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ORIGINAL RESEARCH ARTICLE

Comparison of Prices and Affordability of Cancer Medicines in 16 Countries in Europe and Latin America

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Abstract

Background There are concerns that high prices of cancer medicines may limit patient access. Since information on prices for cancer medicines and their impact on affordability is lacking for several countries, particularly for lower income countries, this study surveys prices of originator cancer medicines in Europe and Latin America and assesses their affordability.

Methods For 19 cancer medicines, public procurement and ex-factory prices, as of 2017, were surveyed in five Latin American (LATAM) countries (Brazil, Chile, Colombia, Mexico, and Peru) and 11 European countries (Austria, France, Germany, Greece, Hungary, the Netherlands, Poland, Romania, Spain, Sweden, and the UK). Price data (public procurement prices in LATAM and ex-factory prices in Europe) in US dollar purchasing power parities (PPP) were analyzed per defined daily dose. Affordability was measured by setting medicines prices in relation to national minimum wages.

Results The prices of cancer medicines varied considerably between countries. In European countries with higher levels of income, PPP-adjusted prices tended to be lower than in European countries of lower income and LATAM countries. Except for one medicine, all surveyed medicines were considered unaffordable in most countries. In European countries of lower income and LATAM countries, more than 15 days' worth of minimum wages would be required by a worker to purchase one defined daily dose of several of the studied medicines.

Conclusions The high prices and large unaffordability of cancer medicines call for strengthening pricing policies with the aim of ensuring affordable treatment in cancer care.

1 Introduction

Cancer is a leading cause of mortality worldwide [1]. In middle-income (MICs) and high-income (HICs) countries cancer contributes to a considerable burden of disease [2–4]. Worldwide, MICs account for 68% of all deaths due to cancer, while HICs account for 29% [5]. This impacts the health systems in these countries as they aim

Key Points for Decision Makers

Lower-income countries tend to pay higher PPP-adjusted cancer medicine prices than countries with higher income. Given high PPP-adjusted prices, cancer medicines are largely unaffordable in Latin America and also Europe, in particular in countries of lower income.

These study findings point to more affordable cancer medicine prices in countries with national pricing policies to enhance patient access as a result of policy action to ensure coverage.

Policymakers should consider the study results when they opt for external price referencing as a policy and define the reference countries for benchmarking.

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to guarantee sustainable access to cancer care with comprehensive pharmaceutical treatment as a key component [1, 6–10].

For many types of cancers, pharmaceutical treatment accounts for a considerable share of healthcare expenditure [11–13]. Medicines exist for the treatment of most oncology diseases, and additional new medicines are expected to enter the market. Some medicines have provided better health outcomes, with fewer side effects [14], while the health benefits of other cancer medicines were assessed to be rather marginal [15–17].

Cancer medicines are usually expensive for both governments and patients [14, 18, 19]. Policymakers in MICs and HICs have been applying a mix of pricing and reimbursement policies, including external price referencing (EPR), health technology assessments (HTAs), price negotiations, and managed entry agreements (MEAs), to maintain the financial sustainability of the system while using various policy tools to promote and encourage access to high-priced medicines, including cancer medicines [20–31].

Evidence suggests that there is not necessarily an association between the income of a country and its medicine price level as lower income countries can pay higher procurement prices than countries of higher income [32–36]. Medicine price studies tend to focus on HICs [32, 34, 37–41]. Although some price studies were conducted in MICs [42–46], medicine prices of MICs are much less in the focus of research. In particular, little is known about the differences in prices of cancer medicines between MICs and HICs. Therefore, this study surveys the prices of originator cancer medicines in some MICs and HICs to identify possible cross-country differences in prices and affordability.

2 Materials and Methods

2.1 Selection of Countries

The study included 16 countries in Latin America (LATAM) and Europe: five upper MICs (UMICs) and 11 HICs, according to the World Bank classification in 2017 [47]. Within the two regions, we aimed to select countries of different gross national income (GNI) per capita. All European countries included in the study were HICs (except for Romania), but we classified these countries into two groups related to income: a group consisting of Austria, France, Germany, the Netherlands, Sweden, and the UK whose GNI per capita ranked among the highest world-wide—hereafter referred to as upper HICs (UHICs); and a group consisting of Greece, Hungary, Poland, Romania (a UMIC), and Spain with comparably lower income—hereafter referred to as lower HICs (LHICs). The five selected LATAM countries represent a mix of UMICs (with Chile as a HIC) that differ in economic data and welfare distribution (Table 1). The selection of the LATAM countries was also guided by the practical rationale of whether, or not, a country had access to medicine price data.

