




A Scoping Review of Different Methods of Assessing the Impact of New Medical Technologies at Early Stages of Development

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Abstract

Background: Investing in the R&D sector of new medical technologies is associated with the risk of being rejected by paying organizations because of the lack of value-for-money. The purpose of this study is to investigate the different methods of evaluating the impacts of emerging medical technologies.

Methods: Using scoping review method, we analyzed studies that investigated methods for assessing the impacts of emerging medical technologies on development. To find these studies, the Cochran Library, ISI Web of Knowledge, Embase, Ebsco and Pubmed databases from 2000 to 2018 were searched. The methodological quality of the studies was assessed using the STROBE Checklist. Two reviewers independently selected the qualified studies. Charting and collating the data were used based on the method proposed by Arksey and O'Malley.

Results: Overall, 38 studies met the inclusion criteria. Sixteen methods were identified and put in five distinct categories: forecasting, Pro-HTA, Early-HTA, priority setting, and HHS were found to measure the impact of emerging technologies. The quality of these studies was acceptable. Few studies were conducted on emerging pharmaceutical technologies, and they were mostly on emerging medical devices. The Early HTA methods were often used to measure the effects of pharmaceutical technologies and medical devices technologies. The Pro-HTA method used dynamic modeling to examine the impact of medical technologies on a broad range of dimensions, while the HTA and Early-HTA methods used cost-effectiveness techniques throughout the development process. The HHS method used a multivariate decision-making technique.

Conclusion: Different methods were used to investigate the impacts of emerging medical technologies. Chronologically Pro-HTA methods are new ways for investigating emerging medical technologies beyond clinical and economic impacts. Assessing the feasibility of implementing Pro-HTA in real environments deserves further research.

Keywords: Early Stages of Technology Development, New Medical Technologies, Health Technology Assessment, Emerging Pharmaceuticals

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Introduction

Medical Technological advances threaten financial sustainability in many health care systems; thus the efficient

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↑What is “already known” in this topic:

Classical Health Technology Assessment (HTA) is commonly used in the evaluation of medical technologies with sufficient available evidence. But some approaches are increasingly being used to support health economic evidence development during the early stages of technology development.

→What this article adds:

Sixteen methods were identified that investigated the impacts of emerging medical technologies. Chronologically Pro-HTA is a new method using a dynamic simulation approach for investigating emerging medical technologies beyond clinical and economic impacts. Assessing the feasibility of implementing Pro-HTA in real environments deserves further research.

and optimal allocation of resources are important challenges for the system (1). One of the ways to manage the consequence of technological pressure involves the presence of a health care system in charge of emerging technologies as soon as possible before the product is fully developed. The health care system would track emerging technologies and try to invest in products that are potentially cost-effective in addition to their significant clinical benefit (2).

Emerging medical technologies are always accompanied by uncertainty. On the one hand, the emergence of medical technologies leads to the expansion of national wealth, increased competitiveness, increased exports, and increased welfare and quality of life. On the other hand, it can lead to problems such as increased induced demand, increased medical costs without necessary efficacy, increased patients' life span with poor quality of life (3, 4). So it is important to assess the clinical and economic consequences of emerging technologies. Common approaches, such as health technology assessment (HTA) reports, have not helped policymakers much in selecting and evaluating technologies (5).

Over the past two decades, the use of product assessment models in their early stages of development has been of interest to provide timely information for the ongoing process of development, market access, and technology pricing. The primary purpose of this study was to undertake a comprehensive review of the literature in the early stages of development to identify methods of a technology evaluation. The second purpose is to identify new methods to assess the potential impact of emerging medical technologies.

Methods

Study Design

This scoping review was conducted to identify different methods of evaluating emerging medical technologies in their early stages of development. We followed the methodology proposed by Arksey and O'Malley in five steps (6).

Stage 1, Research question and eligibility criteria

The research question concerns the current methods to evaluate potential impacts of new medical technologies in terms of clinical and economic consequences in the early stage of development to make a better decision regarding the governance of these technologies?

Inclusion criteria were all studies evaluating medical technologies at various stages of development before entering the market, such as seminal research, laboratory phase, animal phase, clinical phase, and pre-market launch. Medical technologies include those emerging health technologies used directly to diagnose or treat a health condition, e.g., medicines, medical devices, diagnostic tests or medical equipment.

Stage 2, Identifying relevant studies

The studies included a broad category of study designs to capture comprehensiveness. We included surveys, cross-sectional, descriptive, qualitative, national, and in-

ternational reports, systematic reviews, and discussion studies. PubMed, Cochrane Library (through own website), ISI Web of knowledge, and Embase (through the Ovid website) from 2000 to 2018 were electronically searched to find potential eligible studies. We also tracked references of marker studies, the website of related organizations and conferences to find more relevant studies. Moreover, the studies presented in International Society for Pharmaceutical and Outcome Research (ISPOR) conferences (up to 2018) were also searched.

