Analysis of drug consumption and expenditure of WHO essential medicines for cancer in 40 countries and regions between 2012 and 2022: a multinational drug use study

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Summary

Background WHO introduced the Model List of Essential Medicines (EML) for neoplasm in 1977, with updates every 2 years. Addressing inequities in access is crucial for ensuring that the benefits of treatment advancements are accessible. We aimed to evaluate international patterns in the consumption and expenditure of cancer medicines listed by the WHO EML.

Methods In this multinational drug use study, we annualised consumption and expenditure data of 65 WHO essential cancer medicines between Jan 1, 2012, to Dec 31, 2022, from the MIDAS database, covering 30 high-income, seven upper-middle-income, and three lower-middle-income economies. Trends over the decade were assessed using rank-sum test, trends regression, and the Lorenz curves. Panel regression assessed associations between consumption, country income levels, disability-adjusted life-years (DALYs) by neoplasm (cancer-related DALYs), Gini index, and the universal health coverage (UHC) index. The constitutes of medicines regarding WHO-documented overall survival benefits at least 4 months were examined.

Findings By 2022, we found no significant difference in annual consumption of WHO essential cancer medicines between high-income and middle-income economies (median 436·82 [IQR 92·66–800·14] standard units *vs* 609·52 [278·44–762·50] standard units; p=0·84). Differences in expenditure on EML cancer medicines between high-income and middle-income economies were evident in 2022 (high-income economies: US$33 198·82 [IQR 18 123·61–51 818·48]; middle-income: $4034·42 [2502·68–5805·27]; p=0·0007). Over the 11 years, consumption of EML cancer medicines had an average annual growth rate of 16·79% (IQR 10·62 to 24·07) for middle-income economies compared with 1·81% (0·51 to 6·37) in high-income economies and expenditure had an average annual growth rate of 8·96% (3·38 to 18·82) compared with –0·06% (–1·94 to 2·95) in high-income economies. UHC index was positively associated with consumption (adjusted coefficient: 11·35 [95% CI 6·59–16·10]; p<0·0001), whereas we found no significant effects with country income, DALYs, or the Gini index. Middle-income economies consumed more medicines with documented overall survival benefits of more than 4 months compared with high-income economies (57·1% *vs* 37·8%; p=0·004).

Interpretation Over the past decade, the consumption gap of WHO essential cancer medicines has narrowed among different economies, especially in middle-income economies. Improved UHC might be associated with improved treatment access.

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Introduction

Cancer continues to be one of the most substantial global health challenges, as reflected in the approximately 20 million new cancer cases and 9·7 million cancer-related deaths in 2022.[1] Pharmacological interventions are important in cancer management, serving both curative and palliative purposes alongside primary modalities.[2] However, significant disparities in the availability and affordability of cancer therapeutics persist, particularly in low-income and middle-income economies. These disparities have led to poorer survival outcomes for patients in these regions compared with those in high-income economies.[3–5] Although the majority of cancer indications are considered non-curative, new treatment approaches have increased clinical benefits.[6,7] Additionally, from 1991 to 2022, the cancer mortality rate in the USA declined by 33%, leading to an estimated 3·8 million averted deaths. This reduction can be attributed to advancements in both pharmacological and non-pharmacological treatments.[8] Therefore, addressing these inequities is crucial for ensuring that the benefits of cancer treatment advancements are accessible to all patients, regardless of economic status.

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Research in context

Evidence before this study

Although the WHO Model List of Essential Medicines (EML) represents essential and cost-effective cancer treatments, it has not had global adoption. To evaluate gaps in the adoption of WHO essential cancer medicines, we searched PubMed for articles published between Jan 1, 2014, and Nov 20, 2024, using the following search terms: (essential list) AND ((cancer drug) OR (cancer medicine)) AND ((consumption) OR (use) OR (expenditure) OR (affordability) OR (accessibility)). This search resulted in 222 records. After screening for relevance based on the criterion of reporting on cancer medications listed in the WHO EML, we identified 30 pertinent studies. 11 of these studies focused on accessibility and affordability, eight on childhood cancer, seven reviewed the EML policy and national EML formation, two discussed the adoption issues of EML medicines, one provided methodology to forecast volume and cost, and one on the overall survival benefits of cancer medicines listed in the WHO EML. Most of the accessibility studies focused on the comparison of drug inclusion on national EMLs (including approval and drug reimbursement) with WHO EML. Only three studies further explored the pricing of WHO essential cancer medicines by reimbursement policy or survey. However, no cross-sectional or longitudinal studies were found that tracked international trends in the usage of WHO essential cancer medicines in high-income or middle-income economies. Additionally, no studies have explored the factors influencing the consumption of EML.

