original reports abstract

Access to WHO Essential Medicines for Childhood Cancer Care in Trinidad and Tobago: A Health System Analysis of Barriers and Enablers

Brandon Tang, MD, MSc[1,2]; Curt Bodkyn, MD[3]; Sumit Gupta, MD, PhD[4,5]; and Avram Denburg, MD, PhD[4,5]

PURPOSE Improving access to essential medicines is necessary to reduce global mortality resulting from childhood cancer. However, there is a lack of context-specific data in many low- to middle-income countries on the determinants of access to essential childhood cancer medicines. We conducted a mixed-methods case study of the barriers to and enablers of access to WHO essential medicines for childhood cancer care in Trinidad and Tobago, in response to domestic calls for policy attention and reform.

METHODS We interviewed stakeholders (N = 9) across the pharmaceutical supply system using a novel analytic framework and qualitative interview guide. Interviews were recorded, transcribed, and analyzed with constant comparative methods to capture emergent themes. Quantitatively, we examined alignment of the national essential medicines list with the 2017 WHO Essential Medicines List for Children (EMLc). National buyer prices for EMLc cancer medicines were compared with median international prices, with calculation of median price ratios to assess procurement efficiency.

RESULTS Principal barriers identified included a lack of data-driven procurement, low supplier incentive to engage in tenders, reactive rather than proactive processes in response to stockouts, and siloed information systems. Recurring themes of regionalization, standardization, and proactivity emerged as priorities for policy reform. Quantitative analysis of the national essential medicines list and median price ratios for procured medicines aligned with findings reported qualitatively.

CONCLUSION Our study contributes to global efforts to improve childhood cancer care by identifying policy-relevant evidence on access to essential childhood cancer medicines and providing a model for future studies in other jurisdictions.

JCO Global Oncol 6:67-79. © 2020 by American Society of Clinical Oncology

INTRODUCTION

Improving access to essential cancer medicines is recognized as a cornerstone of efforts to reduce worldwide mortality resulting from childhood cancer, in line with the United Nations Sustainable Development Goals, WHO Noncommunicable Disease Global Monitoring Framework, and recently launched WHO Global Initiative for Childhood Cancer.[1-3] Childhood cancer medicines are included on the WHO Essential Medicines List for Children (EMLc)[4]; however, ongoing barriers to accessing these medicines in low- and middle-income countries (LMICs) impede the delivery of high-quality care.[5] Access to medicines is influenced by multiple health system factors, including medication availability, accessibility, acceptability, affordability, and quality.[6] National and institutional efforts to ensure access to childhood cancer medicines are limited by a lack of robust data in many LMICs on the context-specific determinants of drug access.[7]

Childhood cancer outcomes across the English-speaking Caribbean (ESC) lag behind those achieved in most high-income countries (HICs), despite wide variation in per capita gross domestic product (GDP) and health system context in the region. ESC countries endorse many of the issues with drug access described here and have identified improved access to essential pediatric cancer medicines as a regional priority.[8] In response to this, we undertook an in-depth case study of drug access dynamics in Trinidad and Tobago (T&T) to support the development of evidence-informed policies and practices for improved childhood cancer drug access along the pharmaceutical value chain.

T&T is a Caribbean island country with a population of 1,369,125,[9] governed by a parliamentary democracy. Citizens generally have free access to health care, without fees or copayments for medicines in the public health sector, although these exist in the private health system.[10] Although it is classified as an HIC by gross

Author affiliations and support information (if applicable) appear at the end of this article.

Accepted on December 10, 2019 and published at ascopubs.org/journal/go on January 10, 2020: DOI https://doi.org/10.1200/JGO.19.00300

national income per capita,[9] T&T experiences health system challenges similar to those of many LMICs. For example, the country's total health expenditure (5.7% of the GDP) and per capita expenditure on health (US $895.26) are on par with LMICs such as Colombia and Mexico.[10,11]

At present, despite a political emphasis on improving access to medicines in T&T and growing recognition of childhood cancer as a health system priority, few to no local data exist on the determinants of access to essential medicines for pediatric cancer care. The purpose of this study was to perform a mixed-methods analysis of barriers to and enablers of access to essential pediatric cancer medicines in T&T. We also aimed to develop and test a rigorous approach to analyzing childhood cancer drug access that can be applied in a range of LMIC health systems.

METHODS

Framework for Mapping Determinants of Pediatric Oncology Drug Access: POSIT and MDS-3

We conducted a convergent parallel mixed-methods analysis of the determinants of childhood cancer drug access in T&T.[12] Our conceptual approach was guided by the Pediatric Oncology System Integration Tool (POSIT), an expert-informed and peer-reviewed framework for the analysis of childhood cancer care in the health system context (Figs 1 and 2)[13], and by the Management Sciences for Health Managing Drug Supply (MDS-3) framework (Fig 3),[14] an established and widely used reference for examining drug access in LMICs.[15-17]

We developed a semistructured qualitative interview guide drawing on POSIT and MDS-3 to understand key aspects of the pharmaceutical value chain that influence access to childhood cancer medicines. The 3 substantive categories used in our interview guide mirrored those of MDS-3: policy and economic issues, pharmaceutical management (selection, procurement, distribution, and use), and management support systems. Within these broad categories, open-ended interview questions were constructed to explore barriers to and enablers of drug access for children with cancer. Institutional approval was obtained from the Research Ethics Board at the Hospital for Sick Children in Toronto, Ontario, Canada, and the Office of the Chief Medical Officer in Port of Spain, T&T.

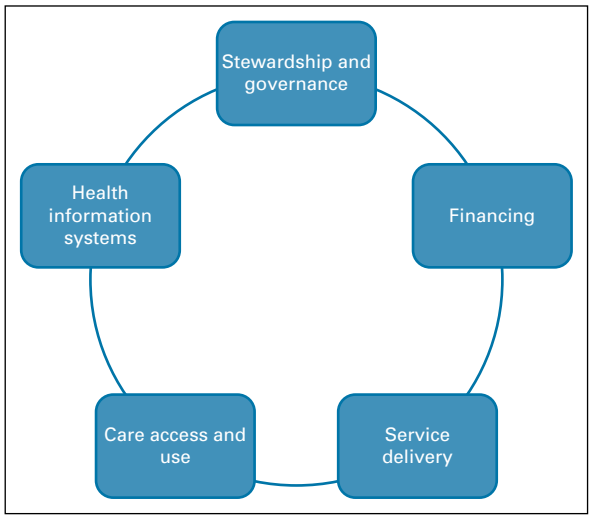

FIG 1. Overview of Pediatric Oncology System Integration Tool analytic domains.

