Racial and Ethnic Differences in Pediatric Pulmonary Hypertension: An Analysis of the Pediatric Pulmonary Hypertension Network Registry

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Objective To investigate racial and ethnic differences in pulmonary hypertension subtypes and survival differences in a pediatric population.

Study design This was a retrospective analysis of a cohort of patients with pulmonary hypertension (aged ≤18 years) enrolled in the Pediatric Pulmonary Hypertension Network registry between 2014 and 2018, comprising patients at eight Pediatric Centers throughout North America (n = 1417).

Results Among children diagnosed after the neonatal period, pulmonary arterial hypertension was more prevalent among Asians (OR, 1.83; 95% CI, 1.21-2.79; P = .0045), lung disease-associated pulmonary hypertension among blacks (OR, 2.09; 95% CI, 1.48-2.95; P < .0001), idiopathic pulmonary arterial hypertension among whites (OR, 1.58; 95% CI, 1.06-2.41; P = .0289), and pulmonary veno-occlusive disease among Hispanics (OR, 6.11; 95% CI, 1.34-31.3; P = .0184). Among neonates, persistent pulmonary hypertension of the newborn (OR, 4.07; 95% CI, 1.54-10.0; P = .0029) and bronchopulmonary dysplasia (OR, 8.11; 95% CI, 3.28-19.8; P < .0001) were more prevalent among blacks, and congenital diaphragmatic hernia was more prevalent among whites (OR, 2.29; 95% CI, 1.25-4.18; P = .0070). An increased mortality risk was observed among blacks (HR, 1.99; 95% CI, 1.03-3.84; P = .0396), driven primarily by the heightened mortality risk among those with lung disease-associated pulmonary hypertension (HR, 2.84; 95% CI, 1.15-7.04; P = .0241).

Conclusions We found significant racial variability in the prevalence of pulmonary hypertension subtypes and survival outcomes among children with pulmonary hypertension. Given the substantial burden of this disease, further studies to validate phenotypic differences and to understand the underlying causes of survival disparities between racial and ethnic groups are warranted. *(J Pediatr 2019;211:63-71)*.

In adults with pulmonary hypertension, several studies have documented racial and ethnic differences in survival, with increased mortality reported among racial and ethnic minorities when compared with non-Hispanic white patients.[1-4] Other studies have documented racial and ethnic variability within pulmonary hypertension subtypes, including a higher incidence of connective tissue disease and sickle cell disease-associated pulmonary hypertension among black patients,[5-10] familial and idiopathic pulmonary hypertension among white patients,[5,11] and congenital heart disease-associated pulmonary hypertension among Hispanic patients.[5] Historically, racial and ethnic minority populations are disproportionately affected by poor access to healthcare services, and treatment disparities may have resulted in poorer survival outcomes.[5] Heterogeneity in clinical phenotypes and underlying genotypes may also have contributed to the observed survival disparities among minority races with pulmonary hypertension, because disease progression and availability of treatment vary substantially by pulmonary hypertension subtypes.

There are currently no published data examining racial and ethnic differences among children with pulmonary hypertension, and understanding racial and ethnic differences in pulmonary hypertension manifestations and outcomes is crucial for disease diagnosis and management. We used the Pediatric Pulmonary Hypertension Network (PPHNet) registry, which includes patients enrolled from established interdisciplinary pulmonary hypertension programs at 8 pediatric pulmonary hypertension centers throughout North America,[12] to investigate

BPD	Bronchopulmonary dysplasia
PPHN	Persistent pulmonary hypertension of the newborn
PPHNet	Pediatric Pulmonary Hypertension Network
PVOD	Pulmonary veno-occlusive disease

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racial and ethnic differences in pulmonary hypertension subtypes and outcomes in the pediatric population.

Methods

This was a retrospective analysis of the PPHNet registry. The study protocol was approved by the institutional review boards of all participating centers and all study participants signed informed consent. The cohort included 1417 incident and prevalent children (≤18 years old) enrolled in the registry between 2014 and 2018. Demographics (including age, sex, race, ethnicity), pulmonary hypertension subtypes, and survival outcomes were extracted. To examine the potential impact of socioeconomic status on survival outcomes, we linked patients' zip code of residence to the 2016 US Census Bureau Small Area Income and Poverty Estimates to derive a neighborhood socioeconomic indicator quantifying the percentage of children aged <18 years living in poverty at the county level, as defined by the US Census Bureau.[13]

The primary variables of interest were racial/ethnic variability in pulmonary hypertension subtypes and survival. Race was classified into six categories: American Indian/Alaska Native, Asian, black, Native Hawaiian/other Pacific Islander, white, or multiracial. Ethnicity was categorized as Hispanic/Latino and non-Hispanic/Latino. Because pulmonary hypertension in the first 4 weeks of life may be transient, we conducted separate analyses comparing patients diagnosed in the first 4 weeks of life with those diagnosed beyond the neonatal period.

We performed a survival analysis on the overall study population, as well as for specific pulmonary hypertension subtypes, with a focus on lung disease-associated pulmonary hypertension and pulmonary arterial hypertension—the subtypes with the largest sample sizes in our cohort. Recognizing the registry included patients enrolled at different stages of disease progression and to ameliorate potential survival bias (patients who survived longer were more likely to be enrolled in the study), survival analysis was limited to an incident cohort, defined as patients enrolled in the registry within 180 days of disease diagnosis. We further conducted sensitivity analyses to assess survival outcomes in both the prevalent and incident cohorts for the overall study population, as well as for a subset of patients with pulmonary hypertension subtypes that present in the neonatal period, including congenital diaphragmatic hernia and persistent pulmonary hypertension of the newborn (PPHN). In the sensitivity analysis involving patients with congenital diaphragmatic hernia and PPHN, survival time was measured from the date of birth to the date of death.

Statistical Analyses

Logistic regression models were used to estimate ORs and 95% CIs for the associations between racial/ethnic subgroups and pulmonary hypertension subtypes. Kaplan–Meier estimates and Cox regression models were used to examine racial and ethnic variability in all-cause mortality. We examined the unadjusted mortality risk of individual racial and ethnic subgroups and mortality risk adjusted for patients' age at diagnosis, sex, and socioeconomic status (ie, county-level childhood poverty rate). Survival time was defined as the time elapsed between the date of diagnosis and date of death. Patients still alive on February 22, 2019 (the date of registry data extraction) and those lost to follow-up before this date were censored on February 22, 2019, and the last day of enrollment, respectively. Patients without a self-identified race were excluded from analyses examining racial variability in pulmonary hypertension subtypes and survival outcome, and patients without a self-identified ethnicity were excluded from analyses comparing ethnic subgroups.

