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Market Access Newsletter

Editorial

by Prof. Mondher Toumi
EMAUD Chairman

Dear Colleagues & Friends,

Even though the US decision making policy is different from that of Europe, the fragmentation of both markets, the prevailing model of Value Based Pricing (VBP), and the need to enforce an increase to comparative/relative effectiveness research make both continents more alike.

The fragmentation of the market appears to be historically prominent in the US. Pharmaceutical companies have the infrastructure to cope with the issues perfectly, whereas in Europe it becomes a very complicated, and often unpredictable hurdle to deal with. To overcome this hurdle many efforts have been developed but they remain very much disseminated, generic, and are insufficiently coordinated, which allow regional authorities to act in a discretional way. This will continue until there is more structure.

VBP is a model that seems to be quite ubiquitous in the field of drugs. By definition, a better product will always achieve better price. Of course we trust humans to be instinctive enough to keep finding better products. In the meantime, the production of wealth has tended to flatten in developed countries. A gap begins to develop between budgetary constraints and expenses. Therefore, it is not unthinkable to assume that the model will be questioned in its nature or in the way it is managed, with the inclusion of a well defined ceiling price, as the actions to implement such changes are attempted in France.

The recent International ISPOR meeting highlighted the trend of real life evidence as an unavoidable piece of evidence in drug assessment. There is still a long way to go before we handle the methodology of these hurdles and limits, and before we are able to interpret such data. There will certainly be a difficult period of transition, further complicated by the different attitudes between payers and marketing authorisation stakeholders. The disparity will lie in the nature of the set up and the meaning of the results. It is not a matter of not acting properly, as new actors appear as 'impartial referees' of the interpretation of these studies.

The US and European models are different in many ways; however, challenges for the pharmaceutical industry will be the same. What will be the solution for each of them? Will there be a convergence in the solutions? Even though most of the models are based on VBP, the definition of the value drastically varies from one country to another.

Yet, there is something that has not changed among all these regulations. Patients are still excluded from the discussions and the decision making of value for drugs. Nowadays, two viewpoints are mostly considered in the decision making process: the expert opinion and the societal viewpoint. They are both legitimate since the expert has got the technical knowledge, and society mandates him to make a judgment. Besides, through various taxes, it is society that finances the National Health Service. However, patients are the first line of contact between the benefit of medicines and the expected outcomes.

Today, no decisions actually incorporate the patient perspective. Measuring each perspective is complex, and there is little knowledge on how to do it. However, there are validated and recognized techniques on how to measure these values, such as the Discrete Choice Experiment (DCE) that provides a clear and concise understanding of the patient perspective and preference. But these need to be extended. The patient point of view, as expressed within decision making committees, remains something very much linked to emotion and therefore it is not really used in decision processes. It is quite surprising that methods of DCE have not been systematically used in decision making processes. Yet, it is another thing that is becoming unavoidable in the future.

America's Patient Access Scheme: Coverage with Evidence Development

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Notwithstanding the rhetoric often heard in political circles declaring "we don't ration healthcare in America," healthcare is invariably rationed in the US. Mostly, care is rationed implicitly, through a patient's ability to pay, or qualitative differences in health insurance. Despite the fact that the majority of clinical- and cost-effectiveness studies are published in the US, their impact has been limited. Traditionally, US policymakers have been reluctant to pursue an explicit approach towards rationing, or allocating healthcare in accordance with some distributive rule, given limited resources. As a result, findings from effectiveness analyses have rarely led to changes in prescribing and reimbursement practices.

However, a significant policy shift may occur in the near future, based in part on a renewed focus on the sustainability of Medicare and Medicaid, but also healthcare reform coupled with a massive infusion of funding directed towards comparative effectiveness research (CER). The US National Institutes of Health broadly defines CER as the "generation and synthesis of evidence that compares the benefits and harms of alternative methods to prevent, diagnose, treat, and monitor a clinical condition or to improve the delivery of care."

In the US context, CER findings are technically precluded from determining Medicare and Medicaid prescribing and reimbursement decisions. Needless to say, CER's ultimate objective is to connect prescribing and reimbursement decisions to an evidence base. That is, to inform decisions on whether to prescribe or reimburse a particular drug, what kinds of conditions to impose on that drug's reimbursement, and how much cost sharing to levy on the patient, based on data underlying the drug's clinical- and cost-effectiveness, i.e., its "value."

In recent years, in the private healthcare sector, there have been cautious attempts at establishing evidence-based risk sharing (or patient access) agreements, or what Americans call "paying for pills by results." Notably, the insurer UnitedHealthcare and the life science company Genomic Health signed a deal, in which UnitedHealthcare agreed to pay for a genetic test (Oncotype Dx®) while results are monitored. The contract stipulated that Genomic Health would grant UnitedHealthcare rebates if patients who should not be placed on chemotherapy are. And, Merck agreed to link the amount the insurer Cigna pays for the diabetes drugs Januvia® and Janumet® to how well type 2 diabetes patients are able to control their blood sugar, and how adherent they are to their prescription regimen. Cigna will review A1c laboratory values, and, if A1c improve over time, the discounts Merck offers on Januvia® and Janumet® will increase.

