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Survival outcomes of adapted paediatric cancer treatment protocols in Cameroon and collaborating sub-Saharan African centres: a systematic review and meta-analysis

Yvonne Nyiambam Waindim[1,2a], Glenn Mbah Afungchwi[2,3], Fongang Che Landis[3], Angele-Hermine Pondy-Ongotsoyi[4,5] and Mary Bi-Suh Atanga[3]

[1]Department of Public Health, Faculty of Health Sciences, The University of Bamenda, PO Box 39, North West Region, Bambili, Bamenda, Cameroon
[2]World Child Cancer, First Floor, Abunde's Building, Up Station, Bamenda, Cameroon
[3]Department of Nursing and Midwifery, Faculty of Health Sciences, The University of Bamenda, PO Box 39, North West Region, Bambili, Bamenda, Cameroon
[4]Department of Oncology/Hematology, Mother and Child Center, Chantal Biya Foundation, PO Box 1936, Yaoundé, Cameroon
[5]Department of Pediatrics, Faculty of Medicine and Biomedical Sciences, University of Yaounde 1, PO Box 1364, Yaoundé, Cameroon
[a] https://orcid.org/0000-0002-3253-0984

Abstract

Survival outcomes for childhood cancers remain substantially lower in low- and middle-income countries than in high-income countries, largely due to late diagnosis, limited supportive care and treatment abandonment. In response to these challenges, Cameroon and collaborating Sub-Saharan African centres have implemented adapted paediatric cancer treatment protocols designed to balance effectiveness with feasibility in resource-constrained settings. Yet, the survival impact of these adaptations has not been systematically synthesised. We conducted a systematic review of studies published over the past 20 years that reported treatment protocols and survival outcomes among children and adolescents with cancer in Cameroon or in multicentre African studies that included Cameroonian patients. Searches were run in PubMed, Google Scholar, African Journals Online and grey literature sources. Study selection followed the Preferred Reporting Items for Systematic Reviews and Meta-Anal 2020 guidelines, and risk of bias was assessed using ROBINS-I. A random-effects meta-analysis was used, given the expected clinical and methodological heterogeneity. Twelve studies, including 1,984 participants, were included; four were conducted only in Cameroon, and eight were multicentre African studies including Cameroon. Most protocols were adapted from the International Society of Paediatric Oncology and Groupe Franco-Africain d'Oncologie Pédiatrique guidelines. Because studies differed in reported outcomes, study design and comparator structure, comparative odds ratios (ORs) were pooled for exploratory purposes only and were not interpreted as a single causal measure of protocol effectiveness. An initial random-effects model showed substantial heterogeneity (I^2 = 85%). The strongest and most consistent pattern was seen in stage-based comparisons, where children diagnosed earlier had much better outcomes than those presenting with advanced disease (pooled OR 5.89, 95% CI 3.38–10.29). By contrast, implementation/time-based comparisons and protocol-versus-protocol comparisons were smaller and less stable in sensitivity analysis. Overall, adapted protocols appear to support encouraging outcomes, but the clearest advantage was linked to earlier diagnosis rather than to a uniform protocol effect. More standardised outcome reporting and stronger prospective studies are needed.

Keywords: *paediatric cancer, adapted treatment protocols, survival outcome, Cameroon, sub-Saharan Africa, LMICs*

Review

Correspondence to: Yvonne Nyiambam Waindim
Email: waindimy@gmail.com

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Introduction

Where a child lives remains one of the strongest determinants of their chances of surviving a cancer diagnosis [1]. While more than 80% of children diagnosed with cancer in high-income countries (HICs) now survive, outcomes in many low- and middle-income countries (LMICs), including Cameroon, remain substantially poorer, with survival rates often below 30% [2]. Over the past several decades, survival gains in HICs have been driven by advances in multimodal therapy, cooperative group clinical trials, improved supportive care and innovations in risk-adapted treatment strategies [3, 4]. In contrast, childhood cancer care in LMICs continues to be challenged by limited infrastructure, shortages of specialised personnel, constrained diagnostic capacity and higher rates of both late presentation and treatment abandonment [3, 5, 6].

In response, paediatric oncology programmes in LMICs have increasingly adopted adapted treatment protocols, often because locally conducted clinical trials are scarce and programmes must modify protocols developed elsewhere to fit available diagnostic, supportive care and treatment resources. The adaptation often involves reduced-intensity chemotherapy regimens designed to minimise toxicity in settings where supportive care resources are limited [3, 5, 7]. Several collaborative initiatives, including the Groupe Franco-Africain d'Oncologie Pédiatrique (GFAOP) [8] and the Collaborative African Network for Childhood Cancer Care (CANCaRe Africa) [9], have successfully implemented such adapted protocols across Sub-Saharan Africa. These initiatives aim to balance treatment effectiveness with local feasibility while addressing challenges related to late diagnosis, comorbidities and health system constraints. Evidence suggests that adapted protocols can improve survival outcomes, particularly for highly curable cancers such as Wilms tumour, Burkitt lymphoma and Hodgkin lymphoma [10–12].

