HEALTH POLICY ANALYSIS

Implementing Pharmacoeconomic Guidelines in Latin America: Lessons Learned

Introduction

Latin America is a large and diverse region. Therefore it is no surprise that the development and implementation of pharmacoeconomic (PE) guidelines is proceeding at a different pace in different jurisdictions.

The first three articles in this special issue of *Value in Health* focusing on Latin America outline the challenges in the development and implementation of guidelines in three country clusters. The three clusters represent countries at different stages in the development and implementation of guidelines at the time the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Latin American conference was held in Brazil (September 2009). However there have been rapid changes in some countries during the past year, especially in Colombia. In Argentina, Colombia, Guatemala, Uruguay, and Venezuela, PE guidelines were only under consideration at the time of the conference. In Chile and Mexico, PE guidelines were being developed, or were already developed. In Brazil, PE guidelines were already in the implementation phase and formed the basis of industry submissions to the Office of Economic Regulation at the Brazilian Health Surveillance Agency (ANVISA), the agency that decides on the regulatory approval and reimbursement of drugs and other health technologies[1,2](see Augustovski et al. for a review and comparison of the PE guidelines currently existing in the Latin American region).

Each step in the development and use of PE guidelines raises its own challenges. In addition, the characteristics of each country’s health care system have important influences on the process. Nevertheless, several common lessons were learned.

Consideration of PE Guidelines (Argentina, Colombia, Guatemala, Uruguay, and Venezuela)

When considering the development of PE guidelines, it is important to take account of how a new policy of requiring evidence on clinical and cost-effectiveness of drugs or other health care technologies will operate alongside the existing health care system. In particular it is important to note how health care is financed (e.g., through general taxation, social security contributions, or patient payments), how drugs and other health technologies currently receive market approval, how reimbursement is determined, how prices are set, and what existing controls are in place (e.g., hospital formularies or generic substitution). There is considerable diversity on these issues in the countries being considered in this cluster.

In most countries in Latin America social security represents the largest financier and provider of health care, complemented by public and private systems. Therefore the development of PE guidelines must recognize the needs of all three sectors. Nevertheless, in most countries there is a compulsory package of benefits to be provided by social security, an approved list of drugs for public subsidy, and in some countries a special fund for high-cost technologies. Although no fourth hurdle is currently formally in place in any of the countries in this cluster, consideration of clinical and cost-effectiveness—through the application of PE guidelines—is being considered to be and could well be incorporated within the existing set of policy instruments.

Development of PE Guidelines (Chile and Mexico)

In Mexico a set of PE guidelines has already been developed and a law established requiring a PE dossier before inclusion of a technology in the national formulary. After inclusion of a technology in the national formulary, each health care institution can then decide whether or not to purchase the technology, based on its cost, budget availability, previous experience with the technology at the institution concerned, and priority of disease. In Chile, clinical guidelines have been established in several different pathologies based on a prioritization process. A particular concern is to obtain more efficiency without infringing on some of the basic principles of community solidarity and equal access to health care.

In both Mexico and Chile the advantages of considering clinical effectiveness and cost-effectiveness, through the implementation of PE guidelines, are well recognized. These include establishing a more objective basis for purchasing decisions and enabling decision makers to have a better estimate of the budgetary effects of adopting new technologies. Several potential disadvantages, however, have also been identified. These include differences of opinion on the need for guidelines, the lack of adequately trained personnel to submit and review PE dossiers, and the fact that guidelines might be the subject of controversy between the government and health care industries.

Implementation of PE Guidelines (Brazil)

So far Brazil is the Latin American country with the most experience in the implementation of PE guidelines. The implementation is the responsibility of ANVISA and the Ministry of Health. PE is applied in pricing decisions for new drugs. If the new drug is no better than existing care a cost-minimization analysis is used. If the drug is found to be superior to existing care, the ceiling price is set at the lowest price among nine reference countries.

To develop and implement the PE guidelines, an expert working group was established in 2006. After revision of the first draft of the guidelines, two workshops were convened, involving experts in economic evaluation and representatives from the Ministries of Health and Finance. Discussions were also held with a broader
group of participants at the second ISPOR Brazilian Chapter Congress before publication of the guidelines in 2009.