Added value of this study

This study provides 11-year patterns in consumption and expenditure on 65 EML cancer medicines from 2012 to 2022, covering 40 countries or regions. Furthermore, we examine the association between essential cancer medicine consumption, economic status, disease burden, social equity, and service of universal health coverage (UHC). Our findings revealed stable trends on per capita expenditure and consumption of EML cancer medicines in high-income economies. In middle-income countries, we observed sustained growth in consumption alongside effective expenditure control. Although moderate differences in consumption were noted between high-income economies and middle-income economies, the gap has narrowed over the past decade. Our analysis suggests that the consumption of EML cancer medicines could be significantly associated with UHC service coverage but independent of economic status, disease burden, and social equity. Additionally, our results suggest that the proportion of consumption of medicines with WHO Technical Report Series-documented evidence of overall survival benefits more than 4 months was higher in middle-income economies.

Implications of all the available evidence

EML is revised by WHO expert committees and includes medications that meet specific criteria of efficacy, safety, and cost-effectiveness to prioritise high-value treatments that address the most pressing health-care needs of populations. Differences in global consumption of EML cancer medicines have decreased or narrowed over the past decade due to sustained increases in middle-income economies, although significant differences in expenditure and unit price remain.

In 1977, WHO introduced the Model List of Essential Medicines (EML), which is revised biennially to assist countries and regional bodies in crafting national essential medicines lists based on the criteria of efficacy, safety, and cost-effectiveness, without cost being the topmost consideration.[9,10] The WHO EML offers evidence-based recommendations to national and subnational policy makers, facilitating the prioritisation of high-value medications that address the primary health-care needs of populations, a key factor in defining essential medicines, to close the gap of medical treatment.[9] In countries facing resource constraints and inadequate health technology assessment capacities, national essential medicines lists tend to have a relatively high alignment with the WHO EML to enhance accessibility to the most effective therapeutics.[2,11] For cancer, four categories of main treatments and supportive medicines are included, which represent frequently selected high-priority cancer medicines by practising oncologists.[3] However, the rapid approval of new pharmaceuticals that often show marginal or uncertain benefits, coupled with exorbitant pricing, complicates the selection and procurement of cancer medicines.[12] Due to variations in institutional design, governance structures, disparities in capacities of evidence management, and complex stakeholder involvement, the national adaptation and implementation of the WHO EML is challenging.[13] WHO has proposed specific criteria for selecting cancer medicines; however, deviations in adherence to these guidelines occur. The clinical value of cancer medicines included in the WHO EML remains unclear, as only 68% of the targeted cancer medicines listed in the EML documented evidence of overall survival benefit of at least 4 months in the WHO Technical Report Series.[14]

In this study, we used data from the IQVIA Multinational Integrated Data Analysis System (IQVIA MIDAS) database to examine the global market dynamics of cancer medicines listed on the WHO EML (appendix pp 1–2), emphasising global trends in consumption and expenditure. Additionally, we assessed the influence of various factors on the medical use of these medicines. We also explored the variations in the constitution of WHO essential cancer medicines regarding documented

See Online for appendix

evidence on overall survival benefits. This analysis aims to provide insights into the different accessibility and adoption patterns of countries of WHO essential cancer medicines in response to cancer disease burden and economic conditions.

Method

Data source and study design

All sales data for cancer medicines listed on the WHO EML were sourced from the IQVIA MIDAS database. This commercial database consolidates local product volumes, trends, and market shares by drug molecules from IQVIA local audits. The data extracted from MIDAS includes national and regional monthly expenditure and consumption figures from Jan 1, 2012, to Dec 31, 2022, from hospital settings regardless of public or private channels, and these data are increasingly used for drug utilisation and expenditure studies.[15,16] This longitudinal study spans 11 years and includes data from 30 high-income economies, seven upper-middle-income economies, and three lower-middle-income economies, according to the World Bank.[17] Our analysis included 65 EML cancer medicines and therapeutic alternatives (appendix pp 1–2).

MIDAS database provides monthly data on consumption volumes in standard units and their corresponding monetary values in US$ over the study period. The pack price data were derived from local industry standard sources, which could reflect either the list price or the average invoice price, depending on country and available information. A standard unit is defined as the smallest common dose of a product form, which facilitates the comparison of medicine consumption across different forms, especially when the defined daily dosage is not available for specific cancer medicines.[18] Given the high cost associated with cancer treatments, we assumed that the sales volumes approximate the actual consumption of EML cancer medicines. We aggregated the national monthly sales and calculated the annual number of standard units sold per 1000 capita for the included countries or regions to account for seasonal time lag in data auditing.[19] For expenditure analysis, we assumed that the reported sales volume equated to medicine expenditure. Annual expenditure was measured in US$ per 1000 capita. To account for economic fluctuations over the period, total sales in US$ were standardised to 2022 values using the inflation rates for average consumer price provided by the International Monetary Fund.[20] The aggregated standard unit price was the quotient of overall expenditure and consumption.

Exploratory factors

We included gross national income per capita, disability-adjusted life-years (DALYs) by neoplasm (cancer-related DALYs), Gini index, and universal health coverage (UHC) service coverage index as exploratory factors for consumption association analysis (appendix p 3). We divided the targeted drugs (ie, targeted therapies [section 8.2.2] and immunomodulators [section 8.2.3]), into two groups referring to criterion according to the WHO Technical Report Series: targeted drugs having documented evidence of overall survival benefit of at least 4 months and others (appendix pp 4–5).[14,21] We compared drug adoption during 2019–22, 4 years following WHO's quantification of overall survival evidence, between the two groups across countries or regions. Considering the unique health-care system, pricing mechanism, and market dynamics of medicines in the USA, we did a complementary analysis to test the robustness of results.