According to the study question and having reviewed the studies, the search strategies were written according to the guidelines of each database. Details for search strategies in two databases and retrieved records are available in a [Appendix](#). The basic search strategies are as follows:

1- Model (Title/Abstract) OR tool (Title/Abstract) OR Simulation (Title/Abstract) OR forecast(Title/Abstract) OR foresight (Title/Abstract) OR (Title/Abstract) future foresight process (Title/Abstract) OR technology foresight (Title/Abstract) OR health technology assessment (Title/Abstract) OR horizon scanning (Title/Abstract) OR prospective simulation (Title/Abstract) OR Pro HTA (Title/Abstract) OR dynamic model (Title/Abstract) OR prospective assessment (Title/Abstract)

2- Pharmaceutical innovation (Title/Abstract) OR Pharmaceutical diffusion (Title/Abstract) OR health technology diffusion (Title/Abstract) OR Emerging innovation (Title/Abstract) OR emerging drug (Title/Abstract) OR new drug (Title/Abstract) OR new medicine (Title/Abstract) OR drug entity (Title/Abstract) OR medicine entity (Title/Abstract) OR emerging health technology (Title/Abstract) OR healthcare innovation (Title/Abstract) OR medical device (Title/Abstract)

3- #1 AND #2

Stage 3, Study selection

We followed the PRISMA guidelines to find relevant studies. We included studies with methods to assess the impacts of emerging technologies on the health care system, such as new pharmaceutical and medical devices. Studies that had at least an English abstract were included in the evaluation. The results of the selected databases were entered into the Endnote Software (X.9.33 version). After removing duplicate studies, the titles and abstracts were studied. After unrelated studies were removed, the full texts of the remaining studies were reviewed. Two authors individually performed the above steps. They also independently assessed the quality of the studies included using the STROBE checklist.

Stage 4, Charting the data

A datasheet was then used to extract the data. Data were extracted independently by two individuals. The information extracted included authors' names, year of publication, country of study, dimensions, and variables influencing the access to emerging technologies, evaluation methods, and techniques, and studies' title, language, perspective, and outcome index.

Stage 5, Collating, summarizing, and reporting the result

This stage of a scoping study involves collating, summarizing and reporting the results. At first, we summarized the main characteristics of the studies such as year of publication, country of origin, type of method used to assess an emerging technology in the early stage of development, quantitative or qualitative algorithms to assess, criteria used to make decisions and perspective of the studies. We also divided the studies according to the type of emerging technologies. Then, the included studies were counted and ordered chronologically in terms of the types of medical technologies. A clear distinction was made between identified methods and comparative analysis of included studies based on the main characteristics.

Results

This study which was a scoping review, included 10,578 records in total and 8 studies that were added manually. A total of 3,275 studies were excluded after duplicate records were excluded and 7,303 records remained for assessment.

After reviewing the titles/abstracts, 319 abstracts remained. Among them, 58 records were eligible after reading the full text, but 21 studies were excluded as they were not original, lacked data sufficiency or the full text, or were not related to the health system. Finally, 38 records met the inclusion/exclusion criteria (Fig. 1).

Most of the studies were conducted in the Netherlands (13 studies), Germany (6 studies), and UK (6 studies) and the other conducted in Belgium (2 studies), Switzerland (2 studies), Denmark (3 studies), Sweden (3 studies), United States (3 studies), New Zealand (1 study) and Korea (1

study). Among these, 23 studies focused on medical equipment and diagnostic tests, 7 studies on pharmaceuticals and 8 studies were related to all new technologies and not specifically to a distinct category of medical technologies. Table 1 provides more detailed information about the studies.

Five general approaches to evaluate new technologies were identified at an early stage of development. Overall, 27 studies evaluated technologies using the early HTA approach, 4 studies using the pro-HTA method, 2 studies using horizon scanning, 3 studies using priority-setting techniques, and 3 studies using forecasting methods. Figure 2 shows these studies based on the time of the study and the type of intervention. The figure shows that in recent years most of the researchers used the early HTA approach to assess the effectiveness of emerging medical technologies.

Methods used in evaluating emerging technologies

1- *Early health technology assessment*: This approach is often undertaken in the context of economic evaluation studies in combination with clinical trial development strategies. The main purpose of this model is to evaluate the cost and effectiveness of interventions in the early stages of development. The first study using this approach was published in 1993 by Clemens, et al. (7). A review of the literature from 1993 to 2006 shows that this approach has often been used in the evaluation of emerging drugs in stages 1 and 2 of clinical trials, suggesting an uncertainty of evidence in a clinical trial or suggestions to improve or stop further trials (7-11). Dong, Van Til, and Hjelmgren reported the results of medical device evaluation (12-14).

