Practical Use of Early Stage Health Technology Assessment of Medical Devices: Systematic Literature Review

Mariia Simonova(✉), Vladimír Rogalewicz, Gleb Donin, and Peter Kneppo

Department of Biomedical Technology, Faculty of Biomedical Engineering, Czech Technical University, Prague, Kladno, Czech Republic
mariia.simonova@fbmi.cvut.cz

Abstract. The early stage HTA (eHTA) is a commonly used tool for identifying economic indicators of health technology in early phases of research and development. It provides powerful influence instruments to manage the manufacturer's investment risks and to improve the device design.

There is no uniform generally accepted standard of eHTA implementation, but an analysis of several large-scale theoretical studies showed that, in general, the eHTA process for medical devices consists of three stages: conceptual modelling of the new medical technology, determination of new technology parameters by expert elicitation methods, and simulation allowing for an analysis of commercial options.

The aim of this study is a systematic review of studies published from 2014 till 2019 and an analysis of selected articles in terms of the methods used in each step of the early stage health technology assessment.

Most of the analyzed case studies deal only with a part of the early stage medical device assessment, probably because of its confidential character. But we have found the popularity of decision-making models, the applicability of AHP (the analytic hierarchy process) methods to the elicitation process, and information on the use of CEA (cost-effectiveness analysis) methods and headroom methods as economic analysis tools.

Keywords: Early stage HTA · eHTA · Health technology assessment · Medical device assessment · Medical device development

1 Introduction

Advanced society is based on knowledge and modern technologies [1]. Technology has a critical role, especially in connection with the acquisition, processing and application of information [2]. At present, monitoring, evaluating, and detecting new trends in various medical devices is an exclusively interdisciplinary issue [3]. The interdisciplinary approach is one of the ways to cope with the growing complexity, dynamism and variability of the society [4, 5].

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The emerging demand for health technology assessment at the early stage of development is caused by several factors. The introduction of the new Medical Devices European Regulation EU 2017/745 belongs to the most important ones. Under the new regulation, medical devices manufacturers have to focus more on clinical trials. The clinical trial may be based on the device clinical data only if the technical, biological and clinical equivalence with the device concerned can be demonstrated (Section 3, part A, Annex XIV, MDR 2017/745). In addition, in the case of implantable devices and Class III devices, the clinical trial must be definitely carried out, unless the device falls under one of the exceptional rules (Section 4, Article 61, Chapter 4, MDR 2017/745) [6]. This fact means that most new medical devices and new health technologies will have to go through a clinical trial. For the manufacturers, clinical trials always mean a huge expense, especially in case of implantable medical devices and medical devices with a metabolic effect. In this situation, there is a growing need for a full-scale implementation of a methodological process that would allow for health technology assessment at an early stage of development, before clinical testing, and even before design finalization. Such a solution is provided by the early stage HTA that possesses powerful tools to manage the manufacturer's investment risks and to improve the device design.

The early stage HTA (eHTA) is an assessment of health technologies at the stage of research and development. The eHTA is most commonly used as a tool for identifying economic indicators of health technologies. Early stage models can be used to gain information for the design and management stage of new health technologies to mitigate the risks associated with placing the technology on the market and its inclusion into the public insurance reimbursement systems [7].

eHTA, combined with early health economics modelling, is being increasingly used by manufacturers as an approach to identifying the added value of new health technologies. The results of such a process are useful for:

- deciding on the next direction of development,
- setting minimum efficiency limits for a new technology compared to currently available comparators,
- providing support for pricing and payment settings [8].

An analysis of several large-scale theoretical studies showed that, in general, the eHTA process for medical devices consists of three stages as shown in Fig. 1.

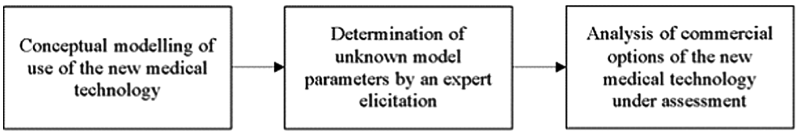

Fig. 1. eHTA steps. (Source: own analysis).

The first step is detailed conceptual modelling of use of the medical technology. It is important to consider all possible situations and conditions. Subsequently, the model parameters are determined. In the case that these parameters are not generally

known, expert elicitation methods are mostly used in eHTA. Finally, statistical evaluation and introduction of unknown parameters into the model, simulation, and an analysis of commercial options are carried out after the elicitation.