Cameroon provides a particularly relevant context for examining the effectiveness of adapted paediatric cancer treatment protocols. As an LMIC with a population of over 28.4 million [13], Cameroon is among the Global Initiative for Childhood Cancer (GICC) focus countries in the WHO Afro Region [14]. Childhood cancers account for approximately 1%–2% of all cancers in the country, with lymphomas, acute leukaemias, nephroblastomas and retinoblastomas being the most prevalent [15]. Before the year 2000, there were no dedicated paediatric oncology services in Cameroon [16]. Significant progress has since been made with the establishment of two specialised paediatric oncology programmes: one at the Mother and Child Center-Chantal Biya Foundation (MCC-CBF) in Yaoundé and another within the Cameroon Baptist Convention Health Services (CBCHS), with a hub at Mbingo Baptist Hospital [16]. These programs offer paediatric chemotherapy, surgery and palliative care, although radiotherapy and nuclear medicine services remain largely unavailable nationally [15]. Nonetheless, recent progress in the provision of radiotherapy has been made, with the Cameroon Oncology Centre now providing radiotherapy [17], and the construction of a bunker for radiotherapy at Mbingo Baptist Hospital is underway.

The treatment protocols implemented in these centres are largely adaptations of international guidelines, modified to reflect local resource availability and supportive care capacity [16]. While individual studies from Cameroon and collaborative African trials have reported encouraging survival outcomes following the introduction of these adapted protocols, the available evidence remains fragmented [16]. Although the number of Cameroon-only outcome studies remains modest, paediatric oncology in Cameroon has developed substantially through multicentre African collaboration that included Cameroonian centres. Excluding those studies would therefore omit a portion of the evidence relevant to Cameroon.

To date, however, there has been no systematic synthesis of survival outcomes associated with adapted paediatric cancer treatment protocols in Cameroon and in collaborating Sub-Saharan African Centres that included Cameroonian children. Such a synthesis is essential to understand the extent to which these adaptations have translated to meaningful survival gains, identify areas of progress and highlight gaps that require policy and health system responses. This systematic review and meta-analysis therefore aimed to collate the treatment protocols used in Cameroon and to assess their associated survival outcomes across major paediatric cancer types.

Methods

Literature search

We framed the review question using a PICOT-informed approach: among children and adolescents (0–19 years) with cancer treated in Cameroon or in multicentre African studies that included Cameroonian centres (Population), what adapted paediatric cancer treatment protocols

(Intervention), compared with baseline cohorts, alternative adaptive regimens or other within-study comparative groups when reported (Comparator), were associated with better survival outcomes (Outcome) in studies published over the last 20 years (Time)?

We conducted a systematic search of the literature to identify studies reporting treatment protocols and survival outcomes in these settings. Electronic databases searched included MEDLINE via PubMed, Google Scholar and African Journals Online. The search covered studies published over the past 20 years. PubMed searches combined MeSH terms and free-text words. A representative search string was as follows: (child* OR adolescent* OR paediatric OR paediatric) AND (cancer OR neoplasm* OR "Burkitt lymphoma" OR "Wilms tumour" OR nephroblastoma OR retinoblastoma OR "Hodgkin lymphoma" OR lymphoma) AND (survival OR outcome* OR mortality) AND (protocol* OR treatment OR chemotherapy) AND (Cameroon)). Equivalent concept-based adaptations were used for Google Scholar and African Journals Online.

To minimise publication bias and capture locally relevant evidence, grey literature sources were also searched. These included government reports, such as the Ministry of Public Health: National Strategic Plan for Prevention and Cancer Control (2020–2024) [15], as well as global reports, including the CureAll framework (WHO GICC) [18].

Study selection

Studies were selected based on the following predefined eligibility criteria. Included studies were those that: (1) focused on children and adolescents (0–19 years) diagnosed with cancer; (2) reported both treatment protocols and survival outcomes; (3) were conducted in Cameroon or were multicentre African studies that included data from Cameroon; (4) used interventional, clinical trial, or cohort designs with sufficient data for outcome extraction; and (5) were published in English or French, Cameroon's official languages, within the past 20 years.

Studies were excluded if they focused exclusively on adults or mixed-age populations without disaggregated paediatric data, were unrelated to the Cameroonian context, lacked survival outcome data, or were case reports, editorials, expert opinions or letters to the editor. Conference abstracts without sufficient outcome data were excluded. Randomised trials were not excluded a priori, but none were identified in the final sample.

Study screening was conducted independently by four reviewers (YW, GA, FL and MA), all of whom have advanced training in research methods. Titles and abstracts were screened first, followed by a full-text review of potentially eligible studies. Discrepancies were resolved through discussion and majority consensus. The study selection process adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines [19].

