Tampere University

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TECHNOLOGY ASSESSMENT: A TOOL OF TECHNOLOGY FAILURE PREVENTION

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ABSTRACT

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Technology plays an increasingly important role in health care. Failures and unpredicted effects of health technology may lead to disastrous consequences such as injuries and casualties, but they also mean huge financial costs, waste of resources, legal issues and loss of public trust for medical care systems and health technology industry. Therefore, technology failures should be prevented for the sake of patients, functional health care systems and technological advancement. The objective of this thesis is to indicate, that properly conducted technology assessment (TA) is critical for preventing failures. Short theoretical background is presented draw a more comprehensive picture of TA, its functions and origins. A literature review has been performed to find those ingredients of technology assessment, which are essential from the perspective of failure prevention. Such elements are objectivity and impartiality, planning, choosing assessment criteria, foreseeing adverse effects, technology comparison, and periodical reassessments.

To underline the vitality of properly conducted TA, an example of metal-on-metal hip implants failure is introduced. The reasons for failure are analysed and prevention steps, which should have been implemented, are proposed.

This thesis is an approach to TA seen as a practical and essential tool. It is an attempt to demonstrate, that TA should be of great interest for biomedical engineering. Since biomedical engineers are professionals, who design and manufacture health technology, TA provides a great methodology for them to improve the whole innovation process. TA is also important for better understanding of technology development paths and their consequences.

Keywords: technology assessment, technology failure, failure prevention

PREFACE

This bachelor's thesis conforms to the Guide to Writing a Thesis in Technical Fields at Tampere University (2019).

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Tampere, 24 October 2019

Paula Rakowska

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LIST OF SYMBOLS AND ABBREVIATIONS

ASR	articular surface replacement
BME	biomedical engineering
CoCrMb	cobalt-chrome molybdenium
ECHTA	European Collaboration for Health Technology Assessment
EUnetHTA	European network for Health Technology Assessment
FDA	the Food and Drug Administration
GDH-PQQ	Glucose dehydrogenase pyrroloquinolinequinone
HTA	health technology assessment
INAHTA	the International Network of Agencies for Health Technology Assessment
ISTAHC, HTAi	International Society for Technology Assessment in Health Care
MHRA	Medicines and Healthcare products Regulatory Agency
MoM	metal-on-metal
OTA	the Office of Technology Assessment
TA	technology assessment
THR	total hip replacement
WHO	the World Health Organization
WSI	whole slide image

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1. INTRODUCTION

Technology has become an inseparable part of everyday life. We increasingly depend on technology, not only at work and at home, but also health care and medicine rely on technology more than ever. This growth of technology use has changed the way businesses, societies and medicine work. In business world, technological difference between product offerings has become a key factor in establishing competitive advantage. Similarly, research teams often distinguish themselves by implementing novel technologies. Technologies and their optimal use are critical for obtaining meaningful research results and scientifically important discoveries.

The position of technology and public reliance on it have brought modern society to a point, where newer, improved technologies are on high demand. Consequently, new technologies are being reported and put into use at probably the highest rate ever. There is a rush to innovate in attempt to keep up with the expectations of the market and to survive in a competitive environment. [1] Investing in or adoption of an innovation generate risks, but organizations, which stay behind may lose the race for competitive advantage or even disappear from the stage [2]. Sometimes this hunger for new technology leads to early diffusion of new technologies without adequate measurements of their effects [3]. Undoubtedly, technological innovations introduce opportunities to facilitate medicine, well-being, research, education and simple everyday life activities; however, they also carry along unintended, unknown short- or long-term effects. Those effects may be a threat to human safety or life, or they may be harmful for the environment. They can be both economically and socially costly. Health technology failures are among the most dangerous incidents from the perspective of human safety and life, and they can cause serious public traumas and mistrust in health care systems. Unfortunately, failure of medical technologies is not rare.[4] For this reason, a society, which is constantly seeking new benefits from technology, should have a means to minimize the scale and frequency of technology failures, with emphasis on health technology failures, to ensure their own safety.

The objective of this thesis is to introduce technology assessment (TA) as a tool of getting an adequate picture of biomedical technologies, and to illustrate the scientific basis of TA through analysis of selected instances of technology failure. A list of TA elements,

critical for technology failure prevention, will be proposed. An example of technology assessment misconduct, resulting in technology failure, will be presented. The reasons of failure will be analyzed in order to demonstrate, how technology assessment could have been used to avoid reversal. TA is a vast field and this thesis attempts to distill key elements of TA, then illustrate their utility in the context of known technology failures. It is not an exhaustive review. The aim is to propose a point of view on developing adequate tools for technology failure prevention.

The significance of technology assessment and prevention of technology failure for BME is inherently apparent. Biomedical engineers actively contribute to the rush of innovation by designing and producing medical devices, which are later adopted by health care institutions. Thus, biomedical engineers are or should be qualified to assess the performance of those devices. In fact, the World Health Organization (WHO) recommends engaging biomedical engineers in the process of medical device evaluation by employing them in health technology assessment agencies [5]. The need to incorporate BME professionals into the teams conducting HTA has been identified also by several authors [5],[6],[7],[8]. Concurrently, occasional negligence related to health technology assessment has been observed in the field of biomedical engineering. It is thought that there is less training than needed, too scarce debate, and not enough recognition of health technology assessment as being one of the core tasks of biomedical engineering [5],[8]. This thesis is an attempt to drag more attention toward technology assessment as an extremely important tool for biomedical engineering, which, however, may serve many different functions for different stakeholders and in variety of situations. After all, as Feigal et. al wrote in their article regarding safety of medical devices, “[e]nsuring that medical devices are safe and effective is everyone’s business” [9].

2. TECHNOLOGY ASSESSMENT IN BIOMEDICAL ENGINEERING

It is important to agree on the meaning of terms used in the discussion to avoid misunderstanding and confusion, and to define the frames of the subject. In addition, the origins of technology assessment will be introduced to help in understanding the significance of this tool. The importance of technology assessment in the context of biomedical engineering and technology failure is further discussed in the last sections of this chapter.

2.1 Technology, biomedical engineering, health technology

We focus here on the assessment of technological solutions in the context of biomedical research and health care. The term “technology” should be the starting point for any attempts of formulating technology evaluation criteria. Technology is a broad term, understood differently by different people, and as such does not have one unique definition. It is often defined as the practical application of knowledge [2],[3], however, this definition includes virtually anything. E. Braun proposes a more specific definition of technology, which is: “the material artefacts used to achieve some practical human purpose and the knowledge needed to produce and operate such artefacts”[2] and this is how technology is understood in this work. This explanation clearly distinguishes two elements of technology: (1) physical tools, machines and other means, and (2) immaterial knowledge, processes, ways and ideas.