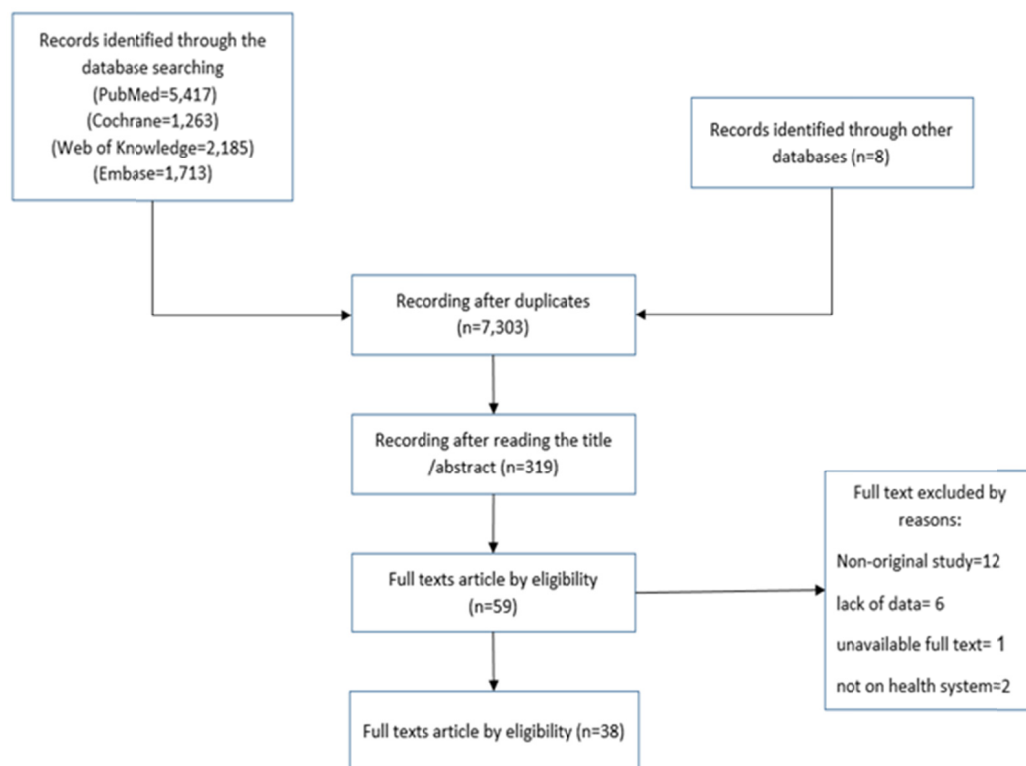


Fig. 1. PRISMA flowchart to find included studies

Table 1. Characteristics of included studies

Authors	Published year	Country	Intervention	R & D stage	Method	Technique of modeling	Perspective	Type of study
Kirsten J.M (31)	2017	USA	Diagnostic trajectory	Before trial	Early HTA	Headroom analysis	Stockholder	Observational study
Aris Angelis (32)	2017	UK	Medicines, medical devices and other health interventions	Market launch	Context of HTA	MCDA	Decision maker	Qualitative
Kolominsky Rabas (5)	2016	Germany	Device (Mobile Stroke Units)	Pre trial	Pro-HTA	System Dynamics and agent base model	Decision maker	Descriptive
Aastha Gupta (33)	2016	Switzerland	Medicine (anti-retroviral treatment (ART))	Pre market	Forecast Analysis	Predict market shares	Decision maker	Descriptive
Katarzyna Markiewicz (27)	2016	Netherlands	Device		Early HTA	Headroom analysis & ROI analysis	Manufacturers	Case study
Michelle MA Kip (34)	2016	Netherlands	triple biomarker test (copeptin, heart-type fatty acid binding protein, and high-sensitivity troponin (HsTn))	Technology available but not used	Early HTA	Decision tree \$ expert elicitation	Societal	Observational study
Middelkamp H.H (35)	2016	Netherlands	Device (Organs-on-Chips)	Early stage of development	Early HTA	MCDA	Stockholders	Observational study
Isabel Püntmann (36)	2010	Germany	Medicine	Early stage clinical research	Early HTA	EVITA	Physicians and other professionals	Descriptive
Jilles (37)	2016	Netherlands	Forty-one technologies (16 pharmaceuticals and 25 non-pharmaceuticals) were NGS-based molecular diagnostics	Premarket	Priority setting	Best-worst scaling	Stockholders	Descriptive
Joosten SE (38)	2016	Netherlands		Pre clinical	Early HTA	Scenario drafting, expert elicitation	Stockholder	Observational study
Huygens SA (39)	2016	UK	Device (tissue-engineered heart valves)	Early stage clinical research,	Early HTA	Delphi panel with experts	Societal	
Alan Girling (40)	2015	UK	Device	Early stage clinical research	Early HTA	Headroom analysis	Manufacturers	Descriptive
Tommy S (41)	2015	Netherlands	Instant MSC Product accompanying Autologous Chondron Transplantation	Early stage clinical research, tests are available	Early HTA	Markov model, headroom analysis	Societal	Observational study
Georg Ruile (42)	2015	Germany	Computed tomography (CT) system	Early stage of trial	PRO-HTA	Simulation with scenario drafting	Society	Observational study
Kolominsky Rabas (15)	2014	Germany	Sensor for managing pulmonary artery in heart failure patients	Implementation of a new device to guide health services planning	Pro-HTA	System dynamic	Societal	Observational study
Wieke Haakma (43)	2014	Switzerland	Photoacoustic mammography (PAM) imaging for detecting breast cancer	Early stage of development	Early HTA	Expert elicitation	Decision maker	Observational study
Marion Gantner (23)	2014	Germany	Prostate specific antigen test	Early research and concept phase of an idea and before major investments are made.	Early HTA	EVITA	Stockholders	Descriptive
Bengt Jonsson (44)	2014	Sweden	Medicine (ipilimumab for the treatment of metastatic melanoma)	Early development phases	Early HTA	Markov model	Decision maker	Descriptive

