HTA128

EU HTA JCA PICO Consolidation Process Examples: Key Trends And Remaining Uncertainties

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Introduction and Objectives

- Joint Clinical Assessments (JCAs), required under the EU HTA Regulation (EU HTAR)[1], are EU-wide evaluations that provide a scientific analysis of the clinical and safety data of a health technology, focusing on its relative effects on health outcomes. The resulting report must be endorsed within 30 days of marketing authorisation and is shared with all EU Member States and made publicly available to support national decision-making.

- The PICO (population, intervention, comparator, outcome) framework determines the scope of the JCA under the EU HTAR. PICO consolidation is a crucial final step of the JCA PICO scoping process. Due to limited understanding of the real-life application of the consolidation process, Health Technology Developers (HTDs) may use simulation of PICO scoping as a strategic tool to guide the development of high quality, robust JCA submission dossiers.

- We aimed to gather insights in the JCA PICO scoping/consolidation process by (1) reviewing previously published multi-country PICO scoping exercises and (2) conducting a PICO scoping exercise designed to follow official guidance on the scoping process.

Methods

1: Review of available literature focused on previous multi-country PICO scoping exercises

- Our review examined previously published multi-country PICO scoping exercises based on (1) published HTA documents, with member states PICOs extracted and consolidated based on EUnetHTA guidelines or (2) conducted by EUnetHTA, EFPIA or the EU HTA CG. Publications were identified through key word searches conducted in 2024, without date restrictions. Included publications were reviewed to determine the number of individual PICO exercises conducted, which indications they concerned, and the average number of countries involved per exercise. The number of consolidated PICOs per analysis was extracted and the average number of consolidated PICOs across all identified exercises in a given indication was calculated.

2: JCA PICO scoping simulation

- A JCA PICO scoping simulation was conducted during Q3-Q4 2024, aiming to replicate the official JCA scoping process as per published guidance[2]. The exercise focused on an upcoming asset planned for the treatment of metastatic non-small cell lung cancer (mNSCLC) in adults without EGFR, ALK or ROS genomic tumour aberrations, not restricted by histology or PD-L1 status. This indication was selected due to it being in a dynamic therapy area with a complex and evolving treatment landscape, also characterised by diverse subpopulation considerations defined by biomarkers and histological differences.

- To reflect diverse perspectives across the region, 25 EU countries were invited to participate in the exercise. The exercise followed a step-wise approach, beginning with drafting preliminary PICOs based on clinical guidelines and background research. These were then shared via a survey with participating countries, who reviewed and provided feedback based on anticipated responses from their national HTA bodies. They could also suggest additional PICOs if not already included but considered locally relevant. After collecting input within a set timeframe, a meeting was held to consolidate the feedback and define a final set of anticipated PICOs.

Results – Review of available literature

- 14 publications[3-16] (representing 35 individual PICO exercises across 21 indications; 74% in the oncology therapy area; Figure 1) were included in the review. On average, 7 countries participated per exercise (range 3-23) and the average number of consolidated PICOs per analysis was 8 (range 1-15). In therapy areas such as NSCLC where multiple PICO exercises were identified from difference sources, the number of countries involved in each exercise and the resulting number of PICOs was variable (Figure 2).
  - Seven[3-9], exercises relied mainly on published HTA documents from where each member state's proposed PICOs were extracted. The resulted PICOs were then consolidated as per EUnetHTA guidelines
  - Three exercises[10-12] were conducted by EUnetHTA for medicinal products that had already obtained a positive CHMP opinion
  - One exercise[13] was conducted by EFPIA in collaboration with Evidera, where both published HTA documents as well as local clinical guidelines were used in the identification of local PICOs for three products/indications
  - Three exercises[14-16] were conducted by the JCA member states Coordination Group.

