



# The impact of health insurance coverage on racial/ethnic disparities in US childhood and adolescent cancer stage at diagnosis

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**BACKGROUND:** Racial/ethnic minority children and adolescents are more likely to have an advanced cancer diagnosis compared with non-Hispanic Whites, which may relate to the lack of consistent health care access. This study aims to describe racial/ethnic disparities in cancer diagnosis stage among children and adolescents and assess whether health insurance mediates these disparities. **METHODS:** Data on individuals  $\leq 19$  years of age diagnosed with primary cancers from 2007 to 2016 were obtained from the Surveillance, Epidemiology, and End Results 18 database. Prevalence ratios (PRs) and 95% confidence intervals (CIs) for the association between race/ethnicity and cancer diagnosis stage were calculated using Poisson regression. Analyses addressing health insurance as a potential mediator were also performed. **RESULTS:** Compared with non-Hispanic Whites, racial/ethnic minorities had a higher prevalence of a distant cancer diagnosis, with PRs of 1.31 (95% CI, 1.23–1.40) for non-Hispanic Blacks, 1.14 (95% CI, 1.04–1.24) for non-Hispanic Asian/Pacific Islanders, and 1.15 (95% CI, 1.09–1.21) for Hispanics. These associations were attenuated when adjusting for health insurance, with PRs of 1.24 (95% CI, 1.16–1.33) for non-Hispanic Blacks, 1.11 (95% CI, 1.02–1.21) for non-Hispanic Asian/Pacific Islanders, and 1.07 (95% CI, 1.01–1.13) for Hispanics. Any Medicaid or no insurance at diagnosis mediated 49%, 22%, and 9% of the observed association with distant stage in Hispanics, non-Hispanic Blacks, and non-Hispanic Asian/Pacific Islanders, respectively. **CONCLUSIONS:** Disparities in cancer diagnosis stage in racial/ethnic minority children and adolescents may be partially explained by health insurance coverage. Further research is needed to understand the mechanisms. *Cancer* 2022;128:3196–3203. © 2022 American Cancer Society.

**KEYWORDS:** adolescent, early diagnosis, healthcare disparities, neoplasm, pediatric.

## INTRODUCTION

In the last 2 decades, the overall 5-year relative survival among US childhood and adolescents with cancer has improved markedly from 62% to approximately 86% due to advances in therapeutics, supportive care, and high rates of participation in clinical trials.<sup>1</sup> However, survival rates vary by diagnosis stage. Based on estimates from the Surveillance, Epidemiology, and End Results (SEER) program 18 registries data, the 5-year relative survival rates for children and adolescents with localized, regional, and distant solid cancers between 2007 and 2011 were 95.3%, 86.3%, and 79.0%, respectively.<sup>2</sup>

Cancer stage describes the extent of disease at presentation and is also a marker of disease progression and the basis of treatment planning.<sup>3</sup> Children and adolescents with advanced stage cancer diagnoses usually need more aggressive, intensive, and adapted therapies, resulting in more side or late effects, such as organ dysfunction, decreased fertility, and a worse overall quality of life.<sup>4–6</sup> Early diagnosis is important because it allows for more timely treatment, usually with less aggressive therapy.<sup>3</sup> However, early detection in children with cancer is complicated by various factors including the rarity of the disease, distinct biological properties and clinical behaviors compared with adult cancers, and the knowledge, attitudes, and behaviors of parents, caregivers, and providers about cancer in this young age group.<sup>3</sup>

Along the cancer diagnosis pathway, timely access to health care optimizes prognosis. Regular health insurance coverage facilitates routine physician checkups and access to health care resources and increases the likelihood of early cancer detection. A previous study has shown that compared with privately insured children and adolescents, those enrolled in public insurance and who are uninsured are more likely to have a metastatic cancer diagnosis.<sup>7</sup>

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Substantial racial/ethnic disparities in cancer diagnosis stage have been reported in multiple studies. For example, findings from childhood central nervous systems tumors and melanoma studies have shown that racial/ethnic minorities are more likely to receive an advanced-stage cancer diagnosis than non-Hispanic Whites.<sup>8,9</sup> Given the higher proportion of racial/ethnic minorities in non-privately insured and uninsured populations,<sup>7</sup> we hypothesized that being uninsured or having Medicaid might mediate some of the observed advanced cancer diagnoses among racial/ethnic minority children and adolescents. Recent findings from US breast cancer patients provide evidence that nearly half of the observed racial/ethnic differences in the risk of being diagnosed with advanced breast cancer can be explained by differences in health insurance coverage.<sup>10</sup>

To our knowledge, no prior studies have described differences in cancer stage at diagnosis by race/ethnicity among children and adolescents overall and by cancer type and quantitatively estimated the extent to which health insurance coverage mediates these differences. This information can help inform further research and targeted cancer control strategies to reduce the proportion of cancers diagnosed at an advanced stage.

