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TO WHAT EXTENT IS ROMANIA PREPARED TO JOIN HEALTH TECHNOLOGY ASSESSMENT COOPERATION AT EUROPEAN LEVEL

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TO WHAT EXTENT IS ROMANIA PREPARED TO JOIN HEALTH TECHNOLOGY ASSESSMENT COOPERATION AT EUROPEAN LEVEL (Abstract): An increasing number of EU States are using the Health Technology Assessment (HTA) approach, and as health technologies, pharmaceuticals are one of the main fields of application in HTA. This is a review aiming to identify the current status of the HTA collaboration efforts in EU and in Romania, taking into consideration the growing role of HTA in decisions about the level of price and reimbursement in some EU countries or, in other countries, in decision on whether to reimburse a new product or to reject its funding totally. Romanian HTA system needs further development, both in terms of financial resources and, probably more important, human resources; the efforts in the long run will bring great returns to the entire health system, allowing better, safer, and more efficient use of pharmaceuticals and other health technologies. The scientific evidence provided may support the decision-making process. **Keywords**: HEALTH TECHNOLOGY ASSESSMENT, EVIDENCE BASED DECISION-MAKING HTA CORE MODEL.

The evidenced based decision-making process relays increasingly at EU level on assessing technologies that includes pharmaceuticals, devices, procedures, programmes, and even organizational aspects of health care systems. A widely accepted definition of Health Technology Assessment (HTA) was provided by European Network for Health Technology Assessment (EUnetHTA): "a multidisciplinary process that summarises information about the medical, social, economic and ethical issues related to the use of a health technology in a systematic, transparent, unbiased, and robust manner" (1).

HTA concept has been introduced in Europe stepwise since 1970s, and the formal collaboration among the national HTA agencies started in 1990s with financial support from the European Commission (EC) (2).

EUnetHTA Collaboration (3) was launched in November 2008, following an EC funded project aiming to connect national HTA agencies, research institutions and health ministries in order to enable an effective exchange of information on health technologies effectiveness thus assisting the EU Member States and candidate countries to plan, deliver and monitor health

services effectively (3). The first EUnetHTA Joint Action (2010-2012) built on the previous project results for developing an effective and sustainable HTA collaboration in Europe (3). EUnetHTA Joint Action 2 (2012-2015) improved the EUnetHTA tools and methodologies based on results of cross-border collaborative practical application of these (3). EUnetHTA Joint Action 3 (2016-2020) is strengthening the collaboration among EU Member States by an increased number of commonly evaluated technologies, revision of methodologies, development of quality standards and mechanisms to ensure uptake at national level, in order to establish a permanent HTA working structure for Europe (3).

Despite all attempts starting in early 1990s, Romania has set an HTA agency in 2012 only as a consequence of Directive 2011/24 EU. Initially established as a unit within the Ministry of Health, since 2014 it passed under the National Agency for Medicines and Medical Devices (NAMMD) (4). A 2017 World Bank financed project on Technical Assistance for institution building of HTA structure, including training for the NAMMD had the objective of making recommendations on further development of HTA system in Romania.

MATERIAL AND METHODS

The current study is a review of the main EU regulations, of national HTA legislation, of literature and working documents regarding the HTA Romanian system and EU cooperation in HTA. For the main consulted documents see first table.

TABLE I

Main consulted documents

- Directive 2011/24/EU of the European Parliament and of the Council of 9 March 2011 on the application of patients' rights in cross-border healthcare;
- Commission Implementing Decision of 26 June 2013 providing the rules for the establishment, management and transparent functioning of the Network of national authorities or bodies responsible for health technology assessment;
- Rules of Procedure of the Health Technology Assessment Network adopted by the HTA Network on 10 november2016;
- Proposal for a Regulation of The European Parliament and of The Council on Health Technology Assessment and amending Directive 2011/24/EU;
- Commission Staff Working Document on Impact Assessment Strengthening of the EU Cooperation on Health Technology Assessment (HTA) Accompanying the Proposal for a Regulation of the European Parliament and of the Council on Health Technology Assessment and amending Directive 2011/24/EU;
- Law 95/2006 on the Healthcare Reform;
- Ministry of Health Order 861/2014 for the approval of HTA criteria, documentation to be submitted by applicants, methodological instruments used in the assessment process concerning inclusion, extension of indications, non-inclusion or exclusion of medicines in/from the List of INNs of medicines from which the insured persons benefit, as well as INNs of medicines granted in national health programmes, and the means of challenge;
- Studies on mapping of HTA organizations and methodologies commissioned by European Commission;
- Technical assistance reports of the World Bank project conducted in Romania.