2.2 Selection of Medicines

In the study, prices of 19 medicines (13 active ingredients) for the treatment of breast cancer, leukemia, colorectal cancer, and renal cancer were surveyed and analyzed (Table 2). The selection of medicines was based on a previous study (pricing survey) conducted in Mexico in 2017. In that study [48], medicines were selected based on their clinical relevance confirmed by their inclusion in the national formulary, their reimbursement by the public health insurance, and their inclusion in national treatment guidelines. Additionally, acknowledging the dynamics in medicine prices following patent expiry, the current study aimed to focus on on-patent medicines; thus, medicines that were included were under patent protection in Mexico in 2017 (time of the survey). To ensure comparability, since few medicines (e.g., imatinib, mercaptopurine) had lost patent protection in some countries at the time of the analysis, only the originator versions were considered.

2.3 Data Sources

Prices for Mexico were collected in 2017 through a primary price data survey using the World Health Organization (WHO)/Health Action International (HAI) methodology [48, 49]. The WHO/HAI methodology [50] is an internationally acknowledged tool for measuring medicine prices, availability and affordability. It surveys and analyzes government procurement prices and patient prices in the public and private sectors, and it studies the price components along the supply chain. Public procurement prices (also referred to as institutional prices) of medicines in the four other LATAM countries (Peru, Colombia, Brazil, and Chile) were sourced from publicly available repositories maintained by governments (Table 3) [51]. Price data of official national price lists and price databases in European countries were provided by the Pharma Price Information (PPI) service of the Austrian National Public Health Institute [51].

Affordability was measured by the minimum wage as reported by countries to the Organization for Economic Co-operation and Development (OECD) (Table 3) [52].

Table 1 Characteristics of the countries included in the study

Country	Country code	Region	World Bank classification	GINI index	GNI per capita	GDP (2017) (US$/1000.000)	Daily minimum wage
Austria	AT	Europe	UHIC	30.5	45,440	416,595.67	60.25
Brazil	BR	LATAM/SA	UMIC	51.3	8580	2,055,505.50	15.22
Chile	CL	LATAM/SA	LHIC	47.7	13,610	277,075.94	22.06
Colombia	CO	LATAM/SA	UMIC	50.8	5830	309,191.38	22.14
France	FR	Europe	UHIC	32.7	37,970	2,582,501.31	62.71
Germany	DE	Europe	UHIC	31.7	43,490	3,677,439.13	65.30
Greece	EL	Europe	LHIC	36.0	18,090	200,288.28	37.23
Hungary	HU	Europe	LHIC	30.4	12,870	139,135.03	30.84
Mexico	MX	LATAM/NA	UMIC	43.4	8610	1,149,918.79	8.85
Netherlands	NL	Europe	UHIC	28.2	46,180	826,200.28	69.96
Peru	PE	LATAM/SA	UMIC	43.8	5970	211,389.27	17.52
Poland	PL	Europe	LHIC	31.1[a]	12,710	524,509.57	37.57
Romania	RO	Europe	UMIC	35.9	9970	211,803.28	28.65
Spain	ES	Europe	LHIC	36.2	27,180	1,311,320.02	49.40
Sweden	SE	Europe	UHIC	29.2	52,590	538,040.46	60.88
United Kingdom	UK	Europe	UHIC	33.2	40,530	2,622,433.96	57.93

All values are expressed in US$ and for the year 2017. We used the GINI Index to have a perspective on the levels of inequality across countries included in the study. The GNI per capita is the measure used by the World Bank Classification to categorize countries by level of income. GDP measures the market value of goods produced in a country.

GDP gross domestic product, *GINI* Gini coefficient, *GNI* gross national income, *LATAM* Latin America, *LHIC* lower high-income country, *NA* North America, *SA* South America, *UHIC* upper high-income country, *UMIC* upper middle-income country, *US$* United States dollars

Sources for: World Bank Classification—The World Bank (https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups)

GINI Index—The World Bank (https://data.worldbank.org/indicator/si.pov.gini)

GDP—The World Bank (https://data.worldbank.org/indicator/ny.gdp.mktp.cd)

Daily Minimum Wage—Organization for Economic Co-operation and Development (OECD) real minimum wages (https://stats.oecd.org/Index.aspx?DataSetCode=RMW) and the Wageindicator.org

[a]Poland's last reported GINI Index relates to 2015

2.4 Specifications for Analysis

The analyzed prices were public procurement prices as of 2017 in the LATAM countries, given the relevance of the procurement prices in their public health systems, and ex-factory prices (list prices before any deduction of discounts) as of September 2017 in European countries.

