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Health system determinants of access to essential medicines for children with cancer in Ghana

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ABSTRACT

Background Evidence of the context-specific challenges related to childhood cancer drug (CCD) access is vital to improving outcomes for children with cancer in low- and middle-income countries, such as Ghana. We sought to determine the availability and cost of essential CCD in Ghana and identify the underlying determinants of access.

Methods Our study integrated quantitative data on drug prices and availability with qualitative insights into health system and sociopolitical determinants of CCD access in Ghana. We analysed retrospective monthly price and stock data for 41 cancer and supportive care drugs on the WHO Essential Medicines List (EML) from private retail and public institutional pharmacies. Non-parametric analyses evaluated relationships between drug price and availability, and impacts of drug class and formulation on availability and procurement efficiency. We assessed the determinants of drug access through thematic analysis of policy documents and semi-structured interviews (n=21) with key health system stakeholders.

Results Ghana lists only 47% of essential CCD on its National EML, revealing gaps in domestic formulary inclusion. Stock-outs occurred for 88% of essential CCD, with a 70-day median stock-out duration; 32% had median price ratios above internationally-accepted efficiency thresholds. Drugs procured inefficiently were more susceptible to stock-outs (p=0.0003). Principal determinants of drug access included: (1) lack of sociopolitical priority afforded childhood cancer and (2) the impact of policy and regulatory environments on drug affordability, availability and quality. Establishment of a population-based cancer registry, a nationally-coordinated procurement strategy for CCD, public financing for childhood cancer care and policies to control drug costs emerged as priority interventions to improve drug access in Ghana.

Conclusion Our study provides context-specific evidence to enable responsive policy development for efficient drug procurement and supply management in Ghana and establishes a rigorous approach to the analysis of childhood cancer drug access in similar health system settings.

Key questions

What is already known?

- The effective care of children with cancer requires equitable access to quality chemotherapeutic and supportive care medicines.
- Little rigorous data exists on the availability of, and determinants of access to, essential medicines to treat childhood cancer in low- and middle-income countries (LMICs), including Ghana.

What are the new findings?

- Access to essential medicines for children with cancer in Ghana is determined by the political and societal priority afforded childhood cancer.
- Policy legacies fostered by sustained system focus on communicable disease control and primary care strengthening have engendered neglect in the realm of non-communicabledisease drug policy, including childhood cancer.
- Weak drug price controls, inefficient procurement models and lack of financial coverage of childhood cancer have significant impacts on the availability of, and access to, childhood cancer medicines in Ghana.

What do the new findings imply?

- Efforts to improve access to essential medicines for children with cancer in LMICs, including Ghana, hinge on a nuanced understanding of system-level impediments to access.
- Our study highlights the impacts of existing policy, regulatory and health service delivery approaches on childhood cancer drug availability, affordability and quality in Ghana, emphasising the role of inherited political priorities and system siloes in perpetuating access barriers.

INTRODUCTION

The mounting threat that non-communicable diseases (NCDs) pose to health outcomes in low- and middle-income countries (LMICs) has galvanised global efforts to thwart premature mortality from NCDs, including cancer.[1] Of the estimated 397 000 children with cancer worldwide,[2] 80% of cases reside in LMICs, with an expected 30% increase in diagnosed cases of childhood cancer by 2020.[3] While 80% of children in high-income countries are cured, only 10% to 50% of children survive cancer in

LMICs due to health system and resource constraints.[3 4] The WHO Global Initiative for Childhood Cancer aims to achieve a global survival rate of 60% by 2030.[5] Bridging the survival gap will require addressing system-level challenges through the development and implementation of evidence-based national childhood cancer strategies.[6]

The effective care of children with cancer necessitates equitable access to quality chemotherapeutic and supportive care medicines.[7 8] Elucidating context-specific determinants of drug access can inform national and institutional planning and facilitate childhood cancer drug (CCD) procurement.[9] Such evidence can also empower stakeholders to address systemic issues including limited formularies, unsuitable product formulations and erratic drug prices.[10 11]

In Ghana, limited access to essential medicines compromises treatment across a range of health conditions, including cancer.[4 9 12 13] A recent assessment by the Ghana National Drugs Programme reported poor availability of palliative and anti-cancer drugs at Korle-Bu Teaching Hospital (KBTH) and Komfo-Anokye Teaching Hospital (KATH)—Ghana's principal cancer treatment facilities, and only centres for paediatric oncology care.[14] However, little rigorous data exists on the availability of, and determinants of access to, essential medicines to treat childhood cancer in Ghana. We sought to generate policy-relevant evidence on the state of and challenges related to access to essential CCD in Ghana.

METHODS

Study design

Our study mapped and analysed the determinants of CCD access in Ghana through in-depth, mixed-methods analysis of: (1) the availability and cost of essential CCD; and (2) the health system and socio-political determinants of drug access for children with cancer. We employed a convergent parallel mixed-methods case study design.[15] The quantitative and qualitative strands of inquiry were analysed separately. Integration of the strands occurred at the level of interpretation and reporting through a contiguous narrative approach.[16] The qualitative findings helped explain and contextualise the quantitative results to expand our understanding of drug access in Ghana.

Patient and public involvement

Patients and members of the public were not involved in the design, conduct, reporting or dissemination of this research as it focussed on the perspectives of health system decision-makers and care providers, and the collection of institutional data on drug availability.

Data collection

We assessed alignment of the 2017 version of the Ghanaian National Essential Medicines List (NEML) with the WHO Essential Medicines List for Children (EMLc) to gauge priority-setting for childhood cancer drugs at a national level.[17] Quantitative data consisted of monthly patient price and stock-out data for 41 essential cancer and supportive care drugs. Data on oncology drugs derived from Rock Chemist, a private retail pharmacy that supplies the vast majority of CCD to KBTH and KATH; data on supportive care drugs were obtained from the Child Health Unit (CHU) at KBTH. We defined stock-out a priori as the lack of medicine availability at the point of patient care. Our sources of drug data were selected to balance data completeness and relevance to real-world availability to patients: Rock Chemist for cytotoxics (direct to KBTH patients and direct to KATH paediatric oncology pharmacy) and KBTH CHU pharmacy for supportive care agents. Drug stock and price data were retrospectively collected for the period of 1st January 2018 to 31st March 2019. Different formulations of the same drug were assessed independently. Qualitative data consisted of in-person, semi-structured interviews with a stratified purposive sample of health system stakeholders, to generate a context-specific understanding of the Ghanaian health system and pharmaceutical value chain for CCD. Key informants were identified through purposive and snowball sampling techniques, including review of relevant policy and academic literature, scans of institutional websites and policy documents and recommendation by participants. Of those invited to participate in qualitative interviews, none declined, terminated the interview early or withdrew their data following interview completion. Twenty-one key stakeholders were interviewed between 1st October 2018 and 5th December 2018, representing policymakers and civil servants (n=8), health professionals (n=9), private pharmaceutical representatives (n=2) and members from civil society organisations (n=2). Our sample size was determined by the identification of thematic saturation through constant comparison with emergent themes. The interviews, ranging from 35 to 90 min, were conducted in English.