The development and implementation of guidelines has proved to be a complex task. The main lessons learned are: 1) the process must involve a broad range of stakeholders, including experts in the field and the researchers who will carry out the studies; 2) the process is as important as the final product; and 3) it is important to undertake periodic revisions of the recommendations and this will take place after 2 years, based on the feedback given by users.

Country Groups

Argentina, Colombia, Guatemala, Uruguay, and Venezuela

The organizing team started working long before the plenary for this activity, undertaking projects from grouping the countries to deciding the contents. The report of the first country group, “When to consider pharmacoeconomic guidelines” [2] was so titled to reflect the position of countries that are thinking about developing guidelines or are currently developing them in earlier phases. Five countries are presented in this cluster.

What is the framework in each country?

Argentina’s framework is a multiter system divided into three large sectors: public, social security, and private. It has a compulsory medical package called the Plan Médico Obligatorio from the social security system, which has 24 provinces. Each province has its own health care system in place. Colombia has a social security system based on health insurance with two main schemes: the contributive scheme, with wider coverage for technologies, and the subsidized scheme, mainly for poor citizens. It has a compulsory plan of health called Plan Obligatorio de Salud (POS). Guatemala has social insurance that provides health care services for workers and pensioners. The uninsured population has access to free consultations and tests via the public network. Uruguay has recently changed its legislation into what is called the Nationally Integrated Health System, which includes a national health insurance regulated by a national health insurance body (Fondo Nacional de Salud [FONASA]) and a national board of health (Junta Nacional de Salud [JUNASA]). The federal government provides coverage to the entire population via Plan Integral de Atención a la Salud (PIAS), an integrated plan and a mandatory health benefit package, and Fondo Nacional de Recursos (FNR), an agency that specializes in high-complexity, high-cost technologies. Venezuela has two contributive government programs, the solidario health system with compulsory affiliation, and a complementary system with voluntary affiliations. The main players in the Venezuelan health care field are the Ministerio de Sanidad y Asistencia Social, the Instituto Venezolano de los Seguros Sociales, the Instituto de Previsión Social del Ministerio de Educación, and the Instituto de Previsión Social de las Fuerzas Armadas.

Approval policies regarding health technologies

Argentina has a typical, classic licensing agency, the Agencia Nacional de Medicamentos Alimentos y Tecnologías (ANMAT) and there is no formal fourth hurdle in place. There’s currently no need of any PE information for approval or reimbursing of new drugs or devices. The superintendence of health services is responsible for maintaining the benefit package. In Colombia all new drugs and medical devices that have to be or want to be included in the benefit package must be approved by the Comisión Reguladora de Salud, which is advised by the Committee of Assessments of Medicines and Health Technology. This group has recently been involved in developing health economic and budget impact guidelines. Guatemala has no independent licensing agency; it is within the Ministry of Health. It has no fourth hurdle in place. In Uruguay there is no independent regulatory agency (there is a division in the Ministry of Health known as DIGESA) nor a fourth hurdle system although a presidential decree issued after the plenary recommends the compulsory use of economic evaluations. The Ministry of Health regulates new inclusions in the PIAS, and in the therapeutic drug formulary. For high-cost technologies the FNR performs reviews of the economic evaluations and budget effects (although there is no formal guideline in place). In Venezuela all new drugs and devices are approved by the Ministry of Health. There is no fourth hurdle system in place.

Pricing policies

In Argentina there is no formal price regulation and insurance companies make arrangements for discounts with the pharmaceutical and device industry depending on their scale. In Colombia the Ministry of Commerce defines the top price of each medication package. Insurance companies, clinics, and hospitals make private arrangements. In Guatemala there are multilateral agreements for open contracting and a bidding process for essential drugs. In Uruguay there is no price regulation. The Direction of Commerce controls prices in pharmacies and drugstores and allows a maximum 25% discount. The FNR acts as a monopsony. Venezuela has had a mixed price system since 1994 and a list of essential drugs with prices is published by the Ministry of Commerce. There is no price regulation for other technologies.