The list of the main consulted documents

A comparative analysis was performed following the developments of HTA at the European Union level and the development of HTA system in Romania.

RESULTS AND DISCUSSION

EU cooperation on HTA.

It is unanimously accepted all over EU that HTA has an important input on evidence-based decision-making.

The EC has supported the cooperation between HTA bodies, through substantial financing of three Joint Actions (JAs): 2010-2012 JA1 (6 million Euros), 2012-2015 JA2 (9.5 million Euros), 2016-2020 JA3 (20 million Euros) (fig. 1).

EU has facilitated the cooperation on HTA in Europe by creating the legal basis of an HTA Network. The article 15 of Directive 2011/24/EU on the application of patients' rights in cross-border healthcare introduces the setting up of a voluntary network to support cooperation between national authorities or bodies responsible for HTA (5). All EU countries have applied for membership and participate. Romania applied for membership and participated in all the Network's meetings through the MoH, mandated by the Law 95/2006, article 922 (6).

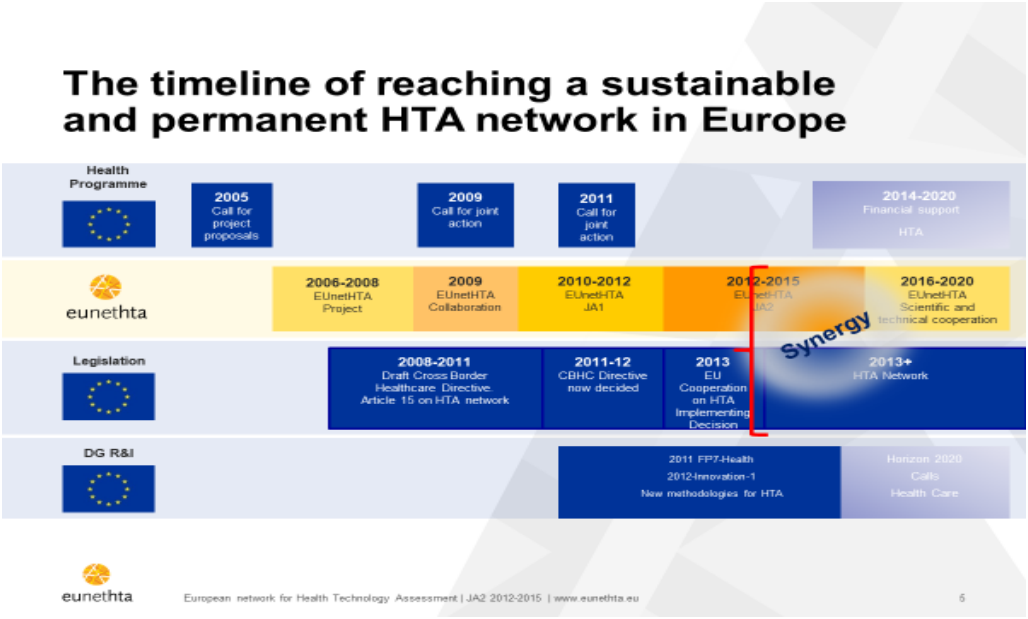

Fig. 1. The timeline of reaching a sustainable and permanent HTA network in Europe
Source: General Presentation on EUnetHTA
(https://www.eunethta.eu/general-presentation-on-eunethta)

The HTA Network's activity is regulated by the Commission Implementing Decision of 26 June 2013 providing rules for the establishment, management, and transparent functioning of the Network of national authorities or bodies responsible for HTA, that created a synergy between HTA Network and EUnetHTA Joint Actions (7),

stating "HTA Network shall be supported by a scientific and technical cooperation mechanism" (8). The HTA Network has also adopted owns Rules of procedures, a 2016-2020 Strategy for EU cooperation on HTA and developed Multiannual Working Programmes.

Thus, while the HTA Network is focusing on strategic issues and takes decisions relevant to EU cooperation on HTA, the currently EUnetHTA JA3 ensures scientific and technical cooperation for the HTA Network.

EUnetHTA collaboration. The scientific work in EUnetHTA Joint Actions, over the last 10 years, resulted in a specific set of tools and methodologies, handbooks and toolkits for users, teaching materials, internal strategies and methodological standards, guidelines and procedures manuals, databases, recommendations on the implementation of sustainable European network for HTA, position papers and reports. The final outcome of these JA consisted in the Joint or Collaborative Assessments of different health technologies produced by partners from different European countries.

