Variations in global prices of chemotherapy for childhood cancer: a descriptive analysis

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Summary

Background The stark disparity in survival for children with cancer across the world has inspired a global call to expand chemotherapy access in low and middle income countries. Among the numerous barriers to success, a paucity of reliable information regarding chemotherapy pricing hinders the ability of governments and other key stakeholders to make informed budget decisions or negotiate lower medication prices. The aim of this study was to generate comparative price information on both individual chemotherapy agents and comprehensive treatment regimens for common childhood cancers using real-world data.

Methods Chemotherapy agents were selected based on their inclusion in the World Health Organization (WHO) Essential Medicines List for Children (EMLc) and their use in frontline regimens for the tracer cancer types prioritized by the WHO's Global Initiative for Childhood Cancer (GICC). Sources included IQVIA MIDAS data, obtained under license from IQVIA, and publicly available data from Management Sciences for Health (MSH). Data on chemotherapy prices and purchase volumes spanning 2012–2019 were aggregated according to WHO region and World Bank (WB) income classification. Cumulative chemotherapy prices for treatment regimens were compared across WB income classification.

Findings Data representing an estimated 1.1 billion doses of chemotherapy were obtained for 97 countries: 43 high income countries (HICs), 28 upper middle income countries (UMICs), and 26 low and lower middle income countries (LLMICs). Median drug prices in HICs were 0.9–20.4 times those of UMICs and 0.9–15.5 times those of LMICs. Regimen prices were generally higher for HICs, hematologic malignancies, non-adapted protocols, and higher risk stratification or stage, albeit with notable exceptions.

Interpretation This study represents the largest price analysis to date of chemotherapy agents used globally in childhood cancer therapy. The findings of this study form a basis for future cost-effectiveness analysis in pediatric cancer and should inform efforts of governments and stakeholders to negotiate drug prices and develop pooled purchasing strategies.

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Keywords: Pediatric oncology; Global child health; Essential medicines; Health economics; Health policy

Introduction

In high income countries (HICs), five-year net survival for children with cancer is approximately 80%[1] and continues to improve with advances in diagnostics, therapeutics, and mechanisms of supportive care. In contrast, survival among children diagnosed with cancer in low- and middle-income countries is estimated to be less than 30%,[2] resulting in a stark gap in outcomes for children who receive treatment for cancer worldwide. A major driver contributing to these differences in

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Research in context

Evidence before this study

The scarcity of publicly available data on the price of chemotherapy impedes efforts to ensure equitable and affordable access to treatment for childhood cancer. We searched PubMed from January 1, 2011, to December 31, 2020, for English language publications using a combination of the search terms "childhood," "cancer," "chemotherapy," "price," "global," and "low- and middle-income countries." Publications containing price information on chemotherapy agents for childhood cancer were limited in number and primarily reflected single-country data. The largest study previous study, conducted by the Essential Medicines Working Group of the International Society of Pediatric Oncology (SIOP), obtained price data from 42 facilities in 37 countries and noted wide variability in medication prices as well as an inconsistent relationship of prices across income groups.

Added value of this study

This study is the largest and most comprehensive real-world dataset to generate comparative price information on chemotherapy agents and regimens used in the treatment of childhood cancer, with data spanning all geographic regions and income groups and representing an estimated 1.1 billion doses between 2012 and 2019. The findings of this study corroborate prior research on the wide variability in chemotherapy pricing globally and higher drug prices in high income countries (HICs), though there was considerable overlap of prices in HICs with those of non-HICs. Generally, estimated prices of regimens were higher for non-adapted protocols, hematologic malignancies, and higher risk stratification or stage. The results provide summary price points for individual chemotherapeutics and regimen-level costs across geographic and economic groupings, which can directly inform policy decisions at local, regional, and global levels.

Implications of all the available evidence

The economic burden of cancer medicines is a particularly salient policy issue for low and middle income countries, where pharmaceuticals constitute approximately one third of total healthcare costs, and where the major source of payment is out-of-pocket expenditure. To our knowledge, the results of this study represent the first comprehensive real-world analysis of purchasing trends and costs of medications used to treat childhood cancer. As the Global Platform for Childhood Cancer Medicines and Access to Oncology Medicines begin implementing their action plans to improve global drug access, these data can provide critical inputs to support each group in drug forecasting, pooled purchase approaches, budget impact analyses, and strategic policy planning efforts.

outcomes is access to essential cancer medications. In recent years, recognition of this inequity, despite inclusion of these drugs on the World Health Organization (WHO) model list of essential medications, has inspired a global call to action. The 70th World Health Assembly (WHA) resolution on cancer prevention and control, published in 2017, highlighted the importance of ensuring access to safe, effective, and affordable medicines as part of a comprehensive cancer strategy.[3] One year later, in 2018, the WHO launched the Global Initiative for Childhood Cancer (GICC), with the goal of increasing global survival rates for childhood cancer to 60% by 2030.[4] Over the past four years, global efforts through the initiative have resulted in the formulation of the CUREALL framework and technical package with a key priority action focusing on ensuring the reliable supply of quality medicines.[5]

A major barrier to enabling access to medications is a lack of transparently available data on the purchasing price and volume of chemotherapy. Without access to this type of information, governments in low and middle income countries are unable to conduct effective forecasting, budgetary planning, and price negotiation activities related to drug procurement.[6,7] To date, existing information on the price of medicines for childhood cancer has primarily been generated by nonprofit organizations and academic institutions using adaptations of the WHO and Health Access International (HAI) survey methodology.[8,9] A recent facility-based study conducted by the International Society of Pediatric Oncology (SIOP), found wide variability in chemotherapy pricing,[6] keeping with prior work that has demonstrated variations in the price of cancer medicines across countries and regions, between medication classes and brands, and between the private and public sectors.[10]

To improve access to chemotherapy for children worldwide, greater transparency of procurement trends in the existing global marketplace is required. Stakeholders should use real-world chemotherapy costs at a national or global level and integrate these data with disease burden measures, resource-appropriate regimens, and contextually-defined treatment goals.[7,11] To address this major barrier, the goal of this study was to utilize two databases with real-world procurement data to examine global chemotherapy prices and procurement volume in order to inform multilevel policy decision-making related to drug purchasing for childhood cancer treatment.

Methods

Chemotherapy agents

Twenty-three chemotherapy agents were selected based on their use in frontline therapy for the WHO Index Cases for Childhood Cancers (acute lymphoblastic

leukemia (ALL), Burkitt lymphoma (BL), Hodgkin lymphoma (HL), retinoblastoma (RB), Wilms tumor (WT), and low-grade glioma (LGG)). Eighteen of these agents were selected from the 2015 WHO Essential Medicines List for Children (EMLc)[12]: asparaginase, bleomycin, carboplatin, cisplatin, cyclophosphamide (intravenous formulation (IV)), cytarabine, dacarbazine, dactinomycin, daunorubicin, doxorubicin, etoposide (IV), ifosfamide, mercaptopurine, methotrexate (IV and tablet), thioguanine, vinblastine, and vincristine. Five additional agents—idarubicin, pegaspargase, procarbazine, rituximab, and thiotepa—were added to the analysis based on their use in common regimens for the above cancers. Supportive care medications (e.g., mesna, leucovorin, and filgrastim) were excluded from the analysis. Steroids (e.g., dexamethasone and prednisone) were also excluded based on their common use in non-malignant conditions.

Data sources and procedures

Data sources included the *International Medical Products Price Guide*, compiled by the Management Sciences for Health (MSH), and IQVIA MIDAS® data. MSH is a global nonprofit advisory organization that supports the development of healthcare systems in low- and middle-income countries. The *International Medical Products Price Guide* contains drug prices from pharmaceutical suppliers, development organizations, and government agencies, and is a publicly available resource.[13] IQVIA is a biotechnology company that provides advanced analytics, technology solutions, and clinical research services in the health sciences industry. The MIDAS platform integrates pharmaceutical data from IQVIA national audits to generate estimates of product volumes, trends, and market share through retail and non-retail channels.[14] IQVIA MIDAS proprietary data is available only under license from IQVIA. Data were retrieved from IQVIA MIDAS and MSH databases on February 5 and February 19, 2020, respectively and analyzed using Python programming language (Python Software Foundation. Python Language Reference, version 3.10.3. Available at http://www.python.org/).

