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Social determinants of health impact on cancer affecting children, adolescents, and young adults: systematic review and meta-analysis

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Objective: To analyze the impact of social determinants of health (SDH) on cancer outcomes of children and adolescents and young adults (AYA) treated for cancer.

Study design: The protocol for this study was registered at PROSPERO (CRD402022346854). A search strategy was implemented across six databases over the last two decades. The focus narrowed to 31 studies conducted in the United States, involving patients between the ages of 15 and 39, assessing survival outcomes based on SDH factors. The Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Analytical Cross-Sectional Studies was employed for risk of bias assessment.

Results: The most extensively examined SDH factors were neighborhood socioeconomic status (nSES) and health insurance status. Other variables investigated were location of care (6/31), poverty level (5/31), education level (3/31), marital status (4/31), median income (3/31), travel distance to medical facility (3/31), language isolation (2/31), and unemployment (1/31). The primary outcome evaluated was overall survival (OS) and cancer-specific survival (CSS). Meta-analyses focusing on hematological malignancies revealed statistically significant associations, such as lowest nSES correlating with worse OS [hazard ratio (HR):1.46, 95%-CI:1.29–1.66] and CSS (HR:1.43, 95%-CI:1.20–1.72), Medicaid/public insurance linked to worse OS (HR: 1.21, 95%-CI:1.16–1.26), and no insurance associated with worse OS (HR:1.35, 95%-CI:1.17–1.55).

Abbreviations
ADI, area deprivation index; ALL, Acute lymphoblastic leukemia; AML, Acute myeloid leukemia; APL, Acute promyelocytic leukemia; AYA, adolescents and young adults; CI, Confidence interval; CSS, cancer-specific survival; HR, hazard ratio; OS, overall survival; SDH, social determinants of health; SEER, Surveillance, Epidemiology, and End Results Program; SES, socioeconomic status; nSES, neighborhood socioeconomic status.

Conclusion: The study highlights the fragmented and incomplete nature of research on SDH in cancer treatment in this age group. Health insurance coverage and nSES were the most studied, revealing significant impacts on patient survival. Identifying vulnerable patients through such analyses could inform policy decisions and address existing gaps in SDH research more effectively.

Systematic Review Registration: https://www.crd.york.ac.uk/prospero/, PROSPERO (CRD402022346854).

KEYWORDS

social determinants of health, hematological malignancies, pediatric, adolescents, survival, young adults, cancer, hematology

Introduction

Cancer is among the leading causes of death for children and for adolescents and young adults (AYA) (1, 2). In the United States (US), it is anticipated that 5,280 adolescents in addition to 9,910 children will be diagnosed with cancer by the end of 2023 (1). Among those, 1,040 and 550, respectively, will die from the disease. In the last few decades, remarkable progress in the medical field has resulted in improved prognosis of cancer affecting this specific population (2). However, barriers remain to access advanced diagnostic methods and therapeutic modalities.

Social medicine is traced to the middle of the 20th century, when scientists began to study the root of the disease rather than focusing only on its biological mechanisms (3). In 1948, the World Health Organization (WHO) included "social well-being" in its definition of health for the first time (4). Currently, WHO recognizes the pivotal role of factors other than biological on the diseases and defines the Social Determinants of Health (SDH) as "conditions in which people are born, grow, work, live and age, and the wider set of forces and systems shaping the conditions of daily life" (5). SDH has been grouped into 5 domains: (i) education access and quality, (ii) health care access and quality, (iii) economic stability, (iv) neighborhood and built environment, and (v) social and community according to the Healthy People 2030 (6, 7). Over the past few decades, the population's lifestyle has dramatically changed with the increase in urbanization and industrialization (8), leading to disparities across all levels of quality of life.

It is a consensus that a broad array of SDH plays a significant role in determining survival and treatment-related outcomes in pediatric and AYA patients with cancer. However, the precise effect of each SDH domain and the connection between these domains has to be defined (9). Several studies have analyzed the effects of SDH on children and AYA diagnosed with cancer, but the number of studies that were able to utilize SDH measures at individual-level and tailored for medical research is still scarce. In fact, most studies with higher number of patients rely on public registries such as SEER and NCDB. Although such databases represented a revolution in terms of representation of the US population's clinical features, they were not initially designed to address SDH. In this context, recent initiatives by the National Health Institute's National Institute on Minority Health and Health Disparities (NIMHD) have been focused on building consensus measures on SDH (10) and the hope is that the prospective studies will benefit from this tool.

Therefore, we designed the present study to identify what SDH have been studied in the US, how they were evaluated, and what impact they have on the survival of children and AYA with cancer. Our goal was to provide a resource to inform policy decisions and identify the gaps in SDH research so they can be addressed.

Methods

Eligibility criteria, information sources, and search strategy

This systematic review and meta-analysis were registered at the Prospective Register of Systematic Reviews (PROSPERO) under the registration number CRD42022346854. This study is part of a series of systematic reviews including all types of cancer and followed the same protocol (11–13). In this particular study, we covered tumors arising exclusively in children and AYA. We conducted a thorough search encompassing manuscripts published from January 2001 to September 2022, utilizing six databases, namely PubMed, Scopus, Web of Science, Embase, Cochrane, and Google Scholar (grey literature). Patient, intervention, comparison, outcome, and study design (PICOS) strategy was employed as follows: Population- Patients diagnosed with any type of cancer (specifically for this study, the population was restricted to children and AYA within the age range of 0–39 years) treated for cancer in the United States; Intervention- Any SDH according to the five major domains by the Healthy People 2030 (6, 7): economic stability; neighborhood and built environment; education access and quality; social and community context; health care access and quality; Comparison —None; Outcome measures- Cancer treatment outcomes related to the survival of the patients; Types of studies- Observational studies. We excluded studies in which (i) results were not stratified according to cancer type, (ii) survival-related outcomes were not presented, (iii) outcomes of the patients were assessed exclusively according to their geospatial location (for example, living in a rural or metropolitan setting; comparison between two

or more cities, counties or states), (iv) cancer survival was evaluated over time only, not considering any SDH; (v) outcome was analyzed only according to the race and/or ethnicity of the patients, not considering any directly modifiable SDH, and (vi) pre-clinical studies, case reports, reviews of the literature, conference reports, letters, personal opinions, book chapters (vii) studies written in a language other than English.

Study selection

In Phase 1 of the study selection, two authors independently screened all titles and abstracts identified through the search strategy. Studies that did not fulfill the inclusion criteria were eliminated. In Phase 2, the full text of the manuscripts selected in Phase 1 were examined independently by each author. Disagreements in all phases were resolved through discussion and an expert in Pediatric Oncology was consulted when necessary.

Data collection and data items

We collected all information using the qualitative analysis software NVivo (Lumivero, Denver, CO, USA), as previously described (11, 12). A second author cross-checked the data collection. Data about the study characteristics, interventions, results, main findings, and main conclusion was collected. Survival outcomes collected included overall survival (OS) and cancer-specific survival (CSS) hazard ratio (HR) or in months.

Assessment of bias in individual studies

The risk of bias in individual studies was assessed using the Joanna Briggs Institute Critical Appraisal Checklist for analytical cross-sectional studies (11). Two authors independently applied the checklist, and any disagreements were resolved through consultation with a clinical expert. The risk of bias was categorized into three levels: High (0%–50% of items scored as "Yes"), Moderate (50%–70% of items scored as "Yes"), and Low (70%–100% of items scored as "Yes").

Synthesis methods

SDH were grouped according to the five domains as defined by the World Health Organization: economic stability, neighborhood and built environment, education access and quality, social and community context, and health care access and quality.

The significance of the results was assessed based on *p*-value (significant if $p < 0.05$) when it was available, by the authors' statement or 95%-confidence intervals (95%-CI). The study encompassed quantitative and qualitative analysis. For the qualitative analysis, MS collected the author's name, year of publication, sample size, age group, social determinants studied, survival outcomes effect size (HR and 95%-CI), and *p*-value if available. Authors crosschecked the retrieved information. Any disagreement was solved by discussion and mutual agreement, and experts were consulted when required.

