

Improving Health Through Healthcare Technologies Assessment Development: Further Perspectives for HTA Tools Development

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Abstract: The HTA progress requires analyses of existing and forthcoming needs as well as the development of tools meeting these needs. The proposed research presents hierarchical scheme for HTA development created based on Environmental Scanning and Analytic Hierarchy Process (AHP). The scheme presents the overall prognosis of HTA development indicating the key blocks of needs and relevant tools. Each of these tools are considered to be exclusively important for HTA development. Local registries are considered to be the priority for further HTA improving meeting more needs and providing less risks comparing to other tools.

Keywords: Health Technology Assessment, HTA development, patients registries, prognosis, forecast, Environmental Scanning, Analytic Hierarchy Process.

1. INTRODUCTION

Healthcare Technologies Assessment (HTA) is at the very end of the data generation chain assessing the value of medical intervention and allowing putting together the entire set of data on the risks and benefits associated with its use. Consistent data generation includes information on the effectiveness of individual clinical trials and systematic reviews that allow assessing the full range of clinical effects associated with the use of a specific technology or treatment of nosology, and summarizing them in the form of clinical guidelines in accordance with WHO requirements. Following these stages, a comprehensive clinical and economic assessment of medical technology makes it possible to assess not only medical, but also economic and social consequences of the intervention. [20] Since the eighties of the last century, organizations specializing in complex clinical and economic assessment of medical technologies (or medical interventions) have been established in countries. These organizations carry out their activities at the level of an individual health facility, a region within the country, at the level of a country or even a group of countries. They may have different lists of tasks to be solved and methods used. The existing progress of research as well as changes in the epidemiological, economic and social environment present new requirements for Health Technologies Assessment (HTA), which is the base for the rational use of medical technologies. HTA was initially established in high income countries but low- and middle-income countries also understand the need for rational approach in healthcare technologies applications and consider it as the basis for effective healthcare systems, achieving social stability and providing labor resources for economic development. In line with this the Member States of World Health Organization approved the resolution "Health intervention and technology assessment in support of universal health

coverage» at the World Health Assembly in May 2014 (WHA67/2014/REC/1 (who.int) WHA 67.23). Initially, there were different approaches regarding assessment and allocating or redistributing resources for the implementation of innovative healthcare interventions in high- and low-middle-income countries but currently, there is a process of harmonization of the requirements and methodology of HTA in both high- and low-middle-income countries. There is also a revision of the tasks facing HTA as well as, the development of new methods of evaluation and interaction with decision-making systems. In addition, a legislative regulation for HTA at a regional level has been approved recently (REGULATION (EU) 2021/2282 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 15 December 2021 on health technology assessment and amending Directive 2011/24/EU). However, the process of modern HTA creation is not finished yet [12, 13]. The harmonization of HTA objectives and methodology allows us to assess the key principles of development of HTA as a tool ensuring Global Health [2, 4, 8, 9, 10, 16, 19, 24, 25].

2. OBJECTIVES

The objectives of this research were:

1. To create a comprehensive hierarchical structural scheme presenting the key information and technological blocks and reflecting the forecast of the HTA development;
2. To highlight and determine the most relevant areas of development of practical tools meeting existing and promising HTA needs which can be considered the objectives for further research and development of practical tools.

3. METHODS

Two key methods were used to conduct the study. Environmental Scanning was used to search and analyze data on the current state and prospects of HTA development. As a result, key information messages were identified and then structured into a hierarchical scheme using the Analytic Hierarchy Process (AHP) by 11 experts specialized in HTA and Healthcare Management.

