Sales of anti-cancer medicines; China, Indonesia, Kazakhstan, Malaysia, Philippines and Thailand

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Objective To assess sales of anti-cancer medicines in the 2017 World Health Organization’s WHO Model list of essential medicines in China, Indonesia, Kazakhstan, Malaysia, Philippines and Thailand from 2007 (2008 for Kazakhstan and Malaysia) to 2017.

Methods We extracted sales volume data for 39 anti-cancer medicines from the IQVIA database. We divided the total quantity sold by the reference defined daily dose to estimate the total number of defined daily doses sold, per country per year, for three types of anti-cancer therapies (traditional chemotherapy, targeted therapy and endocrine therapy). We adjusted these data by the number of new cancer cases in each country for each year.

Findings We observed an increase in sales across all types of anti-cancer therapies in all countries. The largest number of defined daily doses of traditional chemotherapy per new cancer case was sold in Thailand; however, the largest relative increase per new cancer case occurred in Indonesia (9.48-fold). The largest absolute and relative increases in sales of defined daily doses of targeted therapies per new cancer case occurred in Kazakhstan. Malaysia sold the largest number of adjusted defined daily doses of endocrine therapies in 2017, while China and Indonesia more than doubled their adjusted sales volumes between 2007 and 2017.

Conclusion The use of sales data can fill an important knowledge gap in the use of anti-cancer medicines, particularly during periods of insurance coverage expansion. Combined with other data, sales volume data can help to monitor efforts to improve equitable access to essential medicines.

Introduction

The sustainable development goals (SDG) identify access to quality medicines as a key component of universal health coverage (UHC). 1 The SDGs also reflect a global recognition of the need to tackle the growing burden of noncommunicable diseases, including cancer. The World Health Organization’s WHO Model list of essential medicines includes a section on anti-neoplastic medicines that countries can use to inform the development of their own national essential medicines lists. Beyond inclusion in national essential medicines lists, little is known about the use of cancer medicines at a country level. This is an important gap, particularly as countries are striving to improve access to care and financial protection through UHC.

The Lancet Commission on Essential Medicines for Universal Health Coverage 9,10 called for the continuous and global monitoring of access to essential medicines (including anti-cancer medicines) in the form of routine data disaggregated by gender, ethnicity, education, residential location and wealth quintile. As these data are not readily available in many settings, it is important to leverage different sources of evidence to inform progress. 9,10 Multicountry studies on access to anti-cancer medicines in low- and middle-income countries have used the inclusion of medicines in national essential medicines or reimbursement lists and formularies 11–14 and their availability on the market and applicable copayments 15 as proximate indicators of access. Country-level studies have used national essential medicines lists and formularies, sales data, 16–18 surveys 17 and patient-level data from medical records 19–21 to access anti-cancer medicines in low- and middle-income countries. However, to our knowledge, few of the existing studies 15 or official statistics 22 have assessed the changes in use of anti-cancer medicines during the past decade of coverage expansion in low- and middle-income countries.

As the number of new cancer cases worldwide is expected to increase from 18.1 million in 2018 to 29.5 million in 2040 25 and the need to improve access to medicines is high on the global agenda, 9 we need evidence on the use of anti-neoplastic medicines at a country level. In this study, we use routinely collected market sales data to assess how sales of the anti-cancer medicines included in the 2017 WHO Model list of essential medicines 26 have evolved over time in six countries.

Methods

Country selection

We selected countries to include in our study based on the following criteria. First, we identified countries working towards UHC, and that have set up national public or private third-party payment systems or implemented other relevant pharmaceutical coverage policies within the government health system, in the last decade. Second, we chose countries in which IQVIA sales data on the medicines of interest were available and cover both public and private sectors, and hospital, as well as retail sectors. Third, we focused on countries from the same income group (i.e. middle income) and continent to make comparisons more meaningful. China, Indonesia, Kazakhstan, Malaysia, Philippines and Thailand met these criteria. We provide a summary of the demographic and socioeconomic characteristics of these six countries in Table 1.