Data analysis

To estimate the overall trends in consumption and expenditure of WHO's essential cancer medicines over the study period, we calculated the average annual growth rates starting from the earliest market year of the medicines included in the study. The annual growth rate was calculated by dividing the increased expenditure or consumption value with value of the previous year (appendix p 6). A negative annual growth rate indicates a decrease in expenditure or consumption compared with the previous year.

To compare the expenditure and consumption trends of WHO essential cancer medicines between income groups over the 11-year study period, we fitted a linear regression model incorporating an interaction term between income groups and year. The interaction term tests whether the trend over time (slope) significantly differs between the two groups. We employed the Lorenz curve to visualise the global inhomogeneity in the consumption of EML cancer medicine. The degree of inhomogeneity was quantitatively assessed using the concentration index, derived from the area between the Lorenz curve and the line of equality.[22] To explore the relationship between exploratory factors with the consumption of EML cancer medicines over the 11-year study period, we implemented a panel regression model (appendix p 7).

The Shapiro–Wilk test was used to assess the normality of the data distribution. Based on the results, a *t* test was applied for data with a normal distribution, whereas the rank-sum test was used for non-normal distribution. A p value less than 0·05 was used as the cutoff point for statistical significance. Two independent co-authors (YJ and JW) cross-checked all analyses. Summary statistics are presented as mean (SD) for symmetrical distribution and as medians (IQR) for non-symmetrical distribution to mitigate the effect of outliers and skewed data distributions.

All data analysis and visualisation were done using R version 4·3.3.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Based on IQVIA MIDAS retail data of the hospital sector from 2012 to 2022, we identified 378 cancer medicines with WHO's Anatomical Therapeutic Chemical code L01 or L02 (appendix pp 1–2). 65 (17·2%) of 378 of these were listed or suggested as therapeutic alternatives in the WHO EML (34 [52·3%] cytotoxic medicines; 11 [16·9%] targeted therapies; six [9·2%] immunomodulators; and 14 [21·5%] hormones and antihormones; appendix pp 1, 8).