IQVIA national audits and MIDAS reflect local industry standard source of pack prices, which might be list price or average invoice price, depending upon the country and the available information; they do not reflect net prices realized by the manufacturers or achieved by the payer. Most of the drugs in question are purchased by hospitals which can receive commercial rebates, regulated rebates and claw-back, details of which are normally confidential. Sales values reflected in these IQVIA audits are calculated by applying such relevant pricing to the product volume data collected for, and reflected in, such audits. In addition, to allow the national audit sales values to be viewed at a common sales level, MIDAS applies a single average industry margin to the locally reported values. The drug price provided is an estimated price and its intended function is to convert volumes to sales—this estimated price is not intended to be used as a metric in its own right. An understanding of market dynamics in each country is required to make cross country pricing comparisons.

Data on purchase volumes and manufacturer price levels were obtained from both IQVIA MIDAS and MSH for each of the selected chemotherapy agents for the period spanning 2012 to 2019 (Table 1). Data were merged from the two sources at the country level and cross-checked for concordance when both datasets were available for a given country (Supplemental Table S1). When both datasets were available, IQVIA MIDAS data were selected for analysis due to the robustness of the dataset. Negative prices, zero quantities, unlicensed products, and products with units not typically used clinically were excluded from the analysis.

Country-level price data were available for the majority of countries in both datasets. Only regional-level data were available for the IQVIA MIDAS regions of Central America (Guatemala, Honduras, El Salvador, Nicaragua, Costa Rica, and Panama) and French West Africa (Benin, Burkina Faso, Cameroon, Chad, Gabon, Guinea, Ivory Coast, Mali, Niger, Republic of the Congo, Senegal, and Togo). For these countries we applied regional-level price values uniformly to each country in the region. All prices were reported in United States dollars (USD or $). Prices were converted to 2019 USD using the OECD inflation rate.[15]

Countries were stratified according to WHO regional classifications (African Region (AFR), Region of the Americas (AMR), Eastern Mediterranean Region (EMR), European Region (EUR), South-East Asia Region (SEAR), Western Pacific Region (WPR))[16] and 2019 World Bank (WB) income classifications (high income country (HIC), upper middle income country (UMIC), lower middle income country (LMIC), and low income country (LIC)).[17] Due to the limited number of LICs, LICs and lower middle income countries were collapsed into a single category—low and lower middle income countries (LLMICs)—for analysis. Countries in the IQVIA MIDAS regions of Central America and French West Africa had heterogeneous WB income classifications. For these countries, regional-level price data were imputed into the rest of the WB income classification groups to create a combined weighted average, using the purchase volumes and number of countries in each merged group as weights.

Statistical analysis

Adult-equivalent doses (AEDs) for each chemotherapy agent were estimated using mid-range doses for each agent and a body surface area (BSA) of 1.7 m^2 (Table 2 footnote). Estimated numbers of purchased doses were calculated using purchase volumes and AEDs. Weighted means and standard deviations were calculated for each chemotherapy agent by weighting by purchase volume.

Descriptive statistics were calculated according to country, WHO region, and WB income classification. Normality was assessed using box-and-whisker plots before applying non-parametric methods. Differences in chemotherapy prices across WB income classifications were analyzed using the non-parametric Kruskal–Wallis test. Variance in drug prices were calculated based on global values and compared across chemotherapy agents. Threshold for statistical significance was set at $p < 0.05$.

Cumulative price estimations

Cumulative doses of chemotherapy were abstracted from published protocols from international cooperative groups (e.g., International Society of Pediatric Oncology (SIOP), Children's Oncology Group (COG), Malaysia–Singapore (MASPORE)), national cooperative groups (e.g., UK Medical Research Council (MRC), Japan Association of Childhood Leukemia Study (JACLS), and academic institutions (e.g., St Jude Children's Research Hospital (SJCRH)). Protocols adapted for resource-limited settings with less capacity for supportive care (i.e., "adapted protocols") were also included (e.g. SIOP Pediatric Oncology for Developing Countries (SIOP PODC), Franco-African Pediatric Oncology Group (GHFAOP), International Network for Cancer Treatment and Research (INCTR)) (Supplemental Tables S7–S12).

Epidemiologic data from Surveillance, Epidemiology, and End Results (SEER),[18] Centers for Disease Control (CDC),[19] and WHO[20] were used to estimate the mean age (years), weight (kg), and body surface area (BSA) (m^2) of a typical patient with each cancer subtype (ALL: 5.5 years, 19.2 kg, 0.77 m^2; BL: 8.1 years, 25.8 kg, 0.96 m^2; HL: 10.7 years, 35.4 kg, 1.18 m^2; RB: 1.2 years, 9.9 kg, 0.47 m^2; WT: 3.2 years, 14.5 kg, 0.62 m^2; LG: 6.8 years, 22.3 kg, 0.86 m^2). Cumulative chemotherapy doses were calculated for each treatment regimen based on BSA, with the exception of regimens for retinoblastoma. Cumulative doses for these regimens were calculated based on weight, consistent with standard practice for patients weighing less than 10 kg. Doses of intrathecal chemotherapy were calculated based on age for ALL and BL. CNS2 status (presence of leukemic cells in a cerebrospinal fluid sample containing fewer than 5 white blood cells (WBCs)/μL) was used for ALL treatment regimens as a simplifying assumption. The duration of maintenance therapy was estimated to be the same for males and females. As pegaspargase was not available in LLMICs, an equivalent cumulative dose of native *E. coli* asparaginase was estimated using a bioequivalence ratio of one unit of pegaspargase to 24 units of *E. coli* asparaginase.[21] (A range of bioequivalence approaches from 1:6 to 1:24 could be appropriate because pegaspargase is dosed at 2500 International Units (IU)/m^2 and native *E. coli* asparaginase has a range of dosing from 6,000 to 25,000 IU/m^2, from every other day to weekly, with two weeks of native *E.coli* asparaginase dosing for each dose of pegasparaginase.) No other drug substitutions were used. Cumulative doses of chemotherapy for all treatment regimens were calculated without modifications for treatment toxicities and assuming completion of therapy.

Role of the funding source

TY and YC accessed the IQVIA MIDAS and MSH databases on February 5 and February 19, 2020, respectively. All authors and IQVIA approved the decision to submit for publication. While authors received grant funding for separate research as disclosed, there was no funding directly for the research presented in this manuscript.

Results

Chemotherapy

Data on selected chemotherapy agents were available for 97 countries: 43 (44.3%) HICs, 28 (28.9%) upper middle income countries (UMICs), and 17 (17.5%) lower middle income countries (LMICs), and 9 (9.3%) low income countries (LICs). Nineteen countries (19.6%) were part of AFR, 20 (20.6%) AMR, 9 (9.3%) EMR, 33 (34.0%) EUR, 5 (5.2%) SEAR, and 11 (11.3%) WPR. Estimated market segment coverage by IQVIA MIDAS (percentage of the total national pharmaceutical market represented by the audit) ranged from 35% to 100% (median 89%, IQR 80–99). Eleven (11.3%) countries had price data on one to nine chemotherapy agents, 3 (3.1%) had 10 to 14, 51 (52.6%) had 15 to 20, and 32 (33%) had 20 or greater.

The total purchase volume for all selected chemotherapy agents exceeded 180,000 kg and represented an estimated 1.1 billion adult doses globally from 2012 to 2019 (Tables 1 and 2, Supplemental Tables S2 and S3). Of the total number, an estimated 734 million doses (65.9%) were purchased by HICs, 229 million (20.5%) were from UMICs, 150 million (13.4%) were from LLMICs, and one million (0.1%) were from regional data and unclassifiable by income (Table 2).

Globally, the weighted mean price per mid-range dose for a pediatric patient (BSA 1.0 m^2) was lowest for mercaptopurine ($1.67) and highest for thiotepa ($3,450.20). Differences in weighted mean prices were statistically significant across income levels for all agents except thiotepa, for which prices were similar across income categories (Supplemental Table S4). In general, median drug prices were highest in HICs, ranging from 0.9–20.4 times those of UMICs and 0.9–15.5 times those of LMICs (Table 3). Deviations from this trend included cytarabine and idarubicin, for which median prices were highest in UMICs, and bleomycin, for which median prices were highest in LLMICs (Supplemental Table S4). The trend towards higher prices in HICs was not driven solely by higher drug prices in the United States (Supplemental Table S4).