Qualitative Data Collection and Analysis

We identified key health system and political stakeholders involved in systems of pediatric oncology care or pharmaceutical supply management in T&T through reviews of academic literature and policy documents,[10] a priori identification by key informants, and snowball sampling throughout the interview process. We conducted 9 interviews with key health system stakeholders, including health care providers, civil servants involved in oversight of the pharmaceutical system, and national and international policymakers. The size and breadth of the sample were determined through constant comparison with existing themes as the analysis of interviews proceeded, with a view toward thematic saturation. Interviews were audiotaped and transcribed verbatim, imported into NVivo 11 (QSR International, Melbourne, Victoria, Australia), and coded by 2 members of our team. Coding occurred deductively, employing preset coding schemes derived from the MDS-3 framework, as well as inductively, following a grounded theory approach with constant comparative methods to capture emergent themes.[18] Parallel to thematic analysis, process maps of the pharmaceutical value chain were developed based on document review[10] and inference from stakeholder interviews.

Quantitative Data Collection and Analysis

To triangulate our qualitative findings, we performed quantitative analyses of cancer drug selection and procurement. We examined alignment of the 2017 WHO EMLc and the most recent T&T Pharmaceutical Vital, Essential, and Necessary (VEN) list (2010). To assess procurement efficiency, we compared National Insurance Property Development Company (NIPDEC; Port of Spain, T&T) data on national buyer prices with international median buyer prices using the 2015 Management Sciences for Health (MSH) International Medical Products Price Guide.[19] For each drug, the median price ratio (MPR) was calculated as the ratio of the country buyer price to the MSH median buyer price, given the predominance of public sector procurement in the country.[20] We defined an MPR of ≤ 1 as indicative of efficient public sector procurement and an MPR of ≤ 3 as efficient private sector procurement, modeled on WHO norms.[20,21]

RESULTS

Key Stakeholders, Process Maps, and Summary of Barriers to and Enablers of Drug Access

Stakeholders and their roles in the childhood cancer pharmaceutical value chain are summarized in Table 1. To

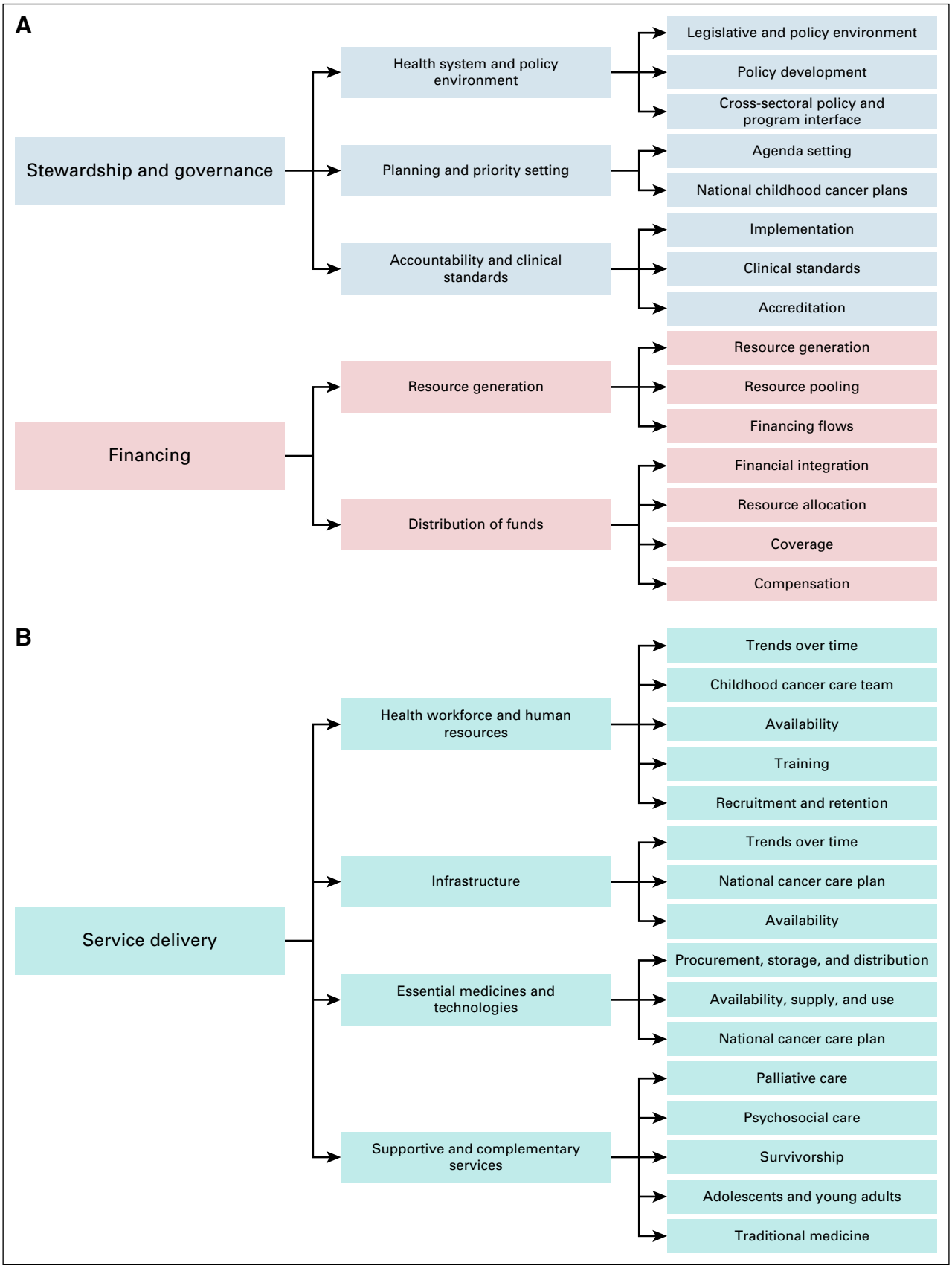

FIG 2. Detailed Pediatric Oncology System Integration Tool analytic domains.

