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Economic Evaluation for Pricing and Reimbursement of New Drugs in Spain: Fable or Desideratum?



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ABSTRACT

Background: The economic evaluation of healthcare technologies has become in many countries a basic tool for reimbursement, pricing and purchasing decisions.

Objective: The objective of this article is to examine the institutional, legal, and political factors that have impeded the application of economic evaluation and the criterion of efficiency in the process of pricing and reimbursement of new medicines in Spain.

Methods: Narrative description of the current institutional framework for the use of economic evaluation in pricing and reimbursement in Spain, legal and policy framework in the field of evaluation of new medicines, and stakeholder initiatives and policies related to the use of economic evaluation outside of the pricing and reimbursement process.

Results: Spain has an institutional framework created and established over the last years that could have facilitated a formal use of economic evaluation in the process of pricing and reimbursement. Nevertheless, the real use of economic evaluation at the central or regional level is still unknown, although application of the efficiency criterion, linking to cost-effectiveness, has been clearly required by Spanish laws and regulations at the national level. We highlight a certain degree of moral hazard from the central government that is not directly responsible for the budget impact of reimbursement and pricing decisions. There are currently a number of ongoing initiatives in the field of economic evaluation by various agents, but they remain uncoordinated.

Conclusions: Poor governance at the highest level of decision making is the main reason for the lack of interest in economic evaluation. A profound political change, supported by transparency and accountability, is required before the criterion of efficiency can be fully considered in the process of pricing and reimbursement of new medicines in Spain.

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Introduction

The economic evaluation (EE) of healthcare technologies has become in many countries in Europe and worldwide a basic tool for reimbursement, pricing, and purchasing decisions.^{1–3} Public decision makers have the difficult task of combining a double objective: on one hand, they should identify and favor access of

citizens to those therapeutic advances that bring additional health benefits; on the other hand, they should prioritize and implement those interventions, strategies, and policies with acceptable value for money under increasingly tight public budget constraints to advance the solvency (capacity to respond to the present and future demands and needs of citizens) of public health systems.⁴ The EE is a tool of undoubted utility when it comes to

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establishing an explicit and comprehensive framework in which health and social costs are compared with therapeutic and social benefits and considered in the decision process to improve value for money.

In 2016, Spain invested 9.0% of its gross domestic product into healthcare (70% publicly funded; 30% privately funded) and represents the fifth largest pharmaceutical market in Europe and the seventh in the world according to sales. Healthcare is organized in Spain in a framework of a National Health Service (NHS) mainly financed by general taxes and based in the principles of universality, free access, and equity. From an organizational point of view, it has 2 main levels: national and regional. Health competences are transferred to the 17 regions (autonomous communities), with the national level being responsible, under the governance of the Interterritorial Council for the NHS, for certain strategic areas as well as for the overall coordination of the health system.⁵ Regional governments are responsible for the management of 90% of public health expenditure. Nevertheless, decisions on public reimbursement and establishment of the maximum price of medicines remain centralized in the hands of the Spanish Ministry of Health ("MSCBS" in its Spanish initials). Regional governments are not legally allowed to deny access to medicines with centrally approved public reimbursement, but as those in charge of purchasing, managing, and paying healthcare providers, regional payers can establish guidelines, incentives, objectives, and systems for monitoring the rational use of medicines in clinical practice, especially for those with high economic or clinical impact.

Spain could have been a pioneer country in the field of EE and its application in health decision making. At the beginning of the 1990s, when the first countries began to apply cost-effectiveness criteria in the process of public reimbursement of medicines, Spanish researchers had developed proposals for methodological standardization,⁶ and several regional health technology assessment (HTA) agencies had already been established, which could have applied principles of EE in the decision-making process. Nevertheless, over the years, it does not appear that EE has occupied a meaningful place when it comes to informing decisions for pricing and reimbursement (P&R) of new medicines and other health technologies. What are the reasons why, starting from favorable conditions, EE has not been more firmly integrated in the decision-making process?

