Current and Future Trends in the HTA of Medical Devices

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Abstract— **Health Technology Assessment (HTA) has been defined as a 'multidisciplinary approach studying the clinical, economic, social and ethical implications of development, diffusion and use of health technology'. While the general definition of HTA is widely accepted and its role in policy making is increasingly established in EU countries, the currently adopted methodological framework for HTA does not fully encounter the challenges rising from different types of health technologies, such as medical devices. This paper provides i) an introduction to the HTA methodology, highlight on ii) specific challenges medical devices pose in addition to other health technologies (i.e. short lifecycle and rapid changes, clinical outcomes often depend on training and experience of operator, dynamic pricing), iii) current HTA practices for medical devices and iv) the results of a FP7 funded project, "Methods for Health Technology Assessment of Medical Devices: a European Perspective" (MedTecHTA n. 305694) completed in December 2015. The general objective of MedtecHTA was to enhance HTA methods for medical devices that would acknowledge complexities rising from their integration into clinical practice and to develop recommendations for a wide range of stakeholders in the field. Overall, this paper provides a summary of the current and expected future trends in the assessment of medical devices technology to inform coverage and reimbursement decisions in healthcare within Europe and beyond.**

Keywords— **HTA; medical devices; MedTecHTA.**

I. Introduction

Medicines regulatory agencies internationally have agreed on evidentiary requirements to receive marketing authorization for pharmaceuticals for more than 50 years now. In order to prove their efficacy and safety, randomised controlled trials (RCTs) that assess new compounds are needed.

On top of the evaluation for licensing purposes, due to increasing financial pressure on limited budgets, the health-care policy agenda has had to develop and embrace a broader approach to evidence gathering and synthesis to inform reimbursement and coverage decisions. Health technology assessment (HTA) has developed as a tool to govern the diffusion of costly medical technologies in early 1970s [1]. HTA has been defined as a multidisciplinary activity that systematically examines the safety, clinical efficacy and effectiveness, cost, cost-effectiveness, organisational implications, social consequences, legal and ethical considerations of the application of a health technology – usually a drug, medical device or clinical/surgical procedure [2].

Specific features of HTA are seeking of comparative effectiveness evidence (i.e., what is the health benefit of a technology relative to alternative options already available in the health-care system?), cost-effectiveness (i.e., are the additional costs justified by these additional benefits?) and relevant intended and unintended impacts of real-world technology implementation. Because of these additional requirements, HTA has been also described as the "fourth hurdle" in addition to the traditional evidential requirements of efficacy, safety, and manufacturing quality [3].

HTA has to be intended as an iterative process starting with a scoping exercise to identify technologies potentially suitable for the evaluation and to establish what are the priorities for the health-care system. Then a scientific assessment of the comparative clinical and economic evidence for the technology under evaluation is conducted. The appraisal of the evidence is the phase where the decision on whether to fund, fund with restrictions or not to fund the particular technology occurs, based also on consideration of political, social, ethical factors [4].

Since its inception, HTA has developed and mostly been applied across the world to inform local and national policy guidelines on the use of drugs, however in recent years its application has spread to non-drug technologies, that include diagnostic and screening methods, health promotion, surgical or clinical interventions and, of course, medical devices.

A medical device is "any instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, including the software intended by its manufacturer to be used specifically for diagnostic and/or therapeutic purposes and necessary for its proper application, intended by the manufacturer to be used for human beings" according to European Union Medical Devices Directive. As such, medical devices cover a variety of products, from pads to clips for neurosurgery.

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The European Association of medical devices companies (EUCOMED) estimates a market size of about €100 million in 2013. The industry includes 25000 companies, of which 95% are small and medium enterprises, employing over 575000 people [5]. To reflect the high innovativeness and dynamism of the industry, it is important to observe that medium lifecycle of technologies is 18-24 months and one patent is filed every 50 minutes [5].

In the following sections we will describe some of the key challenges of HTA for medical devices in contrast to the drug technologies, provide an overview of current HTA practice related to medical devices and a summary of the recommendations recently drawn from the results of a FP7 funded project, "Methods for Health Technology Assessment of Medical Devices: a European Perspective" (MedTecHTA n. 305694).