The Network has been growing fast. If the first EUnetHTA JA counted 33 partners and 26 collaborators from 25 countries, the 3rd JA includes 81 organizations from 29 countries. The National School of Public Health, Management and Professional Development Bucharest joined EUnetHTA in 2011, and two more Romanian institutions in 2016: The National Institute of Public Health and the "Babes-Bolyai" University from Cluj-Napoca (3).

The main methodological framework for production and sharing of HTA information is *HTA Core Model* that collects information on nine domains: Health problem and current use of technology, Description of health technology, Safety, Clinical effectiveness, Cost and economic effectiveness, Ethical analysis, Organisational aspects, Social aspects, Legal aspects. The model reflects the broad scope and multidisciplinary nature of HTA (9).

Designed in EUnetHTA 2006-2008 project, the model has been refined along the 3 JAs, especially following its piloting, being currently at its 3rd version, and is still under revision. The HTA Core Model for the production of core HTAs (version 3.0) consists of three main components: (1) Standardised set of HTA questions (the ontology) that helps to define specific research questions; (2) Methodological guidance to assist in answering the research questions; (3) Common reporting structure. In its development, the Core model has been piloted on seven non-pharmaceutical technologies. The HTA Core Model is accessible free of charge but subject to the HTA Core Model Licence (10).

Given the complexity of the HTA Core Model, it was also developed an application for rapid assessments – *the HTA Core Model for Rapid Relative Effectiveness Assessments (REA)* that covers only four domains: Health problem and current use of technology, Description of health technology, Safety and Clinical effectiveness (fig. 2). REA was initially developed for pharmaceuticals in order to allow the assessment in the limited timeframe of 90-180 days imposed by the European Transparency Directive 89/105/EEC. Equally the Full Core Model, the Core Model for REA was continuously improved based on several pilots and its application was expanded to non-pharmaceutical technologies such as devices, diagnostics, surgical interventions, and screening (10).

The aim of EUnetHTA JA 3 is to define and implement a sustainable model for cooperation on HTA in Europe after 2020 by supporting the collaborative production of HTA and encourages the use of the HTA reports at national level (11).

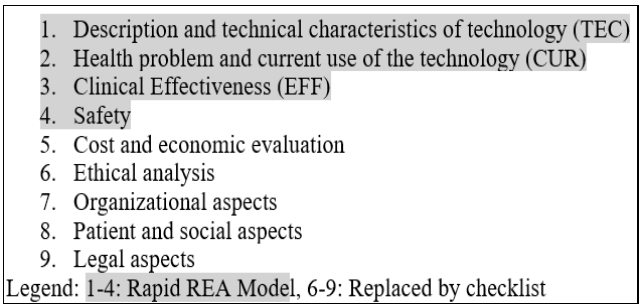

Fig. 2. The domains of the HTA Core Model and relative effectiveness assessment. Source: EUnetHTA WP5. HTA Core Model for rapid relative effectiveness, 2015

The updated list of assessments performed during EUnetHTA JA3 or planned to be performed is available on EUnetHTA website (12). The National School of Public Health, Management and Professional Development Bucharest (NSPHMPDB) has been involved as co-author in five REAs, and as dedicated reviewer in one REA, all for non-pharmaceutical technologies, adding on the experience acquired in JA2 from participation of the piloting of three Full Core HTA assessments. A list of technologies assessed during the EUnetHTA JA 3 with NSPHMPDB' contribution is present ed in second table.

TABLE II

List of technologies assessed during the EUnetHTA JA 3, with contribution of NSPHMPDB.

Pharmaceutical technologies assessed	Publication of Final Assessment
Hypoglossal nerve stimulation systems for treatment of obstructive sleep apnoea	21.05.2020
Biodegradable rectum spacers to reduce toxicity for prostate cancer	24.04.2020
Point-of-care Tests (POCT): D-Dimer and Troponin	14.08.2019
Screening for osteoporosis in the general population	19.12.2018
Bioresorbable Stents in cardiovascular indications (coronary artery disease)	20.08.2018
Antibacterial-coated sutures versus non-antibacterial-coated sutures for the prevention of abdominal, superficial, and deep, surgical site infection (SSI)	06.10.2016
Use of Intravenous immunoglobulins for Alzheimer's disease including Mild Cognitive Impairment.	30.11.2015
Structured telephone support (STS) for adult patients with chronic heart failure.	30.11.2015
Fecal Immunochemical Test (FIT) versus guaiac-based fecal occult blood test (FOBT for colorectal cancer screening.	31.07.2014

Source: Assessments REA (2016 – 2021) (https://eunethta.eu/rapid-reas/)

EU collaboration after EUnetHTA. During JA3, there were performed several evaluations to identify challenges and shortcomings of EU collaboration on HTA

after 2020, either by EUnetHTA, having in mind the aim of preparing for a sustainable network post 2020, or by the European Commission, in the view of preparing further regulations.

