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EDITORIAL

Could or Should We Use Cost-Effectiveness Thresholds in the French Value-Based Pricing Process for New Drugs?

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1 Introduction

Many countries have developed some form of 'value-based pricing (VBP)' to establish the prices of innovative health products. VBP avoids the use of a 'cost-based' approach that would attempt to calculate prices to cover the costs of production along with an 'appropriate' profit margin [1, 2]. VBPs, in contrast, begin with the clinical benefit for patients and end by comparing it with the cost of the product to assess its '*value for money*' [3]. In general, there are five regulatory/pricing approaches (including or excluding VBP): (1) an approach based on comparing health gains to cost-effectiveness thresholds (CETs) (e.g., in the UK), (2) a 2-step process involving appraising added clinical benefit and performing an economic assessment but without predefined CETs (e.g., in France), (3) an approach focusing on relative clinical efficacy without cost-effectiveness analysis (CEA) (e.g., in Germany), (4) a pricing framework driven mainly by affordability and access to essential drugs or regional external price referencing as a benchmark (e.g., in low- and middle-income countries) [4], and (5) a privately supplied process (i.e., by the Institute for Clinical and Economic Research in the US) with no relationship to official governmental health technology assessments (HTAs) but with estimation and dissemination of a suggested emergent VBP benchmark intended to influence negotiations between payers and manufacturers (ICER, 2020) [5].

The determination of the price of health products (e.g., advanced therapy medicinal products) is the subject of debate regarding the issue of '*sustainable/fair price*' [6, 7]. Attempting to apply the concept of a *fair price* first requires that the term be defined. There is no generally accepted or consensus definition, although the general idea is that it must balance meeting the most important health needs of patients with supporting the sustainability of the industry while controlling expenditures. Some authors want to go beyond the VBP component to consider other factors, such as the transparency of R&D costs and the expected return on investment [8, 9]. Since the implementation of an accompanying economic evaluation of innovative health products in France in 2013, questions have been raised regarding the importance of assessing the economic impact of the VBP process. A key aim is to make economic evaluation a real and effective decision aid for guiding health resource allocation and price determination in a manner that enables it to contribute to addressing unmet healthcare needs and reward innovation. In 2019, the French health technology assessment agency (Haute Autorité de Santé [HAS]) addressed some of these questions by publishing the main strategic actions for the HAS [10], including proposing some reflection on a potentially greater role for CETs to aid in promoting a more efficient allocation of available resources. In a collective book describing the challenges of the French health system [11], it is also suggested to consider different CETS regarding the added clinical benefits. However, this suggestion is subject to the methodological limitations mentioned in Sect. 4.1. With no single correct answer, the purpose of this editorial is to present potential perspectives that can be evaluated by the HAS to improve the use of economic evaluation tools in French VBP. This editorial focuses on innovative drugs and the potential use of CETs in France, but it may also serve as a starting point to emphasize the challenges of introducing aspects from other countries' HTA processes.

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2 French VBP: Independent 2-Step Approach

In France, reimbursement decisions for innovative drugs are based on their clinical benefits. Economic impact assessments (also called 'efficiency opinions') and approval by the Economic Evaluation and Public Health Committee (CEESP) constitute one potential criterion among a set of predefined criteria considered in the process of price negotiation between the *Comité Economique des Produits de Santé* (CEPS), an interministerial healthcare product pricing committee independent of the HAS, and pharmaceutical companies. The CEPS negotiates drug prices to maintain total drug spending within a legally established annual national healthcare spending target. The remaining criteria include (a) the improvement in actual clinical benefits (*Amélioration du Service Médical Rendu* [ASMR]) provided in the medical assessments of drugs and approved by a committee (Transparency Committee [CT]), (b) the European prices of comparators (in England, Germany, Italy, and Spain), (c) the expected sales volume, and (d) the security of supply for the French market guaranteed by the establishment of French production sites [12]. The process of the economic evaluation of innovative drugs submitted by pharmaceutical companies has been implemented by the HAS since October 2013, and the eligibility criteria were updated in 2022 [13, 14].

