# Effective Use of Health Technology Assessment TO MAXIMIZE MARKET ACCESS: START EARLY AND UPDATE OFTEN

Contributed by

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We all know that the face of drug discovery and the market for new pharmaceutical products (and medical devices/diagnostic technologies) is changing. The era of the blockbuster appears to be over, the cost of bringing a new product to market has skyrocketed and when a new product is eventually licensed, sceptical payers are increasingly demanding evidence, not only of the product's efficacy, but also its value for money. This demand on the part of payers for evidence of value has led to an increasing need for health technology assessment (HTA) to support reimbursement and market access strategies. The drug development pyramid (see Figure 1) is a familiar concept to those working in clinical research.

With so many candidate substances screened for development just to support the launch of a single product, it would be tempting to see it as folly to embark on a formal assessment of potential value for a product prior to launch before it has even been shown whether the product works. To wait for successful demonstration of efficacy before thinking about demonstrating value, risks coming to market totally unprepared, with the consequent danger that the successfully licensed product will fail to hit the ground running. Furthermore, the formal assessment of value early in a product lifecycle has much more to offer than helping a fast exit from the starting gates for those products that do make it through clinical development.

Pharmaceutical companies generally spend too long persisting with clinical development of products that have a very low chance of making it to market. When you consider the costs involved in the clinical development process, this is true folly. And this is where formal techniques of HTA — in particular economic analysis — can help. Using the very tools that reimbursement authorities use to assess value, cost-effectiveness models, employed early in the lifecycle, can help identify the road to value — the chain of evidence required to take something in early human studies (or even preclinical studies) through to showing a measureable impact on health. Of course, there will be uncertainties — and the earlier in the development process you start, the greater those uncertainties will be — but it is precisely in quantifying those uncertainties that the value of the exercise is obtained. Once the uncertainties are mapped out, strategies to reduce those uncertainties can be developed and the appropriate research studies commissioned.

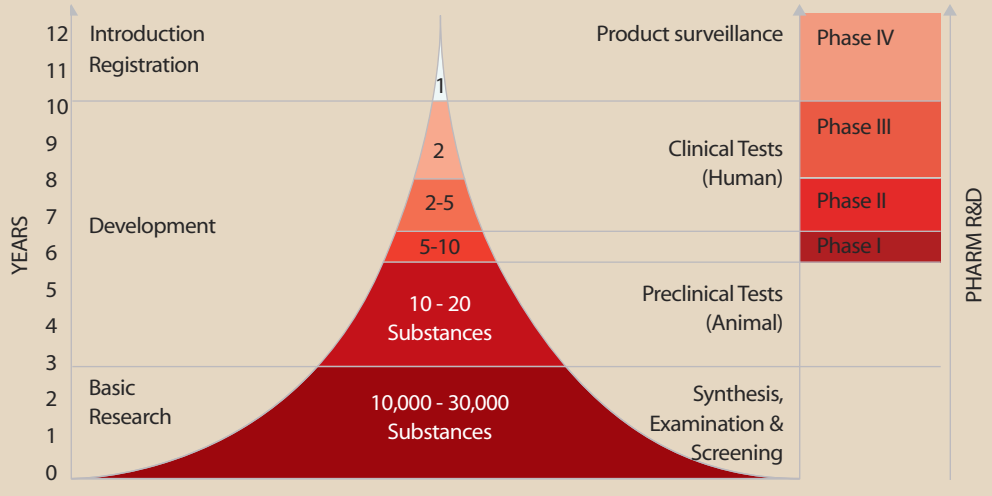
## The Preferred Basis for HTA

The growth in formal HTA has been driven in recent years by the mandating of a fourth hurdle by reimbursement agencies, such as PBAC in Australia, CADTH in Canada, and NICE/SMC in the United Kingdom. Other countries are following suit with increasing demand for HTA by agencies across Asia and South America. Even in the United States, despite protestations, the comparative effectiveness agenda has been viewed by some as the first step on the road towards HTA.

In the arena of publically funded trials and formal HTA, Mark Sculpher and colleagues at the University of York, UK, have argued that the preferred funding base of HTA should precede formal data collection.

They persuasively argue that all too often a clinical trial is performed and at that point a cost-effectiveness analysis is piggy-backed onto the trial to show value. Often, rather than just being trial-based, the economic assessment will incorporate other data and project beyond the time-frame of the study in order to overcome the limitations of the trial framework and estimate lifetime cost-effectiveness. However, they argue that the optimal basis for undertaking formal HTA would be to start with a formal decision problem (what is the value of treatment X), to then construct a model that synthesises

**Figure 1: The Drug Development Pyramid**



currently available evidence about treatment X and to use that model of current evidence to identify research priorities to reduce uncertainty. At that stage, primary data collection (most likely a clinical trial) would be performed, but one that was fundamentally designed with the information needs of the model in mind. Once the trial had reported, the information generated is incorporated into the next iteration of the updated model, allowing a more informed assessment of the technology to be made.