Drug (dosage form)	Total purchase volume (%)				
	HIC	UMIC	LLMIC	Regional[a]	Total
Asparaginase (IV)	6,160,000,000 IU (26.3%)	12,900,000,000 IU (55.1%)	4,370,000,000 IU (18.7%)	2,430,000 IU (<0.1%)	23,415,000,881 IU (100%)
Bleomycin (IV)	202 kg (41.5%)	156 kg (32.0%)	129 kg (26.5%)	20 g (<0.1%)	487 kg (100%)
Carboplatin (IV)	9134 kg (62.4%)	3770 kg (25.7%)	1737 kg (11.9%)	3 kg (<0.1%)	14,644 kg (100%)
Cisplatin (IV)	1740 kg (41.7%)	2002 kg (48.0%)	431 kg (10.3%)	1 kg (<0.1%)	4173 kg (100%)
Cyclophosphamide (IV)	20,476 kg (50.1%)	17,160 kg (42.0%)	3207 kg (7.8%)	16 kg (<0.1%)	40,860 kg (100%)
Cytarabine (IV)	14,253 kg (62.5%)	7214 kg (31.6%)	1340 kg (5.9%)	2 kg (<0.1%)	22,809 kg (100%)
Dacarbazine (IV)	1744 kg (65.7%)	757 kg (28.5%)	156 kg (5.9%)	228 g (<0.1%)	2657 kg (100%)
Dactinomycin (IV)	274 g (35.9%)	422 g (55.3%)	67 g (8.8%)	–	764 g (100%)
Daunorubicin (IV)	62 kg (45.7%)	60 kg (43.7%)	14 kg (9.9%)	13 g (<0.1%)	136 kg (100%)
Doxorubicin (IV)	947 kg (55.0%)	442 kg (25.7%)	169 kg (9.8%)	1.31 kg (0.1%)	1559 kg (100%)
Etoposide (IV)	2870 kg (53.5%)	2193 kg (40.9%)	301 kg (5.6%)	816 g (<0.1%)	5365 kg (100%)
Idarubicin (IV)	12 kg (58.2%)	8 kg (40.3%)	296 g (1.4%)	1 g (<0.1%)	20 kg (100%)
Ifosfamide (IV)	11,591 kg (56.7%)	7699 kg (37.7%)	1156 kg (5.7%)	1 kg (<0.1%)	20,447 kg (100%)
Mercaptopurine (tab)	19,611 kg (86.6%)	1973 kg (8.7%)	1074 kg (4.7%)	603 g (<0.1%)	22,658 kg (100%)
Methotrexate (IV)	9105 kg (62.9%)	4078 kg (28.2%)	1273 kg (8.8%)	3 kg (<0.1%)	14,459 kg (100%)
Methotrexate (tab)	13,693 kg (62.5%)	4284 kg (19.6%)	3890 kg (17.8%)	46 kg (0.2%)	21,913 kg (100%)
Pegaspargase (IV)	689,809,452 IU (46.4%)	798,307,440 IU (53.6%)	–	–	1,488,116,892 IU (100%)
Procarbazine (IV)	623 kg (82.6%)	84 kg (11.1%)	48 kg (6.3%)	–	754 kg (100%)
Rituximab (IV)	10,761 kg (85.8%)	1571 kg (12.5%)	203 kg (1.6%)	3.1454 kg (<0.1%)	12,538 kg (100%)
Thiotepa (IV)	26 kg (98.1%)	500 g (1.9%)	–	–	26 kg (100%)
Thioguanine (tab)	324 kg (90.4%)	22 kg (6.2%)	12 kg (3.5%)	–	358 kg (100%)
Vincristine (IV)	29 kg (70.0%)	10 kg (23.9%)	3 kg (6.1%)	2 gm (<0.1%)	41 kg (100%)

HIC: high income countries; UMIC: upper middle income countries; LLMIC: low and lower middle income countries; IV: intravenous; tab: tablet; IU: international unit; kg: kilogram; g: gram. Source: This is based on internal analysis by Catherine Habashy, Tatenda Yemeke, Nancy Bolous, Yichen Chen, Sachiko Ozawa, Nickhill Bhakta, and Thomas Alexander using data from the following source: IQVIA MIDAS Quarterly Sales for the period 2012–2019 reflecting estimates of real-world activity. [a]Regional category comprised of the Central America region (Guatemala, Honduras, El Salvador, Nicaragua, Costa Rica, and Panama) and the French West Africa region (Benin, Burkina Faso, Cameroon, Chad, Gabon, Guinea, Ivory Coast, Mali, Niger, Republic of the Congo, Senegal, and Togo).

Table 1: **Total purchase volume by World Bank Country income classification (97 countries, 2012–2019).**

The relationship of drug prices in UMICs and LLMICs was inconsistent, with instances of higher drug prices in LLMICs compared with UMICs. Wide variations in pricing were noted with considerable overlap of prices in HICs with those of non-HICs (Fig. 1). While not powered for statistical significance, there may be a relationship between increasing purchase volumes or estimated AEDs and decreasing variance in price (Supplemental Table S6). This relationship should be explored with future chemotherapy pricing datasets. No suggestion of associations were observed between variance in drug pricing of chemotherapy agents and the number of manufacturers or length of time the drug had been on the market (Supplemental Table S6).

Treatment regimens

Wide ranges in estimated regimen prices were observed for all cancer subtypes. Estimated regimen prices were highest for ALL, with median regimen prices 2.0–8.2 times higher for ALL than other cancer subtypes when compared within income classifications.

Estimated prices for ALL regimens ranged widely from $519 (SIOP 1, LLMIC) to $34,960 (SJ TOTALXVI SR/HR) (Table 4). Prices for all regimens followed a predictable trend with the highest prices in HICs, lowest prices in LLMICs, and intermediate prices in UMICs. Within income classifications, median prices for non-adapted regimens were 1.7–2.3 times higher than those of adapted regimens (SIOP 1–4). Among adapted regimens, mercaptopurine was the primary driver of price, constituting 43–60% of the total regimen price for LLMIC and 42–57% of the total regimen price in UMIC (Fig. 2). Increasing intensity of adapted regimens for ALL had only minor influence on regimen price ($516 for SIOP 1 versus $660 for SIOP 4 in LLMICs). Among non-adapted regimens, pegaspargase was the primary driver of prices, constituting 37–89% of the total regimen price. Median prices for high-risk treatment regimens were 1.9–2.6 times higher than regimens for low-risk disease, primarily due to higher cumulative dosages of pegaspargase.

Estimated prices for BL regimens also ranged widely from $38 (SIOP Risk Group 1, UMICs) to $15,303 (ANHL 1131 Arm C, HICs) (Fig. 3). In general, median regimen prices were 3.7 times higher in HICs compared with UMICs and LLMICs, which were equivalent. For several regimens (SIOP, Malawi CHOP, INCTR, JOORTH, BFM, POG 9219), estimated prices in LLMICs exceeded those of UMICs, due to higher prices of cyclophosphamide, doxorubicin, and ifosfamide in

Drug (Dosage form)	Estimated number of adult-equivalent doses[b]				
	HIC	UMIC	LLMIC	Regional[a]	Total
Asparaginase (IV)	603,922	1,264,706	428,431	238	2,297,297
Bleomycin (IV)	11,890,300	9,187,429	7,590,894	1200	28,669,824
Carboplatin (IV)	13,432,005	5,544,250	2,553,904	4618	21,534,778
Cisplatin (IV)	13,644,515	15,701,673	3,378,593	8498	32,733,279
Cyclophosphamide (IV)	16,059,863	13,459,110	2,515,115	12,770	32,046,858
Cytarabine (IV)	4,192,125	2,121,828	394,152	533	6,708,638
Dacarbazine (IV)	2,736,444	1,186,689	244,061	358	4,167,551
Dactinomycin (IV)	161,413	248,472	39,471	–	449,357
Daunorubicin (IV)	815,866	780,922	176,756	163	1,773,708
Doxorubicin (IV)	11,140,778	5,203,585	1,984,311	15,400	18,344,074
Etoposide (IV)	16,883,987	12,902,134	1,768,036	4802	31,558,959
Idarubicin (IV)	583,735	404,770	14,515	44	1,003,064
Ifosfamide (IV)	5,681,916	3,774,132	566,580	270	10,022,898
Mercaptopurine (tab)	192,268,861	19,340,329	10,526,248	5909	222,141,347
Methotrexate (IV)	5,355,806	2,398,830	748,935	1500	8,505,071
Methotrexate (tab)	402,739,733	126,013,883	114,410,730	1,347,432	644,511,778
Pegaspargase (IV)	162,308	187,837	–	–	350,145
Procarbazine (IV)	6,103,249	823,475	466,319	–	7,393,043
Rituximab (IV)	16,879,789	2,463,701	318,450	4934	19,666,873
Thiotepa (IV)	60,750	1178	–	–	61,928
Thioguanine (tab)	3,172,992	217,120	121,341	–	3,511,453
Vincristine (IV)	6,830,591	4,133,413	1,134,354	11,569	12,109,926