Constant change is the most characteristic feature of technology.[2] The change can be aimed at one of the following goals: better performance (e.g. higher speed, higher efficiency, more automated features, etc.) or executing tasks, which earlier were performed by humans. The motivation for changes may be either an actual need expressed by customers or identified as existing in the market (market pull) or introducing a revolutionary technology, for which market is hoped to be created or increased (technology push). The change can also be incremental (gradual improvements of already existing technology based on pre-existing skills and knowledge) or radical (revolutionary technology based on new solutions and requiring new skills). When it is believed that an improvement has been achieved, the result is an innovation: “a new or essentially improved technology, or product of technology, that is offered for commercial transactions on the market.”[2]

Technology can be applied to specific areas and hence become a narrower concept.[10] Examples of such specific areas are biomedical engineering and health technology. Biomedical engineering can be defined as “the use of the principles and techniques of engineering to solve problems in biology and medicine” and its development rate is said to be among the fastest.[6] This interdisciplinary field of technology, practiced both as business and academic discipline, serves as a tool for medical and life research, and provides solutions and innovations for health care. Biomedical engineering includes elements of wide spectrum of other sciences, e.g. biology, nanomedicine, space medicine, molecular and cellular engineering, electrical engineering, robotics and tissue engineering.[1],[6] Medicine and health care increasingly rely on technologies and devices provided by biomedical engineering. Biomedical technologies can be observed as tools for prevention, imaging, diagnosis, treatment, rehabilitation and prostheses. The mutual connection is so deep that the boundaries between terms biotechnology and medical device have become indistinguishable.[1] It is expected that the relationship between medicine and biomedical engineering will remain close also in the future, and that biomedical engineering will play the key role in delivering health care to the patients.[1],[6]

Medvedec defines health technology as “a test, device, medicine, vaccine, procedure, program or system developed to prevent, diagnose or treat medical conditions, promote health, provide rehabilitation or organize healthcare delivery” and underlines the tight connection between it and biomedical engineering.[7] Often health technology is a product of biomedical engineering. Examples of health technology are diagnostic and treatment methods, medical equipment, pharmaceuticals, rehabilitation and prevention methods, organizational and supportive systems within which health care is provided [11]. In this work the focus is on the physical technological solutions: devices and equipment used in medicine and health care.

2.2 Technology Assessment

Technological solutions provided by biomedical engineering have significantly contributed to the development and improvement of health care.[1] Medicine and health care increasingly rely on biomedical devices. Patients’ safety, health and life are at stake. However, in addition to intended effects, a technology may well have unintended influence on the consumer or its environment. Technology’s adverse effects or its complete failure may lead to severe injuries, permanent damage to health, or even deaths, which consequently imply technology recall, legal issues, huge financial costs, public mistrust and loss of prestige for health care centers using the failed technology, and for research

institutions or private companies who designed and produced those technologies. Therefore, all possible influences of any technology, particularly a new one, must be explored before the technology diffuses and becomes an established method for medical practice. Authors assign the moral responsibility resulting from manufacturing or using medical devices to both physicians and biomedical engineers.[4] In addition to desired and undesired consequences of utilization of a given technology, the purpose of the technology and the most efficient ways to use it must be known in order for the technology to be a valuable factor of the successful business or health treatment. Efficient, or optimal, use of technology is understood here as such use, which enables obtaining the best results with the least overall cost in the application the technology was designed for. Recognizing features and functionality of a given technology helps health care institutions to choose the best possible option for treatment in a given case, and facilitates research groups and firms in deciding whether investment and development of a particular technology makes sense [1]. Ensuring the safety and effectiveness of health technology as well as informed decision-making related to health technology are not possible without **technology assessment**.

Technology assessment (TA) can be defined as an interdisciplinary research field, which attempts to produce information for educated and well-reflected decision-making.[12] It is a tool to investigate technologies thoroughly and with foresight in its full context: what opportunities and limitations this technology offers within frames of the organization's interests, resources, skills, structure, and social environment the organization operates in.[2] It is a systematic evaluation of properties of a technology and it should address aspects such as safety, efficacy, effectiveness, costs and cost-effectiveness of the evaluated solution [13]. It is often emphasized in the literature, that a broader context has to be considered in technology assessment, namely, all direct and indirect impacts and side-effects of technology adoption, social, legal ethical and safety implications.[3],[2],[13],[14] All these aspects must be considered in evaluation process, as change of technology will affect all of them [15]. However, the attention payed to each of them will vary between TAs conducted for different technologies, depending on their application and context.[13] Context-specificity is among the most characteristic features of TA often emphasized in literature.[3],[13],[14],[16] Any evaluation is dedicated and conducted for a specific audience and is designed to answer specific questions, and those frames dictate the extent of the assessment and methods used to perform it.[14]

TA is also methodologically sound; it is a process of collecting the best available evidence in a systematic, transparent and reproducible way. Evidence in this context means the result of systematic observation or experiment.[14] The product of TA is assessment

report, which is a technically detailed document, demonstrating the validity of the evidence and making the evidence accessible and usable also by those, who are not the direct auditions of the report.[14]

2.3 Health technology assessment

Technology assessment applied to health care management and policy results in health technology assessment (HTA)[1]. Initially, terms such as “medical technology assessment” and “healthcare technology assessment” were used, but they have nearly disappeared from the literature [10]. Although HTA has emerged from TA, it has been emphasized that there are several differences between these two disciplines. First, HTA is very complex due to it requiring expertise in multiple scientific fields: technological and engineering knowledge must be compatible with clinical use. There are many stakeholders involved, and many external factors influence the process, for instance legal regulations, social judgement, medical constraints, and fragmentation of health care industry. Also, there is a vast ethical and moral burden related to HTA.[1],[16] Nevertheless, despite differences between HTA and TA applied to other disciplines, the methods used in both approaches are the same [1].

Health technology assessment is defined based on its purpose and not methodology [17]. European network for Health Technology Assessment (EUnetHTA) defines HTA as “a multidisciplinary process that summarizes information about the medical, social, economic, and ethical issues related to the use of health technology in a systematic, transparent, unbiased, robust manner. Its aim is to inform the formulation of safe, effective, health policies that are patient focused and seek to achieve best value. Despite its policy goals, HTA must always be firmly rooted in research and the scientific method.” [11] HTA is usually performed by groups of professionals of multiple specializations, who use different analytical methods [3]. Similarly to TA, HTA is context-embedded.[13] Since HTA grew out from technology assessment, it also focuses on providing the best available evidence. HTA shares the principles of evidence-based analysis with evidence-based medicine and clinical practice guidelines, and together with them constitutes the best practice initiative.[14]

Several authors observe that HTA has been criticized for emphasizing too much on efficacy and cost-effectiveness of health technologies, and not enough on ethical and sociopolitical implications [10],[13]. Banta is even concerned that because of this shortcomings, HTA may become dysfunctional [10]. In turn, Integlia and Mazzoni argue, that ethical issues cannot be measured with reliable quantitative methods, and thus can cause disagreements, so that excluding them from HTA may be justified.[13]

2.4 Brief history of technology assessment

The need for technology assessment in its modern form arose in 1950s and 1960s in the United States.[2],[10] In that time, it started becoming apparent, that besides benefits, technology can bring also undesirable effects. Moreover, investing in technological innovations became more expensive and riskier. Thus, demands for technology control and support started growing and increasing pressure was put on the United States Congress.[2] As a response to those demands, in 1972 Congress established Office of Technology Assessment (OTA) [2],[10]. Its scope was to provide Congress with ready, reliable and comprehensive information about technologies, so that Congress could make decisions. OTA existed until 1995 and during its tenure it produced around 750 studies on variety of topics. It was criticized as being redundant to other governmental activities. On the other hand, some referred to its shutdown as “an example of politics overriding science”. It stimulated development of technology assessment in the US and internationally, however, it did not inspire any greater, international initiatives. Individual technology assessment programs are run by governments, universities, research institutions and industry in North America and Europe. [10]

Nevertheless, HTA, which at present seems to be much more institutionalized than TA, is said to have its roots in OTA as well [13],[17]. In 1975 OTA started its health program and this date is provided by some authors as the beginning of HTA [13]. Others date HTA back to 1976, when the Office of Health Technology Assessment was established under the USA Health Care Financing Administration [18]. Likewise, HTA emerged in Europe in 1970s, when concerns related to economic effects of health technologies started arousing. The first institutions, whose task was HTA, were established in France and Spain in 1980s, but their influence was limited to local activity.[14] Sweden was the first European country to have its national HTA institution, opened in 1987 [13],[14]. Since then the institutionalization of HTA in Europe has progressed. In 1985 the first meeting of the International Society for Technology Assessment in Health Care (ISTAHC, today called HTAi) took place. Moreover, there were three projects funded by European Commission, which gave foundations for the modern HTA in Europe, and those were EUR-ASSESS project, HTA Europe project and the European Collaboration for Health Technology Assessment (ECHTA). The most important outcome of the last one, ECHTA, is the formulation of best practice guidelines for performing and reporting HTAs. In 1993 The International Network of Agencies for Health Technology Assessment (INAHTA) was established. [14]. This network exists also today and it unites 51 HTA agencies from 32 countries worldwide [19].