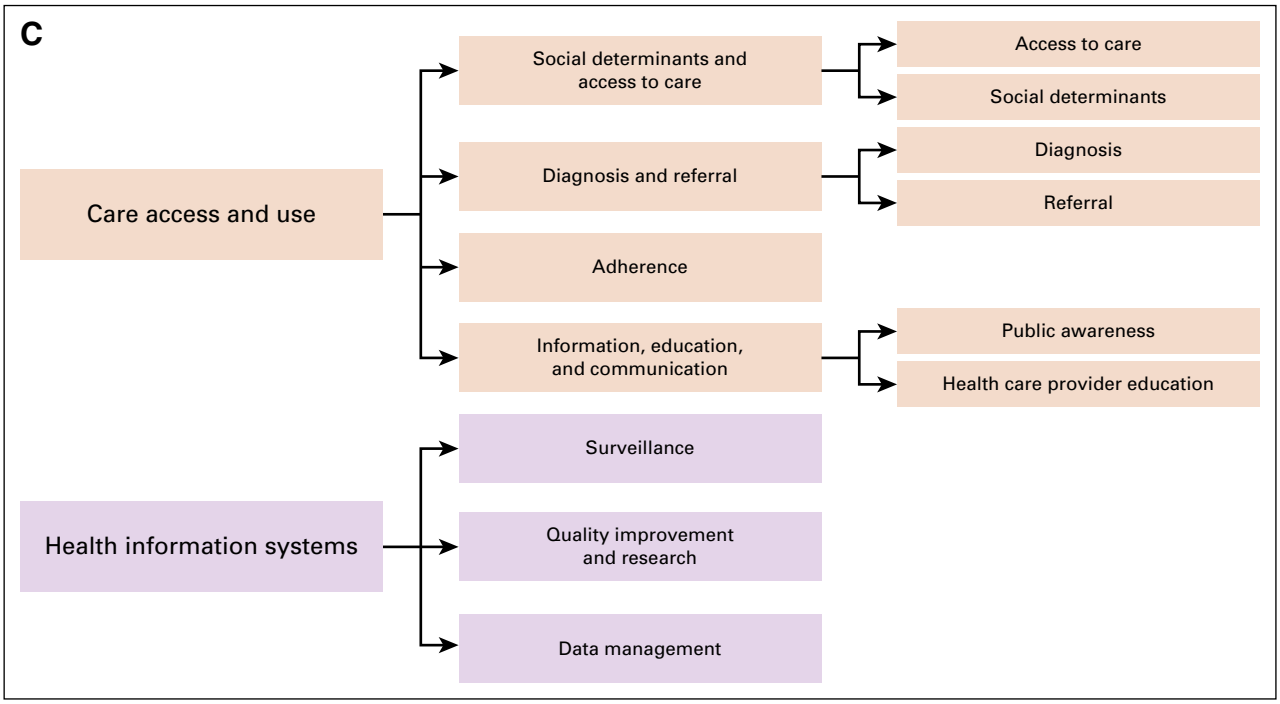

FIG 2. (Continued).

highlight relationships and interactions among stakeholders, we developed process maps to summarize the processes of selection and procurement (Fig 4) as well as distribution (Fig 5) of essential pediatric oncology medicines.[22]

Policy and Economic Issues

i. Policy and legal framework. **Delays in regulatory approval.** Study participants stated that delays in regulatory approval at various levels of the pharmaceutical supply system posed a barrier to accessing essential childhood cancer medicines. For example, the registration of novel medications through the T&T Ministry of Health Chemistry Food and Drugs Division (CFDD) can take up to 6 months, preventing access to potentially useful medications.

> There are some … good generics that are out there, just stuck in the process to get registered … [they] are effective and you can [purchase them] cheaper, but you can't [access them] because they are still waiting to filter through that system.
> —Health care provider

Participants highlighted a recurring phenomenon wherein delayed approval at the hospital level inhibited access to essential cancer medicines during stockouts, when procurement was necessary from alternative private sector suppliers.

> [The] ad hoc purchase outside of the tender … has to go to the manager, the financial officer, the CEO [chief executive officer], the board, then this, then that … by the time you actually do it, you might get it 3 months down the road and time is of the essence … there doesn't seem to be that urgency.
> —Health care provider

Failure to recognize external prequalification mechanisms. T&T is a member of a regional pharmaceutical regulatory authority known as the Caribbean Regulatory System (CRS). However, even when a pharmaceutical product has received CRS market authorization, the country does not automatically recognize this endorsement, and additional processes are required to obtain local registration.

> Instead of reinventing the wheel, we should … utilize the systems that are already developed … and therefore build our systems based on [the Caribbean Regulatory System], so we [can] ensure quality of medicines … it will help speed up the process of [drug] registration.
> —Civil servant

ii. Financing and sustainability. Participants estimated that limited public sector capital has led to an annual shortfall of T&T $300 to $400 million allocated for the purchase of essential childhood cancer medicines, relative to forecasted estimates of need. Strategies to address this limited capital included potential creation of a dedicated pediatric allocation within the national oncology budget and greater use of the Pan American Health Organization (PAHO) Strategic Fund to purchase oncologic medicines, which would contribute to cost savings.

Pharmaceutical Management

i. Selection. **Streamlining of VEN list generation.** Although individual physician advocacy has played an important historical role in VEN development, participants highlighted that T&T recently developed national treatment protocols to standardize the use of adult cancer medicines.

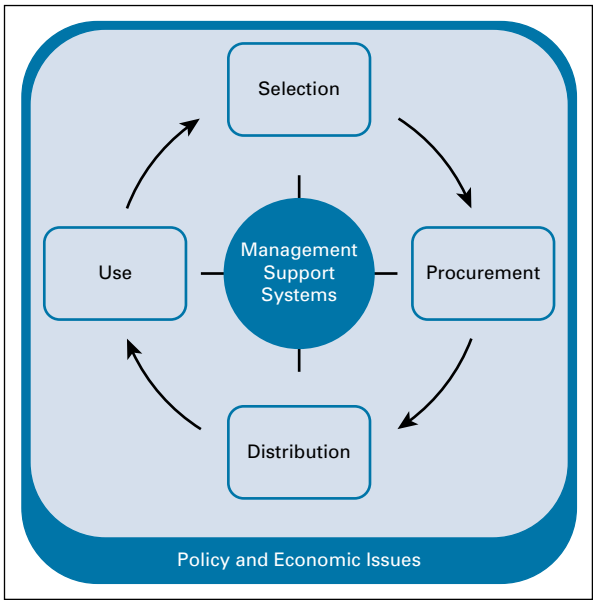

FIG 3. Management Sciences for Health Managing Drug Supply framework for understanding pharmaceutical supply management systems. Data adapted.[30]

> Before, [the Pharmaceutical Vital, Essential, and Necessary list] didn't have things like ifosfamide … topotecan … irinotecan … but all of those things are on now. There's a process for that, where the clinician would write to the [Drug Advisory Committee], provide data supporting the addition of the drug onto the list, and that's how you get it on. —Health care provider

Although there is existing consensus among pediatric oncologists on which treatment protocols to use, childhood cancer care still stands to benefit from the creation of national protocols for adult cancers. A range of stakeholders agreed that streamlined protocols would reduce overall waste of cancer medicines, thereby enhancing the availability of medicines common in the treatment of both adults and children, where waste in the adult sector could indirectly affect the supply of pediatric medicines.

Alignment of VEN list with WHO EMLc. From a quantitative perspective, selection of essential childhood cancer medicines in T&T corresponded with WHO recommendations, as the T&T VEN list contained 20 of 22 drugs included on the 2017 WHO EMLc for cytotoxic and adjuvant medicines (90.9% alignment; Table 2). However, all cancer medicines on the WHO EMLc were procured for use in T&T, including dacarbazine and thioguanine, which were not on the national VEN list.

ii. Procurement. **Limited supplier incentive and availability.** Study participants highlighted that the NIPDEC restricted tendering system, which requires suppliers to register with NIPDEC before participating in bids for tenders, collaterally limits the available supplier pool, estimated to range from 10 to 30, for childhood cancer medicines. This issue is exacerbated in a niche field such as pediatric oncology, in which the volumes of procured medicines unique to childhood cancer treatment are orders of magnitude smaller than those in the adult sector.

