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RESEARCH ARTICLE

Socioeconomic status significantly impacts childhood cancer survival in South Africa

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Abstract

Background and aims: Significantly discrepant survival rates have been documented in single disease childhood cancer cohorts in South Africa; those from higher socioeconomic groups were shown to have a significantly lower risk of death than those from less affluent households. This study aimed to determine the impact of socioeconomic status (SES) on childhood cancer survival using pooled South African data.

Methods: Five databases spanning January 2000 to December 2021 were interrogated. SES status was assigned based on a public sector annual household income classification. H0 households (formally unemployed) received free healthcare. H1, H2 and H3 (annual income > United States Dollar [USD] 19,000) households paid for healthcare relative to their income. The Spearman test assessed correlations between SES and disease stage in patients with solid tumours. Hazard ratios were

Abbreviations: COVID, corona virus disease; H (0,1,2.3), household income category; LMIC, low- and middle-income country; NHL, non-Hodgkin lymphoma; OS, overall survival; SAAPHO, South African Association of Paediatric Haematology Oncology; SES, socioeconomic status; USD, United States Dollar.

determined using Cox regression modelling. The Kaplan–Meier procedure estimated overall survival (OS).

Results: A total of 1598 children were eligible for analysis; 1269 had a solid tumour with a negative correlation between SES and stage (Spearman rho = −.178; $p < .001$). Patients with solid tumours and lower SES showed proportionately higher numbers of stage III and IV disease ($p < .01$). This proportion decreased with higher SES categories. In the multivariate analyses adjusted for sex, age, tumour type and stage, higher SES was associated with lower mortality risk ($p < .001$), indicating that the impact of SES on survival was in excess of any effect that could be explained by lower stage disease alone. There was a strong positive correlation between race and SES (Fisher's exact tests, $p < .001$) across all groups and all SES strata. Five-year OS was 85.3% in children from H3 households versus 46.3% in children from H0 households ($p < .001$).

Conclusion: SES significantly impacts childhood cancer survival for children with solid tumours in South Africa. SES is a robust surrogate for race in South Africa as a prognostic metric of disease outcome in childhood cancer. Advocacy to increase social support for impoverished patients is essential to achieve equitable improvements in outcomes treated with standardised national treatment guidelines.

KEYWORDS
childhood cancer outcomes, low- and middle-income country, socioeconomic status, South Africa, wealth disparity

1 | INTRODUCTION

South Africa remains the most socioeconomically unequal country in the world according to the Gini Index reported by the World Bank Poverty and Inequality Platform,[1,2] with an income distribution skewed towards the top 20% of the population,[3] and a poverty index indicating that almost a fifth of the population live on just United States Dollar [USD] 1.90 per day.[4] The country has a heavily racialised labour market in which most low-income earners have a poor education and are Black. Closely linked is a marked gender bias given that women earn 30% less than men with an equivalent education.[4] Additionally, the majority (60%) of households depend more on social (government funded) grants for their day-to-day survival than household income.[5] Downstream health outcomes indicate that the burden of major categories of ill health and disability are greatest amongst the most economically disadvantaged.[6]

In 2012, a national study used 17 metrics (e.g., household type, access to water and sanitation and household assets) to calculate healthcare outcomes that fit multiple dimensions of access to the healthcare pathway. Results showed that the socioeconomically disadvantaged were discriminated against across the whole spectrum of healthcare access (e.g., healthcare needs, health seeking and health service utilisation).[6,7] There has been a general economic downturn for all South Africans since 2010 (driven by multiple factors such as severe shortages in electricity supplies affecting economic activity and more recently high rates of unemployment in women and youth post-corona virus disease [post-COVID]),[8] particularly for Black South Africans, where the scale of the impoverishment is most acute. This situation is now set against a backdrop of the sharply escalating cost of living in high-income countries driven by the high costs of the COVID pandemic, the war in Ukraine and resultant rising energy costs. As these factors impact the cost of cancer care, patients are forced to choose between paying for their basic needs or accessing cancer treatments for which out-of-pocket expenses can comprise up to 15% of their income.[9] In low- and middle-income countries (LMICs), the situation is much worse, with out-of-pocket expenses for cancer care approaching as much as 40% of income.[9] Although costing studies have not been conducted in South Africa for childhood cancer, in India for family out-of-pocket expenses, one study found that nonmedical expenses accounted for 46% of the monthly household income of rural parents compared to 22% for their urban counterparts. Families from rural areas spent four times the normal amount for their daily food expenditure, and 38% had procured high-interest loans trapping them in long-term debt.[10]

