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LETTER TO THE EDITOR

Anticancer medicines in China: Trends in daily therapy cost and relative procurement volume and spending

Dear editors,

Cancer is a critical public health concern worldwide. The number of cancer patients in developing countries accounts for ~50% of the total number of cancer patients worldwide, however, over 70% of cancer deaths are from developing countries [1]. In China, cancer has been a leading cause of death since 2010, with a substantially lower 5-year survival rate, compared to developed countries [2]. Several factors, including different levels of access to cancer treatment, may contribute to this gap [1]. Due to financial reasons, few people in developing countries can afford and benefit from novel anticancer medicines, especially targeted therapies. Previous studies have documented increasing trends in the use and costs of anticancer medicines in developed countries [3]. China implemented innovative policy-based approaches to improve anticancer medicine accessibility; however, the evidence is limited. Therefore, we aimed to analyze trends in anticancer medicines use in China.

We retrospectively analyzed quarterly (Q) trends in daily therapy cost, relative procurement volume (measured by defined daily doses), and spending of anticancer medicines procured by 594 tertiary hospitals in China, from January 2013 to December 2018 (Supplementary Figure S1). We identified 110 generic names of anticancer medicines, comprising of 70 traditional chemotherapies and 40 targeted therapies, corresponding to 624 products (Supplementary Tables S1-S3). Overall, the average daily therapy cost of all anticancer medicines decreased by 11.5% from 2013Q1 to 2018Q4 ($P = 0.164$; Figure 1A). The procurement volume of anticancer medicines nearly doubled from 2013Q1 to 2018Q4 (Figure 1B), while the procurement spending increased from United States (US) dollars ($)512 million to $927 million (Figure 1C). The proportion of anticancer medicine procurement volume accounted for all medicine procurement volume increased by 39.5% from 0.43% in 2013Q1 to 0.60% in 2018Q4 ($P = 0.022$; Figure 1B), and the proportion of procurement spending increased by 39.2% from 7.9% to 11.0% ($P = 0.019$; Figure 1C).

The average daily therapy cost of targeted oral and intravenous (IV) therapies decreased by 67.3% and 78.6% from 2013Q1 to 2018Q4, respectively ($P < 0.001$ and $P = 0.013$; Figure 1D). Relative procurement volumes of targeted oral and IV therapies increased significantly by 331.0% and 504.8% from 2013Q1 to 2018Q4, respectively ($P < 0.001$ and $P = 0.003$; Figure 1E), while the relative procurement spending on targeted oral and IV therapies increased by 59.8% and 46.8%, respectively ($P = 0.004$ and $P < 0.001$; Figure 1F).

For brand-name products, the average daily therapy cost significantly decreased by 48.6% from 2013Q1 to 2018Q4 ($P = 0.044$), while no trend change was found in generics ($P = 0.753$). By the end of 2018, the average daily therapy cost of brand-name products was still about 2.6 times more than that of generics (Figure 1G). The relative procurement volume for brand-name products increased by 78.1% from 2013Q1 to 2018Q4 ($P = 0.033$; Figure 1H), whereas the relative procurement spending on brand-name products remained at around 55% ($P = 0.440$; Figure 1I).

For medicines listed in the National Reimbursement Drug List (NRDL medicines) and those not listed (non-NRDL medicines), the average daily therapy cost decreased by 32.9% and 11.0% from 2013Q1 to 2017Q2, respectively. There was an abrupt rise in the daily therapy cost of NRDL medicines and non-NRDL medicines after the 2017 NRDL implementation (Figure 1J). From 2013Q1 to 2017Q2, the relative volume of NRDL medicines decreased from 91.4% to 84.8% (Figure 1K), whereas the relative procurement spending on NRDL medicines decreased from 57.8% to 48.9% (Figure 1L). After the 2017 NRDL implementation, relative procurement volume and spending of NRDL medicines increased by 10.9% and 29.2% from 2017Q2 to 2017Q4, respectively (Figure 1K and L).