HIC: high income countries; UMIC: upper middle income countries; LLMIC: low and lower middle income countries; IV: intravenous; tab: tablet; IU: international unit; kg: kilogram; g: gram. Source: This is based on internal analysis by Catherine Habashy, Tatenda Yemeke, Nancy Bolous, Yichen Chen, Sachiko Ozawa, Nickhill Bhakta, and Thomas Alexander using data from the following source: IQVIA MIDAS Quarterly Sales for the period 2012–2019 reflecting estimates of real-world activity. [a]Regional category comprised of the Central America region (Guatemala, Honduras, El Salvador, Nicaragua, Costa Rica, and Panama) and the French West Africa region (Benin, Burkina Faso, Cameroon, Chad, Gabon, Guinea, Ivory Coast, Mali, Niger, Republic of the Congo, Senegal, and Togo). [b]Estimated number of adult doses calculated using BSA of 1.7 m^2 and the following dosages: Asparaginase 6000 IU/m^2; Bleomycin 10 USP/m^2; Carboplatin 400 mg/m^2; Cisplatin 75 mg/m^2; Cyclophosphamide 750 mg/m^2; Cytarabine 2000 mg/m^2; Dacarbazine 375 mg/m^2; Dactinomycin 1000 mcg/m^2; Daunorubicin 45 mg/m^2; Doxorubicin 50 mg/m^2; Etoposide 100 mg/m^2; Idarubicin 12 mg/m^2; Ifosfamide 1200 mg/m^2; Mercaptopurine 60 mg/m^2; Methotrexate IV 1000 mg/m^2; Methotrexate tab 20 mg/m^2; Pegaspargase 2500 IU/m^2; Procarbazine 60 mg/m^2; Rituximab 375 mg/m^2; Thiotepa 250 mg/m^2; Thioguanine 60 mg/m^2; Vinblastine 6 mg/m^2; Vincristine 1.5 mg/m^2.

Table 2: **Estimated number of adult-equivalent doses by World Bank Country income classification (97 countries, 2012–2019).**

LLMICs. Among adapted regimens, the primary drivers of prices were cyclophosphamide and methotrexate (IV). Among non-adapted regimens, the primary driver of price was rituximab, which increased cumulative prices by 2.9–12.2 times when added to the chemotherapy backbone.

Estimated prices for HL regimens ranged from $153 (Malawi OEPA, LLMIC) to $3,005 (BEACOPP, HICs). Regimen prices in HICs were 2.8 and 3.4 times those in UMICs and LLMICs respectively. For certain regimens (ABVD, ABVE-PC), estimated prices in LLMICs exceeded those of UMICs, due to higher prices of bleomycin, cyclophosphamide, doxorubicin, etoposide, and vinblastine in LLMICs.

Estimated prices for WT regimens ranged from $116 (SIOP LOC1, LLMICs) to $4,397 (SIOP MET, 9 pre-op, AV26 post-op) for adapted regimens and $260 (EE4-A, LMICs) to $2,197 (Reg UH-1, HICs) for non-adapted regimens. Overall, median prices in HICs were 6.2 and 6.5 times higher than those of UMICs and LLMICs respectively. Dactinomycin was the primary driver of price for adapted regimens and contributed to their prices being 1.4–1.6 times higher than non-adapted regimens.

Estimated prices for LGG regimens ranged from $140 (SIOP 2, UMICs) to $1,638 (single agent Carboplatin, HICs). For regimens containing vinblastine (SIOP LGG 2, ARIA 3), estimated prices were 27% higher in LLMICs compared with UMICs due to the higher price of vinblastine in LLMICs. Estimated prices for RB regimens ranged from $95 (SJ RET5 VDC-VCE, LLMICs) to $1,601 (SIOP CE/CIV, HICs) for those without autologous transplant and up to $5,222 (ARET 0321, HICs) for regimens utilizing thiotepa for pre-transplant conditioning.

Discussion

Over the past four years, the WHO GICC has increased awareness among all childhood cancer stakeholders that global solutions to address gaps in quality drug access are necessary. Two major initiatives targeting this issue were launched in response over the past year. The WHO-St. Jude Children's Research Hospital Global

Chemotherapy		WB income classification			WHO region					
Name (Dosage form)	Dose range	HIC	UMIC	LLMIC	AFRO	AMR	EMRO	EURO	SEARO	WPRO
Asparaginase (IV)	6000 IU/m^2	31.10	21.50	21.03	47.56	43.13	21.05	36.17	15.78	18.78
Bleomycin (IV)	5 mg/m^2–15 mg/m^2	5.02–15.06	3.83–11.48	5.52–16.55	7.46–22.37	9.74–29.22	6.33–18.99	2.66–7.98	5.83–17.48	10.44–31.31
Carboplatin (IV)	100 mg/m^2–600 mg/m^2	19.24–115.44	9.02–54.12	8.63–51.78	5.97–35.82	7.27–43.62	9.74–58.44	20.44–122.64	9.33–55.98	19.91–119.46
Cisplatin (IV)	20 mg/m^2–100 mg/m^2	7.67–38.35	1.89–9.46	1.38–6.90	3.04–15.19	4.00–20.01	0.32–1.61	3.88–19.38	1.29–6.44	6.22–31.10
Cyclophosphamide (IV)	250 mg/m^2–2100 mg/m^2	40.88–343.35	2.00–16.80	2.93–24.57	2.48–20.79	99.28–833.91	1.45–12.18	6.25–52.50	3.30–27.72	2.70–22.68
Cytarabine (IV)	50 mg/m^2- 3000 mg/m^2	1.35–81.00	1.45–87.00	0.65–39.00	1.00–59.70	0.55–32.70	0.79–47.10	1.32–79.20	1.06–63.30	2.03–121.80
Dacarbazine (IV)	375 mg/m^2–800 mg/m^2	28.76–61.36	24.64–52.56	19.91–42.48	48.30–103.04	22.95–48.96	15.83–33.76	19.43–41.44	38.59–82.32	49.09–104.72
Dactinomycin (IV)	45 mcg/kg	583.99	82.22	64.47	148.25	1632.56	247.56	120.71	13.57	77.00
Daunorubicin (IV)	20 mg/m^2–60 mg/m^2	37.02–111.07	4.17–12.52	7.72–23.15	14.36–43.09	69.97–209.91	8.51–25.52	18.56–55.67	7.47–22.40	7.89–23.66
Doxorubicin (IV)	20 mg/m^2–75 mg/m^2	12.12–45.47	6.84–25.65	8.61–32.28	5.24–19.67	6.22–23.34	6.15–23.07	11.37–42.65	11.10–41.63	14.25–53.45
Etoposide (IV)	75 mg/m^2–200 mg/m^2	9.45–25.20	2.18–5.80	2.63–7.00	6.83–18.20	5.27–14.04	4.06–10.82	7.54–20.10	3.14–8.38	5.67–15.12
Idarubicin (IV)	5 mg/m^2–12 mg/m^2	79.49–190.78	126.57–303.76	82.31–197.53	51.55–123.72	52.33–125.58	61.89–148.54	74.47–178.73	102.34–245.62	139.92–335.80
Ifosfamide (IV)	1800 mg/m^2–5000 mg/m^2	59.58–165.50	32.58–90.50	60.48–168.00	72.54–201.50	56.16–156.00	46.98–130.50	57.60–160.00	69.12–192.00	35.82–99.50
Mercaptopurine (tab)	50 mg/m^2–75 mg/m^2	1.55–2.33	0.49–0.74	0.22–0.33	2.77–4.16	1.30–1.94	0.59–0.88	1.96–2.93	0.20–0.29	1.04–1.55
Methotrexate (IV)	100 mg/m^2–12000 mg/m^2	8.64–1036.80	2.89–346.80	2.80–336.00	3.13–375.60	5.39–646.80	3.23–387.60	9.17–1100.40	2.64–316.80	6.36–763.20
Methotrexate (tab)	20 mg/m^2	4.69	1.16	0.41	0.78	6.17	0.75	1.00	0.44	5.95
Pegaspargase (IV)	2500 IU/m^2	3254.50	333.25	–	–	4384.75	1139.25	1166.00	–	313.00
Procarbazine (IV)	50 mg/m^2–100 mg/m^2	5.57–11.13	3.00–5.99	0.51–1.02	6.56–13.12	56.33–112.66	3.54–7.08	4.20–8.39	0.34–0.68	1.03–2.05
Rituximab (IV)	375 mg/m^2	1737.68	867.26	650.03	756.19	2336.44	1138.05	1064.55	624.41	1186.76
Thiotepa (IV)	200 mg/m^2–300 mg/m^2	2766.46–4149.69	2435.14–3652.71	–	–	9055.38–13,583.07	–	1914.32–2871.48	–	707.28–1060.92
Thioguanine (tab)	30 mg/m^2–100 mg/m^2	5.72–19.05	2.40–8.01	0.37–1.23	4.44–14.79	10.06–33.54	1.67–5.55	4.81–16.03	0.54–1.80	4.16–13.88
Vinblastine (IV)	6 mg/m^2	12.48	3.12	3.98	1.20	17.12	4.55	8.22	2.95	14.35
Vincristine (IV)	1 mg/m^2–2 mg/m^2	8.73–17.46	3.00–6.01	2.64–5.28	3.64–7.27	4.93–9.86	3.46–6.92	6.05–12.10	2.64–5.28	8.35–16.70