Data extraction and quality assessment

Data were extracted using a data extraction sheet. Extracted information included: (a) study characteristics (first author, publication year, study design, study location, study period, cancer type, population and sample size); (b) treatment protocol characteristics and survival outcomes as reported by the primary study authors. Four reviewers (YW, GA, FL and AP) independently assessed the methodological quality of the included studies using the Risk of Bias in Non-Randomised Studies of Interventions tool [20]. Seven domains of bias were evaluated for each study. Overall study quality was classified as high (low risk of bias across all domains), medium (moderate risk of bias in one or more domains), or low (serious or critical risk of bias in one or more domains). Disagreements were resolved through re-examination of the original studies and group discussion guided by the ROBINS-I criteria, with the final consensus requiring the agreement of at least three reviewers.

Survival endpoints were extracted exactly as defined in the primary studies (e.g., end-of-treatment survival, event-free survival and overall survival) and were not assumed to be interchangeable.

Statistical analysis

Study-specific odds ratios (ORs) and 95% confidence intervals were calculated from the reported counts of outcomes in individual studies. Because the included studies differed in both endpoint definition and comparison structure, these estimates were treated as exploratory comparative measures rather than as effect estimates from a single common intervention contrast.

Comparator groups differed across the included studies and included implementation-versus-baseline cohorts, early-stage versus advanced-stage disease comparisons and protocol-versus-protocol or protocol-evolution comparisons. Accordingly, pooled ORs were calculated exploratorily by comparator category using random-effects meta-analysis with the DerSimonian-Laird method. Comparator categories were retained in the results table and considered explicitly during interpretation. Heterogeneity was assessed using Cochran's *Q* statistic, the I^2 statistic to quantify the proportion of variability attributable to between-study heterogeneity, and Tau2 (τ^2) to estimate between-study variance. An initial exploratory overall random-effects model across all study-specific ORs was used to characterise the degree of between-study heterogeneity. A leave-one-out sensitivity analysis by comparator category was conducted to assess the robustness of subgroup comparative patterns. A *p*-value of <0.05 was considered statistically significant. However, statistical significance was interpreted cautiously and always alongside the effect size magnitude, confidence interval and heterogeneity, particularly because the number of studies was small.

Because reported outcomes were not uniform across studies and included end-of-treatment survival, event-free survival, projected survival and overall survival, these outcomes were synthesised narratively rather than pooled into a single summary survival proportion. Formal assessment of publication bias (e.g., funnel plot asymmetry) was not undertaken because the limited number of included studies would render such analyses underpowered and their interpretation unreliable. All statistical analyses were performed using R software (version 4.3.1).

Results

Literature search and study selection

The systematic search identified 313 studies across the selected databases and grey literature sources. Of these, 150 were retrieved from PubMed, 110 from Google Scholar, 50 from African Journals Online and three from grey literature sources. After screening titles for relevance, 250 articles were excluded. Sixty-three abstracts were subsequently screened, of which 43 were excluded due to conference-only publication (*n* = 7), adult-only populations (*n* = 11), non-Cameroonian study populations (*n* = 20) or duplication (*n* = 5).

Twenty full-text articles were assessed for eligibility. Eight were excluded following full-text review because they focused on non-communicable diseases without specific paediatric cancer data (*n* = 2), included mixed-age populations without disaggregated paediatric outcomes (*n* = 4), or reported data published more than 20 years ago (*n* = 2). Ultimately, 12 studies met all eligibility criteria and were included in the final systematic review and meta-analysis. The study selection process followed PRISMA 2020 guidelines and is summarised in Figure 1.

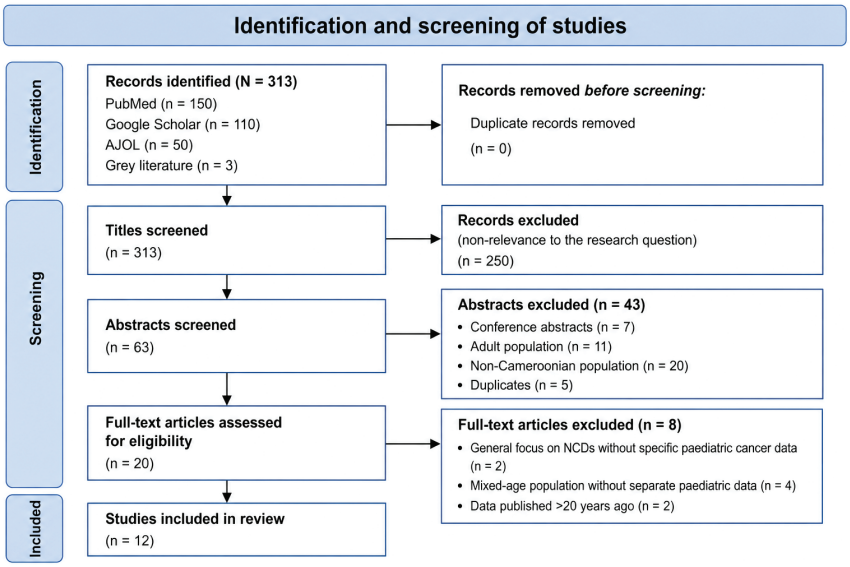


Figure 1. PRISMA 2020 flow diagram for selection of studies included in the review.