Public procurement and ex-factory prices were made comparable by determining unit prices per defined daily dose (DDD). Due to the non-assignment of a DDD by the WHO Collaborating Centre for Drug Statistics Methodology, DDDs as reported by Germany were used (Table 3).

The prices of all medicines were converted into United States dollars (US$) using conversion rates of purchasing power parities (PPP) (see Table 3), which is the number of units of a country's currency required to buy a product in the domestic market that US$ would buy the same product in the USA [51, 53].

Affordability was measured by the number of daily minimum wages (of each country) required to purchase one DDD in the selected medicines. This calculation is a modified version of the affordability assessment outlined in the WHO/HAI methodology [50] that computes the median price of 1 month or one course of treatment of one medicine against the wage of the lowest-paid unskilled government worker (or the minimum wage) in a country.

Price and affordability comparisons were carried out through a descriptive statistical analysis.

3 Results

3.1 Medicine Price Differences Between Countries

In Europe, UHICs (Austria, Germany, UK, the Netherlands, France, and Sweden) reported lower PPP-adjusted prices than countries of lower income (LHICs: Romania,

Table 2 Medicines included in the study and their characteristics

INN—medicine	Presentation	DDD (mg)
Bevacizumab	100 mg/4 mL, 1 vial	45
Bevacizumab	400 mg/16 mL, 1 vial	45
Cetuximab	100 mg/20 mL, 1 vial	65
Dasatinib	50 mg, 60 tablets	120
Everolimus	10 mg, 30 tablets	10
Everolimus	5 mg, 30 tablets	10
Imatinib	100 mg, 60 tablets	500
Imatinib	400 mg, 30 tablets	500
Mercaptopurine	50 mg, 25 tablets	175
Nilotinib	200 mg, 112 tablets	600
Panitimumab	100 mg/5 mL, 1 vial	30
Pazopanib	200 mg, 30 tablets	800
Pazopanib	400 mg, 60 tablets	800
Rituximab	100 mg/10 mL, 2 vial	32
Rituximab	500 mg/50 mL, 1 vial	32
Sorafenib	200 mg, 112 tablets	800
Sunitinib	12.5 mg, 28 tablets	35
Trastuzumab	440 mg, 20 mL × 1 vial	20
Trastuzumab	150 mg, 1 vial	20

INN International Nonproprietary Name, *DDD* defined daily dose, *mg* milligram, *mL* milliliter

Poland, Hungary, Spain, and Greece). All prices in UHICs remained below US$300 PPP/DDD, while prices in some European LHICs and LATAM countries ranged from less than US$50 PPP/DDD to more than US$500 PPP/DDD. European UHICs showed lower prices than LATAM countries and LHICs, and the prices for different medicines did not vary as much compared to LHICs and LATAM countries. While some medicine prices in LATAM countries were similar to those in HICs, some other medicines had higher prices in LATAM countries than in HICs (Fig. 1).

Across all medicines, mercaptopurine 50 mg showed the lowest prices (median: US$10.85 PPP/DDD – Netherlands; minimum (min) = US$0.89 PPP/DDD – Spain; maximum (max) = US$26.02 PPP/DDD – Colombia) in all countries. Prices of imatinib 100 mg (median = US$78.24 PPP/DDD – Colombia; min = US$6.71 PPP/DDD – Peru, max = US$162.89 PPP/DDD – Germany) and imatinib 400 mg (median = US$87.51 PPP/DDD; min = US$11.54 PPP/DDD – Peru, max = US$189.10 PPP/DDD – Hungary) were also lower than other medicines, but they differed considerably between countries. For nilotinib 200 mg, pazopanib 200 mg, pazopanib 400 mg, rituximab 100 mg, and rituximab 500 mg, prices ranged from approximately US$50 PPP/DDD to US$200 PPP/DDD; for these medicines Poland reported the highest prices, while the lowest prices were reported for Mexico and Brazil. For most analyzed medicines, Sweden and the UK reported the lowest prices, while prices in Poland and Romania were among the highest.