Results

A total of 1417 patients enrolled in the PPHNet registry were included in the analysis. Of the patients, 60.1% self-identified as white, 13.1% black, 9.1% Asian, 1.6% multiracial, 1.0% American Indian or Alaska Native, and 0.7% Native Hawaiian or other Pacific Islander. Hispanic or Latino ethnicity comprised 16.0% of the study cohort (**Table I**). The mean and median follow-up duration of the study cohort were 943.7 and 995 days, respectively. Approximately 1 in 4 patients (n = 340 [24.0%]) were diagnosed with pulmonary hypertension within the first 4 weeks of life (**Figure 1**; available at www.jpeds.com), the majority of whom were male (59.1%) and white (67.1%). The most common pulmonary hypertension subtypes among neonates were congenital diaphragmatic hernia (72.9%), PPHN (10.9%), and bronchopulmonary dysplasia (BPD; 10.0%). Compared with other racial and ethnic subgroups, black children (OR, 1.10; 95% CI, 1.07-1.13; $P < .0001$) and Hispanic children (OR, 1.03; 95% CI, 1.01-1.06; $P = .013$) were more likely to live in counties with a high childhood poverty rate, whereas Asian children (OR, 0.95; 95% CI, 0.91-0.98; $P = .007$) and white children (OR, 0.97; 95% CI, 0.95-0.99; $P = .002$) were less likely to live in counties with a high childhood poverty rate.

Lung disease–associated pulmonary hypertension and pulmonary arterial hypertension comprised 90.2% of the cohort (n = 688 [48.6%] and n = 591 [41.7%], respectively; **Table I**). Lung disease–associated pulmonary hypertension was the most common subtype among black, white, and multiracial patients, and pulmonary arterial hypertension was most common among Asian, American Indian/Alaska Native, and Native Hawaiian/Pacific Islander patients (**Table II**). Among Hispanic patients, lung disease–associated pulmonary hypertension and pulmonary arterial hypertension were the most common pulmonary hypertension subtypes.

Bivariate analysis revealed associations between race/ethnicity and several pulmonary hypertension subtypes (**Table III**). Notably, Asian patients were more likely to have pulmonary arterial hypertension (OR, 2.04; 95% CI, 1.41-2.97; $P = .0002$) and less likely to develop lung

Table I. Demographics (n = 1417)

Variables	No. (%)
Age at diagnosis, years	
First quartile	0.0
Median	1.0
Mean	2.7
Third quartile	4.0
Range	0-18
Sex	
Female	690 (48.7)
Male	727 (51.3)
Race	
American Indian/Alaska Native	14 (1.0)
Asian	129 (9.1)
Black	186 (13.1)
Native Hawaiian/other Pacific Islander	10 (0.7)
White	852 (60.1)
Multiracial	23 (1.6)
Not specified	203 (14.3)
Ethnicity	
Hispanic/Latino	227 (16.0)
Non-Hispanic/Latino	1056 (74.5)
Not specified	134 (9.5)
Pulmonary hypertension subtypes	
Pulmonary arterial hypertension	591 (41.7)
Idiopathic	163 (11.5)
Heritable	26 (1.8)
Drugs/toxins	2 (0.1)
Associated pulmonary arterial hypertension	403 (28.4)
Connective tissue disease	7 (0.5)
HIV	0
Portal hypertension	6 (0.4)
Congenital heart disease	390 (27.5)
Schistosomiasis	4 (0.3)
PVOD	9 (0.6)
PPHN	46 (3.2)
Left-heart disease	49 (3.5)
Lung disease	688 (48.6)
Chronic thromboembolic pulmonary hypertension	7 (0.5)
Unclear mechanisms	31 (2.2)
Hematologic	8 (0.6)
Systemic disorders	7 (0.5)
Metabolic disorders	3 (0.2)
Segmental pulmonary hypertension	3 (0.2)
Others	3 (0.2)
Neighborhood socioeconomic indicator	
Percentage of children living in poverty at the county level	
First quartile	8.3
Median	11.1
Mean	12.5
Third quartile	15.3
Range	3.0-36.2

disease-associated pulmonary hypertension (OR, 0.51; 95% CI, 0.34-0.74; $P = .0005$); black patients were less likely to have pulmonary arterial hypertension (OR, 0.57; 95% CI, 0.40-0.79; $P = .0009$). A higher incidence of chronic thromboembolic pulmonary hypertension was observed among black patients (OR, 5.60; 95% CI, 1.03-30.5; $P = .0357$). To examine if the association between chronic thromboembolic pulmonary hypertension and black patients was driven by a higher incidence of hematologic disease–associated pulmonary hypertension among black individuals, we examined the number of patients co-diagnosed with chronic thromboembolic pulmonary hypertension and hematologic disease–associated pulmonary hypertension. There were no patients in our study cohort with a co-diagnosis of chronic thromboembolic pulmonary hypertension and hematologic disease–associated pulmonary hypertension. However, given the small number of patients with chronic thromboembolic pulmonary hypertension (n = 7) and the lack of association between chronic thromboembolic pulmonary hypertension and black patients when neonates were excluded from the analysis (Table III), this finding should be interpreted with caution.

We observed a higher risk of lung disease–associated pulmonary hypertension among black children who were diagnosed beyond the neonatal period (OR, 2.09; 95% CI, 1.48-2.95; $P < .0001$), but not among those diagnosed in the neonatal period (Table III). To investigate this inconsistency, we examined separately the risk of congenital diaphragmatic hernia and BPD—the 2 most common causes of lung disease-associated pulmonary hypertension among neonates. The analysis showed that black neonates were more likely to develop BPD (OR, 8.11; 95% CI, 3.28-19.8; $P < .0001$) but were less likely to have a congenital diaphragmatic hernia (OR, 0.16; 95% CI, 0.06-0.36; $P < .0001$). The heightened risk of BPD in black children persisted when we extended the analysis to include children diagnosed beyond the neonatal period (OR, 3.21; 95% CI, 2.32-4.45; $P < .0001$). Among white children diagnosed in the neonatal period, an increased risk of lung disease-associated pulmonary hypertension was observed (OR, 3.51; 95% CI, 1.92-6.45; $P = < .0001$); an increased risk of congenital diaphragmatic hernia (OR, 2.29; 95% CI, 1.25-4.18; $P = .0070$) and a reduced risk of BPD (OR, 0.38; 95% CI, 0.17-0.88; $P = .0190$) were also observed among white children (Table III). The reduced risk of BPD among white patients persisted when we extended the analysis to include children diagnosed beyond the neonatal period (OR, 0.46; 95% CI, 0.35-0.61; $P < .0001$). Among neonates, a higher risk of PPHN was observed in black children (OR, 4.07; 95% CI, 1.54-10.0; $P = .0029$), and a lower risk of PPHN was observed in white children (OR, 0.29; 95% CI, 0.13-0.65; $P = .0020$).

A higher incidence of schistosomiasis-associated pulmonary hypertension was detected among American Indians/Alaska Native and Native Hawaiians/other Pacific Islander patients; however, given the small number of patients with schistosomiasis, this finding should be interpreted with caution.