Environmental scanning was based on the systematic review of literature (PubMed and EMBASE; 353 relevant publications) and other modes of communication including available English-language websites of organizations assessing healthcare technologies and the search for "grey" literature using Google Search as well personal messages [18, 21]. The determined emerging issues presented both the specific topics and their general environment making possible identifying important emerging issues that may constitute either obstacles or opportunities. [22, 17, 32,]

The obtained data was used for Analytic Hierarchy Process (AHP) which is a structured technique for organizing and analyzing complex decisions using accurate approach to quantifying the weights of decision criteria estimating the relative magnitudes of factors through pair-wise comparisons. First step in AHP was the decomposing of decision problem into a hierarchy of more easily comprehended sub-problems, each of which can be analyzed independently. Next step included systematical evaluation of various elements of hierarchical structure by comparing them to each other two at a time, with respect to their impact on an element above them in the hierarchy. In making the comparisons, the experts assessed both concrete data about the elements and their judgments about the elements' relative meaning and importance based on "environmental scanning" data. These numerical values reflected the number of links with higher hierarchical elements and the capability of the lower element to meet needs of these higher elements. Thus, the higher numerical weight was delivered to the element providing the most significant impact on the whole hierarchical structure and represented the ability to achieve developing HTA needs [7, 26, 27, 29].

4. RESULTS

The hierarchical structure of the main information blocks for HTA development is shown in Fig. 1. It demonstrates the following hierarchical levels: key needs and requirements for HTA; addressing of these needs to more specific questions and participants; possible solutions and practical tools; threats and conflicts that may arise when using the proposed tools for implementing solutions and also the description of potential conflicts resolution.

The key needs included relevance, reliability and timelines for the interventions availability and were addressed in more detailed subjects.

Relevance of expert opinion with local and regional peculiarities and the needs of the local healthcare systems. It can be addressed to availability and use of local data reflecting the morbidity, mortality, epidemiological and demographic data as well as the other features of the territory or administrative unit including the results of local clinical trials and local Real World Data evidence (RWD/RWE). The expert opinion must be relevant to the interests of various stakeholders in addition to healthcare authorities and patients, that can somehow be involved in the implementation of management decisions and are associated with the outcomes of their implementation. A separate need concerns the compliance of expert opinions with formalized requests, regulatory documents and standard operating procedures of the local healthcare systems.

Reliability of expert opinion ensured by the quality of the source data, analysis methods and evaluation criteria. The quality and reliability of source data means appropriate amount of evidence including disease burden, reports on international and local clinical and academic trials, systematic reviews and clinical recommendations (Global evidence) related to safety, efficacy, efficiency and effectiveness. Reliable methods and criteria assure that practical results of regulatory decision and redistribution of resources will match the expert forecast both in the same criteria and figures.

Timelines are the dates when the medical technologies in question become available to those who need them. Modern medical technologies can significantly add years of life and improve its quality. Ensuring early availability means added years of quality life (QALY) for patients. It is provided by various schemes of early access of patients to therapy before market authorization, by shortening of market authorization timelines and market entry of the medicines or by using more effective scenarios providing medications to patients after market authorization. Shortening the timelines for reimbursement has also an impact on ensuring accessibility through the interest of the industry. On the other hand, since the industry is one of the stakeholders in the evaluation of healthcare technologies and its interests should be taken into account together with the interests of other participants.

Identified solutions included stakeholders and patients' involvement, access to local, regional and Global research and disease burden data, data and expertise sharing, pre-launch access for patients, early access to clinical trials data and faster data processing. Early HTA was also reviewed as a solution shortening timelines for reimbursement.

The development and humanization of society lead to an increase in social groups that have their own interests in ensuring the availability of medical technology to patients. Often these stakeholder groups have conflicting interests, which, however, should be taken into account when making a decision. Stakeholders' needs can be met by their involvement in the HTA process. The involvement of patients is presented in most publications as a separate task, which is due to their obvious exclusive role in the assessment and decision-making process. A necessary element ensuring effective involvement of stakeholders is access to local information on the clinical, economic and social burden of the disease, as well as possible solutions and their outcomes is necessary for the effective participation of various stakeholders in the process of analysis, consensus finding and decision-making.

