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VIEWPOINT
Health Policy

Increasing Drug Costs in the United States: Time for Reform?

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The ever-increasing burden of US healthcare costs—currently 18% of GDP—remains a priority for policymakers, as illustrated by the numerous efforts that have been initiated to reduce costs. However, relatively little attention has been paid to the relationship between drug approval processes or pricing strategies and the cost of drugs in the US, currently the highest in the world. Given the significant potential for cost savings in this field, federal legislation could play an important role in pharmaceutical regulation. Here, we will discuss cost-effectiveness criteria and their potential for introduction into the US drug approval process.

INTRODUCTION

The ever-increasing burden of US healthcare costs—currently 18% of GDP—remains a priority for policymakers, as illustrated by the numerous efforts that have been initiated to reduce costs. However, relatively little attention has been paid to the relationship between drug approval processes or pricing strategies and the cost of drugs in the US, currently the highest in the world. Given the significant potential for cost savings in this field, federal legislation could play an important role in pharmaceutical

regulation. Here, we will discuss cost-effectiveness criteria and their potential for introduction into the US drug approval process.

MECHANISMS OF COST DIFFERENCES

Pharmaceutical spending per capita in the US has increased from approximately $540 in 2000 to $1,010 in 2012, compared to $300 in 2000 to $498 in 2012 for the Organization for Economic Cooperation and Development (OECD) average [1]. Differences in drug costs between the US and other developed countries are particularly evident for cancer drugs, the second largest category of medications sold in the US and the largest proportion (41%) of medications sold worldwide at $37.2 billion USD [2]. For example, Avastin and Erbitux, used for treating metastatic colorectal cancer, are priced at $103,950 and $128,160 per 12-month cycle in the US, while in the UK, they are priced at ~£38,620 and ~£36,154 ($65,635 and $61,445 USD, respectively) [3].

One possible reason for this difference is that the US government does not negotiate with pharmaceutical companies, thus leaving the price subject to market competition. One of the drivers of this policy is the "non-interference" provision in the Medicare Prescription Drug, Improvement, and Modernization Act (MMA) of 2006, which states that the Department of Health and Human Services (HHS) is prohibited from interfering with (price) negotiations for drugs that are covered under the Medicare Prescription Drug Coverage (Part D) [4]. This is unlike many other countries, where governments have enacted caps on drug prices and are able to negotiate prices based on therapeutic benefits. Absence of drug pricing regulation leads to higher drug prices, leaving the burden on taxpayers and businesses.

Another potential mechanism driving drug costs is the approval process of the US Food and Drug Administration (FDA). Indeed, the FDA is relatively efficient in terms of the time for drug review and approval (median 322 days) compared to regulatory agencies in Europe (median 366 days) and Canada (median 393 days) [4]. This is due in part to the Prescription Drug User Fee Act (PDUFA), which was enacted in 1992 and authorized the FDA to collect fees from drug manufacturers. However, despite this apparent efficiency, the FDA's approval process has been questioned on several fronts, including the absence of cost-effectiveness criteria in the process of drug approval [5]. This makes sense, as the FDA's main role is to oversee the safety of drugs, medical devices, food, cosmetics, and other health-related products. However, while the FDA has no role in price setting, it could leverage its position as one of the primary overseers of medications in the US to create another avenue of accountability through the inclusion of cost-effectiveness criteria within the drug approval process.

Incorporating cost-effectiveness criteria into decision-making on healthcare coverage could be accomplished through the Centers for Medicare & Medicaid Services (CMS), which is responsible for health insurance for those with low incomes, the elderly, and the disabled; there are currently around 100 million beneficiaries in the US Indicative of CMS's substantial influence is that commercial payers often follow the lead set by CMS on issues concerning coverage and payment guidelines. Despite the potential for inclusion of cost-effectiveness criteria, one important political driver exists against its use: the Affordable Care Act explicitly prohibits the use of these criteria to make recommendations regarding approved drugs (although not explicitly mentioned in the context of FDA approval processes). More specifically, this is geared towards the Patient-Centered Outcomes Research Institute (PCORI), which was created to fund comparative effectiveness research in which healthcare interventions (e.g., drugs) are compared. This motion was permitted in order to increase access to treatment and put to rest fears of denial of care [6].

ABSENCE OF COST-EFFECTIVENESS CRITERIA

The absence of cost-effectiveness criteria in the drug approval process distinguishes the US from other Western countries, which utilize the Quality Adjusted Life Year (QALY), a measure of disease

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burden that takes both the quantity and quality of life lived into account. QALYs are calculated by the amount of time spent in a particular health state weighted by the utility score given to that state; 1 year spent in "perfect health" is equal to 1 QALY, while 1 year spent in "poor health" could be equal to 0.5 QALY. This measure is used in cost-effectiveness analyses (coined "cost-utility" when QALYs are utilized) to allow for a comparison of cost-per-QALY ratios for different interventions or drugs [7]. In the context of the drug approval process, QALYs are a valuation of health benefit resulting from a new treatment or drug.