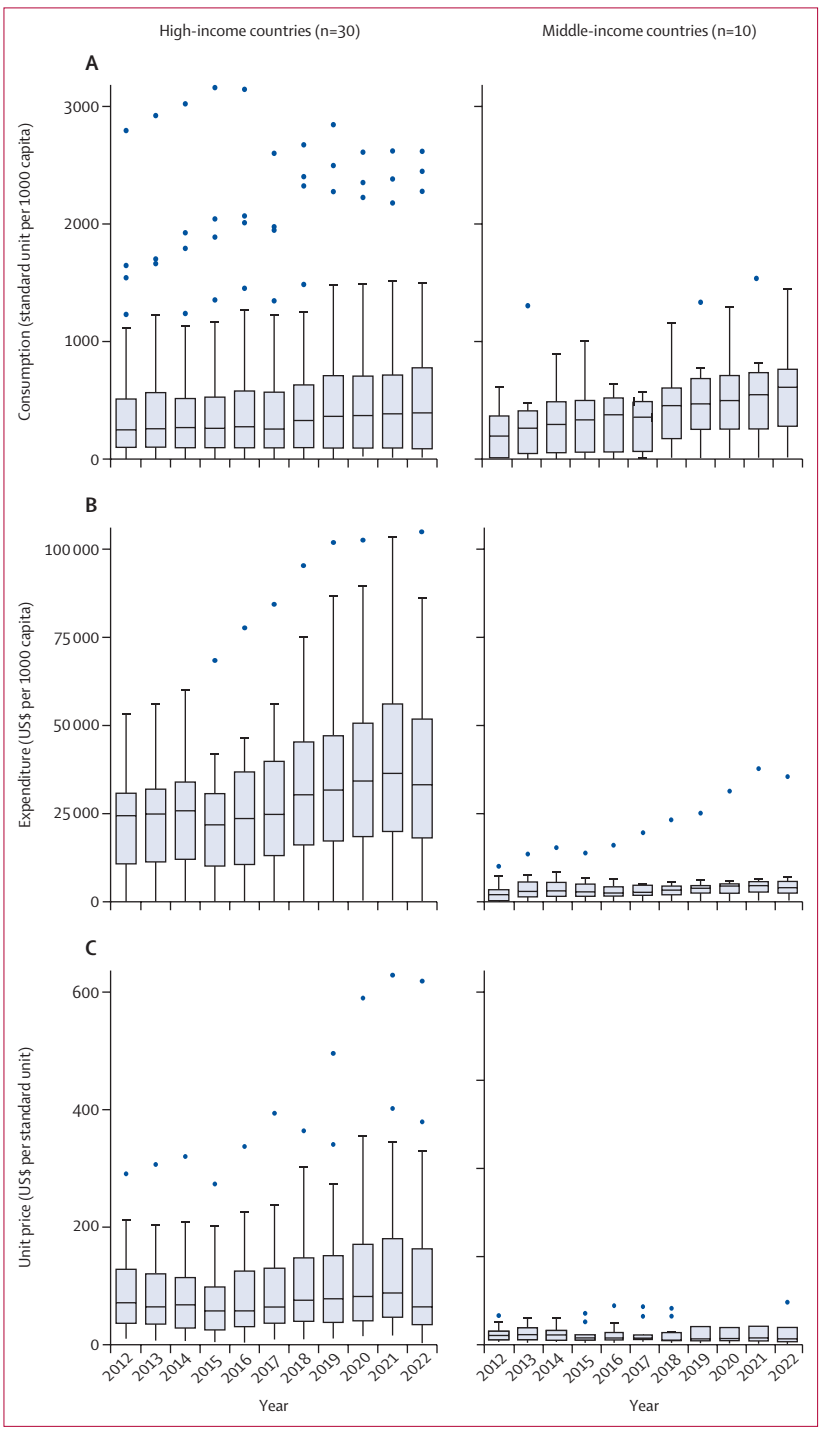

Figure 1: **Annual trends of the WHO Model List of Essential Medicines, by country income level**
(A) Annual consumption. (B) Annual expeniture. (C) Unit price. The yearly consumption of 2022 in New Zealand (7393 standard units) was omitted for better visualisation.

High-income economies showed relatively stable trends in both consumption and expenditure of EML cancer medicines, whereas middle-income economies had increases from 2012 to 2022 (figure 1), and substantial variations in both expenditure and consumption were observed among countries or regions (appendix pp 9–11). At the end of the study period (2022), the median consumption per 1000 capita reached a similar level between high-income and middle-income economies, with no statistically significant difference (high-income economies: median 436·82 standard units [IQR 92·66–800·14] per 1000 capita year; and middle-income economies: median 609·52 standard units [278·44–762·50] per 1000 capita year; p=0·84). Differences in expenditure per 1000 capita on EML cancer medicines remained pronounced in 2022 (middle-income economies: US$4034·42 [2502·68–5805·27] per 1000 capita year; and high-income economies: $33 198·82 [18 123·61–51 818·48] per 1000 capita year; p=0·0007).

Targeted therapies and immunomodulators accounted for the most expenditures on WHO essential cancer medicines (high-income economies: 83·5%; upper-middle-income: 61·8%; lower-middle-income: 65·7%). These medicines also showed, relative to other categories, higher average annual growth rates in both consumption and expenditure, particularly within upper-middle-income and lower-middle-income economies. Expenditure on cytotoxic medicines, along with hormones and antihormones listed in EML was stable or slightly reduced across all income groups (table 1; appendix p 12).

For middle-income economies, an increased consumption of EML cancer medicines was observed, indicated by an average annual growth rate of 16·79% (IQR 10·62 to 24·07) compared with 1·81% (0·51 to 6·37) in high-income economies (p<0·0001), whereas expenditure was of modest increase, reflected by an average annual growth rate of 8·96% (3·38 to 18·82) compared with –0·06% (–1·94 to 2·95) in high-income economies (p<0·004). The three lower-middle-income economies showed the most significant increase in EML cancer medicines use between 2012 and 2022 (average annual growth rate of consumption: 25·58% [17·91 to 31·3]; average annual growth rate of expenditure: 19·44% [11·05 to 29·04]). The average annual growth rate of expenditure was generally lower than the average annual growth rate of consumption, especially in middle-income groups (appendix pp 9–11, 13).

The Lorenz curve of yearly consumption lay below the line of equality, an indication that consumption of EML cancer medicines was more concentrated among countries or regions that ranked high on the gross

national income per capita (figure 2). The concentration index for EML cancer medicines consumption was stable at about 0·53–0·61 between 2012 and 2022. There was an approximate 10% drop in the concentration index in 2020 and 2021 at the start of the COVID-19 pandemic, with a return to baseline (initial value of 0·61 at 2012) in 2022.

Further analysis investigated the relationship between exploratory factors and consumption of EML cancer medicines from 2012 to 2022 (table 2). Gross national income per capita was positively associated with the consumption of EML cancer medicines but was not statistically significant. DALYs per 1000 capita (crude analysis: 11·51 [95% CI 1·29 to 21·73]; p=0·028) and the Gini index (crude analysis:–19·71 [–33·41 to –6·00; p=0·005) showed significant associations with consumption in crude analyses. However, neither DALYs nor the Gini index remained significant in the multivariable panel regression (adjusted analysis). UHC service coverage index was positively associated with the consumption of EML cancer medicines in both crude analysis (estimate: 12·70 [8·27 to 17·12]; p<0·0001) and adjusted analysis (estimate: 11·35 [6·59 to 16·10]; p<0·0001).