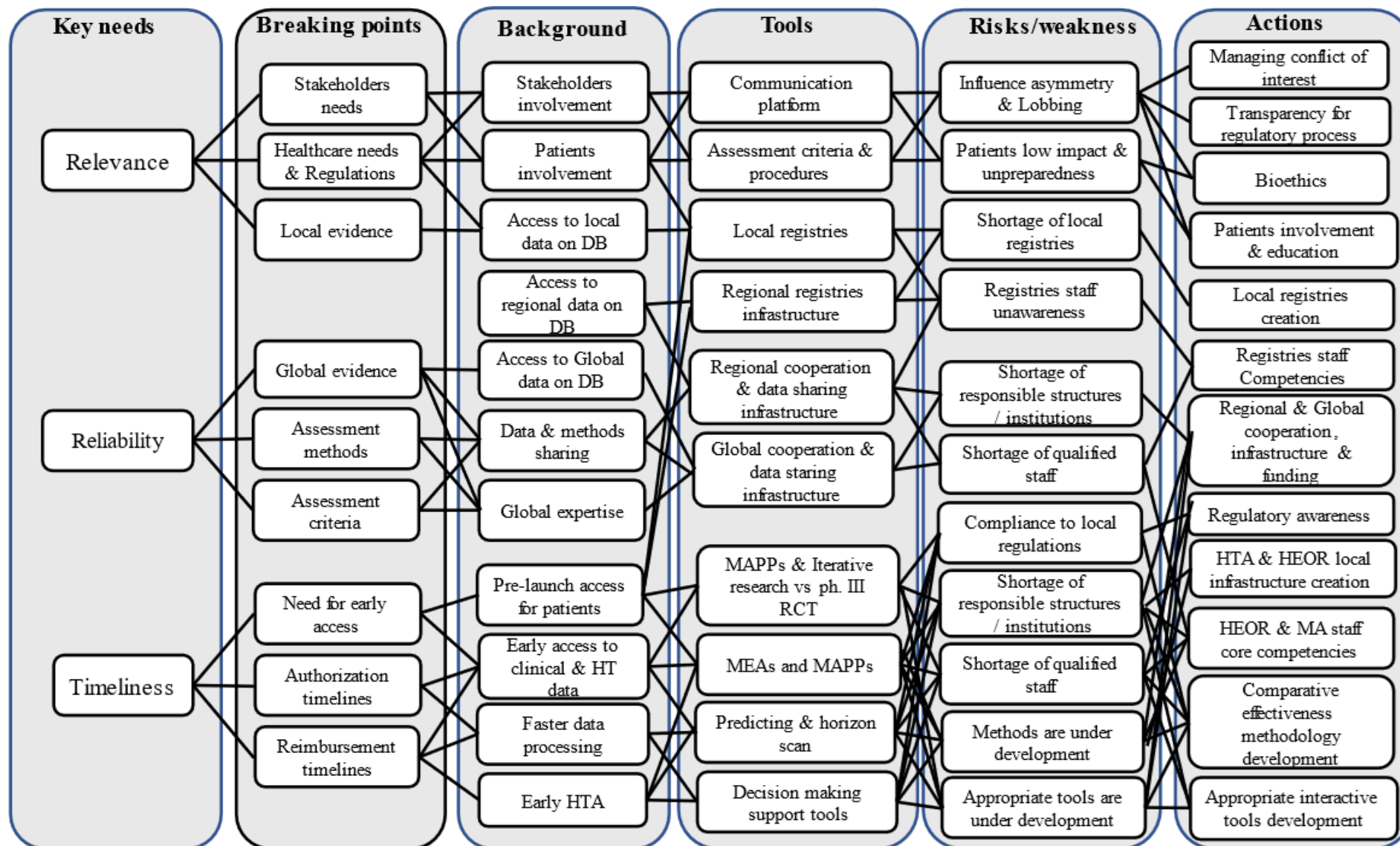


Fig. 1. The hierarchical structure of the main information blocks for HTA development

Local laws and regulations are the background on which the assessment takes place and the results should correspond to this legislation. At the same time, however, there is also feedback, which consists in the influence of stakeholders, especially patients, who, based on local data on the burden of the disease, have the opportunity to change legislation in accordance with social needs.