Statistical analysis

Meta-analysis was performed depending on data availability. Hazard ratios were pooled for SDH and health insurance. Subgroup analysis for hematological malignancies was performed for both variables. Fifteen studies were chosen for the quantitative analysis based on having similar reference and/or measures to assess nSES. The heterogeneity of the analysis was verified using Cochran's Q (x^2 test) and I^2 test I^2 value ranging from 50 to 90% was interpreted as indicative of significant heterogeneity. Meta-analyses were presented using forest plots to determine associations between SDH and either OS or CSS. HR was used to estimate the outcome effect on the meta-analysis. RevMan 5.3 review manager software was used for all statistical analyses.

Results

Study selection

We identified 38,654 manuscripts across the 6 databases queried and 23,335 duplicates were excluded. After screening the title and abstract (phase 1), 44 records were eligible for full-text analysis. Fifteen of these studies were excluded in phase 2 (Supplementary Table S1) (14–26) and 2 studies were added from the reference lists (27, 28). In summary, 31 studies were examined in this systematic review, and 15 manuscripts were eligible for the meta-analysis (Supplementary Figure S1A).

Studies characteristics

Despite the search covering the period from 2001 to 2022, all included studies were published between 2008 and 2022. Leukemias ($n = 9$, 29%) (29–37), lymphomas ($n = 7$, 23%) (27, 38–44) and central nervous system (CNS) tumors ($n = 5$, 16%) (28, 45–48) were the most extensively researched cancer types. Most studies focused on children and adolescents (0–20 years-old, $n = 14$, 45%) followed by AYA (15–39 years-old) ($n = 9$, 26%). Sample size ranged between 235 and 80,855 patients and most studies were based on state or national registries. Noteworthy, the California cancer registry ($n = 10$, 32%) and Surveillance, Epidemiology, and End Results Program (SEER, $n = 7$, 23%) were the most frequently cited.

Risk of bias of included studies

The risk of bias (ROB) assessment showed that 1 study had high ROB (27), 1 study had moderate ROB (42), and 29 studies

had low ROB (Supplementary Figure 1B). All the included studies defined their inclusion criteria while some 18 did not state strategies to deal with any confounder (27, 28, 31, 32, 35, 39, 42, 43, 45, 46, 49–56).

Results of individual studies

Ten SDH variables were investigated across the 31 studies. In terms of the five SDH domains by Healthy People 2023, healthcare access and quality ($n = 3$, 30%) and economic stability ($n = 4$, 40%) had the most studied variables, followed by the social and community context ($n = 2$, 20%), and the education access and quality ($n = 1$, 10%). Notably, no SDH within neighborhood and built environment domain was examined in the studies included in this review.

The most frequently studied variables were socioeconomic status (SES, $n = 19$) and health insurance status ($n = 18$). Other variables included: type of treatment facility ($n = 6$), poverty ($n = 5$), median income ($n = 4$), marital status ($n = 4$), education ($n = 3$), travel distance to treatment facility ($n = 3$), language isolation ($n = 2$) and unemployment ($n = 1$). Overall survival was the main outcome in all studies while the secondary outcome CSS was evaluated in 32% ($n = 10$, 32%).

Health care access and quality

Within the health care access and quality domain, three SDH variables, all at patient level, were explored in the included studies: health insurance (18/31), type of treatment facility (6/31), and travel distance to the treatment facility (3/31, Table 1). Health insurance was captured at the diagnosis and at patient level in all studies. There was a direct impact on children and

TABLE 1 Key findings from studies assessing the influence of social determinants of health (SDH) within the "health care access and quality" domain on treatment-related outcomes in pediatric and adolescent and young adult (AYA) patients with cancer.

Author (year)	Diagnosis	Database (Sample)	Age (yrs.)	SDH indicator	Cohorts	HR (95% CI)[a,c]	Worst survival predictor
Jamy et al. (36)	APL	SEER (816)	0–39	Type of health insurance	Insured	Reference	Uninsured
					Medicaid	1.27 (0.84–1.94)	
					Uninsured	**2.33 (1.32–4.10)**	
Abrahao et al.[f] (31)	APL	State Registry (772)	0–39	Type of health insurance	Private	Reference	Uninsured
					Public	1.00 (0.67–1.31)	
					None	**2.00 (1.20–3.31)**	
					Unknown	0.64 (0.35–1.17)	
Seif et al. (32)	ALL	State Registry (8,516)	0–19	Type of health insurance	Private/Other	Reference	–
					Public	1.41 (0.89–2.25)	
Abrahao et al.[e] (30)	ALL	State Registry (9,295)	0–19	Type of health insurance	Private	Reference	–
					Public	1.15 (1.01–1.32)	
					Uninsured	1.22 (0.83–1.89)	
					Unknown	1.77 (1.38–2.26)	
Rotz et al. (34)	ALL	NCDB (12,301)	0–39	Type of health insurance	Private	Reference	Government insurance or Uninsured
					Government	**1.26 (1.17–1.35)**	
					Uninsured	**1.27 (1.13–1.43)**	
	AML	NCDB (22,683)	0–39		Private	Reference	Government insurance or Uninsured
					Government	**1.19 (1.12–1.27)**	
					Uninsured	**1.26 (1.13–1.41)**	
Kent et al. (29)	Leukemia NOS	State Registry (7,688)	0–39	Type of health insurance	Any	Reference	Uninsured
					None/unknown	**1.31 (1.16–1.47)**	
					Any	Reference	
					None/unknown	**1.27 (1.12–1.44)**[b]	
Keegan et al. (40)	HL	State Registry (9,353)	15–39	Type of health insurance	Private/military insurance	Reference	Public insurance/no insurance
					Public insurance/no insurance	**2.05 (1.58–2.66)**	
					Unknown	1.25 (0.70–2.24)	
					Private/military insurance	Reference	Public insurance/no insurance
					Public insurance/no insurance	**2.08 (1.52–2.84)**[b]	
					Unknown	1.25 (0.62–2.51)[b]	
Abrahao (42)	Lymphoma NOS	State Registry (11,337)	15–39	Type of health insurance	Private	Reference	Medicaid/ uninsured
					Continuous Medicaid	**1.93 (1.63–2.29)**	
					Discontinuous Medicaid	**2.17 (1.83–2.58)**	
					Medicaid/uninsured	**2.14 (1.83–2.49)**	
					Other public	1.13 (0.66–1.93)	

(*Continued*)

