



# Cancer Drug Pricing and Reimbursement: Lessons for the United States From Around the World

DANIEL A. GOLDSTEIN,<sup>a,b</sup> MICHAL SARFATY<sup>a,c</sup>

<sup>a</sup>Davidoff Cancer Center, Rabin Medical Center, Petach Tikvah, Israel; <sup>b</sup>Winship Cancer Institute, Emory University, Atlanta, Georgia, USA;

<sup>c</sup>Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel

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The current system of drug pricing and reimbursement in the United States (U.S.) is under intense scrutiny. Much has been written about perverse incentives and legislation [1, 2] that have led to an exponential increase in drug prices [3], with U.S. prices being significantly higher than those in the rest of the world [4]. The U.S. now needs to look to the rest of the world to understand how to best improve its pricing and reimbursement system. In this article, we will describe drug pricing and reimbursement mechanisms used in other countries to understand the features of an optimal system.

## COST EFFECTIVENESS ANALYSES

Cost effectiveness studies combine data regarding both cost and efficacy to understand economic value. In several countries, cost effectiveness analyses are used to understand the economic value of a new technology and then to guide coverage decisions. A cost effectiveness study uses an economic model to understand the amount of money required to provide an additional health benefit. The results are provided in the form of an incremental cost effectiveness ratio, and one can understand the money needed to gain one quality-adjusted life year (QALY). For example, bevacizumab was estimated to cost \$571,000 per QALY in the first-line management of metastatic colorectal cancer in the U.S. [5]. Governments or insurance companies can then use the results of such studies to understand the cost effectiveness of the technology and subsequently make decisions regarding coverage.

Although these techniques are used in many countries, The U.K.-based cost effectiveness system is perhaps the most widely understood and publicized system. The National Institute for Health and Care Excellence (NICE) was initially created in 1999 under a different guise. Its task was to use cost effectiveness analyses to decide whether the National Health Service should provide specific new technologies. It is frequently quoted that it uses a threshold of £20,000–£30,000 per QALY to decide whether an intervention is cost effective. However, in reality, the threshold is considerably higher—at approximately £13,000 per QALY [6]. Many cancer drugs did not gain approval by this mechanism, and political pressure grew to make additional funds available. As a result, the

Cancer Drug Fund (CDF) was established by the government in 2010 to provide many of these drugs [7]. As funds within the CDF became depleted, many approved drugs subsequently became “disapproved” to balance the budget. The long-term sustainability of this fund remains unclear.

## PAYMENT BY REAL-WORLD RESULTS

Italy uses a unique payment-by-results approach [8]. In this model, all premium-priced medicines are reimbursed at a fixed nominal price, with an agreed upon rebate depending on the specific indication, if a poor level of efficacy is proven. These agreements are made by the Italian Medicines Agency and require the drug companies’ acceptance. Thus, all patients treated with these drugs must be listed in an online registry and their clinical outcome is deemed as a success or failure according to predefined outcomes at a predefined timeframe. In case of failure, the National Health System receives payback from the drug manufacturer. This model achieves a “real-world” cost effectiveness analysis by taking into account actual individual patient outcomes.

## BUDGET IMPACT

Budget impact studies seek to understand how a decision will impact a budget, but do not seek to understand anything regarding value. Such studies estimate the number of patients within a population who would be eligible for a specific therapy, and then the studies estimate the cost of the therapy per person and, thus, the total cost for all eligible individuals within a population. Although a budget impact study does not make any estimate of value, it is a practical analysis that defines what is possible and what is not possible within budget constraints when several new technologies are competing for sections of a budget.

The government of Israel uses a system of clinical efficacy linked to budget impact to make coverage decisions. Every citizen is entitled to health services included in the “Health Basket.” Each year, a public committee advises on which new technologies are high priority to be included in the basket, subject to a fixed budget decided by the government [9]. The committee is made up of representatives from the

Correspondence: Daniel A. Goldstein, M.D., Davidoff Cancer Center, Rabin Medical Center, Petach Tikvah, Israel. Telephone: 1-646-522-9582; E-Mail: dgolds8@emory.edu Received March 14, 2016; accepted for publication June 7, 2016; published Online First on July 6, 2016. ©AlphaMed Press 1083-7159/2016/\$20.00/0 <http://dx.doi.org/10.1634/theoncologist.2016-0106>

government, the health maintenance organizations, and the public. They evaluate each technology, considering clinical, economic, social, ethical, and legal aspects according to predefined criteria [10]. The budget impact analysis estimates the extra cost to the annual budget, considering the cost of the treatment for a patient multiplied by the size of the patient population minus the cost of alternative treatments. After a decision by the basket of services committee, individual health maintenance organizations negotiate prices with the drug suppliers.

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### REFERENCE PRICING

Many countries rely on external reference pricing (ERP) in price negotiations. This means the regulated price is related to drug prices from a group of reference countries, with usually similar incomes. The advantage of ERP is its relative simplicity, as it does not require significant technical/analytical ability and is thus convenient in low-income countries. The primary disadvantage is the uncertainty regarding whether the prices set at the reference countries are, in fact, appropriate. There have been examples of pharmaceutical companies maintaining high prices despite loss of local market share to ensure high reference prices. This has been demonstrated for certain medicines in both Germany and New Zealand [11].