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Submitted: 8 September 2019 – Revised version received: 17 April 2020 – Accepted: 20 April 2020 – Published online: 28 May 2020
We considered all 49 anti-neoplastic medicines (defined on the basis of their active ingredients) listed in sections 8.2 “Cytotoxic and adjuvant medicines” and 8.3 “Hormones and antihormones” of the 2017 WHO model list. We excluded five supportive medications used to prevent or relieve the side-effects of anti-neoplastic treatment. We also excluded five medications that are listed in other therapeutic classes, as well as in sections 8.2 or 8.3. For example, methotrexate is also listed in section 30.2 of the model list for the treatment of rheumatoid arthritis; based on the formulation of methotrexate, it is not possible to distinguish between indications (further details available in the data repository).

The number of medicines that we selected for this study was therefore 39 (Box 1).

**Data source**

IQVIA conducts multisample audits of pharmaceutical purchase data based on invoices from pharmacies, wholesalers, distributors and manufacturers in the hospital and retail sectors in several countries worldwide (further details available in data repository). The proprietary data are extrapolated to represent national-level sales. Quality checks (e.g. comparison with manufacturer data) are conducted to ensure the accuracy and representativeness of the data. We extracted quarterly data on sales volumes of all anti-neoplastic medicines of interest from 2007 to 2017 from the IQVIA database; complete data for Kazakhstan and Malaysia were only available from 2008 onwards, so we used 2008 as the baseline for both these countries. The data set included country, setting (retail or hospital), generic name, quarter, year, strength, formulation, units per pack and number of packs sold. The assumed average maintenance dose per day for a medicine used for its main indication in adults, defined by the Anatomical Therapeutic Chemical Classification System according to its administration route, is referred to as the defined daily dose. The defined dose provides a common unit of analysis that can be used to study the use of medicines over time and across therapeutic classes and population groups. The WHO Collaborating Centre for Drug Statistics Methodology assigns a defined daily dose index for many drugs, but made the decision not to assign defined daily doses for medicines with highly individualized treatment schedules, such as anti-neoplastic medicines.

We used country-specific estimates of new cancer cases available by year for...
the entire study period from the 2017 Global Burden of Disease (GBD) study.21

Analysis
Using information on the strength of each medicine, number of units per pack and number of packs sold, we estimated the total milligrams (or active units for asparaginase) sold. We divided the total quantity sold by the reference defined daily dose for that particular medicine to estimate the total number of defined daily doses sold. We defined sales volume as the estimated number of defined daily doses sold per country and per year for each of the three types of anti-cancer treatment (traditional chemotherapy, targeted therapy and endocrine therapy). We also calculated the number of defined daily doses sold per new cancer case.

Ethics
Ethical approval was granted by the Institutional Review Board of Harvard Pilgrim Health Care.

Results
Cancer incidence
Of the countries studied, China is the most populous and also, according to GBD data,21 the country with the highest all-cancer incidence (325 per 100,000 in 2017; Table 1). The highest number of new cancer cases for both 2007 and 2017 was observed in China, as well as the largest absolute (1,807,036.83 cases) and relative (1.65-fold) increase (Table 2). GBD data21 indicate that Indonesia, the second-most populous of the countries studied, had the second-highest number of cancer cases in both 2007 and 2017 and the second-largest increase in absolute numbers (68,505.81 cases), but not in relative numbers (1.28-fold). We noted that the second-highest relative increase in the number of new cancer cases (1.53-fold; from 2008 to 2017 in this case) occurred in Malaysia.

Sales volumes
The sales data indicated that, of the six countries studied, the highest number of defined daily doses of traditional chemotherapy was sold in China in both 2007 and 2017 (Table 2); China also demonstrated the highest absolute increase in defined daily doses of traditional chemotherapy sold from 2007 to 2017. However, the largest relative increase (12.16-fold) was observed in Indonesia.

Overall, the number of defined daily doses of traditional chemotherapy, targeted therapy and endocrine therapy sold per new cancer case increased over time for all six countries studied, with the exception of traditional chemotherapy in Malaysia (Fig. 1, Fig. 2 and Fig. 3).

In terms of defined daily doses per incident cancer case, for traditional chemotherapy the greatest relative increase from baseline occurred in Indonesia, where sales increased from 3.98 in 2007 to 37.75 in 2017. The highest number of defined daily doses per new case in 2017 was sold in Thailand (78.23). Although the total sales volume (in defined daily doses) increased in Malaysia from 2008 (2023,814.87) to 2017 (2715,687.49), this increase was by a lower proportion (1.34-fold) than the reported increase in the number of new cancer cases (1.53-fold); Malaysia therefore observed a decrease from 65.19 defined daily doses sold per new case in 2008 to 57.06 in 2017.