2.5 The importance of technology assessment in the context of technology failure

Technology is subject to constant change – it “is never so perfect that it could not be improved, and new knowledge brings with it new technological possibilities”.[2] As a result, innovations, new or significantly improved technologies, emerge in the market all the time. In fact, *replacement* (a process in which an old technology has become obsolete, and it is being *replaced* with a new, better technology) is one of the two reasons why a decision to abandon an old technology is made.[4] The other reason is *reversal*: an established technology is abandoned, because it has been discovered that it has not fulfilled its purpose all along, or that it causes harms, which are greater than its benefits. While replacement is a natural consequence of technological development, reversal should be an extremely rare phenomenon, especially in case of health and medical care technology, however, it is reported to be ubiquitous. [4] Reversal reveals that multiple mistakes have been made on the path from an idea to a product diffused in the market, it usually ends up with technology recall, and its effects are dangerous. Having all these features, reversal is synonymous with failure. Although technology failure cannot be completely eliminated, it is crucial that failure is diminished to the lowest possible level, especially for medical devices. [4],[20] TA and HTA are instruments in hands of policy-makers, physicians and biomedical engineers, which can be used to minimize the risks of technology failure.

Technology assessment provides evidence-based, detailed information about a technology, not only as absolute values, but also in relation to competitive technologies. The information is contextualized and precise, it is gathered and recorded in a systematic and methodologically sound manner. Such data is easier to interpret or compare, it can be used better by stakeholders and enables wide propagation of information. Therefore, by producing high-quality information, TA supports educated decision making on many different levels of organizations [1],[13], helps allocate resources efficiently and adequately, and enables organizations to choose the best technology available on the market for a given application [21]. Consequently, TA and HTA allow diffusion of relevant technologies, and prevent diffusion of marginally useful methods [3],[16], as well as those technologies, which are potentially harmful.

In the context of research centers focused on BME, high-quality, timely technology assessment can most importantly improve the quality of research by assuring with methodologically sound methods the validity of data collected with help of the assessed technology. In addition, HTA helps identify research gaps [22]. It can also speed up the

progression rate of a study, be a tool for better resource management and allocation, and thus become a key factor in achieving competitive advantage. HTA also enables verification, if stakeholders' needs have been satisfied by the technology. Eventually, it provides evidence for the significance of a research or for the contribution of a product to the development of health care [22]. Well-designed and widely used TA and HTA for research institutions would establish a habit of conducting technology management based on scientific and local evidence [18] and promote the principles of responsible research and innovation [23]. All these functions of HTA facilitate technology failure prevention.

HTA is thus a bridge between biomedical engineering and health care delivery [1]. It is fundamental for ensuring safety, efficacy and effectiveness of health technologies [3]. There will always be a certain amount of risk related to health technologies [18], but TA and HTA can help make a decision, whether in given circumstances the risk is worth taking or not [2]. Those two methodologies are also crucial for reducing the frequency of device failure and medical reversals.

3. LITERATURE REVIEW

A collection of the most significant technology assessment elements from the perspective of preventing technology failure, was formed based on an analysis of the literature discussing the topic of technology assessment and health technology assessment. The selected works include scientific articles published in peer-reviewed journals related to medicine, biomedical technology, engineering and industrial management; reports published by health policy monitoring organizations, as well as books and monographs. The texts were chosen according to their scientific value, relevance to the topic, availability and author's interest. The objective was to use possibly newest publications. The selected literature was published between years 1989 and 2019. It is noteworthy that not all most relevant publications grant free access for readers, and those were excluded from the review.

As emphasized earlier, this work is not an attempt to create a detailed description of the whole technology assessment process nor to conduct an exhaustive literature review. This thesis presents an approach to technology assessment in the context of technology failure, built on the existing material provided by earlier studies, and filtered through author's personal judgement as a biomedical engineer at the beginning of their professional career. In addition, the process of TA elements selection was influenced by the case of biomedical technology failure analysed in chapter 5: Case Study. Cited case is a well-known incident, widely discussed in literature: metal-on-metal hip implants failure.

4. THE ELEMENTS OF HTA CRITICAL FOR TECHNOLOGY FAILURE PREVENTION

The result of conducted literature review is a short list of the HTA and TA components, which are critical for preventing technology failure. The selection of the elements is subjective; however, it has been influenced by the opinions and reasoning demonstrated in the study material and the frequency of elements' reappearance in those texts. The order of the elements reflects the logical propagation of a TA process, yet it is also subjective and just as the order of TA steps can be changed depending on the research matter, the order introduced below could be subject to modifications as well.

4.1 Element 1: Impartiality and objectivity

This list opens with principles of HTA and TA, which should be imperative and undisputed signpost all along the process, starting from the assembly of an assessment group. Those principles are impartiality and objectivity.

Several authors report concerning phenomena which may be observed in certain type of HTAs. Namely, industry sponsored assessments tend to be biased [22],[24]: flawed, favourable methodology is used, the results are too optimistic, and some data may even be withheld from the public to provide a misleading picture of the technology [4]. Conflicts of interest within the group conducting an evaluation may also lead to unreliable results and is mentioned by many authors as hazards related with TA and HTA [4],[15],[21],[24]. Some authors are worried, that temptation of benefit may lead to corruption of scientific research [24]. It has been observed that malpractice within medical device approval processes and lapses in regulatory mechanisms facilitated by misleading reports from industry, have occurred [4]. Those practices are obviously dangerous, morally improper and through the practice of sound HTA should be prevented as they may lead to catastrophic consequences.

Impartiality and objectivity are the only guarantee of an unbiased, methodologically sound assessment, undue optimism and unreported uncertainties. They are crucial for reliability of information produced by technology assessments and therefore are placed on the top of the list of TA elements essential for technology failure prevention. Although impartiality and objectivity are impossible to measure, they should be for TA assessors what Hippocratic Oath is for physicians and should always point the direction of assessment. Absolute objectivity is out of human reach, but a reasonable approximation can be

achieved by assessors, who put an effort into being as truthful as possible, are not afraid to say what they see as the truth, who gather data from all available sources in a methodologically sound process and who identify and admit the shortcomings of their study [2]. Forming a team of experts, who do not have conflicts of interests, do not receive benefits from the organization of technology's origin nor from their competitors, and who have inquisitive and sceptical attitude, results in closeness to impartiality.