USD: United States dollars; WB: World Bank; WHO: World Health Organization; HIC: high income countries; UMIC: upper middle income countries; LLMIC: low and lower middle income countries; AFR: African Region; EMR: Eastern Mediterranean Region: EUR: European Region; AMR: Region of the Americas; SEAR: South-East Asian Region; WPR: Western Pacific Region; IV: intravenous; tab: tablet; IU: international unit; kg: kilogram; g: gram; mg: milligram; m: meter. Source: This is based on internal analysis by Catherine Habashy, Tatenda Yemeke, Nancy Bolous, Yichen Chen, Sachiko Ozawa, Nickhill Bhakta, and Thomas Alexander using data from the following source: IQVIA MIDAS Quarterly Sales for the period 2012–2019 reflecting estimates of real-world activity.

Table 3: **Weighted mean prices of typical chemotherapy doses in USD, standard pediatric patient (29 kg, BSA 1 m^2).**

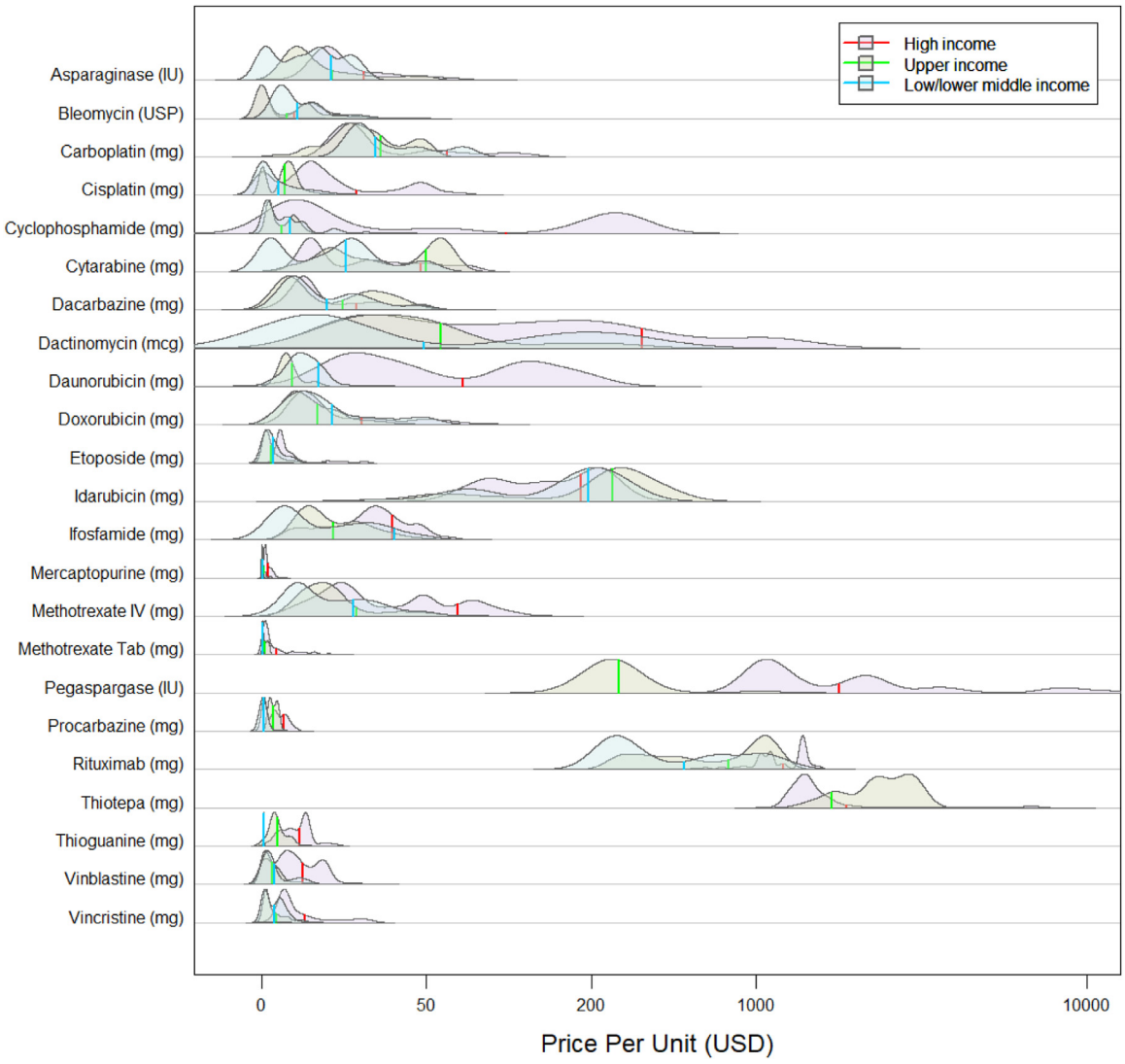

Fig. 1: **Price distribution (in USD) per unit by World Bank income classification.**

Platform for Childhood Cancer Medicines (GPCCM) was announced in 2021 as part of a USD $200 million commitment by St. Jude to ensure an uninterrupted supply of quality childhood cancer medications in 50 countries over the next six years.[22] Additionally, a partnership of multiple organizations, led by the Union for International Cancer Control, announced the Access to Oncology Medicines (ATOM) Coalition in early 2022 with the goal of increasing the availability and affordability of cancer medicines.[23] As these initiatives begin to implement their programs, methods utilizing real-world data to guide planning and monitor progress are needed.

As these initiatives and others begin to scale-up activities in the coming months, the data from this study will provide the stakeholders the largest price analysis to date of chemotherapy agents and regimens used in the treatment of childhood cancer. To our knowledge, this is also the first study to leverage multi-year real-world market data, rather than facility-based data, to evaluate trends and variations in procurement prices and volumes at the country level. Broadly, our findings do corroborate prior smaller research studies demonstrating wide variation of individual chemotherapy prices at the facility level.[8–10] However, with a more representative dataset, these outputs should help provide more certainty for both the large initiatives recently announced as well as individual ministries of health when planning procurements and negotiating prices.