TABLE 1 Continued

Author (year)	Diagnosis	Database (Sample)	Age (yrs.)	SDH indicator	Cohorts	HR (95% CI)[a,c]	Worst survival predictor
Kent et al. (38)	NHL	State Registry (3,489)	15–39	Type of health insurance	None	Reference	–
					Managed or Private	0.82 (0.62–1.08)	
					Government	1.32 (1.00–1.75)	
					Unknown	0.96 (0.69–1.33)	
					None	Reference	–
					Managed or Private	0.96 (0.66–1.39)[b]	
					Government	1.16 (0.79–1.70)[b]	
					Unknown	0.89 (0.65–1.20)[b]	
Huang (44)	Lymphoma NOS	SEER (21,149)	15–39	Type of health insurance	Insured	Reference	Any Medicaid
					Any Medicaid	**1.08 (1.03–1.13)**	
					Insured/no specifics	0.96 (0.91–1.02)	
					Uninsured	1.06 (0.99–1.14)	
Derouen et al. (57)	Leukemia NOS	State Registry (80,855)	15–39	Type of health insurance	Private/military	Reference	Public insurance/ Uninsured (all cancer sites except ovary)
					Public/uninsured	**1.16 (1.04–1.29)**	
					Unknown	1.10 (0.85–1.42)	
	HL				Private/military	Reference	
					Public/uninsured	**2.22 (1.74- 2.84)**	
					Unknown	1.24 (0.71- 2.16)	
	NHL				Private/military	Reference	
					Public/uninsured	**1.69 (1.45–1.98)**	
					Unknown	**1.46 (1.08–1.96)**	
	Breast				Private/military	Reference	
					Public/uninsured	**1.62 (1.47–1.80)**	
					Unknown	1.19 (0.96–1.47)	
	Thyroid				Private/military	Reference	
					Public/uninsured	**2.27 (1.41–3.63)**	
					Unknown	**3.33 (1.37–8.10)**	
	Melanoma				Private/military	Reference	
					Public/uninsured	**2.61 (2.13–3.20)**	
					Unknown	0.98 (0.64–1.51)	
	Testis				Private/military	Reference	
					Public/uninsured	**2.12 (1.71–2.62)**	
					Unknown	**1.90 (1.22–2.96)**	
	Cervix				Private/military	Reference	
					Public/uninsured	**1.23 (1.05–1.46)**	
					Unknown	1.08 (0.74–1.59)	
	Sarcoma				Private/military	Reference	
					Public/uninsured	**1.47 (1.29–1.68)**	
					Unknown	1.28 (0.95–1.71)	
	Colorectal				Private/military	Reference	
					Public/uninsured	**1.29 (1.13–1.46)**	
					Unknown	0.93 (0.69–1.26)	
	CNS				Private/military	Reference	
					Public/uninsured	**1.37 (1.20–1.57)**	
					Unknown	**1.39 (1.03–1.88)**	
	Ovary				Private/military	Reference	
					Public/uninsured	0.97 (0.76–1.24)	
					Unknown	0.99 (0.54–1.80)	
Mitchell et al. (48)	CNS	SEER (9,577)	0–19	Type of health insurance	Insured (Private)	Reference	–
					Insured (Medicaid)	1.01 (0.87–1.16)	
					Insured (Unknown type)	0.82 (0.66–1.02)	
					No insurance	0.97 (0.61–1.53)	
					Unknown	1.36 (0.94–1.96)	
Fineberg et al. (28)	CNS	SEER (1,881)	0–19	Type of health insurance	Private	Reference	–
					Public/No Insurance	1.19 (0.97–1.46)	
Penumarthy (49)	Sarcomas	Academic registry (1,106)	0–39	Type of health insurance	Private	Reference	Low-income public insurance
					Low-income public insurance	**1.27 (1.02–1.57)**	
Wolfson et al. (46)	CNS	State Registry (1,344)	0–39	Type of health insurance	Private	Reference	–
					Public/no insurance	1.10 (0.74–1.64)	

(*Continued*)

TABLE 1 Continued

Author (year)	Diagnosis	Database (Sample)	Age (yrs.)	SDH indicator	Cohorts	HR (95% CI)[a,c]	Worst survival predictor
Lee et al. (50)	Rectal	NCDB (3,295)	15–39	Type of health insurance	Insured	Reference	Medicaid and uninsured
					Medicaid/Medicare/ Government	**1.86 (1.33–2.59)**	
					Uninsured	**1.71 (1.08–2.70)**	
Keegan et al. (58)	Thyroid	State Registry (16,827)	15–39	Type of health insurance	Private/military insurance	Reference	Public insurance/ Uninsured
					Public insurance/no insurance/unknown	**2.56 (1.39–4.71)**	
					Private/military insurance-	Reference	–
					Public insurance/no insurance/unknown	1.61 (0.34–7.69)[b]	
Kahn (43)	Lymphoma NOS	State Registry (1,231)	1–39	Type of medical facility	NCI-CC/COG affiliate	Reference	–
					Community setting	1.49 (0.99–2.22)	
					NCI-CC/COG affiliate	Reference	Community setting
					Community setting	**2.71 (1.47–4.98)**[b]	
Abrahao et al.[e] (30)	ALL	State Registry (9,295)	0–19	Type of medical facility (Pediatric CC)	Yes	Reference	No pediatric CC
					No	**1.35 (1.23–1.48)**	
Abrahao et al.[f] (31)	APL	State Registry (772)	0–39	Type of medical facility (Pediatric CC)	Yes	Reference	–
					No	1.26 (0.79–1.99)	
Derouen et al. (54)	Breast	NCDB (19,906)	15–39	Type of medical facility (NCI-CC facility)	No	Reference	Not in NCI-CC
					Yes	**0.86 (0.76–0.98)**	
					No	Reference	Not in NCI-CC
					Yes	**0.80 (0.70–0.92)**[b]	
Keegan et al. (40)	HL	State Registry (9,353)	15–39	Type of medical facility (NCI-CC facility)	No/missing	Reference	–
					Yes	0.99 (0.83–1.20)	
					No/missing	Reference	–
					Yes	0.98 (0.76–1.25)[b]	
Wolfson et al. (46)	CNS	State Registry (1,344)	0–39	Type of medical facility	NCI-CC	Reference	Community facility
					Community facility	**1.73 (1.09–2.72)**	
Rotz et al. (34)	ALL	NCDB (12,301)	0–39	Travel distance to medical facility	>50 mi	Reference	>–50 mi
					20–50 mi	**0.87 (0.79–0.96)**	
					12–20 mi	**0.86 (0.78–0.95)**	
					<10 mi	**0.91 (0.84–0.95)**	
	AML	NCDB (22,683)			>50 mi	Reference	–
					20–50 mi	0.93 (0.86–1.01)[d]	
					12–20 mi	0.94 (0.87–1.03)[d]	
					<10 mi	1.05 (0.98–1.13)[d]	
Austin et al. (45)	CNS	State Registry (2,421)	0–18	Travel distance to medical facility	<25 mi	Reference	–
					25–49 mi	0.89 (0.72–1.1)[d]	
					≥50 mi	0.87 (0.73–1.05)[d]	
					<25 mi	Reference	
					25–49 mi	0.97 (0.78–1.20)	
					≥50 mi	0.91 (0.76–1.11)	
Austin et al. (56)	Solid tumors	State Registry (4,603)	0–18	Travel distance to medical facility	<25 mi	Reference	–
					25–49 mi	1.1 (1.0–1.3)	
					≥50 mi	1.1 (1.0–1.3)	

ALL, acute lymphocytic leukemia; AML, acute myelogenous leukemia; APL, acute promyelocytic leukemia; CC, Cancer Center; CI, confidence interval; CNS, center nervous system; COG, Children's Oncology Group; CRC, colorectal cancer; HL, hodgkin lymphoma; HR, hazard ratio; KPSC, Kaiser Permanente Southern California; NCDB, National Cancer Database; NCI-CC, National Cancer Institute-Designated Cancer Center, NHL, non-hodgkin lymphoma; NOS, not otherwise specified; SEER, Surveillance, Epidemiology, and End Results Program; yrs, age in years.

[a]Data based on overall survival analysis unless stated otherwise.

[b]Data based on cancer-specific survival analysis.

[c]Values for multivariate analysis unless stated otherwise.

[d]Values for univariate analysis.

[e]Represent the first study for Abrahao et al. team in 2015 which is Racial/Ethnic and Socioeconomic Disparities in Survival Among Children With Acute.
Lymphoblastic Leukemia in California, 1988–2011: A Population-Based Observational Study.

[f]Represent the second study for Abrahao et al. team in 2015 which is Disparities in Early Death and Survival in Children, Adolescents, and Young Adults with Acute Promyelocytic Leukemia in California.

Bold values stand for statistically significant (as reported by authors or depending on the 95%-CI).

AYA cancer outcomes in 12 (63%) of the 18 studies that investigated this variable. Being uninsured (29, 31, 34, 36, 40, 42, 57–59) or covered by Medicaid or public insurance (34, 40, 42, 44, 49, 50, 57, 58, 60) was associated with shorter OS (32, 36, 48, 49). Four studies discussed the association between health insurance coverage and CSS. Two studies found a significant association between public insurance or uninsured status and worse CSS (29, 40). Derouen et al. stratified the risk of death depending on the type of cancer. They found a significant association between non-private insurance and worse OS in 11 types of cancer (57).