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### RELATIVE EFFECTIVENESS

France and Germany include relative effectiveness in their decision making, comparing the health gain and added cost for a new product to current standards of care [12].

In France, a 5-level scale is used to determine the added therapeutic benefit (major, significant, modest, minor, or none) [13]. Price and reimbursement rates are negotiated with manufacturers considering relative effectiveness, the price in other countries, and sales volume forecast. The price and reimbursement rates are then reassessed after 5 years. In Germany, manufacturers set their own official list prices with full reimbursement (“free pricing”) with a scheduled price renegotiation set at 1 year [14]. Benefit assessment begins 3 months after market entry and considers information about the drug’s indication, additional benefit compared with alternatives, cost, and number of patients requiring treatment. The drug is then funded up to the recommended ceiling price. If the drug shows additional benefit, a reimbursement price is negotiated and is then binding, but it does not alter the list price (thus retaining the original reference price for other countries). If no additional benefit is found, the drug will be assigned to the same reimbursement price as its comparator, and patients are required to pay the difference with their own funds if using that medication [12].

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### ADVANTAGES AND DISADVANTAGES OF DIFFERENT SYSTEMS

There are distinct advantages and disadvantages of the different pricing and reimbursement systems. Cost effectiveness studies demonstrate value; however, they make no attempt to say whether it is actually possible to pay for the interventions. For example, a drug that potentially cures patients of a fatal disease may come with a high price tag. However, given that it has a major health benefit, it may still be considered “cost effective.” If many patients require the therapy, it may be literally impossible for the insurance company to foot the bill.

A good example is the recent introduction of drugs to treat hepatitis C. Although these drugs are priced highly, the health outcomes are astonishingly good. Thus, in economic studies, they have been proven to be cost effective [15]. However, many insurance companies and payers have been unable to pay for the drugs for all patients with the disease.

Budget impact studies are highly practical and may favorably influence decision making for drugs for rare diseases. However, they must be used in conjunction with an analysis that seeks to understand value. Payment based on real-world outcomes is theoretically the most just payment mechanism. However, the practicality, accuracy, and transparency of this method may create additional challenges and costs. The theory and ideology, however, is appealing. Consider, for example, the purchase of a television. If the television did not work, the consumer would demand the money back. Some would argue that this should also be the case for cancer drugs. With varying levels of efficacy for drugs in different patients, perhaps the payment should vary based on the magnitude of individual response.

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### ANALYTICAL INSTITUTIONS

Different countries have developed analytical institutions to guide these studies and decisions [16]. Their work requires significant funding. The annual budget of NICE in 2014 was £67 million [17]. There is also the potential for sharing resources and analyses. For example, EUnetHTA was established to create an effective and sustainable network for health technology assessments throughout Europe. Groups from different countries work together to develop reliable, timely, transparent, and transferable information.

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### LESSONS THE U.S. MUST LEARN

By analyzing the different systems, we can learn that certain principles are paramount in developing a new system:

1. The ability to say no is important. The payer must be able to walk away from the negotiating table; otherwise, it is not a real negotiation [2]. If the vendor knows that the payer will never say no, prices will continue to rise.
2. The methodology must be highly robust and transparent [18]. If not robust, the methodology will be continually plagued by complaints and attack. Furthermore, when making decisions regarding potentially life-prolonging drugs, any methodology used must be highly granular and accurate.
3. The system must be binding. Any system that is for informational purposes only will not work to improve value.
4. The system must be free from political interference. It is highly likely that any new system will come under political attack. However, the system should remain strong under attack. In the U.K., the political creation of the Cancer Drug Fund made the recommendations by NICE essentially irrelevant, and it led to prices being maintained at relatively high levels.
5. The system must be enabled by appropriate legislation. Payers must be legally allowed to both negotiate prices and deny coverage for low-value treatments. Current legislation does not allow this and needs to be reformed.

6. Elements of both cost effectiveness and budget impact are required. Whether cost effectiveness is based on real-world data or economic models remains an open question. However, although value is intensely important, it is impractical to consider value in isolation from budget. When purchasing a car, one may consider a new car to be more valuable than a used car. This may be due to less frequent breakdowns, added comfort, or higher resale price. However, if the payer has only enough money for a used car, the added value of a new car is largely irrelevant. The same concept applies when assessing health technologies.
7. Funding must be made available for the analytical process.

## CONCLUSION

The U.S. is in desperate need of a new system for drug pricing and reimbursement to incorporate cost and value. Although

no system is perfect, we can learn from around the world of different approaches to this problem. In Europe, the first health technology assessment organizations were created in France and Spain in the early 1980s and in Sweden in 1987 [19].

Recent discussions in the oncology community have focused on value but have largely ignored the consideration of budget impact. We must seek to understand the advantages and disadvantages of the many different systems. Although the exact mechanism that should be developed in the U.S. is open for debate, some principles are essential if a new system is to be considered in the U.S.

## DISCLOSURES

The authors indicated no financial relationships.

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