Supplementary table S1: Search strategy applied per database

Database	Search String (representative)	Additional Filters Applied
PubMed / MEDLINE	("paediatric oncology" OR "pediatric oncology" OR "childhood cancer" OR "childhood malignancy") AND ("adapted" OR "graduated" OR "low-income" OR "resource-limited" OR "LMIC") AND ("guideline" OR "protocol" OR "treatment regimen") AND ("Africa" OR "sub-Saharan" OR "developing countr*" OR "SIOP PODC" OR "GFAOP")	English; French; Portuguese January 1990 – February 2026; Human; Age: birth–18 years (where filter available)
EMBASE	('pediatric oncology'/exp OR 'childhood neoplasm'/exp) AND ('treatment protocol'/exp OR 'clinical guideline'/exp OR 'adapted treatment') AND ('developing country'/exp OR 'Africa'/exp OR 'low income country'/exp)	January 1990 – February 2026; English, French and Portuguese
Cochrane Library (CENTRAL)	'Childhood cancer' AND 'low-income' AND 'treatment' AND 'Africa'	All years; all publication types
Global Index Medicus (AFRO/EMRO)	Free-text: 'paediatric oncology' AND 'Africa' AND 'protocol' OR 'guideline'	Specifically searched for African-language journals and grey literature indexed by WHO AFRO

Web of Science (WoS Core Collection)	TS=(('pediatric oncolog*' OR 'childhood cancer') AND ('adapt*' OR 'graduated') AND ('Africa' OR 'LMIC' OR 'low-income') AND (guideline OR protocol OR regimen))	January 1990 – February 2026; English, French and Portuguese
Supplementary: SIOP/GFAOP websites; Pediatr Blood Cancer archive; manual reference chaining	Manual review of all issues of Pediatric Blood & Cancer, 1993–2026, and SIOP PODC working group publication lists	Grey literature search: WHO Global Initiative for Childhood Cancer (GICC) documents; GFAOP annual reports; CureAll framework documents

Abbreviations: IT-MTX = intrathecal methotrexate; PODC = Paediatric Oncology in Developing Countries; GFAOP = Groupe Franco-Africain d'Oncologie Pédiatrique.

ODMJ

Supplementary Table S2: The AGREE II instrument of the SIOP-PODC guidelines evaluated in the manuscript.

Guideline*	Source status	Scope	Stakeholder	Rigour	Clarity	Applicability	Editorial	Overall	Recommendation
SIOP-PODC ATR Framework	Full text reviewed	83.3%	61.1%	64.6%	83.3%	91.7%	33.3%	6/7	Yes, with modifications
SIOP-PODC Wilms tumour	Full text reviewed	83.3%	61.1%	58.3%	83.3%	87.5%	16.7%	6/7	Yes, with modifications
SIOP-PODC Graduated-Intensity Retinoblastoma	Full text reviewed	83.3%	61.1%	58.3%	94.4%	91.7%	16.7%	6/7	Yes, with modifications
Management of paediatric Kaposi sarcoma in resource-limited settings	Full text reviewed	77.8%	55.6%	52.1%	77.8%	75.0%	16.7%	5/7	Yes, with modifications
SIOP-PODC Neuroblastoma	Full text reviewed	88.9%	61.1%	62.5%	94.4%	91.7%	16.7%	6/7	Yes, with modifications
SIOP-PODC Standard-Risk Medulloblastoma	Full text reviewed	83.3%	61.1%	58.3%	88.9%	87.5%	16.7%	6/7	Yes, with modifications
SIOP-PODC Low-Grade Glioma	Full text reviewed	88.9%	66.7%	68.8%	94.4%	95.8%	25.0%	6/7	Yes, with modifications
PROS-LMIC/SIOP-PODC Paediatric Radiotherapy	Full text reviewed	83.3%	61.1%	58.3%	83.3%	95.8%	16.7%	6/7	Yes, with modifications

SIOP-PODC Acute Myeloid Leukaemia	Full text reviewed	88.9%	61.1%	70.8%	88.9%	91.7%	25.0%	6/7	Yes, with modifications
SIOP-PODC Craniopharyngioma	Full text reviewed	94.4%	72.2%	72.9%	100.0%	95.8%	33.3%	7/7	Yes

*Guidelines with full descriptions and full text were evaluated.