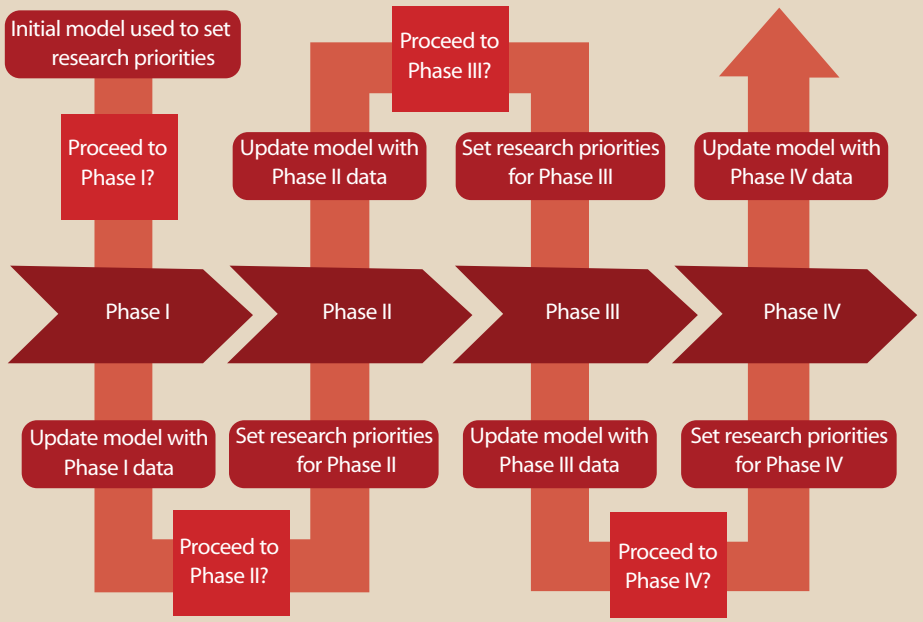
## An Iterative Approach to Research Priority Setting

If we see each clinical development phase as an opportunity for data gathering, then the principles outlined by Sculpher and colleagues could be applied at each stage. Such a process is illustrated in Figure 2. Even before first in-human studies are performed, it should in principle be possible to outline a simple model that links the molecule under development to the disease. At this stage, the simple model would lay out the rational for the product and should include the potential size of the market that could be captured by an effective (and cost effective) new product in the disease area in question. If the potential gains outweigh the costs of development, then the product should enter Phase I of development. At the end of that phase, information should be available on safety of the product.

The model should be updated with any safety concerns and another assessment made as to whether to enter the product into Phase II of clinical development. A similar process repeats once Phase II data become available — now the dose ranging information should allow the optimized dose to be suggested along with further information on the likely side-effect profile at this dose, and most importantly, an updated assessment of the likely range of effectiveness that may be possible. If the decision is made to proceed to a Phase III study, then there will be an opportunity not only to use the model to help influence the optimal design and data collection alongside the Phase III trial, but also to design any supplementary studies that will be needed upon successful completion of a Phase III trial. For example, epidemiological, cost, and health-related quality of life data are all requirements for a fully completed health economic model to support reimbursement and market access. While the Phase III trial will undoubtedly offer some opportunities for data collection, it will often be the case that such data are better collected outside of the trial as part of an observational study.

If the development and iteration of the economic model proceeds in this way, at the end of Phase III and in the event of a successful licence being obtained, the value story to support market access and reimbursement processes will also be available in a timely fashion. In the event that authorities request continuation into Phase IV post-marketing studies, then the economic model is again available and can be used to optimize data collection and can be updated as additional data become available.

**Figure 2: An Iterative Approach to Economic Modeling to Guide Clinical Research Priority Setting**




Business cases, target product profiles, value propositions, trial simulations, etc. are all tools that are used to support decision making around clinical development. The difference is that a formal economic model brings these tools together in a single unified framework that relates all of these concepts back to the most important goal of all — the use of the product in the market place and the appropriate reimbursement by health care systems internationally.

Of course, one of the many things that will be uncertain early in the life of the product is its price. Therefore this sort of health economic assessment has a crucial role in exploring the potential prices that could be charged for a product — and relating that potential to both the effectiveness of the product as eventually shown and the prevailing market conditions in terms of the size of the patient population that could be treated, the competitor landscape and the timing of market entry. Crucially, early economic assessment through the iterative approach to modeling can assist with effective planning and managing expectations regarding price with the client early in the process.

## Strategic Client Relationships

In closing, it is worth reflecting on two important aspects of the above process with respect to the relationship between a consulting company and the client company. Firstly, for this process to work effectively, a very high degree of trust is required between the client company and the consultancy team. Long-term commitment to the process is required on both sides and a willingness to share confidential information that gets to the heart of a client company's long-term future. Secondly, this sort of strategic consulting over the lifetime of products in development may appear at first pass to be a costly addition to the already high costs of development. However, that would be to miss the point about the overall value of the approach in terms of streamlining the clinical development process through the effective design of each stage of clinical development and improving the potential to gain market share at a given price. Seen in this light, the potential costs of the process are easily outweighed by the considerable potential for benefits. PV

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