Meta-analysis was employed to assess the impact of health insurance status on the survival of children and AYA with cancer. Pooling data from six studies examining hematological malignancies, we found that Medicaid/Public insurance (HR = 1.21, 95%-CI:1.16–1.26) and lack of insurance (HR = 1.35, 95%-CI: 1.17–1.55) emerged as significant predictors of poorer OS ($p < 0.0001$; Figure 1).

Types of health care facility impacted survival in 4 (66%) of the 6 studies that examined this variable. Noteworthy, patients treated in specialized cancer centers demonstrated improved outcomes (31, 43, 46, 54) (Table 1). Only 1 study (Rotz et al) reported that travelling more than 50 miles to the treatment facility adversely affected survival in ALL patients (34). However, no significant association was found in other studies for patients with AML, CNS tumors, or non-CNS solid tumors (34, 45, 56).

Economic stability

Four SDH variables were found in the economic stability domain, including: SES (19/31), poverty (5/31), median income (4/31), and employment (1/31, Table 2). All SDH were reported at community-level. Various approaches were employed to measure the SES, with none based on individual data; instead, county, neighborhood, or zip code-level data were utilized. It is worth mentioning that, although the indices used to assess SES of the population are also based on variables falling in domains other than Economic stability continuum, we described these measurements under this subgroup as most variables pertain to the economic status of the local community. The nSES (Yost index) was the most frequently used approach (11/19, 57.9%) (29–31, 38, 40, 42, 48, 51, 54, 57, 58).

Six studies (32%) revealed no significant association between OS and SES. Four studies (21%) showed a significant association between CSS and nSES, where the lowest nSES correlated with the worst CSS. Derouen et al. stratified according to cancer type and showed a higher HR with Hodgkin, non-Hodgkin lymphoma, and colorectal cancer (27). Considering these findings collectively, nSES had a significant association with OS and CSS. However, the precise effect of nSES varies according to cancer type.

For the meta-analysis, we included eight studies for the examination of OS. Focusing particularly on hematological malignancies, we observed a more pronounced impact on OS in

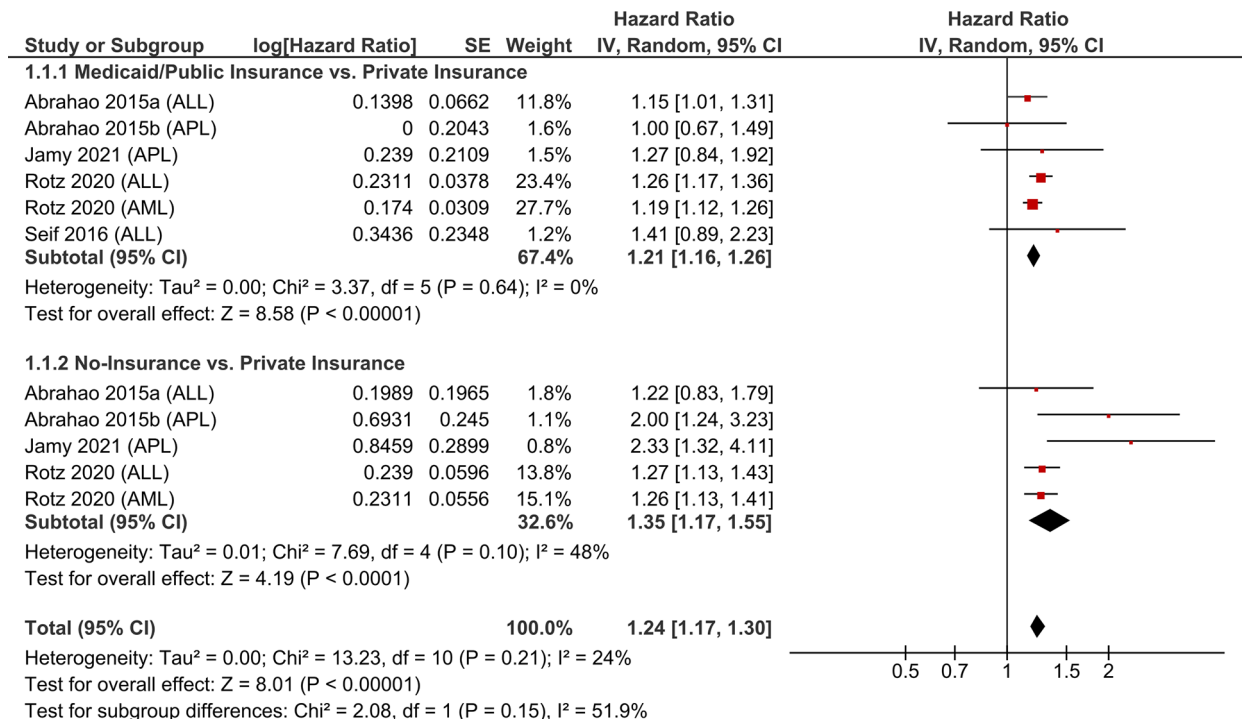

FIGURE 1
Pooled hazard ratios for overall survival according to the health insurance coverage of children and AYA with hematological malignancies.

TABLE 2 Key findings from studies assessing the influence of social determinants of health (SDH) within the "Economic stability" domain on treatment-related outcomes in pediatric and adolescent and young adult (AYA) patients with cancer.

Author (year)	Diagnosis	Database (sample)	Age (yrs.)	SDH indicator	Cohorts	HR (95% CI)	Worst survival predictor
Abrahao et al.[g] (31)	APL	State Registry (772)	0–39	Neighborhood SES (Yost index quintiles)	5 (Highest)	Reference	–
					4	0.72 (0.44–1.18)	
					3 (Medium)	0.93 (0.60–1.46)	
					2	0.94 (0.60–1.46)	
					1 (Lowest)	0.90 (0.57–1.41)	
Abrahao et al.[f] (30)	ALL	State Registry (9,295)	0–19	Neighborhood SES (Yost index quintiles)	Highest	Reference	Lowest SES
					High	1.20 (0.95–1.51)	
					Middle	1.06 (0.84–1.34)	
					Low	1.15 (0.91–1.44)	
					Lowest	**1.30 (1.04–2.27)**	
Kent et al. (29)	Leukemia NOS	State Registry (7,688)	0–39	Neighborhood SES (Yost index quintiles)	Highest	Reference	Lower SES
					High	1.10 (0.94–1.29)	
					Middle	**1.19 (1.02–1.39)**	
					Low	**1.20 (1.03–1.40)**	
					Lowest	**1.31 (1.13–1.54)**	
					Highest	Reference	Lower SES
					High	**1.18 (0.99–1.39)**[b]	
					Middle	**1.24 (1.05–1.47)**[b]	
					Low	**1.27 (1.07–1.49)**[b]	
					Lowest	**1.37 (1.16–1.61)**[b]	
Knoble et al. (35)	AML	SEER (3,651)	0–19	SES status	Cluster 1 (Highest)	Reference	Lower SES
					Cluster 2	1.13 (0.94–1.37)	
					Cluster 3	1.19 (1.00–1.42)	
					Cluster 4	1.10 (0.90–1.34)	
					Cluster 5	1.13 (0.97–1.31)	
					Cluster 6	**1.23 (1.01–1.51)**	
					Cluster 7 (Lowest)	1.04 (0.88–1.23)	
Schraw et al. (37)	ALL	State Registry (4,104)	0–20	Area deprivation index	Least disadvantaged	Reference	More disadvantaged area
					Third-most disadvantaged	1.23 (0.97–1.57)	
					Second-most disadvantaged	1.27 (0.99–1.62)	
					Most disadvantaged	**1.57 (1.23–2.00)**	
Keegan et al. (40)	HL	State Registry (9,353)	15–39	Neighborhood SES (Yost index quintiles)	5 (Highest SES)	Reference	Lower SES
					4	1.16 (0.96–1.41)	
					3 (Medium SES)	**1.44 (1.20–1.74)**	
					2	**1.53 (1.26–1.85)**	
					1 (Lowest SES)	**1.88 (1.53–2.30)**	
					5 (Highest SES)	Reference	Lower SES
					4	1.17 (0.90–1.51)[b]	
					3 (Medium SES)	**1.54 (1.20–1.99)**[b]	
					2	**1.52 (1.17–1.97)**[b]	
					1 (Lowest SES)	**1.77 (1.34–2.33)**[b]	
Kent et al. (38)	NHL	State Registry (3,489)	15–39	Neighborhood SES (Yost index quintiles)	Highest	Reference	Lower SES
					High	1.15 (0.93–1.42)	
					Middle	1.20 (0.97–1.48)	
					Low	**1.39 (1.12–1.71)**	
					Lowest	**1.40 (1.13–1.75)**	
					Highest	Reference	Lower SES
					High	1.08 (0.81–1.41)[b]	
					Middle	1.21 (0.93–1.59)[b]	
					Low	**1.49 (1.14–1.96)**[b]	
					Lowest	**1.38 (1.04–1.84)**[b]	