Global evidence consists of the data that is received and stored at the local, regional and global levels which sometimes have differences in quantity and quality of data. Global databases, such as Cochrane, G-I-N and others, accumulate and process with all available data providing this way the most complete and evidence-based information on diseases and treatments. Local data are included in global data as an integral part, but they are also of some interest, reflecting local specifics and, obviously, should be taken into account when conducting local assessments. Regional databases allow to expand the sample and increase the reliability by combining similar local evidence based on epidemiological, medical, economic, cultural, linguistic community of countries in the region. Regional cooperation serves also as an intermediate link between local and global collaboration making possible accelerating accumulation and increasing accessibility of evidence for global cooperation. Methodology and criteria of assessment are rather related blocks, and their development is more intensive and efficient in case of data and expertise sharing making possible to spend as much resources as possible but to have an opportunity to use the entire results of cooperation.

Early access to patients can be achieved by pre-launch participation in clinical studies or any other similar activities. To some extent it is also linked to patients' data making possible to speed up the process of screening and enrollment of eligible patients into studies. Authorization timelines in terms of HTA are closely related with early access to clinical trials data as well as faster data proceeding. It also makes possible to use early HTA technology and finally to reduce the time for reimbursement.

Section tools is of the very interest for the development of health technology assessment, since it allows you to identify the main areas of research, as well as to rank them by selecting the most effective, promising and relevant.

Communicational and informational platforms

The first thing that experts face when assessing various outcomes and developing predictive scenarios is the need to combine multidisciplinary information and compress it into several verbal statements that can be used to formulate regulatory documents that determine the allocation of resources. Information platforms serve as a tool for information transformation, structuring the studied information into blocks, which, in turn, are connected by certain relationships and algorithms.

Clinical trial was reviewed as an example of such platform. Data generation consists of thousands of data flows between blocks of information represented by dozens of clinical indicators obtained at various stages of screening, treatment and follow-up of hundreds or thousands of patients observing in dozens of clinical centers. Upper levels of information blocks include, but are not limited to, comprehensive information on individual patients (case report form), on clinical centers (investigator file), aggregating information on individual safety and efficacy indicators for all included patients or stratified groups, for example, by age or by presence of concomitant diseases. Obtaining and processing of all this information require qualified personnel, appropriate equipment for measurements, recording, transmission, accumulation and processing of multidisciplinary data resulted in expert analysis and a conclusion that fits just few statements.

These activities require coordinated action of various specialists including physicians, laboratory specialists, pharmacists, data management specialists, medical writers and others. HTA requires also assessment of economic and social outcomes alongside with the clinical

ones generating the need for interdisciplinary interactions between specialists and stakeholders with conflicting interests developing mutually acceptable solution. The concept of "informational platform" also includes blocks of information and transparent algorithms making possible communicating specialists and stakeholders with different background and areas of interests.

As a result, further HTA development requires a hierarchical complex of information and communication platforms assessing data, ranging from monitoring and forecasting of public health, preclinical, clinical and clinical-economic research to social outcomes forecasting and resulting in prognostic scenarios on various issues related to public health management.

Modern information and technology platforms have a complex system of connections, and a change in one of the elements of this complex leads to a change in other elements. Every intervention, from the simplest to the most complex, has an impact on the overall system, and the overall system affects every intervention [30]. Further developing of the hierarchical structure and interactions between these platforms as well as the existence of regulatory and legislative bodies determining these elements and the degree of their impact on the system as a whole, we get a classic "blockchain" structure which is rather plausibly describes the interaction of elements of the overall public health management information platform. [3].

The creation and further development of these information and communication platforms requires the appropriate development of digital infrastructure and digital technologies capable of proceeding with big data and identifying links and dependencies between health indicators and multidisciplinary factors forming these indicators.

The main risks identified by experts in connection with the creation of communication platforms are the possibility of incomplete or asymmetric representation of stakeholders and their unpreparedness, primarily of patients as the main stakeholders. Accordingly, the resolution of these conflicts is associated with transparency of the assessment decision making process, and conflict-of-interest management mechanisms and training of key stakeholders. Bioethics is of great importance for creation of communication platform considering it as a science and technology that provides solutions to interdisciplinary and interdepartmental issues related to human health in conditions of conflicting interests.