Table 3 Data sources

Indicators	Data source
Medicine price data	
Mexico	Primary data collected by the first author using the WHO/HAI methodology
Peru	General Directorate of Medicine Supplies and Drugs (Dirección General de Medicamentos Insumos y Drogas, DIGEMID) (http://www.digemid.minsa.gob.pe/Main.asp?Seccion=705)
Colombia	Price Thermometer (Termómetro de Precios) (https://www.minsalud.gov.co/salud/MT/Paginas/termometro-de-precios.aspx)
Brazil	Health Price Bank (Banco de Preços em Saúde) (http://bps.saude.gov.br/login.jsf)
Chile	ChileCompra (https://www.mercadopublico.cl/Home/BusquedaLicitacion)
EU countries	Pharma Price Information service of the Austrian Public Health Institute (https://ppri.goeg.at/pharma_price_information), average wholesale margins for countries that regulate pharmacy purchasing prices to calculate ex-ex-factory prices: "Regelung für die Vorgehensweise der Preiskommission für die Ermittlung des EU-Durchschnittspreises gemäß § 351c Abs. 6 und Abs. 9a ASVG" (Regulation for the Procedure of the Pricing Committee to Calculate the EU Average Price in accordance to § 351c para. 6 and para. 9a Austrian Social Health Insurance Law)
Other data	
Minimum wage	OECD's Real Minimum Wages (https://stats.oecd.org/Index.aspx?DataSetCode=RMW) For Austria and Sweden: data of minimum real wage of the lowest-skilled worker from Wageindicator.org
PPP	OECD's Purchasing Power Parities Indicator (https://data.oecd.org/conversion/purchasing-power-parities-ppp.htm)
DDD values	Germany's "Anatomisch-Therapeutisch-chemische Klassifikation mit Tagesdosen für den deutschen Arzneimittelmarkt" (Anatomical Therapeutic Chemical (ATC) Classification of daily doses for the German pharmaceutical market) (https://www.wido.de/fileadmin/Dateien/Dokumente/Publikationen_Produkte/Arzneimittel-Klassifikation/wido_arz_atc_gkv-ai_2017.pdf)

DDD defined daily dose, *EU* European Union, *HAI* Health Action International, *OECD* Organization for Economic Co-operation and Development, *WHO* World Health Organization