## MATERIALS AND METHODS

### Population

Data for individuals  $\leq 19$  years old that were diagnosed with primary cancers from January 1, 2007 to December 31, 2016 were obtained from the SEER Program 18 database consisting of 18 population-based cancer registries and representing approximately 28% of the US population. Individuals diagnosed with leukemias, myeloproliferative diseases, and myelodysplastic diseases were excluded because all individuals were marked as having distant stage diagnoses.

### Variables

The outcome variable stage at diagnosis was defined using the “SEER Combined Summary Stage 2000 (2004+)” variable and categorized as early (localized and regional stages) and advanced (distant stage). Race and ethnicity were collapsed into non-Hispanic White, non-Hispanic Black, non-Hispanic Asian/Pacific Islander, and Hispanic using the “Race recode (W, B, AI, API)” and “Origin recode NHIA (Hispanic, Non-Hisp)” variables. Non-Hispanic American Indian/Alaskan Native individuals were excluded due to their small sample size. Health insurance coverage type at diagnosis was defined using the

“Insurance Recode (2007+)” variable<sup>11</sup> and categorized as insured (insured and insured/no specifics), any Medicaid, and uninsured. Other covariates were identified using a directed acyclic graph (Figure S1, available at <http://www.dagitty.net/dags.html?id=wVPRB2>) and include age, sex, and county-level socioeconomic status indicators. Age was categorized as <1, 1–4, 5–9, 10–14, and 15–19 years and further dichotomized into children (0–14 years) and adolescent (15–19 years) categories using the “Age at diagnosis” variable. Sex was defined as male and female using the “Sex” variable. Selected socioeconomic status indicator quartiles based on county-level attributes ascertained from the 2013–2017 American Community Survey included median household income, unemployment percentage, and rural/urban residence area. Cancer types were defined using the “ICCC site recode ICD-O-3/WHO 2008 variable”.<sup>12</sup>

### Statistical analyses

Prevalence ratios (PRs) and 95% confidence intervals (CIs) for the associations between cancer diagnosis stage and race/ethnicity were calculated using Poisson regression with robust error variance. The  $p$  value for the interaction between race/ethnicity and age group (children and adolescents) was estimated using likelihood ratio test. Subgroup analyses by age group were further performed. Mediation analyses were performed using the R package *mma* developed by Yu et al.<sup>13</sup> Under the counterfactual framework, this method applies generalized mediation analysis to estimate the total, direct, and indirect effects based on the changing rate in the outcome to accommodate the outcome, exposure variables, and mediators in any format (e.g., continuous, binary, or multi-categorical). It calculates 95% CIs for these effects using the bootstrap method. The proportion mediated was calculated as the ratio of the logs of the PRs for the indirect and total effects.<sup>13</sup> We conducted sensitivity analyses using datasets with missing data imputed by the multiple imputation by chained equations method in the R *mice* package.<sup>14</sup> Age, sex, and cancer type were included in the imputation procedure as auxiliary variables. Another sensitivity analysis that excluded uninsured cases at diagnosis was performed to examine the contribution of any Medicaid alone at diagnosis versus insured to the observed distant stage disparities by race/ethnicity. All statistical analyses and data visualization were performed using R (version 4.0.2). Code for data management and analyses can be found at <https://github.com/Xiaoyan0221/Racial-ethnic-disparities-in-stage-and-health-insurance>.