Assessment criteria

The allocation of resources in healthcare is a rather complex process that ensures a transparent and rational procedures resulting in clear decisions. As a result, various criteria have to be considered within the framework of HTA and simplified to a one-dimensional solution – to "include or not include" technology in the reimbursement lists or similar documents [1, 6, 11]. These are criteria that often conflict with each other [15]. Insufficient awareness of the value elements considered throughout the decision-making continuum, as well as the lack of transparency in decision-making, can potentially create tension among stakeholders [31]. As a result, a comprehensive "value assessment approach" is increasingly being used in the assessment of healthcare technologies, which requires a clear list of criteria to be taken into account [23]. In addition, it is a generally accepted principle that decision-making in the field of healthcare should be based on evidence-based scientific data [26], which call for the need for a scientifically based method of evaluating more than one aspect of the problem of decision-making at the same time.

Usually the country data, even obtained on the basis of an integrated approach are almost never complete and can only reflect the main trends in the development of the local HTA, which imposes certain restrictions on the results of any analysis in this area. As a rule, countries use a set of methods even if only some of these methods are fixed by law. The multicriterial approach leads to attempts creating the universal tool assessing multiple criteria at once and providing clear conclusion on the matter.

The development of evaluation criteria (and, accordingly, evaluation methods) face the need to combine local data and global data based on local legislation, taking into account numerous interdisciplinary factors, forming a forecast of medical, economic and social outcomes and the possibility of a simple conclusion acceptable with local regulatory procedures.

The key risks and potential conflict are also linked to stakeholder's unpreparedness and asymmetric representation of particular stakeholders needs. This may include, for example, the creation of assessment criteria aimed at saving money when the position of payers is dominant or, conversely, the criteria which may cause unjustified expenses when the position of industry is dominated.

Conflict resolution is related to the transparency of criteria and procedures, education of stakeholders and especially patients, conflict of interest management and the organization of communication platforms based on bioethics principles.

Local registries

Patient registers are a special case of information platforms allowing receiving and analyzing data on a specific disease. The term local implies that the register collects limited information that is not integrated into larger unified registers, and serves to accumulate and analyze information on individual diseases at its own level (hospitals, cities, countries).

Local registers are the most effective and reliable tools for obtaining RWD/RWE information about the number of patients, health determinants and other factors related to the occurrence of the disease, the course of the disease, treatment features and outcomes. Depending on the registries structure and the information entered, they can be a source of data on the economic and social consequences of the disease. Local registries are the basis for regional and, potentially, global registries that provide comprehensive information on diseases. There are two main directions for the further development of registries. The first one is linked to increasing number of parameters including information about social health determinants as well as economic and social outcomes that can be very helpful for HTA and healthcare decision making. The second direction is linked to merging of registries databases wherever possible and increasing the sample size of the studied population. Combining of both makes possible increasing the reliability of expertise and relevance to stakeholders and healthcare authorities' needs. An opportunity to speed up patient's enrollment in clinical trials and to use the existing patients' databases for early access schemes and iterative studies can be considered as additional advantage of such development of registries.

Difficulties and conflicts are primarily related to the insufficient number of available local registers (and appropriate institutions capable creating such registries) and their characteristics. The majority of registers were created to address specific issues and included only patients who received the studied therapy for specific diseases or by medical institutions for their specific tasks and research programs. The infrastructure and financing of registers need a major reassessment that they can meet harmonization requirements and could be used beyond these existing tasks. The lack of qualified personnel with sufficient skills ensuring harmonization and extension of the of registers functions are also an issue.

Accordingly, the resolution of these problems is associated with the reassessment of infrastructure and funding of registries and education of qualified staff as well as creation of specific tools that allow obtaining the necessary data, processing them and presenting real time assessments and. The creation of such tools is closely connected with cloud information technologies that provide optimal opportunities for obtaining and processing information at the current level of science and technology development, as well as the harmonization of registers at various levels (local, regional and global) and the integration of the entire complex of RWD/RWE in HTA process and decision making in healthcare.