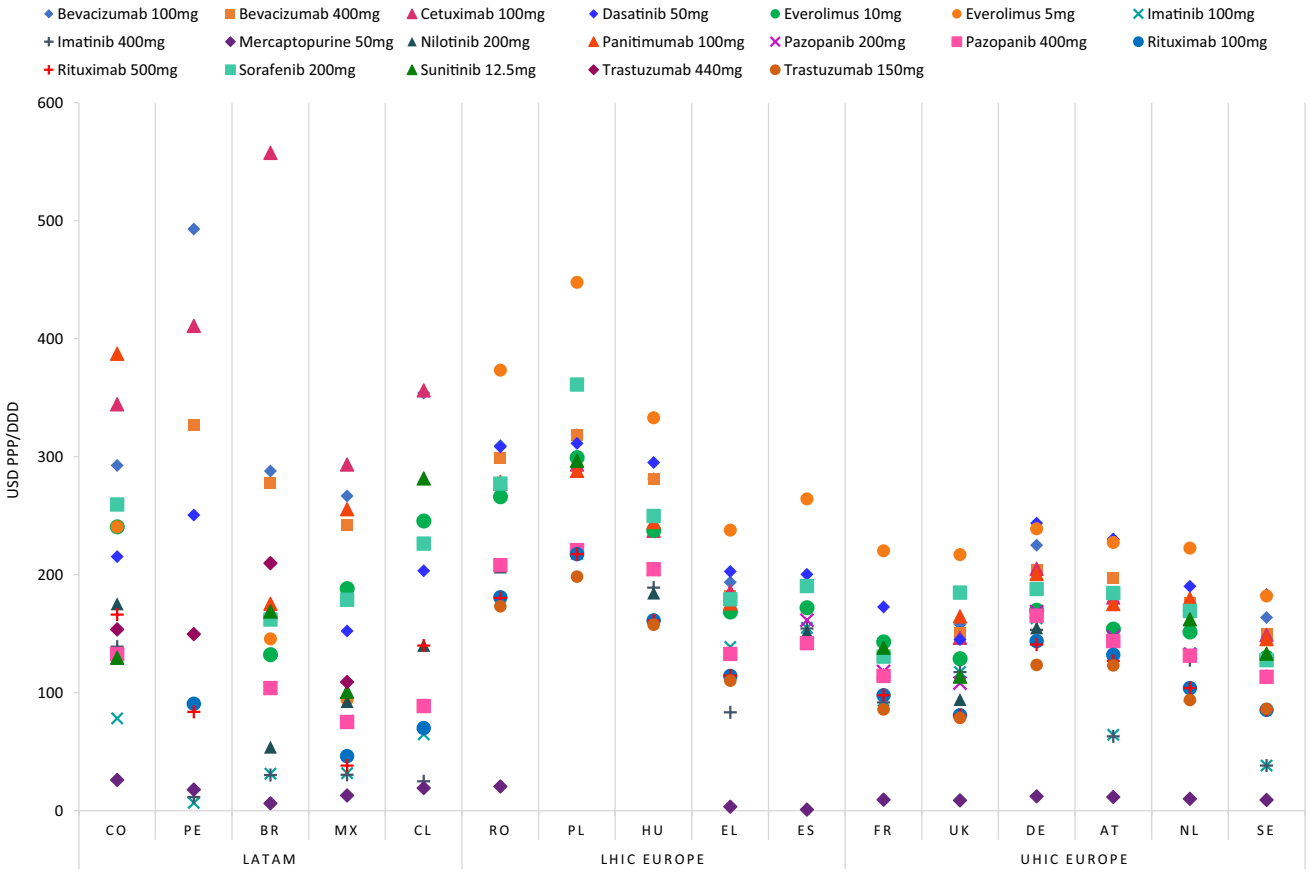

Fig. 1 Prices of originator cancer medicines in 11 European countries and five LATAM countries. *DDD* defined daily dose, *LATAM* Latin America(n countries), *LHIC* lower high-income countries, *mg* milligrams, *UHIC* upper high-income countries, *US$ PPP/DDD* price per medicine, adjusted to purchasing power parity (PPP) in US dollars per DDD, country code—see Table 1

For some medicines, Peru and Brazil reported the highest prices (e.g., bevacizumab 100 mg and 400 mg, and cetuximab 100 mg; see also Online Supplemental Material: A1, A2, and A3).

3.2 Affordability Differences Between Countries

The affordability assessment showed that medicines were more affordable in HICs than in MICs (Fig. 2). For all medicines, less than 5 days' wages were required to purchase one DDD in all UHICs (median = 2.04 days/DDD), whereas the requirement increased to 5–13 days' wages in European LHICs (median = 6.79 days/DDD). Across European countries, medicines were the least affordable (0.72–13.03 minimum wages) in Romania. In LATAM countries, for most medicines, 5 to more than 20 days' wages were required to buy one DDD of a medicine (median = 10.53 days/DDD). Overall, medicines in Mexico were the least affordable (Online Supplemental Material: A4 and A5).

Across all countries, mercaptopurine 50 mg (median = 0.19 day/DDD), trastuzumab 150 mg (median = 1.97 day/DDD), imatinib 100 mg (median = 2.06 day/DDD), and imatinib 400 mg (median = 2.01 day/DDD) were the most affordable medicines. Eight medicines (bevacizumab 100 mg, bevacizumab 400 mg, cetuximab 100 mg, dasatinib 50 mg, everolimus 5 mg, panitumumab 100 mg, sunitinib 12.5 mg, and trastuzumab 440 mg) reported the highest rates of unaffordability. For all other medicines, median affordability values ranged from 3 to up to nearly 5 days/DDD (Online Supplemental Material: A4 and A5).

4 Discussion

The study shows price differences for originator cancer medicines between LATAM countries and European countries and across European countries of different income levels. In general, PPP-adjusted prices in HICs tended to be lower than in LICs.