There is no uniform generally accepted standard of eHTA implementation. That´s why the aim of this study is to provide a review of the most popular methodologies used for a practical implementation of early assessment of medical devices in the last five years.

2 Methodology

The study is based on a systematic literature review of published papers on eHTA of medical devices. One of the aims of this study is to provide topical information on the current state of development and use of early stage HTA methodologies. It will show the real range and specificities of eHTA usage.

A citation analysis of the early HTA was performed using keywords and subsequent manual search in Scopus. The period was selected from 2014 to February 2019. The following keywords and their various combinations were used for the search: Health Technology Assessment, Biomedical Technology Assessment, Medical Devices, Early Health Technology Assessment. Results from pharmacology, toxicology and pharmacy were excluded. A total of 118 results were found.

Subsequently, a review of the title and abstract of all identified studies was conducted, and finally 37 studies were selected for a detailed analysis. After reading full texts of all 37 documents, another choice was made. Selected articles should include at least a partial description of the methodological procedure or a case study of health technology assessment at an early stage of design and development (see Fig. 2).

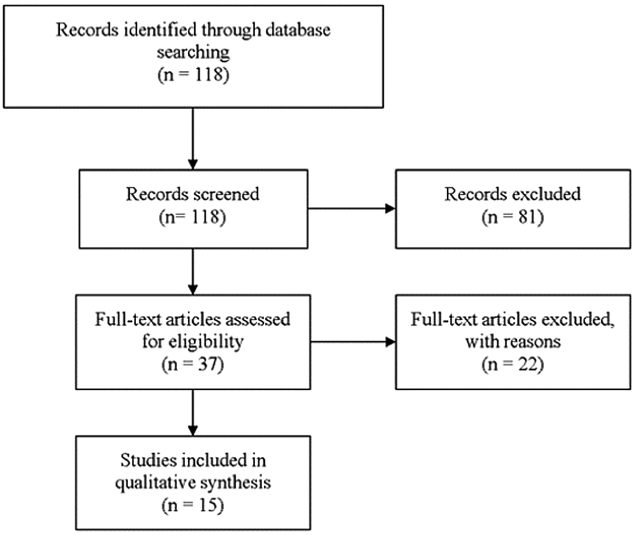

Fig. 2. The PRISMA flow chart of the systematic literature review (Source: own analysis).

In the end, 15 articles published from 2014 to February 2019 that met the requirements were included in the study. The following criteria were analyzed in the selected papers: the kind of health technology, the modelling method, the way of data receiving/elicitation, and the methods of economic analysis.

3 Results

eHTA is still a relatively new area, and it is quite difficult to find published studies. Neither terminology nor keywords are properly unified. Some ambiguities also arise from confusing translations of terms.

Table 1 shows methods used in each step of early stage health technology assessment at each of the selected studies.

Table 1. Methods used in each step of early stage health technology assessment

Author	Kind of health technology	Modelling method	Data receiving/elicitation	Method of economic analysis
Chapman [9]	Stapled Hemorrhoidectomy	N/A	Statistic data	The headroom method
Cancela [10]	Telehealth system for parkinson's disease management	N/A	AHP focus groups	N/A
Kolominsky-Rabas [11]	Mobile Stroke Units	Hybrid simulation consisting of system dynamics models for macro-simulation and agent-based models for micro-simulation	Statistic data	N/A
Buisman [12]	Diagnostic test to detect early rheumatoid arthritis (RA) and Prognostic test to assess the risk of a recurrent ischemic stroke	N/A	N/A	Early-CEA
Girling [13]	Implantable Heart Device	N/A	N/A	The headroom method

(*continued*)

Table 1. (*continued*)

Author	Kind of health technology	Modelling method	Data receiving/elicitation	Method of economic analysis
Markiewicz [14]	The Injectable healing plasters (IHP), A portable point-of-care device (POC-CKD), Continuous blood pressure measurement device (CBPM), A computed tomography photo-acoustic instrument for imaging inter-phalangeal joints in the hand (RAPAI), The flexible endoscopy robot (FLEX), Home Brain Monitoring device (HBM)	N/A	Elicitation and literary data without specifying of methods	Headroom method combined with ROI-analysis
Van Nimwegen [15]	Complex pediatric neurology	N/A	N/A	The headroom method
Miquel-Cases [16]	Predictive biomarkers in breast cancer	Decision model	AHP	The headroom method and Early-CEA
Degeling [17]	Biomarker-Based Treatment	Discrete event simulation and timed automata models	N/A	CEA
Hummelin [18]	Bilateral DIEP flap breast reconstruction	Decision model	Elicitation and literary data without specifying of methods	The headroom method
Khoudigian-Sinani [19]	Predictive technology "StraticyteTM" for the early detection of oral cancer	Decision-analytic model	Belief elicitation method, systematic review and meta-analysis	Early-CEA