ODMJ

Supplementary Table S3. SIOP-PODC treatment guidelines with African authors and clinically tested regimens originating in African paediatric oncology units (n = 19)

		Tumour	Protocol Type	Authors/ group	Year	Setting†	Design/ method	Key outcome/ contribution
Guidelines								
Guideline	**SIOP PODC ATR Framework**	All cancers	**ATR**	Howard, Davidson et al.	2013 / 2017	African authors	Cross-cutting framework; three-tier service-level model; expert consensus + evidence synthesis	Defined principles for context-sensitive protocol adaptation across all paediatric malignancies in LMICs; established the three service-level resource classification underpinning all subsequent PODC disease-specific guidelines
Guideline	**SIOP PODC Wilms**	Wilms tumour	**ATR**	Israëls et al.	2013 / 2015	African authors / Africa-focused	Multi-stakeholder guideline; tiered by resource level; diagnosis, preoperative chemo, nutritional and	Tiered, resource-stratified management recommendations for nephroblastoma; explicitly addressed preoperative imaging constraints and abandonment reduction — directly

Category	Protocol	Tumour	Protocol Type	Authors/ group	Year	Setting†	Design/ method	Key outcome/ contribution
Guidelines								
							social support all addressed	implemented in CWT Africa Project
Guideline	**SIOP PODC Graduated-Intensity Retinoblastoma Guidelines**	Retinoblastoma	**GTR**	Chantada, Luna-Fineman et al. (SIOP PODC)	2013	African authors	International expert committee; teleconferences via Cure4Kids; NCI levels of evidence applied; presented at SIOP Africa and Asia 2012 meetings; cooperative group input (AHOPCA, RetMex, GALOP, INCTR); explicitly modelled on Hunger–Howard ALL graduated-	First GTR framework for retinoblastoma in developing countries: three-tier, resource-stratified recommendations covering staging (IRSS; CT minimum, MRI preferred), enucleation principles (upfront for unilateral intraocular disease; pre-enucleation chemotherapy for buphthalmic eyes, family refusal, or absent pathology expertise), chemotherapy regimens by setting (Regimens 1–5: carboplatin/etoposide/vincristine for Settings 1–2; high-dose +

ODMS

Category	Protocol	Tumour	Protocol Type	Authors/ group	Year	Setting†	Design/ method	Key outcome/ contribution
Guidelines								
							intensity framework; three-tier resource classification system (Setting 1: low-income; Setting 2: lower–middle-income; Setting 3: upper–middle-income)	autologous HSCT for stage IV in Setting 3), conservative therapy (limited to Settings 2–3; EBRT available in Setting 2; cryotherapy/laser/intra-arterial chemotherapy for Setting 3), treatment abandonment management (pre-enucleation chemotherapy as bridge where refusal rate is high), and orbital/metastatic disease (aggressive carboplatin-based regimens + radiotherapy for stage III; palliative low-dose chemotherapy for stage IV in Settings 1–2). Unique inclusion of parental compliance as a primary

ODMS

Category	Protocol	Tumour	Protocol Type	Authors/ group	Year	Setting†	Design/ method	Key outcome/ contribution
Guidelines								
								clinical management variable — directly addressing the African and developing-country context in which abandonment can reach 75% of cases
Guideline	**Karposi sarcoma**	Karposi sarcoma	**GTR**	Molyneux et al.	2013	African authors	Multi-stakeholder guideline; tiered by resource level; diagnosis, preoperative chemo, nutritional and social support all addressed	Tiered, resource-stratified management recommendations for KS. Consensus was sought for the management of childhood HIV-associated KS in varied resource setting.
Guideline	**SIOP PODC Neuroblastoma**	Neuroblastoma	**GTR**	Parikh et al.	2015 / 2016	African authors	Multi-stakeholder guideline; expert consensus; risk stratification	LMIC-adapted diagnostic and treatment framework; addressed drug availability and supportive care thresholds; highlighted

ODMJ

Category	Protocol	Tumour	Protocol Type	Authors/ group	Year	Setting†	Design/ method	Key outcome/ contribution
Guidelines								
							adapted to LMIC diagnostic capacity	diagnostic infrastructure gaps in Africa
Guideline	**SIOP PODC Medulloblastoma**	Medulloblastoma	**ATR**	Parkes et al.	2014 / 2015	African authors	Multi-stakeholder guideline; expert consensus; adapted radiotherapy and chemotherapy recommendations by resource level	Adapted treatment framework for medulloblastoma in resource-constrained settings; highlighted CNS tumour diagnostic infrastructure gaps in Africa
Guideline	**SIOP PODC Low Grade Glioma (LGG)**	Low grade glioma	**ATR**	Hessissen, Parkes, Amayiri et al.	2017	African authors	Multi-disciplinary writing group (neurosurgeons, radiation and paediatric oncologists, medical physicist, neuroradiologists);	Five-tier resource-stratified management recommendations covering diagnosis (CT vs MRI thresholds by service level), surgery (resection principles by anatomical site and expertise), chemotherapy (vincristine + monthly carboplatin first-line;