This means the beginning of a new paradigm in the early HTA strategy, which provides adequate knowledge along with reimbursement and regulatory approaches for consumers and suppliers through the incorporation of the health system and industry perspectives. Based on the study results, this method uses various techniques to test technologies which are briefly listed in Table 2.

2- Pro-HTA: The primary purpose of pro-HTA is to evaluate emerging medical technologies from the perspective of health systems and technology makers. By simulating the potential impacts of new technologies, this model identifies the potentials and shortcomings of these technologies in the health system and seeks to predict the potential of the product in the future market. The main dif-

Table 1. Ctd

Authors	Published year	Country	Intervention	R &D stage	Method	Technique of modeling	Perspective	Type of study
Qi Cao (45)	2013	Netherlands	Device (point-of-care testing (POCT))	Market launch	Early HTA	Headroom analysis, Markov model, expert elicitation	Stockholders	Case study
Anatoli Djanatliev (22)	2013	Germany	Markers for Prostate Cancer Screening & Mobile Stroke Units	Before the design and development phase has started	Pro HTA	System Dynamics and Agent-Based	Decision maker	Descriptive
Valesca P. Retèl (46)	2013	Netherlands	(70G-FFT), (70G-PAR)	Early stages of development	early HTA	Markov model	Societal	Descriptive
Wim H van Harten (26)	2012	Netherlands	70-gene signature for breast cancer	Early stages of promising new technologies	Early HTA	Scenario analyzing	Stockholders	
Douwe Postmus (47)	2011	Netherlands	A novel biomarker technology for identifying individuals at risk of developing a chronic disease	Early stages of promising new technologies	Early HTA	Markov	Industry	Cohort study
Ofra Golana (48)	2010	New Zealand	Medicine or device	Technology available but not used	Priority setting	Conjoint-analysis	Decision maker	Qualitative
Pietzsch JB (49)	2008	USA	Device	Early stage of development	Early HTA	engineering risk analysis	Industry	Descriptive
Emma Cosh (50)	2007	UK	Technology	As early as possible in the development cycle	Early HTA	Headroom analysis, and revenue analysis	Industry	Descriptive
Filip Mussen (51)	2007	Belgium	Medicine	Market launch	Early HTA	MCDA	Decision maker	Descriptive
Hengjin Dong (52)	2006	UK	Knee replacement (TKR) using computer-assisted surgery	Early in the life-cycle of new technologies	Early HTA	Markov model	Decision maker	Descriptive
Karla Douw (53)	2006	Denmark	Medicine or no medicine	Early stage of clinical trial (1-2-3)	Horizon scanning systems	Delphi panels	Decision maker	Descriptive
Karla Douw (54)	2006	Denmark	Device	1,2,3 clinical trial	Horizon scanning	MCDA	Societal	Qualitative
Van Til JA (55)	2006	Netherlands	Percutaneously neuromuscular electrical stimulation	Stage II trial	Early HTA	-	Society	Clinical Trial
Jonas Hjelmgren (56)	2006	Sweden	Cell replacement therapy in Parkinson's disease	Early stage in trial	Early HTA	-	Decision maker	Observational study
Paul Miller (57)	2005	Sweden	Medicine	Early development phases	Early HTA	Clinical trial simulation, option pricing, investment appraisal, threshold analysis, and value of information (analysis)	Stockholders	Observational study
Robert Phaal (58)	2004	UK	Every technology	Early stage of development	Forecasting	Road mapping	Industry, multiorganizational	Descriptive
Karla Douw (59)	2004	Denmark	Medicine or no medicine	Early stage of development	Early HTA	Clinical experts	Decision maker	Descriptive
Jeong-Dong LeeT (60)	2003	Korea	Multigenerational product		Forecasting	Time-series analysis & discrete choice models	Consumer	Descriptive
Joseph A (61)	2001	USA	Medicine	Early development phases	Early HTA	discrete,	Stockholders	Descriptive
Lieven Anne-mans (62)	2000	Belgium	Medicine	Early development phases	Early HTA	-	-	Descriptive

