Economics, expenditures and evaluations

Health economics and outcomes research play very important roles in marketing pharmaceutical products in the UK, but there is a lot to take into consideration...

Welcome to the second in an occasional series of articles designed to take an in-depth look at some of the key issues facing pharmaceutical marketers today. Each supplement includes real-life case studies and provides readers with new marketing perspectives and practical advice to challenge the way their organisation currently thinks about key market issues.

There are few developments in the pharmaceutical industry that have presented marketers with greater challenges than the increasing requirement for health economics and outcomes research (HEOR).

It will no longer suffice for marketers to consider health economics as a peripheral issue delegated to their clinical colleagues or to some arcane health economic group. Health economics needs to become a central element of brand management and as such it is vital that marketers in today’s healthcare industry immerse themselves in this area as well as they might in a clinical profile or a market research strategy.

Whereas health economics and outcomes research was previously considered as a somewhat peripheral activity appended to the delivery of phase III clinical data and finished with once the brand was launched, it has now become an important strategic consideration throughout the development and brand lifecycles. Because of this, marketers need to diligently manage the strategic implications of health economics for their brands ensuring that the right type of economic and outcomes evidence is gathered from as early as phase II through phase IV and beyond.

Managing the communication of economic and outcomes evidence has also developed into a critical success factor. Running parallel to this, environmental changes have led to a fragmentation of the marketplace generating many more stakeholders – all of whom have a requirement for health economic or outcomes evidence, but each will have a particular perspective on the evidence or a preference on how it ought to be presented and interpreted.

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Because healthcare customers are becoming more sophisticated in how they understand and appraise health economic and outcomes evidence, the successful marketer should ensure they fully grasp the needs of their customers in this area and how they can most effectively develop and deliver health economic and outcomes research strategies. This supplement is intended to give marketers an overview of the critical aspects of HEOR in the UK market and provide fresh insights into how the development and use of health economic and outcomes research may be optimally approached.

**HEALTH ECONOMICS AND OUTCOMES RESEARCH IN THE UK MARKET**

Increasing healthcare expenditure in the UK has necessitated considerations of value for money in healthcare provision. The health economics and outcomes research disciplines provide an array of analytical techniques with which to ascertain the value for money of this investment. In the UK, these concerns are the remit of national bodies including The National Institute for Health and Clinical Excellence (NICE), the Scottish Medicines Consortium (SMC) and the All Wales Medicines Strategy Group (AWMSG). These bodies produce guidance about usage based on an assessment of the costs and benefits of new healthcare technologies at a national level. Critically from a marketer’s perspective, economic considerations are becoming increasingly important to broader audiences from PCOs down to individual prescribers.

This paper examines the roles and experience to date with the national health technology assessment bodies. It also highlights that expertise and knowledge based on health economics and outcomes research can be used effectively in supporting marketing activities at a local level.

**1. THE TREND OF INCREASING HEALTHCARE EXPENDITURE IN THE UK**

In the UK, demand for new healthcare technologies and drugs outstrips the government’s capacity to pay. NICE was established in 1999 with a remit to obtain maximum health benefits from the use of NHS and PSS (Personal Social Services) resources. Achieving value for money is a primary objective of government health policy. "The new Public Service Agreement includes a value for money target which will require the NHS to improve its cost efficiency and treat even more patients than before,” (Chancellor of the Exchequer 2002).

These objectives for health policy are borne out of an environment where demand for health services is growing at a rate greater than the rest of the economy. The graph above shows that public expenditure on health in the UK, relative to total Gross Domestic Product (GDP), grew by approximately 40 per cent between 1990 and 2004.

Within the same time period the proportion of healthcare expenditure spent on pharmaceutical products has increased from 12 per cent in 1975 to 16 per cent in 2000 (OECD Health data 2006). This increase in demand for healthcare is not expected to subside, with growth primarily driven by:

1. Increased patient expectation
2. Introduction of more expensive novel technologies
3. An ageing population.

Crucially, this demand is expected to be met solely by increased public expenditure, with no growth in the level...
of private expenditure anticipated (see table, above). With healthcare expenditure growing faster than the total economy it follows that there is a focus on curbing the rate of expenditure. However, cutting existing services is too simplistic to be an acceptable public healthcare policy given the potential to worsen health outcomes. Therefore, health policies need to ensure that expenditure represents good value for money and the UK government has sought to introduce a series of both supply-side and demand-side measures to improve the efficiency of provision. Such measures have included: policies that address provider incentives, expansion of generic prescribing, introduction of user charges/patient cost sharing activities and a proliferation in the use of health economic evaluation to justify value for money.