> There are some drugs that are in short supply because … there is not a supplier that will supply it to the region or to the area. This happens with drugs that have been around for quite some time and are not very lucrative for the companies. It is difficult to entice companies to bring it in for the quantities that we use in the Caribbean. If it's a very large

TABLE 1. Summary of Key Stakeholders and Their Roles in Childhood Cancer Pharmaceutical Supply Management System in T&T

Stakeholder	Role in Pharmaceutical Supply Management
Office of CMO	Holds ultimate responsibility for deciding which drugs are selected and procured in T&T
NDAC	Develops and maintains national VEN list
	Adjudicates requests for additions to VEN list
NIPDEC	Third-party agent that purchases pharmaceuticals for public health system as directed by Ministry of Health
	Oversees national drug procurement via its CMS subdivision
CFDD	Mandatory registration of potential suppliers and pharmaceutical products before procurement can occur by CMS (although ad hoc purchases approved by CMO may bypass this registration process)
RHAs	T&T is divided into 5 semiautonomous RHAs, which have administrative oversight over public health system
	Report annual pharmaceutical use data to CMS to guide procurement forecasting
	Actively engage in procurement process, including deciding which medicines to procure and quantifying procurement needs
EWMSC	National center of excellence for pediatric oncology
NGOs	Provide both social and financial support for children undergoing cancer treatment, such as arranging short-term housing near hospitals and financing transportation to treatment centers
PAHO	Coordinates group-based multinational procurement service known as Strategic Fund

Abbreviations: CFDD, Chemistry Food and Drugs Division; CMO, Chief Medical Officer; CMS, Central Medical Stores; EWMSC, Eric Williams Medical Sciences Complex; NDAC, National Drug Advisory Committee; NGO, nongovernmental organization; NIPDEC, National Insurance Property Development Company; PAHO, Pan American Health Organization; RHA, regional health authority; T&T, Trinidad and Tobago; VEN, VEN, Pharmaceutical Vital, Essential, and Necessary.

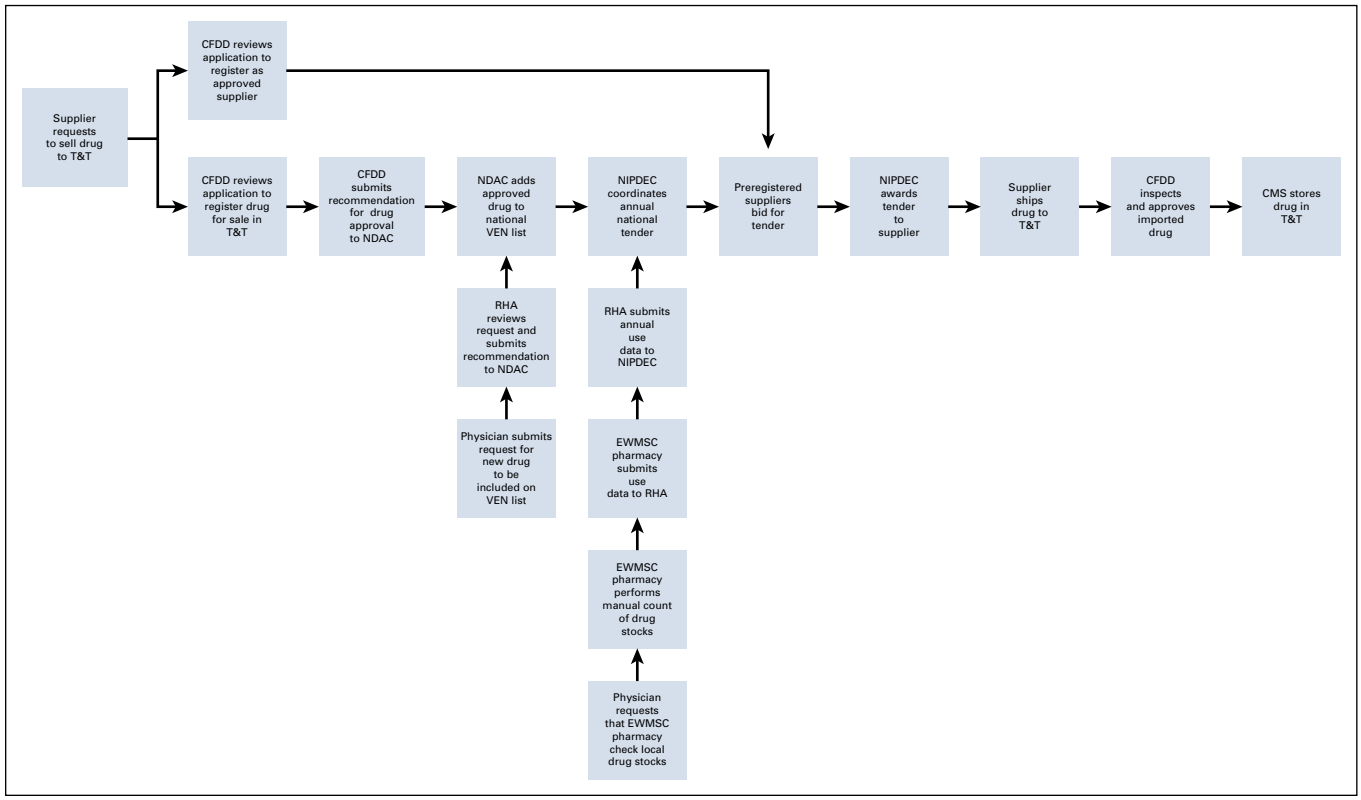

FIG 4. Process map for selection and procurement of essential pediatric oncology medicines in Trinidad and Tobago (T&T). This process map assumes that registration of both suppliers and drugs is ultimately approved. The National Drug Advisory Committee (NDAC) is chaired by the Chief Medical Officer. CFDD, Chemistry Food and Drugs Division; CMS, Central Medical Stores; EWMSC, Eric Williams Medical Sciences Complex; NIPDEC, National Insurance Property Development Company; RHA, regional health authority; VEN, Pharmaceutical Vital, Essential, and Necessary.

> market, then sure they probably would be willing to do that. But if you're talking about an island that just has about 1.3 million people … they're not as enticed to do it. So, it has been difficult in some cases to even get a supplier for the drug.
> —Health care provider

The limited number of interested suppliers further limits accountability, because even those with poor performance records may still have been awarded tenders.

> [For asparaginase], we are now dependent on a sole supplier … that is a problem because [for a supplier] that gets 100% of the tender … if [they are] unable to do that, then we have no other options.
> —Health care provider

One solution proffered by study participants was to combine the pharmaceutical purchasing power of T&T with that of other countries, via initiatives such as the Organization of Eastern Caribbean States (OECS)[23] or the PAHO Strategic Fund. With respect to the PAHO Strategic Fund in particular, participants described key benefits as the ability to achieve a low price point for pharmaceuticals through multicountry pooled procurement and the existence of rigorous quality assurance mechanisms.

> What is helpful … for countries that are very small, where the quantities that you're asking are very limited, is to have some sort of bargaining power by purchasing as a group of countries rather than purchasing individually. That works well usually through established organizations [such as the Pan American Health Organization].
> —Health care provider

Procurement forecasting challenges. Participants emphasized key challenges in the accurate and effective forecasting of childhood cancer drug needs in T&T. Current approaches to forecasting at both facility and national levels are almost entirely premised on drug use data from the previous year. This presents a particular challenge in pediatric oncology, where the annual incidence rates of cancers can be low and variable between years.