Despite good policy development since the dawn of South African democracy in 1994, the current government's actions have fallen short in implementation, monitoring and evaluation of new health policies, dogged by a lack of leadership and poor governance of the public health sector.[11] Begun in 1948, South Africa endured a history of racial segregation imposed by the Apartheid political regime enmeshed with socioeconomic deprivation borne of the subjugation and dispossession of Black people to support the dominance of a White minority.[11] The United Nations opposed the discriminatory racial policies of the South African government from 1948 to 1990 and declared

TABLE 1 Definitions of race categorisation by the apartheid government, South Africa, Population Registration Act, No 30, 1950.

Race category	Definition
Black (originally referred to as a '*native*')	*'a person generally accepted as a member of any aboriginal or tribe of Africa'*
White	*'a person who in appearance obviously is, or who is generally accepted as a White person, but does not include a person who, although in appearance is obviously a White person, is generally accepted as a coloured person'*
Coloured	*'not a White or native'* (to be understood as a brown-skinned person or someone of mixed ancestry)
Asian/Indian	Included further subcategories

Apartheid a crime against humanity in 1966 (resolution 2202 A (XXI) of 16 December).[2] South Africa's current socioeconomic dilemmas are rooted in this race-based classification system instituted by the Apartheid government under the Population Registration Act, No. 30 of 1950.[10] Herein, the word *race* could be interchangeably substituted for skin colour and other physical features purported to be the defining characteristics of specific groups of people.[12] It broadly classified people as Black, White, coloured, or Asian/Indian (Table 1).[13] In this system, White people were positioned at the apex of the socio-political hierarchy, with Asians, Indians and coloureds sequentially next in line, placing Black people at the bottom. This constructed system of entrenched externally imposed racial 'identity' permeated every sector of society, and these racial classifications persist today in corporate environments and state systems of social welfare, education and health, amongst others.[14–16] Although race has historically been used as a biological indicator of genetic ancestry in medicine, it is widely contested as holding little scientific merit.[17] The terms *race* and *ethnicity* are now considered to be socio-political descriptors with no relationship to population genetics,[18] and infusing connotations of superiority into historical racial categories has been roundly dismissed as inapplicable in biology and genetic research.[19] Despite these contestations, race as a biological identifier is often incorrectly reported as influencing health outcomes, when in fact it can be argued that it is socioeconomic deprivation resulting from social disenfranchisement and the dysfunctional health systems that result, which are the real drivers of these adverse outcomes.[20]

Since 2010, race as a demographic identifier was excluded from disease-specific interrogations of large national retrospective datasets,[21–23] performed by the South African Association of Paediatric Haematology Oncology (SAAPHO), and rather substituted by indices of socioeconomic status (SES) like annual household income and maternal education level. A previous national South African report demonstrated a significant relationship between a lower risk of death and higher SES status in children with malignant extracranial germ cell tumours cancer (hazard ratio 0.071; $p = .039$).[23] To validate this finding in a larger, diagnostically more diverse cohort of patients, we analysed pooled data using combined, contemporaneous disease-specific databases and hospital registries from institutions in the Gauteng province, which is the most densely populated and socioeconomically diverse region of the country.

2 | METHODS

Five databases spanning January 2000 to December 2021 were combined and interrogated: three disease-specific datasets for paediatric malignant extracranial germ cell tumours, neuroblastoma and Hodgkin lymphoma (9–14 hospitals per database) and two additional hospital-based registries from Gauteng. All children with cancer diagnoses from birth to 16 years of age were eligible for inclusion. Demographic data included age, sex, disease diagnosis, stage, SES and survival outcomes. Ex post facto, we retrieved all available (patient-assigned) race coding to perform a correlation analysis between SES and race. SES status was assigned based on a public sector annual household income classification according to parental self-reported income. H0 households (formally unemployed and all children under 6 years of age) received free healthcare. H1, H2 and H3 households paid healthcare costs relative to their income according to a State needs assessment. Households classified as H3 (highest income) earned more than USD19,000 per year. In addition, families with private insurance or private funding were also included and identified as such. Datasets were aligned and cleaned to remove duplicate entries, and any patient missing one or more demographic, socioeconomic or survival data points. Patients with incurable malignancies were excluded as well as those treated on intent-to-palliate regimens. Patients with histiocytosis were excluded (Figure 1). An incurable illness was defined as one that was untreatable (due to the poor clinical condition of the patient and/or extent of the disease) or a disease in which available evidence suggested that no known treatment instruments existed, which when employed singularly or in combination would render the patient salvageable. Patients were identified as such by diagnosis.