Regional and Global Registries

Merging and harmonization of registries beyond the countries was appointed as a special task due importance of the Global access to clinical data. [14]

Local legislation provides country-special requirements on data transfer but there are some opportunities in case of existing agreements of legislative uniformity in groups of countries [5]. As a rule, these countries have similar historical linguistic and cultural background as well as exiting economic and healthcare cooperation. Thus, regional registries were considered as a separate tool and intermediate stage on the global data flow significantly facilitating the task of transparency and integrity of clinical, economic and social data on disease burden and treatment effects.

The development of such registries also needs to merge and combine the data from the smaller and subordinated ones as well as the expanding the list of indicators including different diseases data and social health determinants, clinical, economic and social outcomes. The amount of interdisciplinary data and need for processing previously blinded (personal data) or generalized information (due do local legislations) requires implementation of specialized digital capable collecting and processing with this data in real-time frames.

Difficulties and solutions associated with local and global registries are the same as for the local ones: restructuring and re-targeting registers to more complex tasks and the corresponding reallocation of resources and information structures, staff training and creation of appropriate tools (including cloud-based technologies) for the registries maintenance and data analysis in real time frames.

Regional and Global Cooperation

HTA development reviewed in this study concerns only the one block of the information platform for expert support of healthcare decision-making. [6]. The main objective of the platform is to ensure the continues and appropriate transformation of the multidisciplinary data flow. International cooperation allows to merge local data and to use a win-win strategy in methodology development and achieving global core competencies when each party invests as much resources as it can, but has the opportunity to use the complete results of the research or education. Each party invests as much resources as it can, but has the opportunity to use the complete results of the research or education programs.

Regional structuring of cooperation may significantly increase efficiency of this cooperation. Common cultural, linguistic, economic, educational features as well as the traditions of scientific activity facilitate and accelerate the exchange of information. Consistent collaboration on local level followed by regional and global cooperation and the counterflow of expertise from global to regional and local levels considered to be more effective comparing to the flat structureless global cooperation. As a positive example, we can consider Guidance International Network (<https://g-i-n.net>), which unites 7 regional associations (GIN Africa, GIN Arab, GIN Asia, GIN Australia & New Zealand (ANZ), GIN Iberoamerica, GIN Nordic, GIN North America (NA)).

Difficulties related with regional and global cooperation are similar to those ones related with registries. The main are the lack of appropriate organizations and staff. These issues can be solved by creation of relevant infrastructure and development of the personnel global core competencies.

Facilitating and/or ensuring early access to interventions

This block consists of different methods aimed at proving earlier access for more patients and thus increasing the global value outcomes for global health. Initially they were reviewed

as different methods with similar characteristics including: supplementary role in current healthcare decision making; developmental status or opportunities for improvements and the requirement for better implementation in decision making process.

Managed Entry Agreements (MEA) are complementing the established decision-making schemes for medicines budgeting. The application of MEAs requires the development of more advanced algorithms and procedures for their application, which is associated with certain difficulties caused by differences in legislation and application experience even in countries of the same region (Central and Western Europe). Nevertheless, these agreements are considered as one of the promising areas of expert support for decision-making on reimbursement (conditional or unconditional) of medicines, which increases their accessibility for patients and, in some cases, provides earlier access.

Adaptive Pathways or Medicines Adaptive Pathways for Patients (MAPPs) is an approach aimed at maximizing the positive impact of new medicines on public health, achieved by balancing the need for timely patient access through phased (iterative) implementation using both existing tools and a more flexible application of the existing regulatory framework. Thanks to adaptive pathways, a drug can follow an "iterative" process in which it can be initially approved for only a small group of patients (based on limited scientific evidence), and then, when more evidence is collected, the drug can be approved for extended group of patients. In addition, a drug may be first approved based on surrogate endpoints, which should subsequently be tested with more clinically important outcome endpoints

Predicting and Horizon Scanning incorporated into the model of proactive public health management and allowing the necessary set of activities to be formed in advance, increasing the efficiency of bringing medical technologies to market and creating decision support tools that allow adequate and timely allocation of necessary resources. Currently used for particular tasks and investigation of competitive landscape for interventions in short- and medium-term forecast.