3 Questions Raised by the Current Use of Economic Assessments in French VBP

This current process of economic evaluation has allowed the CEPS to use these economic impact assessments of innovative drugs as useful information to support its ability to negotiate with manufacturers to establish VBPs. This framework has the flexibility to determine both a confidential net price and a public price; this is an important feature that allows price adjustments to provide patient access given the multiplicity of considerations. It should also be noted that the CEAs submitted by pharmaceutical companies are based on the prices claimed by pharmaceutical companies, which do not generally reflect the ICERs corresponding to the negotiation of net prices between the CEPS and the pharmaceutical companies.

The HAS doctrine for economic evaluation, as approved by the CEESP [15, 16], outlines the key principles of the assessment of the economic evaluations of health products without considering a predefined CE threshold. Within this framework, regardless of the magnitude of the estimated incremental cost-effectiveness ratio (ICER) (i.e., the health benefit gained per additional amount of money spent), the conclusions of these assessments inform only whether the estimate of the ICER is acceptable from a methodological perspective; that is, there are no major methodological flaws or limitations that would invalidate the results of the CEA. They do not, however, provide any efficiency assessment or recommendation on CETs.

Several questions arise in this public debate and may lead to at least three questions. (i) Is it worth incorporating a CET in the current framework to provide recommendations on the efficiency of innovative interventions, which in turn may help address the limitations of the current process of describing efficiency in the French context? (ii) Does such an alternative perspective fit with the French legal and value-based healthcare system? (iii) Should the current doctrinal HAS framework be updated by incorporating a '*health benefit price benchmark*' level reflecting an acceptable range of CE thresholds?

4 Examples of Perspectives for Improving the Use of Economic Evaluation in French VBP

4.1 Incorporating CETs as a Decision Aid for Assessing the Efficiency of Innovative Drugs

This perspective enables the formulation of a recommendation to aid health policy makers in their decisions in terms of the health benefits and opportunity costs to society of new and generally more costly drugs. Such a recommendation requires the implementation of CETs, making "*the lambda (λ) nonsilent*" [17] (i.e., placing a price or value on the gain of a healthy year of life). This approach has the potential to improve the degree of consistency and transparency in the decision-making process across diseases. However, implementing CETs is subject to the following issues:

- *Methodological issues related to the determination of CETs*. The first question that arises is as follows: Which type of CET perspective should be adopted? Should it be based on willingness to pay for health improvement (i.e., on the 'demand' side) or on the 'supply' side, reflecting the marginal health productivity of healthcare system expenditures [18, 19]? While the demand-side perspective should not be completely excluded, a supply-side perspective appears more appropriate for reflecting the opportunity costs of funding decisions through the inclusion of supply-side constraints and budget holders [20–23]. The choice of approach depends mainly on whether the health budget is constrained. If the budget is flexible, the opportunity cost may not be borne in terms of forgone health services but rather in consumption

more generally. Today, very few French economic studies provide estimates of CETs that facilitate the exploration and comparison of these two approaches. These studies are not funded by French public institutions. Using the French value of statistical life as a demand-side indicator of willingness to pay, Téhard et al. [24] estimated reference values for the ICER based on revealed preferences of citizens making choices about the risk of death, and Pichon-Riviere et al. [25] estimated CETs based on international data on per capita health expenditures and life expectancy.

Other issues regarding the inclusion of disease severity and equity modifiers have recently been discussed in the guidelines of various HTA agencies, such as the National Institute for Health and Care Excellence (NICE) [26]. These approaches introduce flexibility into decision making and should help evaluate the extent to which the proposed solutions are transferable to the French context. Finally, a clearer view of the importance of quality-adjusted life-years (QALYs) as the main health benefit outcome for informing healthcare resource allocation decisions is needed, as well as of the relevance of QALYs compared with that of potential alternative measures provided in the recent literature [27, 28].