> What you often hear is, yes, we purchase all these [topotecan] vials, nobody used it for a year, and therefore, we're not going to purchase that much next year. Then you have 3 patients come at the same time, and you can't get hold of it.
> —Health care provider

Procurement inefficiencies contribute to higher buyer prices. Quantitative analysis of drug prices suggested that nearly half of childhood cancer medicines were procured inefficiently, corresponding with stakeholder concerns regarding the procurement process. Comparison of local versus international buyer prices demonstrated that 15

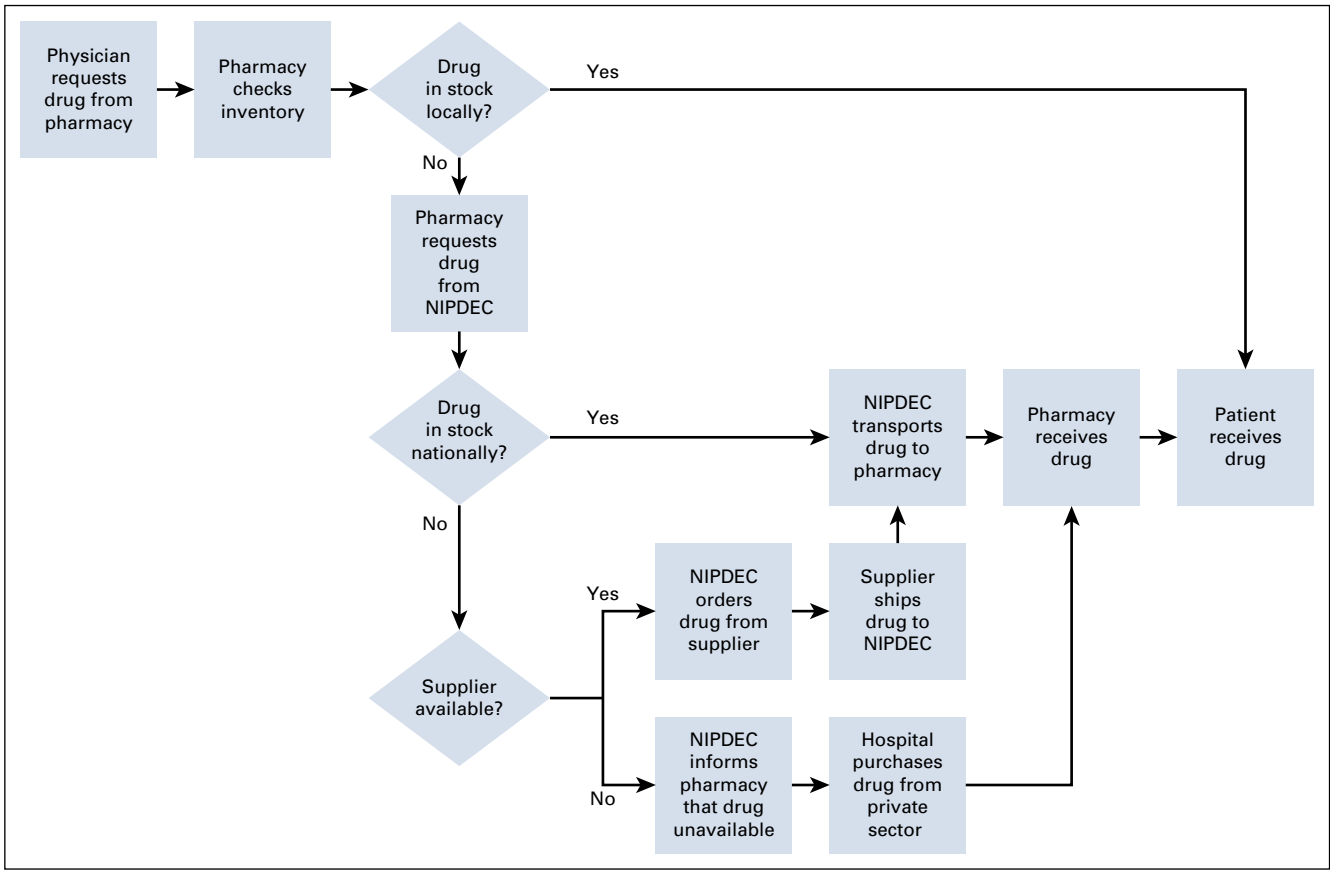

FIG 5. Process map for distribution of essential medicines to Eric Williams Medical Sciences Center, particularly during times of stockouts. NIPDEC, National Insurance Property Development Company.

(53.6%) of 28 formulations had an MPR of < 1, suggesting efficient public sector procurement, whereas 13 (46.4%) of 28 formulations had an MPR of > 1, suggesting inefficient public sector procurement (Table 3). Notably, dactinomycin is purchased on an ad hoc basis rather than via the NIPDEC coordinated annual tender, perhaps explaining the highly inefficient procurement process (MPR, 16.98). The average MPR for generic medicines was 1.09 (12 formulations), compared with 1.33 for brand-name formulations (15 formulations), although this difference was not statistically significant (t[25], 0.93; $P = .18$). Additional information on NIPDEC versus MSH buyer prices is listed in Table 4.

iii. Distribution. **Pharmaceutical stock is distributed via a reactive pull system.** Participants described the overall pull system of distribution as problematic, in which additional medicines are requested only after low stocks are identified at various levels of the pharmaceutical system (Fig 5). The Eric Williams Medical Sciences Complex (EWMSC) only holds a 4- to 6-week supply of most medications and often reactively identifies a stockout after a drug is requested by a physician, given the limited inventory tracking system of the pharmacy. Participants estimated that a stockout of an essential childhood cancer medicine occurred at least 4 to 5 times per year at EWMSC, with each stockout possibly prompting NIPDEC to recognize a national stockout of the same medicine; NIPDEC only houses data on annual drug procurement and is not necessarily privy to the use and stock data held by local oncology centers. In response to a national stockout, NIPDEC creates a new tender to source the medication for the public sector, but this may not be fulfilled for up to 6 months, often compelling facilities to urgently explore private sector avenues to secure an essential medicine. However, participants spoke to quality concerns with private routes of procurement, noting the lack of quality assurance mechanisms comparable to those of public procurement channels. Hence, at both the local and national levels, limited inventory tracking systems drive a pull system of distribution, leading to reactive, as opposed to proactive, practices in drug procurement.

iv. Use. **Expired medicines are used during stockouts.** A number of participants underscored the impact of stockouts of medicines for which there are no substitutes, such as asparaginase in the treatment of acute lymphoblastic leukemia. While parallel attempts are made to source these medicines from public and private sectors, such circumstances may necessitate that pediatric oncologists use recently expired medicines. However, use of expired medicines was highly conditional and only occurred when there was no

TABLE 2. Summary of Key Barriers to and Enablers of Access to Essential Medicines for Childhood Cancer Care in T&T