We also reviewed relevant policies to confirm, explain and expand findings from interviews. These included: Standard Treatment Guidelines 2017, Ghana's National Medicines Policy (2017), Essential Medicines List (2017), 2018 New Operational Prices of Medicines on the National Health Insurance Scheme (NHIS) List (2018), National Strategy for Cancer Control in Ghana 2012 to 2016 (2011) and Guidelines for the Registration of Medicinal Products Classified for Fast-track Processing (2015). Qualitative insights deriving from policy documents in the results are referenced.

We employed the Pediatric Oncology System Integration Tool (POSIT)[18] and the Management Sciences for Health's (MSH) Managing Drug Supply (MDS-3)[19] framework as heuristics for the development of the interview guide. POSIT is an expert-informed framework that identifies key health system components impacting the delivery of childhood

cancer care in LMICs. MDS-3 is a pharmaceutical management framework that facilitates insights on determinants of access to medicines through comprehensive analysis of the pharmaceutical value chain. We drew on both frameworks to develop a conceptually-integrated interview guide structured around three key areas: (1) policy and economic issues; (2) pharmaceutical management; and (3) management support systems (online supplemental appendix).

Data analysis

We undertook quantitative analysis of the selection, availability and price of essential CCD in Ghana. Descriptive statistics were employed to analyse mean and median stock-out durations. We analysed temporal variance in drug availability over the period of interest by quantifying the number of stock-out days for each drug and the total number of drugs unavailable per month. To gauge the efficiency of essential drug procurement, we calculated the median price ratio (MPR) of cytotoxic and supportive medicines using international median supplier prices from the 2015 MSH International Medical Products Price Guide.[20] Where supplier prices were not available, we used available buyer prices. Based on established WHO norms, we designated an MPR ≤1.5 as efficient public sector procurement, and an MPR ≤2.5 as efficient private sector procurement.[21] We employed Spearman's rank correlation coefficient to evaluate the relationships between drug price, procurement efficiency and availability; and used Wilcoxon rank sum tests to analyse the impact of drug class and formulation on availability and procurement efficiency.

Qualitative interviews were audio-recorded with written consent and transcribed verbatim. Data analysis was guided by the Braun and Clarke[22] thematic analysis framework and conducted using NVivo 11 software. To enhance coding reliability, two members of the research team (RB and KP) independently coded an initial sample of interviews, compared codes and established a consensus coding structure with input from AD. Codes were both deductively derived based on the conceptual domains of the interview guide and inductively generated from interview transcripts. Codes were analysed to draw out themes that were subsequently reviewed and refined to generate integrated insights into the determinants of CCD access in Ghana.

RESULTS

Alignment, availability and cost of childhood cancer drugs

NEML alignment

Ghana's NEML sets a normative bar for medicines deemed to satisfy the priority healthcare needs of the population, and influences both public and private drug procurement in the country. Only drugs listed on the NEML are considered for public coverage under the NHIS; listing does not guarantee coverage or availability. The NHIS enables financial access to healthcare by covering the cost of drugs and health services for Ghanaians whose disease conditions are included in its benefits package. Nine of 19 cytotoxic drugs (47%) and 36 of 50 supportive care drugs (72%) on the WHO EMLc are listed on NEML, equating to 65% aggregate alignment. EML alignment and NHIS coverage are displayed in table 1.

Drug availability

Figure 1 represents the number of drugs out of stock per month and figure 2 illustrates the number stock-out days per drug. The first quarter of 2018 had the highest number of unavailable drugs. Over a 15-month period, the average and median duration of stock-out days were 101.5 and 70 days, respectively (range=0 to 455). Cytotoxic medicines were out of stock for a median duration of 72.5 days (range=14 to 311), and supportive care medicines for a median duration of 31 days (range=0 to 455). Stock-out days were significantly higher for injectable cytotoxic drugs (median=75; range=31 to 311) than oral cytotoxics (median=14; range=14 to 81) (p=0.044, 95% CI (2 to 112)). Our data also indicate a significant positive correlation between cytotoxic drug price and number of stock-out days (r_s=0.5, p=0.009, 95% CI (0.18 to 0.82)).

Drug procurement efficiency, availability and costs

Forty-five relevant cytotoxic and supportive care drugs are listed on both the EMLc and NEML; we were able to obtain availability and price data for 41 formulations (30 distinct agents). Twenty-six different generic formulations of 21 CCD were accessible to KATH and KBTH. Seven out of 26 cytotoxic medicines (26.9%) had MPR >2.5. The median and mean MPR for cytotoxic drugs were 1.89 and 2.69, respectively (range=0.35 to 9.1). Of a sample of 15 supportive care drugs, 12 had sufficient information to yield an MPR. Four supportive care medicines had MPR >1.5. The median and mean MPR for supportive care medicines were 1.42 and 3.62, respectively (range=0.07 to 19.71). Overall, 11 of 38 drugs (29.0%) were subject to inefficient procurement (table 2).

Our data evince a significant positive correlation between cytotoxic drug price and MPR (r_s=0.56, p=0.004, 95% CI (0.24 to 0.88)). Moreover, our analysis demonstrates a positive relationship between MPR and number of stock-out days (r_s=0.56, p=0.0003, 95% CI (0.33 to 0.91)). There was no significant difference in stock-out days between cytotoxic drugs (median=72.5) and supportive care drugs (median=31) (p=0.25; 95% CI (−25 to 67)), suggesting that drugs procured inefficiently experienced more prolonged unavailability, regardless of class. While there was no significant difference in procurement efficiency among cytotoxic drug formulations (injections and tablets), there was a significant difference in MPR between cytotoxic drugs (median=1.89) and supportive care drugs (median=1.42) (p<0.0001, 95% CI (1.4 to 2.29)).