According to a study commissioned by EC in 2017, there is a large variety of organizational structures of national HTA models in EU and EEA countries, from large single HTA bodies, specially assigned working groups in the Ministry of Health, to systems with two or more organizations performing various functions in the national HTA processes or constituted in regional networks (13).

As well, an impact assessment performed in the view of issuing the Proposal for a Regulation of the European Parliament and of the Council on HTA and amending Directive 2011/24/EU, reveals that national HTA systems in Member States differ not only in the procedural frameworks and methodologies, but also there are significant differences in the available resources. Having identified all shortcomings, the study also presents an in-depth analysis of four policy options as further steps: (1) No Joint Actions after 2020; (2) Project-based cooperation on HTA activities; (3) Permanent cooperation on common tools, procedures, and early dialogues; (4) Permanent cooperation on common tools, procedures, early dialogues, and joint REA (14).

Based on the previously mentioned study, the EC adopted in 2018 a legislative proposal by which to reinforce cooperation amongst Member States, building on the policy option 4. Thus, the Member States will work together on joint clinical assessments of new medicines and certain new medical devices, on joint scientific consultations for developers, on identification of emerging health technologies and on voluntary cooperation in other areas. Individual EU countries are responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology and making decisions on pricing and reimbursement (15). The proposal is still under discussions, even if according to initial planning it should have been adopted by the Parliament and the Council in 2019. The last published progress report dates from June 2019, when the Council was under Romanian Presidency (16).

Stage of development of HTA system in Romania. The national competent authority for HTA in Romania is set as a unit within the National Agency for Medicines and Medical Devices, and the evaluation methodology is provided by the Ministry of Health Order no. 861/2014. The methodology is not relaying on assessment of evidence but is based on a scorecard system that relays mainly on decision-making in other countries (4,17,18).

As well, the HTA unit is not supported by adequate human resource capacities. A World Bank project was undertaken in Romania in order to provide recommendations for the further development of the national HTA system. In June 2017, the Technical Assistance Report presented three alternative models for the institutionalisation of HTA in Romania, taking into consideration the spread limited capacities in the country (19). At the time of writing no decision was taken in this regard.

Until developing the capacity of doing own assessments, Romania cannot actively participate to the joint clinical assessments as envisaged by the European Commission for the further EU collaboration on HTA. For being able to participate to this process, further steps should be taken in developing

the legislation, training human resources, and ensuring collaboration between existing experts in the field at national level.

CONCLUSIONS

The EU collaboration on HTA still faces a lot of challenges and barriers, from language use and reporting structure to differences in national processes and methodologies and the use of HTA report in decision-making. The EUnetHTA collaboration is aiming to develop an effective and sustainable HTA collaboration, through 1) reducing repetitions and improve the efficiency in the use of resources; 2) facilitate growing impact of HTA in EU Member States; 3) consolidation the relation between HTA and health care decision-making; and 4) supporting countries with less experience in HTAs. The benefits for HTA agencies that contribute to and use EUnetHTA assessments are resource- and time-savings. But, to achieve this, the national agencies should align to EUnetHTA practices in terms of topic selection, scope, and quality of the assessment (11). These initiatives intend to harmonize or standardize the HTA processes so to improve their level of transparency, quality and comprehensiveness, and facilitate the extraction of relevant information that can then be transferred cross-border.

In many countries, even high-income countries, the staffing levels of public authorities tasked with HTA, pharmaceutical pricing, procurement and reimbursement are low, and this is also true for the Romanian health system (20).

As well, EU collaboration on HTA require not only HTA agencies commitment, but also clear involvement and engagement from all stakeholders: industry, patients, healthcare providers and payers (18,19,21). From this perspective it can be argued the role of HTA in Romania is still undervalued, even if calls for increased efficiency and better methods for reimbursement and pricing for drugs are ten years old (20,22). In order to be able to use HTA and to participate to EU collaboration, Romanian HTA system needs further development, both in terms of financial resources and, probably more important, human resources; the efforts in the long run will bring great returns to the entire health system, allowing better, safer, and more efficient use of pharmaceuticals and other health technologies.

CONFLICT OF INTEREST

The authors reveal no conflict of interest concerning the manuscript.

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