Overall survival benefits of at least 4 months among targeted drugs alongside the corresponding consumption and expenditure from 2019 to 2022 were recorded (figure 3). Among high-income economies, 37·8% of the overall consumption of EML cancer medicines included medicines with documented evidence of overall survival benefit, compared with 57·1% in middle-income economies—a significantly higher proportion. When measured by health expenditure, similar proportions of consumed medicines with documented overall survival evidence in the WHO Technical Report Series (43·7% in high-income economies and 39·9% in middle-income economies) were observed between income groups. With the exclusion of the USA, the results remain unchanged. Compared with middle-income economies, high-income economies (excluding the USA) recorded a lower proportion of overall consumption (38·0%) and a similar proportion of expenditure (44·8%) on EML cancer medicines with documented overall survival benefits.

Discussion

Our study, encompassing 40 countries with varying income levels, revealed an overall upward trend in total EML cancer medicine consumption and expenditure

	Consumption			Expenditure			Unit price, US$ per standard unit
	Standard unit per capita year	Proportion of total	Average annual growth rate	US$ per capita year	Proportion of total	Average annual growth rate	
High income							
Targeted therapies	41·98 (15·99 to 120·25)	16·46%	7·19 (3·6 to 10·83)	14 332·05 (7102·61 to 16 018)	55·07%	0·32 (–3·48 to 4·93)	178·53 (88·73 to 497·65)
Immunomodulators	16·63 (6·64 to 36·75)	6·52%	4·02 (2·09 to 12·08)	7406·83 (4003·4 to 16 190)	28·46%	–1·29 (–4·03 to 4·7)	476·76 (255·27 to 679·15)
Hormones and antihormones	43·2 (25·98 to 184·12)	16·94%	3·98 (0·59 to 9·16)	1167·72 (169·38 to 4095)	4·49%	–7·02 (–9·69 to 0·09)	11·31 (5·57 to 28·7)
Cytotoxic medicines	153·25 (57·77 to 297·96)	60·08%	–0·29 (–1·34 to 1·89)	3116·35 (1595·28 to 6401)	11·98%	0·27 (–2·39 to 4·23)	19·77 (10·24 to 33·13)
Upper middle income							
Targeted therapies	46·9 (20·59 to 72·43)	12·25%	26·11 (21·03 to 45·99)	1947·25 (1005·73 to 2313)	49·33%	7·37 (2·29 to 20·11)	52·8 (34·32 to 85·21)
Immunomodulators	5·24 (3·67 to 8·37)	1·37%	22·34 (18·03 to 120·32)	491·38 (365·2 to 825)	12·45%	16·48 (6·49 to 28·05)	110·56 (65·47 to 271·61)
Hormones and antihormones	135·31 (65·23 to 220·89)	35·33%	18·85 (9·26 to 23·68)	519·77 (194·99 to 788)	13·17%	0·57 (–10·49 to 4·37)	3·89 (3·56 to 17·58)
Cytotoxic medicines	195·49 (113·14 to 274·26)	51·05%	6·72 (4·89 to 8·22)	988·88 (826·47 to 1197)	25·05%	3·07 (–2·05 to 10·99)	6·65 (5·04 to 7·27)
Lower middle income							
Targeted therapies	25·76 (13·17 to 33·3)	13·16%	47·63 (29·4 to 48·38)	556·03 (320·87 to 2319)	58·68%	31·13 (19·52 to 38·75)	99·92 (60·75 to 122·99)
Immunomodulators	1·74 (0·98 to 7·5)	0·89%	36·66 (25·26 to 60·16)	66·27 (55·41 to 127)	6·99%	32·81 (19·06 to 37·44)	38 (26·09 to 125·46)
Hormones and antihormones	119·05 (61·27 to 180·64)	60·82%	16·13 (10·93 to 18·34)	125·23 (67·63 to 468)	13·22%	12·38 (–4·03 to 23·67)	2·88 (1·97 to 3·11)
Cytotoxic medicines	49·17 (27·39 to 181·45)	25·12%	19·46 (12·9 to 26·37)	200·07 (146·39 to 508)	21·11%	13·8 (7·9 to 24·05)	4·07 (3·33 to 10·29)

Data are median (IQR) or %.

Table 1: **Average annual growth rate of WHO Model Lists of Essential Medicines of cancer drugs**

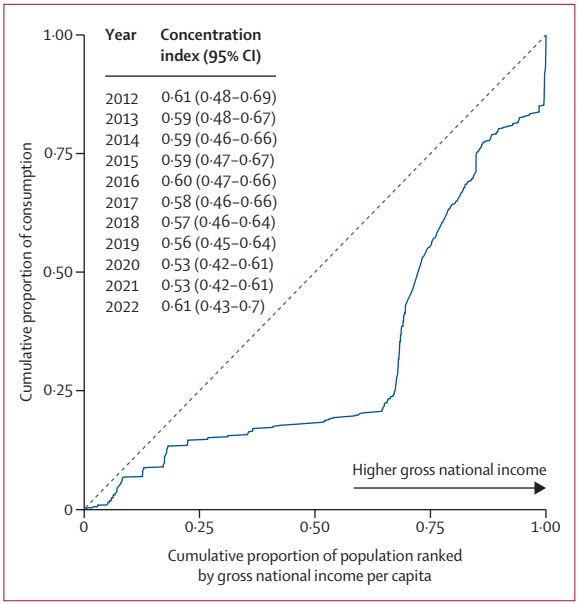

Figure 2: **Lorenz curve of yearly consumption for gross national income per capita (2012–22)**
The dashed line indicates the line of equality and the solid line indicates Lorenz curve.