## RESULTS

The initial study population included 30,598 children and adolescents with cancer. After excluding cases with missing values on race/ethnicity ( $n = 677$ ), cancer stage ( $n = 1376$ ), insurance coverage ( $n = 1260$ ), and any of the socioeconomic status indicators ( $n = 76$ ), a total of 27,830 cases were included in the analyses. Of these, over half were non-Hispanic White, 27.6% were Hispanic, 11.6% were non-Hispanic Black, and the remaining 7.9% were non-Hispanic Asian/Pacific Islander. In general, non-Hispanic Whites and Asian/Pacific Islanders were more likely to be reported as

insured at diagnosis and residents in areas with higher median household incomes and lower unemployment rates (Table 1). Additionally, there was a higher proportion of individuals diagnosed at a distant cancer stage in racial/ethnic minorities versus non-Hispanic White (23.0%–26.5% vs. 20.4%) (Table 1) and across the majority of cancer types (Table S1). No obvious patterns were observed across age groups, sex, or cancer type (Table 1).

In multivariable models, racial/ethnic minority children and adolescents were more likely to be diagnosed at a distant cancer stage after adjustment for age,

**TABLE 1.** Demographic Characteristics of Children and Adolescents with Cancer According to Race and Ethnicity, 2007–2016 ( $n = 27,830$ )

Characteristic	Non-Hispanic White, No. (%)	Non-Hispanic Black, No. (%)	Non-Hispanic Asian/Pacific Islander, No. (%)	Hispanic, No. (%)
Total	14,741 (53.0)	3219 (11.6)	2195 (7.9)	7675 (27.6)
Age, y				
<1	953 (6.5)	227 (7.1)	186 (8.5)	528 (6.9)
1–4	2643 (17.9)	678 (21.1)	417 (19.0)	1518 (19.8)
5–9	2287 (15.5)	578 (18.0)	352 (16.0)	1230 (16.0)
10–14	3014 (20.4)	676 (21.0)	431 (19.6)	1598 (20.8)
15–19	5844 (39.6)	1060 (32.9)	809 (36.9)	2801 (36.5)
Sex				
Female	6987 (47.4)	1563 (48.6)	1038 (47.3)	3568 (46.5)
Male	7754 (52.6)	1656 (51.4)	1157 (52.7)	4107 (53.5)
Health insurance type				
Insured	11,547 (78.3)	1576 (49.0)	1585 (72.2)	3394 (44.2)
Any Medicaid	2957 (20.1)	1551 (48.2)	575 (26.2)	4048 (52.7)
Uninsured	237 (1.6)	92 (2.9)	35 (1.6)	233 (3.0)
Median household income quartile				
First	4122 (28.0)	1329 (41.3)	155 (7.1)	1372 (17.9)
Second	2715 (18.4)	729 (22.6)	547 (24.9)	2970 (38.7)
Third	4063 (27.6)	759 (23.6)	430 (19.6)	1665 (21.7)
Fourth	3841 (26.1)	402 (12.5)	1063 (48.4)	1668 (21.7)
% Unemployed quartile				
First	5242 (35.6)	447 (13.9)	919 (41.9)	1453 (18.9)
Second	4085 (27.7)	783 (24.3)	536 (24.4)	1771 (23.1)
Third	2367 (16.1)	734 (22.8)	407 (18.5)	2195 (28.6)
Fourth	3047 (20.7)	1255 (39.0)	333 (15.2)	2256 (29.4)
Rural–urban				
Metro	12,818 (87.0)	2985 (92.7)	2140 (97.5)	7438 (96.9)
Rural/urban	1923 (13.0)	234 (7.3)	55 (2.5)	237 (3.1)
Stage				
Localized/regional	11,736 (79.6)	2365 (73.5)	1690 (77.0)	5894 (76.8)
Distant	3005 (20.4)	854 (26.5)	505 (23.0)	1781 (23.2)
Cancer type <sup>a</sup>				
Lymphomas and reticuloendothelial neoplasms	2904 (19.7)	723 (22.5)	444 (20.2)	1371 (17.9)
CNS and miscellaneous intracranial and intraspinal neoplasms	3679 (25.0)	731 (22.7)	447 (20.4)	1581 (20.6)
Neuroblastoma and other peripheral nervous cell tumors	967 (6.6)	234 (7.3)	145 (6.6)	390 (5.1)
Retinoblastoma	1229 (8.3)	397 (12.3)	199 (9.1)	774 (10.1)
Renal tumors	268 (1.8)	95 (3.0)	60 (2.7)	235 (3.1)
Hepatic tumors	710 (4.8)	255 (7.9)	82 (3.7)	428 (5.6)
Malignant bone tumors	249 (1.7)	52 (1.6)	75 (3.4)	196 (2.6)
Soft tissue and other extrasosseous sarcomas	1009 (6.8)	215 (6.7)	147 (6.7)	584 (7.6)
Germ cell tumors, trophoblastic tumors, and neoplasms of gonads	1185 (8.0)	195 (6.1)	255 (11.6)	1067 (13.9)
Other malignant epithelial neoplasms and malignant melanomas	2496 (16.9)	309 (9.6)	331 (15.1)	1023 (13.3)
Other and unspecified malignant neoplasms	45 (0.3)	13 (0.4)	10 (0.5)	26 (0.3)