Characteristics of the selected studies

Four studies (33.3%) were conducted exclusively in Cameroon, whereas eight (66.7%) were multicentre studies undertaken through collaborative African initiatives, principally GFAOP and CANCaRe Africa, that included Cameroonian participants. A total of 1,984 children, aged 0–18 years, across all studies were included. Study periods spanned from 2001 to 2022. An equal number of studies were conducted within the CBCHS Childhood Cancer Program and the MCC-CBF. The most frequently studied malignancy was Wilms tumour (n = 5, 41.7%). Six studies were rated as high quality and six as medium quality based on ROBINS-I assessment. The characteristics of the 12 included studies are summarised in Table 1.

Treatment protocols

For Wilms tumour, all included studies reported the use of adaptations of the International Society of Paediatric Oncology (SIOP) protocols, which emphasise preoperative chemotherapy to reduce tumour size and surgical complications. Yao *et al* [29] employed the GFAOP-NEPHRO-02 protocol, an adapted version of SIOP2001, which combined vincristine and actinomycin, occasionally with doxorubicin, depending on stage. Similarly, Fufa *et al* [22] in the second CANCaRe study adapted protocols to local limitations but emphasised early surgery after preoperative chemotherapy. In the first CANCaRe Africa study, Chagaluka *et al* [21] used a consensus SIOP-adapted treatment guideline that also incorporated social support interventions to reduce treatment abandonment and avoided radiotherapy where unavailable.

For Burkitt lymphoma, three different protocols were used across the included studies. Two studies used regimens adapted by the GFAOP. Bouda *et al* [31] in the third GFAOP study implemented the adapted Groupe Franco-Africain (GF)-LMB2009 protocol, which involved intensified induction chemotherapy followed by reduced maintenance therapy, while Traoré *et al* [27] in the second GFAOP study employed cyclophosphamide monotherapy as first-line treatment and a multidrug second-line chemotherapy for refractory/relapsed patients. In contrast, Hesseling *et al* [24] applied the Cameroon 2008 Burkitt lymphoma protocol, which relied on a cyclophosphamide-based regimen with intrathecal chemotherapy.

Both studies on Hodgkin lymphoma used the COPP/ABV hybrid protocol without radiotherapy. For Retinoblastoma, the SIOP-paediatric oncology in developing countries (PODC) retinoblastoma guideline for Setting 1 was used. Two modified LMB89 regimens modified African treatment protocol ("MAT" and "GFA") were applied in the study on B-cell lymphoma.

The reporting of treatment completion was inconsistent across studies. Some authors reported completion of the full protocol, while others reported completion through end-of-treatment assessment, and others did not directly report on this indicator. Because these measures were not directly comparable, the treatment completion rate was not pooled quantitatively. Instead, Table 2 summarises each protocol together with the closest study-reported treatment delivery or completion indicator.

Comparative findings and survival outcomes

Comparative analyses were performed for 10 of the 12 studies and fell into three main categories. Implementation-versus-baseline or time-based comparisons showed mixed findings. Chagaluka *et al* [21] reported an increase in end-of-treatment survival after the implementation of the adapted Wilms tumour protocol (OR = 2.05, 95% CI; 1.5–2.6), and Israels *et al* [25] also reported improved outcomes in the Cameroonian implementation cohort, although with imprecise estimates (OR = 2.07, 95% CI:0.61–7.11). In contrast, Fufa *et al* [22] reported lower survival in the second African Wilms cohort than in the earlier cohort (OR = 0.54, 95%CI; 0.37–0.81).

Stage-based comparisons consistently favoured earlier disease at presentation. Yao *et al* [29] and Hesseling *et al* [30] demonstrated better outcomes for children with Wilms tumour diagnosed at earlier stages (stages I and II) than for those with advanced disease (stages III and IV) (OR = 4.13, 95% CI; 1.90–8.99 and OR = 7.00, 95% CI; 1.39–35.34, respectively). A similar pattern was observed for Burkitt lymphoma in the Cameroon 2008 protocol study [24] and for Retinoblastoma [26], where early-stage disease had higher survival than advanced-stage disease (OR = 10.27, 95%CI; 3.21–32.81)

Table 1. Characteristics of studies included in the systematic review and meta-analysis.