Patients were grouped into three main groups: leukaemias, brain tumours and solid tumours, which included lymphomas. The Spearman rank correlation coefficient test was used to assess relationships between SES and disease stage at diagnosis in children with solid tumours. Children with leukaemia and brain tumours were excluded from this specific analysis, as they are differently risk stratified and graded, respectively, and could not be homogenously combined. The Fisher's exact test was used to test the correlation between SES and race across all race categories and SES strata. Adjusted hazard ratios were determined using Cox regression modelling, and the Kaplan–Meier procedure was used to estimate overall survival (OS) (confidence interval [CI] 95%), where statistical significance was defined as a p-value less than .05.

Ethical approval was obtained from the Human Ethics Review Committee of the University of Cape Town (002/2018), with reciprocal approval from the University of Stellenbosch (S18/07/138) and Witwatersrand University (M1711100).

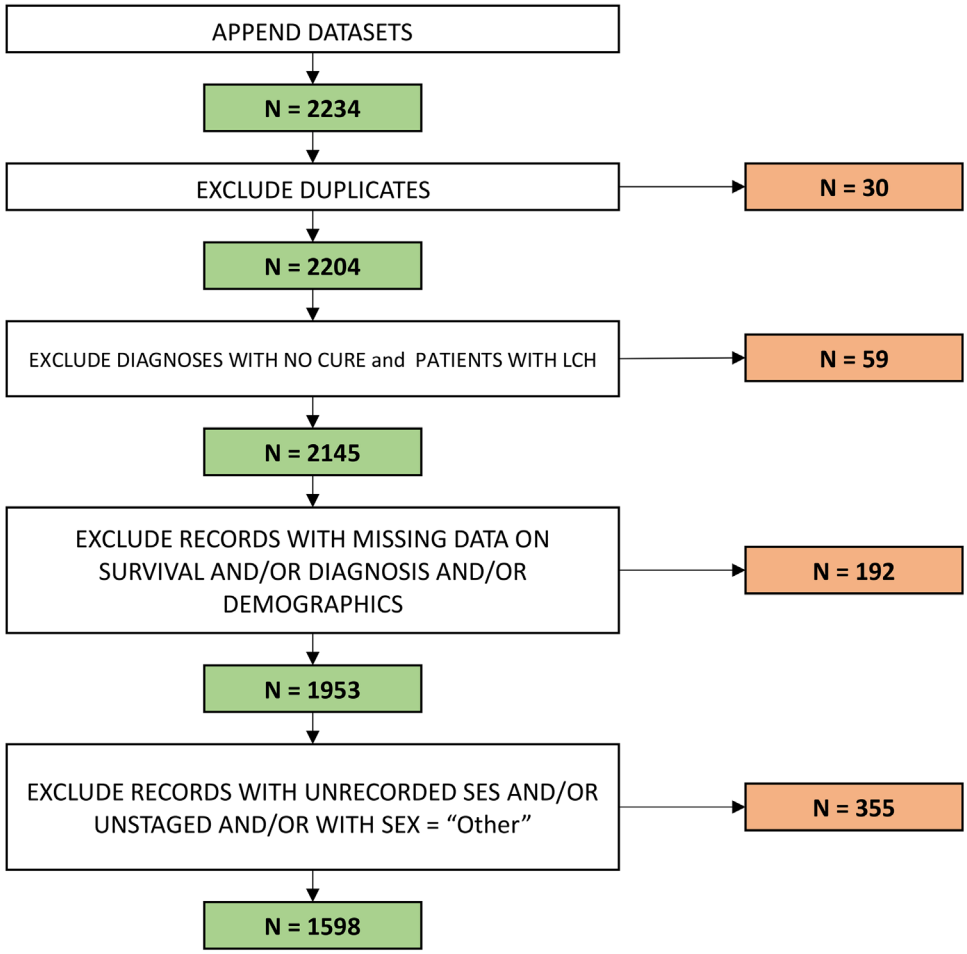

FIGURE 1 Consort diagram showing selection of children's data from combined datasets, January 2000 to December 2021.