Price fluctuation

No notable drug price fluctuations were experienced over the 15-month period. Overall, the price of two cytotoxic and one supportive care drug varied between January 2018 and March 2019: the prices of doxorubicin

Table 1 Alignment of WHO EMLc, Ghana NEML and NHIS

Cytotoxic and supportive care medicines	WHO EMLc 2017	NEML 2017	NHIS
Asparaginase	X		
Bleomycin	X		
Carboplatin	X	X	NR
Cisplatin	X	X	NR
Cyclophosphamide	X	X	Injection 200 mg: NR Injection 500 mg: R Tablet 50 mg: NR
Cytarabine	X		
Dacarbazine	X		
Dactinomycin	X		
Daunorubicin	X		
Docetaxel			
Doxorubicin	X	X	NR
Etoposide	X	X	NR
Hydroxycarbamide (hydroxyurea)	X	X	NR
Ifosfamide	X		
Imatinib			
Irinotecan			
Mercaptopurine	X		
Methotrexate	X	X	R
Paclitaxel	X		
Tioguanine	X		
Vinblastine	X	X	NR
Vincristine	X	X	NR
Acyclovir		X	R
Allopurinol	X	X	R
Amikacin	X		
Amitriptyline	X	X	R
Amoxicillin	X	X	R
Amoxicillin + clavulanic acid	X	X	R
Amphotericin B	X		
Ampicillin	X	X	R
Aprepitant			
Azithromycin	X	X	R
Benzathine benzylpenicillin	X	X	NR
Benzylpenicillin	X	X	R
Calcium folinate	X		
Cefalexin	X		
Cefazolin	X		
Cefotaxime	X	X	R
Ceftazidime	X		
Ceftriaxone	X	X	R
Chloramphenicol	X	X	R
Ciprofloxacin	X	X	R
Clindamycin	X	X	R
Cloxacillin	X	X	R
Dexamethasone	X	X	R

Continued

Table 1 Continued

Cytotoxic and supportive care medicines	WHO EMLc 2017	NEML 2017	NHIS
Diazepam	X	X	R
Dimenhydrinate (Gravol)			
Docusate sodium	X		
Domperidone		X	R
Doxycycline	X	X	R
Erythromycin	X	X	R
Filgrastim (granulocyte colony-stimulating factor)	X		
Fluconazole	X	X	R
Fluoxetine	X	X	R
Gabapentin		X	R
Gentamicin	X	X	R
Granisetron		X	R
Ibuprofen	X	X	R
Imipenem + cilastatin	X		
Lactulose	X	X	R
Meropenem	X		
Mesna	X		
Metoclopramide	X	X	R
Metronidazole	X	X	R
Midazolam	X	X	R
Morphine	X	X	R
Nitrofurantoin	X	X	R
Olanzapine		X	R
Ondansetron	X	X	R
Paracetamol	X	X	R
Phenobarbitone/phenobarbital	X	X	R
Phenoxymethylpenicillin	X	X	R
Phenytoin	X	X	R
Prednisolone	X	X	R
Procaine benzylpenicillin	X	X	
Senna	X	X	NR
Sulfamethoxazole + trimethoprim (co-trimoxazole)	X		
Trimethoprim	X		
Vancomycin	X	X	R

R: Drugs covered by NHIS and reimbursed by National Health Insurance Authority.
NR: Drugs not covered by NHIS.
EMLc, Essential Medicines List for Children; NEML, National Essential Medicines List; NHIS, National Health Insurance Scheme.

and cyclophosphamide tablets demonstrated one-time increases by 10 cedis (Ghanaian cedi) (14%) and 0.5 cedis (20%), respectively. To deplete stocks due to imminent expiry, the price of ceftriaxone (2 g) was reduced once from 75 to 60 cedis (20%).

Determinants of childhood cancer drug access

Despite governmental acknowledgement of childhood cancer on national policy agendas, as exemplified in Ghana's *National Strategy for Cancer Care 2012–2016*,[23] multiple systemic barriers at the national and institutional levels impede access to CCD. Two dominant themes emerged: (1) lack of political and societal priority for childhood cancer, due to competing health system priorities coupled with limited scientific and lay knowledge of the problem; and (2) the influence of existing policy and regulatory milieu on CCD affordability, availability and quality. Together, these themes reveal the role of policy legacies and the interplay of political, economic and societal factors shaping CCD access.

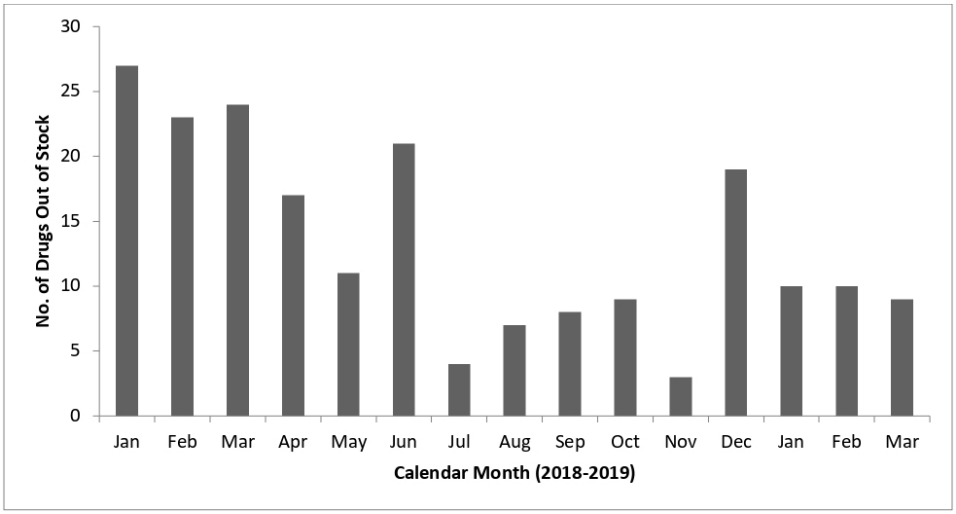

Figure 1 Annual trend of stock outs from January 2018 to March 2019.