Category	Barrier	Enabler
Policy and economic issues		
i. Policy and legal framework	Delays in regulatory approval at various levels of pharmaceutical supply system Failure to recognize external prequalification mechanisms	Continue clear political and legal mandate to promote access to essential medicines Standardize regulatory approval processes, including approval of new medicines, use of pre-existing generic medicines, and local responses to stockouts Expedite acceptance of external or regional prequalification mechanisms (eg, CRS, PAHO)
ii. Financing and sustainability	Limited public sector capital to purchase essential childhood cancer medicines	Dedicate national budget for oncology, including allocation for pediatric oncology Purchase oncology medicines from PAHO Strategic Fund
Pharmaceutical management		
i. Selection	Failure to include pediatric oncologists in initial VEN list generation Variation or waste in adult sector while selecting cancer medicines common in treatment of adults and children	Continue formal channels for physicians to advocate for inclusion of essential medicines on VEN list Streamline national oncology treatment protocols for both adults and children
ii. Procurement	Limited supplier availability Lack of supplier incentive because of small market size Inaccurate forecasting of childhood cancer medicine needs Lack of dedicated pediatric supply of oncologic drugs common in adult and pediatric treatment protocols Unanticipated stockouts necessitate procurement from private sector	Diversify supplier base (eg, consider open tendering mechanism *v* current restricted system) Engage in group-based procurement (eg, purchase oncology medicines from PAHO Strategic Fund) Strengthen data infrastructure at all levels of pharmaceutical supply system (eg, NIPDEC, EWMSC) Consider multiyear or larger volume procurement
iii. Distribution	Pharmaceutical stock distributed via reactive pull system Lack of safety stock at EWMSC	Harmonize connectivity of data infrastructure at all levels of pharmaceutical supply system (eg, NIPDEC, EWMSC) Consider multiyear or larger volume procurement Maintain safety stock
iv. Use	Expired medicines used during stockouts	Prevent stockouts Maintain safety stock Continue availability of unique pediatric formulations
Management support systems		
i. Information management	Poor communication and integration of information systems across different levels of pharmaceutical supply system Information systems largely paper based Epidemiologic and quality assurance data lacking to support procurement decisions	Develop harmonized, computer-based pharmaceutical management system to connect data infrastructure at all levels of pharmaceutical supply system (eg, NIPDEC, EWMSC) Enhance national cancer registry Develop formal system to monitor supplier performance
ii. Human resource management	Lack of stable human resources (eg, NIPDEC, CFDD) Lack of interinstitutional communication protocols Individual advocacy insufficient to address systemic issues	Develop standard procedures for collaboration and communication among stakeholders and manage stockouts

Abbreviations: CFDD, Chemistry Food and Drugs Division; CRS, Caribbean Regulatory System; EWMSC, Eric Williams Medical Sciences Complex; NIPDEC, National Insurance Property Development Company; PAHO, Pan American Health Organization; T&T, Trinidad and Tobago; VEN, Pharmaceutical Vital, Essential, and Necessary.

TABLE 3. Alignment of Cancer Medicines on 2017 WHO EMLc and 2010 T&T VEN List

Cytotoxic or Adjuvant Medicine on WHO EMLc	Drug on T&T VEN List	Drug on WHO EMLc but Not T&T VEN List
Allopurinol	X	
Asparaginase	X	
Bleomycin	X	
Calcium folinate	X	
Carboplatin	X	
Cisplatin	X	
Cyclophosphamide	X	
Cytarabine	X	
Dacarbazine		X
Dactinomycin	X	
Daunorubicin	X	
Doxorubicin	X	
Etoposide	X	
Filgrastim	X	
Ifosfamide	X	
Mercaptopurine	X	
Mesna	X	
Methotrexate	X	
Paclitaxel	X	
Tioguanine		X
Vinblastine	X	
Vincristine	X	

Abbreviations: EMLc, Essential Medicines List for Children; T&T, Trinidad and Tobago; VEN, Pharmaceutical Vital, Essential, and Necessary.

other source of the essential cancer medicine nationally and the medicine was within 1 month of the expiration date.

Management Support Systems

i. Information management. **Poor communication and integration of information systems.** Participants noted that poor communication and integration of information systems across different institutions, such as NIPDEC, regional health authorities (RHAs), and EWMSC, was a prominent access barrier to essential childhood cancer medicines. As a result, there is no harmonized system or process to track the procurement, distribution, and use of medicines through the pharmaceutical supply chain.

> As it is right now, all systems are not integrated ... our inventory management system is just for Central Stores. And each of the institutions [has] their own inventory. Each regional health authority has their own inventory management system … and that's one of our shortfalls because in a supply chain management system we have the flow of medicines in one direction, but we need to have a flow of information in the other which feeds back to the health planner, and that's not happening.
> —Civil servant

Furthermore, data accuracy is affected by a reliance on paper-based information systems, and there is a lack of epidemiologic data to support procurement decisions, because the T&T national cancer registry was last updated in 2011. Hence, the current understanding of cancer prevalence, incidence, and medication use patterns is incomplete.

ii. Human resource management. **Lack of stable human resources.** Several stakeholders described how human resource limitations adversely affected their ability to oversee the pharmaceutical supply chain. For example, the lengthy registration process for novel medicines at CFDD was attributed to a reliance on clinical expert volunteers for drug application reviews, as opposed to dedicated in-house personnel. Human resource concerns were also cited in relation to NIPDEC, where turnover of management-level employees led to the loss of tacit information about the governance and processes of the organization, without concomitant standard operating procedures to guide new employees.

DISCUSSION

Across all domains of the pharmaceutical system, 3 common themes for policy change emerged: regionalization, standardization, and proactivity. Regionalized solutions encompass many of the systemic enablers described by study participants. For example, acceptance of regional prequalification would expedite drug registration processes by recognizing the market authorization of authorities such as the CRS or US Food and Drug Administration. Group-based procurement through existing collaboratives, such as the OECS or PAHO Strategic Fund, is another regionalized solution that would address an important procurement barrier by expanding the pool of available suppliers. Despite the potential benefits, participants also highlighted the political and administrative challenges of pursuing regional solutions to drug access. For instance, regional approaches would require significant engagement and coordination with key external stakeholders (eg, PAHO) and a willingness to accept reduced autonomy over certain aspects of pharmaceutical management, through adherence to the stipulations of supranational initiatives.

The importance of standardizing core processes in the pharmaceutical supply system was another emergent theme from our stakeholder interviews. Developing a systematic process for monitoring drug stocks in the EWMSC pharmacy would enable proactive identification of stockouts and reliably push more accurate data to NIPDEC at the national level to guide procurement decisions. Standard protocols for stakeholder responsibilities and communication during stockouts among groups such as NIPDEC, RHAs, and EWMSC would increase overall awareness of the national state of drug stocks and improve coordination during stockouts.