3 | RESULTS

3.1 | Patient characteristics

A total of 1598 children (772 male and 826 female) were eligible for inclusion. The median age was 53 months (interquartile range [IQR]: 21–116). Datasets were merged, and children excluded as shown in the consort diagram (Figure 1). There were 231 patients with leukaemia, 110 with brain tumours and 1257 with solid tumours. A detailed list of patient diagnoses is shown in Table 2.

3.2 | Stage

Disease stages for children with solid tumours were: stage 1 ($n = 250$), stage 2 ($n = 158$), stage 3 ($n = 285$), stage 4 ($n = 562$) and stage 5 ($n = 2$).

3.3 | SES

In the SES strata from poorest to most affluent, the results were: H0 ($n = 688$), H1 ($n = 386$), H2 ($n = 46$), H3 ($n = 59$) and privately funded or insured patients ($n = 419$).

3.4 | Race

In the cohort, 1186 children had a documented self-declared race assignment: Black ($n = 921$), coloured ($n = 108$), Asian/Indian ($n = 36$) and White ($n = 121$). In the solid tumour subgroup specifically, the disaggregation was: Black ($n = 728$), coloured ($n = 97$), Asian/Indian ($n = 24$) and White ($n = 92$).

3.5 | Statistical analysis

3.5.1 | SES and stage

A total of 1257 children with solid tumours (including lymphoma) were eligible for inclusion in this analysis (Table 2). There was a negative correlation between SES and disease stage (Figure 2). Children with solid tumours and lower SES presented with proportionately higher numbers of stage III and IV tumours ($p < .01$), and this decreased with higher SES status. In the multivariate analysis adjusted for age, sex, tumour type and stage, higher SES was associated with a lower risk of death ($p < .001$), indicating that the impact of SES on survival was in excess of any effect explained by lower stage disease alone.