The objective of this article is to examine the institutional, legal, and political factors that have influenced, or indeed, impeded, the adoption of EE for P&R of new medicines in Spain. The structure of the article is as follows. First, we review the P&R process in Spain and the HTA and decision-making institutions. The second section reviews the legal and policy framework regarding EE for P&R of medicines. The third section examines the initiatives adopted in practice by the different stakeholders in the Spanish pharmaceutical market. We finally conclude with a discussion and interpretation of the contradictions and political barriers limiting the role of EE as a value-based tool in the Spanish NHS.

Overview of P&R in Spain and the Role of the HTA and Decision-Making Institutions

Before any new drug can be marketed in Spain, the initial decision for setting the price and whether it can be financed by the NHS is made centrally by the Interministerial Committee on Pricing of Medicines and Healthcare Products ("CIPM" in its Spanish initials). This committee includes 8 members from the Ministries of Health, Finance, Economics and Industry, plus 3

members nominated by the 17 regions on a rotating basis. The minutes of these meetings record the approved list prices but the process of assessment and deliberations remains under the veil of confidentiality, although recently, Spring, 2019, the authorities have begun publishing very brief reasons for rejecting reimbursement.

Once a new medicine is approved by the European Medicines Agency, the Spanish Agency for Medicines and Healthcare Products (AEMPS) notifies the Ministry of Health–MSCBS and initiates the HTA process. AEMPS is a national agency under the direct control of the MSCBS. The manufacturer is asked to submit a dossier containing technical information about the drug, incidence and prevalence of the indication, the proposed ex-factory price that the manufacturer is seeking, expected sales, budget impact, cost-effectiveness evidence, the market price in other European countries, information about the company's research and manufacturing base in Spain, and whether the sale of the product will benefit Spain's economy and reduce its trade deficit.

At the same time, AEMPS drafted a clinical HTA report (therapeutic positioning report; IPT). The IPT summarizes evidence about the relative efficacy and safety of the drug, the severity, incidence and prevalence of the disease, the existence of other therapeutic alternatives, whether there are any especially vulnerable groups who may benefit from the treatment, and any social-medical aspects that may be of interest. The theoretical purpose of this IPT is to inform about the added therapeutic value of a new drug. Although the conclusions of the IPTs frequently refer to the need to consider the criterion of efficiency, these documents do not include data on the cost or cost-effectiveness of the evaluated drugs.

Spain operates a dual pricing system for the sale of new hospital medicines put on the market in the country. The official price is the published list price, which operates for patients paying privately. Nevertheless, at the same time, the MSCBS may also choose to negotiate a "reimbursed price," which is the price the manufacturer receives when the drug is used in the NHS. This may be at a discount to the official price, and this is confidential. Once the manufacturer and MSCBS have negotiated a consensus about the price, all documentation is passed to the CIPM (the final decision maker), who authorizes public reimbursement of the new drug at that price.

The P&R decision should take into account the following criteria, although none have been operationalized: (1) severity of the disease, (2) the specific needs of certain groups of people, (3) the therapeutic and social value of the medicine and incremental clinical benefit taking into account its cost-effectiveness, (4) the rational use of public expenditure and the budget impact to the health service, (5) the existence of therapeutic alternatives at lower price, and (6) the degree of innovation of the medicine.⁷

In Spain, after a drug has received P&R approval at the national level, regional payers can negotiate prices under the maximum official price and make recommendations to purchasers and prescribers about appropriate purchasing and prescribing decisions. The regional agencies of evaluation and rational use of the medicine and the commissions of pharmacy of the hospital centers can establish recommendations of use and positioning of medicines and participate in guides to pharmacotherapeutic use. In the case of outpatient drugs, these restrictions are rarely strict in practice, except for new medicines of high expected budgetary impact, and are usually limited to initiatives such as procurement or encouraging use of generic prescribing. Regions and hospitals have more discretion about whether to include an inpatient drug in the hospital formulary and may conduct local HTA. The recommendations of these entities can be included in the contracts, programs, and incentives to centers and professionals.

