia	428	81 (18.9)		
Pulmonary atresia-VSD	175	36 (20.6)		
Pulmonary atresia-IVS	286	69 (24.1)		

CHAMPUS, Civilian Health and Medical Program of the Uniformed Services; *IVS*, intact ventricular septum; *VA*, US Department of Veterans Affairs; *VSD*, ventricular septal defect.
For CCHD lesions, categories are mutually exclusive. When >1 CCHD was present, lesion is listed as a complex combination.

Table VIII. Multivariable models of characteristics associated with preterm delivery among the subgroup of infants with CCHD most likely to be prenatally diagnosed

Models	RR per year (95% CI), 1999-2004 (era 1)	RR per year (95% CI), 2005-2016 (era 2)	Interaction *P* value*
Model 1: Adjusted only for hospital	1.14 (1.04-1.16)	0.97 (0.94-1.01)	.002
Model 2: Adjusting for hospital, poverty, race/ethnicity, and sex	1.12 (1.01-1.25)	0.98 (0.95-1.01)	.012
Model 3: Adjusting for poverty, race/ethnicity, and significant interactions, stratified by race/ethnicity†			
Non-Hispanic white	1.08 (0.93-1.26)	0.95 (0.88-1.03)	.136
Hispanic	1.15 (0.96-1.38)	0.99 (0.94-1.04)	.088
Non-Hispanic black	1.10 (0.84-1.44)	0.99 (0.95-1.05)	.498
Others	1.22 (0.79-1.90)	0.98 (0.89-1.08)	.337
Model 4: Adjusting for hospital, poverty, race/ethnicity, and significant interactions, stratified by poverty†			
Low poverty	1.10 (0.99-1.21)	0.95 (0.91-0.99)	.021
High poverty	1.24 (0.94-1.63)	1.01 (0.97-1.05)	.098

*Compares the RR per year of era 1 and era 2.
†Interaction noted between race/ethnicity and era.