Reimbursement policies

In Argentina a group of essential drugs is delivered to all primary care centers in the country. Ambulatory drugs are subsidized in a variable proportion and there is a special fund (Administración de Programas Especiales [APE]) that reimburses the social security system for most high-cost technologies. In Colombia insurance companies provide all services included in the POS. In most countries when an insurance company denies the provision of health care, a patient can go to the courts; Colombia has a special fund for reimbursing these cases (Fondo de Garantía de Pagos [FOSYGA]). In Guatemala there is no reimbursement system in place for the public sector and all reimbursement occurs in the private sector. In Uruguay drugs in the compulsory formulary are bought by each provider. Consumers have some co-pay in the private sector. Those technologies covered and funded by FNR have no co-pay. In Venezuela reimbursement only occurs in the case of high-cost drugs for chronic and end-of-life illnesses for which coverage reaches all citizens.

Financial control policies

In Argentina there is national reference pricing for approximately 200 essential drugs. Recently there was a strong stimulus for prescribing drugs using the generic name. The benefit package (Plan Médico Obligatorio) has currently no clear system in place for updating the package; but before 2007 there was a fourth hurdle system in place with PE requirements. In Colombia, the Comisión Reguladora de Salud defines and updates the per capita unit payment each year, as well as its benefits. Also, guidelines have been published that make economic evaluation of budget impact compulsory. In Guatemala the process has begun of elaborating national guidelines that will include health and economic information as well as efficiency principles to update or to change the national formulary. In Uruguay all pharmacies and pertinent parties have to report selected indicators to the information technology system on a monthly basis. The FNR is externally audited and results are publicly available. Venezuela has no current financial control policies in place. There’s a strong preference for generics in case there is a choice.

Although these countries were grouped in the same cluster these are very heterogeneous countries in many aspects. Most have a rather fragmented health care system, and have designed a compulsory benefit package for the social security system. There
is no formal fourth hurdle or PE system in place, but methodologic guidelines are being considered, developed, or advanced in some of them (e.g., Colombia). There’s also no formal drug price regulation, except for reference prices for essential drugs in some countries, and many countries have specific reimbursement policies for selected high-cost technologies (e.g., Argentina, Uruguay, and Venezuela). Also, most have a list of essential drugs that are provided or subsidized by the government or social insurance. Finally, the financial control policies in these countries range from reference pricing or providing a mandatory positive list to open bidding processes. The incorporation of formal fourth hurdle systems is also under consideration.

Chile and Mexico

During the past 60 years life expectancy in Latin-American countries extended from 51 to 74 years [3]; this gain in the population’s longevity represents several challenges for the regional health systems: 1) predominant causes of death are transitioning from infectious (less expensive to treat) to chronic degenerative diseases (more expensive to treat); 2) aging of the population results in a number of disabilities requiring dedicated assistance from the family or from the health system to perform tasks of day-to-day living; and 3) the increasing demand for health care is stretching the existing health system budgets to their maximums and allocation in a wise manner becomes compulsory to optimize the limited available resources in the countries.

The science of economic assessment of health technology has appeared during a time when clear statements of what and how to evaluate are most important. The techniques facilitate a more objective approach to the assessment of the best options for the society to invest in, aligned with the specific necessities of jurisdictions. The existence of health technology assessment guidelines eases communication among involved parties because all clearly understand the rules in the appraisal process.

Latin American countries are now at three different stages in the implementation of guidelines for health technology economic evaluation. Most advanced countries (mainly Brazil) have already developed and implemented their own guidelines for conducting economic assessments. Other countries, such as Chile and Mexico, are just embarking on guidelines implementation and intend to empower decision makers with a clearer and more transparent methodology that bring certainty to all participants in the acquisition of new technology.

Mexico has recently released its PE guidelines [4], anticipating that the submission protocol of new products before the Health General Council for approval into the national formulary be clearer for all stakeholders. The exercise took about 2 years from the conception of the guidelines to the final deliverable document.

The Chilean government is seeking to reduce the inequality gap in health care by guaranteeing access for all members of the population to treatment for a specific portfolio of diseases, selected by the authorities. To finance such an ambitious goal, the government is planning to increase the VAT general tax (value added tax) 1% from the current value and the surplus will be dedicated to ensuring that this health access policy is properly implemented.

Finally, there are countries that have not yet incorporated a formal framework of economic assessment of health technology guidelines to help better allocate their resources. Some examples from the first cluster include Venezuela or Costa Rica.

The spectrum of cases addressed here are to help those countries thinking of carrying out their own health technology economic evaluation guidelines.