For targeted therapies, the highest number of defined daily doses per new cancer case in 2017 was sold in Kazakhstan, in which we observed the largest relative increase from 0.04 in 2008 to 9.49 in 2017. Of the five targeted therapies considered in this study (Box 1), trastuzumab and imatinib were sold in the largest quantities per new cancer case in all countries. For endocrine therapies, the largest numbers of defined daily doses of endocrine therapies per new cancer case (112.17) were sold in Malaysia in 2017, while both China and Indonesia more than doubled their numbers of defined daily doses sold per new cancer case from 2007 to 2017. Of the four endocrine medicines included in this study (Box 1), tamoxifen was the most widely sold endocrine therapy in all countries.

Discussion
Our data show an overall increase in the sales of anti-cancer therapies in China, Indonesia, Kazakhstan, Malaysia (increase in overall chemotherapy sold, although a slight decrease per new cancer case), Philippines and Thailand during our study period. During this time, the six countries continued working towards the goals of achieving UHC. Given the high cost of cancer treatment, the expansions these countries have made in health-care coverage over the last decade will likely have played an important role in enabling greater use of these medicines. The largest increase occurred in defined daily doses of traditional chemotherapy sold in Indonesia between 2014 and 2015, which is when implementation of UHC began in that country. In addition to a higher availability of cancer medicines, improved access to a health-care system as a result of progress in UHC could have led to earlier diagnoses (at a stage amenable to treatment), contributing to an increased use of cancer medicines.

While the overall increase in sales of anti-cancer medicines from 2007 (or 2008) to 2017 in each country suggests increased access by the populations, aggregated results hide potential disparities in access between groups within a population. Two studies in Thailand found differences in the use of medicines between members of different insurance schemes. One study described differences in the type of treatment received and health outcomes between individuals with colorectal cancer insured under the UHC scheme for the general population and those in the civil servant scheme.22 Disparities in survival were also found for lymphoma patients, and mainly attributed to limited access to rituximab for UHC-insured patients at the time of the study (2003–2006).21 Two studies from China on patterns of prescribing for patients with breast cancer highlighted limited access to trastuzumab for patients overexpressing human epidermal growth factor receptor 2 (HER-2).18,20 One of these two multicentre studies found that, between 2011 and 2014, only 31 (28.4%) of 109 patients overexpressing HER-2 were treated with trastuzumab.20 A 2011 study in Malaysia found that only 19% of 172 patients younger than 70 years with HER-2-positive breast cancer stage I to II received trastuzumab within 1 year of diagnosis, which the authors attributed to its high cost and insufficient public funding for the treatment.21 Despite these earlier findings highlighting limited access, official statistics show that the use of trastuzumab has increased over time (particularly in the public sector) following inclusion in the national formulary in 2008.20

As global spending on cancer treatment continues to rise, new therapies continue to enter the market and new indications are being approved for medicines already available,32 countries will increasingly face challenges in enabling access to new therapies in an equitable way. Budgetary constraints play an important role in access to highly priced...
medicines, such as the five targeted therapies included in this study. In the absence of large discounts as part of differential pricing or industry access programmes, it will be challenging for middle-income countries working towards UHC to provide cancer medicines equitably to all patients in need. In Thailand for example, UHC-insured patients have access to medicines on the national essential medicines list and civil servants have access to all medicines on the Thai market. To facilitate the coverage of highly priced medicines, Thailand has engaged in compulsory licensing, price negotiation and health technology assessment, and created a separate section on the essential medicines list (E2) used for centralized procurement, among other measures. Similarly, in China, coverage of medicines differed between provinces and insurance schemes before 2018. Generally, coverage with the Urban Employee Basic Medical Insurance scheme is more generous than the Urban Resident Basic Medical Insurance scheme and both provide greater coverage than the New Rural Cooperative Medical Scheme. To help municipalities (ultimately responsible for payment of medicines) cover medicines in the Basic Medical Insurance scheme, the Chinese Government has engaged in price negotiation with manufacturers to secure more competitive prices. Further, since 2019, provinces are required to cover all medicines included in the Basic Medical Insurance list (including the national essential medicines list); previously there was some flexibility for provinces to either exclude some medicines listed as essential (in the national list) from