2. THE PRACTICE OF HEALTH ECONOMIC EVALUATION

The role of health economic evaluation in achieving these policy objectives is to quantify the costs and benefits of competing health technologies so that decision makers can determine whether or not public funding of various technologies represents good value for money.

If an intervention is ‘cost-effective’ then allocating resources to this intervention may be deemed to be an appropriate use of money. The discussion below briefly describes some of the methods used in health economic evaluation. These methods include cost-effectiveness analysis, cost-utility analysis and cost-benefit analysis.

Cost-effectiveness analysis (CEA) is a technique used to assess the trade-off between extra cost and the improvement in outcomes from a new technology. Results of this type of analysis are expressed in natural units. Natural units reflect the specific objective of treatment and include outcomes such as ‘adverse events avoided’ and ‘life years gained’. In essence, a CEA communicates the value of a technology compared to the existing technology and other direct competitors. From a marketer’s perspective these types of analyses can be used as an important element of a brand’s differentiation.

A cost-utility analysis (CUA) incorporates the impact of a treatment on a patient’s quality of life as well as length of life (often expressed as Quality Adjusted Life Years – QALY). Increasingly, national decision makers require that CUA rather than CEA be performed in order to assess the value for money of a product. This preference for CUA is primarily because it allows assessment of the relative value for money of different interventions across different therapeutic areas with QALYs being considered as the ‘common currency’ with which health outcomes may be measured. In a CUA, an intervention would be said to be cost-effective if the incremental cost per QALY gained is less than some pre-determined threshold. In the UK, this pre-determined threshold is often quoted at £30,000. However, this threshold value is not absolute and will be discussed further into the article.

Cost-benefit analysis (CBA) is a technique used to

“There the government has introduced supply- and demand-side measures to improve the allocation of scarce healthcare resources and to curb escalating costs”
compare the costs and benefits of a technology in purely monetary terms. If the total monetary value of benefits from a technology outweighs the total cost, the technology should be adopted. Willingness-to-pay values are often used and these can be derived using techniques such as contingent valuation or conjoint analysis. CBA can provide decision makers with an understanding of two fundamental questions. Firstly, how people value the improvements in health outcomes achieved from using a service and secondly, whether people using the service place sufficient value on the improvement in health outcomes to justify the cost. However, this technique is rarely used in public policy due to the inherent difficulties in placing a monetary value on health.

In each of the types of economic evaluation described above, a number of techniques may be used in order to accurately predict the costs and benefits of the interventions being evaluated. Some of these are described in the table below.

### Economic evaluation and techniques

<table>
<thead>
<tr>
<th>Technique</th>
<th>Description and purpose</th>
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<tbody>
<tr>
<td>Meta-analysis</td>
<td>The process of combining the data from a number of independent studies (usually drawn from the published literature) and synthesizing summaries and conclusions addressing a particular issue (health technology assessment or economic evaluation for example). It aims to utilise the increased power of pooled data to clarify the state of knowledge on that issue. Meta-analysis is often used in health technology assessment to evaluate therapeutic effectiveness.</td>
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<tr>
<td>Preference and utility valuation studies</td>
<td>These studies are used to inform a health economic evaluation in terms of the willingness to pay for an intervention (preference studies) or the quality of life associated with that intervention (utility valuation studies).</td>
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<tr>
<td>Epidemiological and disease modelling</td>
<td>Is commonly used when clinical trials or clinical evidence alone is not sufficient to determine the full impact in terms of costs and benefits of the interventions being evaluated. Modelling techniques such as decision analysis, Markov models and microsimulation models can be used to predict the longer term costs and outcomes for the patient group being treated with the interventions being evaluated. These models can be used to extrapolate results from a clinical trial setting to the real world setting where patient demographics and/or treatment practices may differ.</td>
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<tr>
<td>Budget impact modelling</td>
<td>Is focussed mainly on the monetary implications on the uptake of a new healthcare intervention. This modelling can be used to calculate the expected number of patients likely to receive the respective interventions and therefore the total financial implications of those interventions. This information can then be used by government departments and the pharmaceutical industry alike for determining affordability, planning and budgeting.</td>
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### 3. THE BIRTH OF HEALTH TECHNOLOGY ASSESSMENT IN UK HEALTH POLICY