ODMS

Category	Protocol	Tumour	Protocol Type	Authors/ group	Year	Setting†	Design/ method	Key outcome/ contribution
Guidelines								
							five-tier PODC service-level framework; qualitative survey of 8 referral centres in Africa, Asia and Central America informing resource constraints; ratified by SIOP board	weekly vinblastine second-line or carboplatin allergy), radiotherapy (minimum 3D-CRT requirement; 2D only as last resort), and late effects monitoring. Survey confirmed most African LGG centres lack specialised pathology, routine MRI, paediatric neurosurgeons, and MDT structures — directly shaping the tiered recommendations
Guidelines	**PROS-LMIC/SIOP PODC radiotherapy guidelines**	All cancers	**GTR**	Parkes et. Al.	2017	African authors	PROS-LMIC/SIOP PODC developed adapted RT treatment guidelines for treatment of	Recommendations for the technical delivery of radiotherapy to children in LMIC, taking regional challenges into account. A distinction based between low-

ODMS

Category	Protocol	Tumour	Protocol Type	Authors/ group	Year	Setting†	Design/ method	Key outcome/ contribution
Guidelines								
							children with cancer in LMIC based on a tiered system, with levels of service defined according to available resources in a specific unit	income countries (LIC) and middle-income countries (MIC), which are composed of lower-middle income countries (L-MIC) and upper- middle incomecountries (U-MIC) and the RT management resources available.
Guideline	**SIOP PODC AML**	AML	**ATR**	Bansal, Davidson et al.	2019 / 2020	African authors	Multi-stakeholder guideline; GRADE-informed; prephase concept; high-dose cytarabine (HDAC) consolidation; adapted for Level 2 LMIC settings per PODC framework	Stratified recommendations for AML in LMICs; prephase designed to reduce early death by partial remission induction prior to full-intensity treatment; directly implemented and evaluated in Kenya (van Weelderen et al., 2023)

ODMS

Category	Protocol	Tumour	Protocol Type	Authors/ group	Year	Setting†	Design/ method	Key outcome/ contribution
Guidelines								
Guideline	**SIOP PODC Craniopharyngioma**	Craniopharyngioma	**ATR**	Amayiri, Spitaels, Zaghloul, et al.	2020 / 2023	African authors	Multi-disciplinary group (neurosurgeons, radiation and paediatric oncologists, radiologists, paediatric endocrinologists, ophthalmologist); five-tier PODC service-level framework; WHO EML/EMLc used as minimum hormonal treatment reference; online Cure4Kids	First LMIC-adapted, risk-stratified, multidomain management framework for craniopharyngioma covering: surgery (hypothalamic-sparing maximal safe resection; keyhole approaches; intracystic interferon-alpha for predominantly cystic lesions to delay/avoid radiotherapy); radiotherapy (2D only when referral impossible; 3D-CRT minimum standard; tiered target volume and QA guidance by service level; 50–55 Gy in 1.8 Gy fractions); endocrine replacement using WHO EML medicines

ODMS

Category	Protocol	Tumour	Protocol Type	Authors/ group	Year	Setting†	Design/ method	Key outcome/ contribution
Guidelines								
							meetings; ratified by SIOP board; every decision node stratified by resource availability	(hydrocortisone, levothyroxine, DDAVP, sex steroids — with specific dosing tables); and long-term follow-up framework. Uniquely addressed panhypopituitarism, diabetes insipidus, and hypothalamic obesity as primary management challenges in LMIC where endocrinological expertise, PICU capacity, and rehabilitation services are severely limited
Tested								
Tested	**GFAOP BL Multicentre**	Burkitt lymphoma	**ATR**	GFAOP BL Committee	2001–05	Africa-specific	Prospective multicentre; modified LMB protocol (reduced	First systematically documented adapted BL protocol in Africa; established feasibility and