During the follow-up period, 105 patients (7.4%) patients died, on average 1220 days from the time of pulmonary hypertension diagnosis. To define an incident cohort, we identified 528 patients who were diagnosed within 180 days of study enrollment, 57 (10.8%) of whom died, on average 802.8 days from the time of pulmonary hypertension diagnosis. Of the 119 neonates in the incident cohort, 18 (15.1%) died during the study period. In comparison, of the 409 incident cases diagnosed after the neonatal period, 39 (9.5%) died during the study period. Younger age at diagnosis was associated with a poorer survival outcome (HR, 0.91; 95% CI, 0.83-0.99; $P = .0311$). Survival outcome was

Table II. Pulmonary hypertension subtypes by race and ethnicity

Pulmonary hypertension subtypes	Race							Ethnicity		
	American Indian/ Alaska Native (n = 14)	Asian (n = 129)	Black (n = 187)	Native Hawaiian/ other Pacific Islander (n = 10)	White (n = 852)	Multiracial (n = 23)	Not specified (n = 203)	Hispanic (n = 227)	Non-Hispanic (n = 1056)	Unknown (n = 134)
Pulmonary arterial hypertension	8 (57.1)	75 (58.1)	58 (31.2)	6 (60.0)	361 (42.4)	6 (26.1)	77 (37.9)	101 (44.5)	440 (41.7)	50 (37.3)
Idiopathic	1 (7.1)	20 (15.5)	10 (5.4)	2 (20.0)	109 (12.8)	4 (17.4)	17 (8.4)	26 (11.5)	125 (11.8)	12 (9.0)
Heritable	0	5 (3.9)	2 (1.1)	0	14 (1.6)	1 (4.3)	4 (2.0)	4 (1.8)	19 (1.8)	3 (2.2)
Drugs/toxins	0	0	0	0	0	0	2 (1.0)	1 (0.4)	0	1 (0.7)
Associated pulmonary arterial hypertension	7 (50.0)	50 (38.8)	46 (24.7)	4 (40.0)	241 (28.3)	1 (4.3)	54 (26.6)	70 (30.8)	299 (28.3)	34 (25.4)
Connective tissue disease	0	0	2 (1.1)	0	2 (0.2)	0	3 (1.5)	0	3 (0.3)	4 (3.0)
HIV	0	0	0	0	0	0	0	0	0	0
Portal hypertension	0	1 (0.8)	1 (0.5)	0	3 (0.4)	0	1 (0.5)	2 (0.9)	4 (0.4)	0
Congenital heart disease	7 (50.0)	49 (38.0)	41 (22.0)	4 (40.0)	238 (27.9)	1 (4.3)	50 (24.6)	68 (30.0)	292 (27.7)	30 (22.4)
Schistosomiasis	1 (7.1)	0	0	1 (10.0)	2 (0.2)	0	0	1 (0.4)	3 (0.3)	0
PVOD	0	0	3 (1.6)	1 (10.0)	2 (0.2)	1 (4.3)	2 (1.0)	4 (1.8)	5 (0.5)	0
PPHN	0	5 (3.9)	9 (4.8)	0	22 (2.6)	1 (4.3)	9 (4.4)	7 (3.1)	32 (3.0)	7 (5.2)
Left-heart disease	0	3 (2.3)	4 (2.2)	1 (10.0)	32 (3.8)	1 (4.3)	8 (3.9)	7 (3.1)	34 (3.2)	8 (6.0)
Lung disease	6 (42.9)	43 (33.3)	100 (53.8)	2 (20.0)	417 (48.9)	14 (60.9)	106 (52.2)	105 (46.3)	516 (48.9)	67 (50.0)
Chronic thromboembolic pulmonary hypertension	0	0	3 (1.6)	0	3 (0.4)	0	1 (0.5)	1 (0.4)	6 (0.6)	0
Unclear mechanisms	0	3 (2.3)	10 (5.4)	0	17 (2.0)	0	1 (0.5)	5 (2.2)	24 (2.3)	2 (1.5)
Hematologic	0	2 (1.6)	3 (1.6)	0	3 (0.4)	0	0	0	7 (0.7)	1 (0.7)
Systemic disorders	0	0	2 (1.1)	0	5 (0.6)	0	0	2 (0.9)	5 (0.5)	0
Metabolic disorders	0	0	1 (0.5)	0	1 (0.1)	0	1 (0.5)	2 (0.9)	1 (0.1)	0
Segmental pulmonary hypertension	0	1 (0.8)	0	0	2 (0.2)	0	0	0	2 (0.2)	1 (0.7)
Others	0	0	1 (0.5)	0	2 (0.2)	0	0	1 (0.4)	2 (0.2)	0

Values are number (%).

Table III. Pulmonary hypertension subtypes significantly associated with specific racial and ethnic subgroups

Races/ethnicities	Pulmonary hypertension subtype	OR (95% CI)	*P* value
Analyses including all patients			
American Indian/Alaska Native	Schistosomiasis	30.7 (1.47-258.6)	.0034
Asian	Pulmonary arterial hypertension	2.04 (1.41-2.97)	.0002
	APAH	1.66 (1.13-2.42)	.0084
	Pulmonary arterial hypertension- congenital heart disease	1.67 (1.14-2.44)	.0152
	Pulmonary hypertension-lung	0.51 (0.34-0.74)	.0005
Black	Pulmonary arterial hypertension	0.57 (0.40-0.79)	.0009
	Idiopathic pulmonary arterial hypertension	0.37 (0.18-0.69)	.0035
	Chronic thromboembolic pulmonary hypertension	5.60 (1.03-30.5)	.0357
	Unknown	2.86 (1.27-6.09)	.0079
Native Hawaiian/other Pacific Islander	PVOD	22.2 (1.12-149.9)	.0061
	Schistosomiasis	44.5 (2.09-388.1)	.0016
White	PVOD	0.17 (0.02-0.78)	.0335
Multiracial	APAH	0.11 (0.01-0.53)	.0312
	Pulmonary arterial hypertension- congenital heart disease	0.11 (0.01-0.55)	.0342
Analysis including only patients diagnosed after the neonatal period			
American Indian/Alaska Native	Schistosomiasis	45.8 (2.03-517.9)	.0025
Asian	Pulmonary arterial hypertension	1.83 (1.21-2.79)	.0045
	Pulmonary hypertension-lung	0.61 (0.39-0.93)	.0236
Black	Pulmonary arterial hypertension	0.44 (0.30-0.62)	<.0001
	Idiopathic pulmonary arterial hypertension	0.29 (0.14-0.56)	.0006
	APAH	0.67 (0.45-0.97)	.0393
	Pulmonary arterial hypertension- congenital heart disease	0.62 (0.42-0.91)	.0164
	Lung disease	2.09 (1.48-2.95)	<.0001
Native Hawaiian/other Pacific Islander	PVOD	42.8 (1.57-260.7)	.0031
	Schistosomiasis	65.6 (2.86-769.5)	.0011
White	Idiopathic pulmonary arterial hypertension	1.58 (1.06-2.41)	.0289
Multiracial	APAH	0.10 (0.01-0.47)	.0238
	Pulmonary arterial hypertension- congenital heart disease	0.10 (0.01-0.49)	.0259
	Pulmonary hypertension-Lung	2.77 (1.12-7.43)	.0316
Hispanic	PVOD	6.11 (1.34-31.3)	.0184
Analysis including only patients diagnosed during the neonatal period			
Black	PPHN	4.07 (1.54-10.0)	.0029
	Pulmonary hypertension-lung	0.25 (0.11-0.56)	.0008
	BPD	8.11 (3.28-19.8)	<.0001
	Congenital diaphragmatic hernia	0.16 (0.06-0.36)	<.0001
White	PPHN	0.29 (0.13-0.65)	.0020
	Pulmonary hypertension-lung	3.51 (1.92-6.45)	<.0001
	BPD	0.38 (0.17-0.88)	.0190
	Congenital diaphragmatic hernia	2.29 (1.25-4.18)	.0070

APAH, associated pulmonary arterial hypertension.

not significantly associated with specific pulmonary hypertension subtypes, sex, or county-level childhood poverty rate.