	Crude effect		Adjusted effect	
	Estimate (95% CI)	p value	Estimate (95% CI)	p value
Gross national income per capita, US$1000	2·89 (–1·54 to 7·32)	0·20	2·20 (–2·07 to 6·47)	0·31
Disability-adjusted life-years per 1000 capita	11·51 (1·29 to 21·73)	0·028	4·76 (–5·26 to 14·78)	0·35
Gini index	–19·71 (–33·41 to –6·00)	0·005	–8·45 (–22·39 to 5·48)	0·24
Service coverage index for universal health coverage	12·70 (8·27 to 17·12)	<0·0001	11·35 (6·59 to 16·10)	<0·0001

Table 2: **Panel regression of economic, health burden, social equality, universal health coverage indicators, and consumption of WHO Model Lists of Essential Medicines of cancer drugs**

over the past decade, with noticeable individual differences and generally valid price control. The consumption of EML cancer medicines was significantly associated with the service coverage of UHC. Additionally, middle-income economies had a higher composition of consumption on EML target therapies with documented overall survival benefits longer than 4 months in the WHO Technical Report Series.

The EML cancer medicine consumption and expenditure trends varied by country income levels. Middle-income economies showed fast-growing trends in the consumption and expenditure of EML cancer medicines. The increased access to relatively newer treatments, such as targeted therapies and immunomodulators, in middle-income economies might partially be attributed to the time-lag approval of newer medicines that were previously adopted in high-income economies. However, significant difference remained in per capita expenditure, with about a five-fold difference between income groups. The expenditure difference in WHO essential cancer medicines between high-income and middle-income economies aligns with accessibility evaluations from global survey-based studies, which have identified inequities in access and a high risk of catastrophic expenditure (defined as spending >40% of total consumption net of spending on food) in both middle-income economies and low-income economies.[3,23] There are several explanatory factors potentially related to the change in consumption and expenditure of EML cancer medicines. First, the introduction of emerging cost-effective products, coupled with increased market competition, has most likely contributed to the reduction in unit prices of EML cancer medicines. Second, the availability of more affordable alternatives outside the WHO EML, which were not captured in this study, might have influenced some economies to shift toward these options. This shift could have affected both the consumption and expenditure patterns observed. Third, national pharmaceutical policies are instrumental in shaping investments and reimbursement strategies, which in turn influence the consumption and expenditure of EML cancer medicines, including ongoing system-level health-care cost control measures in the past decade.[24–28]

In most countries and regions, expenditure growth was lower than the corresponding consumption growth (appendix p 13), particularly in middle-income economies, suggesting a decrease in unit prices (figure 1C). The decrease in unit prices can be partially attributed to new alternatives and biosimilars. Another possible explanation is national medicine expenditure control over the past decade, such as China's national drug price negotiations.[24,29] Although health care in the USA is often characterised by overspending,[30,31] the USA recorded stable consumption and expenditure on EML cancer medicines. Considering the nature of economic growth and inflation, adopting cheaper alternatives in clinical practice resulting from reimbursement policy amendments might partly explain such observations.[32] Beyond national efforts in price negotiations and reimbursement policies, factors such as the market share of private sectors, the capacity of reimbursement channels, and the scope of subsidised cancer medicine lists could also influence the consumption of EML cancer medicines.

Beyond mere differences in purchasing power, the different compositions of expenditure also help to explain the generally lower unit prices in middle-income economies. Middle-income economies tend to allocate relatively less funding to targeted therapies and immunomodulators, which constitute a significant portion of expenditures in high-income economies. Nevertheless, this allocation is understandable, given that targeted therapies and immunomodulators, which have emerged as first-line cancer treatments in the past decade, command higher prices due to the burgeoning nature