Internationally, different types of agencies and organizations (with various responsibilities and mandates) involved in healthcare evaluation utilize this measure. However, the QALY thresholds appear somewhat arbitrary and vary substantially by country. In the Netherlands, a maximum threshold value of €80,000 (~$109,500 USD) per QALY gained has been suggested, while in New Zealand and Australia, threshold values of NZ$20,000 (~$17,094 USD) and AU$69,900 (~$65,748 USD) are implicitly used in the drug approval process [8]. In the UK, the National Institute for Health and Care Excellence (NICE) (https://www.nice.org.uk) develops guidance, standards, and information on not only high-quality health care but also social care. Unlike the FDA, NICE is charged with using existing knowledge to inform decisions regarding which treatments should be covered by the UK's publicly funded single-payer system, the National Health Service (NHS). In the case of cost-effectiveness assessment of new drugs, NICE applies a threshold of £20,000–£30,000 (~$33,000–$50,000 USD) per QALY gained. If the QALY-adjusted cost of a new drug exceeds this threshold, there is a substantial risk that the drug will not be approved.

The most important result of the FDA not using cost-effectiveness criteria is that quite a few drugs that are approved in the US (although they might not be covered under public or commercial payers) are rejected in countries such as the UK if they are conveyed to be too expensive with only marginal effects. The 2013 FDA approval of the cancer drugs Kadcyla and Xofigo, for metastatic breast cancer and advanced prostate cancer, respectively, clearly illustrates this effect. While approved by the FDA, the drugs were rejected by NICE based on their cost per QALY gained: Kadcyla and Xofigo currently cost approximately $74,405 and $40,000 per course of treatment, respectively [9,10]. As these new and expensive drugs become preferentially available in the US, they contribute increasingly to the overall high drug prices in the US compared to other Western countries that benefit from value-based pricing methods.

ARE QALYS THE ANSWER?

The combination of increasing drug costs and absence of QALYs in the regulatory process makes it difficult for decision-makers to objectively determine the added value of a drug in such an expansive open market. This complexity and ambiguity is demonstrated by the comparison of 12 cancer drugs approved by the FDA in 2012. Of these, nine were priced at over $10,000 per month, while only three prolonged survival, and two of them by less than two months [11]. While these high costs of care are problematic, the use of QALYs as a standard metric for assessing drug efficacy is not without controversy. One ongoing concern is that the approach discriminates on age and disability. For example, the QALY metric values young and healthy populations more highly than illness-struck, disabled, or elderly populations [6].

Another primary argument against the use of QALYs is its subjective nature. Quality of life varies between individuals and is heterogeneous in meaning, depending on an individual's preferences, circumstances, and experience. The QALY metric assumes that patients value quality of life over length of life, where alternatively, some patients may find more importance in living longer without regard for quality [12]. Additionally, quality of life for an individual does not take into account the individual's impact on caregivers or family. This also entrenches into an ethical dimension of the metric, as it breaches concerns related to subjective conclusions about the benefits and disadvantages of treating different dis-

eases and using different treatment methods, and the evident ethical complications of putting a dollar value on extending a patient's life [12].

CONCLUSIONS

Although there are concerns about the role of QALYs as the sole benchmark of health gains for purposes of allocating resources, decision-making bodies in the US and UK, along with the World Health Organization, have found that they are preferred compared to alternative measures of health improvement [7]. The QALY metric is an important metric to consider in efforts to reduce healthcare costs in the US, as it encompasses both the quality and the quantity of life lived. The QALY allows, in one single metric, a basis with which to compare the effects associated with the use of an intervention. That is, with one metric, there is a means of comparing one treatment against another, or a treatment against no intervention at all. Moreover, this metric is a vehicle for decision-makers to best determine how to allocate scarce resources to maximize health benefits [6,12]. Although the incorporation of QALYs in measuring and comparing health effects will increase the length of the drug review process, it can eventually be a tool to increase due diligence and accountability. By encouraging prices based on real value, drugs could become more affordable and less burdensome to consumers. Although QALYs are heavily debated, there still exists no viable superior alternative method of measuring health benefits in the context of decision making for resource allocation. Moreover, even in case of rejection of the QALY metric, the needs of decision-makers will persist with QALY alternatives that are likely to share many of its attributes.

Although current provisions prevent government-led negotiation of drug prices, if ever approved by Congress, this could be a cornerstone of decreasing drug costs. Additionally, with increasing drug prices and its burden on overall health expenditures, a reform in the drug approval processes and pricing strategies seems imperative. We have highlighted and evaluated just one possibility, introduction of QALYs, but there are potentially many other means. The current emphasis on changing healthcare in the US sets the stage for daring and innovative initiatives to not only improve healthcare but also increase value across the continuum of care. Utilizing healthcare resources in the most optimal manner would benefit all of society.

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