ference between this approach with early HTA and horizon scanning is that by simulating the system, it explores the potential benefits and disadvantages of using pre-product technology. In fact, by integrating technologies and processes into simulation scenarios, it depicts the effects of technologies on stakeholders, processes, and reimbursements throughout the system (15).

3- *Horizon scanning*: Horizon scanning studies are part of a broader field of health technology assessment. By determining priorities and the most important technologies for evaluation, and ultimately the evaluation of treatments

among the selected technologies, provides health policy-makers with the information needed to make decisions. Initial evaluation includes information such as aspects of safety, effectiveness, and financial, organizational, ethical, and other factors related to the anticipation of new technology releases.

The main difference between health technology assessment and the horizon scanning system is that the latter focuses mainly on evaluating and prioritizing new products at different stages of their fabrication, while health technology assessment studies focus on evaluating newly

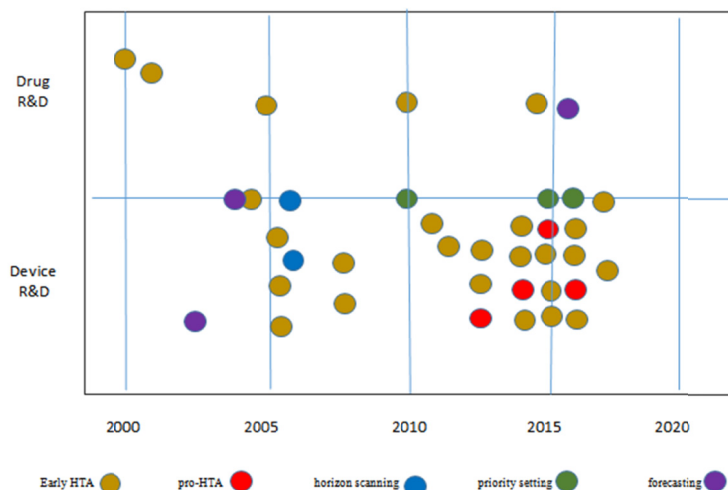


Fig. 2. Review studies presenting iterative economic evaluation in drug and medical device development, based on technology evaluation methods

made technologies. The general steps of this approach include 1. Identification: identification of emerging pharmaceutical and non-pharmaceutical technologies. 2. Filtering: Selecting the most important and most efficient technologies from the experts' point of view. 3. Priority setting: Prioritize these technologies based on different evaluation criteria from the perspective of each country. 4. Assessment: using evaluation methods for comparing two drugs or interventions in two different therapies (16).

4- *Priority setting*: Given the accelerating development of technology and the increasing demand for services as

well as resource limitations, the past decade has experienced the increasing use of rational and transparent approaches in service prioritization (17). Therefore, this method identifies a wide range of accessible services by prioritizing services according to some specific criteria, including demographic factors, epidemiology, infrastructure, reimbursement mechanisms, costs, and potential benefits of service utilization. As mentioned earlier, this technique is one of the HSS (Horizon Scanning System) steps, but some studies have used it separately to evaluate technologies (18).

Table 2. Various techniques are used in different approaches to evaluate technologies

Modelling	Technic	Definition	Study
Early HTA	EVITA ¹	An algorithm for initial evaluation of risk and benefit of new drugs. In this approach, the benefits of pharmaceutical treatment are calculated by: (1) the purpose of treatment; (2) disease category; (3) trial setting; and (4) the average score of risk and benefits of the new drug.	(23, 36)
	Headroom analysis	It is a QALY* approach that evaluates emerging technologies by considering the maximum potential of the effect of technology, the maximum willingness to pay (WTP) for this EFFECT, and decreases the potential costs involved in applying this technology.	(27, 31, 40, 45)
	Expert elicitation	It is a method to measure unknown parameters for evaluating a new technology at the early stage of development from the experts' point of view.	(45, 43, 38, 34)
	Scenario analyzing	In this technique, a team of experts and analysts delineate the path and dissemination of technologies across multiple scenarios and then monitor and predict these technologies using specific criteria such as efficiency, logistics, ethical/legal aspects, patient centeredness and cost-effectiveness at the early stage of development.	(26, 38, 42)
	Engineering risk analysis	This technique assesses the risk of failure by evaluating new technology compared to existing alternatives, and this method ultimately depends on the decision maker's preferences and his degree of risk taking.	(49)
Early HTA	MCDA	In these methods, several options are compared against multiple criteria; the best option or the most appropriate order of options are selected. MADM methods, based on mathematical reasoning, determine the best decision-making option out of the available options by prioritizing them.	(35, 51)
	Markov	In this model, disease states are used to represent all the possible consequences of an intervention. These models are fully exclusive. So, every individual can be in just one disease state at any time.	(44-46, 52)
	System dynamic	Dynamic modeling is a simulation of the real world that is presented in mathematical terms with nonlinear relationships of the real world.	(5, 15, 22)