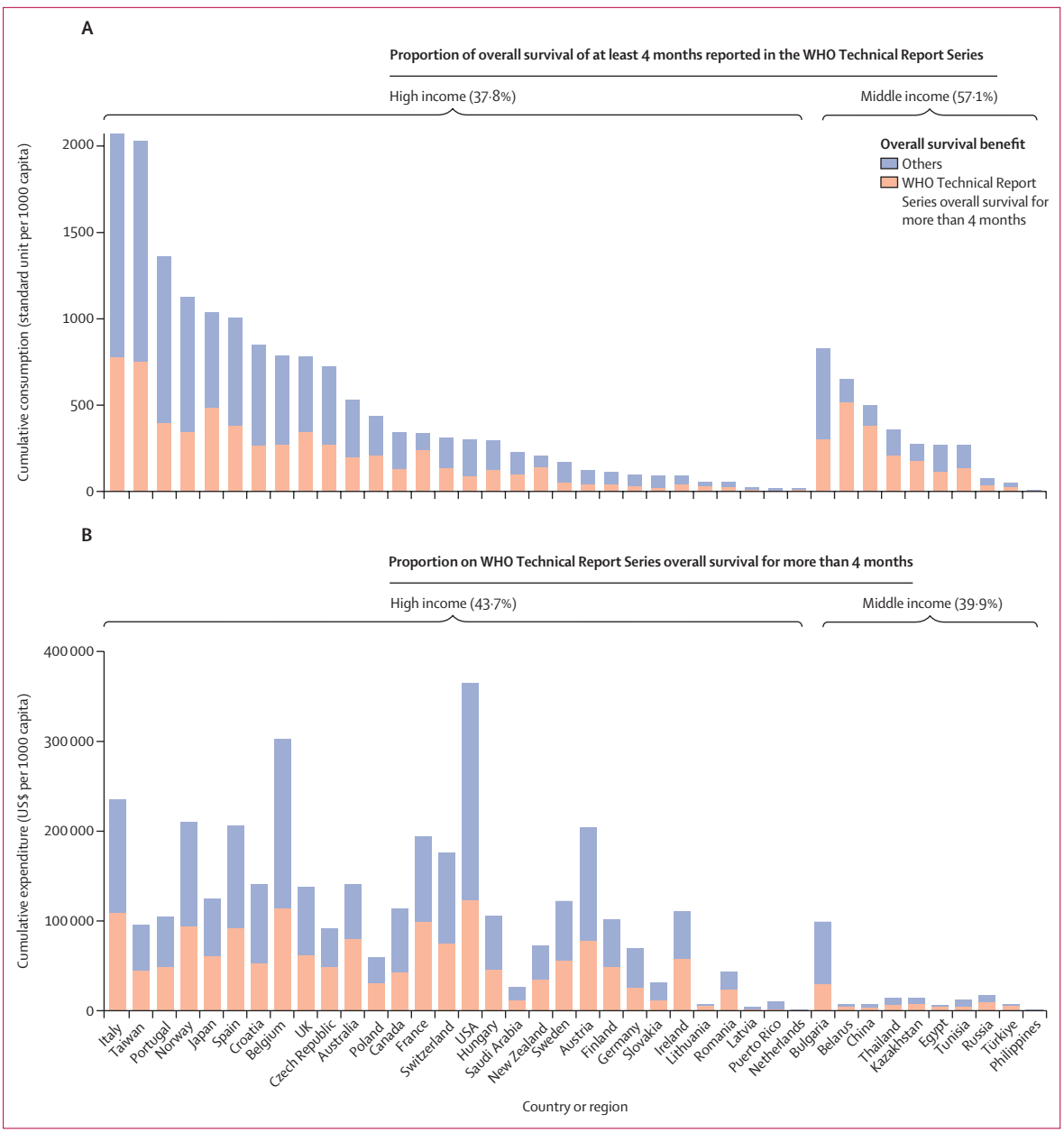

Figure 3: **Expenditure and consumption of the cancer drugs listed in the WHO Model List of Essential Medicines with or without documented overall survival benefit for at least 4 months**

(A) Consumption from 2019 to 2022. (B) Expenditure from 2019 to 2022.

and evolving evidence of benefits.[33] Although advances in developing targeted therapies bring more opportunities for anticancer treatment, previous research showed that among molecular-targeted cancer therapies approved by US Food and Drug Administration in 2015–22, fewer than a third showed substantial patient benefits at approval.[34] Since the 2015 EML updates, WHO has considered meaningful, comparable improvements in overall survival over the existing standard of care as a key criterion for adding new, high-cost targeted cancer drugs. In 2019, the WHO EML adopted a threshold requiring a survival benefit of at least 4–6 months for a drug to be considered for inclusion.[2,14,21] For example, according to the WHO Technical Report Series, the WHO Expert Committee on Selection and Use of Essential Medicines recommended listing new relatively high-priced cancer medicines, including bortezomib and lenalidomide, for specific indications on the complementary list of the 2019 EML on the basis of good evidence showing substantial improvement in survival outcomes with acceptable safety for patients with newly diagnosed multiple myeloma.[21] It should be noted that, given WHO

EML's inclusion of essential cancer drugs with full consideration of benefits, harms and toxicity estimates, affordability, availability, and others, this grouping is based on documented overall survival benefit evidence and unrelated to the clinical value of these drugs. We merely determined whether the targeted therapies met the criteria for overall survival benefit evidence according to their own technical reports. Our results revealed that middle-income economies had a higher proportion of consumption in medicines with WHO-documented overall survival benefits of at least 4 months, compared with high-income economies. This observation potentially suggests that documented survival benefit evidence on WHO Technical Report Series serves as a solid reference for middle-income economies. However, when evaluated based on monetary expenditure, the proportions were similar between the two groups. Further qualitative and quantitative research should be done to elucidate the effect of the WHO EML inclusion on national drug policies as well as drug use.