As highlighted by the GICC, the economic burden of chemotherapy is a particularly salient policy issue for many low- and middle-income countries, where

Regimen	HICs	UMICs	LLMICs
ALL (5.5 years, 19.2 kg, 0.77 m^2)			
Adapted regimens			
SIOP regimen 2	$2542	$903	$607
SIOP regimen 4	$2841	$960	$660
Non-adapted regimens			
COG AALL 0932 SR, Arm C	$7130	$1176	$709[a]
COG AALL 1131 HR	$16,377	$2442	$1481[a]
St Jude TOTAL XV LR	$3870	$1634	$1372
St Jude TOTAL XV SR/HR	$5961	$2802	$2438
St Jude TOTAL XVI LR	$18,759	$2521	$1647[a]
St Jude TOTAL XVI SR/HR	$34,960	$4532	$2987[a]
UK MRC SR	$6271	$1079	$646[a]
UK MRC HR	$16,650	$2156	$1401[a]
MA-SPORE 03 SR	$2644	$942	$708
MA-SPORE 03 HR	$5730	$2005	$1546
JACLS ALL 202-U (CNS pos)	$3684	$1486	$1408
Burkitt lymphoma (8.1 years, 25.8 kg, 0.96 m^2)			
Adapted regimens			
Malawi CHOP (6 Cycles)	$974	$139	$174
GFAOP Stage I-III (COPM-CYM)	$1606	$402	$386
INCTR LR	$629	$53	$61
INCTR HR	$1259	$105	$122
JOORTH	$2710	$281	$326
MWI LMB 89 (COP-COMP-CYM-COMP)	$1205	$340	$322
Non-adapted regimens			
BFM Risk Group 1	$519	$166	$217
BFM Risk Group 2	$1160	$370	$481
BFM Risk Group 3[b]	$2874	$1178	$1082
BFM Risk Group 4[b]	$3243	$1521	$1243
COG ANHL1131B (COP-COPADM-CYM)	$1662	$445	$438
COG ANHL1131B (COP-R-COPADM-R-CYM)	$11,671	$5441	$4183
Hodgkin lymphoma (10.7 years, 35.4 kg, 1.18 m^2)			
ABVD (6 Cycles)	$941	$622	$647
ABVE-PC (5 Cycles)	$1849	$340	$428
OPPA-COPP (2 Cycles/4 Cycles)	$2285	$812	$310
OEPA-COPDAC (2 Cycles/4 Cycles)	$1560	$453	$441
BEACOPP (4 Cycles/4 Cycles)	$3005	$761	$546
Low Grade Glioma (6.8 years, 22.3 kg, 0.86 m^2)			
Adapted regimens			
SIOP 1 CV	$1601	$721	$684
ARIA 1 Carbo (12 months)	$1092	$512	$490
ARIA 1 Carbo (18 months)	$1638	$768	$735
ARIA 2 COG A9952	$1462	$648	$612
ARIA 3 VB	$752	$188	$239
Retinoblastoma (1.2 years, 9.9 kg, 0.47 m^2)			
Adapted regimens			
SIOP 1 VCE (6 Cycles)	$281	$117	$114
SIOP 3/4 CE/CIV (4 Cycles/4 Cycles)	$1061	$643	$481
Non-adapted regimens			
SJCRH RET5 VCE/VCD (3 Cycles/3 Cycles)	$380	$89	$95
COG ARET 0321	$5222	$3750	–
Wilms Tumor (3.2 years, 14.5 kg, 0.62 m^2)			
Adapted regimens			
SIOP Loc 1	$942	$146	$116
SIOP AFR Coop Met 6 Pre/AV14 Post	$2523	$408	$343
SIOP AFR Coop Met 9 Pre/AV26 Post	$4397	$708	$594
Non-adapted regimens			
EE 4A	$2159	$327	$260
DD 4A	$1653	$284	$242
DD 4A-regimen M	$1937	$281	$277
Regimen UH-1	$2197	$356	$397

(Table 4 continues on next column)

(Continued from previous column)

Source: This is based on internal analysis by Catherine Habashy, Tatenda Yemeke, Nancy Bolous, Yichen Chen, Sachiko Ozawa, Nickhill Bhakta, and Thomas Alexander using data from the following source: IQVIA MIDAS Quarterly Sales for the period 2012–2019 reflecting estimates of real-world activity. Copyright IQVIA. All rights reserved. [a]Asparaginase substituted using ratio 1 IU/m^2 Pegaspargase: 24 IU/m^2 native *E.coli*-Asparaginase. [b]Price data on Vindestine not included in total regimen price.

Table 4: **Comparative regimen prices in USD by World Bank Country income classification.**

pharmaceuticals constitute approximately one third of total healthcare costs and where the major source of payment is out-of-pocket expenditure.[24] Medicines in these settings are commonly the largest family expenditure item after food,[25] and financial constraints are a more important cause of treatment refusal than misperceptions about the curability of childhood cancer.[26] A recent study examining the affordability of cancer medicines in Ghana estimated that the cost of medicines to treat a child with ALL or retinoblastoma exceeded 400-days wages for the lowest-paid unskilled worker.[8]

Examining prices of chemotherapy as regimens rather than individual drugs provide a template for future market-shaping initiatives. The evaluation of costs and procurement planning of single drugs in isolation may lead to practices that inadvertently limit improvements in childhood cancer survival. In this manuscript, we provide a reproducible approach to costing that other groups may incorporate as a factor when designing and choosing between regimens where variations in survival outcomes may exist. For example, our data shows wide variation in estimated prices between treatment regimens for the same cancer subtype. On specific occasions, estimated prices of adapted protocols surpassed those of non-adapted protocols; adapted protocols for WT were more expensive than non-adapted protocols due to the costs and cumulative dose of dactinomycin. Although an older, generic medication, dactinomycin is not used in adult cancers and thus global volumes are small, a likely contributing factor to the higher price observed. These findings

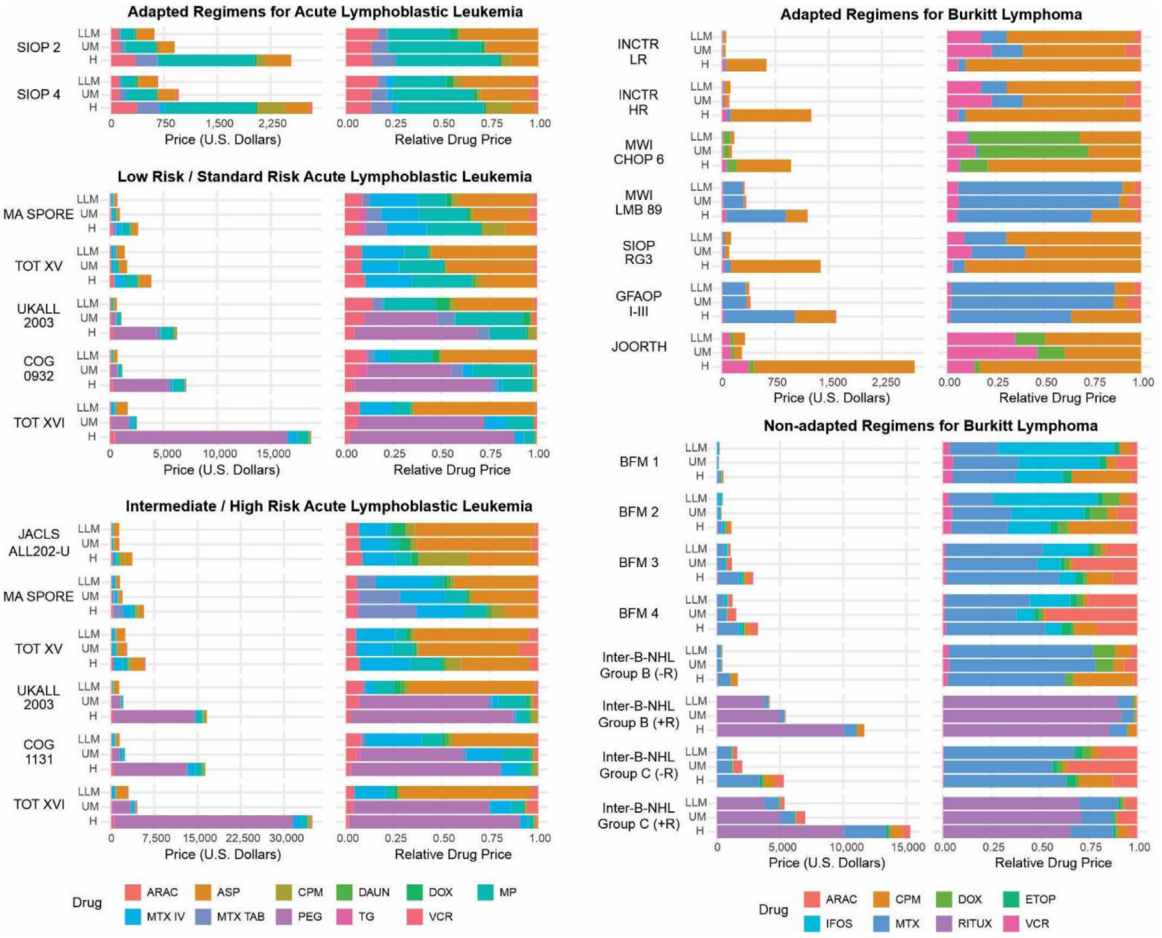

Fig. 2: **Estimated Prices of Treatment Regimens for Acute Lymphoblastic Anemia and Burkitt Lymphoma Compared Across World Bank Country Income Groups.** LLM: low and lower-middle income countries; UM: upper middle income countries; H: high income countries; ARAC: cytarabine. ASP: asparaginase. CPM: cyclophosphamide. DAUN: daunorubicin. DOX: doxorubicin. ETOP: etoposide. IFOS: ifosfamide. MP: mercaptopurine. MTX: methotrexate. PEG: pegaspargase. RITUX: rituximab. TG: thioguanine. VCR: vincristine. Source: This is based on internal analysis by Catherine Habashy, Tatenda Yemeke, Nancy Bolous, Yichen Chen, Sachiko Ozawa, Nickhill Bhakta, and Thomas Alexander using data from the following source: IQVIA MIDAS Quarterly Sales for the period 2012–2019 reflecting estimates of real-world activity.

highlight the importance of judicious selection of upfront treatment regimens based upon toxicity, efficacy, and cost, in concert with attempts to reduce prices of individual agents.