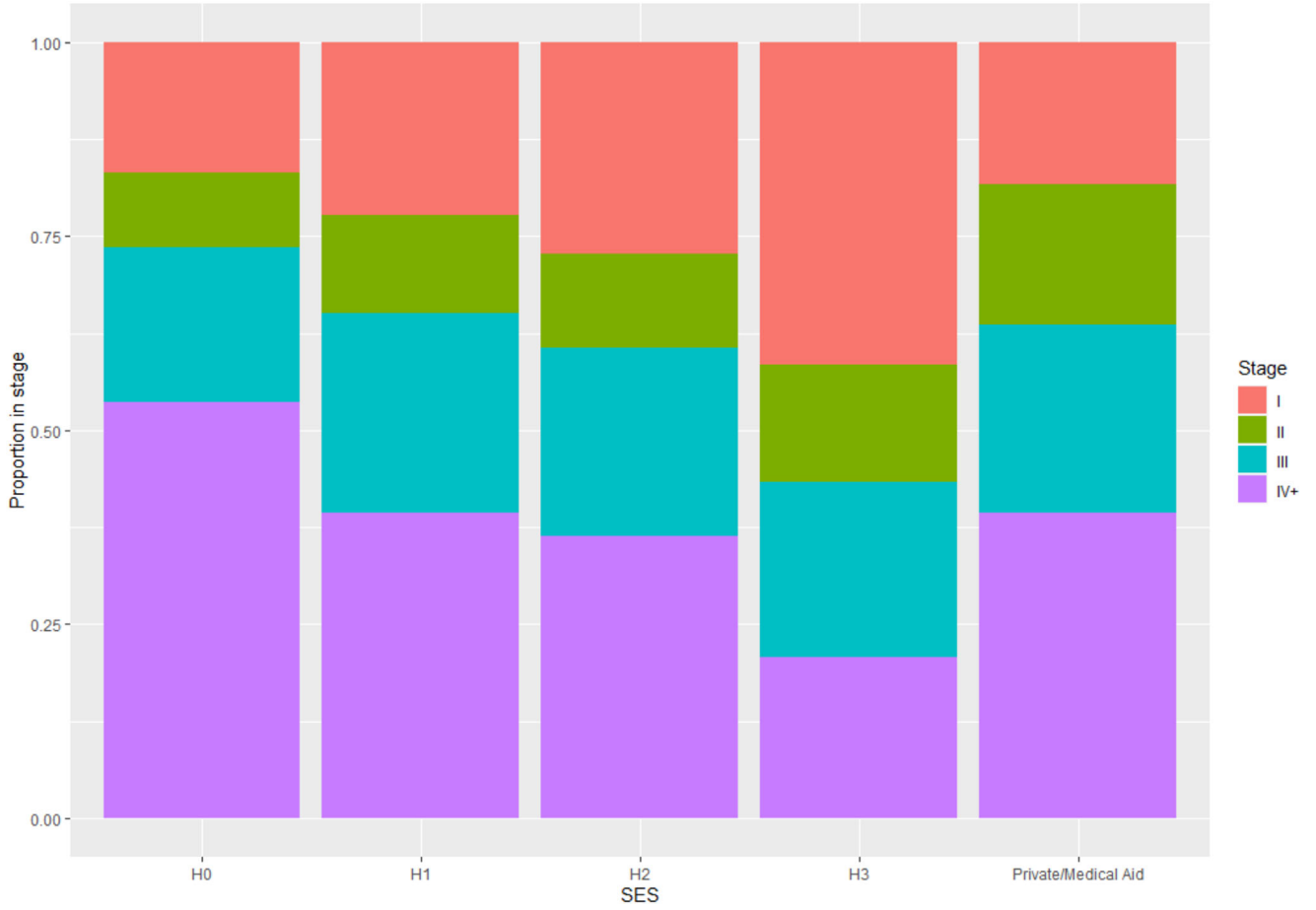

FIGURE 2 The relationship between disease stage and socioeconomic status (SES) in patients with solid tumours, January 2000 to December 2021 ($n = 1257$).

3.5.2 | SES and race

In both the solid tumour subgroup and the combined cohort, race and SES were strictly correlated ($p < .001$). In the solid tumour subgroup, there was a significant positive correlation between SES (from H0 to private insurance/funding) and race (for Black, coloured, Asian/Indian and White), with SES increasing, moving from one category to the next; thus, Black patients were most financially disadvantaged and White patients most affluent (Spearman rho = .21, $p > .001$). The same significant correlation was seen in the combined cohort (solid tumours, leukaemia and brain tumours) (Spearman rho = .18, $p < .001$).

3.6 | Outcome

In the combined cohort, there was a stark difference in 5-year OS between children from the poorest households (H0, 46.3.%) and incrementally more affluent households: H1, 65.3% ($p < .001$); H2, 57.9% ($p = .04$) and H3, 85.3% ($p < .001$). Children with medical insurance also did significantly better in survival (OS 64.0%, $p = .002$), although not as well as those in the H3 group (Figure 3).

4 | DISCUSSION

We were able to show a significant relationship between poverty and a lower survival outcome in a large and diagnostically heterogenous group of South African children with cancer, similar to the relationship previously reported in South African children with malignant extracranial germ cell tumours.[23] This was consistent with our first hypothesis that a significant relationship exists between SES and childhood cancer outcome in South Africa. Moreover, we demonstrated an incontrovertible correlation between SES and race, confirming our second hypothesis that race, as it impacts survival in our context, is a function of socioeconomic deprivation rather than any biological characteristic like the arbitrary assignment of racial category by skin colour. A recent South African study has demonstrated a significant relationship between food insecurity and an increased risk of death (HR 3.2; $p = .046$), implying a relationship between poverty and unfavourable childhood cancer outcomes by proxy.[24] A large population-based study from the United States has shown SES to be a significant mediator of racial (physical traits) and ethnic (religion, language, culture, nationality) childhood cancer survival disparities (acute lymphoblastic leukaemia [ALL] $p < .001$; acute myeloid leukaemia [AML] $p = .01$;