The UK government has introduced various supply- and demand-side measures to improve the allocation of scarce healthcare resources and to curb the escalating costs of providing care, with the most important arguably being the introduction of the ‘fourth hurdle’ being a ‘cost-effectiveness’ recommendation for new products and/or new indications.

At the national level, NICE provides guidance for England and Wales, and the SMC provides advice for Scotland. Additionally, AWMSG provides interim advice on new drugs and/or new indications prior to a review being completed by NICE.

**The National Institute for Health and Clinical Excellence (NICE)**

NICE is a government body set up in 1999 to produce recommendations for healthcare professionals, patients and carers to better enable them to make informed treatment and healthcare decisions. NICE does not license drugs or devices – this is done in the UK by the Medicines and Healthcare products Regulatory Agency (MHRA).

NICE produces guidance on health technologies and on clinical practice for the NHS in England and Wales. The underlying policy objective of NICE is that the efficiency of the healthcare sector will improve as a result of better decision making by healthcare professionals. Improved efficiency in the healthcare sector will therefore mean a greater production of ‘health’ within a constrained budget.

NICE’s technology appraisal programme reviews and make recommendations about:

- New medicines and major new indications for existing medicines
- Medical devices (for example, hearing aids or inhalers)
- Diagnostic techniques (tests used to identify diseases)
- Surgical procedures (such as repairing hernias)
- Health promotion activities (for example, ways of helping people with diabetes manage their condition).

In contrast to the SMC and AWMSG, NICE does
not review all new medicines and/or indications at the time of launch. The Department of Health commissions NICE to develop clinical guidelines and guidance on public health and technology appraisals. NICE is asked to look at particular drugs and devices when there is confusion or uncertainty over the value of a drug or device or when prescribing practices vary across the country (‘postcode prescribing’).

Another unique feature about NICE is that, until recently, the procedure for evaluating new technologies always included an independent assessment of the clinical and economic evidence by an academic group. This is different from the SMC and AWMSG process, where the principal evidence is the submission from the manufacturer or sponsor. However, a Single Technology Appraisal (STA) process was introduced by NICE in 2005 to expedite the evaluation of some technologies. The STA process is specifically designed for the appraisal of single products, with single indications. This process will normally be used to ensure that NICE is able to issue guidance to the NHS in England and Wales on new technologies close to their introduction into the UK market. Under the STA process, as with the SMC and AWMSG, the manufacturer’s submission is the principal source of evidence. It is, of course, subject to a structured critical appraisal.

The Scottish Medicines Consortium (SMC)
The SMC was set up in 2002 to provide advice to NHS Boards and their Area Drug and Therapeutics Committees (ADTCS) across Scotland about the status of all newly licensed medicines, all new formulations of existing medicines and any major new indications for established products (licenced from January 2002).

The SMC is the source of advice for Scotland on new drug therapies and the NICE STA process has no status in Scotland. If a NICE STA endorses a drug that was not recommended by the SMC, manufacturers need to resubmit the drug to SMC with new evidence. However, the SMC say that NICE Multiple Technology Appraisals (which examine a disease area or a class of drugs) usually contain new evidence gathered after the launch of drugs or new economic modelling, and therefore NHS Quality Improvement Scotland (NHS QIS) reviews this type of appraisal and decides whether the recommendations should apply in Scotland. Where NHS QIS decides that such an appraisal should apply in Scotland, the NICE guidance supersedes SMC advice.

A review by the SMC in 2004 found that of 12 products reviewed by both NICE and the SMC, every decision was the same.