ODMS

Category	Protocol	Tumour	Protocol Type	Authors/ group	Year	Setting†	Design/ method	Key outcome/ contribution
Guidelines								
							cyclophosphamide, adjusted IT prophylaxis); francophone Africa	baseline survival data informing GFALMB protocol refinement
Tested	**GFAOP GFALMB**	Burkitt lymphoma	**ATR**	GFAOP	2006–15	Africa-specific	Prospective multicentre; iterative refinement of BL protocol incorporating HD-MTX (3000 mg/m²) based on toxicity data from prior GFAOP BL study	Improved EFS over prior GFAOP BL regimen; 1-yr OS improved from 33% to 60% across successive protocol iterations; exemplar of iterative toxicity-driven African protocol adaptation
Tested	**GFAOP HL**	Hodgkin lymphoma	**ATR**	GFAOP	2006-12	Africa-specific	Prospective multicentre feasibility study in 5 countries (n=106).	OS 82%, EFS 67% at median 30 months follow-up; chemotherapy-only strategy feasible in radiotherapy-absent

ODMS

Category	Protocol	Tumour	Protocol Type	Authors/ group	Year	Setting†	Design/ method	Key outcome/ contribution
Guidelines								
							Paediatric HL treated with only COPP/ABV hybrid chemotherapy (cyclophosphamide, vincristine, procarbazine, prednisone, adriamycin, bleomycin and vinblastine) where radiotherapy is unavailable.	settings; 85.8% patients unfavourable prognosis (G2 - stages IIB, III or IV, MTI ≥0.45, lymphadenopathy ≥6 cm or presence of visceral involvement.); predominant histology nodular sclerosis (36%); haematologic toxicity main adverse effect; supportive care limitations identified as key barrier to improved outcomes
Tested	**GFAOP-NEPHRO-02**	Wilms tumour	**ATR**	GFAOP	2010	Africa-specific	Prospective multicentre; modified SIOP nephroblastoma	Demonstrated acceptable survival with adapted preoperative chemotherapy approach in

ODMS

Category	Protocol	Tumour	Protocol Type	Authors/ group	Year	Setting†	Design/ method	Key outcome/ contribution
Guidelines								
							backbone; preoperative chemotherapy adapted to surgical and imaging constraints of francophone African referral centres	settings without routine upfront histology or CT imaging
Tested	**CWT Africa Project**	Wilms tumour	**GTR**	Paintsil, Israels et al.	2014–20	Africa-specific	Prospective multicentre clinical trial (NCT01991652); 8 centres, 5 countries (Ghana, Malawi, Cameroon, Uganda, Ethiopia); SIOP PODC adapted WT	End-of-treatment survival 52% vs. 68% (p=0.01) and abandonment 23% vs. 13% (p=0.03) in first 2 years; 2-yr EFS 49.9% confirmed in 2020 publication; most extensively evaluated Africa-specific adapted guideline to date

ODMP

Category	Protocol	Tumour	Protocol Type	Authors/ group	Year	Setting†	Design/ method	Key outcome/ contribution
Guidelines								
							guideline with preoperative chemo, nutritional + social support; common outcome monitoring infrastructure	
Tested	**Malawi Lymphoma Programme**	Burkitt and Hodgkin lymphoma	**ATR**	UNC–Malawi	2018–21	Africa-specific	Prospective consecutive cohort; adapted BL and HL regimens; systematic abandonment-rate and treatment-completion tracking as primary outcome measures alongside survival	Demonstrated that treatment abandonment tracking is as critical as survival data in evaluating LMIC protocol success; low abandonment rates attributed to social support and transport coverage

ODMS

Category	Protocol	Tumour	Protocol Type	Authors/ group	Year	Setting†	Design/ method	Key outcome/ contribution
Guidelines								
Tested	**BCCOE Hunger Protocol — Arm 1**	ALL	**GTR**	Rubagumya, Xu et al.	2012–15	Africa-specific	Retrospective cohort (n=42); Hunger GTR Arm 1 (low-intensity, anthracycline-free); non-oncologist delivery with remote Dana-Farber support; rural Rwanda (BCCOE); first published Hunger protocol outcomes in sub-Saharan Africa	2-yr EFS 22–26%; TRM 3% (below 4% Hunger advancement threshold); 83% disease-related mortality confirmed insufficient intensity; Rwanda MoH approved advancement to Arm 2 based on documented acceptable toxicity
Tested	**BCCOE Hunger Protocol — Arm 1 to 2 Transition**	ALL	**GTR**	Manirakiza, Dugan et al.	2012–17	Africa-specific	Retrospective + prospective cohort; sequential	Arm 2 (n=17): TRM 0%, 65% in remission at end of delayed intensification; confirmed