Variability in survival outcomes was observed across racial and ethnic subgroups (**Table IV** and **Table V**; available at www.jpeds.com). For children diagnosed after the neonatal period, increased mortality risk was observed in black patients (HR, 2.46; 95% CI, 1.17-5.17; $P = .0176$; **Figure 2**; available at www.jpeds.com), and the risk remained significant after adjusting for age at diagnosis, sex, and county-level poverty rate (HR, 2.42; 95% CI, 1.12-5.23; $P = .0243$). A poorer survival outcome was also observed among Native Hawaiian/other Pacific Islander children diagnosed beyond the neonatal period (HR, 4.50; 95% CI, 1.08-18.8; $P = .0393$), and mortality risk remained significant after adjusting for age at diagnosis, sex, and county-level poverty rate (HR, 4.97; 95% CI, 1.16-21.3; $P = .0308$). No significant racial and ethnic variability in mortality risk was observed in children diagnosed during the first 4 weeks of life. The majority of neonatal deaths (n = 11) were infants with congenital diaphragmatic hernia (n = 9). In sensitivity analyses including both prevalent and incident cases, an increased mortality risk was observed in black children and reduced mortality risk was observed in white children in both adjusted and unadjusted models (**Table VI**; available at www.jpeds.com).

We evaluated the survival outcomes of patients with lung disease-associated pulmonary hypertension and pulmonary arterial hypertension. Survival analysis of the incident cohort of patients with lung disease-associated pulmonary hypertension showed that black patients experienced poorer survival outcomes compared with white patients (**Figure 3**; available at www.jpeds.com), and this association remained significant after excluding neonates and adjusting for age at diagnosis, sex, and county-level childhood poverty rate (HR, 2.91; 95% CI, 1.01-8.42; $P = .0489$; **Table IV**). However, a subgroup analysis of neonates with lung disease–associated pulmonary hypertension did not reveal statistically significant racial and ethnic differences in survival. We performed a sensitivity analysis that included prevalent and incident cases of patients with congenital

Table IV. Cox regression analysis of survival outcome by race and ethnicity

Variables	Unadjusted HR (95% CI)	Unadjusted *P* value	Adjusted* HR (95% CI)	Adjusted* *P* value
Analyses including all pulmonary hypertension subtypes				
All incident cases				
Race				
American Indian/Alaska Native	1.73 (0.24-12.6)	.5860	1.43 (0.20-10.4)	.7256
Asian	0.65 (0.23-1.82)	.4132	0.75 (0.27-2.09)	.5826
Black	1.99 (1.03-3.84)	.0396	1.93 (0.98-3.78)	.0934
Multiracial	1.09 (0.26-4.49)	.9059	1.17 (0.28-4.85)	.8300
Native Hawaiian/other Pacific Islander	3.23 (0.78-13.3)	.1047	3.36 (0.80-14.1)	.0969
White	0.63 (0.35-1.12)	.1142	0.61 (0.34-1.08)	.0896
Ethnicity				
Hispanic	0.45 (0.16-1.26)	.1289	0.45 (0.16-1.27)	.1329
Incident cases diagnosed after the neonatal period				
Race				
American Indian/Alaska Native	2.51 (0.34-18.4)	.3652	2.13 (0.29-15.9)	.4600
Asian	0.65 (0.20-2.13)	.4763	0.80 (0.24-2.64)	.7120
Black	2.46 (1.17-5.17)	.0176	2.42 (1.12-5.23)	.0243
Multiracial	1.43 (0.34-5.99)	.6228	1.57 (0.37-6.64)	.5420
Native Hawaiian/other Pacific Islander	4.50 (1.08-18.8)	.0393	4.97 (1.16-21.3)	.0308
White	0.46 (0.23-0.90)	.0244	0.42 (0.21-0.83)	.0134
Ethnicity				
Hispanic	0.47 (0.14-1.54)	.2135	0.50 (0.15-1.64)	.2547
Incident cases diagnosed during the neonatal period				
Race				
American Indian/Alaska Native	0.00 (0.00-∞)	.9983	0.00 (0.00-∞)	.9980
Asian	0.76 (0.10-5.83)	.7937	0.60 (0.07-4.89)	.6330
Black	1.08 (0.24-4.83)	.9203	1.04 (0.23-4.69)	.9600
Multiracial	0.00 (0.00-∞)	.9983	0.00 (0.00-∞)	.9983
Native Hawaiian/other Pacific Islander	0.00 (0.00-∞)	.9983	0.00 (0.00-∞)	.9980
White	1.40 (0.39-5.01)	.6087	1.68 (0.44-6.31)	.4460
Ethnicity				
Hispanic	0.43 (0.06-3.25)	.4102	0.32 (0.04-2.56)	.2810
Subgroup analyses of patients with lung disease-associated pulmonary hypertension				
All incident cases				
Race				
American Indian/Alaska Native	0.00 (0.00-∞)	.9979	0.00 (0.00-∞)	.9979
Asian	0.52 (0.07-3.87)	.5232	0.52 (0.07-3.88)	.5210
Black	2.84 (1.15-7.04)	.0241	3.01 (1.18-7.65)	.0207
Multiracial	0.90 (0.12-6.72)	.9197	0.98 (0.13-7.47)	.9870
Native Hawaiian/other Pacific Islander	0.00 (0.00-∞)	.9979	0.00 (0.00-∞)	.9979
White	0.59 (0.25-1.40)	.2338	0.59 (0.25-1.41)	.2330
Ethnicity				
Hispanic	0.73 (0.17-3.12)	.6683	0.80 (0.19-3.45)	.7650
Incident cases diagnosed after the neonatal period				
Race				
American Indian/Alaska Native	0.00 (0.00-∞)	.9978	0.00 (0.00-∞)	.9978
Asian	0.63 (0.08-4.81)	.6574	0.64 (0.08-4.93)	.6710
Black	2.96 (1.05-8.32)	.0395	2.91 (1.01-8.42)	.0489
Multiracial	0.96 (0.13-7.32)	.9703	1.01 (0.13-7.91)	.9960
Native Hawaiian/other Pacific Islander	NA	NA	NA	NA
White	0.50 (0.18-1.37)	.1765	0.50 (0.18-1.41)	.1900
Ethnicity				
Hispanic	1.00 (0.22-4.42)	.9968	1.17 (0.26-5.21)	.8370
Incident cases diagnosed during the neonatal period				
Race				
American Indian/Alaska Native	0.00 (0.00-∞)	.9990	0.00 (0.00-∞)	.9990
Asian	0.00 (0.00-∞)	.9990	0.00 (0.00-∞)	.9990
Black	4.05 (0.47-34.7)	.2014	4.04 (0.47-35.1)	.2050
Multiracial	NA	NA	NA	NA
Native Hawaiian/other Pacific Islander	0.00 (0.00-∞)	.9990	0.00 (0.00-∞)	.9990
White	0.82 (0.10-6.99)	.8531	0.81 (0.09-7.58)	.8500
Ethnicity				
Hispanic	0.00 (0.00-∞)	.9987	0.00 (0.00-∞)	.9987
Subgroup analyses of patients with pulmonary arterial hypertension				
All incident cases				
Race				
American Indian/Alaska Native	3.14 (0.42-23.7)	.2670	2.36 (0.31-17.9)	.4067
Asian	0.86 (0.25-2.97)	.8112	1.17 (0.33-4.14)	.8026
Black	0.96 (0.22-4.17)	.9551	0.69 (0.16-3.05)	.6210