Abbreviations: $, US dollars; EGFR, epidermal growth factor receptor; HER2, human epidermal growth factor receptor 2; IV, intravenous; non-NRDL medicines, medicines not listed in the National Reimbursement Drug List; NRDL medicines, medicines listed in the National Reimbursement Drug List; Q, quarterly

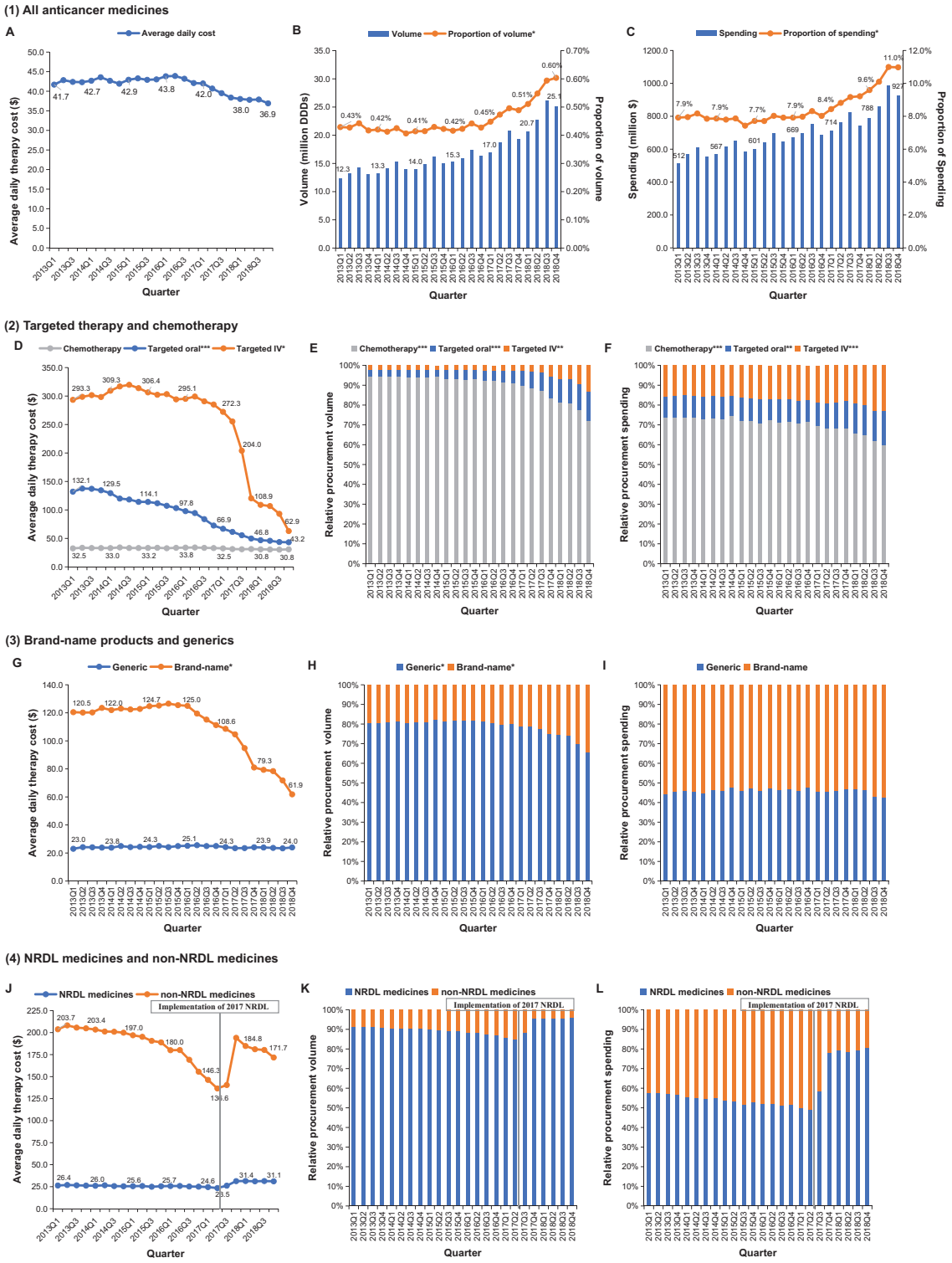

FIGURE 1 Average daily therapy costs, relative procurement volumes, and relative procurement spending of anticancer medicines in China from 2013Q1 to 2018Q4. **(1) All anticancer medicines**: A. Average daily therapy cost; B. Absolute medicine volume and proportion of medicine volume of all medicines; C. Absolute medicine spending and proportion of medicine spending of all medicines. **(2) Targeted therapy and chemotherapy**: D. Average daily therapy cost; E. Relative procurement volume; F. Relative procurement spending. **(3) Brand-name products and generics**: G. Average daily therapy cost; H. Relative procurement volume; I. Relative procurement spending. **(4) NRDL medicines and non-NRDL medicines**: J. Average daily therapy cost; K. Relative procurement volume; L. Relative procurement spending. Note: *, $P < 0.05$, **, $P < 0.01$, and ***, $P < 0.001$ for the modified Mann-Kendall trend test. The modified Mann-Kendall test was not conducted for subgroup analysis of NRDL medicines and non-NRDL medicines due to the non-monotonicity of the data. Abbreviations: NRDL medicines, National Reimbursement Drug List; NRDL medicines, Medicines listed in the National Reimbursement Drug List; non-NRDL medicines, Medicines not listed in the National Reimbursement Drug List