ODMS

Category	Protocol	Tumour	Protocol Type	Authors/ group	Year	Setting†	Design/ method	Key outcome/ contribution
Guidelines								
							graduated-intensity escalation (Arm 1 → Arm 2 + delayed intensification with doxorubicin, cyclophosphamide, cytarabine); task-shifted model; rural Rwanda	feasibility of rapid-cycle graduated intensification in a rural LIC; groundwork laid for Arms 3–4 for high-risk patients
Tested	**SIOP PODC AML Guidelines Implementation — Kenya ††**	AML	**ATR**	van Weelderen, Wijnen, Njuguna et al.	2010–21	Africa-specific	Retrospective before–after cohort (n=122); Pre-implementation period (2010–2019): pre-guideline (doxorubicin + cytarabine	Abandonment 19% vs. 3% (Period 1 vs 2); 2-yr pEFS 5% vs. 15% (p=.53); 2-yr pOS 8% vs. 16% (p=.93) — trends not statistically significant; TRM remained high (36% vs. 47%); early death 46% in both periods predominantly from sepsis;

ODMS

Category	Protocol	Tumour	Protocol Type	Authors/ group	Year	Setting†	Design/ method	Key outcome/ contribution
Guidelines								
							induction, etoposide consolidation); Post-implementation period (2019–2021): SIOP PODC AML guideline (IV etoposide prephase, intensified induction I, HDAC consolidation); Moi Teaching and Referral Hospital, Eldoret, Kenya; Level 2 PODC setting	relapse rate 57% vs. 17%; guideline implementation feasible but survival remains dismal; inadequate infection control and supportive care identified as primary modifiable barrier
Tested	**SACCSG HL-2018**	Hodgkin lymphoma	**ATR**	Geel et al. (SACCSG)	2016–22	Africa-specific	Prospective multicentre (17	2-yr OS 92.6% vs. historical 84% (p=.004); HIV+ 2-yr OS 89% vs.

ODMP

Category	Protocol	Tumour	Protocol Type	Authors/ group	Year	Setting†	Design/ method	Key outcome/ contribution
Guidelines								
							units, n=132); risk-stratified, response-adapted ATR; ABVD ± COPDac by risk tier; HIV-specific protocol modifications; consolidation radiotherapy for SER/bulky disease; South Africa	historical 46%; risk stratification correlated with prognosis; improvement primarily attributed to standardised supportive care and protocol harmonisation across 17 centres
Tested	**SIOP PODC Retinoblastoma Guidelines**	Retinoblastoma	**ATR**	Kruger et al.	2016–22	Africa-specific	Prospective multicentre (2 units, n=82); stage-based, proof of feasibility ATR; Laser and cryotherapy;	2-yr OS 50.0% total cohort, but 68.8% for limited disease. Causes of death included disease progression/ relapses (60.5%), neutropenic sepsis (15.9%), unknown causes

ODMS

Category	Protocol	Tumour	Protocol Type	Authors/ group	Year	Setting†	Design/ method	Key outcome/ contribution
Guidelines								
							Preoperative chemotherapy (IV vincristine, carboplatin, adriamycin) followed by enucleation and postoperative chemotherapy (total of six cycles) based on stage; Cameroon	(18.4%), unrelated infection (2.6%), and death post-surgery (2.6%). Stage was the most significant, guidelines demonstrated efficacy and feasibility

Abbreviations: ALL = acute lymphoblastic leukaemia; AML = acute myeloid leukaemia; ATR = adapted treatment regimen; BCCOE = Butaro Cancer Center of Excellence; BL = Burkitt lymphoma; CWT = Collaborative Wilms Tumour; EFS = event-free survival; GFAOP = Groupe Franco-Africain d'Oncologie Pédiatrique; GTR = graduated treatment regimen; HL = Hodgkin lymphoma; IT = intrathecal; KS = Kaposi sarcoma; LMIC = low- and middle-income country; MoH = Ministry of Health; OS = overall survival; PODC = Paediatric Oncology in Developing Countries; PROS = Pediatric Radiation Oncology Society; RT = radiotherapy; SACCSG = South African Children's Cancer Study Group; SIOP = International Society of Paediatric Oncology; TRM = treatment-related mortality.

ODMS

Protocol Type: ATR = adapted treatment regimen (single protocol modified for a specific resource-constrained setting); GTR = graduated treatment regimen (prospectively tiered framework with sequential intensity escalation based on documented toxicity thresholds); FRAMEWORK = cross-cutting conceptual or governance document applicable across disease types.

† Africa-specific = protocol developed and tested exclusively within African clinical settings. African authors = protocol developed through international collaboration with substantive African co-authorship.

†† The Kenya AML study (van Weelderen et al., 2023) represents the only published before–after evaluation of a SIOP PODC guideline implementation in sub-Saharan Africa

ODMJ