(*continued*)

Table IV. Continued

Variables	Unadjusted HR (95% CI)	Unadjusted *P* value	Adjusted* HR (95% CI)	Adjusted* *P* value
Multiracial	2.20 (0.29-16.6)	.4458	2.83 (0.36-22.0)	.3206
Native Hawaiian/other Pacific Islander	6.15 (1.40-26.9)	.0159	8.61 (1.81-40.8)	.0067
White	0.58 (0.23-1.47)	.2538	0.56 (0.22-1.42)	.2187
Ethnicity				
Hispanic	0.47 (0.11-2.03)	.3104	0.31 (0.07-1.47)	.1422
Incident cases diagnosed after the neonatal period				
Race				
American Indian/Alaska Native	3.90 (0.51-29.8)	.1900	2.61 (0.34-20.2)	.3580
Asian	0.74 (0.17-3.32)	.6979	1.10 (0.24-5.03)	.9050
Black	1.32 (0.30-5.90)	.7153	0.98 (0.21-4.53)	.9790
Multiracial	2.49 (0.32-19.1)	.3801	2.62 (0.33-20.6)	.3610
Native Hawaiian/other Pacific Islander	7.00 (1.56-31.2)	.0111	8.29 (1.67-41.2)	.0097
White	0.44 (0.15-1.26)	.1248	0.41 (0.14-1.20)	.1045
Ethnicity				
Hispanic	0.30 (0.04-2.27)	.2425	0.24 (0.03-1.94)	.1819
Incident cases diagnosed during the neonatal period				
Race				
American Indian/Alaska Native	NA	NA	NA	NA
Asian	0.99 (0.10-9.69)	.9949	0.75 (0.06-9.98)	.8280
Black	0.00 (0.00-∞)	.9991	0.00 (0.00-∞)	.9991
Multiracial	NA	NA	NA	NA
Native Hawaiian/other Pacific Islander	NA	NA	NA	NA
White	2.50 (0.24-26.1)	.4441	2.08 (0.19-22.3)	.5450
Ethnicity				
Hispanic	0.71 (0.07-7.25)	.7731	0.10 (0.00-3.76)	.2113

NA, Not applicable.
*Adjusted by age at diagnosis, sex, and county-level childhood poverty rate.

diaphragmatic hernia and PPHN and measured survival time from the date of birth to the date of death; poorer survival outcome was observed among Native Hawaiian/other Pacific Islander children in both the unadjusted and adjusted models (**Table VII**; available at www.jpeds.com). Survival analysis of an incident cohort of patients with pulmonary arterial hypertension showed an increased mortality risk among Native Hawaiian/other Pacific Islander children, and the risk persisted following adjustment for age at diagnosis, sex, and county-level childhood poverty rate (**Table IV**).

Discussion

In this analysis of a large, pediatric-focused pulmonary hypertension registry, we found significant variability in the prevalence of pulmonary hypertension subtypes and survival outcomes among children of different racial and ethnic backgrounds. Among children diagnosed after the neonatal period, Asian patients were more likely to have a diagnosis of pulmonary arterial hypertension and less likely to develop lung disease–associated pulmonary hypertension, black patients were more likely to have a diagnosis of lung disease–associated pulmonary hypertension and less likely to have pulmonary arterial hypertension, white patients were more likely to have a diagnosis of idiopathic pulmonary arterial hypertension, and Hispanic patients were more likely to have a diagnosis of PVOD (pulmonary veno-occlusive disease). A higher incidence of idiopathic pulmonary arterial hypertension has been previously reported in populations of adult white patients, but the other relationships have not been previously reported. We further observed that PVOD was over-represented among Native Hawaiian/other Pacific Islander patients, and schistosomiasis-associated pulmonary hypertension was over-represented among American Indian/Alaska Native and Native Hawaiian/other Pacific Islander children. However, because American Indian/Alaska Native and Native Hawaiian/other Pacific Islander children represented <2% of the study cohort, study findings pertaining to these racial subgroups should be interpreted with caution. Among neonates, we observed an increased risk of PPHN and BPD among black children, and an increased risk of congenital diaphragmatic hernia among white children.

The relationship between lung disease–associated pulmonary hypertension and specific racial subgroups may be mediated by differences in preterm birth rates, a known risk factor for lung disease–associated pulmonary hypertension in children. Historically, Asian infants have the lowest preterm birth rate in the US, and black infants have the highest.[14] The increased risk of PPHN and BPD among black infants observed in our analysis has been documented in previous studies,[15-17] highlighting the need to address this disparity. Inhaled nitric oxide improves survival and decrease the risk of BPD in preterm black infants but not white infants,[18,19] and genetic variability may contribute to the differential response.[19] These findings combined with ours may provide a rationale for considering inhaled nitric oxide therapy for preterm black infants with severe early respiratory failure who are at high risk of developing BPD.

Previous studies on adult populations documented a higher burden of pulmonary hypertension among black patients with connective tissue disease[6,7]; however, this relationship has not been consistently demonstrated.[20] In our study cohort, black children were over-represented among those with connective tissue disease-associated pulmonary arterial hypertension (2/7 [29%]); however, a risk analysis did not attain statistical significance. Although others have reported a higher risk of familial pulmonary arterial hypertension among white adults[5,11] and a higher prevalence of congenital heart disease–associated pulmonary arterial hypertension among Hispanic individuals,[5] these relationships were not observed in our study cohort. Sampling bias, inadequate sample size, and differences between childhood-onset and adult-onset pulmonary hypertension may explain some of the observed inconsistencies.

Importantly, our study demonstrates a 2-fold increased risk of mortality in black children with lung disease-associated pulmonary hypertension. These findings are consistent with previous studies that reported a poorer prognosis among black adults with pulmonary hypertension.[1-4,21] One study reported a 3-fold increased risk of death among African American adults with interstitial lung disease-associated pulmonary hypertension compared with white patients.[21] A number of factors may contribute to these observed disparities. Historically, racial and ethnic minority populations are disproportionately affected by poor access to healthcare services. Treatment disparities among racial minorities with pulmonary hypertension have been reported in a number of studies.[5,8] Because the prognosis of pulmonary hypertension depends on early diagnosis and treatment, poor access to care likely results in worse outcomes. In our study, we attempted to account for the impact of socioeconomic status by examining the childhood poverty rate in the county where patients reside. Although black and Hispanic patients in our study cohort were more likely to live in counties with higher poverty rates, county-level childhood poverty rate did not seem to be associated with survival outcome. Further studies are needed to investigate other socioeconomic determinants that may contribute to survival disparities not currently captured in our data source, including the type of insurance coverage and treatment access.