(*Continued*)

TABLE 2 Continued

Author (year)	Diagnosis	Database (sample)	Age (yrs.)	SDH indicator	Cohorts	HR (95% CI)	Worst survival predictor
Abrahao et al. (42)	Lymphoma NOS	State Registry (11, 351)	15–39	Neighborhood SES (Yost index)	Highest	Reference	Lowest SES
					Medium	1.09 (0.94–1.26)	
					Lowest	**1.26 (1.08–1.47)**	
Mitchel et al. (48)	CNS	SEER (9,577)	0–19	Neighborhood SES (Yost index quintiles)	5 (Least deprived)	Reference	Most deprived area
					4	1.07 (0.88–1.30)	
					3	1.17 (0.96–1.42)	
					2	1.20 (0.98–1.46)	
					1 (Most deprived)	**1.26 (1.03–1.55)**	
Fahmideh et al. (47)	CNS	State Registry (5,477)	0–20	Area deprivation index	Least disadvantaged	Reference	More disadvantaged area
					Third-most disadvantaged	**1.18 (1.02–1.37)**	
					Second-most disadvantaged	**1.18 (1.01–1.38)**	
					Most disadvantaged	**1.29 (1.09–1.51)**	
Austin et al. (45)	CNS	State Registry (2,421)	0–18	SES index	75–100	Reference	–
					50–75	0.97 (0.77–1.22)	
					25–50	1.17 (0.93–1.48)	
					<25%	1.13 (0.90–1.43)	
Wolfson et al. (46)	CNS	State Registry (1,344)	0–39	SES status	High/mid	Reference	–
					Low	1.27 (0.85 –1.90)	
Chalfant et al. (55)	Wilms' tumor	SEER (3,406)	0–18	At-risk Social deprivation index	Low-risk	Reference	High risk (Social deprivation)
					High-risk	**1.25 (1.02–1.53)**	
					Low risk	Reference	–
					High-risk	1.22 (0.99–1.56)[b]	
Hamilton et al. (52)	Melanoma	State Registry (235)	0–18	SES quartile	76%–100% (Highest)	Reference	–
					51%–75%	0.9 (0.3-3.6)	
					26%–50%	1.6 (0.4–6.3)	
					≤25%(Lowest)	2.8 (0.8–9.6)	
Lara et al. (51)	Bladder	SEER (1,688)	15–39	Neighborhood SES (Yost index)	High	Reference	Low SES
					Low	**1.28 (1.26–1.30)**	
					High	Reference	Low SES
					Low	**1.21 (1.17–1.24)**[b]	
Austin et al. (56)	Solid tumors	State Registry (4,603)	0–18	SES	75–100 (Highest)	Reference	–
					50–75	1.0 (0.8–1.2)	
					25–50	1.0 (0.8–1.2)	
					<25% (Lowest)	1.1 (0.9–1.3)	
DeRouen et al. (54)	Breast	State Registry (80,855)	15–39	Neighborhood SES (Yost index)	Highest	Reference	Lower SES
					High	**1.13 (1.03–1.25)**	
					Middle	**1.22 (1.10–1.35)**	
					Low	**1.36 (1.23–1.51)**	
					Lowest	**1.37 (1.23–1.53)**	
					Highest	Reference	Lower SES
					High	**1.14 (1.03–1.26)**[b]	
					Middle	**1.19 (1.07–1.33)**[b]	
					Low	**1.36 (1.22–1.52)**[b]	
					Lowest	**1.29 (1.14–1.45)**[b]	
Keegan et al. (58)	Thyroid	State Registry (16,827)	15–39	Neighborhood SES (Yost index)	High (quintile 3–5)	Reference	Low SES
					Low (quintile 1–2)	**1.85 (1.48–2.31)**	
					High (quintile 3–5)	Reference	Lower SES
					Low (quintile 1–2)	1.25 (0.72–2.17)[b]	

(*Continued*)

TABLE 2 Continued

Author (year)	Diagnosis	Database (sample)	Age (yrs.)	SDH indicator	Cohorts	HR (95% CI)	Worst survival predictor
DeRouen et al. (57)	Breast	State Registry (80,855)	15–39	Neighborhood SES (Yost index)	Highest	Reference	Lower SES
					Higher middle	1.08 (0.93–1.25)	
					Middle	**1.29 (1.11–1.49)**	
					Lower-middle	**1.50 (1.29–1.73)**	
					Lowest	**1.48 (1.26–1.73)**	
	Thyroid				Highest	Reference	–
					Higher middle	0.81 (0.42–1.56)	
					Middle	0.85 (0.43–1.66)	
					Lower-middle	1.43 (0.77–2.67)	
					Lowest	1.12 (0.55–2.25)	
	Melanoma				Highest	Reference	Middle SES
					Higher middle	0.98 (0.76–1.26)	
					Middle	**1.50 (1.17–1.92)**	
					Lower-middle	1.28 (0.98–1.67)	
					Lowest	1.24 (0.91–1.68)	
	Testis				Highest	Reference	–
					Higher middle	1.21 (0.85–1.72)	
					Middle	1.00 (0.70–1.42)	
					Lower-middle	1.09 (0.77–1.55)	
					Lowest	1.22 (0.86–1.74)	
	NHL				Highest	Reference	Lower SES
					Higher middle	1.12 (0.88–1.43)	
					Middle	1.09 (0.85–1.39)	
					Lower-middle	**1.42 (1.12–1.81)**	
					Lowest	**1.72 (1.34–2.19)**	
	HL				Highest	Reference	Lower
					Higher middle	1.19 (0.80–1.76)	
					Middle	1.37 (0.93–2.01)	
					Lower-middle	**1.59 (1.08–2.34)**	
					Lowest	**1.85 (1.23–2.78)**	
	Leukemia NOS				Highest	Reference	Lower SES
					Higher middle	1.13 (0.94–1.37)	
					Middle	**1.30 (1.08–1.56)**	
					Lower-middle	**1.31 (1.09–1.57)**	
					Lowest	**1.42 (1.18–1.71)**	
	Cervix				Highest	Reference	–
					Higher middle	0.87 (0.64–1.17)	
					Middle	1.08 (0.81–1.44)	
					Lower-middle	0.98 (0.73–1.31)	
					Lowest	1.32 (0.99–1.75)	
	Sarcoma				Highest	Reference	Lower SES
					Higher middle	1.21 (0.99–1.48)	
					Middle	**1.21 (1.00–1.47)**	
					Lower-middle	1.14 (0.94–1.39)	
					Lowest	**1.27 (1.04–1.55)**	
	CRC				Highest	Reference	Lower SES
					Higher middle	**1.43 (1.18–1.73)**	
					Middle	**1.46 (1.20–1.77)**	
					Lower-middle	**1.65 (1.35–2.01)**	
					Lowest	**1.88 (1.54–2.30)**	
	CNS				Highest	Reference	–
					Higher middle	1.01 (0.84–1.21)	
					Middle	0.95 (0.79–1.15)	
					Lower-middle	1.09 (0.90–1.33)	
					Lowest	1.11 (0.90–1.37)	

(*Continued*)