SN	Author	Year	Study design	Study period	Study location	Population studied (age range as reported)	Sample size	Quality of evidence	Main reported survival outcome
1	Chagaluka *et al* [21]	2020	Multi-centre non-randomised clinical trial by CANCaRe Africa	2014–2018	Ghana Malawi Cameroon (MBH, BBH, BHM)	Children with Wilms tumour (0.3–13 years)	201	High	2-year EFS 49.9%; EOT without disease 68.5%
2	Fufa *et al* [22]	2024	Multi-centre non-randomised intervention study by CANCaRe Africa	2021–2022	Ghana Ethiopia Malawi Zimbabwe Uganda Cameroon (MBH)	Children with Wilms tumour (0.5–14) (0.5–14 years)	230	High	2-year EFS 41.3%; EOT without disease 54.3%
3	Harif *et al* [23]	2008	Multicentre non-randomised intervention study by GFAOP	2001–2004	Algeria, Madagascar Morocco Senegal Tunisia Cameroon (MCC-CBF)	Children with B-cell lymphoma (1–17 years)	306	Medium	3-year OS 61%
4	Hesseling *et al* [24]	2012	Non-randomised intervention study	2008–2009	BBH MBH BHM	Children with Burkitt lymphoma (2–17 years)	129	High	1-year EFS 61%
5	Israels *et al* [25]	2018	Multi-centre, non-randomised clinical trial by CANCaRe Africa	2011–2015	Ghana Malawi Cameroon (MBH,BBH,BHM)	Children with Wilms tumour (< 18 years)	122	Medium	EOT no disease 68%
6	Kruger *et al* [26]	2022	Non-randomised intervention study	2012–2017	MBH BHM	Children with retinoblastoma (1–112 months)	82	Medium	24-month OS 50%
7	Traoré *et al* [27]	2011	Multi-centre non-randomised intervention study by GFAOP	2005–2008	Burkina Faso Ivory Coast Mali Senegal Cameroon (MCC-CBF)	Patients with Burkitt lymphoma (≤18 years)	178	Medium	OS 50.5%
8	Traore *et al* [28]	2020	Multi-centre, non-randomised study by GFAOP	2006–2012	Mali Senegal Madagascar Burkina Faso Morocco Cameroon (MCC-CBF)	Patients with histologically confirmed Hodgkin Lymphoma (2-18 years)	106	Medium	OS 82% (median follow-up 30 months)

Continued

Table 1. Characteristics of studies included in the systematic review and meta-analysis. *Continued*

9	Yao *et al* [29]	2019	Non-randomised Intervention study by GFAOP	2005–2011	Senegal Mauritius Ivory Coast Mali Togo Burkina Faso Cameroon (MCC-CBF)	Children diagnosed with Wilm's tumour (6 months-18 years)	169	High	3-year OS 72%
10	Hesseling *et al* [30]	2019	Non-randomised intervention study	2007–2012	MBH	Children diagnosed with Wilm's tumour	35	High	Projected survival 44% (median follow-up 84 months)
11	Bouda *et al* [31]	2019	Multi-centre non-randomised intervention study by GFAOP	2009–2015	Senegal Mauritius Ivory Coast Mali Togo Burkina Faso Cameroon (MCC-CBF)	Patients with BL (8 months–18 years)	400	High	12-month OS 60%
12	Pondy *et al* [32]	2018	Non-randomised intervention study	2007–2016	(MCC-CBF)	Children with Hodgkin disease (7–16) years	26	Medium	5-year OS 82%

MBH-Mbingo Baptist Hospital: BBH-Banso Baptist Hospital; BHM-Baptist Hospital Mutengene; MCC-CBF-Mother and Child Centre-Chantal Biya Foundation; GFAOP- Groupe Franco-Africain d'Oncologie Pediatrique; CANCaRe- Collaborative African Network for Childhood Cancer Care and Research; EFS-event-free survival; OS-Overall survival; EOT-end of treatment

Protocol-versus-protocol and protocol-evolution comparisons were less consistent. Bouda *et al* [31] reported higher survival for stage III Burkitt lymphoma in the third GFAOP study than in the first GFAOP cohort (OR = 1.92, 95% CI: 1.07–3.44), and Harif *et al* [23] found better outcomes in the MAT regimen than with the GFA regimen for B-cell lymphoma (OR = 2.48, 95% CI 1.49–4.12). By contrast, Traoré *et al* [27] found no statistically clear difference between first-line cyclophosphamide monotherapy and second-line multi-drug therapy (OR = 0.88, 95% CI; 0.50–1.58). For Hodgkin lymphoma, both Pondy *et al* [32] and Traore *et al* [28] reported high study-level survival using COPP/ABV hybrid regimens without radiotherapy, but comparative ORs were not estimable because favourable risk groups achieved 100%.

Across the included studies, survival was reported using different endpoints, including end-of-treatment status, event-free survival and overall survival. These measures were not treated as interchangeable. Accordingly, Table 3 presents study-specific comparative ORs as exploratory measures only, and these should be interpreted in the context of each study's reported endpoint and comparator group.

Meta-analysis

An initial exploratory random-effects model across all study-specific comparative ORs showed substantial between-study heterogeneity ($Q = 59.9$, $p < 0.0001$; $I^2 = 85\%$; $\tau^2 = 0.66$), indicating marked variation in comparative estimates across studies. Because comparison groups differed across studies, we did not interpret this as a single pooled treatment effect. Instead, ORs were pooled exploratorily by comparator category.