*QALY: Quality Adjusted Life Years/MCDA: Multiple Criteria Decision Analysis

¹. Evaluation of Pharmaceutical Innovation with regard to Therapeutic Advantage

<http://mjiri.uums.ac.ir>

Table 2. Ctd

Modelling	Technic	Definition	Study
	Agent base model	This model performs simulation simultaneously at three levels of people, organization, and community. In this model, people are called agents and can have individual characteristics as well as dynamic behavior.	(5)
Pro-HTA	Clinical trial simulation (CTS):	This model uses mathematical synthesis to integrate simultaneously models of pharmacokinetics and pharmacodynamics drug action, disease progression, placebo effects, and patient variability.	(57)
	Best & worse scaling	Having chosen the list of objects, the researcher presents choice sets of these to respondents to get the best and worst option data.	(57)
Priority setting	conjoint-analysis	This is a survey-based statistical method used in market research. In fact, this technique is based on evaluating people's preferences of technologies based on specific criteria such as potential benefits, processes, organizational aspects.	(48)
	Delphi	The insights of experts are combined on a given question.	(53)
Horizon scanning	MCDCA	This method is described in the early HTA approach.	(54)
	Road mapping	This method assesses potential opportunities and threats for technology and market development during product development and delivery. Road-mapping has great potential in technology development strategies and provides companies with relevant information about their manufacturing processes and tools.	(19)
Forecasting	Discrete-event simulation:	Discrete event simulation can also be used to forecast the impact of changes in patient flow, to examine resource needs (either in staffing or in physical capacity), or to investigate the complex relationships among the different model variables (for example, rate of arrivals or rate of service).	(60, 61)

*QALY: Quality Adjusted Life Years/MCDA: Multiple Criteria Decision Analysis

5- Forecasting: This method is often used for industry. It attempts to graphically illustrate the future relationship between services, status, and the developed and under developing market variables. Once the future status and the path of technology are clear, there will be appropriate and timely feedback to continue the process of product development (19).

The perspective of the included studies

Conventional HTA approaches are limited in the pro-

cess of health care decision-making in integrating a variety of preferences and stakeholder's perspectives (20). In other words, patient and public involvement are more focused and are not able to identify and respond to all stakeholders. According to Daniel's ethical framework of 'accountability for reasonableness, all reasons and criteria for funding health care should be accessible to all stakeholders (21).

Therefore, with different stakeholders in the health system, in decision-making about new technologies, the

Table 3. Dimension and criteria extracted from studies on emerging technologies evaluation

Dimension	Criteria	Reference
Patient relevant outcome	Compliance, mortality, progression rate, control of symptoms, restoration or preservation of functionality, QALY ¹ , accessibility to the service, affordability to the individual	(14),(29),(13), (35), (15), (11), (13), (57), (41), (43), (58), (59), (11), (55)
Technology relevant outcome	Materials, market access, compatibility with existing technology, market share, off label use, efficiency, price, cost, marketing factor, need to extra services	(5), (7), (27), (36) (9), (9), (40), (33), (48), (15), (1), (1), (26), (14), (45), (47), (13), (57), (41), (43), (58), (59), (18), (55)
Innovation level	Clinical novelty, nature of treatment, ease of use, training	(30), (49), (41),
Socioeconomic impact	Public health, budget impact, social production, WTP ² , financial access, equity, threshold, patient's interest	(14),(30),(40),(35), (13), (14), (41), (43), (11), (55)
Social outcome of health care	Burden of disease, treatment effectiveness, net monetary benefit, severity of illness, hazard ratio, access, lifesaving, impact on future generation, number of preventions, number of treatments, safety (adverse event, tolerability, interaction, contraindication)	(30), (7), (29), (9), (40), (13), (35), (48), (15), (1), (1), (11), (26), (14), (49), (47), (13), (41), (43), (58), (59), (11), (55)
Population dynamic environment	Birth, death, immigration, number of patients Organizational consequences, ethical, legal, national policy relevance, need, current treatment strategy, patient characteristics	(5) (14),(45), (47), (41), (11), (55)
Financing	Reimbursement, public and private health insurance, pay for extra services	(5), (26), (41), (43), (11), (55)

¹ Quality Of Life Years; ² Willingness To Pay

views of different stakeholders must be considered at the same time and when there is agreement on access to new technology from a variety of perspectives, including health, insurance, industry and the public, a decision that helps products develop and are based on real community's demand and prevent waste of resources is helpful (5, 22, 23).