Abbreviation: CNS, central nervous system.

<sup>a</sup>Categorized based on the International Classification of Childhood Cancer Third Edition (ICCC-3),<sup>12</sup> excluding leukemias, myeloproliferative diseases, and myelodysplastic diseases, which were all staged as distant.

sex, and socioeconomic status. Specifically, the prevalence of having a distant cancer stage diagnosis was higher for non-Hispanic Blacks (PR, 1.31; 95% CI, 1.23–1.40), non-Hispanic Asian/Pacific Islanders (PR, 1.14; 95% CI, 1.04–1.24), and Hispanics (PR, 1.15; 95% CI, 1.09–1.21) compared with non-Hispanic Whites. These associations were slightly attenuated when further adjusting for health insurance category at diagnosis for non-Hispanic Blacks (PR, 1.24; 95% CI, 1.16–1.33), non-Hispanic Asian/Pacific Islanders (PR, 1.11; 95% CI, 1.02–1.21) and Hispanics (PR, 1.07; 95% CI, 1.01–1.13), respectively, versus non-Hispanic Whites (Table 2). When stratified by cancer type, non-Hispanic Blacks and Hispanics had a higher

prevalence of a distant cancer stage diagnosis versus non-Hispanic Whites for most cancers, whereas a higher prevalence was only observed for non-Hispanic Asian/Pacific Islanders versus non-Hispanic Whites for central nervous system (CNS) and miscellaneous intracranial and intraspinal neoplasms, neuroblastoma and other peripheral nervous cell tumors, renal tumors, soft tissue and other extrasosseous sarcomas, and other malignant epithelial neoplasms and malignant melanomas (Table 2). However, results for specific cancer types are imprecise and most were not statistically significant.

The observed racial/ethnic disparities in cancer diagnosis stage also differed by age group ( $P_{\text{interaction}} < .001$ ). In general, the PRs for adolescents were higher than