Our study findings also highlight the financial implications of treating advanced disease. Not surprisingly, regimen prices were generally higher for cancers of higher risk stratification or stage. This finding is particularly relevant for policy makers in low- and middle-income countries, where late presentation of disease is much more common than in HICs.[27] Implementation of early detection programs targeted at treatable cancers may have both survival and financial benefits in these settings. Additionally, these data can play an important role when exploring opportunity costs for novel therapies in low- and middle-income countries. Novel therapies introduced in HICs are rarely available in low- and middle-income countries for a variety of regulatory and practical reasons.[28] However, affordability is also a key barrier. For example, the addition of rituximab to a chemotherapy backbone for the treatment of pediatric mature B-cell lymphoma has become standard of care in HICs but remains out of reach in many low- and middle-income countries due to the near order in magnitude increase in price. While the additional survival benefit of rituxmab in HICs has been modest, it is conceivable that the addition of targeted therapies, such as rituxumab for mature B-cell lymphoma or blinatumomab for B-ALL to lower intensity regimens in LMICs could result in a more significant survival benefit with lower treatment-related toxicity.[28] Using a comparative regimen approach, combined

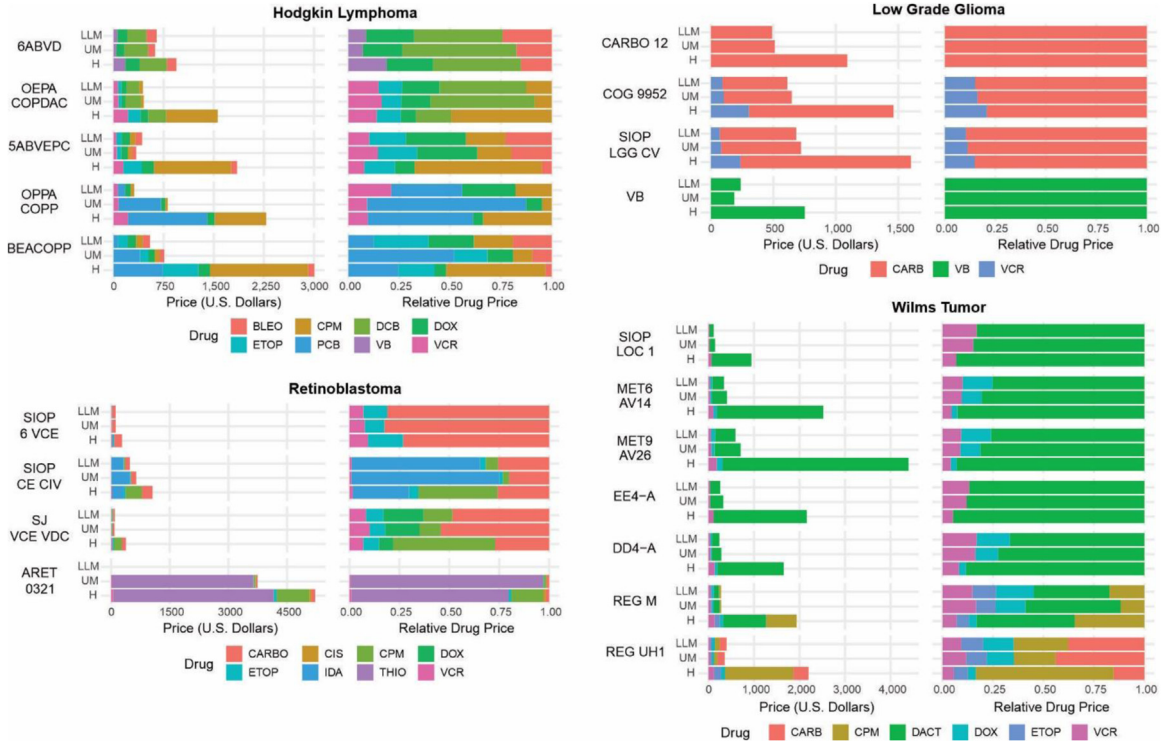

***Fig.* 3: Estimated Prices of Treatment Regimens for Hodgkin Lymphoma, Low Grade Glioma, Retinoblastoma, and Wilms Tumor Compared Across World Bank Country Income Groups.** Abbreviations: CARBO: carboplatin. CIS: cisplatin. CPM: cyclophosphamide. DACT: dactinomycin. DOX: doxorubicin. ETOP: etoposide. IDA: idarubicin. THIO: thiotepa. VCR: vincristine. Source: This is based on internal analysis by Catherine Habashy, Tatenda Yemeke, Nancy Bolous, Yichen Chen, Sachiko Ozawa, Nickhill Bhakta, and Thomas Alexander using data from the following source: IQVIA MIDAS Quarterly Sales for the period 2012–2019 reflecting estimates of real-world activity.

with increased transparency and graphically depicting price variations, advocates can use the data from this study to support market-shaping initiatives and ultimately increase access to novel therapies in low- and middle-income countries.

From a policy perspective, these data highlight the power of pooled procurement interventions. Prior work has posited that income-related price discrimination and market competition alone are unlikely to lead to affordable medication prices in low and middle income countries.[29] Governments in these settings participate in a number of cost control strategies including internal and external reference pricing, promotion of generic medicines, regulation of mark-ups, application of cost-based pricing, and tax exemptions and reductions for pharmaceutical products.[30] The recent technical report to the WHO highlights the potential roles of negotiated tendering and pooled procurement as additional price control strategies. The report encourages transparency through disclosure of price information in order to ensure accountability and promote efficiency in pharmaceutical markets.[3] Our data summaries can provide another basis for nongovernmental associations and ministries of health to argue for cost transparency across geographical regions and country income levels.

Pooled procurement refers to the practice of combining financial and non-financial resources across purchasing authorities in order to increase negotiating power.[5] It has historical precedent as a cost-reduction strategy in the treatment of HIV/AIDS, tuberculosis, and malaria, where pooled procurement was demonstrated to reduce originator and generic prices by 42.4% and 35% respectively,[31] and more recently in the treatment of Hepatitis C, where pooled procurement of direct-acting antivirals reduced prices by up to 99%.[32] Our study observed a potential relationship between increasing purchase volumes and decreasing variance in prices, suggesting that pooled procurement may be beneficial in price stabilization. Pooled procurement has the additional benefits of increasing resiliency of supply chains and reducing quality uncertainty by imposing minimum quality standards. It holds potential for cancer treatment, not only as a cost-reduction strategy but also as a stabilizing force for supply chains and as a signal for drug quality in markets where drug regulation may be lacking.[33]

This study has several limitations. As with prior studies, the distribution of data was skewed towards HICs, with less data originating from low- and middle-income countries and particularly sub-Saharan Africa. Regional-level data were extrapolated to country-level data for Central America and West Africa, which may have limited our country level assessment of price variation in these regions. Once the data were weighted by volume, the contribution of these regions to the overall results was negligible as the relative volume of drug purchased in these regions was small (Supplemental Table S13). The data reflects years prior to the COVID-19 pandemic and therefore cannot account for changes associated with the worldwide supply chain disruption. Wholesale prices were used for comparison, thus omitting the contribution of duties, taxes, mark-ups, distribution costs, and dispensing fees, which regularly constitute between 30 and 45% of retail prices.[34] As a result, it is likely that variability in retail drug pricing is higher than is reflected in our findings. Prices were collected from different sources in each country and, as such, completeness can vary although likely not to affect the overall conclusions. The prices used (ex-manufacturing, list price) were normalized values using the same definition between countries. It is unfortunately not possible to estimate uncertainty for each of the point estimates due to the data being post-processing data. IQVIA MIDAS market segment coverage is not uniform, and it is plausible that data may be missing in a nonrandom manner that would impact the study findings. This study did not compare originator and generic drug prices, or examine other dimensions of drug access, such as availability, affordability, accessibility, acceptability, and quality.[35] No price adjustments were made to account for waste or purchasing power parity.