Stage-based comparisons showed the largest pooled association (OR = 5.89, 95% CI: 3.38–10.29), whereas implementation/time-based comparisons (OR = 1.25, 95% CI: 0.43–3.59) and protocol-versus-protocol or protocol-evolution comparisons (OR = 1.63, 95% CI: 0.88–3.00) were smaller and less precise (Table 4). The two Hodgkin lymphoma studies were not included in the comparator-category pooled analysis because the favourable prognostic group had 100% survival in both studies, preventing reliable estimation of study-specific ORs for pooling.

Table 2. Treatment protocols by cancer type.

Cancer type	Author	Treatment protocol	Treatment completion	Study-reported treatment delivery/ completion indicator
Wilms tumour	Fufa *et al* [22]	Wilms Africa Phase II comprehensive SIOP-adapted treatment protocol for Wilms tumour	54.3%	Completion through end-of-treatment assessment
	Chagaluka *et al* [21]	Consensus SIOP -adapted treatment guideline for Wilms tumour	73.1%	Completion through end-of-treatment assessment
	Yao *et al* [29]	GFAOP-NEPHRO-02	65.8%	Completed the whole or major part of the protocol at the end-of-treatment assessment
	Hesseling *et al* [30]	A modified SIOP treatment protocol. No access to radiotherapy	>50%	Completion through end-of-treatment assessment
	Israels *et al* [25] for the Cameroon cohort	Adapted the comprehensive SIOP-PODC Wilms tumour guideline	77.6%	Completion through end-of-treatment assessment
Burkitt lymphoma	Bouda *et al* [31]	GFAOP–LMB 2009 protocol	58%	Completed full treatment protocol
	Traoré *et al* [27]	First-line cyclophosphamide monotherapy with intrathecal methotrexate + hydrocortisone	Not directly reported	Not directly reported
	Hesseling *et al* [24]	The Cameroon 2008 Burkitt Lymphoma protocol	100% (129/129)	Completion through end-of-treatment assessment
Hodgkin lymphoma	Pondy *et al* [32]	COPP/ABV hybrid protocol without radiotherapy.	Not directly reported	Not directly reported
	Traore *et al* [28]	COPP/ABV hybrid chemotherapy only	100%	Completion through end-of-treatment assessment
Retinoblastoma	Kruger *et al* [26]	SIOP-PODC retinoblastoma guidelines for setting 1	84.1%	Chemotherapy + enucleation received through end-of-treatment assessment
B-cell lymphoma	Harif *et al* [23]	Two LMB89-modified regimens ("MAT" and "GFA") were used.	76.8%	Completion through end-of-treatment assessment

Note: These measures are not directly comparable across studies

Sensitivity analysis

Leave-one-out sensitivity analysis showed that the stage-based subgroup was the most robust, with pooled ORs remaining consistently elevated after omission of each study in turn (OR range 4.99–8.59; I^2 = 0% throughout). In contrast, the implementation/time-based subgroup was less stable, with pooled ORs ranging from 0.93 to 2.05 and heterogeneity remaining high in most iterations. Excluding Fufa *et al* [22] increased the pooled OR and eliminated heterogeneity, whereas the exclusion of Chagaluka *et al* [21] or Israels *et al* [25] shifted the pooled estimate toward the null with persistent between-study variability. The protocol-versus-protocol or protocol-evolution subgroup was also sensitive to study omission, becoming statistically significant only after exclusion of Traoré *et al* [27]. Detailed results are presented in Table 5.

Table 3. Study-specific exploratory comparative ORs for reported outcomes, organized by cancer type and classified by comparator type and comparison group.

Cancer type	Author	Comparator type	Comparison group	Computed OR	95% CI
Wilms tumour	Fufa *et al* [22]	Cohort comparison	Second study cohort versus first study cohort	0.54	0.37–0.81
	Chagaluka *et al* [21]	Cohort comparison	Implementation cohort versus baseline cohort	2.05	1.29–3.26
	Israels *et al* [25]	Cohort comparison	Cameroon implementation cohort versus Cameroon baseline cohort	2.07	0.61–7.11
	Yao *et al* [29]	Stage-based comparison	Early stage (I–II) versus advanced stage (III)	4.13	1.90–8.99
	Hesseling *et al* [30]	Stage-based comparison	Early stage (I–II) versus advanced stage (III–V)	7.00	1.39–35.34
Burkitt lymphoma	Bouda *et al* [31]	Historical/stage comparison	Stage III current study versus stage III first GFAOP study	1.92	1.07–3.44
	Traoré *et al* [27]	First line versus second-line treatment comparison	First line CPM versus second line multidrug therapy	0.88	0.5–1.58
	Hesseling *et al* [24]	Stage-based comparison	Early stage (I–II) versus advanced stage (III–IV)	7.60	1.69–34.25
Hodgkin's lymphoma	Pondy *et al* [32]	Prognostic group comparison	G1 versus G2	Not estimable	NA
	Traore *et al* [28]	Prognostic group comparison	G1 versus G2	Not estimable	NA
Retinoblastoma	Kruger *et al* [26]	Stage-based comparison	Early stage (I–II) versus advanced stage (III–IV)	10.27	3.21–32.81
B-cell lymphoma	Harif *et al* [23]	Protocol comparison	MAT versus GFA	2.48	1.49–4.12

Note: ORs were derived from the primary studies and are not directly comparable across studies. They are presented as study-specific exploratory comparative measures and should not be interpreted as estimates of a single common treatment effect

Table 4. Exploratory pooled ORs by comparator category.