- *Legal framework for accessing innovative medicine and pricing innovative medicines*. Incorporating CETs as a tool to recommend efficient interventions may conflict with the other objectives of policy makers, for whom economic assessments constitute only a potential adjustment variable among other criteria used in pricing negotiations. Currently, the recommendation of drugs to be added to the list of reimbursed products is based exclusively on a qualitative assessment of the clinical benefits provided; it does not provide information about the opportunity costs of such funding decisions. In such a situation, using CETs as a primary determinant for price negotiation that maintains the power of negotiation of the CEPS is not guaranteed. In such situations, efficient strategies based on CETs may conflict with a reimbursement decision already made on the basis of only the clinical benefit.
- *Reticence of the French public in terms of the ethical foundations of CEAs*. A part of the French public still expresses its disagreement with the ethical foundations of the utilitarian paradigm originally developed by Jeremy Bentham [29], that is, focusing on the health maximization of the whole population (*the greatest good for the greatest number*) but potentially ignoring individual rights for access to innovative treatments as guaranteed by French laws and the constitution. Moreover, a decision based on a CET may discriminate against patients on the basis of age or disability; this works against equitable access to innovative drugs across all patients.

While the methodological issues may be addressed by establishing acceptable CETs, legal and social issues make assessing the operationality of CETs very challenging, leading to several key questions: (a) Do policy makers need to adjust the requirements of the legal framework of reimbursement since no economic notions (e.g., opportunity costs) are considered in the current criteria of reimbursement decisions? In this sense, can an innovative drug providing both a relevant health benefit and efficiency be included in the list of reimbursable products provided that the concerns related to equity issues are also addressed? (b) If not, then is it worth using CETs only in economic assessments by the HAS (as an independent public institution) to recommend efficient innovative drugs, even if they cannot be systematically used by the CEPS in the current VBP process? Clearly, further discussion and clarification on this issue are needed.

4.2 Using a Range of CETs Through the Process of Obtaining the VBP Benchmark

Without any adjustment of the current process of drug reimbursement or the use of CETs for decision purposes, this scenario permits the minimum-level use of CET(s) through the implementation of a form of '*health benefit price benchmark*' or '*value-based price benchmark*', as currently used by the Institute for Clinical and Economic Review in the US [5]. This approach may propose a range of CETs ideally gravitating around plausible estimates of CETs, which reflect consensual trade-offs between the supply and demand sides. It may provide information on a set of prices that are useful for the process of negotiation determination (e.g., floor or ceiling prices) and optimize the presentation of the health benefit outcome matrix, especially the communication of uncertainty issues related to the economic evaluation of advanced therapeutic medicinal products and rare diseases. Moreover, this perspective may constitute a flexible tool and a reasonable compromise that maintains the power of the CEPS in bargaining while still allowing its use to provide more robust economic assessment findings. This approach is also consistent with the multicriteria decision analysis discussed by Ghabri et al., in which CETs are not used by themselves [30]. Furthermore, the learning curve lessons capitalized on by the Institute for Clinical and Economic Review may be useful in the French context. However, importantly, establishing such an acceptable range of CETs would require a feasibility study that addresses the technical issues mentioned in Sect. 4.1.

5 Conclusion

The above questions and perspectives may offer a starting point for a collective discussion and debate on how to improve the use of efficiency opinions to optimize the

current VBP process. A fruitful way to improve this process is to clarify the importance of prior economic evaluation as a step in a global value-based healthcare system aimed at building a consistent and transparent approach in which health benefits and resources are captured to ensure a sustainable health sector ecosystem. The questions are presented to identify the actions needed to establish and refine the VBP system that are consistent with the values and characteristics of the French healthcare system. They also suggest systematic consideration of the extent to which CETs or a benchmark of CETs or another alternative option can be used as decision aids to guide public decisions in resource allocation and promote access to efficient health innovations. As Henri Poincarré, a French mathematician, stated, "*A problem well understood is a problem half solved*".

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