TABLE 2 Continued

Author (year)	Diagnosis	Database (sample)	Age (yrs.)	SDH indicator	Cohorts	HR (95% CI)	Worst survival predictor
	Ovary				Highest	Reference	–
					Higher middle	0.90 (0.63–1.29)	
					Middle	1.05 (0.74–1.48)	
					Lower-middle	0.95 (0.68–1.34)	
					Lowest	1.13 (0.78–1.63)	
Metzger et al. (39)	HL	Academic Registry (327)	3–22	Children living in poverty rate	≤23.1%	Reference	–
					>23.1%	2.2 (0.5–9.5)	
Bona et al. (33)	ALL	Academic Registry (575)	1–18	Percent of families in poverty	≥20% in poverty	85% (74–92)[e]	Higher poverty
					<20% in poverty	92% (89–94)[e]	
Huang et al. (44)	Lymphoma NOS	SEER (21,149)	15–17	Poverty rate	<10%	Reference	–
					10%–19.99%	0.90 (0.33–2.42)	
					≥20%	1.41 (0.33–5.97)	
			18–25		<10%	Reference	–
					10%–19.99%	0.97 (0.67–1.41)	
					≥20%	1.22 (0.68–2.18)	
			26–39		<10%	Reference	–
					10%–19.99%	0.92 (0.75–1.14)	
					≥20%	0.93 (0.67–1.30	
Gruszczynski et al. (53)	Thyroid	SEER (3,913)	0–19	Poverty Line	Above poverty line Below poverty line	Reference 1.04 (1.00–1.08)	High poverty
					Above poverty line Below poverty line	Reference **1.09 (1.02–1.17)**[b]	High poverty
Fineberg et al. (28)	CNS	SEER (1,881)	0–19	Poverty level	Below Poverty Level rate (all other quartiles)	Reference	High poverty
					Below Poverty Level rate (highest quartile)	**1.26 (1.09–1.46)**	
Rotz (34)	ALL	NCDB (34,984)	0–39	Community median income	≥$63,000	Reference	Lower median income
					$38,000–$62,999	**1.16 (1.07–1.26)**	
					<$38,000	**1.27 (1.15–1.40)**	
	AML				≥$63,000	Reference	Lower median income
					$38,000–$62,999	**1.14 (1.07–1.23)**	
					<$38,000	**1.21 (1.11–1.32)**	
Chao et al. (41)	NHL	KPSC (718)	15–39	Household median income	<$40,000	Reference	Lower house median income
					$40,000–65,000	0.70 (0.47–1.02)	
					>$65,000	**0.60 (0.40–0.92)**	
					<$40,000	Reference	–
					$40,000–65,000	0.74 (0.46–1.19)[b]	
					>$65,000	0.70 (0.41–1.18)[b]	
Huang (44)	Lymphoma NOS	SEER (21,149)	15–17	Median family income	Quintile 1 (25,400–63,170)	Reference	–
					Quintile 2 (63,190–68,850)	2.29 (0.72–7.28)	
					Quintile 3 (68,910–81,820)	3.25 (0.73–14.44)	
					Quintile 4 (81,930–94,400)	1.54 (0.26–9.24)	
					Quintile 5 (94,910–136,900)	1.79 (0.17–18.80)	
			18–25		Quintile 1 (25,400–63,170)	Reference	–
					Quintile 2 (63,190–68,850)	0.88 (0.57–1.38)	
					Quintile 3 (68,910–81,820)	0.69 (0.40–1.19)	
					Quintile 4 (81,930–94,400)	0.70 (0.36–1.35)	

(*Continued*)

TABLE 2 Continued

Author (year)	Diagnosis	Database (sample)	Age (yrs.)	SDH indicator	Cohorts	HR (95% CI)	Worst survival predictor
					Quintile 5 (94,910–136,900)	0.59 (0.22–1.59)	
			26–39		Quintile 1 (25,400–63,170)	Reference	–
					Quintile 2 (63,190–68,850)	1.34 (1.02–1.75)	
					Quintile 3 (68,910–81,820)	1.30 (0.92–1.83)	
					Quintile 4 (81,930–94,400)	1.40 (0.94–2.08)	
					Quintile 5 (94,910–136,900)	1.06 (0.59–1.88)	
Huang (44)	Lymphoma NOS	SEER (21,149)	15–17	Percentage of unemployment	Quintile 1 (1.29–5.45%)	Reference	–
					Quintile 2 (5.46%–6.36%)	0.63 (0.25–1.55)	
					Quintile 3 (6.39%–7.49%)	0.90 (0.39–2.06)	
					Quintile 4 (7.53%–8.53%)	0.54 (0.19–1.55)	
					Quintile 5 (8.54%–20.35%)	0.85 (0.33–2.17)	
			18–25		Quintile 1 (1.29–5.45%)	Reference	–
					Quintile 2 (5.46%–6.36%)	1.33 (0.92–1.92)	
					Quintile 3 (6.39%–7.49%)	1.03 (0.71–1.50)	
					Quintile 4 (7.53%–8.53%)	0.93 (0.62–1.40)	
					Quintile 5 (8.54%–20.35%)	0.91 (0.59–1.39)	
			26–39		Quintile 1 (1.29–5.45%)	Reference	–
					Quintile 2 (5.46%–6.36%)	1.08 (0.87–1.32)	
					Quintile 3 (6.39%–7.49%)	1.12 (0.91–1.38)	
					Quintile 4 (7.53%–8.53%)	1.23 (0.99–1.54)	
					Quintile 5 (8.54%–20.35%)	1.02 (0.80–1.29)	

ALL, acute lymphocytic leukemia; AML, acute myelogenous leukemia; APL, acute promyelocytic leukemia; CI, confidence interval; CNS, center nervous system; CRC, colorectal cancer; HL, hodgkin lymphoma; HR, hazard ratio; KPSC, Kaiser Permanente Southern California; NCDB, National Cancer Database; NHL, non-hodgkin lymphoma; NOS, not otherwise specified; SEER, surveillance, epidemiology, and end results program; SES, socioeconomic status; yrs, age in years.

[a]Data based on overall survival analysis unless stated otherwise.

[b]Data based on cancer-specific survival analysis.

[c]Values for multivariate analysis unless stated otherwise.

[d]Values for univariate analysis.

[e]Probability of 5-year overall survival (95% CI); $P = 0.02$.

[f]Represent the first study for Abrahao et al. team in 2015 which is Racial/Ethnic and Socioeconomic Disparities in Survival Among Children With Acute.
Lymphoblastic Leukemia in California, 1988–2011: A Population-Based Observational Study.

[g]Represent the second study for Abrahao et al. team in 2015 which is Disparities in Early Death and Survival in Children, Adolescents, and Young Adults with Acute Promyelocytic Leukemia in California.

Bold values stand for statistically significant (as reported by authors or depending on the 95%-CI).

the lowest quartile compared to the highest quartile (HR = 1.46, 95%-CI:1.29–1.66) Notably, there was low heterogeneity across all groups, except for the comparison between the lowest and highest quartiles (Figure 2). The analysis of CSS in hematological malignancies, we found a significant association between nSES and CSS in all subgroup analyses. The strongest association was evident in the comparison between the lowest and highest quartiles for nSES (HR = 1.43, 95%-CI: 1.20–1.72) (Supplementary Figure S2).