Early HTA provides algorithms for early access to and analysis of study treatment outcomes as well as early awareness of stakeholders and decision makers reducing the time for HTA process and allocating funding for intervention. There were five main risks closely linked one to another and with the early access methodology: these schemes were not deeply incorporated into regulatory process or were under development or required additional tools (databases or predictive models, etc.). There was also shortage of qualified staff and organizations (local, regional or global). Resolution of these issues was linked with infrastructure and funding for establishing of appropriate institution and personnel competencies as well as for the development of comparative effectiveness methodology and interactive tools for decision making (to summarize comprehensive analyses of big data and different prognostic scenarios in a friendly and assessable format).

Selected tools for prioritization

Comprehensive HTA development requires improvement implementation of all mutually linked blocks. Nevertheless, some of these blocks can provide more impact on the rest and trigger their development or can cause risks and additional tools required for conflict resolution. The analytic hierarchy process (AHP) made possible to range the importance of the proposed HTA tools and their efficacy. The importance was considered to be aligned with number of addressed needs which can solved by the tool. The efficacy was considered as a ratio between the number resolved needs and the number of associated risks.

The number of links between specific tools the addressed need is shown in Fig. 2. Local registries were considered to be the most important tool allowing increasing awareness and involvement of patients into HTA process as well as obtaining data on disease burden and treatment outcomes necessary for local regulatory decisions and also generating data for regional and global cooperation in comprehensive HTA area.

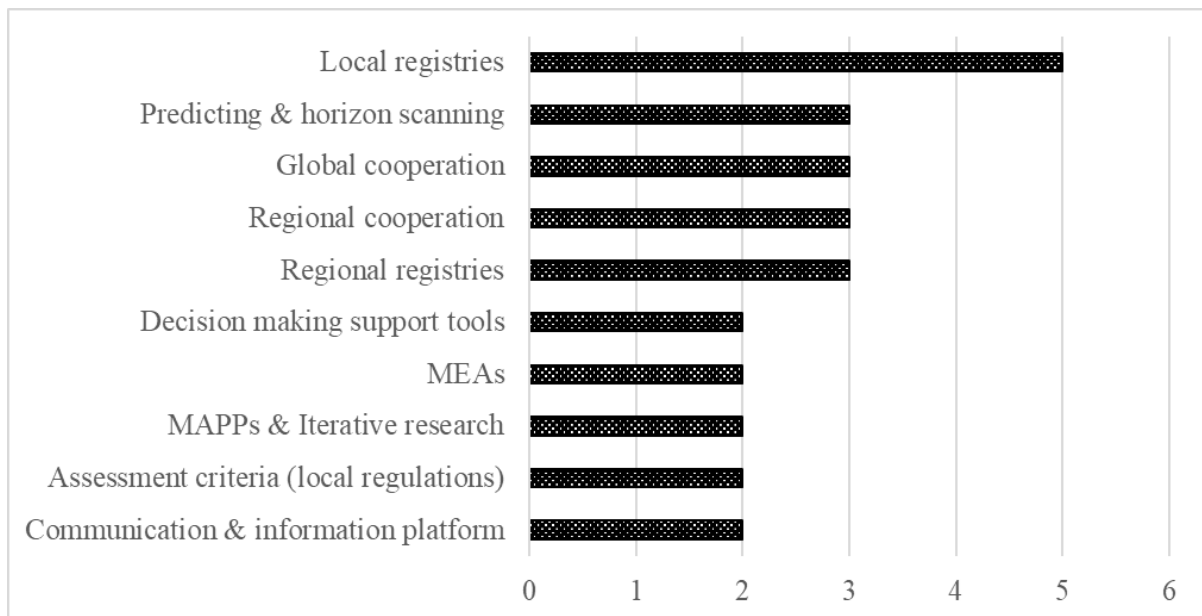


Fig. 2. The number of addressed needs to be solved by perspective tools development

The relative efficacy of the perspective tools is presented on Fig. 3. It indicates that development of local registries can be the most effective step indicating that meeting of 5 needs will cause 3 potential risks (ratio is 1,7) requiring 4 additional activities for conflict resolution.