| Table 2. All-cancer incidence and sales volumes of anti-cancer medicines in six countries in 2007 (or 2008) and 2017 |
|-------------------------------------------------|----------------|----------------|----------------|----------------|----------------|----------------|
| Data                                             | China          | Indonesia      | Kazakhstan     | Malaysia       | Philippines    | Thailand       |
| New cancer cases, all cancers<sup>b</sup>          |                |                |                |                |                |                |
| Year 2007 or 2008<sup>a</sup>                     | 2,781,760.17   | 242,435.72     | 35,281.97      | 31,045.63      | 87,922.57      | 120,420.79     |
| Year 2017                                         | 4,588,797.00   | 310,941.53     | 38,503.55      | 47,594.47      | 126,203.23     | 157,914.48     |
| Absolute increase                                 | 1,807,036.83   | 68,505.81      | 32,211.57      | 16,548.84      | 38,280.66      | 37,493.69      |
| Relative increase, x-fold                         | 1.65           | 1.28           | 1.09           | 1.53           | 1.44           | 1.31           |
| Chemotherapy                                      |                |                |                |                |                |                |
| Total no. defined daily doses sold<sup>c</sup>    |                |                |                |                |                |                |
| Year 2007 or 2008<sup>a</sup>                     | 80,222,871.95  | 965,421.50     | 1,075,377.68   | 2,023,814.87   | 1,594,213.68   | 6,182,965.79   |
| Year 2017                                         | 202,691,916.50 | 11,737,244.72  | 1,307,816.88   | 2,715,687.49   | 3,867,712.03   | 12,354,259.40  |
| Absolute increase                                 | 122,469,044.55 | 10,771,823.22  | 232,439.20     | 691,872.62     | 2,273,498.34   | 6,171,293.91   |
| Relative increase, x-fold                         | 2.53           | 12.16          | 1.22           | 1.34           | 2.43           | 2.00           |
| No. defined daily doses per new cancer case       |                |                |                |                |                |                |
| Year 2007 or 2008<sup>a</sup>                     | 28.84          | 3.98           | 30.48          | 65.19          | 18.13          | 51.34          |
| Year 2017                                         | 44.17          | 37.75          | 33.97          | 57.06          | 30.65          | 78.23          |
| Absolute increase                                 | 15.33          | 33.77          | 3.49           | −8.13          | 12.51          | 26.89          |
| Relative increase, x-fold                         | 1.53           | 9.48           | 1.11           | 0.88           | 1.69           | 1.52           |
| Targeted therapy                                  |                |                |                |                |                |                |
| Total no. defined daily doses sold<sup>c</sup>    |                |                |                |                |                |                |
| Year 2007 or 2008<sup>a</sup>                     | 333,010.55     | 9,685.43       | 1,253.75       | 39,124.13      | 37,116.25      | 125,958.25     |
| Year 2017                                         | 1,128,751.09   | 488,889.37     | 365,575.96     | 400,541.29     | 217,806.95     | 1,104,714.19   |
| Absolute increase                                 | 10,948,740.54  | 479,203.94     | 364,322.21     | 361,417.17     | 180,690.70     | 978,755.94     |
| Relative increase, x-fold                         | 33.88          | 50.48          | 291.59         | 10.24          | 5.87           | 8.77           |
| No. defined daily doses sold per new cancer case  |                |                |                |                |                |                |
| Year 2007 or 2008<sup>a</sup>                     | 0.12           | 0.04           | 0.04           | 1.26           | 0.42           | 1.05           |
| Year 2017                                         | 2.46           | 1.57           | 9.49           | 8.42           | 1.73           | 7.00           |
| Absolute increase                                 | 2.34           | 1.53           | 9.46           | 7.16           | 1.31           | 5.95           |
| Relative increase, x-fold                         | 20.54          | 39.36          | 267.19         | 6.68           | 4.09           | 6.69           |
| Endocrine therapy                                 |                |                |                |                |                |                |
| Total no. defined daily doses sold<sup>c</sup>    |                |                |                |                |                |                |
| Year 2007 or 2008<sup>a</sup>                     | 34,219,204.50  | 1,394,979.75   | 1,771,683.00   | 3,066,676.50   | 2,890,588.06   | 6,003,971.15   |
| Year 2017                                         | 129,391,344.55 | 3,979,765.31   | 2,323,521.75   | 5,338,724.85   | 5,955,772.99   | 11,275,412.09  |
| Absolute increase                                 | 95,172,140.05  | 2,584,785.56   | 551,838.75     | 2,272,048.35   | 3,065,184.93   | 5,271,440.94   |
| Relative increase, x-fold                         | 3.78           | 2.85           | 1.31           | 1.74           | 2.06           | 1.88           |
| No. defined daily doses sold per new cancer case  |                |                |                |                |                |                |
| Year 2007 or 2008<sup>a</sup>                     | 12.30          | 5.75           | 50.21          | 98.78          | 32.88          | 49.86          |
| Year 2017                                         | 28.20          | 12.80          | 60.35          | 112.17         | 47.19          | 71.40          |
| Absolute increase                                 | 15.90          | 7.05           | 10.13          | 13.39          | 14.32          | 21.54          |
| Relative increase, x-fold                         | 2.29           | 2.22           | 1.20           | 1.14           | 1.44           | 1.43           |