**TABLE 2.** Prevalence Ratios and 95% CIs of Distant Diagnosis Stage Associated with Race/Ethnicity by Cancer Type

Cancer type <sup>a</sup>	Race/ethnicity	PR (95% CI) <sup>b</sup>	PR (95% CI) <sup>c</sup>
All cancers	Non-Hispanic White	1 [Reference]	1 [Reference]
	Non-Hispanic Black	1.31 (1.23–1.40)	1.24 (1.16–1.33)
	Non-Hispanic Asian/Pacific Islander	1.14 (1.04–1.24)	1.11 (1.02–1.21)
	Hispanic	1.15 (1.09–1.21)	1.07 (1.01–1.13)
Lymphomas and reticuloendothelial neoplasms	Non-Hispanic White	1 [Reference]	1 [Reference]
	Non-Hispanic Black	1.08 (0.99–1.18)	1.04 (0.95–1.13)
	Non-Hispanic Asian/Pacific Islander	1.00 (0.89–1.12)	0.98 (0.87–1.10)
	Hispanic	1.06 (0.98–1.14)	1.00 (0.93–1.08)
CNS and miscellaneous intracranial and intraspinal neoplasms	Non-Hispanic White	1 [Reference]	1 [Reference]
	Non-Hispanic Black	1.27 (0.95–1.69)	1.25 (0.93–1.67)
	Non-Hispanic Asian/Pacific Islander	1.33 (0.95–1.86)	1.32 (0.94–1.85)
	Hispanic	1.22 (0.98–1.52)	1.20 (0.95–1.51)
Neuroblastoma and other peripheral nervous cell tumors	Non-Hispanic White	1 [Reference]	1 [Reference]
	Non-Hispanic Black	1.09 (0.95–1.24)	1.06 (0.92–1.21)
	Non-Hispanic Asian/Pacific Islander	1.06 (0.90–1.26)	1.06 (0.90–1.25)
	Hispanic	0.92 (0.81–1.04)	0.89 (0.78–1.01)
Renal tumors	Non-Hispanic White	1 [Reference]	1 [Reference]
	Non-Hispanic Black	1.18 (0.92–1.52)	1.16 (0.89–1.49)
	Non-Hispanic Asian/Pacific Islander	1.12 (0.75–1.67)	1.11 (0.75–1.66)
	Hispanic	1.07 (0.85–1.34)	1.05 (0.83–1.32)
Hepatic tumors	Non-Hispanic White	1 [Reference]	1 [Reference]
	Non-Hispanic Black	1.31 (0.78–2.22)	1.19 (0.70–2.04)
	Non-Hispanic Asian/Pacific Islander	0.96 (0.56–1.66)	0.93 (0.54–1.62)
	Hispanic	1.28 (0.89–1.87)	1.14 (0.75–1.73)
Malignant bone tumors	Non-Hispanic White	1 [Reference]	1 [Reference]
	Non-Hispanic Black	0.94 (0.71–1.24)	0.91 (0.69–1.21)
	Non-Hispanic Asian/Pacific Islander	1.02 (0.75–1.39)	1.02 (0.75–1.39)
	Hispanic	1.21 (1.02–1.44)	1.19 (0.96–1.39)
Soft tissue and other extrasosseous sarcomas	Non-Hispanic White	1 [Reference]	1 [Reference]
	Non-Hispanic Black	1.17 (0.94–1.45)	1.04 (0.84 to 1.40)
	Non-Hispanic Asian/Pacific Islander	1.44 (1.11–1.87)	1.38 (1.06–1.80)
	Hispanic	1.37 (1.16–1.63)	1.21 (1.01–1.45)
Germ cell tumors, trophoblastic tumors, and neoplasms of gonads	Non-Hispanic White	1 [Reference]	1 [Reference]
	Non-Hispanic Black	1.35 (0.98–1.84)	1.25 (0.91–1.72)
	Non-Hispanic Asian/Pacific Islander	0.82 (0.58–1.16)	0.79 (0.56–1.12)
	Hispanic	1.25 (1.04–1.51)	1.11 (0.91–1.35)
Other malignant epithelial neoplasms and malignant melanomas	Non-Hispanic White	1 [Reference]	1 [Reference]
	Non-Hispanic Black	3.12 (2.35–4.15)	2.71 (2.02–3.64)
	Non-Hispanic Asian/Pacific Islander	1.93 (1.35–2.74)	1.78 (1.25–2.52)
	Hispanic	1.95 (1.53–2.50)	1.65 (1.27–2.14)

Abbreviations: CI, confidence interval; CNS, central nervous system; PR, prevalence ratio.

<sup>a</sup>Cannot compute results for retinoblastoma due to the small number of cases ( $n = 8$ ) in the distant stage category.

<sup>b</sup>Adjusted for age, sex, median household income quartile, % unemployed quartile, and rural/urban residence area.

<sup>c</sup>Additionally adjusted for health insurance type.

children for non-Hispanic Blacks ( $PR_{\text{adolescents}} = 1.37$ ; 95% CI, 1.22–1.54;  $PR_{\text{children}} = 1.18$ ; 95% CI, 1.08–1.28) and Hispanics ( $PR_{\text{adolescents}} = 1.11$ ; 95% CI, 1.01–1.22;  $PR_{\text{children}} = 1.04$ ; 95% CI, 0.97–1.12) versus non-Hispanic Whites, but comparable in non-Hispanic Asian/Pacific Islanders ( $PR_{\text{adolescents}} = 1.09$ ; 95% CI, 0.94–1.26;  $PR_{\text{children}} = 1.11$ ; 95% CI, 1.00–1.24) (Table 3). Notably, the PRs for Hispanics versus non-Hispanic Whites were only statistically significant among adolescents. The opposite was observed for the PRs of non-Hispanic Asian/Pacific Islanders versus non-Hispanic Whites.