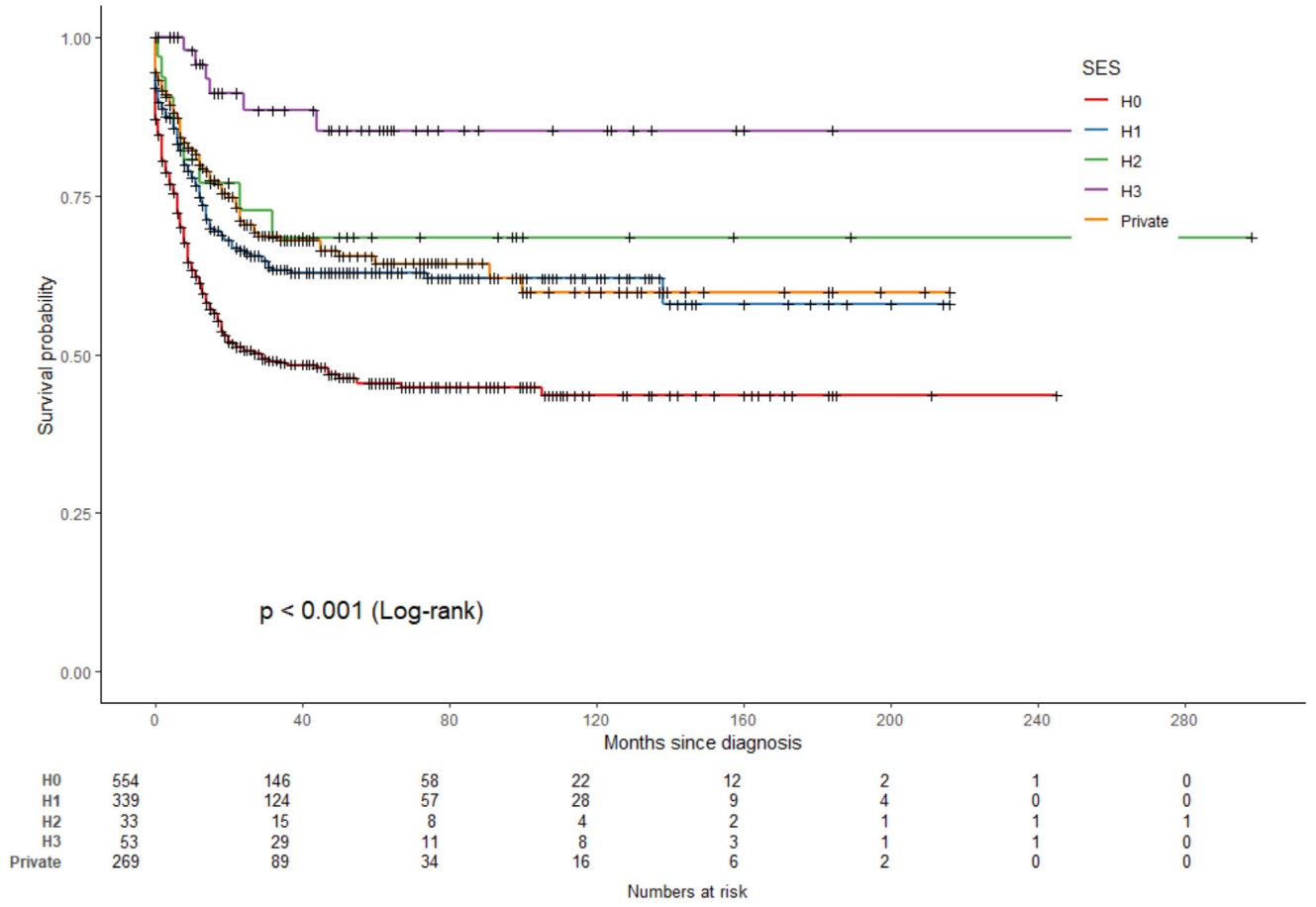

FIGURE 3 Survival in South African children with cancer by socioeconomic status, January 2000 to December 2021 ($n = 1598$).

neuroblastoma and non-Hodgkin lymphoma [NHL] $p = .04$), although this relationship was not consistently demonstrated for all cancers.[25]

An institutional single-disease cohort study from South Africa ($n = 145$) examined the impact of SES factors in patients with neuroblastoma and found that race significantly impacted outcome. White children faired significantly better than Black children (OS 65.3% vs. 29.7%, $p = .0005$).[26] However, only certain SES parameters showed a significant impact on outcome, namely, paternal employment ($p = .02$) and South African nationality ($p = .05$). There was no relationship reported between race and household income (or any other SES measure) to show a correlation between race and any SES factor, but it was hypothesised that the reported differences in outcome due to race were more likely reflecting real differences in socioeconomics given the stark differences in the documented household income between Black and White homes.[26]

By comparison, in a study in Finland, high parental income and education still positively influenced childhood cancer outcome despite a high-quality public health system.[27] Lower health literacy and increased out-of-hospital expenses were proffered as possible reasons accounting for the differences seen in parents with lower incomes and lower levels of education. Double parental incomes significantly influenced outcomes (OS 86%, $p = .003$), although mortality was lower if the mother was unemployed,[27] possibly reflecting the advantage of having a highly literate parent with high levels of agency available for full-time home care.