Political and societal priority for childhood cancer

The political priority afforded to childhood cancer in policy development at the national and institutional levels emerged as a critical determinant of CCD access in Ghana. A majority of participants at all levels of the health system maintained that the absence of a dedicated, consistent focus on childhood cancer as a public health issue has hindered the establishment of national systems for data capture in order to forecast need, impact policy and galvanise momentum for increased health awareness among the public and health providers. Systemic challenges to improved access to CCD included: (1) competing allocative priorities for the health system; (2) inadequate public and health provider awareness of childhood cancer; and (3) weak data systems, resulting in a paucity of evidence for policymaking on childhood cancer.

Competing health priorities

Participants highlighted a range of considerations instrumental to the political prioritisation of health issues in Ghana, including disease burden, cost-effectiveness, return on investment, availability of international donor funds and degree of public awareness. Many noted that both limited data and policymakers' perceptions of these criteria in relation to childhood cancer have constrained its inclusion on national health policy agendas:

> They [government] don't think the survival is good enough for them to invest in the management of childhood cancer. They think it is awfully expensive. So, there is no point in putting money into something with abysmal outcomes. (Healthcare provider)

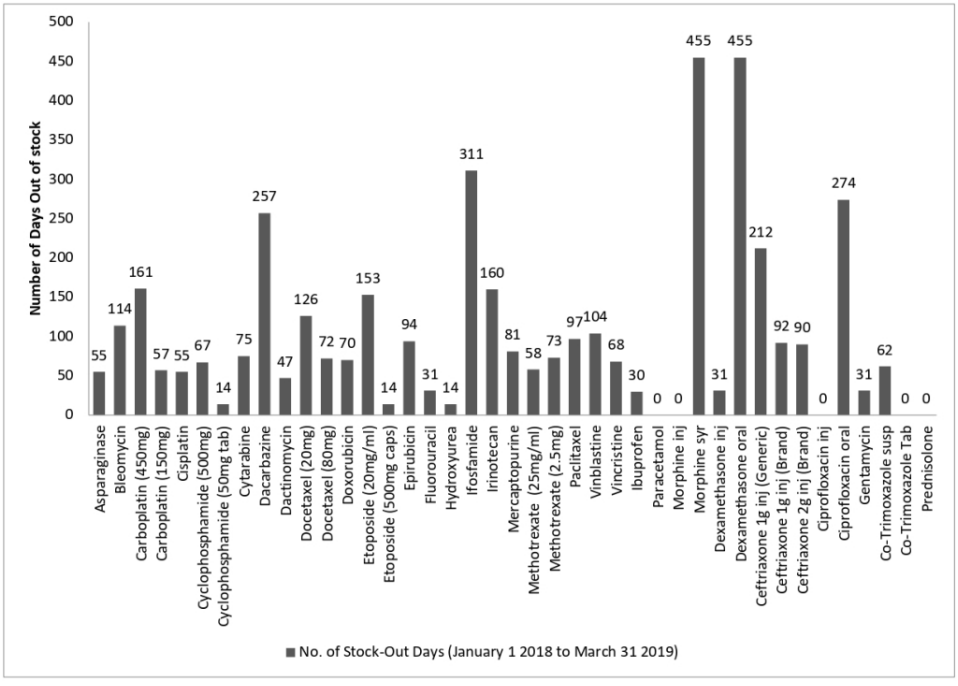

Figure 2 Duration of stock outs per drug from 1st January 2018 and 31st March 2019.

Table 2 Comparisons of wholesale supplier prices with MSH median supplier prices

Cytotoxic and supportive care medicines	Quantity	Method of administration	Purchasing unit	Generic/brand	Wholesale supplier price (GHS)	Wholesale supplier price (US$)*	MSH median supplier price (US$)	Median price ratio
Asparaginase	10 000 IU/ml	Injection	Single dose vial	Generic	350.00	68.63	52.88‡	1.30
Bleomycin	15 IU	Injection	Vial	Generic	150.00	29.41	12.15	2.42
Carboplatin	450 mg	Injection	Vial	Generic	350.00	68.63	34.33	2.00
	150 mg	Injection	Vial	Generic	140.00	27.45	14.89	1.84
Cisplatin	1 mg/mL	Injection	Vial	Generic	1.00	0.20	0.11	1.74
Cyclophosphamide	500 mg	Injection	Vial	Generic	15.00	2.94	8.16	0.36
	50 mg	Oral	Five blisters of 10 tablets	Generic	3.00	0.59	0.30‡	1.94
Cytarabine	100 mg	Injection	Vial	Generic	30.00	5.88	3.11	1.89
Dacarbazine	200 mg	Injection	Vial	Generic	90.00	17.65	6.81‡	2.59
Dactinomycin	500mcg	Injection	Vial	Generic	60.00	11.76	8.70‡	1.35
Docetaxel	20 mg	Injection	Vial	Generic	240.00	47.06	5.17	9.10
	80 mg	Injection	Vial	Generic	780.00	152.94	17.51	8.73
Doxorubicin	50 mg	Injection	Vial	Generic	70.00	13.73	7.26	1.89
Epirubicin	50 mg	Injection	Vial	Generic	250.00	49.02	21.68‡	2.26
Etoposide	20 mg/mL	Injection	Vial	Generic	6.00	1.18	0.39	3.04
	500 mg	Oral		Generic	30.00	5.88	N/A†	--
Fluorouracil	50 mg/mL	Injection	Ampoule	Generic	1.50	0.29	0.20	1.44
Hydroxyurea	500 mg	Oral	Capsules	Generic	2.00	0.39	0.22‡	1.80
Ifosfamide	1g	Injection	Vial	Generic	90.00	17.65	10.78	1.64
Irinotecan	20 mg/mL	Injection	Vial	Generic	180.00	35.29	5.78‡	6.11
Mercaptopurine	50 mg	Oral	Tab	Generic	4.00	0.78	2.24‡	0.35
Methotrexate	25 mg/mL	Injection	Vial	Generic	15.00	2.94	2.63	1.12
	2.5 mg	Oral	Tab	Generic	1.50	0.29	0.16	1.87
Paclitaxel	100 mg/mL	Injection	Vial	Generic	210.00	41.18	11.08‡	3.71
Vinblastine	10 mg/mL	Injection	Vial	Generic	75.00	14.71	2.55	5.76
Vincristine	1 mg	Injection	Vial	Generic	15.00	2.94	3.25	0.90
Ibuprofen	100 mg/5 mL	Oral	60 mL suspension	Generic	0.06	0.01	0.01	2.18
Paracetamol	120 mg/5 mL	Oral	100 mL syrup	Generic	0.03	0.01	0.01	1.13