The comparator category	Studies included	No of studies	Pooled OR	95% CI	Q statistic	I^2 (%)	τ^2
Implementation/time-based	Fufa *et al* [22]; Chagaluka *et al* [21]; Israels *et al* [25] (Cameroon-specific comparison)	3	1.25	0.43–3.59	20.05	90.0%	0.74
Stage-based comparisons	Yao *et al* [29]; Hesseling *et al* [30]; Hesseling *et al* [24]; Kruger *et al* [26]	4	5.89	3.38–10.29	1.83	0.0	0.00
Protocol-versus-protocol/ protocol-evolution comparisons	Bouda *et al* [31]; Traoré *et al* [27]; Harif *et al* [23]	3	1.63	0.88–3.00	7.31	72.6	0.21

Note: ORs were pooled within comparator categories using a random-effects model on the log-odds scale. Comparator categories were defined according to the structure of the comparison in each study. These estimates are exploratory and should not be interpreted as a single common treatment effect across all included studies. The Hodgkin lymphoma studies were not entered into the comparator-category pooled analysis because the favourable prognostic group (G1) had 100% survival in both studies, preventing reliable estimation of study-specific ORs for pooling.

Table 5. Leave-one-out sensitivity analysis of exploratory pooled ORs by comparator category.

1. Implementation/time-based comparisons				
Omitted study	**Pooled OR**	**95% CI**	**I^2 (%)**	**τ^2**
None (full model)	1.25	0.43–3.59	90	0.74
Fufa *et al* [22]	2.05	1.33–3.17	0.0	0.00
Chagaluka *et al* [21]	0.93	0.25–3.37	76.1	0.69
Israels *et al* [25]	1.05	0.28–3.87	94.6	0.84

B Stage-based comparisons				
Omitted study	**Pooled OR**	**95% CI**	**I^2 (%)**	**τ^2**
None (full model)	5.89	3.38–10.29	0.0	0.00
Yao *et al* [29]	8.59	3.86–19.11	0.0	0.00
Hesseling *et al* [30]	5.76	3.18–10.43	0.0	0.00
Hesseling *et al* [24]	5.66	3.11–10.31	0.0	0.00
Kruger *et al* [26]	4.99	2.65–9.42	0.0	0.00

C Protocol-versus-protocol/Protocol-evolution comparisons				
Omitted study	**Pooled OR**	**95% CI**	**I^2 (%)**	**τ^2**
None (full model)	1.63	0.88–3.00	72.6	0.21
Bouda *et al* [31]	1.49	0.54–4.11	85.7	0.46
Traoré *et al* [27]	2.22	1.51–3.26	0.0	0.00
Harif *et al* [23]	1.30	0.60–2.79	71.3	0.22

Note: Leave-one-out sensitivity analysis was performed by omitting one study at a time and re-pooling study-specific log ORs within each comparator category using a random-effects model. These analyses are exploratory and are intended to assess the robustness of subgroup comparative patterns rather than confirm a single common treatment effect.

Discussion

This systematic review synthesised evidence on adapted paediatric cancer treatment protocols used in Cameroon and in collaborating Sub-Saharan African centres that included Cameroonian children. Overall, the reviewed studies suggest that adapted protocols can support encouraging outcomes for several childhood cancers in resource-limited settings. However, the evidence does not support a single pooled estimate of protocol effectiveness. The included studies differed not only in cancer type and study design but also in the outcomes reported and in the structure of comparisons used to derive comparative ORs. As a result, the findings are best interpreted as patterns across centres rather than as a single common treatment effect.

In Wilms tumour, the most frequently studied malignancy in this review, survival improvements were consistently associated with the implementation of adapted SIOP-based protocols. These protocols emphasise preoperative chemotherapy to reduce tumour size and surgical risk, an approach particularly well suited to settings where children often present with advanced disease [12,33–35]. Studies by Chagaluka *et al* [21] and Yao *et al* [29] demonstrated significant survival gains following protocol implementation, especially among children diagnosed

at earlier stages. Similar patterns have been reported across Africa, reinforcing the suitability of SIOP-adapted protocols in resource-constrained contexts [12, 33, 34].

Burkitt lymphoma, the most common childhood cancer in sub-Saharan Africa [36, 37], was managed using a range of adapted regimens across the included studies. Earlier approaches, such as cyclophosphamide, were designed to maximise feasibility and reduce toxicity but were often associated with higher relapse rates [27, 38, 39]. More recent studies adopting intensified but still adapted regimens, including lymphomes malins B (LMB)-based protocols, have reported improved survival even among children with advanced-stage disease [24, 31]. The survival pattern for Burkitt lymphoma in this review aligns with outcomes reported from other LMICs [6, 11, 39] but remains substantially lower than survival achieved in HICs using high-intensity, risk-adapted protocols supported by robust infrastructure [4].