4.2 Element 2: Planning

Prior to the proper conduct of assessment, the whole process should be carefully planned. First, clear and actionable research questions must be formulated, so that the scope of the assessment is known and understood by all assessors [2],[3],[21],[25]. The problem cannot be too narrow nor too wide, otherwise the assessment will miss its primary aim of providing relevant and usable information for decision makers [2]. The technology of interest should be characterized and its intended functionalities and expectations related to them ought to be defined [1],[2] and the feasibility of those tasks and expectations must be evaluated [16]. Also, the end-point in time should be established, so that technology effects over an adequate period of time can be observed [2]. While establishing the time horizon, it is essential to consider, if any delayed consequences are possible. This stage includes also choosing research methods, scientifically justified and relevant to the type of technology being assessed and to its intended application. Transparency and reproducibility are indisputable requirements for method selection [23]. The logistic issues should be addressed, so that no organizational obstacles would interrupt the proper assessment [3]. If the process requires clinical test, the features of population engaged in the trials ought to be designed, so that the assessment is clinically relevant and scientifically valid [3],[22]. Finally, a feedback loop has to be determined. It is important that assessors know how to decide whether the research questions have been answered and when further studying would not produce valuable results anymore.[22] The methods and timing of internal quality control should be defined, and duties related to it ought to be assigned.

As TA and HTA are context-embedded, it is not possible to create one universal strategy or protocol for conducting the evaluation [21]. The assessors can use existing case studies and (H)TA reports as well as recommendations of national and international agencies to deepen their knowledge about methodologies relevant to their study subjects and research questions. Above all, assessors should rely on their experience, expertise and creativity to create the most adequate protocol for a given HTA.

The planning stage is necessary for ensuring systematic study conduct, following the protocol, collecting all relevant data and consistent information record. Furthermore, a well-planned research strategy diminishes bias.

4.3 Element 3: Defining criteria of evaluation

The protocol of conducting HTA is not complete without the criteria according to which the technology is going to be evaluated [1],[3],[26]. Some authors argue that defining evaluation criteria could be the most important step of TA. [25] Those criteria should respond to the problems which need to be addressed. They should also reflect the needs, expectations and preferences of various stakeholders. The criteria can be broken down into sub-criteria and those can acquire single or multiple attributes. Criteria should be ordered hierarchically according to their importance for the purpose of the assessment. The whole system can be formed into value tree, which is one of the tools utilized to estimate the value of technology in a transparent and systematic way. [25],[26]

Criteria can be borrowed from the earlier studies or existing reports, they might be based on interviews with the stakeholders, or designed by the assessors' team. The list of distinctive criteria should be limited to only those necessary for adequate depiction of technology. In any case, ideal criteria are understandable, operational, non-redundant, concise and essential for the research problem. Similarly, the attributes of criteria should be understandable and operational, but also unambiguous, comprehensive and direct. A necessary step is defining such range of attributes, which is acceptable for a given purpose. [25] The measurable features can be described using quantitative scales, and for immeasurable features a qualitative scale consisting of verbal or graphical values often turns out to be more functional [2],[25],[26].

The stage of defining assessment criteria may arouse a practical problem. Since the whole hierarchy of criteria is intended to reflect the preferences of stakeholders, their requests ought to be prioritized as well. The question is, how to do that? Which stakeholders should be taken into account? How to combine their preferences? [25] Designing and applying a suitable strategy to generate adequate indices and their interdependencies is crucial for creating a feasible criteria system.

4.4 Element 4: Forecasting adverse effects

Assessment of technologies is future-oriented by definition [2],[23]. The aspiration of (H)TA is to get a far-sighted and thorough presentation of technology and its effects. Some of those effects may be unintentionally harmful and undesired, but they can be

avoided if HTA is conducted properly.[2] Therefore, methodologies of technology forecasting should be included in the protocol to estimate the most probable direction of development of the studied technology, its effects on patients health, its influence on environment, as well as its economic, social, political and ethical implications [2],[21],[23]. Not only immediate, but also long-term influence of an implemented technology must be evaluated [23],[27]. In particular, the goal is to explore those effects, which may not be inherently obvious, and which may pose a threat [2]. The threats must be analysed thoroughly and objectively: who or what is going to be affected if the technology will be adopted and utilized, what is the most likely chain of events, what could be the consequences and what would be their scale, can anything be done to minimize the risk? [2] Also, all the assumptions made prior to the forecast should be documented. [2]

There exists a variety of technology forecasting methodologies which may be incorporated into HTA protocols. Usually, in order to improve the accuracy of the estimation, a combination of different strategies and methods is employed. [21]

The negative effects induced by an implemented technology are particularly important, because all the difficulty of health technology decision making is related to them. Safety of patients and improving their health instead of worsening it is the most important motivation for HTA. Consequently, there cannot be an assessment without forecasting potential short- and long-term hazards caused by utilization of a technology. Undeniably, this stage is the core of HTA processes.

4.5 Element 5: Technology comparison

Technologies are not suspended in a void. They interact with one another: they compete with rival (alternative) solutions and need complementary technologies to function properly [2]. Moreover, technologies become obsolete, and sometimes a technology is discovered to be harmful and it is withdrawn from the market. In both scenarios, the technology, which has become irrelevant, needs to be replaced with an alternative, either already existing one or one that is to be announced, to enable continuation of research, studies, treatment, etc. Thus, comparative assessment in a natural way is an inseparable stage of technology assessment. The results of assessment are not useful, as long as there is no reference data, which it can be compared to.[3] Rival technologies do not only set up a frame of reference, but they also establish a standard and define the frontiers of the state of art of the studied type of technology.

New technology is always intended to introduce some benefits and improvements in comparison to the older technology, regardless of its application, but this must be proven in a controlled, well-designed and comprehensive manner. The following questions must be asked: is this technology better than alternative technologies? Why is it better, how is it better?[1],[2],[3],[12] When used instead of existing methods, does the technology offer better results? Does it produce new information or improve the effectiveness of treatment when used in combination with existing technologies? [3]

Marginal effectiveness (the relative superiority) of a technology may be measured with respect to different features such as efficiency, safety, lifetime etc. The relative weight of those features in the context of studied technology has to be defined a priori, so that the differences between indices for alternatives may be compared and the clinical significance of those differences can be evaluated. Since technological reversals happen, and individual patients may need personalized treatments, undoubtedly substitutive value of a technology must be estimated. [3] The value tree described in the previous section can be utilized to clarify marginal effectiveness of rival technologies.[26]

One more aspect which could be mentioned within the frames of comparative assessment is how well the technology fits into the environment of already established technologies. Is the assessed technology compatible with commonly used complementary technologies? Does it require additional investments in custom supplements offered by the same company which produces the new technology? Does the use of the new technology differ significantly from the use of rival technologies? Is it complicated? [2] This information will have an influence on the rate and extent of technology diffusion. If adopting and utilization of an innovation requires too much effort and is too costly, it will be rejected by the market and will never reach broader audiences.

Clearly, comparing an innovation and an established technology is challenging. It often requires confronting estimations and hypotheses about the results of a new, unknown solution with well-explored (or at least what is believed to be well-explored) and empirically demonstrated effects of frequently used methods. [27] Luckily, there exist plausible strategies of technology forecasting, which assist the process of comparison, and with well-designed HTA protocol as well as systematic and consistent data recording, technology comparison may be successful.

Surprisingly, it seems that direct comparisons of emerging and established technologies, which would prove supremacy of the first one over the latter one, are too rare [3]. Reportedly, early diffusion of technologies, which have not been adequately assessed in comparison to established technologies has happened [3],[4],[27]. This implies that there

is a possibility of investing in a new, expensive technology, that does not offer any benefits in comparison to the older technology. Moreover, adopting a new technology generates also other costs, such as time spent by staff on learning the new technology and gaining experience on the optimal utilization of it, possible waste of samples and material caused by early improper use of the new technology, etc. HTA can be used to evaluate, whether the established technology has become obsolete and is blocking advancement in studies or improvement of patients' well-being, and also, whether a new technology is worth the effort.