Continued

Table 2 Continued

Cytotoxic and supportive care medicines	Quantity	Method of administration	Purchasing unit	Generic/brand	Wholesale supplier price (GHS)	Wholesale supplier price (US$)*	MSH median supplier price (US$)	Median price ratio
Morphine	10 mg/mL	Injection	Ampoule	Generic	0.18	0.04	0.53	0.07
	10 mg/5 mL	Oral	200 mL syrup	Generic	N/A‡	--	N/A†	--
Dexamethasone	4 mg/mL	Injection	2 mL	Generic	0.40	0.08	0.10	0.79
	0.5 mg	Oral	N/A†	Generic	N/A‡	--	0.01	--
Ceftriaxone	1g	Injection	N/A†	Generic	4.50	0.88	0.40	2.22
	1g	Injection	N/A†	Brand	40.00	7.84	0.40	19.71
	2g	Injection	N/A†	Brand	60.00	11.76	N/A‡	--
Ciprofloxacin	2 mg/mL	Injection	100 mL	Generic	0.03	0.00	0.01	0.49
	250 mg/5 mL	Oral	100 mL suspension	Generic	7.80	1.53	0.13‡	11.93
Gentamicin	40 mg/mL	Injection	2 mL	Generic	0.20	0.04	0.06	0.64
Co-trimoxazole	240 mg/5 mL	Oral	100 mL suspension	Generic	0.04	0.01	0.01	1.43
	480 mg	Oral	Tab	Generic	0.09	0.02	0.01	1.47
Prednisolone	5 mg	Oral	Tab	Generic	0.08	0.02	0.01	1.41

*Exchange rate as at 27 March 2019 was 5.1 Ghanaian cedi to 1 US dollars.
†Information unavailable.
‡MSH buyer price used as MSH supplier price unavailable.
GHS, Ghanaian cedi; MSH, Management Sciences for Health; US$, US dollar.

Despite the upward trend in the incidence of NCDs in Ghana, several participants affirmed that Ghana's health system priorities are largely focussed on and designed for communicable disease control, health promotion and primary care strengthening.[24] The policy legacies produced by this health system milieu were seen to constrain opportunities for policy agenda-setting and development of health services geared toward the management of chronic diseases.

Inadequate awareness

Although cancer control policy focusses largely on awareness generation, participants described childhood cancer knowledge gaps among the public and health providers as a significant barrier to generating policy attention for improved drug access. Both health providers and civil servants drew attention to an ongoing need to broaden public and provider knowledge to encourage early hospital presentation and minimise misdiagnosis:

> People may not know that this is cancer and they may treat for something else for some months even in a health facility before they come to the realisation that this is cancer and then they eventually come to us. So that is where awareness plays an important role even among health workers. (Healthcare provider)

As CCD are mostly accessed through KATH and KBTH, greater awareness could impact referral systems and thus warrant improved mechanisms to forecast and attend to prospective increases in drug need. One civil servant remarked that the efficiency of the referral system is another major determinant of timely CCD access, necessitating greater modes of communication across health institutions.

Weak data systems

The routine absence of data on childhood cancer from national reporting and health information systems was viewed by many participants as both a cause and a consequence of anaemic political priority. Participants cast the lack of rigorous, publicly collected childhood cancer incidence and outcomes data as a foundational constraint to drug access and evidence-informed policymaking. Such data was viewed as essential for determining burden of disease, quantifying CCD need, furnishing justification for NEML inclusion and incentivising both national and private procurement. To improve data collection on incidence, KATH and KBTH maintain hospital-based registries specific to childhood cancer through the support of a civil society organisation. Participants noted, however, that these efforts exist at the margins of health system priorities and stressed that the lack of nationally coordinated childhood cancer data impedes the establishment of effective interventions to improve drug access.

Influence of policy environments on cancer drug affordability, availability and quality

The influence of policies governing drug regulation and financing in Ghana emerged as principal determinant of CCD access. Inadequate policy and regulatory guidance has abetted persistent problems with CCD affordability, availability and quality.

Affordability

Many participants emphasised the cost of drugs as a demand-side factor impeding access to CCD. Children with cancer do not benefit from treatment coverage under the NHIS. Evidence also supports claims that paediatric formulations are typically more expensive than adult formulations.[24] Drug purchases therefore constitute a substantial out of pocket (OOP) expense that most families cannot afford. Patients rely heavily on financial support from donors to provide CCD access. The paediatric oncology unit at KATH uses donor funds to stock vincristine, cyclophosphamide, methotrexate, cytarabine and doxorubicin, which are provided to patients free of charge. While KBTH does not stock CCD, donor funds are provided to caregivers to purchase medicines at local retail pharmacies.

Compounding these demand-side constraints, a number of supply-side determinants of affordability emerged. Participants related high drug costs to both the presence and absence of regulations, including high import duties and taxes, drug registration-related costs, minimal drug pricing controls and limited financing options. The persistent high costs associated with the importation of cytotoxic and supportive care agents were frequently ascribed to prevailing taxation policies, compounded by unfavourable exchange rates. Duties and tariffs routinely constitute 30% to 40% of the final price of imported medicines.[25] In recognition of this burden, a participant affirmed that parliament approved a value added tax (VAT) exemption on imported drugs in November 2017, and reduced benchmark NHIS prices accordingly, with the expectation of a 30% retail drug price reduction. However, participants uniformly affirmed a lack of consequent price reductions at the retail level. For drugs to qualify for public reimbursement, retail prices offered by NHIS-credentialed pharmacies must reflect NHIS operational prices. As a consequence of this policy change, NHIS operational prices were abruptly incommensurate with the prices charged by retail outlets. Consequently, a range of drugs lost NHIS coverage, conferring additional OOP expenses on patients. The unanticipated maintenance of prices in the face of VAT exemption has thus had perverse ramifications for drug affordability. Participants expressed hope that if these unanticipated downstream policy effects are addressed, the VAT exemption policy has the potential to improve affordability of medicines.

Lack of price control measures in the pharmaceutical market were also cited as a key cost driver. Medicine prices in Ghana are among the highest in Africa: an estimated 50% to 200% of a drug's retail price is attributed to retail mark-ups.[25] In Ghana, CCD supply is heavily dependent on the private sector. The few outlets that stock oncology drugs have minimal competition and can dictate prices without government oversight or control.