Racial differences in clinical expression of disease and treatment response may also affect survival outcomes. A pooled analysis of 6 randomized, controlled trials of endothelin-receptor antagonists showed that white patients experienced greater treatment benefit than black patients, highlighting racial heterogeneity in treatment response to pulmonary arterial hypertension medications that remains poorly understood and understudied.[22] Further studies are needed to explore the underlying causes of survival disparities among black children with pulmonary hypertension. The young age of disease presentation in a substantial proportion of patients in our study cohort further highlights opportunities to investigate genetic causes of pulmonary hypertension among different racial and ethnic subgroups.

Contrary to published evidence documenting higher mortality rates in black and Hispanic preterm infants, our study did not detect disparities in pulmonary hypertension survival outcome among black and Hispanic neonates. Several factors may have contributed to this inconsistency. First, survival outcomes for different pulmonary hypertension subtypes vary substantially. Given the small number of neonates in our dataset, who were predominantly white patients with congenital diaphragmatic hernia, our analysis was not adequately powered to examine survival disparities in individual subtypes. Second, our analysis did not account for the full range of clinical variables (eg, birth weight, prematurity, treatment, family history) known to affect survival outcomes in neonates. We were also unable to ascertain cases of transient pulmonary hypertension in this population. Efforts are currently underway to collect these data elements in the registry. Finally, studies have shown that racial and ethnic disparities in neonatal mortality are often driven by systemic factors. Minority populations tend to be served by healthcare facilities that are under-resourced and unable to provide high-quality care.[23-25] A recent study reported that black and Hispanic infants are more likely to be born in hospitals with higher risk-adjusted neonatal morbidity and mortality rates than white infants.[23] Because our study was limited to 8 academic centers, our analysis could not have adequately captured variability in care quality contributing to the observed survival disparities among minority infants.

Contrary to published data reporting survival disparities among Hispanic patients with pulmonary hypertension, we did not detect ethnic differences in survival outcome in our study cohort. We did observe an increased mortality risk among Native Hawaiian/other Pacific Islander children in both the overall cohort and patients with pulmonary arterial hypertension, but the limited sample size prohibits generalization of the findings.

We acknowledge several limitations of this study. First, the study patients were referred to 1 of 8 tertiary referral centers, and our results may not be generalizable to the US population at large. Because racial and ethnic minorities are historically underserved populations, they are likely under-represented in our study cohort. To investigate the extent of referral bias, we compared the racial/ethnic distribution of patients at the referral centers by querying the Pediatric Health Information System database[26] and the population in the counties of the referral centers based on US Census data.[27] Race and ethnicity data were available for 4 of the 8 referral centers. Asian individuals were under-represented at all 4 centers and black and Hispanic individuals were under-represented at two centers (**Table VIII**; available at www.jpeds.com), indicating that referral bias may be present.

Another limitation is that race and ethnicity were self-reported, limited to broad categories that may not adequately capture biological variability among racial subgroups, and

incomplete. Furthermore, the limited sample size of certain patient subgroups and pulmonary hypertension subtypes prohibited a comprehensive analysis of survival disparities. In addition to referral bias, enrollment bias within each referral center may not truly reflect the pediatric pulmonary hypertension population at each center. Future studies that leverage electronic medical records to characterize racial and ethnic variability in childhood-onset pulmonary hypertension will be important. Some of the pulmonary hypertension subtypes, such as schistosomiasis-associated pulmonary hypertension, are rare in the US; thus, caution should be taken in the interpretation of the risk analysis. Finally, although we attempted to control for the duration of disease using the date of first diagnosis, it is possible that the true duration of disease before the diagnosis of pulmonary hypertension varied and, thus, may have skewed the survival analysis.

Our study demonstrates significant racial variability in the prevalence of pulmonary hypertension subtypes and survival outcomes among children with pulmonary hypertension, and highlights the reduced survival among black children with lung disease-associated pulmonary hypertension. Given the substantial burden of the disease, further studies to validate the observed phenotypic differences and to understand the underlying causes of survival disparities are warranted. ■

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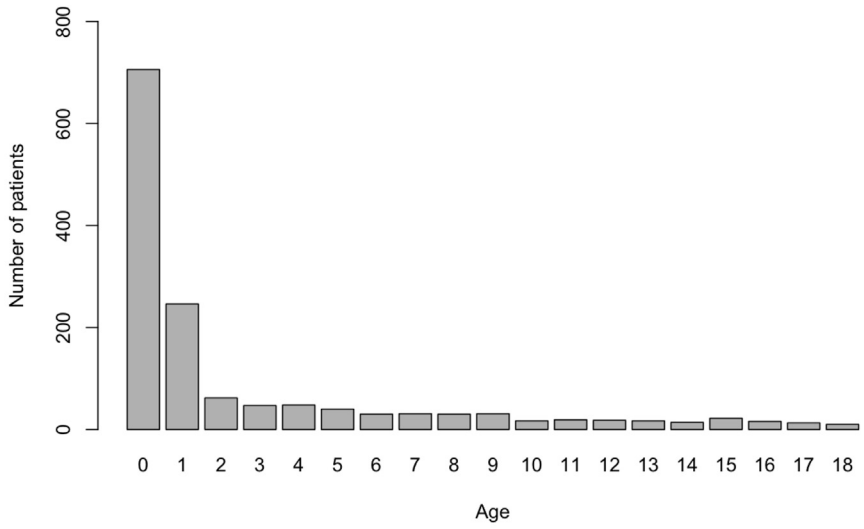

PH subtypes	Age of diagnosis (years)			
	1st quartile	Median	Mean	3rd quartile
PAH	0.0	2.0	4.3	7.0
Idiopathic	1.0	6.0	6.2	9.0
Heritable	3.0	6.0	7.2	12.5
Drugs/toxins	0.8	1.5	1.5	2.3
Associated PAH	0.0	1.0	3.5	5.0
Connective tissue disease (CTD)	4.0	9.0	7.6	9.0
HIV	-	-	-	-
Portal hypertension	1.0	2.0	4.5	7.5
Congenital heart disease (CHD)	0.0	1.0	3.4	5.0
Schistosomiasis	0.8	1.0	1.3	1.5
PVOD	0.0	1.0	4.6	5.0
Persistent PH of the newborn (PPHN)	0.0	0.0	0.2	0.0
Left-heart disease	0.0	1.0	3.3	4.0
Lung disease	0.0	0.0	1.1	1.0
Bronchopulmonary dysplasia	97.0 days	153.5 days	355.8 days	271.5 days
CTEPH	15.5	16.0	16.3	17.5
Unclear mechanisms	0.5	4.0	6.2	12.0
Hematological	1.0	6.0	6.4	9.5
Systemic disorders	4.5	11.0	9.4	14.0
Metabolic disorders	0.0	0.0	6.0	9.0
Segmental PH	3.0	5.0	8.0	11.5
Others	1.0	2.0	4.7	7.0

Figure 1. Distribution of pulmonary hypertension diagnosis age. *CTEPH*, chronic thromboembolic pulmonary hypertension; *PAH*, pulmonary arterial hypertension.