Another South African institutional cancer registry report from Cape Town ($n = 212$) showed a significantly poorer outcome for children with cancer who lived in informal housing with no amenities (water, electricity, sewerage) ($n = 34$; $p = .039$).[28] Contrary to expectation, children in this study who had medical insurance did not have more favourable survival outcomes,[28] in contrast to the findings in our cohort. This could be explained by the fact that insured children in our cohort were economically heterogenous, and not all children with medical insurance necessarily had additional disposable income to cover the out-of-pocket costs of medical treatment. This is a phenomenon seen in other South African childhood cancer cohorts in Gauteng.[29] Many South African children access insurance through their parents' corporate or state employers. The majority of these parents do not have access to higher tier (significantly more expensive) insurance plans, which offer broader-based coverage, so the differences in the groups relate both to the selection of insurance plans by those who have access, as well as their pool of disposable funds, which are both ultimately a function of the family's overall earning potential.

The last decade has seen the development and implementation of national treatment guidelines for retinoblastoma, neuroblastoma, Hodgkin lymphoma and germ cell tumours by the SAAPHO, as we

TABLE 2 Patient cohort by diagnosis ($n = 1598$).

Tumour type	*n*
	1598
Solid tumours	**1257**
Neuroblastoma	469
Germ cell tumours	365
Extracranial, malignant	*217*
Extracranial, mature and immature	*148*
Lymphomas	205
Hodgkin lymphoma	*155*
Non-Hodgkin lymphomas	*50*
Wilms tumour	64
Rhabdomyosarcoma	29
Osteogenic sarcoma	27
Retinoblastoma	26
Sex cord stromal tumours	21
Carcinoma, NOS	12
Ewing's sarcoma/PNET/DSRBCT	11
Rare tumours	8
CCSK/RCC	7
Hepatoblastoma	7
Sarcoma, NOS	6
Leukaemias	**231**
Acute lymphoblastic leukaemia (B+T)	156
Acute myeloid leukaemia	68
Chronic myeloid leukaemia	5
Burkitt Leukaemia	2
Brain tumours	**110**
Low-grade gliomas	38
Medulloblastomas	19
Craniopharyngiomas	19
Ependymoma	12
Brain tumours, NOS	12
Pinealoblastoma	6
Choroid plexus carcinomas	4

Abbreviations: CCSK, clear cell sarcoma of the kidney; DSRBCT, desmoplastic small round blue cell tumour; NOS, not otherwise specified; PNET, peripheral neuroectodermal tumour; RCC, renal cell carcinoma.

aspire to emulate health models pioneered in high-income countries, which are far better funded. Although not without systemic inequalities, these guidelines produce enviable outcomes for children with cancer through standardising and integrating interdisciplinary cooperation and best practices. Identifying the relationship between lower risk of death and higher SES in children with germ cell tumours called into question whether standardising care instruments was enough on its own to achieve these outcomes, thus prompting us to seek validation in a larger, more diagnostically diverse sample. Given that we have corroborated those findings in this pooled analysis, it seems reasonable to determine whether social support should be included as part of the standardised care package, and if so, then the criteria that should be applied to identify eligible candidates, the care package coverage and the payer. We would need more complex modelling than was used in our analysis to determine the answers to some of these questions, and this is recommended for future work. In particular, exploring thresholds for improvement in financial support, including options for funding, could yield significant upward shifts in survival.