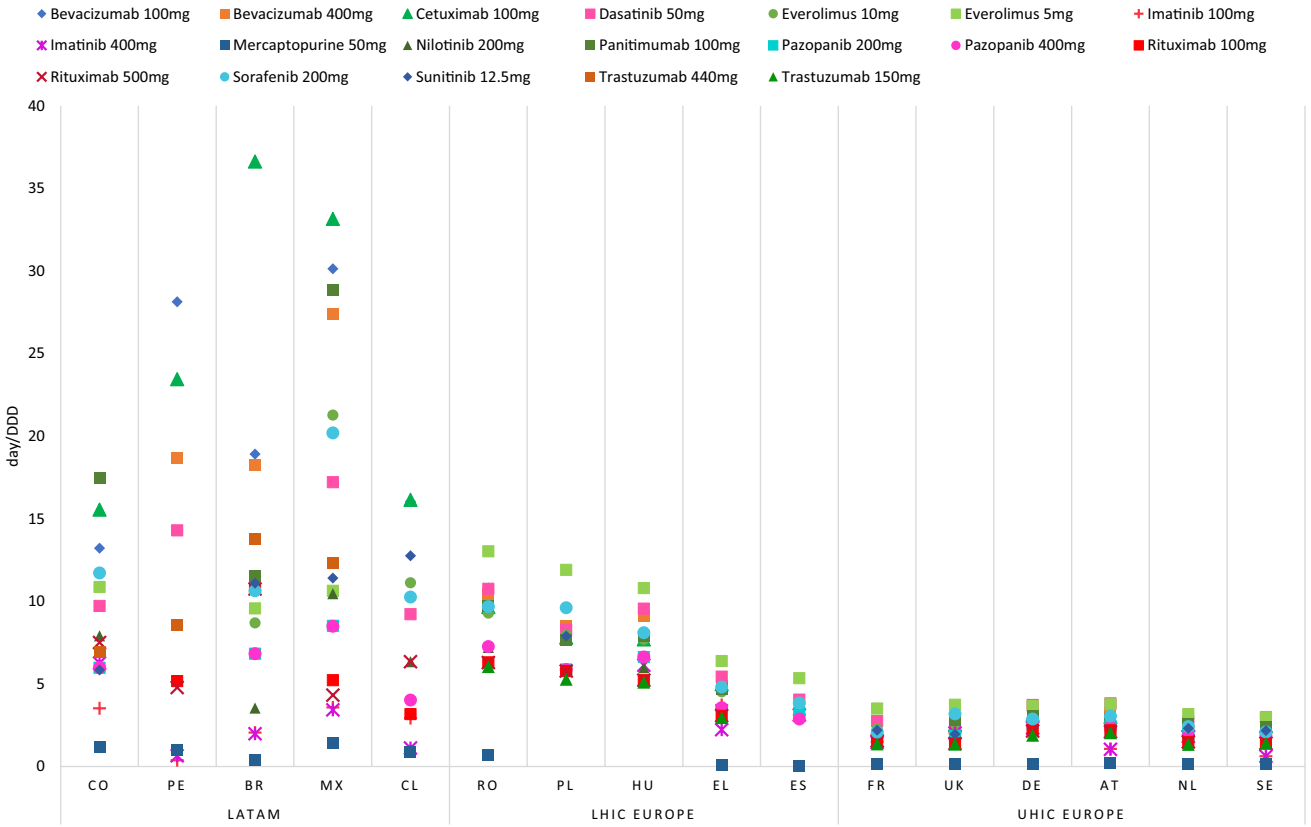

Fig. 2 Affordability of originator cancer medicines in 11 European countries and five LATAM countries. *day/DDD* number of daily minimum wages necessary to buy one DDD, *DDD* defined daily dose, *LATAM* Latin America(n countries), *LHIC* lower high-income countries, *mg* milligram, *UHIC* upper high-income countries, country code—see Table 1

4.1 Prices of Cancer Medicines

Prices of all studied medicines differed between countries. Across Europe, PPP-adjusted prices in UHICs (France, Germany, the Netherlands, the UK, and Sweden) were lower than in LHICs (Spain, Poland, Hungary, Greece and Romania). Prices in European (UHIC and LHIC) countries were similar to or lower than in LATAM countries. This finding confirms previous research that could not identify any positive association between the income of a country and medicine prices [32–36, 54] and suggests a rather inverse relationship between country income and price (i.e., higher prices in LICs).

One explanation for high (PPP-adjusted) prices in LATAM countries compared to European HICs could be the lack of pricing and reimbursement policies, which had been implemented in European countries and have proven to be effective [26, 55–61]. In addition, given their willingness- and ability-to-pay, health systems of HICs can represent attractive markets for the pharmaceutical industry. In contrast, LHICs (Poland, Greece, Hungary, Romania, and Spain) are struggling with very tight budgets and are likely to have less power to bargain with manufacturers. These conclusions are in line with the findings of a cross-country comparison of prices of cancer medicines across Europe, which demonstrated that Central and Eastern European countries (i.e., those with lower incomes) were less able to negotiate discounts [62]. An analysis of list price and actual price data in that study [62] showed discounts of 53% for two medicines in Italy and discounts between 30% and 40% for five medicines in Italy. Spain, Norway, and also Poland were also able to secure a discount in the range of 30–45% for one or two medicines but in several cases discounts for these and further studied countries amounted to less than 10%. No difference between the list price and the discounted price was reported for several medicines by some countries. An earlier study as of 2009 showed that for oncology medicines no or low discounts could be secured by hospital purchasers in five European countries, which was attributed to the fact that oncology medicines were monopoly medicines whereas for medicines with alternatives and with subsequent use in the outpatient sector larger discounts were provided [63]. The same pattern was confirmed in a report of the Austrian Court of Auditors, which identified higher discounts for cytostatic medicines with generics available compared to monoclonal antibodies (findings for two hospitals: average

discounts of 13% and 17%, respectively, for cytostatics in general, and of 7–8% for monoclonal antibodies [64]).