To this end, today, newer approaches such as pro-HTA, early HTA, horizon scanning, priority setting are being tried by different stakeholders to evaluate new technologies using different technics. Among the studies investigated in the present study, 10 studies were conducted from the decision maker's perspective, 1 from the physician's perspective, 7 from the societal perspective, 9 from the stockholders' perspective, 6 from the industry perspective, and one from the patient's perspective.

Criteria extracted from studies on emerging technologies evaluation

To evaluate emerging technologies in the studies under consideration, different criteria have been taken into account, depending on the study's perspective. In this study, we tried to classify these criteria into larger dimensions by examining and aggregating them (Table 3).

Among the studies reviewed, 26 studies examined healthcare outcome criteria, 12 studies examined patient-relevant outcome, 17 studies examined technology relevant criteria, 10 studies examined socioeconomic criteria, 6 studies examined innovation level, 8 studies examined population dynamic, 8 studies examined environmental variables, and 9 studies examined financing criteria in their evaluations of technologies.

The studies used different criteria in their evaluations, but most studies used criteria such as the cost of access to new technology, budget impact, the burden of disease, Willingness To Pay (WTP), safety, effectiveness, and availability. The least attention is paid to technology-level criteria.

Discussion

The limitations of health resources have led researchers to consider the clinical and economic implications of investing in new technologies. Health Technology Assessment is used as a tool to ensure the maximum health of the community and prevent the emergence of inefficient technologies. It helps to ensure that the new technology is good value for money as long as it is ready to enter the clinical practice. However, such calculations at the time of the introduction of new technology into the treatment process will not help to improve the monetary value of the technology by making changes to the new technology. To prevent the loss of R&D investments for new technologies, developers have proposed to evaluate the economic and clinical impacts of technology at an early stage of development.

In this study, 38 studies were found to meet the inclusion criteria, which were then examined based on their different evaluation techniques and perspectives and the criteria for technology monitoring. Five general evaluation methods for monitoring technologies (pharmaceutical and

non-pharmaceutical) in the early stages of development were found, including Pro-HTA, Early-HTA, forecasting, and HSS. These methods are performed at or before the early clinical trial. Since at this stage of technology development, scientific evidence is limited, expert elicitation techniques are used alongside the methods to complete the evidence.

The findings showed that pro-HTA, early HTA, and HSS models, in their evaluations, often take into account the various stakeholders in the health system. They develop technology when there is an agreement on deciding to introduce new technology in terms of health, insurance, industry, and people's perspective. So this method develops products that are based on the community's real demand and help prevent the waste of resources (2, 15, 23).

Chronologically, the pro-HTA method seems more recent than the other methods. Because of the complexity and lengthy scenarios of investigating the effects of emerging technology, the dynamic simulation models used in the PRO-HTA method have become increasingly popular.

Most of the studies we considered used the early HTA method. The Pro HTA method, taking into account various influential criteria in terms of industry, health system, people, and insurance of access to technology, helps corporate managers and the health system make decisions while simulating the results of an emerging product to optimize or reject an innovative product to avoid inappropriate investments (24, 25).

The early HTA approach is principally based on the concept of HTA, and the main difference is at their starting point of analysis. The HTA method is assessed after the technology is completed and before entering the treatment process, while in the early HTA method, it performs analysis during the technology research and development stages. In other words, the HTA approach is based on the results of evidence-based studies, so it is possible to use HTA after the development or implementation of new technology, while the early HTA evaluates technology at the early stage of product development. HSS also prioritizes new developing technologies.

Hartz et al. (2008) conducted the first systematic review in 2008 to identify methods for evaluating technologies at an early stage of development, which was in line with the purpose of the present study. It included 56 studies on pharmaceutical technology assessment and 27 studies on medical devices. In the present study, there were 7 studies on pharmaceutical products, 24 studies on medical devices, and 7 studies on evaluating both technologies.

Retele et al. (2009) studied the methods and results of nanotechnology evaluation in cancer care in the early stages of development and in the process of their diffusion. They found that most studies focused on the regulatory and safety (environmental) aspects and did not provide any structural assessment of dynamics, health economics, or organizational aspects (26).

Katarzyna Markiewicz (2014), in a study from 1996 to 2013, identified different techniques in technology assessment and evaluation. Compared to Hartz's study, they focused on medical devices and identified some qualita-

tive and quantitative methods emphasizing that these techniques must be implemented before the product can be fully developed (27).