Nevertheless, risk sharing arrangements have not taken off in the US. They may not be particularly viable, given the healthcare system's open, fragmented, multi-payer environment. Instead, in terms of patient access schemes, the US relies more on the coverage with evidence development (CED) model, driven by Medicare. CED constitutes an agreement between Medicare, manufacturers of new drugs, diagnostics, or devices, and Medicare beneficiaries, to provide patients who enroll in specially designed post-marketing trials access to new technologies while additional evidence is generated. CED tackles the problem of inadequate evidence base at launch of a product. If, at the end of a given time period outcomes are lacking, manufacturers face the risk of discontinuation of reimbursement by Medicare.

Unlike other jurisdictions, Medicare lacks the authority to negotiate the price paid for pharmaceuticals and must therefore pay the price set by the manufacturer. Medicare's only recourse is to review real-world clinical data, employing CED. In turn, this can lead to limits in coverage to patient groups for whom the evidence is very strong. As such, CED may serve to reconcile the tension between developing fiscally sensible, evidence-based policies and being sufficiently responsive to manufacturers, physicians, and patients.

Recent examples of CED include off-label uses of four colorectal cancer drugs and warfarin's companion diagnostic. In June 2010, Medicare initiated a review, a so-called national coverage determination, of Provenge® - sipuleucel-T, a novel cellular immunotherapy for the treatment of asymptomatic or minimally symptomatic, metastatic prostate cancer. National coverage determinations often precede CED. At $93,000 per treatment cycle, Provenge® is one of the most expensive cancer therapies ever to hit the marketplace. Additionally, with 25,000 prostate cancer patients eligible to take Provenge® annually, the fiscal impact of reimbursement will likely be substantial. Indeed, the anticipated budgetary impact related to Provenge® reimbursement appears to be a major factor in the decision to undertake the review. On March 30, 2011, Medicare issued a provisional decision stating that it will allow nationwide coverage, but only for the FDA-approved indication, explicitly ruling out reimbursement of off-label uses. Further, Medicare said it will continue to monitor outcomes closely, and may revisit its decision.

Medicare covers what it deems is "reasonable and necessary." This clause implies that Medicare considers the broader interests of the program, including the opportunity costs of reimbursing new technologies, i.e., Medicare's fiscal sustainability. With Medicare unable to absorb all the costs of new, high-priced technologies, cases like Provenge® may be a harbinger of things to come.

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Patient-Centered Benefits-Risk Assessment

The case for Multi Criteria Decision Analysis with the Analytic Hierarchy Process

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In recent years health technology assessment (HTA) processes have expanded beyond those countries dominated with a single payer, and with this expansion there has been renewed attention placed on the fundamental evaluation methods that are used. While there has been considerable attention placed on comparative effectiveness research (CER) in the US and efficiency-frontier analysis in Germany, another fundamental issue has emerged: how can technology assessment better involve patients. Here patient centered strategies and methods can be categorized into two types: those that involve patients directly in decision making and those that aim at the study of patients needs and preferences in terms of benefit-risk trade-offs.

Quantitative approaches to benefits-risk assessment

In benefit-risk assessment one may identify two subsequent steps, the (1) quantification of benefits and risks and (2) the judgment to be made about the benefit-risk ratio's in terms of acceptability. Here, decision makers seek for decision thresholds, trading off the amount and severity of risks to the benefits. Although we can provide clinical data on the performance of interventions on these endpoints, they are certainly not equally important. Yet, it is not clear how and with what weight these multiple endpoints contribute to the decision. Although an evaluation of the benefits and risks is part of any drug evaluation process, drug evaluation and regulatory committees do not formally use quantitative benefit-risk assessment methods.

In August 2010, the European Medicines Agency (EMA) published an extensive report on both qualitative and quantitative methods for benefit-risk assessment. Further to that, Guo *et al* (Value in Health, 2010) searched for quantitative methods incorporating benefits and risks into one aggregate measure. Of 12 different measures found in the review, multi-criteria decision analysis (MCDA) was one approach that was mentioned.