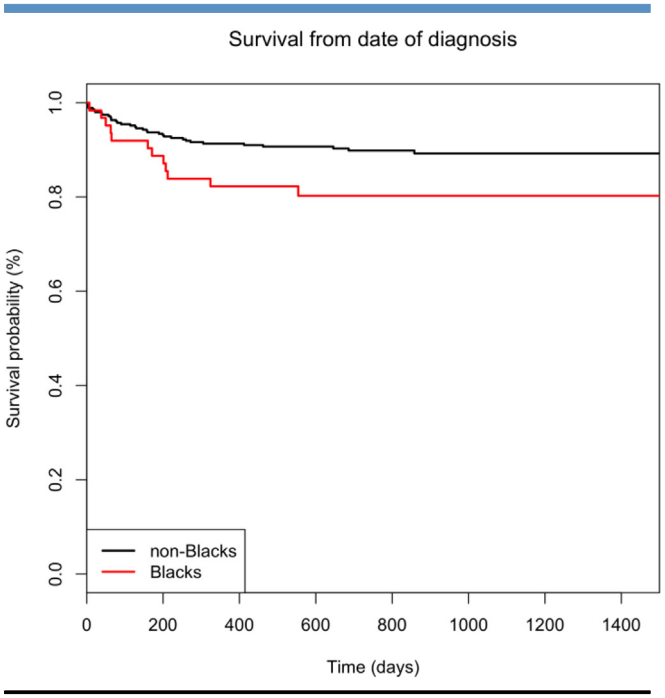

Figure 2. Survival outcomes of non-neonates across all pulmonary hypertension subtypes.

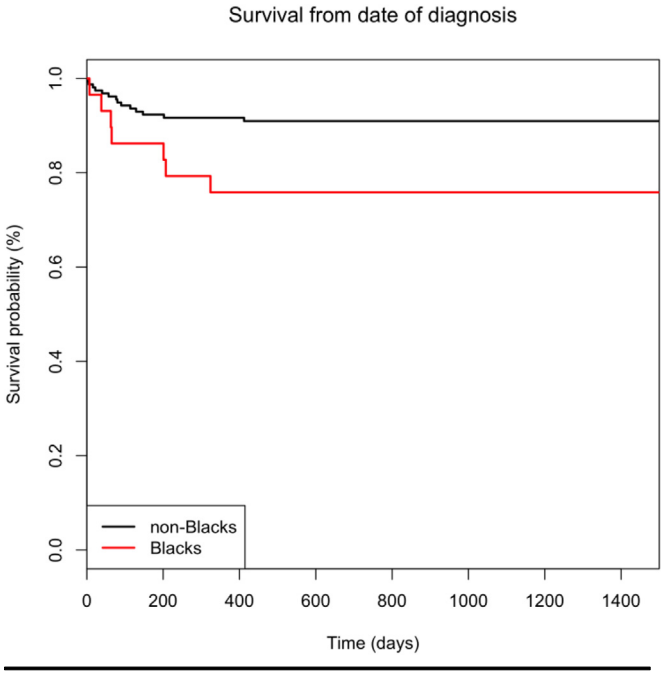

Figure 3. Survival outcomes of non-neonates with pulmonary hypertension due to lung disease.

Table V. Survival outcomes stratified by racial and ethnic subgroups

	Prevalent and incident cases		Incident cohort		Incident cohort, excluding neonates		Incident cohort, neonates only	
Races/ethnicities	**No.**	**Death, no. (%)**	**No.**	**Death, no. (%)**	**No.**	**Death, no. (%)**	**No.**	**Death, no. (%)**
All pulmonary hypertension subtypes								
American Indian/Alaska Native	14	1	4	0	3	0	1	0
Asian	129	11 (7.9)	50	4 (8.0)	42	3 (7.1)	8	1 (12.5)
Black	186	21 (8.6)	64	10 (15.6)	52	8 (15.4)	12	2 (16.7)
Native Hawaiian/other Pacific Islander	10	2 (20.0)	6	2 (33.3)	5	2 (40.0)	1	0
White	852	53 (5.3)	264	21 (8.0)	201	13 (6.5)	63	8 (12.7)
Multiracial	23	2 (9.5)	15	2 (13.3)	14	2 (14.3)	1	0
Missing race	203	15 (4.3)	105	6 (5.7)	76	3 (3.9)	29	3 (10.3)
Hispanic	227	16 (4.9)	73	2 (2.7)	58	2 (33.3)	15	0
Non-Hispanic	1056	78 (6.1)	369	36 (9.8)	289	25 (8.7)	80	11 (13.8)
Missing ethnicity	134	11 (6.0)	66	7 (10.6)	46	4 (8.7)	20	3 (15.0)
Total	1,417	105 (7.4)	517	45 (8.7)	393	31 (7.9)	115	14 (12.2)
Lung disease-associated pulmonary hypertension								
American Indian/Alaska Native	5	0	1	0	1	0	0	0
Asian	42	3 (7.1)	16	1 (6.3)	13	1 (7.7)	3	0
Black	98	7 (7.1)	28	6 (21.4)	26	5 (19.2)	1	1 (100.0)
Native Hawaiian/other Pacific Islander	2	0	1	0	0	0	1	0
White	405	13 (3.2)	120	8 (6.7)	83	4 (4.8)	37	4 (10.8)
Multiracial	11	1 (9.1)	9	1 (11.1)	9	1 (11.1)	0	0
Missing race	107	5 (4.7)	52	5 (9.6)	37	3 (8.1)	15	2 (13.3)
Hispanic	103	4 (3.9)	26	2 (7.7)	21	2 (9.5)	5	0
Non-Hispanic	502	19 (3.8)	167	13 (7.8)	126	8 (6.3)	41	5 (12.2)
Missing ethnicity	65	6 (9.2)	34	6 (17.6)	22	4 (18.2)	12	2 (16.7)
Total	670	29 (4.3)	227	21 (9.3)	169	14 (8.3)	58	7 (12.1)
Pulmonary arterial hypertension								
American Indian/Alaska Native	7	0	2	0	2	0	0	0
Asian	73	6	28	3 (10.7)	26	2 (7.7)	2	1 (50.0)
Black	64	6	22	1 (0.05)	19	1 (5.3)	3	0
Native Hawaiian/other Pacific Islander	6	2	4	2 (50.0)	4	2 (50.0)	0	0
White	353	20	97	7 (7.1)	86	6 (6.8)	11	1 (9.1)
Multiracial	4	1	3	1 (33.3)	3	1 (33.3)	0	0
Missing race	82	2	40	1	33	0	7	1 (14.3)
Hispanic	98	4	34	0	30	0	4	0
Non-Hispanic	436	31	140	14	125	12	15	2
Missing ethnicity	55	2	22	1	18	0	4	1
Total	589	37	196	15 (8.9)	173	12 (6.8)	23	3 (13.0)

Table VI. Cox regression analysis of survival outcome, including prevalent and incident cases