TA and HTA provide not only absolute data about technologies, but also place them in the context of the whole technological universe of a given field, provide frames of reference for those technologies and by doing this also name alternative options available in the market. Comparing an emerging technology to existing ones is a tool of verification, if the technology fulfills the standards of the field, if it offers actual advantages over the rival technologies and it is going to revolutionize the market, or if it is faulty, potentially harmful, and thus inferior to other technologies. Therefore, comparative assessment is essential for preventing technology failure.

4.6 Element 6: Periodical reassessment

Technology assessment does not apply to the beginning of technology's lifecycle curve only. A significant part of HTA and TA methodologies is directed toward future and focused on forecasting. Forecasting produces hypothetical and approximated data. As time passes and technology is being adopted and utilized, new information about it and its functionality becomes available. The new information may change the predictions about technology's future and the most probable development paths. When this knowledge is combined with the fact that technology undergoes constant changes, it becomes obvious that assessment should be repeated on a regular basis.[2],[3],[15] Follow-up studies need to be properly designed and conducted for the technologies, which passed the first examination and became approved by the policy makers or other authorities [3]. Moreover, the technologies which have long been accepted and used as being standard, but there is a suspicion, that their consequences might have not been assessed properly, should be reassessed [4]. A new technology may be included into standard practices, but also a technology believed to be standard may turn out to be harmful or obsolete, and consequently abandoned. Moreover, technologies seen as obsolete for one purpose, may prove to be perfectly suitable for other applications, potentially totally different than their original purpose.[1] Re-evaluation is necessary to avoid adverse effects of a technology, which might have not been discovered during the first

assessment due to incomplete information or lack of proper tools at the time it was conducted.

Figure 1 summarizes the elements of HTA proposed as critical for technology failure prevention.

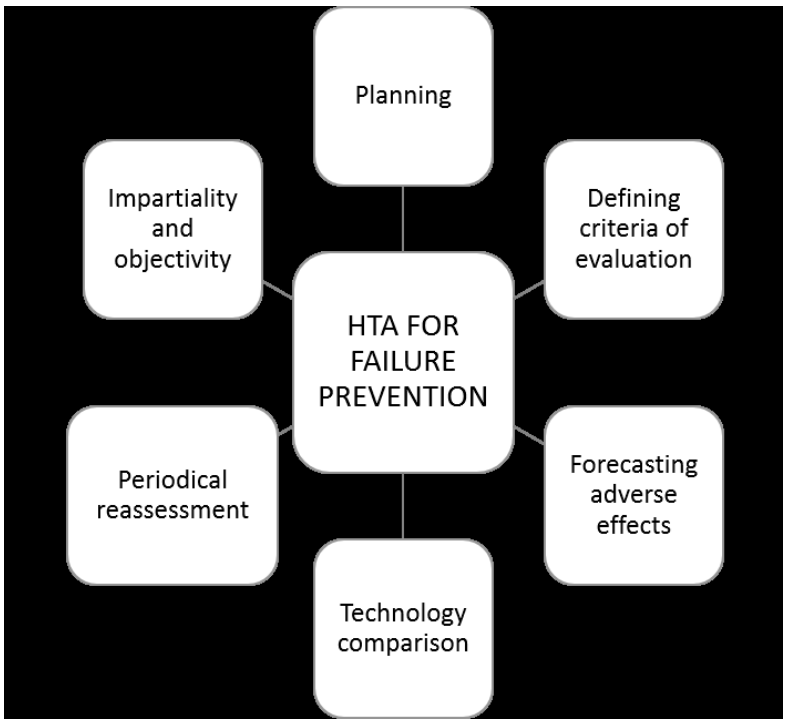

Figure 1. *The elements of HTA which are fundamental for avoiding failure of a technology.*

5. CASE STUDY

Failed technologies are not a rare phenomenon. In this chapter an example of such technology is analysed to expose TA failure on the path of introducing the technology to the market and to demonstrate how a proper TA process could have prevented the failure. The example chosen for this purpose is metal-on-metal hip implants.

5.1 Metal-on-metal hip implants

Hip arthroplasty, or hip replacement, is a surgical procedure which is used to treat osteoarthritis and other disorders leading to painful chronic hip joint degeneration. There are two main types of hip prostheses: (1) total hip replacement devices (THR), which comprise of femoral stems and modular femoral head; (2) resurfacing devices, which replace the femoral head only partially. Figure 2a and Figure 2b present schematics of total hip replacement and hip resurfacing, respectively.

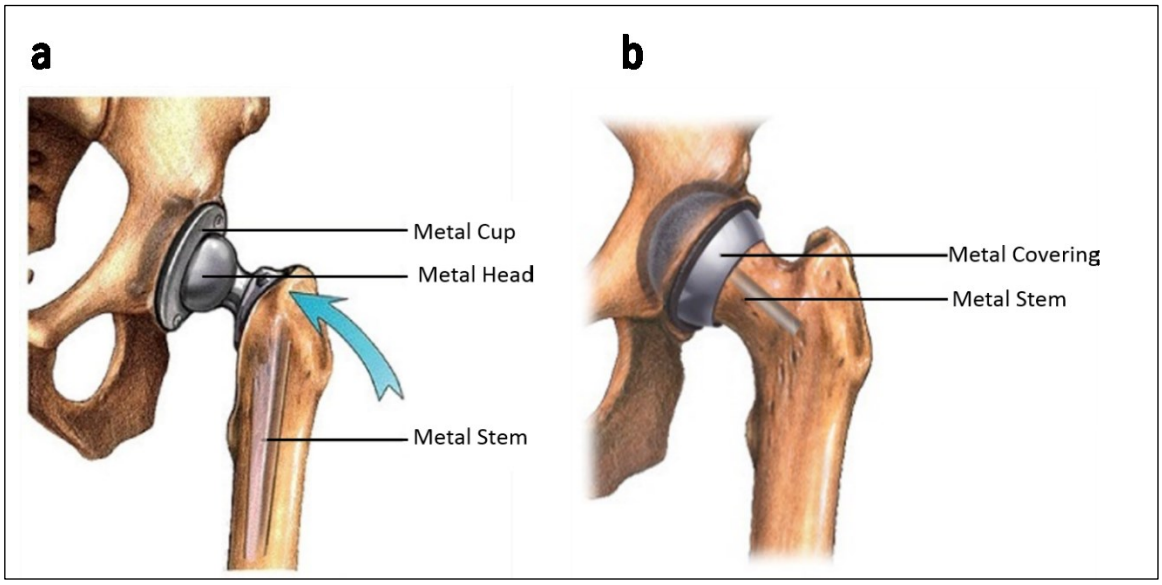

Figure 2. *Schematics of (a) MoM total hip replacement, (b) MoM resurfacing. Adapted from* [28].

One of the materials, which has been used in production of both types of implants, is cobalt-chrome molybdenum alloy (CoCrMb). Prostheses where both the femoral stem and femoral head are made of this alloy are known as metal-on-metal (MoM) hip implants. [29]

5.2 The source of failure and adverse tissue reaction

MoM hip implants were introduced to the European market in 1997 [30] as durable and strong implants with better volumetric wear resistance (the ability to resist material loss in three dimensions) than other implants, and they were targeted at young patients, active and with long life expectancy [29],[31]. Unfortunately, they turned out to fail sooner than implants made of other materials [29],[30]. Safety issues related to MoM implants received public attention when in 2010 the Australian Orthopaedic Association revealed a high number of revision surgeries for Articular Surface Replacement (ASR), resurfacing device produced by an American company, DePuy [34]. The following chain of events resulted in the recall of ASR from the market all over the world.