We found that the anticancer medicine use in China increased and the daily therapy cost decreased over time, especially for targeted therapies and brand-name products. The decreasing cost may have led to increasing utilization of anticancer medicines and plausibly improved the overall survival rate of cancer patients in China [2]. Furthermore, the relative use of anticancer medicines with mandatory insurance reimbursement increased sharply compared to those without mandatory coverage, potentially indicating improved access to selected anticancer medicines.

In contrast to increasing prices of anticancer medicines in the US [3], Australia [4], and France [5], we observed that the daily therapy cost of anticancer medicines decreased in China, especially for targeted therapies. Several factors could contribute to such findings. First, since 2010, provincial centralized bidding and tendering process were gradually implemented across China, which was effective in reducing medicine prices [6]. Second, me-too medicines, such as the tyrosine kinase inhibitors icotinib, were introduced to the market at lower prices compared to first-in-class medicines [7]. In addition, NRDL listing combined with mandatory reimbursement depended on successful national drug price negotiations. The average daily therapy cost of targeted IV anticancer therapies, half of which had prices negotiated by the central government in 2017, decreased sharply thereafter.

We found a considerable increase in the procurement volume of targeted anticancer therapies relative to that of traditional chemotherapies. This shift in volume suggested increased availability of targeted anticancer therapies in China, as targeted therapy may have better efficacy and less toxicity compared to traditional chemotherapy, thus, playing more important roles in clinical practice. For instance, trastuzumab combined with chemotherapies was recommended as the preferred treatment for human epidermal growth factor receptor 2 (HER2) positive breast cancer [8].

However, the prices of targeted therapies have remained much higher than those of chemotherapies. Targeted therapies listed in the NRDL were still likely to be too expensive for most patients to afford, considering the Chinese disposable income per capita in 2018 was US $4265.7 [9]. For instance, the annual treatment cost of trastuzumab after the national drug price negotiation was US $16,096.5 in 2017. The average copayment rate in tertiary hospitals for patients enrolled in urban and rural medical insurance systems was 40.7%. Hence, the annual out-of-pocket cost for HER2 positive breast cancer patients was US $6551.3, which could have been difficult to afford by most patients in China.

Our study had several limitations. First, not all anticancer medicines approved in China were included. We excluded traditional Chinese medicines and hormonal anticancer medicines, which could have led to an underestimation of anticancer medicines used. Second, the Provincial Reimbursement Drug List may be slightly different from the NRDL, leading to potential bias in actual reimbursement. Third, our sampled hospitals only included tertiary hospitals. Caution should be warranted when extrapolating our findings to the whole of China. Finally, our analyses were based on aggregated procurement data, and it was unable to estimate whether the actual overall medicine use per patient increased or decreased.

In conclusion, our analyses showed decreasing daily therapy costs and increasing use of anticancer medicines in China. The costs of targeted anticancer therapies were found to be still high, and spending on reimbursable anticancer medicines was rising rapidly. Future studies on the affordability of targeted anticancer therapies for patient needs and the impacts of shifts in medicine on resource utilization are needed.

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AUTHOR'S CONTRIBUTION

XDG and LWS conceptualized and designed the study. TH and CH screened and completed data and analyses. TH and XDG contributed to interpreting the results. TH, XDG, LB, and LS helped in drafting this work. AKW provided input into the analyses, and critically reviewed and modified the manuscript drafts. All authors have approved the final manuscript. The corresponding authors attest that all listed authors meet authorship criteria and no others meeting the criteria have been omitted.

COMPETING INTERESTS

All authors have no conflicts of interest to declare.

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DATA AVAILABILITY STATEMENT

The datasets used for this study are available from the corresponding author upon reasonable request.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical informed consent exemptions were obtained from the Peking University Health Science Review Board.

CONSENT FOR PUBLICATION

Not applicable.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.