To ensure that economic evaluation guidelines are carried out successfully in Latin America, it is necessary to have all parties agree that the guidelines will benefit everybody involved, as well as facilitate the decision-making process for all stakeholders—from regulators to the health industry—otherwise the guidelines will not be adopted.

It is necessary to have in mind several questions at the conceptual phase of the project:

1. What are the benefits for society if economic evaluation guidelines are implemented in the health system?
2. Is the economic evaluation compulsory by law, is there a practical need to have it, or is it being explored based on convictions of all parties involved?
3. Who wants the guidelines to be implemented?
4. Have all potential stakeholders been identified and reached about the economic evaluation guidelines implementation?
5. Do all stakeholders agree on having the guidelines implemented?
6. Is there a sufficient number of experts on health technology economic assessment in the country to have a balanced number of them working among the stakeholders?

It is also necessary to have in mind several questions during the execution phase of the project:

1. Has a committee with representation from all parties been set to write the guidelines?
2. Has every important issue been considered in the content of the guidelines?
3. Who will review and give feedback, beyond the committee, on the guidelines?
4. Who is the audience for the guidelines?
5. How will financial support to complete the guidelines implementation be obtained?
6. Is there general consensus among the stakeholders on the final draft of the guidelines?
7. Have particular issues of the guidelines been discussed head to head and clarified with those who the guidelines will affect?
8. What is the scope of the guidelines?
9. What methodologies of economic evaluation are best suited for the country?
10. Will the guidelines be used as a tool to align and standardize economic evaluations submission for decision makers regarding new technology approval?

Finally there are questions to be addressed after the guidelines have been set up:

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1. Has a committee been appointed to monitor guidelines performance?
2. Do the guidelines require a short-term review to update or amend?
3. What is the life expectancy of the guidelines before a new, thorough review will be required?
4. Do the guidelines meet expectations for all stakeholders?
5. After a certain period of time, have the economic evaluation guidelines made a difference in the appraisal process?

Setting up economic evaluation guidelines is equivalent to all parties acknowledging that guidelines are the most suitable road map to developing and presenting economic evaluations of new technologies to key decision makers to facilitate their resolutions. Guidelines are like any instruction manual that is carefully revised to explain the rules for decision making regarding new technology to be included in the health system. The eventual goal is to make a decision on if a new technology is worthy of being acquired and how much the health system is willing to pay for it, and if it represents additional benefits to the health status of the society.

It is advisable to get counselling from groups in countries where the guidelines have already been implemented because these individuals can provide important feedback and information derived from their own experience.

The final benefit of economic evaluation guidelines is for the entire society because better decision making might bring both efficiency and equity in opportunities for the whole population.

Brazil

In this article, the Brazilian experience in developing the Methodological Guidelines for Studies in Economic Assessment of Health Technologies is presented. Although one of the authors (MD) participated as a collaborator in the development of these guidelines, credit for the elaboration and revision of the guidelines is, in large part, due to Flávia Elias and her team at the Ministry of Health; to Cid Vianna and Rosângela Caetano, who prepared the basic text that was submitted to a robust discussion process; and to Everton Nunes, who developed the final revision of the guidelines and collaborated in the presentation that gave origin to this article.

It is important to highlight the Brazilian context of health care decision making as it relates to health technologies. Two types of decisions merit emphasis: 1) decisions related to pricing of new medications; and 2) decisions related to incorporation of technologies into the Unified Health System (SUS).

In Brazil, drug prices have been regulated since the end of 2000. The regulation policies are defined by the Chamber of Regulation of Drugs Market (Câmara de Regulação do Mercado de Medicamentos), which is composed of five ministries and headed up by the Ministry of Health. ANVISA, by means of its Office of Economic Regulation, is responsible for policy implementation. With regard to new drugs, it is possible to say that there is an evidence-based pricing regulation policy. The model could be summarized as follows: if the new medication does not present benefits compared to the best therapeutic option available, then its maximum price will be defined based on a cost-minimization analysis. If the scientific evidence supports an additional therapeutic benefit in relation to the chosen comparator, then the peak price will be fixed based on international prices, and cannot be higher than the lowest price from a group of nine reference countries from different regions of the world. In addition, for a specific list of products considered highly important, which are generally high in cost, there is also a mandatory discount, reviewed annually, based on the difference in the revenue index between Brazil and the nine countries that comprise the Human Development Index. Currently this discount is 22.85%.