Prices in LATAM countries showed considerably larger variation, with higher prices for several medicines compared to those in the studied European HICs. This can be the result of ineffective or lack of pricing regulations in these countries [25, 65, 66]. Colombia and Brazil control the prices of cancer medicines, while Peru and Chile have kept a free pricing system (i.e., no price regulation or control) [67, 68], and Mexico has a mixed system of free pricing in the private sector and price control through price negotiations in the public sector [27, 69]. As governments move on expanding health coverage, emerging markets with a large population size, like those in LATAM, could be considered attractive to the pharmaceutical industry [70, 71]. However, manufacturers do not offer prices of (originator) cancer medicines in line with the countries' income level [72]. This points to the necessity of government action to regulate medicine prices, since well-designed price regulation based on evidence-informed selection through HTAs can help sustain medicine prices at more affordable levels [26, 58, 73–75].

A few active substances in the sample had gone off-patent at the time of the study, and the studied originator versions reported lower prices (e.g., imatinib and mercaptopurine). This highlights the impact of (generic) competition. Therefore, governments could use the efficiency gains of generic and biosimilar medicines and complement pricing policies by demand-side measures, such as generic substitution and information campaigns, to enhance the uptake of off-patent medicines [73].

This study adds to previous evidence that showed concerns about the high prices of cancer medicines [3, 15, 16, 18, 19, 76]. It has been argued that their high prices are justified by the value that they bring. While some new cancer medicines have improved health outcomes, others have demonstrated limited evidence of their therapeutic value [15, 17, 57, 77, 78].

4.2 Affordability of Cancer Medicines

In the literature, a medicine was defined as affordable if less than 20% of 1 day of income (minimum wage) is needed to buy one DDD [34, 48, 79]. According to this definition, nearly all surveyed medicines were unaffordable in the studied countries since, except for mercaptopurine in most HICs, in all countries at least more than 1 day's wage to procure one DDD would be required. These findings confirm the conclusions of a recent WHO report suggesting that prices of cancer medicines are unaffordable—to patients paying out of pocket, but very likely also to health systems globally [76].

There was large cross-country variation in the affordability of cancer medicines. While in the UHICs, less than 5 days' wages were required to procure one DDD of most medicines, the respective data for the LHICs in Europe and in LATAM countries were considerably higher (3–7 days' and 5 to more than 10 days' wages, respectively). The lowest affordability for most medicines was found in Mexico. Besides the price level, the unaffordability of cancer medicines in Mexico is also attributable to the country's minimum wage. If Mexico's minimum wage were as high as in Colombia, Peru, or Brazil, medicines would have been more affordable than in the other LATAM countries (see Online Supplemental Material: A6 and A7).

Governments have been implementing different policies to ensure access to high-priced medicines that would otherwise be unaffordable to their citizens. One of the solutions that has been used for cancer medicines in Europe and other HICs is MEAs [24, 31, 80]. MEAs can take different forms (e.g., flat discounts, risk-sharing agreements, price-volume agreements, pay-for-performance), but they have in common that lower prices are kept confidential [24, 38, 80, 81]. While these arrangements help to make medicines affordable for health systems, they negatively impact other countries that use EPR and reference to the officially (higher) published prices in these countries [24, 81]. The use of MEAs can also incentivize the pharmaceutical industry to set even higher prices of new products in expectation of a MEA [80, 82].

