Editorials in Personalized Digital Medicine Sciences

The European Health Technology Assessment Regulation: State of the Art and Challenges

by Rossella Di Bidino

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The goal of Digi-MEd is to critically reflect on issues regarding Digital Medicine and Health from a Medical Humanities perspective, to understand current challenges of medical education from an interprofessional point of view.

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DIGI-MEd
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Rossella Di Bidino

The European Health Technology Assessment Regulation (HTAR) (EU 2021/2281) came into force on January 12, 2025. Its objective is to provide a reference framework and establish a series of procedures aimed at making operational the cooperation of Member States in the assessment of health technologies (Article 1). In practice, from this year onward, Joint Clinical Assessments (JCA) and Joint Scientific Consultations (JSC) will be conducted at the European level.

JCAs will help define the relative effects of a health technology and specify the degree of certainty given the available evidence (Article 9). However, before starting the assessment process, what the regulation calls the "assessment scope" (Article 8) must be defined — this corresponds to the PICO framework. This is one of the most critical aspects of the entire process. Member States must first agree on the Population (P), Intervention (I), Comparators (C), and Outcomes (O) that will be used for the evaluation. The importance of this step lies in the fact that PICO determines what evidence must be included in the assessment, thereby impacting the evidence development plans of health technology developers.

It is possible that different policy questions from Member States lead to different PICO frameworks, even at the European level, with significant consequences in terms of the required evidence and workload for assessors.

To reach a joint definition of the assessment scope, a PICO proposal is drafted at the European level and then sent to Member States, who may confirm or modify its content. Subsequently, at the European level, a "consolidation" process will take place to define the lowest possible number of PICOs that can meet the needs of all Member States.

"[...] while the assessment is conducted at European level, [...] the decision-making process remains the responsibility of individual Member States."

It is no surprise that in 2024, six PICO exercises were conducted—three for medicines and three for medical devices—to test the entire process. The results, particularly for medicines, confirmed initial concerns. Specifically, for the two oncology drugs involved, 13 different PICOs were defined for each, with differences in comparators and outcomes.
These results make even more clear the need for developers to anticipate possible national PICOs, simulate the consolidation process, and validate it with various stakeholders. It will be valuable to optimize the actual duration of a Joint Clinical Assessment.

On the other hand, JSCs are consultations aimed at ensuring that the evidence generated meets the likely requirements for a future joint assessment. These consultations focus on all relevant aspects related to the design of clinical studies or clinical investigations, including all elements of a PICO (Articles 16-17). However, the final document will have any legal effects for any of the parties involved (Member States, the Coordination Group, or the health technology developer).

The technologies currently covered by the regulation include:

- Medicinal products
- Class IIb and III medical devices
- Class D in vitro diagnostic medical devices

A key role is played by the European Coordination Group for HTA (HTACG), composed of representatives from Member States. Several subgroups operate within the HTACG, including one dedicated to Emerging Health Technologies (EHT).

The assessments conducted at the European level do not replace national regulatory processes. For example, Article 9 states that JCAs do not include any value judgment or conclusions regarding the overall added clinical value of the assessed health technology but are limited to a scientific analysis. Furthermore, both the implementing acts and the guidelines issued so far repeatedly reaffirm that while the assessment is conducted at the European level, the appraisal — meaning the decision-making process — remains the responsibility of individual Member States. Additionally, the European assessment is limited to strictly clinical domains, while other HTA domains (economic, organizational, etc.) remain under national jurisdiction.

"From 2026, JCAs will also be conducted for medical devices, from 2028 they will include orphan drugs. By 2030, the activities will cover all medicinal products."

Before the regulation took effect, during the 2024 a series of implementing acts were issued covering JCA, JSC, conflict of interest management, and information sharing with the EMA.

At the same time, various methodological and procedural guidelines were developed, addressing aspects such as the scoping phase, the validity of clinical studies, relevant outcomes for JCAs, and methodologies for conducting direct and indirect comparisons. Notably, digital outcomes have been included as potentially relevant in European-level assessments.

Each November, a work plan is expected to be shared, and for 2025, it includes the launch of 17 joint clinical assessments for oncology drugs and 8 for advanced therapies, as well as between 5 and 7 joint scientific consultations for medicinal products and between 1 and 3 JSCs for medical devices.

The scope of HTAR will gradually expand. From 2026, JCAs will also be conducted for medical devices, and from 2028, they will include orphan drugs. By 2030, the activities provided for by the regulation will cover all medicinal products.

This workload underscores the need to promptly address key issues, such as adapting national procedures and recruiting and training professionals. For HTAR to be effective, it must integrate seamlessly with national regulatory and evaluation processes, avoiding bottlenecks that could compromise its success.

To support national implementation, several countries, including Italy, have leveraged the Technical Support Instrument (TSI) for reorganizing health technology governance.

In terms of training, Italian National Agency for Regional Healthcare Services (AGENAS) has established a registry of qualified trainers for basic HTA education and is selecting advanced courses in Italy, while AIFA is working to enhance and align national procedures with HTAR requirements.

The implementation of the European Health Technology Assessment Regulation marks a significant step toward greater coordination and harmonization in the evaluation of health technologies at EU level. However, its success will depend on the ability to address key challenges. Specifically, aligning EU and national procedures, along with ensuring active stakeholder involvement throughout the process, could serve as crucial facilitators.