The second type of decision refers to incorporation of new technologies. At the end of 2006, a commission was created with the purpose of making recommendations to the Ministry of Health regarding the incorporation of technologies. Based on scientific evidence, cost-effectiveness studies, and estimates of effects on budget, this commission makes recommendations regarding the incorporation of a submitted technology to the Ministry of Health, with the final decision being at Ministry’s discretion. Economic evaluation is one of the requirements established by legislation. This indicates the importance of guidelines for economic evaluation for decision making.

Developing economic evaluation studies is no trivial task. One has to appropriately choose the type of evaluation, the analytical models to be used, the study perspective, the time horizon, the sensibility analysis, and the discount rate. Several countries have followed the path of developing guidelines for economic evaluation to contribute to results comparability and better practical applications for decision making.

The process of developing the Brazilian guidelines started in 2006, with the Health Technologies Evaluation Workgroup (Grupo de Trabalho de Avaliação de Tecnologias em Saúde), of the Ministry of Health. This group congregates all governmental units working with Health Technology Assessment (HTA). Such integration has been very important for advancing HTA in Brazil. This group started, at that time, a discussion on the necessity of specific guidelines for economic evaluation. The first version was then produced, and two workshops were conducted for its evaluation. The workshops included representatives from several government entities and universities. A revised and still preliminary version of the guidelines was presented for the first time to the public at the ISPOR Second Brazilian Chapter Congress in 2008. After that, the guideline development process was opened to the public through a public consultation process. Including worthy contributions that resulted from the public consultation, the final revision was accomplished and, in September of 2009, the guidelines were officially launched after a 3-year process.

The objective of a publication such as this is to establish methodological standards that facilitate the application of economic evaluations in health care decision making. Considering the scarce literature available on this topic, its publication is very important in closing the gap of Portuguese written materials in this area. The objective was not to supply didactic material, but to ensure that economic evaluations become important tools for health care decision making. The public consultation process was very interesting because it allowed for open evaluation throughout the process. The public consultation participation rate was as follows: 37% from government entities, 37% from universities, 19% from industry, and 7% from other sectors. Out of the 23 topics presented in the consultation, all presented a concordance of at least 50%. Only three topics presented a concordance level lower than 60%; the study perspective, the intervention description, and the discount rate. In these topics the approval rate was between 50% and 60%.

Guideline use is already a reality. By the end of 2010 there were about 60 studies granted by the Ministry of Health that followed the guidelines. A multiplier effect is expected, which will be very important to increase awareness of the importance of the guidelines among more and more stakeholders—not only those who develop the studies (either in the university or industry) but also for decision makers. There is a clear trend toward growth in the number of economic evaluations supporting health care decision making, and, therefore, greater utilization of the guidelines.

In the international arena, it is important to highlight the recent adoption of Methodological Guidelines for Economic Evaluation by the Mercado Común del Sur (Southern Common Market or MERCOSUR). Those guidelines were based on the Brazilian text.

It is necessary to emphasize the importance of a participative process in developing guidelines. This process was as important as its final result. An otherwise excellent text, deprived of a participative elaboration process, would not bring the benefit of facili-
ilitating adherence to the guidelines because there would not be any involvement from the main stakeholders from the beginning of the process. During the 3 years of discussion that went into developing the Brazilian guidelines the process benefited greatly from the debate among all stakeholders involved. This participative process was very enriching and, surely, will contribute to the future success of the guidelines.

Conclusions

The fragmentation in Latin American health care systems means that the development and implementation of PE guidelines is a complex task. It has to be consistent with other health care reforms in the countries concerned and involve a broad range of stakeholders, including academic experts, industry, and decision makers in the different sectors of health care (i.e., government, social security, and private as well as citizens). Finally, the implementation of PE guidelines should take account of the need for good local data on resource use and cost, and the need for adequately trained personnel to submit and evaluate PE dossiers. Nevertheless, several countries have decided to embark of this task and are moving forward at different speeds. No one is pretending that this will be easy, but at least in principle it appears that existing health care decision-making processes in Latin America could accommodate PE guidelines, should there be interest in implementing them.

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REFERENCES