<sup>a</sup> Complete sales data for Kazakhstan and Malaysia were only available from 2008; therefore we used the 2008 data as the baseline for these countries.

<sup>b</sup> Global Burden of Disease Collaborative Network.<sup>32</sup>

<sup>c</sup> Data available on request from IQVIA.
coverage, or to cover some medicines not listed as essential.40

Our study had several limitations. First, we used national-level sales data of anti-cancer medicines included in the 2017 WHO Model list of essential medicines; sales data do not tell us whether the medicine was eventually prescribed, dispensed and administered to the patient. If procurement quantities were inaccurate, or less patients presented than in previous years, sales may differ from actual use. Anti-cancer treatments included in the 2017 WHO model list are a subset of all available anti-cancer medicines; this subset is selected by the WHO Expert Committee on the Selection and Use of Essential Medicines by considering the burden of disease and responsiveness of the indicated cancer to pharmacotherapy. We had no access to patient-level data on the actual conditions treated, regimens, insurance status, co-payments, income, education or the many other factors that can influence the use of medicines. Our measure, defined daily dose, is a way to summarize and compare sales volumes across products and does not necessarily reflect the way in which these medicines are actually prescribed. Since we had no information on the indications for which these medicines were used in clinical practice (and most of these medicines can be used for different types of cancers), we could only attempt a crude adjustment for use by the total number of new cancer cases per country and year. Furthermore, the quality of the available data on cancer incidence may differ between countries, which may impact the reliability of inter-country comparisons.

Second, we cannot judge whether the sales levels we observed are sufficient to appropriately treat all cancer patients in a given country. The sales differences we identified between the six countries cannot be attributed to any specific cause, such as financial barriers, training and infrastructure, lack of insurance coverage, differences in clinical guidelines or stage at diagnosis, all of which might partially explain sales differences.

Finally, while IQVIA data are nationally representative and include the relevant channels (public and private sectors; hospital and retail settings) where cancer medicines are transacted, medicines procured through special channels (e.g. donations) may not be included in the IQVIA sample and therefore may not be captured in the data.

Fig. 1. Defined daily doses of traditional chemotherapy sold per new cancer case in six countries from 2007 (or 2008) to 2017

Fig. 2. Defined daily doses of targeted therapy sold per new cancer case in six countries from 2007 (or 2008) to 2017

Fig. 3. Defined daily doses of endocrine therapy sold per new cancer case in six countries from 2007 (or 2008) to 2017
Despite the limitations described here, studies using routinely aggregated sales data over time can fill an important knowledge gap in the use of medicines. Such studies can be complemented by other research based on higher-resolution patient-level data (e.g. health insurance claims data, medical records and socioeconomic status), allowing assessments of equity in access. Future studies also need to assess the affordability of cancer medicines at the household and system level. Monitoring sales in the context of insurance coverage expansions is important to identify progress and challenges in improving access to anti-cancer medicines, contributing to the SDG agenda. Our study has taken a first step in that direction.