Our association analysis indicates that disease burden and social inequity could partially explain the discrepancies in EML cancer medicine consumption, and the UHC service coverage index showed a significant association with EML cancer medicine consumption, with better UHC associated with higher consumption of these medicines. Distinguished from findings in other cancer medicine consumption studies,[35,36] our analysis identified that per capita income level was not significantly associated with access to EML cancer medicines. Although higher disease burden and lower social inequality were individually associated with increased EML cancer medicine consumption, these associations lost significance when adjusted for the UHC service coverage index. Although such observations might be limited by inaccurate assessment of disease burden, a potential explanation could be the strong relationship between UHC and EML cancer medicine consumption. This explanation is reasonable, as UHC aims to ensure that all individuals receive essential health-care services without financial hardship, aligning closely with the purpose of the WHO EML.[37] However, we acknowledge that UHC places greater emphasis on screening and early detection, while EML cancer medicines are primarily intended for treatment. Due to the observational nature of this study and data limitations, we cannot establish causality between UHC service coverage and EML cancer medicine consumption. Besides, bidirectional relationship—improved UHC leading to increased consumption and increased consumption contributing to improved UHC—are plausible and warrant further investigation.

This study has several limitations. First, from a global perspective, consumption and expenditure data from low-income economies remain absent. Additionally, the representation of middle-income economies might be affected due to the selective nature of IQVIA's auditing process. The included economies are typically those with either well-established pharmacy systems or significant market growth potential. Second, the sales volume data used to approximate the consumption and expenditure of EML cancer medicines were obtained from manufacturers. This approach might overestimate actual consumption, as it is based on sales figures, and might not accurately reflect wholesale prices at the institutional or government level. This is due to variations in sales stages, including manufacturer, wholesaler, and pharmacy sales, as recorded in IQVIA's local audits. Additionally, differences in product formulations might affect standard unit counting, and regional variations, such as average weight, might influence dosing and treatment, affecting the comparability of consumption across different medicines. Third, the MIDAS data are commercially sourced, primarily for marketing investigation and auditing purposes, and do not include clinical indication and individual-level data. As a result, we could not exclude the possibility of multiple indications of some cancer medicines. This includes the potential use of specific drugs in non-cancer treatments, which might result in over-estimated consumption of cancer therapies. Fourth, the current analysis counts each country equally rather than weighting observations by market size. Although this helps the study inform readers about what is happening concerning country-specific factors, it does not give extra weight to larger markets that might have an outsized role in global trends. Fifth, due to the variation in cancer prevalence among different income economies, the current presentation expressed per 1000 capita EML cancer medicine consumption cannot explain whether the increasing consumption is due to the increasing number of patients with cancer or improved treatment access. As a result, cross-country comparison should be taken cautiously and the gap in consumption and expenditure might become less pronounced when cancer prevalence is considered. Lastly, to be consistent with the WHO EMLs criteria for target therapies, we classified these medicines into two groups by whether having documented at least 4 months overall survival benefit evidence according to WHO Technical Report Series. This limits the current grouping to that based on WHO-documented overall survival benefit but not on other value-based factors such as progression-free survival, quality of life improvement, alternative treatment and health system feasibility, or evidence from up-to-date pivotal trials, label changes, or exhaustive reviews.

Contributors

XL and XG conceived and designed the study. YJ and JW analysed the data and cross-verified the analysis. LB reviewed the documented evidence of overall survival benefit. YJ and LB wrote the first draft. RN and DMB provided clinical and health economical insights on study design. VKCY and EWC acquitted the data and provided administration and technical support. All authors interpreted the findings, critically reviewed and revised the report, and had final approval of the submitted

paper. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. YJ and XL are the guarantors of this manuscript. All authors have read and approved the final manuscript. All authors had access to all the data reported in the study.

Declaration of interests

XL received research grants or contracts from the Health and Medical Research Fund (HMRF Main Scheme, HMRF Fellowship Scheme, and Hong Kong Special Administrative Region), and from the Research Grants Council Early Career Scheme (HKSAR); is also the former non-executive director of ADAMS Hong Kong; received commission grants from Hospital Authority of Hong Kong, and internal funding from the University of Hong Kong; received consultancy fees from Merck Sharp & Dohme, Pfizer, Open Health, and The Office of Health Economics; and received honoraria for associate editorship from *Nature Springer*. EWC reports grants from the Health Bureau (Hong Kong), the Research Grants Council Hong Kong, National Natural Science Fund of China, Bayer, AstraZeneca, Novartis, RGA Reinsurance Company, Pfizer, and Narcotics Division of the Security Bureau of HKSAR; consulting fees from Pfizer, Novartis, and AstraZeneca; and honorarium from Hospital Authority (Hong Kong) and Pfizer. All other authors declare no competing interests.

Data sharing

The underlying MIDAS data were provided by IQVIA under license. The terms of our agreement do not permit disclosure, sublicensing, or sharing of IQVIA MIDAS data. IQVIA will honour legitimate requests for MIDAS data from qualified researchers. Please contact IQVIA to seek approval for data access; a license fee might be applied. For details on the data access policy and procedure, please contact the corresponding author at sxueli@hku.hk. For inquiries related to the analytical process and other related content of the article, please contact corresponding authors sxueli@hku.hk and guanxiaodong@pku.edu.cn.

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