To determine whether health insurance was a potential mediator of the association between race/ethnicity and cancer stage at diagnosis, we further adjusted for health insurance. As would be expected if

health insurance mediates the association, we observed an attenuation of the PRs for all cancers combined and most cancer types. Notably, non-Hispanic Blacks and Hispanics still had a higher prevalence of a distant cancer stage diagnosis versus non-Hispanic Whites for most cancers but estimates were imprecise and most were not statistically significant. Among non-Hispanic Asian/Pacific Islanders, there was no clear pattern and most results were not significant (Table 2). Results from sensitivity analyses based on multiple imputations concur with these findings (Table S2).

To estimate the proportion of the association between race/ethnicity and stage at diagnosis mediated by health insurance, we conducted formal mediation analyses. We found that approximately half of the association between race/ethnicity and stage at diagnosis was explained by having any Medicaid or no insurance at diagnosis in Hispanic children and adolescents. The percentage explained was 22% in non-Hispanic Blacks and 9% in non-Hispanic Asian/Pacific Islanders (Figure 1; Table S3). The analyses stratified by age group (Table S4) demonstrated similar mediating effects of health insurance type between adolescents and children, with the exception of a higher proportion explained in non-Hispanic Asian/Pacific Islander adolescents versus children (38% vs. 5%). Results from sensitivity analyses that excluded uninsured cases ( $n = 597$ ) were consistent with the main analyses (Table S5).

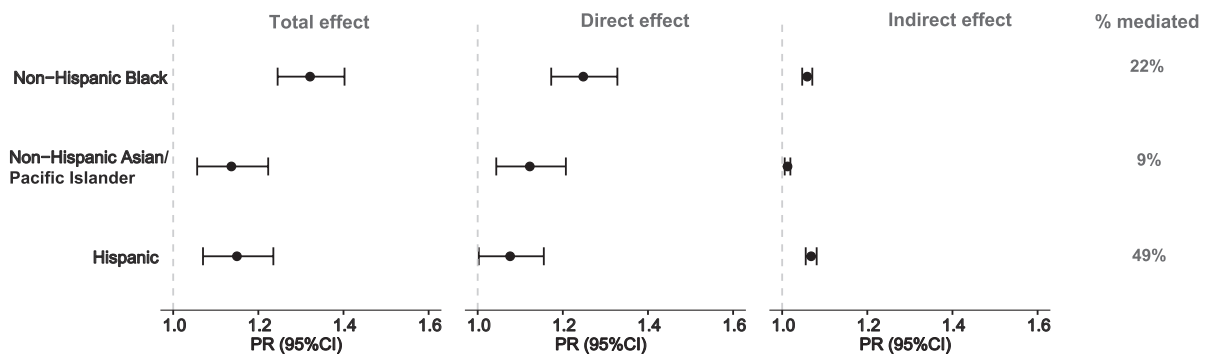
**TABLE 3.** Prevalence ratios and 95% CIs of diagnosis stage for all cancer types combined associated with race/ethnicity by age group<sup>a</sup>

Age group	Race/ethnicity	PR (95% CI) <sup>b</sup>
Children	Non-Hispanic White	1 [Reference]
	Non-Hispanic Black	1.18 (1.08–1.28)
	Non-Hispanic Asian/Pacific Islander	1.11 (1.00–1.24)
	Hispanic	1.04 (0.97–1.12)
Adolescents	Non-Hispanic White	1 [Reference]
	Non-Hispanic Black	1.37 (1.22–1.54)
	Non-Hispanic Asian/Pacific Islander	1.09 (0.94–1.26)
	Hispanic	1.11 (1.01–1.22)

Abbreviations: CI, confidence interval; PR, prevalence ratio.  
<sup>a</sup> $p$  for interaction between age group and race/ethnicity on diagnosis stage was calculated using likelihood ratio test and was  $<.001$ .  
<sup>b</sup>Adjusted for sex, median household income quartile, % unemployed quartile, rural/urban residence area, and health insurance type.