Related to this, there was widespread recognition that the lack of financial incentives for industry to supply CCD, stemming from small aggregate markets and fractured procurement channels, has served to drive up and sustain high cancer drug prices. Participants from the government and pharmaceutical sector affirmed that supplying oncology drugs was perceived by many suppliers as not economically viable due to low demand.

To redress price-related challenges, the government has enacted policies to both augment incentives for cancer drug provision and strengthen central control of drug prices. Ghana's Food and Drugs Authority (FDA) classifies oncology drugs under the orphan drug category.[26] Orphan drugs benefit from a discounted registration fee and FDA decision within 3 months. Measures to control prices include the establishment of a National Medicine Price Committee (NMPC). The NMPC is mandated to manage the pricing system for pharmaceuticals in Ghana, instituting a national drug price reference index—including publication of maximum sales and reimbursement prices for all essential, patented and expensive medicines—and provisions to protect stakeholders from exposure to price fluctuations.[27]

Availability

A range of participants reported recurrent issues with drug availability, attributed to problems at various points along the pharmaceutical value chain. With respect to the quantitative stock-out trends observed (figure 2), no one explanator accounted entirely for this variability over time; rather, participants cited a range of factors including quantification issues, delays in bulk consignments and unanticipated increases in demand for cytotoxic drugs from the veterinary sector that led to erratic stocks, especially in early 2018.

In light of such vulnerabilities to existing supply chains, procurement challenges emerged as a critical determinant of access. A lack of central coordination has resulted in CCD procurement that is poorly calibrated to need, and highly susceptible to both drug shortages and increased manufacturing-to-receipt time. Participants indicated that the lack of nationally coordinated public procurement of CCD, coupled with the unavailability of locally manufactured CCD, serves to both limit drug availability and inflate price. Abstention from institutional and national-level CCD procurement was seen as a major contributor to drug shortages and price inefficiencies through loss of economies of scale. Principal barriers to public procurement noted by participants include: persistent perception of oncology drugs as a risky investment; hesitation of private suppliers to enter into supply contracts with the government due to payment delinquency; and non-response of oncology suppliers to open national tenders. Participants further suggested that institutions were deterred from procuring CCD as a result of a perceived lack of demand that would potentially lead to drug expiry—a situation exacerbated by competition with private retail pharmacies offering select drugs at wholesale prices. A number of participants noted that existing modes of fractured procurement, in conjunction with small-volume tenders, result in delays in drug order processing. Drug manufacturing companies are often compelled to pool multiple orders until a minimal number of vials is met; the added time required for drug production and shipping results in an order fulfilment time of approximately 3 months. Further delays in obtaining FDA approval also emerged as an issue for CCD suppliers.

Participants referenced a range of top-down and grassroots strategies to combat erratic drug availability—ranging in focus from market approval and procurement to distribution and supply management. National and regional approaches by the FDA and West African Health Organization (WAHO) to streamline regulatory approvals were cited as promising levers to enhance availability. WAHO's West Africa Medicines Regulations Harmonization Project harmonises product registration requirements and procedures between Economic Community of West African States member states.[28] The intended goal is to incentivise pharmaceutical companies, suppliers and manufacturers to supply CCD to the small Ghanaian market and foster local antineoplastic production, with a view to expedited drug registration and decreased time-to-market across the region. The FDA's fast-track drug registration process was also highlighted in this context. In addition to the orphan drug category, the FDA has enacted the guidelines which decrease the application processing time for qualified medicinal products from 6 months to 90 days.[29] Oncology drugs and paediatric formulations are eligible for the fast-track process, in the hopes of significantly reducing the time to market availability.

Implementation of a logistics management information system (LMIS) was highlighted as a critical mechanism to improve supply management of medicines in Ghana. As current software systems are siloed by programme drug portfolio and location, participants heralded government plans to launch an LMIS that include all medicine products, including cancer medicines, in public facilities. This was widely perceived as a promising means to facilitate distribution and circulation of medicines between public sector health facilities, with positive knock-on effects for availability. In response to procurement challenges, Ghana has undertaken framework contracting, a nationally-coordinated bulk purchase of 54 NEML-listed essential medicines. While CCD are not yet included, respondents were optimistic that the future inclusion of CCD could render medicines more affordable and readily available.

In recognition of the complexity and cost implications of drug importation, participants from the pharmaceutical sector and government spoke to the merits of generating opportunities for local production, arguing that drugs produced domestically would be cheaper and more readily available. Participants stressed the absence of domestic production capacity, the resource-intensive nature of the

enterprise and the lack of aggregate demand for oncology drugs as major deterrents to the development of local antineoplastic producers. Both the Ghana National Medicines Policy (GNMP) and civil servants emphasised that to foster local production, strategies must include: tax exemption for imported raw materials; quotas on the importation of select already locally-produced agents; and government financial assistance for local manufacturers in the form of low-interest capital loans.[25]

Where such policies have failed to prevent recurrent drug shortages, grassroots-level actors have implemented ad hoc strategies to combat poor availability—often with ancillary impacts on affordability, both positive and negative. Participants highlighted two beneficial strategies that parents and health providers have deployed to circumvent waste mitigation and high drug costs. First, families group purchase, share both costs and medicines. Second, health providers engage in batched administration, coordinating patient appointments to ensure that available vials are given to multiple children and wastage is minimised. In the face of persistent shortages and acute need, CCD suppliers often contract private agencies to acquire drugs and courier them to the point of sale, at a considerable cost to patients.

Quality

Concerns related to the quality of available CCD arose recurrently and were often connected to availability and affordability issues. Participants highlighted a common cost-control practice of institutional sourcing and procurement from markets with lower drug prices, with inadvertent effects on CCD quality. Accordingly, many participants expressed concern that high drug costs were contributing to the proliferation of low-quality drugs. Existing quality assurance measures for cancer drugs in Ghana are weak and piecemeal. The FDA's post-market surveillance programme relies mainly on clinician reporting of adverse drug reactions or ineffectiveness. In addition, participants expressed dissatisfaction with the delay in FDA response after a drug is reported. While hospital manufacturing centres have aided in the conversion of certain medicines, widespread concern persists among paediatric healthcare providers about substandard quality related to CCD compounding, limiting the availability of safe and effective child-friendly formulations and constraining optimal dosing.