	Unadjusted		Adjusted	
Variables	**HR (95% CI)**	***P* value**	**HR (95% CI)**	***P* value**
Analysis including all patients				
Race				
American Indian/Alaska Native	1.10 (0.15-7.93)	.9225	1.05 (0.15-7.57)	.2023
Asian	1.32 (0.70-2.49)	.3869	1.38 (0.73-2.61)	.3243
Black	1.91 (1.17-3.12)	.0100	1.75 (1.06-2.92)	.0303
Multiracial	1.61 (0.40-6.56)	.5060	1.70 (0.42-6.94)	.4588
Native Hawaiian/other Pacific Islander	3.56 (0.88-14.5)	.0760	3.55 (0.87-14.5)	.0770
White	0.51 (0.33-0.78)	.0018	0.53 (0.34-0.81)	.0038
Ethnicity				
Hispanic	1.02 (0.59-1.75)	.9473	0.94 (0.54-1.62)	.8141
Analysis including only patients diagnosed after the neonatal period				
Race				
American Indian/Alaska Native	1.30 (0.18-9.37)	.7948	1.33 (0.18-9.63)	.7759
Asian	1.20 (0.60-2.42)	.6060	1.28 (0.63-2.60)	.4922
Black	1.92 (1.14-3.24)	.0150	1.78 (1.04-3.06)	.0369
Multiracial	1.85 (0.45-7.57)	.3917	1.96 (0.48-8.04)	.3505
Native Hawaiian/other Pacific Islander	4.10 (1.00-16.7)	.0496	3.94 (0.96-16.1)	.0570
White	0.50 (0.31-0.79)	.0032	0.51 (0.32-0.82)	.0053
Ethnicity				
Hispanic	1.14 (0.64-2.00)	.6611	1.09 (0.62-1.91)	.7782
Analysis including only patients diagnosed during the neonatal period				
Race				
American Indian/Alaska Native	0.00 (0.00-∞)	.9973	0.00 (0.00-∞)	.9980
Asian	1.88 (0.43-8.27)	.4408	1.79 (0.41-7.94)	.4410
Black	1.35 (0.31-5.93)	.6931	1.22 (0.27-5.56)	.7960
Multiracial	0.00 (0.00-∞)	.9982	0.00 (0.00-∞)	.9970
Native Hawaiian/other Pacific Islander	0.00 (0.00-∞)	.9979	0.00 (0.00-∞)	.9979
White	0.72 (0.23-2.24)	.5731	0.79 (0.25-2.54)	.6960
Ethnicity				
Hispanic	0.36 (0.05-2.70)	.3173	0.29 (0.04-2.26)	.2370

Table VII. Cox regression analysis of survival outcome, including incident and prevalent cases of patients with congenital diaphragmatic hernia and PPHN

	Unadjusted		Adjusted	
Variables	**HR (95% CI)**	***P* value**	**HR (95% CI)**	***P* value**
Race				
American Indian/Alaska Native	0.00 (0.00-∞)	.9960	0.00 (0.00-∞)	.9957
Asian	0.76 (0.30-1.94)	.5690	1.02 (0.39-2.62)	.9730
Black	1.21 (0.54-2.73)	.6390	1.42 (0.60-3.32)	.4230
Multiracial	0.00 (0.00-∞)	.9969	0.00 (0.00-∞)	.9969
Native Hawaiian/other Pacific Islander	5.76 (1.37-24.2)	.0167	5.04 (1.20-21.2)	.0274
White	0.97 (0.51-1.82)	.9130	0.74 (0.38-1.43)	.3707
Ethnicity				
Hispanic	1.23 (0.62-2.45)	.5520	1.22 (0.61-2.46)	.5726

Table VIII. Racial and ethnic composition of pulmonary hypertension referral centers, compared with racial and ethnic composition of the county in which individual centers were situated

Races/ethnicities	% Hospital visits (95% CI	% County population (95% CI)
Referral center 1		
Race		
Asian	21.4 (20.6-21.4)	33.1 (33.0-33.2)
Black	2.9 (2.8-3.0)	2.8 (2.8-2.8)
Native Hawaiian/other Pacific Islander	2.0 (1.9-2.1)	1.4 (1.4-1.4)
White	46.1 (45.7-46.5)	54.2 (54.1-54.3)
American Indian	0.07 (0.07-0.07)	0.5 (0.05-0.05)
Multiracial	0	7.9 (7.8-8.0)
Unspecified	27.3 (26.9-27.7)	0
Ethnicity		
Hispanic/Latino	40.5 (40.0-40.9)	35.8 (35.7-35.9)
Not Hispanic/Latino	59.4 (59.0-59.8)	64.2 (64.1-64.3)
Unspecified	0.1 (0.1-0.1)	0
Referral center 2		
Race		
Asian	2.8 (2.8-2.8)	6.9 (6.8-7.0)
Black	49.4 (49.3-49.5)	51.3 (51.1-51.5)
Native Hawaiian/other Pacific Islander	0.09 (0.08-0.10)	1.2 (1.2-1.2)
White	32.6 (32.5-32.7)	35.9 (35.7-36.1)
American Indian	0.06 (0.05-0.07)	0.2 (0.2-0.2)
Multiracial	1.9 (1.9-1.9)	4.5 (4.4-4.6)
Unspecified	14.2 (14.1-14.3)	0
Ethnicity		
Hispanic/Latino	8.7 (8.6-8.8)	20.7 (20.6-20.8)
Not Hispanic/Latino	90.9 (90.8-91.0)	79.3 (79.1-79.4)
Unspecified	0.3 (0.3-0.3)	0
Referral center 3		
Race		
Asian	2.2 (2.2-2.2)	3.1 (3.0-3.2)
Black	8.4 (8.3-8.5)	5.1 (5.0-5.2)
Native Hawaiian/other Pacific Islander	0.3 (0.3-0.3)	2.1 (2.1-2.1)
White	59.3 (59.2-59.4)	85.0 (84.9-85.1)
American Indian	0.5 (0.5-0.5)	0.2 (0.2-0.2)
Multiracial	2.5 (2.5-2.5)	4.6 (4.5-4.7)
Unspecified	28.7 (28.6-28.8)	0
Ethnicity		
Hispanic/Latino	56.0 (55.9-56.1)	42.4 (42.2-42.6)
Not Hispanic/Latino	60.1 (60.0-60.2)	57.6 (57.4-57.8)
Unspecified	6.3 (6.2-6.4)	0
Referral center 4		
Race		
Asian	3.3 (3.2-3.4)	7.9 (7.8-8.0)
Black	13.3 (13.2-13.4)	32.0 (31.8-32.2)
Native Hawaiian/other Pacific Islander	0.08 (0.07-0.09)	0.2 (0.2-0.2)
White	44.5 (44.3-44.7)	53.6 (53.4-53.8)
American Indian	0.1 (0.1-0.1)	0.9 (0.9-0.9)
Multiracial	1.9 (1.9-1.9)	5.4 (5.3-5.6)
Unspecified	26.1 (26.0-20.7)	0
Ethnicity		
Hispanic/Latino	20.6 (20.5-20.7)	32.3 (32.1-32.5)
Not Hispanic/Latino	64.2 (64.0-64.4)	67.7 (67.5-67.9)
Unspecified	15.3 (15.2-15.4)	0