Is there a £30,000 cost per QALY threshold?
The incremental cost-effectiveness ratio (ICER) is a summary statistic of economics analysis. Cost per QALY gained is the most commonly used ICER but other examples are cost per life gained or cost per event avoided (eg, fracture). The cost/QALY ICER is useful because it takes into account quality of life as well as quantity, and it allows comparisons with other health services. The latest guidance on methods for health technology assessment issued by NICE uses the following wording about cost/QALY thresholds:

“Below a most plausible ICER of £20,000/QALY, judgements about the acceptability of a technology as an effective use of NHS resources are based primarily on the cost-effectiveness estimate. Above a most plausible ICER of £20,000/QALY, judgements about the acceptability of the technology as an effective use of NHS resources are more likely to make more explicit reference to factors including:

- The degree of uncertainty surrounding the calculation of ICERs
- The innovative nature of the technology
- The particular features of the condition and population receiving the technology
- Where appropriate, the wider societal costs and benefits.

Above an ICER of £30,000/QALY, the case for supporting the technology on these factors has to be increasingly strong.”

Source: NICE Guide to the Methods of Technology Appraisal, April 2004 (page 33).

Surprisingly, there is no clear rationale or evidence supporting a £20,000–£30,000/QALY threshold. This makes it all the more important that NICE considers a number of other factors, not just the estimated cost/QALY. Indeed, analyses conducted on NICE recommendations to date have shown that NICE does not adopt a black (reject over £30k/QALY) and white (accept under £30k) approach to decision making (see table, page 6). The SMC have stated that they also do not have a fixed upper limit on willingness-to-pay for a QALY.
It appears to be in keeping with society’s preferences that the government should not operate with a strict cost/QALY threshold. For instance, if a £20-30,000 per QALY threshold were applied to orphan drugs, it’s likely that no orphan drugs would be funded in the UK. However, based on past decisions and advice from a Citizen’s Council set up by NICE, such a policy is not followed and would not be in keeping with society’s preferences (NICE Citizens Council Report: Ultra Orphan Drugs, November 2004).

What are the chances of success with NICE and the SMC?
Several analyses are in the public domain on approval rates with NICE and the SMC. Summary results are shown in the table on page seven. However, it is important not to read too much into overall approval rates because these figures can disguise important factors. For instance, rates of approval change over time. The analysis of NICE recommendations shows higher approval rates in the initial ‘honeymoon’ period than now, and similarly the SMC have stated that approval rates have decreased over time. More importantly, overall approval rates are heavily influenced by the number and type of submissions. For instance, ‘me-too’ drugs submitted based on cost minimisation analysis (same efficacy, same or less cost) have a relatively a high rate of success compared to innovative and/or high cost drugs that have to justify additional expenditure (increased QALYs, increased cost).

To maximise the chance of a successful submission, it is important to utilise the array of health economic and outcomes research techniques available (see table, page four). A multi-disciplinary approach is important because specialist input is needed from the key areas of clinical research, epidemiology, biostatistics and economics.

What is the impact of a NICE or SMC recommendation?
The implementation of national guidance from NICE or SMC is a matter of considerable attention and concern. Several reviews have been conducted using IMS data. These show that although a case can be made that NICE has improved the appropriate use of medicines, a positive recommendation from NICE is not always sufficient to ensure the appropriate uptake of a new product/indication at a national level, or to ensure consistency across the country.

A review of 28 sets of guidance from the early phase of NICE appraisals, using IMS Disease Analyzer data, identified that 12 cases could be classed as reasonably implemented within the expectations of guidance (based on actual usage versus expected usage). Another 12 were classified as under implemented. There were only four cases where usage exceeded the expectations in NICE guidance (Source: Nice Guidance Implementation Tracking Data Sources, Methodology & Results, January 2005).

Another report has investigated variations in usage of cancer drugs approved by NICE. This review considered 16 cancer drugs appraised by NICE plus four standard cancer drugs as comparators. The report found that overall usage of cancer drugs generally increases following positive appraisals from NICE, but there were cases of significant variation in usage across the country that cannot be accounted for by differences in casemix or cross boundary flows alone. In the most extreme example, there was an 11-fold variation in the use of one drug. However, the report found that variation does appear to lessen over time once a positive appraisal from NICE has been published. There were differences of opinion between the pharmaceutical industry and the cancer networks about whether direct funding restrictions play an important role. The cancer networks reported
that the main issue is constraints in service capacity and differences in clinical practice. (Source: Variations in usage of cancer drugs approved by NICE Report of the Review undertaken by the National Cancer Director, May 2004).