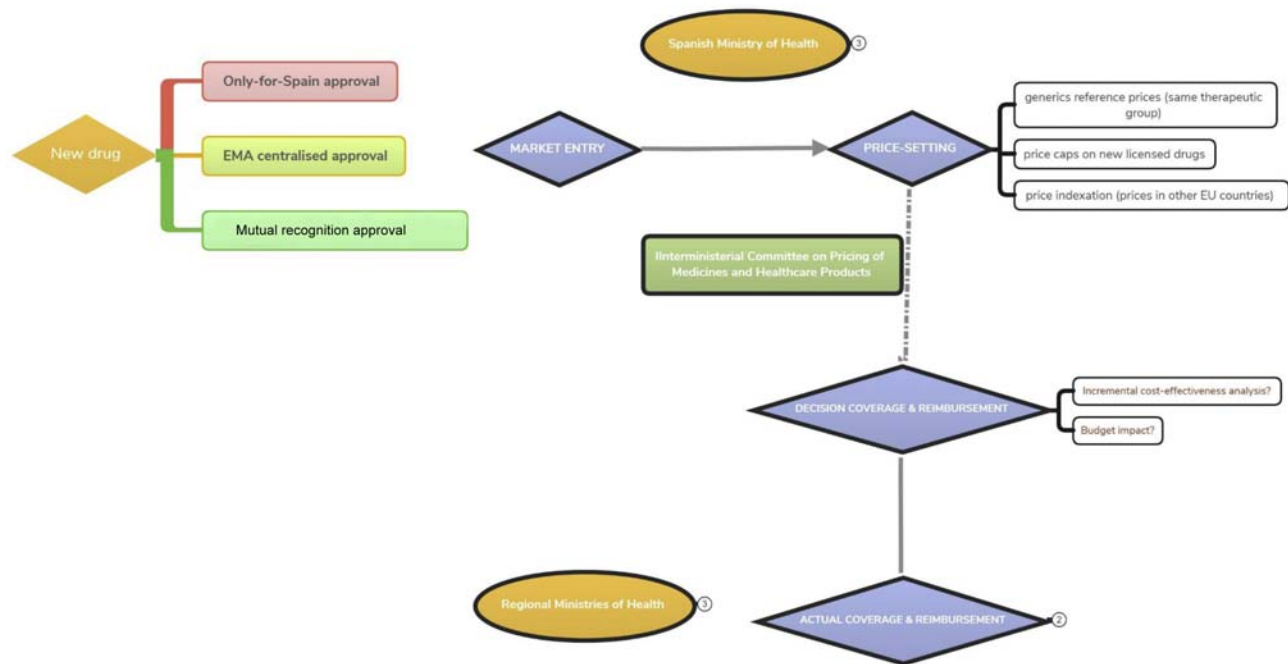
Figure 1. Spanish process for drug coverage and reimbursement.

Figure 1 summarizes the described process for drug coverage and reimbursement.⁸

Development of the Legal and Policy Framework for the Use of EE in Spain

The first factor to consider is whether the Spanish legislation favored or, on the contrary, hindered the use of the criterion of efficiency in the allocation of public resources. In this regard, it should be emphasized that the legal and regulatory framework requires consideration of the efficiency criterion and encourages EE. The Spanish Constitution of 1978 in its article 31.2 includes the principles of equity and efficiency in the allocation of public resources. Successive laws and strategic plans for the health service have gradually moved toward establishing the necessary institutions and policies for implementing EE, but progress has been slow and incomplete. See Table 1 for further details.

Within the health sector, the Medicines Law of 1990 and the Strategic Plan of Pharmaceutical Policy for the Spanish NHS of 2004 seemed to move forward in the path of selective funding (ie, rationing) based, among other criteria, on the principle of efficiency. Nevertheless, in Law 29/2006, of July 26, on guarantees and rational use of medicines and health products, there was a notable absence of any reference to EE.^{9,10} Outside of the scope of the medicines, Order SCO/3422/2007, of November 21, 2007, which developed the procedure for updating the basket of common services of the NHS, again appealed to the principle of efficiency for the ideal application of health techniques, technologies, or procedures.