Analysis of chronic healthcare programmes outside South Africa reveals that these are highly dependent on equitable and well-coordinated health systems, working in an integrated fashion across the healthcare continuum. In LMIC, these programmes place considerable demands on systems where weaknesses in finance, governance, workforce deficits, health information, medical supplies and services are then exposed.[30] In addition, the underlying mechanisms and pathways leading to social inequity in childhood cancer survival are currently not as well elucidated compared to adults in whom lifestyle and co-morbidities have a clearer causal relationship. Erdmann et al. have developed a conceptual framework focussing on social inequities in childhood cancer, to determine mechanisms and pathways by which social determinants may create health inequalities, suggesting that it may have a global application. They propose social inequities become targets for intervention and policy development and include factors like access to diagnostic facilities (contemporary), therapy and supportive care, social support for families, long-term follow-up of vulnerable groups to identify late effects (somatic and psychiatric), adverse socioeconomic conditions and a legal framework to protect survivors from discrimination.[31] Already, most or all of these constitute significant barriers to care in resource-limited environments. These factors are all part of critical conversations that need to be framed in a time of growing economic and environmental uncertainty, increasing basic service insecurity, in particular electricity supply in South Africa, rising costs of healthcare, particularly oncology care, and the incoming National Health Insurance Bill that seeks to increase parity across our unequal health services landscape.

The association between systemic racism and socioeconomic deprivation is not particular to South Africa. In the United States, not unlike South Africa, racism, historically planned residential segregation, poor access to education and housing all drive socioeconomic disparity such that Black people and others experience more adverse health outcomes. As a single example, poor access to education impacts health-related knowledge, literacy and behaviour, negatively impacts access to high-income jobs with good working conditions and benefits like medical insurance, and consequently affects social standing and exposure to stress, all of which cumulatively impact health outcomes.[32] A distinction then between race as a social factor rather than an innate biological determinant has become a core element of critical race theory as a framework developed to acknowledge, understand and unpack the mechanics of racism in social contexts. In this regard, we assert that the only valid determinants of health outcomes are social determinants of health, such as the social construction of race (rather than race as a stand-alone biological descriptor), and established

biological vulnerabilities based on the identification of reproduceable genetic mutations.[33]

4.1 | Strengths and limitations

We acknowledge that hospital classification systems have inherent problems capturing accurate socioeconomic data, and subtle differences between classification systems exist between sites such that these are likely to have impacted data recording. Nevertheless, the findings of the pooled data are compelling and indicate the power of larger samples of children, as these findings were not consistently seen in single-disease cohorts. Additionally, health-seeking behaviour, such as the use of traditional medicines as a forerunner to hospital care, may have impacted children's access to care. It is not uncommon that South African parents of children who are ill, often seek the permission of elders to access medical help or alternative pre-hospital care from traditional healers who are geographically closer and more culturally aligned and accepted, which can delay a diagnosis and negatively influence outcomes.[34]

4.2 | Implications for practice

It is hard to see how modernising and finessing treatment approaches as a national imperative for improving childhood cancer survival will singularly drive the progress that we aspire to without parallel socioeconomic upliftment of the most disadvantaged in our country. It seems almost inevitable that we will reach a ceiling beyond which outcomes for Black children will not match their White counterparts without a commitment to social and financial support by state and private funders. This will mean that additional work will need to be done by already overburdened clinicians and parent support organisations to design and drive this change. The study of race in a socio-political context as a vehicle to understand how structural inequality results in health disparities for defined groups remains critically important.[19] To this end, the current prospectively designed national treatment guidelines for childhood cancer underway in South Africa provide us with a critical opportunity to collect good quality data on social determinants of health[35] and their intersections with race and ethnicity, which may uncover insidious gaps in care and help reinvigorate a more creative and socially responsive health policy space,[36] like the one reimagined by the National Health Insurance policy, if we successfully and responsibly practice good governance.

5 | CONCLUSION

Apartheid has produced a landscape of deep and sustained structural inequity inextricably linked to race, which negatively impacts health outcomes for the most disenfranchised children in South Africa. Establishing evidence-based relationships between childhood cancer outcomes and SES underscores the imperative of creating equality and financial parity for children with cancer from poorer households, so that achieving improved outcomes with standardised national treatment guidelines can be realised across the socioeconomic divide. It also highlights the importance of clinical scientists acting as agents of social justice, in addition to advocating for and providing quality healthcare, if the work of developing and implementing South African national treatment guidelines is to bear fruit in the most unequal society in the world.

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CONFLICT OF INTEREST STATEMENT

The authors declare they have no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data restricted due to ethical considerations, but reasonable requests will be considered by the corresponding author and only with the express consent of the South African Association of Paediatric Oncology (SAAPHO).

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