Mechanical wear, the source of failure of MoM implants, caused aseptic acetabular and femoral loosening [28],[30],[35] as well as femoral neck fracture [28],[30], so that reoperations were necessary. For MoM THR implants failure rate reached up to 13.6 % at seven years, being four times the rate for other types of implants [29]. Although the volume of wear particles released in process of implant surface degradation was smaller than in case of other implants, the particles were much more numerous due to their smaller size and higher number of particles per unit volume [35]. Those wear particles in contact with tissue triggered innate and adaptive immune responses, which resulted in profound necrotic and inflammatory changes [31],[35]. Wear particles passing to bloodstream resulted in elevated chromium and cobalt ion concentrations in patients' blood, many times higher than physiological concentrations [34],[35]. In some patients, metal ions were found even in cerebral fluid [36]. Moreover, hypersensitivity and allergic reaction induced by increased presence of metallic ions have been observed in many patients [28],[31]. Pseudotumors [31],[35] and even neurological changes have been reported as well [37]. Increased risk of failure was discovered to be related with female gender [34].

The exact number of patients around the world, who have gone through the MoM arthroplasties is not known, but it is certain the cases can be counted in hundreds of thousands [30]. Many revisions, meaning open surgeries including changing any part of the implant, have taken place [34]. Indications for revision are usually symptoms of tissue damage, elevated metal ion blood levels [29], solid pseudotumor found through cross-sectional imaging, infection, aseptic loosening and fracture [34]. A revised implant is seen as a failed implant, and asymptomatic implants are assumed to be functioning properly. Consequently, there is a significant number of MoM implants remaining in situ, but their future is uncertain[34].It is disturbing that such a faulty technology spread so widely and was used in large number of patients. To understand the phenomenon and to identify the TA

malpractices related to MoM hip implants, which allowed the adoption of this technology and led to its catastrophic outcomes, the case of DePuy's MoM hip implants has been analysed.

5.3 Introduction of DePuy's implants onto European market

DePuy introduced both types of MoM implants, resurfacing and THR, to European markets in 2003 [36]. Prior to that the company conducted laboratory tests, including mechanical simulator tests intended to assess the materials, the strength and the wear rate of the implants [36]. However, the regulatory bodies in Europe did not require clinical trials for this class of device, and thus no such trials were conducted in relation to the approval process in Europe [34],[35]. Any MoM hip implant could be approved, i.e. receive CE mark, if the manufacturer was able to demonstrate similarity to a product, which had already been on the market, and implants such as metal-on-polyethylene (MoP) hip replacements were already in use for many years [38]. Figure 3 presents the elements of DePuy ASR TM XL total hip replacement.

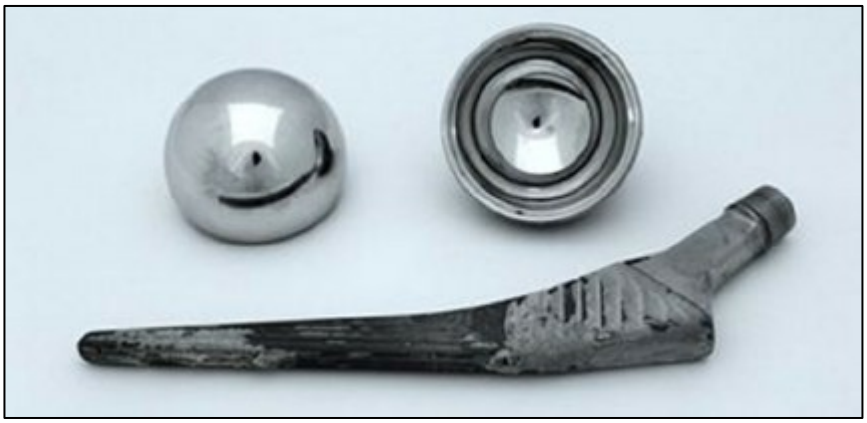

Figure 3. *Elements of DePuy ASR TM XL total hip replacement: femoral head shown top left, acetabular cup shown top right and femoral stem shown in the bottom. Adapted from* [39].

TA alert nr 1: no clinical trial was performed before marketing the product. It has been reported that simulator tests do not adequately reflect conditions imposed on the implant by the living tissue [36]. For surgeons, it is obvious that joint replacements must be clinically tested before they are introduced to the market, so that their functionality and safety can be proven and so that the company can avoid investing in and selling a device, which

would turn out ineffective [36]. And some implants failed as soon as two years after implantation, which means that clinical trials did not have to take many years to expose the flaws of MoM implants [28],[36]. Moreover, regulators in Europe had a flawed approach to definition of “similarity” of technologies. Properly assembled team of professionals should have determined, whether the level of “similarity” of MoM bearings to hip implants made of other materials was sufficient for MoM implants to be approved based on this principle, or insufficient, implying a need for clinical testing. Assessors should always be selected according to the skills needed to adequately evaluate technology and the full range of its properties, advantages and hazards related to it. The proper assemblance of assessors’ team is a manifestation of (H)TA’s context-dependency.

5.4 Lack of transparency of European approval processes

DePuy MoM hip prostheses received CE mark, from a so called “notified body”, a private organisation performing premarket approval of medical devices for EU governments, which in this case was a British company, BSI [35],[36]. The data about the devices delivered by DePuy to BSI have never been revealed to the public due to “confidentiality obligations” [30].

TA alert nr 2: The approval process was performed by a commercial entity based on their internal protocol and criteria, which were not known or verified by any other stakeholders. Such system is not transparent and constitutes a danger, enabling collusions and corruption. Activity of such institutions should be closely monitored by governmental organizations and TA agencies to prevent malpractices and ensure transparency, impartiality and integrity of the approval procedures.

5.5 The approval (and disapproval) for American market

In 2008, DePuy’s THRs were approved by the FDA in the US in a similar way [29]. The so called “510(k) clearance process” grants approval for devices based on “similar equivalence” principle: it is enough to demonstrate that the product is similar to another one already available on the market, and the clinical trials are not required [36],[37]. However, DePuy’s resurfacing method was a new technology in America, therefore it had to go through more scrupulous procedure, which required conducting premarket clinical trials for assuring implants’ safety and effectiveness [35],[36]. During the study MoM resurfacings displayed a concerning rate of femoral neck fractures, even when arthroplasties were performed by experienced surgeons, who cooperated with DePuy in implant design process. This resulted in withdrawing the approval application by the company, and so

their resurfacing implants were never approved by the FDA [36]. Also, the failure to prove device's safety and effectiveness through clinical trials in the US did not cause the company to reconsider marketing of the product in Europe.

TA alert nr 3: If pre-marketing clinical trials had been performed for both resurfacing implants and THRs in the US and Europe, it is possible that MoM implants would have never been accepted for use in patients. At least in the US, failure rate indicated by clinical trials effectively prevented resurfacing implants from wider use. Even small changes in design can dramatically change the performance or survival of a device, especially in biological environment. Therefore, whenever a manufacturer declares "similar equivalence" of their new device with an already approved device, they should be required to specify every alternation the new device introduces in comparison to the older one. Moreover, it should be obligatory that manufacturer clarifies what impact on the patient the differences would have. Subsequently, a properly assembled team of independent assessors should review manufacturer's report and evaluate the new device to confirm or discredit manufacturer's statements. Authorities and regulatory bodies should require, that safety of any medical device is unambiguously proven based on scientific and clinical evidence. Invasive medical treatments, such as hip arthroplasty, should automatically imply a need for premarket clinical verification of technology components' safety, and not as separate parts, but as a whole device. Then, it should be required from the companies to inform all relevant regulators about any prior failed attempts to be granted regulatory approvals for marketing. Such precautions would help the decision makers to make better-educated decisions regarding the device. [29] Optionally, an open database collecting all filed, approved and failed applications, accessible for all interested parties could be created to ensure better exchange of information.