In March 2010, once the severity of the economic crisis was recognized, the Interterritorial Council of the NHS agreed on a series of “actions and measures to promote quality, equity, cohesion and sustainability of the National Health System.” These proposals included measures to strengthen the use of cost-

effectiveness criteria in P&R of new medicines and reinforce the role of HTA agencies in the preparation of scientific evidence.

The Royal Decree-Law 9/2011, of August 19, amended the previous Law on Medicines, revisiting the concept of selective funding and considering the therapeutic and social value of the drug such as general criteria for public reimbursement. Likewise, it was required that the CIPM would take into consideration the evaluation reports prepared by the AEMPS as well as the reports that could be drawn up by a proposed new Committee on the Cost-Effectiveness of Medicines and Health Products. In the same sense, the most recent Royal Decree-Law 16/2012 maintained the same principles, practically unchanged, and required that EE and budget impact analysis should be taken into consideration by the CIPM in P&R decisions. This law also required the creation of an Advisory Committee on the Pharmaceutical Provision of the NHS, which was finally established seven years later, in 2019. As before, 6 years after incorporating this law in statute, this committee has not been created. Two reports issued by the National Commission of Markets and Competition^{11,12} and a third published by the Court of Auditors¹³ denounced the lack of transparency in the procedures for P&R of medicines by the MSCBS and the CIPM. Hence, there is little evidence that neither EE nor criteria of efficiency have been used so far in practice to inform national P&R decisions. The 2016 report of the European Commission on Spain reports “limited progress has been made in improving the cost-effectiveness of the healthcare sector, and rationalising hospital pharmaceutical spending.”¹⁴

Stakeholder Initiatives and Policies Related to the Use of EE Outside of the P&R Process

Although P&R of new medicines is a competence of the national government in Spain, the 17 regions have decentralized responsibility for health management, resource allocation, budget

Table 1. Laws or strategic plans with respect to new medicines.

Law or strategic plan and date	Policy toward use of EE
The use of EE as a criterion for pricing and reimbursement of new medicines	
Medicines Law, 1990	The Medicines Act of 1990 established that the provision of medicines by the NHS should be carried out by means of selective financing (ie, rationing) of medicines according to available resources (ie, budgeted public expenditure).
Strategic Plan of Pharmaceutical Policy for the Spanish NHS, 2004	"A quality pharmaceutical service requires that at the moment of taking the decision on the incorporation of a new drug in its financing by the NHS, the existing scientific knowledge to be taken into account should be both its therapeutic utility and its pharmacoeconomic profile." "The General Directorate of Pharmacy and Health Products will classify the pharmacological novelties that have to be presented to the Interministerial Commission on Drug Prices to decide on their inclusion in the financing of the National Health System according to their therapeutic usefulness and their pharmacoeconomic assessment."
Law 29/2006, of July 26, 2006	States: "Article 81. Support structures for the rational use of medicines and health products in primary care. To contribute to the rational use of medicines, primary care pharmacy units or services will establish information systems on pharmacotherapy management that include clinical aspects of effectiveness, safety and efficiency of the use of medicines and provide correct information and training on medicines and health products to health professionals" (the concept of efficiency and the scope of its application are not explicitly stated).
Royal Decree-Law 9/2011, of August 19, 2011	Amended the previous Law on Medicines. The Interministerial Commission on Drug Prices can consider the therapeutic and social value of the medicine and incremental clinical benefit taking into account its cost-effectiveness. The Spanish Agency of Drugs and Health Products was established in 2013 to produce Health Technology Assessment reports (IPT) to support these decisions.
Royal Decree-Law 16/2012, of 2012	Maintains the same principles as RDL 9/2011, practically unchanged, and introduces the role of EE and budget impact analysis as information to be taken into consideration by the Interministerial Commission on Drug Prices, as well as the providing for the creation of an Advisory Committee on the Pharmaceutical Provision of the NHS.
The use of EE as a criterion for approval of other health technologies	
Order SCO/3422/2007, of November 21, 2007	This order relates to the procedure for updating the portfolio of common services of the NHS. It states in Article 6.8 that "The resulting reports must include the results of the assessment has been carried out on the safety, effectiveness, efficiency , effectiveness and sanitary utility of the technique, technology or procedure, as well as the ethical, legal, social, organizational and economic repercussions of its implementation, the comparison of its usefulness with respect to other techniques, technologies or procedures available and, if applicable, recommendations on the most suitable conditions to apply this technique, technology or procedure."
The Interterritorial Council of the National Health System (18/03/2010)	Agreed on a series of "actions and measures to promote quality, equity, cohesion and sustainability of the National Health System" and states, "It is also considered advisable that the incorporation of new medicines into the SNS service portfolio should be based on cost-effectiveness criteria , as well as working together to develop pharmacotherapeutic guidelines that help clinical decisions are based on criteria of evidence and cost-effectiveness ."