DISCUSSION

Using population-based data, we found racial/ethnic disparities in childhood and adolescent cancer stage at



**FIGURE 1.** Mediation of the association between race/ethnicity and childhood and adolescent cancer stage at diagnosis for all cancer types combined by health insurance coverage. The reference group for all PRs is non-Hispanic Whites. The total effect indicates the combined indirect (race/ethnicity → insurance → stage at diagnosis) and direct (race/ethnicity → stage at diagnosis) causal effects of race/ethnicity on stage at diagnosis. In this simplified scenario, it is important to note that the direct effect can be comprised of a causal path mediated by other variables not considered in this analysis. The percent of the total effect of race/ethnicity on diagnosis stage mediated by health insurance type (i.e., the indirect effect) was calculated as the ratio of the logs of the PRs for the indirect and total effects. CI indicates confidence interval; PR indicates prevalence ratio.



diagnosis across cancer types, with racial/ethnic minorities more likely to be diagnosed with distant stage cancers compared to non-Hispanic Whites. Non-Hispanic Black and Hispanic versus non-Hispanic White disparities were stronger in adolescents than in children. To our knowledge, our study is among the first to quantify the extent to which health insurance mediates these disparities among children and adolescents with cancer. The results broadly indicate that the type of health insurance coverage partially explains the observed disparities in cancer diagnosis stage. It is noteworthy that having any Medicaid at diagnosis or being uninsured is estimated to account for half of the disparities between non-Hispanic White and Hispanic children and adolescents.

Previous literature has documented racial/ethnic differences in childhood and adolescent cancer diagnosis stage. Studies from the Texas Cancer Registry reported that non-Hispanic Blacks and Hispanics with solid tumors were more likely to have an advanced stage of disease at presentation.<sup>8,15</sup> In melanoma, Hispanic children had a three times higher odds of advanced-stage presentation compared with non-Hispanic Whites.<sup>9</sup> Another study of retinoblastoma reported a two times higher odds of having regional/distant disease among Hispanic children versus non-Hispanic children.<sup>16</sup> However, these studies were either based on regional data sources or only focused on one specific cancer type. In our study, we used data from 18 US population-based cancer registries and assessed differences in cancer stage at diagnosis across major solid cancers in children and adolescents. Although we were unable to assess retinoblastoma due to the small number of distant cancer cases, we found racial/ethnic disparities in cancer diagnosis stage in non-Hispanic Black and Hispanic versus non-Hispanic White children and adolescents across most solid tumor types. However, statistically significant evidence was not found for most tumor types, which could be due to insufficient sample sizes. In the non-Hispanic Asian/Pacific Islander population, we found a comparable risk of a distant cancer stage diagnosis among those with lymphomas and reticuloendothelial neoplasms, hepatic tumors, and malignant bone tumors versus non-Hispanic Whites.

Possible explanations for more advanced stage at diagnoses in race/ethnicity minorities, particularly non-Hispanic Blacks and Hispanics, are multifactorial. They are not only related to differences in tumor type but also to social determinants of health that may result in delayed detection of early cancer symptoms.<sup>9</sup> Early diagnosis can be crucial for effective cancer management because it can allow for timely and less intensive treatment with minimal

side or late effects. It is a critical issue for childhood cancer because cancers at younger ages tend to have a shorter latency period and are more aggressive. Nevertheless, early detection and diagnosis is a complicated process with no known effective screening programs in this age group, requiring astute observations and cooperation from multiple parties, including parents/caregivers, primary physicians, and the health care system, and also depends on the accessibility to health care resources.<sup>3</sup> Because diagnostic delay is usually hard to measure and a longer delay in diagnosis could lead to a more advanced disease, a higher diagnosis stage is often considered as a proxy for diagnosis delay. However, the relationship between diagnostic delay and cancer stage can also be complicated by disease aggressiveness with fast-growing cancers showing early symptoms, which may lead parents to seek medical attention for their child much sooner than slow-growing cancers, resulting in an earlier diagnosis.<sup>3</sup> This complexity might partially lead to the inconsistent findings between diagnosis delay and cancer diagnosis stage.<sup>17-19</sup>

Health insurance coverage, as one of the few modifiable resources that may contribute to racial/ethnic disparities, can help ensure timely access to health care resources and high-quality care. Prior studies in newly diagnosed patients with cancer aged 15–29 years have found that those with public or no insurance tend to have a longer delay in diagnosis and present with a more advanced stage, compared with those who are privately insured.<sup>20</sup> Among children and adolescents with cancer, health insurance coverage explained 20% and 48% of the survival disparities between non-Hispanic Blacks and Hispanics versus non-Hispanic Whites.<sup>21</sup> Akin to these findings, our results indicate that the lack of health insurance coverage or being recorded as having any Medicaid at diagnosis accounts for half the observed distant stage at presentation for Hispanics and one-fifth for non-Hispanic Blacks. We additionally analyzed the non-Hispanic Asian/Pacific Islander population, which is often neglected by researchers due to small numbers of childhood and adolescent cancer cases, and found that only 9% of the disparities were attributable to health insurance coverage type. Notably, racial/ethnic disparities in cancer stage at diagnosis remain despite adjusting for health insurance, emphasizing that other factors also contribute to these disparities.