A final theme from our stakeholder interviews was a need for more proactive pharmaceutical management

TABLE 4. Comparison of NIPDEC Buyer Prices With MSH Median Buyer Prices

Cytotoxic or Adjuvant Medicine on WHO EMLc 2017	Quantity and Medium	Method of Administration	Purchasing Unit	Generic *v* Brand	NIPDEC Buyer Price (US$)[a]	MSH Median Buyer Price (US$)	Median Price Ratio
Allopurinol	100-mg tablets	Oral	28-tablet pack	B	0.59[b]	0.66	0.89
Asparaginase	10,000 IU/mL	Injection	Vial	G	40.35	52.89	0.76
Bleomycin	15 IU	Injection	Vial	G	25.70	12.32	2.09
Calcium folinate	50 mg/5 mL	Injection	Vial	G	3.47	2.34	1.48
Carboplatin	150 mg/15 mL	Injection	Vial	B	10.43	16.01	0.65
	450 mg/45 mL	Injection	Vial	B	25.43	40.32	0.63
Cisplatin	50 mg	Injection	Vial	G	6.15	7.25	0.85
	50 mg[c]	Injection	Vial	G	6.89	7.25	0.95
Cyclophosphamide	200 mg/10 mL	Injection	Vial	G	1.99	2.08	0.96
	1 g	Injection	Vial	G	4.65	8.27	0.56
	50-mg tabs	Oral	50-tablet pack	G	0.38[b]	0.30	1.26
Cytarabine	100 mg/1 mL	Injection	Vial	B	4.43	3.48	1.27
	1 g	Injection	Vial	B	11.18	NA[d]	NA
Dacarbazine	200 mg	Injection	Vial	G	15.94	6.81	2.34
Dactinomycin[e]	0.5 mg	Injection	Vial	NA	147.75	8.70	16.98
Daunorubicin[f]	NA	NA	NA	NA	NA	NA	NA
Doxorubicin	10 mg	Injection	Vial	B	4.13	2.12	1.94
Etoposide	100 mg/5 mL	Injection	Vial	B	0.86[b]	0.40	2.12
Filgrastim	300 μg/mL	Injection	Vial	G	13.48	40.04	0.34
Ifosfamide	1 g	Injection	Vial	B	18.90	26.71	0.71
	2 g	Injection	Vial	B	37.00	47.98	0.77
Mercaptopurine	50-mg tablets	Oral	25-tablet pack	B	1.85[b]	2.24	0.83
Mesna	400 mg	Injection	15-vial pack	B	3.94[b]	3.01	1.31
Methotrexate	2.5-mg tablets	Oral	100-tablet pack	G	0.044[b]	0.06	0.69
	50 mg/2 mL	Injection	Vial	B	3.68[b]	2.22	1.65
	1,000 mg/10 mL	Injection	Vial	B	1.90[b]	2.22	0.85
Paclitaxel	100 mg/16.7 mL	Injection	Vial	G	9.45	11.08	0.85
Tioguanine	40-mg tablets	Oral	25-tablet pack	B	11.35[b]	6.82	1.66
Vinblastine	10 mg/mL	Injection	Vial	B	15.90	4.98	3.20
Vincristine	1 mg/mL	Injection	Vial	B	3.68	2.54	1.45

Abbreviations: EMLc, Essential Medicines List for Children; MSH, Management Sciences for Health; NIPDEC, National Insurance Property Development Company.

[a]Exchange rate for January 2019 was 1 Trinidad and Tobago dollar to 0.15 US dollars.

[b]NIPDEC buyer price adjusted to match comparison unit of MSH buyer price (tablet, vial, or mL).

[c]Different manufacturer of cisplatin.

[d]No equivalent MSH comparison unit for quantity and medium procured.

[e]Dactinomycin not procured during annual tender but later in year after legitimate bid received.

[f]Daunorubicin procurement pending receipt of bids for tender.

approaches. For example, the high frequency of stockouts at both the local and national levels suggests that multiyear procurement could be a proactive approach to reduce stockouts. Investment in improved information management systems, in terms of financial resources as well as the development of systematic processes, would also enhance multiple aspects of drug access, through improved data to forecast procurement quantities, quality assurance mechanisms, and ability to monitor drug stocks.

Our findings are relevant to broader health systems strengthening in T&T, because many proposed enablers of drug access would enhance overall health system performance. For instance, recent reports have suggested that institutional process inefficiencies, such as delays in hospital diagnostics resulting from inadequate staffing, create significant barriers to accessing health services in T&T.[24,25] Themes for policy reform from our study, such as increased standardization of intra- and interinstitutional processes in the pharmaceutical sector, may therefore be relevant in addressing other health system inequities as well, including access to diagnostic services and wait times for specialist care.[25]

An underlying objective of our study was to develop health system capacity in T&T by equipping local stakeholders with policy-relevant data. Historically, this has been approached through the development of international collaboratives, known as twinning, in which LMIC and HIC centers create partnerships to enhance institutional capacity.[26] However, the relative absence of explicit national childhood cancer strategies in LMICs limits the ability of such partnerships to enact long-term improvements.[27] By generating context-sensitive data on health policy and system-level challenges, our study provides local stakeholders with information relevant to sustainable health system reform in T&T.

From a global perspective, our mixed-methods study will contribute to future analyses of access to childhood cancer medicines in a range of LMIC settings. Existing frameworks for access to medicines tend to parse pharmaceutical supply systems into conceptual domains such as availability, affordability, and acceptability.[28,29] These approaches offer valuable analytic perspective; however, by examining access to medicines in terms of functional components of the pharmaceutical value chain (ie, selection, procurement, distribution, and use), our framework naturally highlights areas that are amenable to process improvement and system-level change. Moreover, our qualitative, stakeholder-driven interviews ensured that change ideas were grounded in the issues that local experts valued most. Our approach provides a tailored, transposable approach to the analysis of childhood cancer drug access that can inform future studies in a range of LMICs.

T&T is a relatively small Caribbean island nation with a number of characteristics similar to LMICs in terms of health system governance, financing, and service delivery, but it is still classified as an HIC by GDP. Consequently, the findings from our study may not be generalizable to all LMIC contexts, particularly those with larger populations.

Our mixed-methods approach is also limited by the inherently perspectival nature of qualitative research, because our findings may have been influenced by the views of study participants. For instance, certain domains of the MDS-3 framework, such as policy, legal, and financial contexts, organically emerged as less prominent themes in our analysis. However, this limitation is partially mitigated by the thematic saturation achieved with a small number of study participants, especially given the relatively bounded pharmaceutical system context in T&T. Hence, additional stakeholder interviews would have been unlikely to yield new central themes or critical phenomena relevant to our study. In addition, although we endeavored to obtain more local- and national-level data on drug availability, such as stocks and shortage trends, we were limited by the available institutional data holdings, which constrained our ability to triangulate our qualitative findings with quantitative data.

In conclusion, to our knowledge, our study constitutes the first in-depth mixed-methods case study of the determinants of childhood cancer drug access in the health system context. Principal barriers to accessing childhood cancer medicines in T&T include a lack of data-driven procurement, low supplier incentive to engage in tenders, reactive (*v* proactive) processes in response to stockouts, and siloed information systems. Findings from our quantitative analysis aligned with key barriers and enablers reported qualitatively. Regionalization, standardization, and proactivity were identified as key themes to strengthen policies and practices along the pharmaceutical value chain. Our process-oriented analysis has relevance to future studies of access to essential medicines in LMIC settings, as a means of identifying pliable areas for policy change driven by local contexts. Our work contributes to the international agenda focused on improved global childhood cancer outcomes by furnishing novel policy-relevant evidence on access to essential childhood cancer medicines in the health system context and by providing a model for future studies in other jurisdictions.