EE indicates economic evaluation; NHS, Spanish National Health Service; RDL, Royal Decree Law.

decisions, and procurement of medicines. This has resulted in several EE-related initiatives proposed or implemented during the past decade, mainly by regional HTA agencies and the regional purchasers (regional governments and hospitals). We will also show in this section the relevant role played by healthcare professional associations as well as the role of private agents such as the pharmaceutical industry.

Spanish researchers have been proactive in conducting EE. The number of EE published per year by Spanish researchers has been increasing steadily.^{15,16} The debates on methodological aspects and practical application of EE are similar to international ones¹⁷⁻¹⁹ and with common emphasis on the need to improve the quality and credibility of EE.²⁰⁻²⁴

This activity has been carried out by agents from both the public and private sectors. On the public side, the 8 HTA agencies in Spain have been coordinated through the Spanish Network of HTA Agencies (RedETS) since 2012. The reports produced by these agencies are held in a free-access HTA repository (<http://www.redets.mscbs.gob.es/productos/buscarProductos.do?metodo=buscaTipos&tipoid=1>), including methodological guidelines on EE for healthcare interventions,^{25,26} a recent work estimating the

willingness to pay for a quality-adjusted life-year,²⁷ clinical practice guidelines, as well as through their participation in different international networks of health technologies, such as the International Network of Agencies for HTA, the European network for HTA, or the European Network for Cooperation in HTA. Nevertheless, it must be emphasized that the EEs carried out by these HTA agencies focus on the evaluation of nonpharmacological interventions.

Other public institutions participate in the dissemination of EE of health technologies. The Mixed Committee for the Evaluation of New Medicines, formed by the regions Andalusia, Catalonia, the Basque Country, Navarre, Aragon, and Castilla and Leon, evaluates new medicines used in primary care. They have a double mission: (1) to analyze and evaluate the additional value on therapeutics by the new medicines to the supply of already available medicines and (2) to offer the professionals in these regions specific recommendations for the correct use of these medicines. The Canary Islands Health Plan 2004-2008 was the first regional health plan explicitly incorporating cost-effectiveness criteria in health planning.²⁸ The Budget Impact and EE Commission of the Catalan Health Service has promoted constant activity until 2017 in the

field of EE and its use in the decision-making process in Catalonia, issuing public guidelines on EE, budget impact analysis, and risk-sharing agreements. These measures aimed to provide practical, value-based assessment tools to the regional programs of therapeutic harmonization, especially regarding the use and reimbursement of high-cost new drugs at the hospital level.^{29,30} Nevertheless, in 2017, the activity of this commission stopped abruptly, and there is no evidence that the cost-effectiveness criterion is explicitly considered in the decision-making process in Catalonia.

Several regional governments (such as Catalonia, Andalusia, and the Basque Country) and hospital purchasers have developed risk-sharing agreements for drug purchasing that directly or indirectly consider the logic of EE. Nevertheless, the lack of communication of the results of these agreements prevents a realistic assessment of their relevance and transferability in the wider framework of regional policies for funding and purchasing medicines. For instance, the published results of the first payment-by-results scheme in Catalonia for the introduction of gefitinib in the treatment of advanced epidermal growth factor receptor-mutation positive non-small-cell lung cancer estimated the financial consequences of this payment-by-results reimbursement model and the perceptions of the stakeholders involved in the agreement.³¹ This scheme identified a very modest total savings in healthcare direct costs, showing that the extension of this type of value-based scheme crucially depends on the availability of adequate data systems to measure outcomes and provide accountability, as well as requiring the involvement of healthcare professionals.