5.6 Changes of implants' dimensions and manufacturing variations

After introducing their products to markets, DePuy started modifications of the implants with intention to optimise their use and range of applications. And so, the taper connections were made shorter and the neck diameter decreased to enable greater range of motion for the patients [30]. DePuy, inspired by the fact that for other types of implants larger femoral heads were proven to lower the failure rate, started introducing bigger and bigger heads into MoM hip implants [33]. Surprisingly, the surgeons were not informed about the changes; in fact, the products were still marketed with the old specifications [30]. However, bigger femoral heads in combination with shorter tapers caused waggling of the joint, resulting in increased wear and corrosion, and so they started to be noticed

by the surgeons [30]. The company was aware of an increased failure rate, but still over five years after implementing the dimension changes, company's senior engineers were not able to find the reasons for the failure, and finally DePuy sought help from Southampton University. Nevertheless, the implants were still being implanted and the company did nothing to stop it. [30] In addition, later studies discovered that the dimensions of implants did not always meet the specifications. Those manufacturing variations also contributed to increased failure rate, especially for implants manufactured after 2006, which implies that changes in production processes were introduced around that time. [40] The FDA was successful to identify the shortening of tapers but decided this change did not imply safety or effectiveness issues with the device; the regulators in Europe failed to notice any changes in implants' dimensions until they were notified by the surgeons [30].

TA alert nr 4: It has been already mentioned that even small modifications can influence a device's functionality. Therefore, before implementing size changes in MoM implants, DePuy should have thoroughly studied their effects on the implants' performance and survival. Also, surgeons should have been informed about the changes, so that they had been aware they were implanting virtually new implants. Clearly, DePuy's internal quality control of the production processes failed, as it can be seen from the increasing nonconformity in product dimensions leading to earlier failure of implants manufactured after 2006. Acquisition of new production processes, if such took place, should have also been communicated to the surgeons, so that they could follow if any variations in quality or performance of the devices appeared after that. It is unsettling that the FDA failed to recognize the consequences of design changes introduced by DePuy. Even if the agency was not aware of the significance of such modifications for implants, it should have required that DePuy demonstrates their reasonability or at least neutrality for implants' functionality.

5.7 Safety issues of MoM hip implants

Wear particles from MoM hip implants caused immune response, necrosis and inflammation in surrounding tissue. Figure 4 shows explanted elements of DePuy's ASR products and samples of fibrotic and necrotic tissue from the implantation site. Metal debris from the prostheses has been proven to be genotoxic and it is thought to be potentially carcinogenic. DePuy knew about all these hazards, however, the company never issued any warnings [30]. On the contrary, when the concerns about the potential carcinogenicity of metal ions released from MoM implants aroused, the sales representatives were provided with a paper written by one of the prosthesis designers, Thomas Schmalzried,

which was intended to oppose unfavourable evidence [30]. Moreover, the long-term consequences of increased metal ion concentrations in human body are unknown to this day, and no toxicity thresholds have been established; consequently, there were no indications for safety of MoM implants when they were introduced onto the market [30]. In July 2007, after debating on MoM implants safety, MHRA's Committee on Safety of Devices decided that patients should be informed about the potential risks and that they should sign a consent for implanting those prostheses. Unfortunately, the Committee failed to effectively communicate this to surgeons, who were not aware of such recommendation. [30]

Figure 4. *Explanted elements of DePuy's ASR hip implants and samples of fibrotic and necrotic tissue from the implantation site.* [41]

TA alert nr 5: Virtually nothing was known about biocompatibility and long-term safety of MoM implants when they emerged. The technology was adopted too rapidly, without adequate evidence for its reasonability [38]. A similar level of uncertainty would not be acceptable for new medications [30]. The regulatory requirements for implants should not be more forgiving. It is not surprising that some call introduction of MoM implants "a large uncontrolled experiment" [30]. It was unethical of DePuy to induce risks of implanting toxic, genotoxic and potentially carcinogenic material in patients, to hide the suspicions the company had about the adverse effects of metal debris in the body, and to

spread misleading information. The risk taken by the company and the surgeons' community by implanting MoM hip replacements was unnecessary, as there were other options available in the market [31],[35], and there was no scientific evidence not only for superiority of MoM bearings over other ones [30], but even for their reasonability [38]. The continuous incompetence or unwillingness of regulatory bodies to assure patients' safety in this case should not be ignored. Internal periodical revisions of protocols and quality control must be done in such organizations, and a system of personal penalties for incompetent decisions need to be created to avoid corruption and assure patients safety.

5.8 Biased data and intended misinformation

As already mentioned, surgeons who cooperated with DePuy to create MoM implants, helped the company to provide biased, favourable or misleading evidence [35],[36]. They have been paid large royalties for participating in the process of implant design, consulting etc. They were also on a mission of promoting MoM implants and convincing other surgeons to use them [36]. In 2007, DePuy was fined for paying "unlawful payments" to surgeons to use their products in years 2002-2006 [42]. The surgeons, who were not paid by the company, were often misguided by DePuy's marketing campaign. Promotion material was purposefully designed in such a way, that made DePuy's products look like they generated fewer metal debris than other implants [36].

TA alert nr 6: It is now clear that DePuy and surgeons cooperating with the company were driven by the desire of personal benefits, and impartiality or objectivity were excluded from the process of TA. This resulted in producing biased data about their technology, its effects and potential risks it might have brought along. In the light of reports of biased data produced by the commercial organizations, this might not be surprising, however, such practices should be diminished as they constitute a great danger for entire populations. Introducing impartial assessors into companies' evaluation teams could help in controlling the quality of companies' internal assessment processes. Alternatively, independent, parallel TA would provide high-quality, unbiased information, which could be compared to the results provided by the company. More would be known about a given technology and decision makers would be equipped with better tools.

5.9 Delayed requirement for post-marketing studies

After approving DePuy's implants for their markets, the authorities in the US and in Europe did not demand post-marketing follow-up studies. Only in 2011, when the controversies on MoM implants already aroused and spread worldwide, the FDA required manufacturers to monitor the patients, in which implant failure could lead to serious consequences. [30]

TA alert nr 7: Follow-up studies should have been demanded from the manufacturers the moment MoM implants were introduced onto the markets, especially for those implants, whose approval process did not require pre-marketing clinical studies. Those could have exposed the flaws and hazards of MoM implants much sooner and could have led to faster recall of the products.

Clearly, many TA missteps have been taken in the process of introducing MoM implants onto markets, both on the side of the manufacturer and on the side of regulators and authorities. In 2010, DePuy voluntarily recalled one class of their implants, ASR, however, it happened after many years of denial, and new class of MoM implants, Pinnacle, made from the same material, was offered by the company as an "alternative", which shows the company has never accepted the failure [36]. DePuy's delayed recall and lack of adequate reaction regardless concerning evidence and company's awareness of faulty implant design resulted in 20,000 lawsuits around the globe by July 2019 [43]. It is noteworthy that lawsuits regard both ASR and Pinnacle technologies [43]. In the end, the risks of MoM implants received the attention they should have gained from the beginning, nevertheless, by that time hundreds of thousands of patients have been already exposed to toxic substances and have suffered from their adverse effects.

5.10 How the disaster could have been avoided

In the case of MoM implants, adequate HTA was not performed, which led to significant harm for thousands of patients. This disaster, however, could have been prevented, if only several HTA steps have been conducted properly. If premarketing clinical trials have been performed, MoM hip implants would probably have never entered the markets. DePuy, assisted by cooperating surgeons, produced purposefully biased data about the technology, and withheld unfavorable information. The manufacturer did not verify the impact of dimensions changes on the safety of their products prior to implementing them. The company did not inform regulators nor surgeons about those changes. Also, no notification about a rejected approval application in the US was issued to regulators in Europe. The company did not consider it necessary to reflect on the safety of their products

based on the mentioned rejection. In addition, product quality control was not performed, or the manufacturing variations were not considered important enough for the company to try to eliminate them or withdraw the faulty exemplars from the market.