AFFILIATIONS

[1]Department of Medicine, University of British Columbia, Vancouver, British Columbia, Canada
[2]Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada
[3]Child Health Unit, Faculty of Medical Sciences, The University of the West Indies, St Augustine, Trinidad and Tobago
[4]Division of Haematology/Oncology, Department of Paediatrics, The Hospital for Sick Children, Toronto, Ontario, Canada
[5]Institute of Health Policy, Management and Evaluation, Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada

CORRESPONDING AUTHOR

Avram Denburg, MD, PhD, Division of Haematology/Oncology, Department of Paediatrics, The Hospital for Sick Children, 555 University Ave, Toronto, Ontario, Canada, M5G 1X8; Twitter: @AvramDenburg; e-mail: avram.denburg@sickkids.ca.

SUPPORT

Supported by the SickKids-Caribbean Initiative.

AUTHOR CONTRIBUTIONS

Conception and design: Brandon Tang, Sumit Gupta, Avram Denburg
Provision of study material or patients: Brandon Tang, Avram Denburg
Collection and assembly of data: Brandon Tang, Curt Bodkyn, Avram Denburg
Data analysis and interpretation: All authors
Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless otherwise noted. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/go/site/misc/authors.html.

Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

No potential conflicts of interest were reported.

ACKNOWLEDGMENT

We thank the SickKids-Caribbean Initiative for its financial and logistic support of this study, the Office of the Chief Medical Officer in the Ministry of Health, and other institutional partners in Trinidad and Tobago for their instrumental leadership and collaboration and the study participants for their time and the insights they provided.

REFERENCES

1. United Nations: Sustainable development goals. https://www.un.org/sustainabledevelopment/sustainable-development-goals/
2. World Health Organization: World leaders join new drive to beat noncommunicable diseases. https://www.who.int/mediacentre/news/releases/2018/world-leaders-ncds/en/
3. World Health Organization: Global initiative for childhood cancer. https://www.who.int/cancer/childhood-cancer/en/
4. World Health Organization: WHO Model Lists of Essential Medicines. https://www.who.int/medicines/publications/essentialmedicines/en/
5. Mehta PS, Wiernikowski JT, Petrilli JA, et al: Essential medicines for pediatric oncology in developing countries. Pediatr Blood Cancer 60:889-891, 2013
6. Denburg A, Arora B, Arora RS, et al: Access to essential medicines for children with cancer: A joint SIOP-CCI position statement. Lancet Oncol 18:20-22, 2017
7. Denburg AE, Knaul FM, Atun R, et al: Beyond the bench and the bedside: Economic and health systems dimensions of global childhood cancer outcomes. Pediatr Blood Cancer 61:572-576, 2014
8. Denburg A, Cuadrado C, Alexis C, et al: Improving childhood cancer care in Latin America and the Caribbean: A PAHO Childhood Cancer Working Group position statement. Lancet Oncol 18:709-711, 2017
9. World Bank Group: Trinidad and Tobago. https://data.worldbank.org/country/trinidad-and-tobago
10. Pan American Health Organization, World Health Organization. Republic of Trinidad and Tobago: Pharmaceutical Country Profile. https://www.who.int/medicines/areas/coordination/PSCP_TRT_en.pdf?ua=1
11. Organisation for Economic Co-operation and Development: Health spending. https://data.oecd.org/healthres/health-spending.htm
12. Creswell JW, Plano Clark VL: Designing and Conducting Mixed Methods Research (ed 2). Los Angeles, CA, Sage Publications, 2011
13. Maser B, Force L, Friedrich P, et al: Pediatric Oncology System Integration Tool (POSIT): A health systems performance assessment framework for childhood cancer care in low- and middle-income countries. J Cancer Policy 100208, 2019. https://www.sciencedirect.com/science/article/pii/S2213538319300876
14. Management Sciences for Health: MDS-3: Managing Access to Medicines and Health Technologies. Arlington, VA, Management Sciences for Health, 2012
15. Athuraliya N, Walkom EJ, Dharmaratne S, et al: Assessing medication packaging and labelling appropriateness in Sri Lanka. J Pharm Policy Pract 9:38, 2016
16. Kamba PF, Ireeta ME, Balikuna S, et al: Threats posed by stockpiles of expired pharmaceuticals in low- and middle-income countries: A Ugandan perspective. Bull World Health Organ 95:594-598, 2017
17. Bigdeli M, Jacobs B, Tomson G, et al: Access to medicines from a health system perspective. Health Policy Plan 28:692-704, 2013
18. Charmaz K: Grounded theory, in Ritzer G (ed): The Blackwell Encyclopedia of Sociology. Hoboken, NJ, Blackwell Publishing, 2007, pp 2023-2027
19. Management Sciences for Health: International medical products price guide. http://mshpriceguide.org/en/home/
20. Martei YM, Chiyapo S, Grover S, et al: Availability of WHO essential medicines for cancer treatment in Botswana. J Glob Oncol 4:1-8, 2018
21. Gelders S, Ewen M, Noguchi N, et al: Price, Availability and Affordability: An International Comparison of Chronic Disease Medicines. https://apps.who.int/iris/handle/10665/116493
22. Health Quality Ontario: Quality Improvement Guide. Toronto, Ontario, Canada, Queen's Printer for Ontario, 2012
23. Organisation of Eastern Caribbean States: About the OECS. https://www.oecs.org/
24. Bahall M: Health services in Trinidad: Throughput, throughput challenges, and the impact of a throughput intervention on overcrowding in a public health institution. BMC Health Serv Res 18:129, 2018
25. Bahall M: Health equity and access to health care in Trinidad and Tobago. World J Pub Health 3:83-92, 2018
26. Hopkins J, Burns E, Eden T: International twinning partnerships: an effective method of improving diagnosis, treatment and care for children with cancer in low-middle income countries. J Cancer Policy 1:e8-e19, 2013
27. Gupta S, Rivera-Luna R, Ribeiro RC, et al: Pediatric oncology as the next global child health priority: The need for national childhood cancer strategies in low- and middle-income countries. PLoS Med 11:e1001656, 2014
28. Management Sciences for Health: Defining and Measuring Access to Essential Drugs, Vaccines, and Health Commodities: Report of the WHO-MSH Consultative Meeting, Ferney-Voltaire, France, December 11-13, 2000. Geneva, Switzerland, World Health Organization, 2000

29. Frost LJ, Reich MR: How Do Good Health Technologies Get to Poor People in Poor Countries? Boston, MA, Harvard Center for Population and Development Studies, 2010

30. Systems for Improved Access to Pharmaceuticals and Services: Systems for Improved Access to Pharmaceutical Services Annual Report: Project Year 4, October 2014–September 2015. Submitted to the US Agency for International Development by the Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program. Arlington, VA, Management Sciences for Health, 2015