Figure 1: Published JCA PICO scoping exercises by therapy area

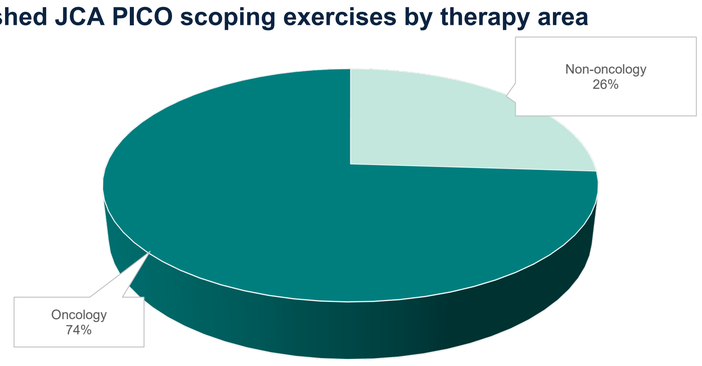
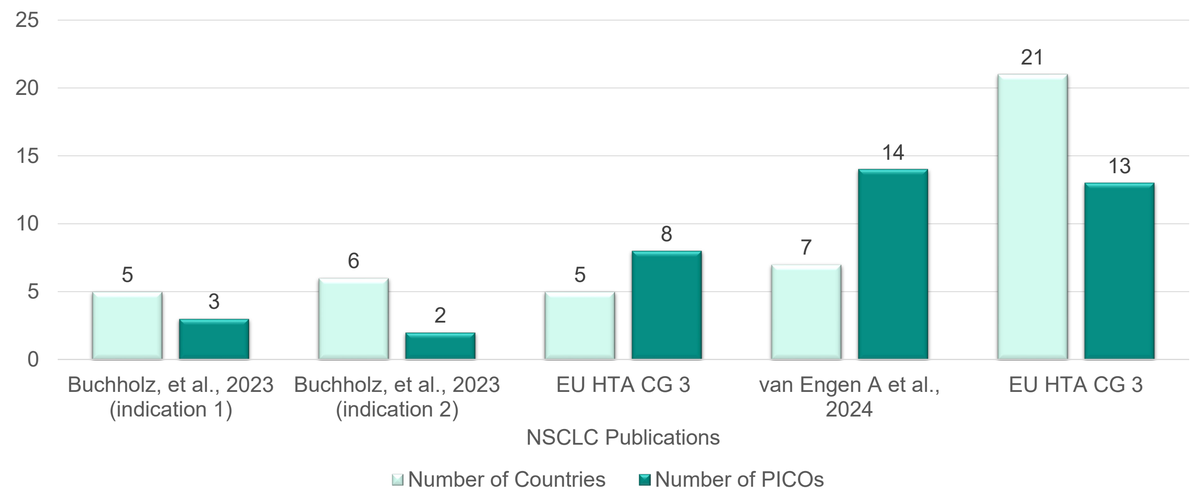


Figure 2: Number of countries involved and PICOs identified per NSCLC PICO scoping exercise



Results – JCA PICO scoping simulation

- 25 countries participated and responded to the JCA PICO scoping conducted during Q3-Q4 2024 (Figure 3). Following a review of the responses, a total of 67 anticipated PICOs were defined (Table 1), based on the understanding that one PICO comprises one population, one intervention (or combination), one comparator (which can include more than one treatment), and at least one outcome. Some countries did request additional comparators and/or additional biomarker cut-off values (leading to new sub-populations) compared to what had been pre-defined, due to local clinical practice and specific member states needs.

Figure 3: Countries participating in JCA scoping exercise

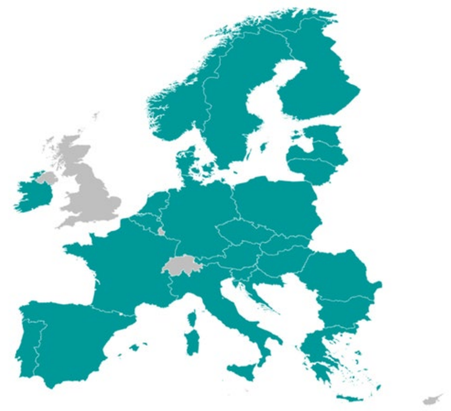


Table 1: Overview of results from JCA PICO scoping simulation in NSCLC

	Number of populations	Number of PICOs
Full population (as per aspirational label/per study	1	7
Sub-populations	15	60

[a] Sub-populations based on histology (squamous and non-squamous) and specific PDL1 biomarker cut-off value

Discussion

- The JCA Implementing Act[17] clearly articulates the vision of member states' input into the PICO scoping process, which should be to translate their clinical requirements into the fewest possible PICO sets. Nevertheless, depending on the condition being treated and the country-specific treatment pathway, the number of potentially relevant PICOs identified by the concerned member states during the scoping process could be highly variable.

- Multiple PICOs can potentially arise due to varied national health priorities, emphasising the need for early coordination and standardised guidelines. Rapid development of new technologies and treatments can outpace the existing evidence base for comparators, adding to the challenge of preparing appropriate comparative evidence

- Uncertainty remains about how PICO consolidation will be applied in a "real" JCA scoping process, and whether certain parameters will be employed (e.g. minimum number of countries requiring a PICO) to define the eventual list of PICOs.

Conclusions

- Limited examples of published JCA PICO scoping exercises along with their attributes (including small number of countries involved) restricts robust analyses and hampers the ability to draw clear conclusions or confidently predict the output of PICO scoping in a real life JCA processes. Additionally, results from a JCA PICO scoping simulation conducted for a highly dynamic indication highlighted uncertainty about whether all distinct sub-populations should be included, or if the number of PICOs would be refined through consolidation discussions.

- The current lack of clarity surrounding the JCA PICO scoping process, including the consolidation step, poses a challenge to the EU HTAR's ambition of delivering harmonised, timely, and high-quality JCAs across Member States. Without clear, consistent guidance on how to define and consolidate PICOs, especially in complex therapeutic areas, there is a risk of misalignment between the evidence prepared for JCA submissions versus the final consolidated set of PICOs, and subsequently EU-level assessments and national HTA expectations.

- Such uncertainties could contribute to delays in evidence generation and slower patient access to innovative treatments. If not addressed, it may undermine the EU HTAR's goal of improving efficiency, transparency, and equity in health technology evaluation across Europe.

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Disclosures

KD is an employee of MSD (UK) Limited, London, UK; ED is an employee of MSD Belgium; AD is an employee of MSD Greece; CG is an employee of MSD France; NS is an employee of MSD Switzerland

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