To improve access to new (cancer) medicines, governments have strengthened cross-country collaboration [83]. Supported by the European Commission, HTA bodies from several European countries have been working together in the European Network for HTA (EUnetHTA) project for over a decade. It fosters collaboration on HTAs by developing further methodologies and reducing overlaps and duplication of efforts. More formalized and sustainable collaboration beyond 2020 on HTAs is being discussed based on a European Commission proposal for a regulation of HTAs [84]. In addition, some cross-country collaborations of a few European countries (e.g., Baltic Procurement Initiative, Beneluxa Initiative, Nordic Pharmaceutical Forum, Valetta Declaration, and Fair and Affordable Pricing) have been established to collaborate on HTAs and horizon scanning, joint procurement, and joint negotiations [83, 85, 86]. These cross-country collaborations are rather new, and first successes (e.g., Beneluxa negotiation for nusinersen's price [85, 87]) have focused so far on therapeutic areas other than cancer. For LATAM countries, the Pan-American Health Organization (PAHO) Strategic Fund has acted as a single entity negotiating and procuring prices of a defined set of medicines (including cancer medicines) and vaccines on behalf of participating member states [88]. PAHO's Strategic Fund has achieved prices lower or equivalent to international reference prices and other procuring agencies (e.g., the Clinton Foundation and the Global Fund); it has also provided better procurement conditions for a more efficient

use of resources [88, 89]. However, these mechanisms have apparently not yet been sufficient to ensure affordability [49]. A possible reason could be that the pricing policies have not yet been designed in the most appropriate way to address national challenges, and more learnings on how to optimize the policy framework are needed. In addition, limitations of the policies' contribution to ensure affordability may also result from the high prices of cancer medicines in recent years that are an issue even for high-income countries with comparably lower PPP-adjusted prices [1, 3, 24, 25].

4.3 Limitations

Our study has some limitations. The ex-factory prices used might not be the actual prices paid, as many European countries concluded MEAs and other confidential arrangements for cancer medicines to obtain discounts. However, as discussed, there are indications that no or low discounts are granted for monopoly oncology medicines.

For the selection of the medicines, Mexico was taken as the starting point. We checked the applicability of the inclusion criteria (e.g., clinical relevance, on-patent status) only for this country and not for all other comparator countries. We acknowledge that a few medicines in a few countries had lost patent protection and this can have an impact on medicine prices, even on originator medicines that were surveyed.

We acknowledge that the WHO/HAI methodology was developed as an instrument for price surveys and affordability measurements in LICs where no medicine price information was published. However, the WHO/HAI methodology is not limited to low-income settings, and the affordability assessments have also been conducted in HICs [32, 90].

4.4 Implications

Findings of international medicine price and affordability comparisons provide evidence for policymakers to adapt and tailor policies towards affordable prices according to the country's characteristics [33, 35]. Knowledge about price levels in other countries is needed for methodological decisions on EPR to assess the appropriateness of the selection of comparator countries. The WHO Guideline on Country Pharmaceutical Pricing Policies, as updated in 2020, recommends selecting reference countries based on a set of explicitly stated factors, mentioning comparability such as in terms of market size, national income, and purchasing power [91]. If MICs choose HICs as their external reference benchmark without any adjustment for purchasing power parities, this might have catastrophic effects on prices and eventually on public budgets and patients who have to co-pay or fully pay out-of-pocket.

Affordability considerations (i.e., budget impact analyses) can constitute a valuable part of an HTA, in addition to the evidence on the additional therapeutic value of a medicine.

By comparing different countries and regions, the findings of this study on prices and affordability can inform the international community in their efforts to develop new models towards fair prices—those that provide a reasonable return of investment at a price that "does not bankrupt health systems" and does not cause "financial toxicity" [54, 92]. The key findings of this study—prices for cancer medicines are variable and largely unaffordable—call upon policymakers to revise their policy framework and develop adequate policy options. There is specific need for policy action in UMICs since they are excluded from "access programs" that LICs enjoy. Furthermore, UMICs can suffer from trade pressure that HICs exercise to intensify intellectual property protection, and overall, these countries receive little international support to promote lower prices of medicines [93].

5 Conclusions

Public procurement and ex-factory prices of originator cancer medicines considerably differ between countries of different income levels and would be largely unaffordable compared to the national minimum wage. For several studied medicines their PPP-adjusted prices were higher in countries of lower income than in those of higher income.

High unaffordability levels constitute a major barrier to access to needed cancer care. Policymakers are urged to implement policies aiming at prices deemed affordable as well as ensuring coverage and public funding for medicines that demonstrate added value. Since access to affordable medicines is a global challenge, collaboration between countries and action at a global level is encouraged to move towards prices that are fair and sustainable for patients, health systems, and the industry.

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Declarations

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Conflict of interest All authors declare that they have no conflict of interest.

Availability of data and material All data generated or analyzed during this study are included in this published article (and its Online Supplementary Material files).

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