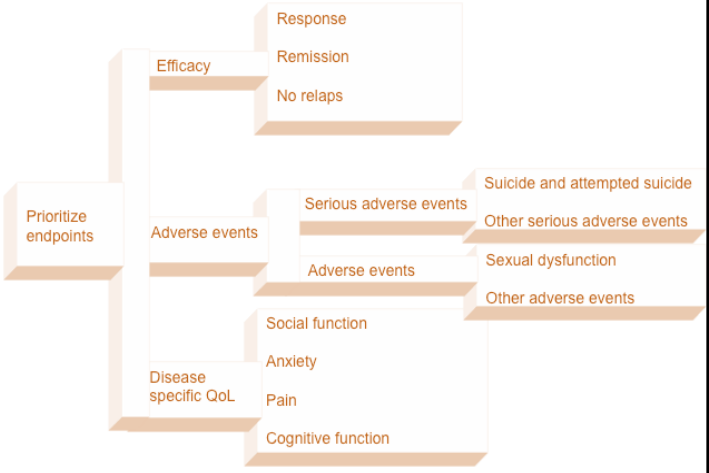
MCDA, the Analytic Hierarchy Process and patient involvement

MCDA stems from operations research and decision sciences, and seeks to quantify decision trade-offs by weighing separate decision criteria. MCDA methods are based upon a (hierarchical) decision structure, involving (sub-) criteria and alternatives relevant for the decision to be made.

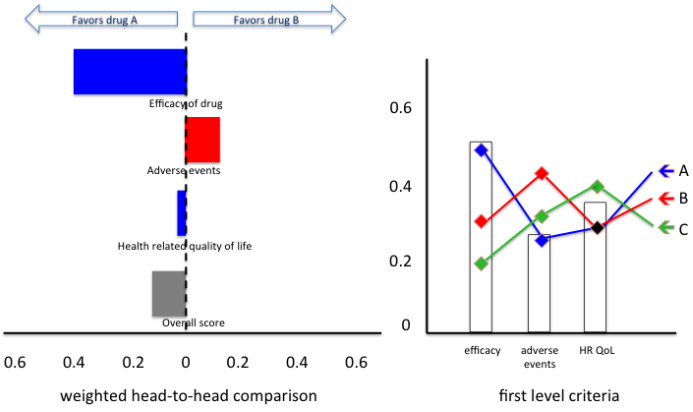
Although several MCDA methods are employed, including SMART, ELECTRE and more recently BRAT, the Analytic Hierarchy Process (AHP) is the most widely used approach in healthcare. In AHP, developed by Thomas Saaty, a decision problem is decomposed and criteria are compared using pairwise comparisons on an 18-point scale. By using the eigenvalue it is possible to calculate the weights. In AHP, different decision-makers can be at stake, including regulators, policy makers and patients. Namely, in today's healthcare, decisions need to be made patient-centered and evidence based. This also applies to benefit-risk assessment, where the patient should be at stake in determining an acceptable trade-off.

An example of patient weighted risk-benefit trade-off

In a recent study about antidepressants, the AHP was used to prioritize patient-relevant endpoints. The decision structure was defined after several discussions with experts involved in the pilot. Following that, two panel sessions were organized with stakeholders. AHP can be used in a group decision mode, which allows all panel members to vote and to discuss the results. The decision structure has three levels of criteria, where "efficacy", "adverse event" and "quality of life" were defined to be the main criteria.



After the elicitation of criteria weights and performance weights (comparison of the interventions), several graphical presentations can be used to provide decision support. A hypothetical example of a head-to-head comparison of two drugs using a criteria weighted score is presented. It presents the overall drug score, weighted for the importance of the three criteria. The complete picture can be seen on the right side of the graph, as it presents both the criteria weights (bars) as well as the performance weights of three hypothetical drugs. Clearly, drug A is to be the preferred drug even though there are more adverse events.



Relevance for health policy

In decision making, clinical evidence remains the most important factor to consider and should never be replaced by patients' preferences. However, each treatment is associated with multiple benefits and risks and where designers of clinical trials may have a certain view on their preferred and primary study endpoints it may be worthwhile to counterbalance that view with a patient perspective. Therefore, the patients' perspective may add supportive evidence in appraisals. An advantage of AHP is it's hierarchical structure, which allows the decision maker to structure endpoints according to the level of aggregation and causality with other surrogate endpoints.

It should be encouraged that decision makers further look into these methods and that they carry out a series of pilot experiments to learn about the most appropriate use in benefit-risk assessment. Even without adding the patients' perspective, the method may add transparency to the decision making process.

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EMAUD News

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Event: 3rd Annual Market Access Day
Coming up soon !

--- Market Access: the New Rules of the Game ---

Stakeholders are still around the table playing the game of Market Access. New concepts and new regulations regularly pop up, but does the content really change? Is Value Based Pricing as proposed for the UK really new? After AMNOG in Germany, what will be the next concept in the game of Market Access?

On the top of major reforms at a national level, increasing pressure at the regional and even local level will force industry to adapt organisational structures and decision processes to take up these highly fragmented new challenges.

The next decade will certainly face the emergence of more sophisticated market access regulations that may be perceived as evolutionary from a conceptual perspective, but for the industry, they will certainly be revolutionary. Therefore, the field of Market Access will become even more crucial to company's success.

If you want to be in the game, come join the debate with stakeholders during the EMAUD Market Access Day.

To be located in Paris, France
by invitation only
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