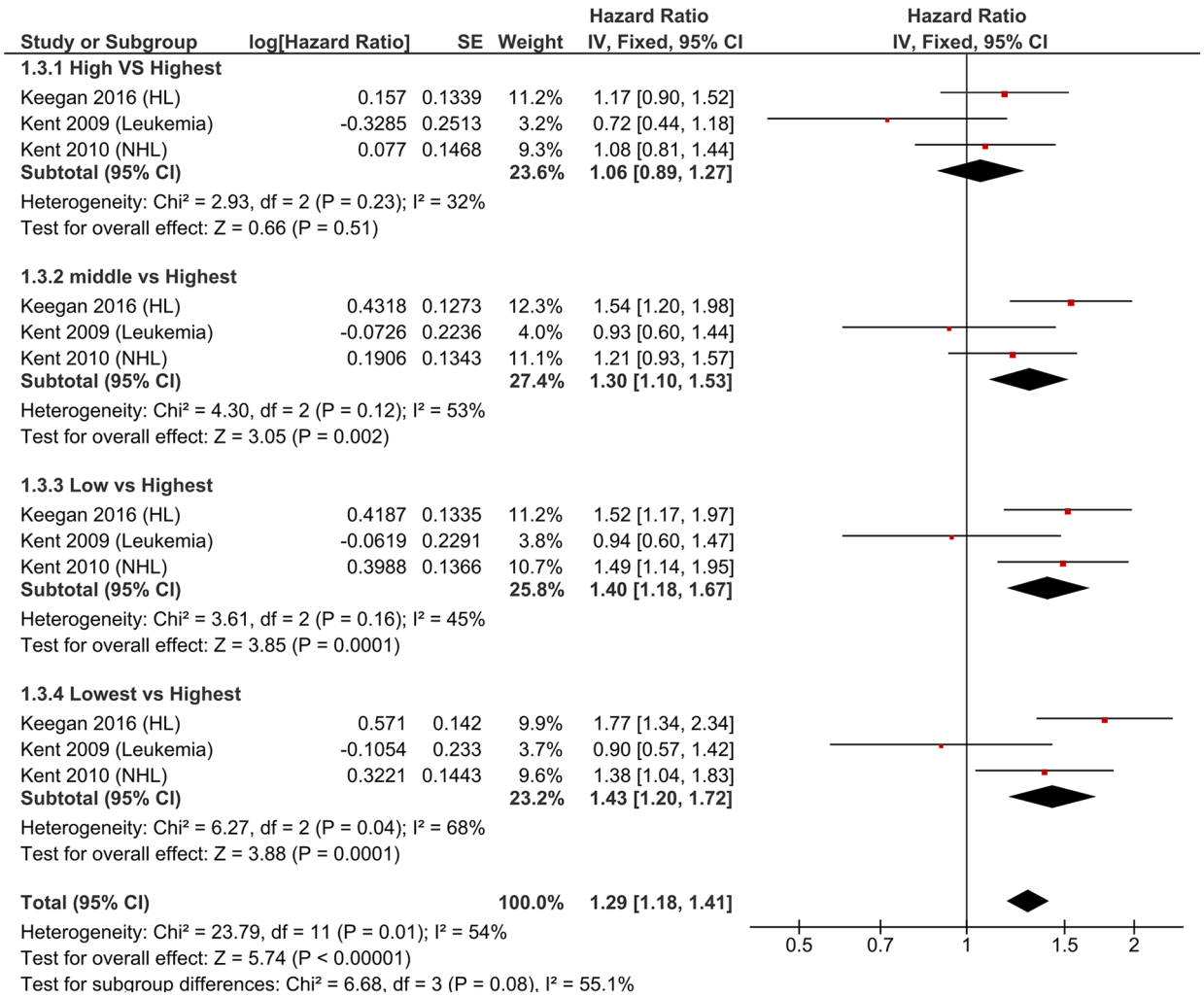

FIGURE 2
Pooled hazard ratios for overall survival according to nSES in children and AYA with hematological malignancies.

The effects of poverty on OS were examined in five manuscripts (Table 2) (28, 33, 39, 44, 53), and three of these studies (60%) found a significant association between poverty and OS (28, 39, 53). Four studies investigated the impact of household/community median income on hematological malignancies patients (27, 34, 41, 44), and 2 of these manuscripts (50%) showed a significant association between incomes level and OS. Huang et al. employed age-stratification and observed a consistent result for patients aged 15–17 years; however, the effect diminished in older age groups (44). There was no significant association between unemployment and survival (44).

Education access and quality

The association between education level at community level and OS was explored in three of the 31 included studies (Table 3) (28, 41, 44). In addition to OS, Chao et al. investigated CSS as a secondary outcome to assess the correlation with census block-level college graduate percentage as a measure of education level; however, neither outcome showed statistical significance (41). Huang et al. studied lymphoma patients using county-level percentages of people with a high school education or less, stratified into three age groups, but once again, the results were not statistically significant (44).

Social and community context

Marital status at individual level and language isolation at community level were the only 2 variables measured in this age group in the manuscripts analyzed. For the marital status, 4 studies (Table 3) used OS as the main outcome (40, 42, 44, 58), and 2 of those used the CSS as a secondary outcome (40, 58). Three reports (75%) assessed lymphoma patients, and one manuscript examined thyroid cancer patients (58). Two of these manuscripts (50%) showed a statistically significant correlation between being married and longer OS (42, 58). For language isolation, one manuscript showed a significant association with OS (53).

Table 3 Key findings from studies assessing the influence of social determinants of health (SDH) within the "Education access and quality" and "Social and community context" domains on treatment-related outcomes in pediatric and adolescent and young adult (AYA) patients with cancer.

Author (year)	Diagnosis	Database (Sample)	Age (yrs.)	SDH indicator	Cohorts	HR (95%-CI)[a]	Worst survival predictor
Chao et al. (41)	DLBCL	KPSC (718)	15–39	Percentage of college graduates	<25%	Reference	–
					25%–49%	1.76 (0.79–2.39)	
					>50%	0.81 (0.35–1.85)	
	NHL				<25%	Reference	–
					25%–49%	1.07 (0.73–1.56)	
					>50%	0.65 (0.36–1.19)	
	DLBCL				<25%	Reference	–
					25%–49%	1.06 (0.53–2.12)[b]	
					>50%	0.89 (0.32–2.43)[b]	
	NHL				<25%	Reference	–
					25%–49%	0.88 (0.55–1.40)[b]	
					>50%	0.58 (0.27–1.25)[b]	
Huang (44)	Lymphoma NOS	SEER (21,149)	15–17	Percentage of persons with less than high school education	2.05%–8.61%	Reference	–
					8.64%–11.30	1.16 (0.46-2.94)	
					11.32%–13.70%	1.14 (0.39–3.26)	
					13.78%–20.80%	1.30 (0.42–3.98)	
					20.83%–37.02%	1.75 (0.51–6.00)	
			18–25		2.05%–8.61%	Reference	–
					8.64–11.30	1.44 (0.99–2.10)	
					11.32%–13.70%	1.26 (0.82–1.93)	
					13.78%–20.80%	1.13 (0.71–1.79)	
					20.83%–37.02%	1.10 (0.67–1.82)	
			26–39		2.05%–8.61%	Reference	–
					8.64%–11.30	1.07 (0.87–1.32)	
					11.32%–13.70%	1.08 (0.85–1.37)	
					13.78%–20.80%	1.27 (0.99–1.63)	
					20.83%–37.02%	1.14 (0.86–1.50)	
Fineberg et al. (28)	CNS	SEER (1,881)	0–19	Population with less than a high school degree	All other quartiles	Reference	–
					Highest quartile	1.16 (1.00–1.35)	
Abrahao (42)	Lymphoma NOS	State Registry (11, 351)	15–39	Marital Status of the patient	Married	Reference	Unmarried
					Unmarried	**1.24 (1.09–1.42)**	
	HL				Married	Reference	Unmarried
					Unmarried	**1.24 (1.07–1.44)**	
	NHL				Married	Reference	–
					Unmarried	1.23 (0.93–1.62)	
Huang (44)	Lymphoma NOS	SEER (21,149)	15–17	Marital Status of the patient	Married	Reference	–
					Single (never married)	1.31 (0.80–2.14)	
					Other	1.20 (0.49–2.99)	
	Lymphoma NOS		18–25		Married	Reference	–
					Single (never married)	0.84 (0.70–1.02)	
					Other	0.67 (0.46–0.99)	
	Lymphoma NOS		26–39		Married	Reference	–
					Single (never married)	1.04 (0.93–1.15)	
					Other	1.03 (0.84–1.26)	
Keegan et al. (40)	HL	State Registry (9,353)	15–39	Marital Status of the patient	Married	Reference	–
					Not married	1.11 (0.98–1.26)	
					unknown	0.95 (0.64–1.41)	
					Married	Reference	–
					Not married	1.14 (0.95–1.36)[b]	
					unknown	1.30 (0.82–2.07)[b]	