Maarten J. Ijzerman et al. identified 10 methods for assessing medical technologies at an early phase before market launch. They named them early HTA methods, while some of these techniques did not follow the principles of early HTA, which had been defined by Pietzsch and Pat'e-Cornell (2008). They defined early HTA on the principles of economic evaluation in the health economics discipline. In this definition, early HTA assesses the safety, effectiveness and cost-effectiveness of new medical technology (28). But MCDA or Horizon scanning techniques are developed to trace new technologies for broader dimensions previously defined for early HTA. MCDA captures some criteria in addition to safety, clinical effectiveness and cost-effectiveness of new technology such as the severity of disease, size of targeted population and equity consideration (29, 30). Horizon scanning not only focused on potential safety, clinical effectiveness and economic impact of emerging technologies but also considered other impacts of emerging technologies. To deal with the above reasons, we revisited the classification for methods in the previous study (28).

Claudia Wild et al. also conducted a systematic review to identify the countries using the HSS approach and its process and practice. Finally, 13 countries were identified that studied the same processes such as identification and filtering, prioritization, initial evaluation, diffusion, and monitoring of the technologies evaluated.

It is noteworthy that studies evaluating pharmaceutical products date back to 2000 and earlier. In recent years this assessment has shifted to medical devices. It could be due to shorter clinical trial lengths for medical devices compared to medicines and, as a result, easier appraisal and estimation of outcomes, the shorter life cycle of equipment, more predictable outcomes in product development compared to pharmaceutical products, more expensive equipment in most cases and consequent costs of technology (repairs, maintenance).

In the future, the use of early technology evaluation strategies such as Early HTA and pro-HTA will be more desirable given the constraints emerging from limited resources, increased demand, complex dynamics of disease, increased pressure on health systems, and increased uncertainty in R&D on the production of medical services. It is expected that the results of these studies will lead to value-dependent pricing.

This study faced some limitations. The timeframe of the present study was limited to studies that were published since 2000. We did not fully search grey literature to find relevant studies. We might have missed some studies which would be potentially included. However, systematic review studies indicate that a specific method to measure the economic and clinical impact of emerging technologies at the development stage has not been eliminated.

Conclusion

Given the limited financial resources of the health sector in most countries, to invest in the R&D sector in the de-

velopment of emerging medical technologies, research should ensure that technology can be incorporated into the therapeutic process. Different methods were used to investigate the impacts of emerging medical technologies. Chronologically Pro-HTA methods are new ways for investigating emerging medical technologies beyond clinical and economic impacts. Assessing the feasibility of implementing Pro-HTA in real environments requires further research.

Conflict of Interests

The authors declare that they have no competing interests.

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Appendix. Search strategy in Pubmed:

- #1 simulat* [T/A] (536,040)
- #2 forecast [T/A] (8,918)
- #3 forecasting [MeSH Subheading] (388,878)
- #4 forecasting [All Fields] (652,477)
- #5 future [All Fields] (886,484)
- #6 emerging assessment [All Fields] (170,413)
- #7 foresight process* [T/A] (303)
- #8 Technology Foresight [T/A] (717)
- #9 health technology assessment [T/A] (4,857)
- #10 horizon scanning [T/A] (195)
- #11 pro HTA[All Fields] (45)
- #12 HTA [T/A] (3,084)
- #13 dynamic model [T/A] (4,430)
- #14 prospective assessment [T/A] (1,584)
- #15 trends [MeSH Subheading] (388,787)
- #16 prospective simulation [T/A] (36)
- #17 early assessment [T/A] (2,445)
- #18 assessment, biomedical technology [MeSH Terms] (11,143)
- #19 health technology [MeSH Terms] (14,210)
- #20 computer simulation [MeSH Subheading] (238,945)
- #21 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20) (1,681,216)
- #22 pharmaceutical innovation [T/A] (229)
- #23 pharmaceutical diffusion [T/A] (23,207)
- #24 health technology diffusion [T/A] (4)
- #25 emerging diffusion [T/A] (7,029)
- #26 emerging drug [T/A] (795)
- #27 new drug [T/A] (17,173)
- #28 new medicine [T/A] (460)
- #29 drug entity [T/A] (85)
- #30 medicine entity [T/A] (22,869)
- #31 emerging health technology [T/A] (12)
- #32 healthcare innovation [T/A] (25)
- #33 medical device* [T/A] (15,393)
- #34 innovation diffusion [MeSH Subheading] (19,985)
- #35 approval, new device [MeSH Subheading] (2,944)
- #36 approval, new drug [MeSH Subheading] (15,530)
- #37 (#24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36) (76,894)
- #38 ("2000/01/01"[Date - Completion]: "2020/08/30"[Date - Completion]) (17,885,956)
- #39 (#23 AND #39 #40) (11,417)