If the company performed proper HTA:

- The company would conduct clinical trials.
- Ideally, based on the high rate of failure, the clinical trial would be stopped, and the product would be identified as not suitable for use in humans. Unbiased reports would be published to spread the knowledge. Possibly, further research and attempts of improving the design would follow. The company would not bribe the experts cooperating with them, so that reliable, high quality data would be produced. The company would seek for their results to be confirmed by independent HTA agencies or research teams. In a perfect world, the motivation for both the company and the surgeons cooperating with them would be solely the will to help patients and to provide high quality scientific evidence.
- Alternatively, if the product would pass onto the marked regardless of unfavorable clinical trial results, DePuy would test any modifications before selling altered implants. The company would find out about the adverse effects and would never market modified implants. The production processes and any innovations of those processes as well as quality of every product would be controlled and monitored. This way non-conformity in product dimensions would be avoided and the failure rates would not rise.
- If any dimensions modifications would turn out to improve implants' performance or survival, they would be communicated to regulators for approval prior to implementing and marketing new devices. If any approval application would be rejected, the company would notify other regulatory bodies, who might be concerned with the rejected product.

HTA missteps happened also on the regulatory bodies end. Their approach to similarity of medical devices was flawed, which led to improper classification of DePuy's MoM hip implants. No independent assessment of DePuy's products nor revision of the company's declaration took place. The approval process in Europe lacked transparency and reliability. Follow-up studies were required only after controversies aroused. The communication between different regulators was non-existent and was ineffective between regulators and surgeons.

If the proper HTA was performed by the regulators:

- An assembly of appropriately selected experts would be formed within both the FDA and European regulatory bodies to perform independent and objective HTA of MoM hip implants. These assemblies would understand that the principle of similarity cannot be applied to hip implants. In general, the definition of similarity would be reconsidered, and similarity requirements would be specified for different categories of devices. Premarketing clinical trials would be required for DePuy's MoM hip implants. The assessors would review reports provided by DePuy and would evaluate the devices to verify the trueness of data from company's reports. Clinical trials would indicate the hazards resulting from implanting MoM hip prostheses, reviews would reveal DePuy's attempt to mislead the audiences, and the technology would be rejected as being harmful for patients.
- Self-regulation, self-monitoring and internal quality control processes would take place periodically to ensure that regulatory bodies fulfil their role as objectively and accurately as possible. Repeated revision of procedures and methods as well as regular trainings for the assessors would be implemented. The assessors would not grant certifications for medical and health technologies easily and the risk of corruption would be avoided.
- A good interorganizational communication system would be developed, so that the regulators could make the best educated decisions. This way the rejection of DePuy's MoM resurfacing technology by the FDA would reach European regulators and the approval of the device for European markets would be revised. Also, effective ways of information exchange between regulators, health care facilities and relevant groups of professionals would be developed to enable fast dissemination of important alerts, warnings and recommendations.

6. CONCLUSIONS

Researchers agree that society, businesses and health care rely increasingly on technology and that the rate of technological innovations is greater than ever before. However, technology is only as good as the research and knowledge standing behind it. Since it is created by humans, who obviously have limited capabilities, technology fails sometimes. As technology plays such an important role in today's world, technology failure can be very costly; especially health technology malfunctioning may have disastrous consequences. It may cause injuries, enduring health problems, or even deaths. From the point of view of health care providers and research facilities, health technology reversals may cause huge economic losses, waste of resources, legal issues, and what is probably most undesirable, loss of credibility and public trust. Therefore, it is necessary that there exists a means to reduce technology failures to minimum. This thesis demonstrates that carefully designed, structured, standardized and well conducted TA allows safe and proper use of technologies and as such can be a powerful tool in preventing technology failure. Based on literature review, a subjective collection of the most significant ingredients and steps of TA in the context of failure prevention was proposed. Those elements are: (1) Impartiality and objectivity; (2) Planning; (3) Defining criteria of evaluation; (4) Forecasting adverse effects; (5) Technology comparison; (6) Periodical reassessment. A TA process containing all these elements is the best strategy to prevent a technology failure and its potential tragic consequences. Those TA ingredients were found by the author to be critical for producing reliable, understandable, standardized and applicable information about technologies. Only such information could assist decision makers on different levels and in various parties of the health technology industry and medical care delivery to create effective and safe system of health care. Such information could also boost research and innovations by providing high quality data, which would be comparable and further processable.

The last chapter of this thesis used real life example of technology failure to demonstrate how misconducted technology assessment led to wide adoption of metal-on-metal implants, which had catastrophic results. Suggestions on what could have been done to prevent this large-scale failure were presented. The cardinal mistake was lack of premarketing clinical trial, which was not required by regulatory instances for approving the implants to the markets. The principle of technological similarity was misinterpreted by regulators in this case. This led to lack of scrutiny in the assessment of MoM hip implants. The missteps taken by the company were unreliable, biased data provided for surgeons,

not revised by independent HTA agencies nor regulatory bodies; intended disinformation; hiding unfavourable evidence; and introducing untested modifications without communicating them to the consumers or regulators. DePuy's case is also an example of scientific evidence replaced by corruption. It should be treated as a warning by health technology assessors, showing that lack of objectivity, impartiality and scepticism in HTA results not only in false information and discredit of science, but also in disastrous consequences for entire populations.

Interestingly, it is not easy to find scientific articles pondering particular cases of technology failure (with the exceptions of glucometers and MoM implants). As technology failure cases indicate how poorly conducted TA can lead to casualties and delays in achieving successful research results, they should be studied more frequently and more intensively, especially by TA specialists. Also, analysing technology reversal incidents ought to be a field of interest for biomedical engineering as a tool of tracing the ways of technological development and mistakes made on the way. Exploring reversals could sensitize engineers to a broader range of problems, which should be addressed when a new technology is developed. Engineers could avoid making mistakes by learning on those made earlier by their peers. Such studies would provide an insight into real history of a technology, indicating the patterns and directions of innovative thinking as well as its outcomes. All of these would result in improvements in the whole research and development area.

Since (H)TA is strongly context-dependent, one universal strategy of (H)TA cannot be created. Nevertheless, some universal rules would significantly improve the quality and compatibility of information produced through (H)TAs. Uniform reporting system and a common database of performed (H)TAs should exist to facilitate future execution, learning and design processes, and to serve as a reliable source of information for all groups of interests. Authorities could publish recommendations and lists of available alternative methodologies for evaluating certain categories of devices to enhance uniformity and comparability of (H)TAs performed for products being within one such group. A system of peer reviews could be created so that possible mistakes or gaps of executed (H)TAs could be pointed out. The events organized by existing organizations focused on (H)TA could be better promoted, so that more professionals and students, for whom this topic is important, could participate in those events and follow their outcomes. As some authors report lack of qualified professionals or insufficient training provided for those already involved in (H)TA processes [5],[7],[8], more attention should be paid to the process of recruiting, educating and training future and present (H)TA professionals. Students of sciences related to health technology ought to get acquainted with the discipline

and its importance already in the early phase of their studies. Those who would find the field of (H)TA interesting, would get a chance to specialize in it and use any opportunity to increase their knowledge and practical skills. Especially BME students and professionals should be increasingly included in the discipline of (H)TA.

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