Aside from these public agencies, institutions, or commissions, other entities have supported the use of EE of medicines. The Group for the Evaluation of Innovation, Standardization and Research in the Selection of Medicines ("GENESIS" acronym in Spanish), within the framework of the Spanish Society of Hospital Pharmacy, has developed an intense activity to introduce EE in the selection of drugs for hospital pharmacies across Spain. They have carried out a high number of drugs evaluation reports incorporating EE and have developed their own methodological guideline.³² The Spanish Health Economics Association, a meeting point for health economists and health professionals, has been generating a continuous debate on health economics for almost 40 years now. Many of its main debates have been published as open documents to better inform healthcare decisions.³³⁻³⁶ Recently, the Collegial Medical Organization and the Spanish Society of Public Health and Health Administration have also publicly positioned themselves in favor of a more transparent use of cost-effectiveness criteria for P&R of medicines.^{37,38}

From the private sector, the pharmaceutical and health technologies industries have also been playing an important role in developing EE. In fact, a significant proportion of the work carried out in the past 2 decades in terms of EE on health technologies has been financed with private funds or directly performed by pharmaceutical industry, and the number of consulting firms and their activity has grown appreciably. The pharmaceutical industry systematically carries out evaluations on the cost-effectiveness of the new drugs that must go through the process of P&R. In most cases, these models are developed in a centralized manner by the manufacturer and then adapted to the different requirements of each country. Nevertheless, in Spain, it is budget impact rather than cost-effectiveness that carries the greatest weight in the price negotiations between the MSCBS and the manufacturer. Hence, in many cases, the value dossiers that are presented by manufacturers to the MSCBS do not even contain information on cost-effectiveness.

Discussion and Conclusions

Although in Europe the use of EE applied to health decisions has been growing in recent years, this process has not yet been satisfactorily implemented in Spain. Spain has laws and institutions (MSCBS, HTA agencies, other regional drug evaluation agencies, professional and scientific associations) that could have facilitated a formal use of EE in P&R. Nevertheless, the lack of development and application of the laws and the functioning of certain institutions, mainly the Ministry of Health, have acted as barriers to the use of EE. During the past 20 years, there has been a constant appeal to health authorities to use EE as a support tool in decision making, starting with the macro level and then moving to meso- and micro-management levels.³³⁻³⁹ Nevertheless, the existing literature indicates that in the first decade of the millennium, its use was very limited and its utility unknown in Spain.⁴⁰⁻⁴² During the recent years of the economic crisis, the official discourse appealed to the need to perform cost-effectiveness analysis as a key tool to apply the efficiency criteria in the allocation of scarce health resources, but indeed, the main policy response to the crisis was to institute deep general cuts across health service providers, far from applying principles of prioritization, value for money, and cost-effectiveness.⁴³ Furthermore, during the years of economic crisis, many price negotiations for new pharmaceuticals were delayed, taking longer than the maximum 180 days required by the European Commission directive.⁴⁴ In other cases, the situation has been the opposite. Media pressure has acted as a catalyst to accelerate process times. In any case, the opacity of the process, including the agreements reached between health authorities and pharmaceutical companies, questions the actions of the public agents involved.⁸