II. CHALLENGES OF HTA OF MEDICAL DEVICES

Because of their intrinsic features, medical devices pose some specific challenges for HTA assessors [6-8]. Key differences when compared to drugs include the ability, or difficulty, to undertake double-blind RCTs, the importance of learning curves over treatment effect and relevant organizational impact of the technology, dynamic pricing, short lifecycle and class effects.

Although RCTs are widely recognised as the preferred study design in order to avoid or minimise bias and are key to establish comparative effectiveness, lower licensing evidentiary requirement has reduced the incentives for device manufacturers to undertake premarketing RCTs [9]. Moreover, single or double blinding is not always easy to implement (e.g. comparison of surgical therapy versus medical management or open surgery versus minimally invasive surgery) and should be replaced by blinding of outcomes assessors', whenever possible. Equipoise can be jeopardized by patients reluctant to enter a randomization where one of the arms can be associated with high surgical risk and the other relatively safe, with a drug therapy already in use. Standard RCT design is also not ideal to track continuous incremental device innovation, occurring throughout the trial development. The tracker trial design has been suggested to take into account technological developments, however there are few applications in practice because of high complexity and implementation costs [10].

As regards the impact of learning curve time on outcomes, given the high level of interaction between a new device performance and the "operator" skills, it is likely that the initial phase of the adoption will be associated with more adverse events or negative outcomes than the mature phase of adoption. A fair comparison between the standard of care and the new technology would be ideally made when clinician experience with the device has reached a saturation point.

In other words, the efficacy or comparative effectiveness of a device depends not only on the device itself but on how it is used, and the resources (e.g. trained staff, logistics) in place for the appropriate implementation may deeply affect their performance.

Another aspect that is particularly relevant with medical devices is extension of recommendations to "within class" products often based on inadequate evidence to avoid differentiation. In the US, the market authorization for devices allows to clear even high risk devices, such as implantables, through the 510(k) procedure that grants licensing approval without clinical assessment for products that demonstrate "substantial equivalence" to previously approved devices. However claiming of "substantial equivalence" from a clinical point of view may not hold under the cost-effectiveness perspective. Extrapolating evidence from one device to another may appear attractive in the short term, but lowering the bar for later-than-first comers could also impact on patient safety.

Finally, because medical devices are often procured through mechanisms more aligned with commodity products than pharmaceuticals, prices are highly dynamic over time and across geographical areas so that the outcome of an economic evaluation and health-care guidance can influence or be influenced by price strategies of the technology and its comparator.

III. CURRENT HTA PRACTICES FOR MEDICAL DEVICES

Around the world, health policy-makers are increasingly turning to HTA in order to manage the entry of new medical technologies. Comparative effectiveness evidence is a requirement of all HTA agencies, but many require also cost-effectiveness data.

A comprehensive survey of non-European Union (EU) HTA agencies has recently undertaken as part of the MedTecHTA project [11]. This survey sought to characterize and contrast HTA agencies in terms of their organizational structure, processes, and methods for handling devices. Out of 36, 27 (75 %) agencies were judged to have adopted HTA-specific approaches for medical devices that were largely organizational or procedural. Although the majority (69 %) of both categories of agency had specific method guidance or policy for evidence submission, only one device-specific agency had developed methodological guidelines specific to medical devices (Brazil). In interviews many device-specific agencies cited insufficient resources (budget, skilled employees), lack of coordination (between regulator and reimbursement bodies), and the inability to generalise findings from evidence synthesis to be key challenges in the HTA of medical devices. The lack of evidence for differentiation in scientific methods for HTA of devices raises the question of whether HTA needs

to develop new methods for medical devices but rather adapt existing methodological approaches to the specific MD issues.