Results from stratification analyses indicated that the extent to which health insurance coverage mediates the association between race/ethnicity and stage at diagnosis varies by cancer type. For soft tissue and other extraosseous sarcomas, approximately 70% of the disparities between non-Hispanic Black and White children and

adolescents were estimated to be attributable to lacking insurance or having Medicaid, whereas for CNS and miscellaneous intracranial and intraspinal neoplasms, the proportion explained by health insurance coverage type is minimal. As briefly discussed above,<sup>7</sup> these variations by cancer type might be partially related to differences in cancer aggressiveness at presentation. In our study, CNS tumor cases predominantly present with a nondistant stage at diagnosis, making the benefits of health insurance coverage type less detectable than soft tissue tumors, in which just over one-fifth had a distant cancer diagnosis.

We also observed an age difference in the racial/ethnic disparities in cancer diagnosis stage, with non-Hispanic Black and Hispanic versus non-Hispanic White adolescents experiencing larger disparities than children in these groups. Adolescents are a particularly vulnerable group with unique physical, emotional, and social challenges and have long been reported to experience a lagged improvement in cancer outcomes compared with other age groups.<sup>22</sup> Although a previous study using California Cancer Registry data reported that the historical survival improvement gap has closed for adolescents and young adults with cancer, this group still experienced a worse race/ethnicity-associated survival trend over time.<sup>23</sup> These racial/ethnic disparities among adolescents with cancer might be related to inequality in care access and delivery due to a higher risk of lacking health insurance.<sup>24</sup>

Notably, the proportions mediated by health insurance of the association between race/ethnicity and stage at diagnosis varied markedly between Hispanics (49%) and non-Hispanic Blacks (22%). Explanations for this difference could be related to language barriers and undocumented immigrant statuses experienced by many Hispanics that could pose challenges to using their health insurance. This is supported by evidence of a longer time from onset of symptoms to diagnosis in Spanish versus English speakers and reports of not seeking timely care because of immigration status concerns.<sup>25</sup>

This study is subject to several limitations. First, although SEER is a well-recognized high-quality population-based data set, SEER 18 registries represent a minority of the US population and intentionally oversamples racial and ethnic minorities,<sup>26</sup> which may not be reflective of the general cancer population of children and adolescents in the United States. In addition, SEER collects the patient's insurance status at diagnosis; children and adolescents without insurance at their time of diagnosis could be enrolled in Medicaid shortly after cancer diagnosis and then recorded as having Medicaid.<sup>27</sup> Therefore, it should not be inferred that Medicaid is

inferior to private insurance (comprising most of the insured group) because of this potential misclassification and because Medicaid may mark individuals with greater social and economic vulnerabilities that may impact stage at diagnosis. In SEER, individual-level socioeconomic status was not available. Therefore, we used county-level variables as surrogates, which might not reflect individual-level socioeconomic status.<sup>28</sup> Finally, the analyses may be limited by unmeasured confounding and small numbers of cases for some cancer types that decreases the precision of our estimates.

In conclusion, we found racial/ethnic disparities in cancer diagnosis stage across many cancer types in children and adolescents, with stronger disparities in non-Hispanic Black and Hispanic versus non-Hispanic White adolescents than in children. Although these disparities remain after taking health insurance coverage into account, improving access to health care through health insurance may help eliminate part of the observed disparities, particularly for Hispanic children and adolescents. Future studies should continue to investigate underlying mechanisms.

## AUTHOR CONTRIBUTIONS

**Xiaoyan Wang:** Conceptualization, formal analysis, methodology, writing—original draft, and writing—review and editing. **Derek S. Brown:** Methodology and writing—review and editing. **Yin Cao:** Methodology and writing—review and editing. **Christine Ekenga:** Methodology and writing—review and editing. **Shenyang Guo:** Methodology and writing—review and editing. **Kimberly J. Johnson:** Conceptualization, methodology, writing—review and editing, and supervision.

## CONFLICT OF INTEREST

The authors made no disclosures.

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