(*Continued*)

Table 3 Continued

Author (year)	Diagnosis	Database (Sample)	Age (yrs.)	SDH indicator	Cohorts	HR (95%-CI)[a]	Worst survival predictor
Keegan et al. (58)	Thyroid	State Registry (16,827)	15–39	Marital Status of the patient	Married	Reference	Unmarried
					Unmarried	**1.78 (1.43–2.23)**	
					Unknown	1.77 (0.94–3.33)	
					Married	Reference	–
					Unmarried	0.76 (0.42–1.37)[b]	
Gruszczynski et al. (53)	Thyroid	SEER (3,913)	0–19	Percentage of the population in language isolation	Yes	**1.09 (1.03–1.15)**	Language isolation
Fineberg et al. (28)	CNS	SEER (1,881)	0–19	Language isolation (quartiles)	Highest quartile All other quartiles	Reference 1.12 (0.84–1.49)	–

CI, confidence interval; CNS, center nervous system; DLBCL, diffuse large B-cell lymphoma; HL, hodgkin lymphoma; HR, hazard ratio; KPSC, Kaiser Permanente Southern California; NCDB, National Cancer Database; NHL, non-hodgkin lymphoma; NOS, not otherwise specified; SEER, surveillance, epidemiology, and end results program; yrs, age in years.

[a]Data based on overall survival analysis unless stated otherwise.

[b]Data based on cancer-specific survival analysis.

Bold values stand for statistically significant (as reported by authors or depending on the 95%-CI).

Discussion

Our study uncovered several risk factors associated with suboptimal outcomes in pediatric and AYA patients. Notably, individuals with non-private insurance, residing in areas marked by low median income, high poverty rates, limited educational resources, lower SES, and who were unmarried (AYA) tended to exhibit the poorest outcomes. Clinicians must be attentive to these factors while evaluating the patients and adapt their therapeutic strategies and prognostic assessments accordingly. Additionally, it is also essential to acknowledge the importance of the multidisciplinary management of these patients and incorporate social professionals in the workflow during the treatment journey of children and AYAs with cancer.

The primary focus of existing research on the role of SDH in the cancer outcomes of children and AYA has been predominantly centered on variables falling within the economic stability and healthcare access domains, i.e., nSES and health insurance. These variables are widely available in most public registries such as SEER and NCDB and, although important, they were not designed to be assessed in patients with cancer. In addition, we also observed that there is a noticeable gap in the study of other SDH domains, namely, neighborhood and built environment, social and community context, and education access and quality.

Medical insurance had a significant association with OS and CSS in several types of cancer; however, it is important to point out that the insurance status is normally registered at the diagnosis, especially in public registries. Changes may occur during the patient's progress through their cancer journey. For example, uninsured patients who become eligible for Medicaid and receive treatment under its coverage might be captured as uninsured. On the other hand, the type of insurance at the diagnosis provides important information about the healthcare access of the patient (or their parents) before their eligibility for Medicaid. In our analysis, individuals with non-private insurance faced the highest risk of early death, suggesting a potential correlation with delayed presentation and advanced disease state among under-insured patients (24, 61). This is particularly concerning given the higher likelihood of AYA, aged 18–34, not having health insurance (62). This demographic may be at an elevated risk of facing increased economic burdens and limited access to care (63). Moreover, beyond insurance status, additional factors may contribute to adverse outcomes, such as the quality of healthcare facilities providing patient care and the distance patients must travel to access care. These considerations highlight the multifaceted nature of challenges faced by individuals with inadequate insurance coverage.

Meta-analyses have revealed statistically significant associations between lower nSES and poorer OS; between lower nSES and worse CSS; between Medicaid/public insurance and worse OS; and between no-insurance and worse OS. These findings underscore the substantial impact of SDH on pediatric age groups. Notably, the influence of SES on survival remains evident even when patients share the same insurance coverage, emphasizing the profound impact of financial burden on survival outcomes (57). On the other hand, it is important to point out that all SES measurements were assessed at community level and there is evidence of poor correlation between the patient and area level SDH measurements (64). Community level measures are indicators of the environment, independently of the individual (64), and should be analyzed with caution. Further investigation is imperative to establish comprehensive criteria for assessing SES. Such criteria should meticulously capture individual and familial resources, as well as the surrounding environment, to enhance our understanding of the nuanced factors influencing health outcomes in these age groups.

This study has some limitations. All examined publications were retrospective studies predominantly utilizing SEER and California Cancer Registry databases. This choice restricts the range of outcomes and variables that can be explored. To comprehensively study all SDH domains and assess other treatment-related outcomes impacted by SDH, there is a clear need for prospective studies encompassing a more diverse

representation of the general U.S. population. As a recurrent limitation of systematic reviews, there was a small number of studies that fulfilled the selection criteria, preventing us from performing a quantitative analysis of most SDH analyzed. Furthermore, the majority of analyzed manuscripts focused on hematological cancers within the specified age group. While these cancers are prevalent in this demographic, it results in an underrepresentation of patients with other cancer types, limiting the generalizability of the findings. In the context of meta-analyses, it is important to acknowledge limitations stemming from heterogeneity in SDH measures and/or reference points across manuscripts. These variations may introduce complexities in comparing and synthesizing results. As such, future studies should strive for standardized approaches in measuring and reporting SDH factors to facilitate more robust meta-analyses. Indeed, this issue has been recognized and in 2018 the National Institute on Minority Health and Health Disparities (NIMHD) launched the initiative to build a consensus toolbox of measures on SDH (10). The goal of the PhenX measures for SDH project is "to establish a collection of Common Data Elements (CDEs) to improve the quality and consistency of data acquisition and facilitate collaboration" (10).

Prominent avenues for future research include the exploration of additional SDH variables and a nuanced understanding of the proportional contribution of each SDH domain, along with their interactions, in influencing objective patient outcomes. Recognizing that quality of life (QOL) outcomes may also be impacted by SDH factors, it becomes crucial to consider the potential ascertainment bias introduced by SDH in the measurement of QOL. For children, particularly in the social and community context domain, factors such as school bullying, domestic violence, parents not living together, nontraditional family arrangements, religious beliefs, nutrition status, and access to healthy food merit thorough investigation. Future studies should aim to identify outcome predictive SDH variables that are unique to specific age strata for pediatric patients. This will not only strengthen the evidence base but also provide insights for tailored interventions aimed at improving health outcomes across diverse patient populations.

Conclusion

This study provided the panorama of how the SDH have been measured in children and AYA patients diagnosed with cancer and highlights the need for improvement in this critical field. The most common SDH variables evaluated were health insurance coverage and nSES, as these are broadly available in most public registries. On the other hand, SDH within the social and community context domain, neighborhood and built environment domain, and education access and quality domains were the least explored. We detected the following factors as predictors of poor outcomes of children and AYA patient diagnosed with cancer: non-private insurance, living in areas with low median income, high poverty rates, limited educational resources, lower SES, and being unmarried (for AYA). Developing tailored methods to measure the SDH and, consequently, identify vulnerable children and AYA diagnosed with cancer is a critical need to inform policy decisions and physicians and, ultimately, decrease the disparities in the outcomes of underserved patients.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

Author contributions

MS: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Visualization, Writing – original draft. KT: Formal Analysis, Investigation, Project administration, Writing – review & editing. MM-G: Conceptualization, Data curation, Formal Analysis, Investigation, Writing – review & editing. BS: Conceptualization, Writing – review & editing. GA: Formal Analysis, Software, Supervision, Writing – review & editing. EB: Conceptualization, Investigation, Supervision, Writing – review & editing. TJ: Conceptualization, Investigation, Supervision, Writing – review & editing. JC: Conceptualization, Investigation, Supervision, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fradm.2024.1441776/full#supplementary-material

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