Although the criterion of efficiency has been clearly reflected in Spanish laws and regulations for P&R at the national level for many years, its application at the national or regional level is still unknown. Higher-level decision makers (MSCBS and regional governments) did not give a clear signal on how to incorporate this criterion in decision making or at what level it should be placed. This lack of definition has resulted in that, beyond the official discourse, EE is missing in the P&R process, and efficiency decisions were transferred to the level of meso and even micro management, which is paradoxical, following the example observed in other countries.^{1-3,39,45} In this sense, we cannot rule out a certain degree of moral hazard. The central government is charged with making P&R decisions but is not directly responsible for the consequences, given that the health and pharmaceutical budget constraints and economic impact fall on regional and provider purchasers. The national P&R committee (CIPM) includes 3 members from the 17 regions on a rotating basis, so it could be argued that regional payers are underrepresented in the decision-making process. In addition, there appears to be a lack of good governance. The concept of "good governance" encompasses compliance with laws; obtaining good results; absence of corruption, mismanagement, and nepotism; and responding to a set of agreed-on rules of democratic participation, transparency, responsibility, accountability, and obedience to codes of conducts. A more transparent and evaluative culture would help to facilitate the incorporation of the efficiency criteria explicitly in the decision-making process. The creation in 2019 of an independent Advisory Committee for the Reimbursement of the Pharmaceutical Provision of the NHS is expected to be a welcome step in this direction.

The IPTs (HTA reports) have been successful in meeting international standards of quality of clinical evidence but are limited to

the analysis of safety and efficacy, with absence of information on costs, cost-effectiveness, and budgetary impact. It also seems curious that there has been no real interest by the central government in using the great evaluative potential of the network of regional HTA agencies to undertake the cost-effectiveness analysis of medicines. Despite the fact that P&R is the legal competence of the national government, regional health services and some direct buyers (hospitals) show a much greater real interest in the application of EE. To meet their responsibilities to promote efficiency and financial sustainability at the local level, these agents have been forced to undertake EE and budget impact analysis in an informal and nonexplicit way when priority setting for hospital formularies and engaging in pharmaceutical procurement and financial schemes.

In all countries, there are administrative, methodological, and practical barriers to implementing value-based P&R.^{40–42} Some countries, such as Germany, have clearly and coherently stated that they do not wish to use cost-effectiveness criteria in health-care decisions. Nevertheless, Germany has applied other methods to introduce the criterion of efficiency, linking price very clearly to the concept of added clinical benefit, in its decision-making process. In Spain, the stated policy has been to use EE, but the barriers to implementation have remained practically unchanged for decades, whereas other countries in Europe and elsewhere, from a similar initial starting point,^{46–49} have successfully advanced from theory to practice. Reports and public positions issued by independent public auditors, competition regulators, and scientific and professional societies^{33–38} seem to have been unsuccessful in influencing the incorporation of EE or improving transparency and accountability of P&R of medicines. Therefore, we do not know explicitly whether EE is applied in these processes or, speculatively, assuming that it was done, how it is considered and the relevance it may have in the decision-making process.

Arriving late allows us to learn from the experiences of others and adapt to our environment those processes that have proven to be useful and adequate. The lack of impact of EE in Spain has not been due to the lack of methodological guidelines and qualified professionals. Many different actors from a variety of backgrounds have contributed to the development of EE in Spain, although this activity has sometimes not been well coordinated. The implementation of the right incentives, coordination, and leadership³⁹ would undoubtedly improve the volume and quality of work carried out. The barriers to the use and application of EE in decision making have already been identified, and their persistence is due to the disinterest shown by the highest-level decision makers and the weakness of those agents who have understood its relevance but have not been able to influence its actual application.

Existing agreements and regulations should have standardized the use of EE as a tool to help decision making. An obvious advantage of EE is that it makes explicit key information in the decision-making process on the allocation of scarce resources among mutually exclusive competing alternatives. It is, perhaps, precisely these elements that allude to transparency and accountability and that have made it attractive in other European countries that have played against it in Spain. Therefore, we cannot but insist that one of the greatest challenges of the Spanish health system is to improve its standards and move toward a culture of good governance.³⁵ The lack of good governance promotes poor ethics and dishonest behavior in general. Failure to consider elements of efficiency in decision making entails an erosion of the quality and solvency of the health system and its ability to respond to present and future social challenges. On contrary, good governance positively influences all the functions of the health system, improves its performance, and, ultimately,

results in better health.⁵⁰ A key driver in the journey toward better governance is to understand that transparency and accountability are not merely optional or abstract concepts. They are 2 basic principles of the cultural change that the Spanish NHS needs in order to guarantee its solvency and legitimacy and for it to continue improving the well-being of society, just as it has done in recent decades.

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