(*continued*)

Table 1. (*continued*)

Author	Kind of health technology	Modelling method	Data receiving/elicitation	Method of economic analysis
Kip [20]	New triple biomarker test	Decision tree model	Elicitation without specifying of methods. Answer options to questions consisted of percentages with a range of 25%, and including 0% and 100%.	CEA
De Graaf [21]	Biomarkers	N/A	N/A	The headroom method
Brandes [22]	Hypothetical vascular closure device	Decision tree model	Meta-analysis	CEA
Grigore [23]	Alternative treatments for prostate cancer	Decision model	The histogram and hybrid elicitation methods	CEA

(Source: own processing)
AHP the analytic hierarchy process, *CEA* cost-effectiveness analysis, *N/A* information not available, *ROI* return on investment analysis

In earlier studies dealing with similar literary reviews and frequently used eHTA methods, the popularity of Markov's models [8, 24, 25], simple stochastic models assuming that future states depend solely on the current state and not the sequence of past events (states), has been widely discussed. However, it is clear that decision-making models are more commonly used in recent years for an assessment of medical devices and technologies at an early stage of development.

Some of the studies that dealt with a comparison of Markov models and decision models have concluded that the algorithms behave in a similar way and that the differences are very small. The primary difference between Markov models and decision models is that the first one models the risks of recurring events in a straightforward manner. It is argued that the decision model is more appropriate for generalizing samples in a particular context, while the Markov model is more appropriate when an exact sample has to be derived [26, 27].

The use of cost-benefit analysis (CEA) in assessing the costs and health impacts of new health technologies comparing to current practice. The estimated cost-effectiveness of the proposed new intervention is compared either with the cost-effectiveness of a set of existing interventions or with a fixed price threshold (cut-off point), which represents the expected social willingness to pay for an additional unit of health [28].

The headroom method of economic evaluation has also been very popular. It can offer a practical way to manage investments, justifying the choice to develop the potential medical product [9, 13–15].

The least described and discussed parts of eHTA studies are methods of obtaining unknown model parameters. The classical concept of health technology assessment at the early stage of development assumes mainly an application of elicitation methods. Some of the analyzed studies describe benefits of AHP-based methodologies within expert elicitation and evaluating the responses. The method of analyzing the hierarchy process has been used for a procedure for the synthesis of priorities calculated on the basis of subjective judgments of experts. However, the details of the use of elicitation methods were only briefly mentioned in one study analyzed (Kip et al. [20]). The authors do not even mention the name of the method, but according to the description it can be assumed that the fixed interval method of expert elicitation was used [23].

4 Discussion and Conclusion

The early stage medical device assessment can be divided into three steps, and this paper is focused on an overview of the practical methods used in the eHTA process. during the last five years.

According to our results decision-making models have been more commonly used in recent years for conceptual modeling of the use of medical technology within the framework of eHTA. Expert elicitation is still the least described process of early assessment of medical devices, but in many studies the authors mention AHP methods as useful tool for objective evaluation of responses. For the methods of economic analysis in recent years, CEA methods and headroom methods are more typical, sometimes in their combination.

Overall, it can be said that the eHTA process is still insufficiently described in published papers. What has been represented especially scarcely are studies about practical usage of medical devices assessment at the stage of research and development. Most of the analyzed case studies published from 2014 to February 2019 deal only with a part of the early stage medical device assessment. Probably because of the confidential character of the studies, medical devices and technologies and their characteristics are not usually described in detail. This is understandable, competitive relationships and industrial espionage force manufacturers to protect their know-how as much as possible until they enter the market. At the same time, it can reasonably and logically be assumed that, based on the findings of the eHTA, the manufacturer can influence and change the final characteristics of the final device or technology model provided the evaluation was carried out in the development phase.

We also assume that the practical methodology of eHTA is used more than it seems to be according to the number and content of published studies. In some European countries, special agencies and organizations are involved in the assessment of medical devices and technologies in the early stage of development. However, there are no European directives, recommendations or approved methodological guidelines. At the same time, different healthcare systems, pricing and reimbursement settings in different countries need to be taken into account. Therefore, the question of the possibility and, above all, the usefulness of introducing a unified system for eHTA is justified.

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