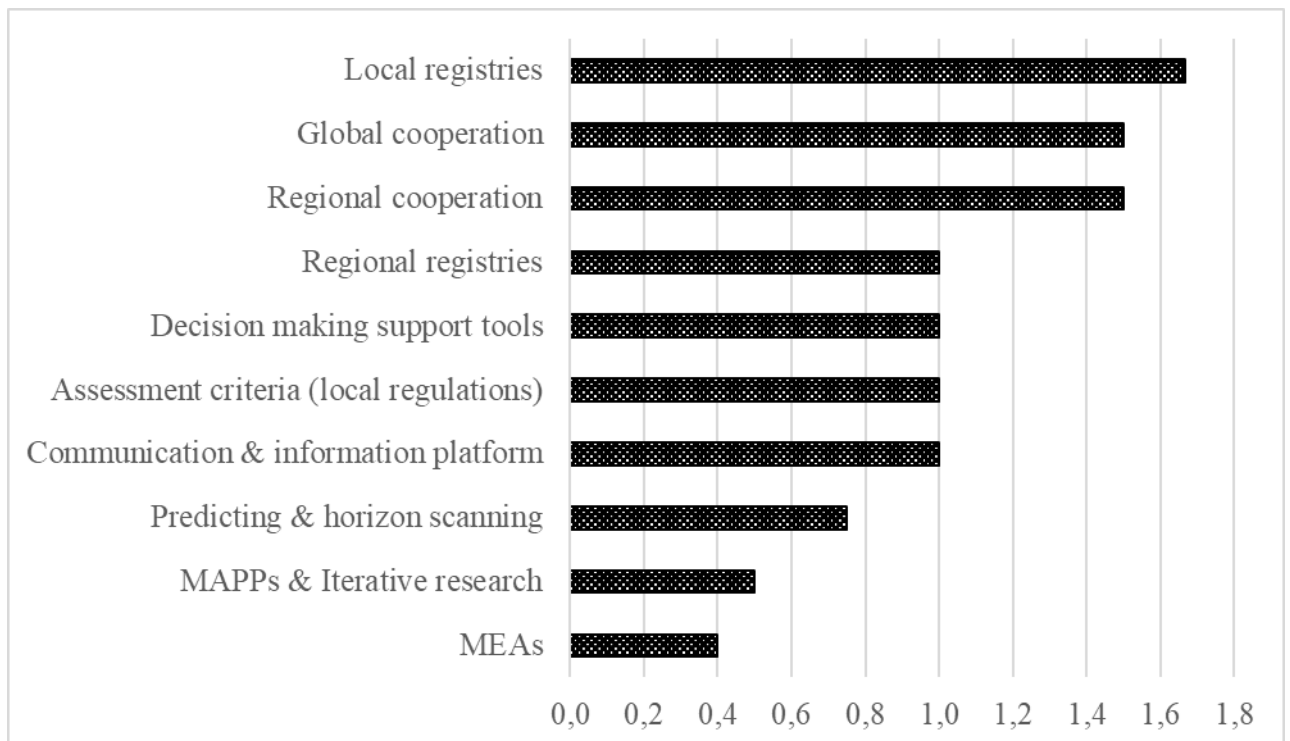


Fig. 3. The ratio between the number resolved needs and the number of associated risks (efficacy of the perspective tool development)

1. CONCLUSION

The proposed hierarchical scheme for HTA development was created based on Environmental Scanning and analytic hierarchy process (AHP). The scheme presents the overall prognosis of HTA development indicating the key blocks of needs and relevant tools. Each of these tools are considered to be exclusively important for HTA development. Local registries are considered to be the priority for further HTA improving meeting more needs and providing less threats comparing to other tools.

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