For Hodgkin lymphoma, both included studies used COPP/ABV hybrid regimens without radiotherapy and reported strong study-level survival [28, 32]. These findings are consistent with reports from other LMICs using similar chemotherapy-only approaches [40, 41]. Notably, survival reached 100% among children in favourable-risk groups, highlighting the curability of Hodgkin lymphoma even in the absence of radiotherapy when chemotherapy is delivered effectively, and the disease is treated early. A similar outcome was also reported by Baez *et al* [42] in Nicaragua. Nonetheless, outcomes remain inferior to those reported in HICs and in settings such as Egypt, where combined-modality therapy is more available [43–45].

The single study on retinoblastoma [26] included in this review demonstrated a strong survival advantage for children diagnosed at early stages (stages I–II). This finding reinforces the central role of early detection and timely intervention in determining outcomes for this malignancy, especially in SIOP-PODC setting 1 environments with only basic imaging, no radiotherapy, minimal pathology services, no genetic testing and no dedicated paediatric oncology ward [26, 46]. The study also highlights key barriers to early detection in Cameroon, noting late diagnosis (median age 24 months in contrast to 14.1 months in HICs) and the use of traditional/complementary medicine by more than 50% of families, which may delay diagnosis. Across LMICs, late presentation, refusal of enucleation and reliance on traditional medicine continue to contribute to poor outcomes (survival rates of 44%–57%), in contrast to HICs, where survival now exceeds 95% [47–50]. Together, these findings suggest that for Retinoblastoma in Cameroon and other LMICs, protocol adaptation is important, but survival is likely to depend just as much on awareness, timely referral, earlier entry into care and acceptance of enucleation where indicated.

The exploratory comparator-category analysis showed that stage-based comparisons consistently showed better outcomes among children presenting with earlier-stage disease than among those with advanced disease [24, 26, 29, 30], whereas implementation/time-based comparisons were smaller and much more heterogeneous. This suggests that the most consistent survival differences in the study are linked to how early children enter care, rather than to protocol adaptation alone.

A further issue highlighted by this review is the inconsistency in outcome reporting. Across studies, authors reported end-of-treatment status, event-free survival, projected survival or overall survival over different follow-up periods. These measures are related but not interchangeable, and this limits cross-study comparability. Future studies in this field would therefore be strengthened by harmonised reporting of end-of-treatment, event-free and overall survival outcomes.

Implication for policy and practice

Findings from this review suggest that survival gains in childhood cancer in Cameroon and collaborating sub-Saharan African centres are achievable when adapted treatment protocols are implemented within functional care pathways. Policy priorities should therefore extend beyond protocol modification alone to include: strengthening early diagnostic and referral systems; ensuring access to minimum supportive care packages, including essential medicines and blood products; integrating social supportive care mechanisms to reduce treatment abandonment; and harmonising national paediatric cancer treatment guidelines. Investments in these areas are likely to yield greater and more sustainable survival gains.

Limitations

This systematic review and meta-analysis has several limitations that should be considered when interpreting the findings. First, the included studies used non-randomised intervention designs, which are inherently subject to selection bias and unmeasured confounding. Although

the use of the ROBINS-I tool enabled structured assessment of study quality, residual bias related to patient selection, disease severity and care-seeking behaviour cannot be fully excluded.

Secondly, there was substantial heterogeneity across studies in terms of cancer types, treatment protocols, comparator groups, follow-up duration and the structure of their comparisons. For this reason, the study-specific ORs and comparator-category pooled estimates should be interpreted as exploratory comparative measures rather than as estimates of a single common treatment effect.

Thirdly, reported outcomes were not uniform across studies. These measures are clinically related but not interchangeable, limiting direct comparability across studies and precluding the synthesis and interpretation of a single pooled survival estimate as a unified outcome.

Fourthly, formal assessment of publication bias (e.g., funnel plot asymmetry) was not performed because the limited number of included studies would render such analyses underpowered and their interpretation unreliable. As a result, the possibility that studies with negative or inconclusive findings are underrepresented cannot be entirely excluded.

Conclusion

Adapted paediatric cancer treatment protocols used in Cameroon and collaborating sub-Saharan African centres are associated with encouraging outcomes, but the available evidence is heterogeneous and should be interpreted cautiously. The most consistent finding was the strong survival advantage associated with earlier-stage disease, underscoring the importance of early diagnosis and standardised outcome reporting in future childhood cancer strategies.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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Ethical approval

This study was a systematic review of published literature and did not involve direct contact with human participants. Ethical approval was therefore not required in accordance with the Declaration of Helsinki.

Author contributions

Study conception and design: YW and GA; data extraction and quality assessment: YW, GA, FL, AP; analysis and interpretation of data: YW, GA, FL, AP, MB; drafting of manuscript: YW, GA, FL, AP, MB; final approval of version to be published: YW, GA, FL, AP, MB.

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