Despite these limitations, this study provides a robust contribution to the existing literature on global chemotherapy pricing for childhood cancer. This data is a critical component for comprehensive models exploring the medical cost of childhood cancer treatment, which also includes diagnosis, supportive care medications, ongoing laboratory evaluation, hospitalization, surgery, and radiation. Comprehensive costing models, in combination with outcome data, form the basis for cost-effectiveness analysis. Our data lends support to the potential role of pooled procurement and the associated negotiation power as a cost reduction strategy in global initiatives. The findings of this study will inform global collaborative efforts, ministry of health cancer control programs, and health system planning for chemotherapy access and will serve as a basis for future drug forecasting and strategic planning in the treatment of childhood cancer globally.

Contributors

The study was conceptualized by NB. Literature search was conducted by CH and NSB. Data collection was performed by TTY and YC and interpreted by CH, TTY, NSB, TA. SO, and NB. The original draft was written by CH with review and editing by TTY, TA, SO, NSB, and NB. Figures were created by YC and TA.

Data sharing statement

The data are proprietary IQVIA MIDAS® data belonging to IQVIA. The authors have permission to use and cite the data in an academic publication but are not otherwise permitted to disclose or share the data. Those seeking to access the dataset should contact IQVIA directly.

Declaration of interests

TA received support from NIH (K12CA120780 and R21CA259926), the University Cancer Research Fund, Lineberger Comprehensive Cancer Center Fund from Lineberger Comprehensive Cancer Center, and St. Jude Children's Research Hospital for grand rounds honoraria. NB received support from National Cancer Institute, American Lebanese Syrian Associated Charities (ALSAC), St. Jude Children's Research Hospital NCI Comprehensive Cancer Center, and Memorial Sloan Kettering for grand rounds honoraria. SO received grant funding from Merck.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2023.102005.

References

1 Bhakta N, Force LM, Allemani C, et al. Childhood cancer burden: a review of global estimates. *Lancet Oncol*. 2019;20:e42–e53.
2 Ward ZJ, Yeh JM, Bhakta N, Frazier AL, Girardi F, Atun R. Global childhood cancer survival estimates and priority-setting: a simulation-based analysis. *Lancet Oncol*. 2019;20:972–983.
3 World Health Assembly. *Pricing of cancer medicines and its impacts*. World Health Organization; 2018.
4 World Health Organization. *WHO global initiative for childhood cancer: an overview*. 2020. published online Dec 10.
5 World Health Organization. *CureAll framework: WHO Global Initiative for Childhood Cancer. Increasing access, advancing quality, saving lives*. 2021. published online Oct 28.
6 Martei YM, Iwamoto K, Barr RD, Wiernkowski JT, Robertson J. Shortages and price variability of essential cytotoxic medicines for treating children with cancers. *BMJ Glob Health*. 2020;5:e003282.
7 Hughes TM, Empringham B, Wagner AK, et al. Forecasting essential childhood cancer drug need: an innovative model-based approach. *Cancer*. 2021;127:2990–3001.
8 Mensah KB, Mensah ABB, Bangalee V, Padayachee N, Oosthuizen F. Evaluating essential medicines for treating childhood cancers: availability, price and affordability study in Ghana. *BMC Cancer*. 2021;21:683.
9 Zhu Y, Wang Y, Sun X, Li X. Availability, price and affordability of anticancer medicines: evidence from two cross-sectional surveys in the Jiangsu province, China. *Int J Environ Res Public Health*. 2019;16:3728.
10 Ocran Mattila P, Ahmad R, Hasan SS, Babar ZUD. Availability, affordability, access, and pricing of anti-cancer medicines in low- and middle-income countries: a systematic review of literature. *Front Public Health*. 2021;9:628744.
11 GBD 2017 Childhood Cancer Collaborators. The global burden of childhood and adolescent cancer in 2017: an analysis of the Global Burden of Disease Study 2017. *Lancet Oncol*. 2019;20:1211–1225.
12 Robertson J, Magrini N, Barr R, Forte G, Ondari C. Medicines for cancers in children: the WHO model for selection of essential medicines. *Pediatr Blood Cancer*. 2015;62:1689–1693.

13 Management Sciences for Health. International medical products price guide. https://msh.org/resources/international-medical-products-price-guide/. Accessed March 12, 2023.
14 IQVIA MIDAS®. https://www.iqvia.com/solutions/commercialization/brand-strategy-and-management/market-measurement/midas. Accessed March 12, 2023.
15 Prices–Inflation (CPI)–OECD Data. https://data.oecd.org/price/inflation-cpi.htm. Accessed May 3, 2022.
16 Regional offices. *Forum*. 1979;Suppl:26–27.
17 World Bank country and lending groups—world Bank data help desk. https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups. Accessed May 3, 2022.
18 Surveillance, Epidemiology, and End results program. https://seer.cancer.gov/. Accessed July 28, 2022.
19 Kuczmarski RJ, Ogden CL, Guo SS, et al. 2000 CDC Growth Charts for the United States: methods and development. *Vital Health Stat 11*. 2002;246:1–190.
20 Growth charts–WHO child growth standards. https://www.cdc.gov/growthcharts/who_charts.htm. Accessed July 29, 2022.
21 Egler RA, Ahuja SP, Matloub Y. L-asparaginase in the treatment of patients with acute lymphoblastic leukemia. *J Pharmacol Pharmacother*. 2016;7(2):62–71.
22 St Jude Global. Global platform for access to childhood cancer medicines. https://global.stjude.org/en-us/medicines.html. Accessed November 22, 2022.
23 Union for International Cancer Control. The access to Oncology medicines (ATOM) coalition. https://www.uicc.org/who-we-work/networks/access-oncology-medicines-atom-coalition. Accessed November 22, 2022.
24 Lu Y, Hernandez P, Abegunde D, Edejer T. *The world medicines situation*. World Health Organization; 2011.
25 *WHO guideline on country pharmaceutical pricing policies*. Geneva: World Health Organization; 2013.
26 Alam A, Kumar A. Prevalence, predictors, causes of treatment refusal and abandonment in children with acute lymphoblastic leukaemia over 18 years in North India. Treatment phase affecting factors: a step towards better focussed counselling. *Cancer Epidemiol*. 2018;57:53–59.
27 Global retinoblastoma study group. Global retinoblastoma presentation and analysis by national income level. *JAMA Oncol*. 2020;6(5):685–695.
28 Duffy C, Santana V, Inaba H, et al. Evaluating blinatumomab implementation in low- and middle-income countries: a study protocol. *Implement Sci Commun*. 2022;3:62.
29 Danzon PM, Mulcahy AW, Towse AK. Pharmaceutical pricing in emerging markets: effects of income, competition, and procurement. *Health Econ*. 2015;24:238–252.
30 Abdel Rida N, Mohamed Ibrahim MI, Babar ZUD, Owusu Y. A systematic review of pharmaceutical pricing policies in developing countries. *J Pharm Health Serv Res*. 2017;8:2017.
31 Waning B, Kaplan W, King AC, Lawrence DA, Leufkens HG, Fox MP. *Global strategies to reduce the price of antiretroviral medicines: evidence from transactional databases*. Bulletin of the World Health Organization; 2009. published online July.
32 Teaima MH, Al-Nuseirat A, Abouhussein D, Badary OA, El-Nabarawi MA. Pharmaceutical policies and regulations of oral antiviral drugs for treatment of hepatitis C in Egypt-case study. *J Pharm Policy Pract*. 2021;14:106.
33 Zenatti PP, Migita NA, Cury NM, et al. Low bioavailability and high immunogenicity of a new brand of E. Colil-asparaginase with active host contaminating proteins. *eBioMedicine*. 2018;30:158–166.
34 World Health Organization and Health Action International. *Measuring medicine prices, availability, affordability and price components*. 2nd ed. 2008.
35 Ozawa S, Shankar R, Leopold C, Orubu S. Access to medicines through health systems in low- and middle-income countries. *Health Policy Plan*. 2019;34:iii1–iii3.