Notably in Europe, the National Institute of Health and Care Excellence (NICE) has set up a specific Medical Technologies Evaluation Programme (MTEP). The process allows for use of non-randomised clinical evidence and cost-consequence rather than cost-effectiveness methods for economic evaluation. However, given the non-binding role of the recommendation given and the voluntary enrollment, the process has been so far received mild feedback among manufacturers [12]. The situation is different with the Technology Appraisal Programme, that is open to both drugs and devices technologies with similar methodological guidance. In this respect, NICE expresses a strong preference for evidence from 'head-to-head' RCTs. Inferences about relative treatment effects drawn from non-RCT evidence should be interpreted cautiously, more than one independent source of such evidence needs to be examined to gain some assurance of the validity of any conclusions drawn. Other agencies have a more restrictive approach, for instance the German agency, Institute for Quality and Efficiency in Health Care, only considers non-RCT data if there is no alternative [13]. For the MDs companies, it becomes of utmost importance to prepare for this type of evaluation and adjust the development plan according to the requirements of a successful coverage or reimbursement decision. Experiences of early stage HTA performed from the perspective of the manufacturers have been described before [14, 15].

IV. FUTURE TRENDS IN THE HTA OF MEDICAL DEVICES

Prediction of future trends within a field sensitive to political will and direction is not an easy task, however based on our experience and three years research project's findings on the topic of the methods for the HTA of medical devices we can identify a set of recommendations that are likely to improve the overall approach to the HTA of devices and produce long term benefits for the patients, the healthcare system and the manufacturers.

The MedTecHTA project started in January 2013 from a consortium of seven academic and scientific institutions around Europe. The project has devoted more than 3000 hours of scientific research to analyse the approaches for HTA of medical devices in the EU and extra-EU countries; to investigate the geographical differences in the uptake of innovative medical devices, with important implications in terms of equity of access; to identify appropriate methods to investigate the three-pillars of HTA: comparative effectiveness, economic evaluation and organisational impact of the devices; to study the uncertainty concerning the approval of new devices and the link with investment in research.

Based on our project results, we have organised our recommendations in three main groups:

A. Improving the process for HTA of medical devices

It is advisable to align regulatory and HTA processes data requirements for devices. For instance, recent experience of joint scientific advice or "early dialogue" between regulatory, reimbursement bodies and manufacturers should be encouraged to facilitate the design of studies that jointly fulfill the requirement of regulators and payers. For what we have seen from our international survey, harmonization of HTA evaluative frameworks across agencies would help companies approaching different organisations for submission. One-off yes or no decisions can be replaced by recurrent appraisals or conditional coverage and evidence development decisions. At the same time, consideration should be given to the likely prospects of research and who should pay for it (i.e. is it priority for public funding or for manufacturers to undertake?).

B. Developing methods for HTA of medical devices

In terms of methods, rather than developing new tools, it would be better to refine existing approaches for handling the common 'complexities' of devices and be able to synthesise observational and trial evidence, incorporate learning curves and incremental innovation into decision analytic models.

It might help framing the assessment of medical devices as being a complex intervention, with consideration of various components, modifying factors and outcomes in the formulation of the research question. Innovative or advanced study designs and analysis methods should be considered to assess the comparative effectiveness of MDs. In this regard, disease-based or device-based registries of high quality, allowing for comparative analyses, are invaluable tools to establish the long-term effectiveness and safety of MDs. The applicability of findings across agencies or settings should be assessed against the challenges arising from patient eligibility, user dependence, study design, and rapid evolution of the technology.

C. Optimising the diffusion of medical devices

The potential of routinely collected data, such as administrative databases, should be exploited to understand diffusion and use of devices, although the coding system should be checked for valid and reliable identification of the technology. A consideration of factors potentially driving adoption and diffusion of medical devices should be given in HTA, including physicians' personal goals and motivation,

manufacturers' actions, geographical and environmental factors.

We believe the project has been successful for the high quality of scientific outputs produced to share within the academic community. Whether it will generate impact at a policy level, within the healthcare systems, for citizens and patients, clinicians and manufacturers, is still early to say, although MedTecHTA has already played a role in shaping the new guidelines for therapeutic medical devices to be adopted by the European Network of HTA agencies (EUnetHTA). We will certainly be ready to follow additional development in the field and keep working on our research interests with the aim of improving the evaluation process to inform funding decisions of health technologies. For additional details and full reports and publications from the project we point the reader to the project website www.medtechta.eu.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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