Our findings reveal that access to CCD in Ghana is the product of a dynamic tension between received policy, regulatory and governance structures and evolving health system realities (figure 3). The provision of CCD within the Ghanaian health system is mediated by a complex series of inter-relationships between public and private sector institutions. These relationships are conditioned by national policy legacies and institutional path dependencies tailored to communicable disease and primary care priorities. The lack of centralised mechanisms for data collection and management on childhood cancer incidence and outcomes has hampered political prioritisation and evidence-informed planning. Weak regulatory controls on drug pricing, limited financing options and fractured procurement practices have engendered siloed pharmaceutical management and supply systems, with ramifications for CCD availability, affordability and quality.

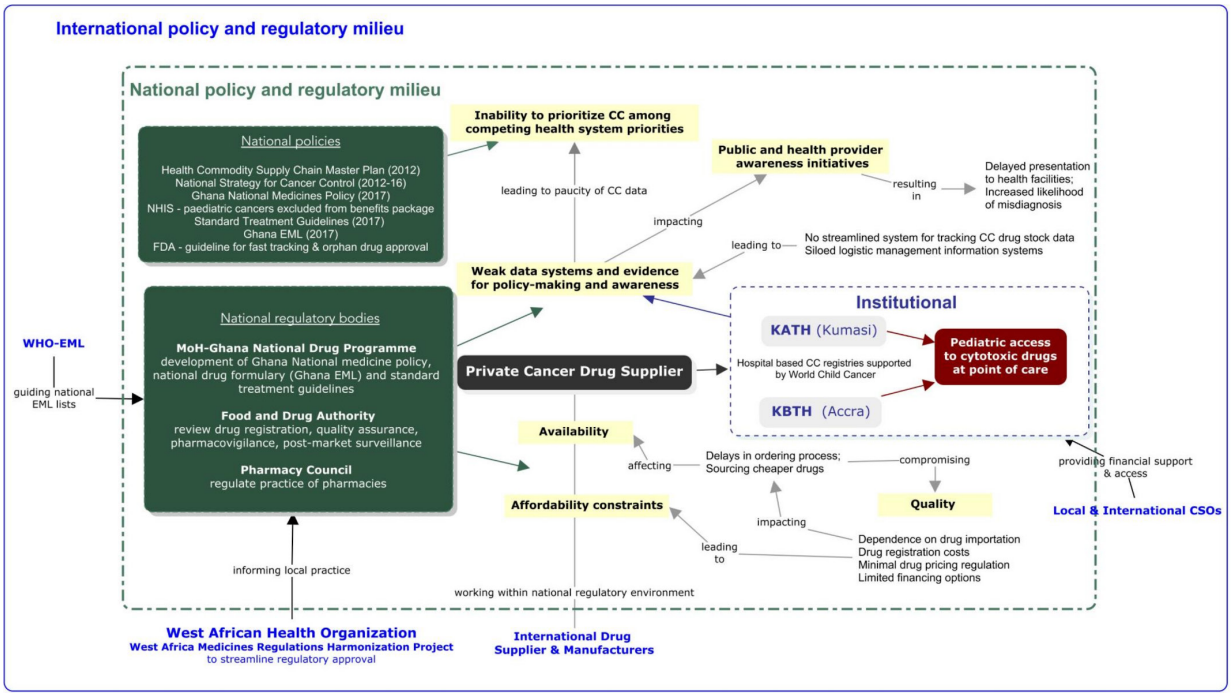

Figure 3 Ghanaian health system determinants influencing childhood cytotoxic drug access. CC, childhood cancer; CSO, Civil society organization; EML, Essential MedicinesList; FDA, Food and Drug Authority; KATH, Komfo-Anokye Teaching Hospital; KBTH,Korle-Bu Teaching Hospital; NHIS, NationalHealth Insurance Scheme.

DISCUSSION

Our study contributes to a small, but growing body of literature that augments understanding of health policy and system considerations for children with cancer in LMICs, and yields valuable theoretical and practical insights relevant to the analysis of drug access in health system context. First, our results underscore path dependence in Ghanaian health policy. Path dependence implies that past decisions frame and limit presently available ones, amplifying the downstream effects of policy over time and constraining future policy options.[30 31] The policy legacies fostered by sustained system focus on communicable disease control and primary care strengthening—issuing from longstanding domestic and international health governance priorities—have engendered neglect in the realm of NCD drug policy, including childhood cancer, despite the ongoing epidemiological transition in the country.[32 33]

Second, recognition of the dynamic interplay between core components of access, and the impact of health system structures and policies, underscores the value of complex adaptive systems theory for understanding drug access.[34] Complex systems are characterised by interdependence of their component parts and cyclical causal pathways between them.[35] Our findings highlight the close inter-relationships between principal dimensions of drug access—affordability, availability and quality—and the foundational impact of governance on these dimensions, separately and in combination.[36]

Together, the path dependence of drug policymaking and interdependence of its downstream effects have cultivated a health system environment minimally receptive to growing childhood cancer needs. The absence of dedicated political priority for childhood cancer amidst a broader push for enhanced NCD coverage has stymied the development of policies on drug procurement, pricing and quality assurance that incorporate childhood cancer, hampering the inclusion of paediatric cytotoxic and supportive care agents in both national and institutional pharmaceutical management practices. Further, the limited alignment between the WHO EMLc and Ghana NEML in respect of essential cytotoxic medicines for children is both a symptom and determinant of a drug policy environment that largely neglects childhood cancer. It underlines a lack of explicit priority in agenda-setting at the national level, and contributes to exclusion from legislative and regulatory provisions, like bulk procurement through framework contracting, that would ensure procurement through established public channels.[37]

Weak data systems compound this neglect by constraining evidence development that could document the scale and contours of the problem, and thereby help surmount it. Coupled with the historical exclusion of childhood cancer from public health coverage in Ghana—a critical demand-side determinant of drug affordability—this lack of evidence has constrained the ability of institutions to forecast accurately, and thus procure and stock essential childhood cancer medicines efficiently. The upshot has been devolution of procurement and supply management responsibilities to private markets, themselves distorted by widespread barriers to individual patient demand in line with need. In the absence of centralised public procurement and sustained institutional provision of CCD, the capacity for public sector quality assurance is limited to the point of initial market entry. The strong incentive for low-cost alternatives that stem from affordability issues has driven multi-source procurement through weakly regulated private channels, compounding erratic availability with concerns of substandard quality. Our analysis of drug pricing and stock data stresses the vulnerability of the system to procurement inefficiencies. This combination of factors relegates real-world access to a function of grassroots efforts by providers, patients and local communities, with resultant inefficiencies and inequities as documented in other LMIC contexts.[38–40] The interconnectivity across sectors, actors and system levels reveals what Atun[41] refers to as 'dynamic complexity'; such interconnectivities warrant greater attention in policy development and implementation.