Funding: IQVIA data were provided in kind. AF is supported by a postdoctoral fellowship from the Swiss National Science Foundation. XG was supported by the China Scholarship Council. AW’s effort was partially covered by the Ebert Award of the Department of Population Medicine at Harvard Medical School and the Harvard Pilgrim Health Care Institute.

Competing interests: AF reports personal fees from the European Society of Medical Oncology, separate from the submitted work. The institution by which PS declares no competing interests.

Sales of anti-cancer medicines in six countries Alessandra Ferrario et al.

Melhours

摘 要
抗癌药物销售情况：菲律宾、哈萨克斯坦、马来西亚、泰国、印度尼西亚和中国

目的
旨在评估世界卫生组织发布的《世卫组织基本药物标准清单》中的抗癌药物于2007年至2017年在菲律宾、哈萨克斯坦、马来西亚、泰国、印度尼西亚和中国（2008年哈萨克斯坦）的销售情况。

方法
我们从IQVIA数据库中选取了39种抗癌药物的销售数据。我们用销售总量除以此参考清单中的限定日剂量来估算每个国家三种抗癌疗法（传统化疗、靶向治疗和内分泌疗法）每年的限定日剂量总销量。我们根据每个国家每年新增癌症病例数调整了这些数据。

结果
我们观察到所有国家各种类型的抗癌疗法的销售额都有所增长。泰国每例新增癌症患者购买传统化疗药物的限定日剂量最大；然而，印度尼西亚每例新增癌症患者的相对增幅最大（9.48倍）。哈萨克斯坦新增癌症患者中，靶向治疗的限定日剂量销售额呈现最大的绝对增幅和相对增幅。2017年，马来西亚调整后的内分泌疗法限定日剂量销量最大，而中国和印度尼西亚的调整后销售量在2007年至2017年增加了一倍以上。

结论
销售数据的使用可以填补抗癌药物使用方面的重要认知缺口，尤其是在扩大保险覆盖范围期间。结合其他数据，销售数据有助于监测改善患者平等获取基本药物方面的工作。

Résumé

Vente de médicaments contre le cancer en Chine, en Indonésie, au Kazakhstan, en Malaisie, aux Philippines et en Thaïlande

Objectif
Évaluer la vente de médicaments contre le cancer figurant dans l’édition 2017 de la Liste modélée des médicaments essentiels publiée par l’Organisation mondiale de la Santé en Chine, en Indonésie, au Kazakhstan, en Malaisie, aux Philippines et en Thaïlande entre 2007 (pour le Kazakhstan et la Malaisie) et 2017.

Méthodes
Nous avons extrait de la base de données IQVIA les informations relatives au volume de vente pour 39 médicaments contre le cancer. Nous avons divisé le nombre total de médicaments vendus par la dose quotidienne déterminée de référence, afin d’estimer le nombre total de doses quotidiennes déterminées vendues par pays et
par an, pour trois types de traitements contre le cancer (chimiothérapie conventionnelle, thérapie ciblée et endocrinothérapie). Nous avons ajusté ces données en tenant compte du nombre de nouveaux cas de cancer diagnostiqués chaque année dans chaque pays.

Résultats Nous avons observé une hausse des ventes pour tous les types de traitements contre le cancer dans tous les pays. C’est la Thaïlande qui vend le plus grand nombre de doses quotidiennes déterminées en chimiothérapie conventionnelle pour chaque nouveau cas de cancer; néanmoins, c’est en Indonésie que nous avons constaté la plus grande augmentation relative pour chaque nouveau cas de cancer (nombre multiplié par 9,48). En termes d’augmentation absolue et relative des ventes de doses quotidiennes déterminées pour lathérapie ciblée, c’est au Kazakhstan qu’elle était la plus élevée. La Malaisie est le pays ayant vendu le plus grand nombre de doses quotidiennes déterminées pour l’endocrinothérapie, tandis que la Chine et l’Indonésie ont plus que doublé leur volume de vente ajusté entre 2007 et 2017. Conclusion L’exploitation des données de vente peut combler un manque de connaissances dans l’utilisation de médicaments contre le cancer, surtout pendant les périodes d’élargissement de la couverture maladie. En les associant à d’autres informations, les données sur le volume de vente permettent de suivre les efforts fournis pour garantir un accès de plus en plus équitable aux médicaments essentiels.
