

SUPPLEMENT PAPER to the Eucomed position paper on Health Technology Assessment (Siebert et al, 2002) aiming to clarify two important topics that were already partly addressed in the first paper: the appropriateness of evidence and the learning curves for medical devices in Europe

Abstract

Eucomed supports the need for robust evidence to substantiate the claims on effectiveness of a medical device. The level of evidence should provide decision-makers with sufficient confidence of relevance and reliability of findings. The latter can clearly be associated with experimental methods but can, in certain cases (discussed below), also be achieved through well-designed observational studies. In these cases, observational data should be considered as a valid alternative to experimental methods.

Learning curves may affect the outcomes of procedures associated with many innovative devices, especially immediately after market introduction. This poses a question on the timing of assessment of new technologies. Too early, an assessment could result in a decision to restrict access to a potentially effective technology and subsequently limit further innovation as a result of the learning curve phenomenon. A later assessment, on the other hand, could be highly beneficial for informing policy-makers on matters of patient access to modern and more effective care. The timing of assessment should be decided on a case-by-case basis in collaboration with stakeholders, including industry.

Based on the two elements mentioned above, together with the points addressed in the first position paper (Siebert et al, 2002), Eucomed considers that HTA methodologies and processes for medical devices must be designed in a transparent and collaborative way that encourages innovation and rapid patient access to innovative, reliable and safe technologies.

Introduction

There is sound and abundant evidence demonstrating that technological innovation in healthcare has brought about significant improvements in patients' health and quality of life (Bethesda, MD: Medtap, 2003; Cutler & McClellan, 2001; Kern & Jaron, 2003; Goldman DP, & al. 2005; Alliance for Aging Research, 2006). However, in times of resource constraints, priorities are set among different healthcare programmes. Health Technology Assessment (HTA) is one of the instruments used by decision-makers to manage the introduction and diffusion of technological innovation (Henshall et al, 1997; Jonsson & banta, 1999; Velasco-Garrido & Busse, 2005).

The European Medical Technology Industry Association, Eucomed, acknowledges that HTA can be beneficial to decision-makers, and the Industry values its potential benefits, and considers it critical to be more involved in the growing number of European/national HTA projects and initiatives. Developments and methodological innovations in HTA need to be endorsed by all relevant stakeholders to be effective.

The aim of the present paper is to set out Eucomed's position on the following issues:

- 1.) The appropriateness of evidence, i.e. experimental and non-experimental studies for technology evaluation in different scenarios.
- 2.) The consideration of learning curves and their impact on the timing of health outcomes assessment.

This paper supplements a previous article (Siebert et al, 2002) that sets forth the position of Eucomed on HTA for medical devices in general.

Non-experimental studies to measure health outcomes of medical devices

Experimental studies are those that try to identify the causal relationship between the intervention and the effect in a controlled way by eliminating the effect of confounding variables and biases as in the case of randomised clinical trials (RCTs).

Non-experimental studies are observational studies with controls (e.g. controlled before-after studies, concurrent cohort studies, case-control studies) or without controls (before-after studies, cross-sectional studies, case series) (Hennekens & Buring, 1987) where the causal relationship between the intervention and the effect is derived from observing patients in the actual clinical practice.

Experimental methods – such as randomised controlled trials (RCTs) – are considered by

the HTA community to be the "gold standard" for outcome evaluation because of internal validity, i.e. likelihood that an observed effect of an intervention is in fact attributable to that intervention.

Non-experimental methods are deemed lower in the hierarchy of evidence than RCTs but are often appropriate to provide good quality evidence, i.e. the level sufficient to inform the decision making process in the interests of optimal patient care.