With the recent emergence of the Ghana Cancer Board and the National Steering Committee for NCDs, a greater opportunity has emerged for coordinated planning and monitoring for childhood cancer care, particularly in light of plans to reform the now-outdated cancer control policy. Recognition of the need for complex systems thinking to apprehend challenges to CCD access can help prioritise high-yield policy responses to them. Policy recommendations and implications are summarised in table 3. First, data infrastructure must be improved and used in drug policy development and implementation. The development of quality population-based cancer registration and evidence-driven pharmaceutical management practices are foundational to evidence-informed policy on cancer control, including drug access. Ultimately, such data could inform nationally coordinated quantification and procurement of CCD that leverages economies of scale to speed manufacturing-to-receipt time, assure consistent availability and reduce drug cost.[42]

Strategies focussed on drug affordability, incorporating both demand-side and supply-side reforms, constitute a second key domain for focussed policy response. CCD and supportive care medicines are financially prohibitive for the majority of patients. Attention to cost-related barriers and public coverage through NHIS could significantly improve access to CCD in Ghana and other comparable health systems. While treatment is expensive, evidence shows that childhood cancer treatment in Ghana and other LMICs is cost-effective.[4 43–45] Efforts to consolidate existing national pricing control strategies will provide essential supply-side complements to health financing reforms. These insights are of direct relevance to evolving efforts at health system strengthening and policy reform in line with the emerging prioritisation of NCDs and universal healthcare coverage expansion in Ghana.

Study strengths and limitations

This study has a number of theoretical and methodological strengths. First, it provides an in-depth analysis of CCD access that combines granular data on drug availability and price with varied system-level stakeholder perspectives on access dynamics to generate a comprehensive

Table 3 Policy and planning recommendations and goals

Stakeholder level	Policy option	Goals
Challenge 1: Weak data systems and evidence for political prioritisation and public awareness		
National	Formal inclusion of childhood cancer in national NCD policy and planning, for example, broadened scope of inclusion of childhood cancer in National Cancer Control Strategy	Catalyse opportunities for greater health system prioritisation of childhood cancer
National Institutional	Development of streamlined national and institutional cancer registration and data management systems	Improve data collection and management procedures for evidence-based policy and planning
National	Strengthen systems for forecasting paediatric cancer drug needs	Minimise procurement inefficiencies Evidence-informed procurement
National Institutional	Implementation of a logistic management system	Enables real-time tracking of institutional tenders, stocks, and prices Inform procurement and supply management premised on evolving patterns of use and need.
National Institutional Community	Increase public awareness of childhood cancer through national health promotional campaign Investment in Ghana Cancer Board, National Steering Committee for NCDs and relevant stakeholders to advance advocacy for policy reform	Increase public awareness Improve early recognition/diagosis of childhood cancers Elevate priority of childhood cancers on policy agendas
Challenge 2: Cancer drug affordability, availability and quality constraints		
International	WHO pre-qualification of essential childhood cancer drugs	Streamline regulatory processes for importation of quality generic cytotoxic and supportive care drugs for childhood cancer
National Private pharmaceutical	Consolidate existing national pricing control strategies through regulatory reform Decrease taxation on imported drugs Coordinated public procurement of childhood cancer drugs Inclusion of childhood cancer in national health insurance scheme benefits package	Improve drug pricing and affordability Leverage economies of scale across institutions to improve affordability Increase adherence/minimise treatment abandonment
National	Expedited FDA approval processes Generic substitution as a policy directive	Minimise stock-outs through decreased order latency and product diversification Enhance affordability

FDA, Food and Drugs Authority; NCD, non-communicable diseases.

picture of access to CCD. Further, this study combines childhood cancer-specific analytical tools, such as the POSIT analytical framework, and systems-based theory on access to medicines, to engender insights into CCD access that are sensitive to health system context.

The study also has several methodological limitations. Retrospective analysis of CCD stocks and prices relied on existing institutional record-keeping processes, with potential implications for data accuracy. One consequence of this was the practical need to source data on drug availability variably from patient-level and supplier-level perspectives across institutions of interest. For KBTH, the WHO definition of stock-out at the point of patient care was adopted: we analysed Rock Chemist retail stocks of cytotoxic medicines, which reflect direct procurement by parents on an as-needed basis; supportive care drug data were obtained from the Child Health Unit pharmacy at KBTH, which likewise reflect patient-level availability. By contrast, as Rock Chemist is the primary supplier of CCD in Ghana, we analysed availability of cancer drugs at KATH at the supplier level. However, significant discordance between KATH pharmacy availability and Rock Chemist availability of these single-source agents is unlikely, and analysis at the supplier level represents a conservative assumption, as pharmacy-level stock-outs may be readily mitigated through reordering from the local supplier, where the latter has available stocks; supplier-level stock-outs were therefore felt to

more likely represent lasting, structural issues with availability. To calculate MPR, 2015 MSH price referencing was related to local price data from 2018, without accounting for increased freight costs and inflation. Finally, there remain limitations to the generalisability of these findings given unique policy and regulatory nuances specific to the Ghanaian context. Even so, our results corroborate findings from literature on drug access that emphasise the need for policy decision-making attentive to existing system networks and dynamics.[34]

CONCLUSION

Ghana's NCD control efforts require concerted evidence and policy development tailored to emergent health system realities. Efforts to improve access to essential medicines for children with cancer in LMICs, including Ghana, hinge on a nuanced understanding of system-level impediments to access. Our study highlights the impacts of existing policy, regulation and health service delivery approaches on CCD availability, affordability and quality in Ghana, emphasising the role of inherited political priorities and system interdependence in perpetuating access barriers. We identify pliable points for focussed policy reform to improve CCD access in Ghana and provide an approach to comparable analyses in other health system contexts. As an economic leader in West Africa, and priority partner country for the WHO's Global Initiative for Childhood Cancer, the strategies Ghana adopts have the potential to influence policy environments in other countries in the region, laying the foundations for broader improvements in access to essential medicines for children with cancer and other NCDs.

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Patient consent for publication Not required.

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Data availability statement Data are available upon reasonable request. Interview transcripts, though anonymised, may reveal the identity of participants, given the limited number of stakeholders involved in childhood cancer care and drug policy in Ghana; excerpts will be made available upon reasonable request.

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