So what other factors and decision makers play a role in achieving product uptake in the UK?
As seen above, a positive NICE recommendation for a product does not necessarily guarantee rapid uptake and/or widespread usage of a product in all parts of the UK. This can, in part, be explained by the fragmented nature of decision making in the UK. There are now an increasing number of stakeholders who are making treatment and purchasing decisions based on health economic data. These stakeholders range from policy makers at the Primary Care Trust level through to the increasing number of commissioning GP practices. It is this proliferation of customers having a greater influence on purchasing decisions that makes health economics and outcomes research such an important focus for marketers.

At a local level, a Primary Care Organisation (PCO) must consider the local budgetary impact a decision might have for a range of sectors, eg, hospital services. Hence, each local body has to interpret NICE’s guidance in light of the local setting and advocate appropriate behaviour to maximise the health status of their local populations. In addition, physicians must act as agents for each patient’s presenting, understanding their individual needs, as well as considering this in the context of society at large (eg, opportunity costs for other patients).

A pharmaceutical company selling into this market must make sure its value proposition can meet the wide range of needs of different stakeholders, eg, they can deliver cost-effective care, help hospitals to reduce admissions (where appropriate), enable PCOs to meet their payments-by-results targets and provide patients with safe, efficacious medication.

Health economic and outcomes research can be used to help each stakeholder understand the likely implications of decisions they make, whether this focuses upon cost-effectiveness, budgetary impact, patient outcome or other incentives. So, the practice of health economic evaluation is highly relevant and transferable to marketing a product across the various local decision makers and throughout a product’s lifecycle. The case studies on page eight show examples where HEOR techniques used at a national level were employed at a local level and at different times of the product lifecycle. In case study one, HE techniques were used with a PCO. In case study two, OR techniques were used with prescribers.

4. CONCLUSIONS
For pharmaceutical companies to be successful in the changing healthcare environment, they must be able to demonstrate the value of their products to stakeholders at both national and local levels. While the importance of health economics and outcomes research is undisputed with bodies such as NICE and the SMC, we believe that the expertise and knowledge required for national health technology assessment processes are applicable to a broad range of local market access issues including product pricing, product differentiation and improving the relevance of communications with both prescribers and payers.

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Case study one

Budget impact model –
Utilising health economic evidence at national and local level – a case study in cardiology

A client approached IMS prior to gaining a new indication for an existing product used in the treatment of a chronic cardiovascular disease. IMS developed a cost-utility Markov-type model using the pivotal clinical trial data for submission to the SMC. The product was recommended for use by the SMC. The client subsequently identified a need to communicate the health benefits and budget implications of prescribing their brand to local healthcare providers.

IMS built a highly visual, fully interactive version of the health economics and budget impact model for this purpose. The company sales representatives’ were trained to communicate the local impact of changes in prescribing behaviour, eg, number of life years gained, number of hospitalisations avoided, number of bed days avoided, drugs costs and savings and net budgetary impact.

Impact: The client was able to communicate to their customers the costs and benefits of the different therapeutic options available and ensured the rapid uptake of their product.

Case study two

Literature review and meta-analysis – case study in NSCLC

This project was carried out post-launch as a means to revitalise product sales. The client had a product competing in the novel agent cytotoxic market. It was difficult to differentiate their product against competitors using the existing clinical trial evidence. IMS conducted a best-in-class meta-analysis, with a focus on head-to-head studies against the main competitor. Maximum credibility was attained by collaborating with Key Opinion Leaders in the field of oncology and an international publication was achieved as a result.

Impact: Provided an evidence base to support discussions with payers and physicians and played an important role in the growth of product sales.

Case study three

Analysing persistence using IMS longitudinal patient data – case study in hypertension

A client approached IMS wishing to understand how the length of time a patient remained on therapy was related to the patient’s characteristics and the therapeutic class. IMS performed a multi-country study using Cox regression modelling on IMS Disease Analyzer data to derive the relative risk factors for patient non-persistence in each country.

IMS Disease Analyzer is a longitudinal patient database collected from office based physicians in Austria, France, Germany and the UK containing a combined total of 15.7 million individual patient records with up to 14 years of history.

Impact: Provided insight into the determinants of patients’ persistence by geography and how to position the client’s product against that of competition.

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