This is the case when:

1. The role played by confounding variables is so small and the effect of the intervention is so dramatic that randomising patients is not required to provide proof. A simple illustration of this is the needle-stick prevention device or the cast around a broken arm. Another example is timely implant of an endo-prosthesis for the rupture of the thoracic aorta, which could prevent a number of complications and subsequent traumas due to major surgery.
2. Incremental improvements are to be evaluated. Innovation in medical devices often progresses via modifications that individually are unlikely to produce demonstrable benefits but which, collectively, may do so (McCulloch, 2005). In these cases, RCTs would slow the progress and access of patients to innovative products, thus reducing incentives for investments in R&D. A popular example for incremental improvements is the weight and size reduction of pace-makers over the years that collectively has resulted in significant patient benefits.
3. Rare adverse events or long term health outcomes need to be detected (Edwards et al, 1998; Lange, 2006). RCTs would need to be unfeasibly large to measure frequency and severity of rare adverse events as well as outcomes that cannot be detected in the short run. Here, post-marketing surveillance activities, such as registries, can provide relevant evidence.
4. Large differences between treatments are expected or when a disease - if left untreated - is very debilitating or lethal and for which there is no known effective treatment (Edwards et al, 1998; Lange, 2006). For example, this is the case for patients with infantile hydrocephalus, where devices (e.g. occipital ventricular catheters) are used to drain the lateral ventricles.
5. External validity, i.e. generalisability, is important. To achieve high internal validity, RCTs generally measure a key clinical efficacy endpoint (e.g. mortality or morbidity)

in a limited population and clinical setting. Confounding factors due to co-morbidities are excluded during the trial, but will be present in “real life”.

Findings drawn from well-conducted observational studies may be more generalisable as often larger samples of patients are enrolled based on wider inclusion criteria than normally used in RCTs. Clinicians and patients can be followed-up without study mandated intervention by investigators, and outcomes and costs are analysed in more real world settings. The outcomes from such studies are thus derived from (and representative of) actual clinical pathways and not influenced by strict protocols. This has relevance especially if results are intended to be used as a basis for reimbursement decisions. Furthermore, if care is taken to minimise the potential for bias (e.g. covariate adjustment, propensity scores), non-experimental studies can effectively provide decision-makers with appropriate, reliable (i.e. internal validity) and relevant (i.e. generalisable) data.

Finally, in light of the growing use of evidence coming from non-experimental studies by healthcare decision-makers (ISPOR Task Force on Real World Data), Eucomed would welcome participation in defining commonly accepted guidelines, such as the CONSORT Statement (Moher et al., 2001), on how to design and evaluate non-experimental studies and, additionally, on whom is to conduct them.

In considering the level of evidence required to support robust decision-making, the value of the additional information requested should be balanced against the level of certainty required and the time, cost and data collection burden likely to be imposed (Claxton KP, Sculpher MJ, 2006).

Learning curves and the timing for assessing medical devices

The effectiveness of an innovative device as part of a medical procedure depends to a large degree on the user’s experience with the device and procedure in question. Innovative technologies are not always straightforward to implement and quality in performance requires training and/or frequent repetitions over time (Cook 2004, Ramsay & Fayers, 2004). This is the so-called “learning curve” phenomenon.

Consideration of the learning curve effect raises a question related to the timing of the assessment of a new technology.

There is ongoing debate on when to assess a product innovation for technologies where learning curves are an important factor in the outcomes achieved. Assessing an innovation

soon after its product market introduction could in theory provide answers for political decision-makers and insurers on the issue of funding the new technology and allow early patient access. On the other hand, there may be limitations to meaningful interpretations that can be made from HTA in the early phase of product introduction. This paradox has become known as Buxton's Law: *It is always too early [for rigorous evaluation] until, unfortunately, it's suddenly too late* (Buxton, 1987).

The early assessment of a technology might ignore both the impact of the user's learning curve, and the fact that the process of innovation in medical devices is one of continuous – often incremental – improvements of the device or the procedure in close interaction with the users of the technology. A too-early assessment of a new device or procedure could give an unrepresentative impression of the long-term value of that device and procedure where there is a strong learning curve component. The Industry recommends a collaborative process of assessment of a technology on a case-by-case basis to determine the appropriate time to conduct meaningful research to establish the full value of the innovation, depending on the technology and the context.

Conclusion

The Industry supports a transparent and collaborative partnership on development of HTA processes and methodologies for medical technologies. Where there is a gap between sufficient and available evidence, the value of additional information should be carefully considered, in particular elements related to technological improvements or a movement on the learning curve

It is recognised that the level of uncertainty in evaluating medical devices may be greater than with other health technologies and that more emphasis may be placed on value judgements. Our goal is to ensure rapid access to innovative medical technologies of value to patients and society.

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