Challenges in predicting the Joint Clinical Assessment (JCA) scope from a stakeholder perspective: a case study in Relapsed/Refractory Multiple Myeloma (r/r MM)

HTA72

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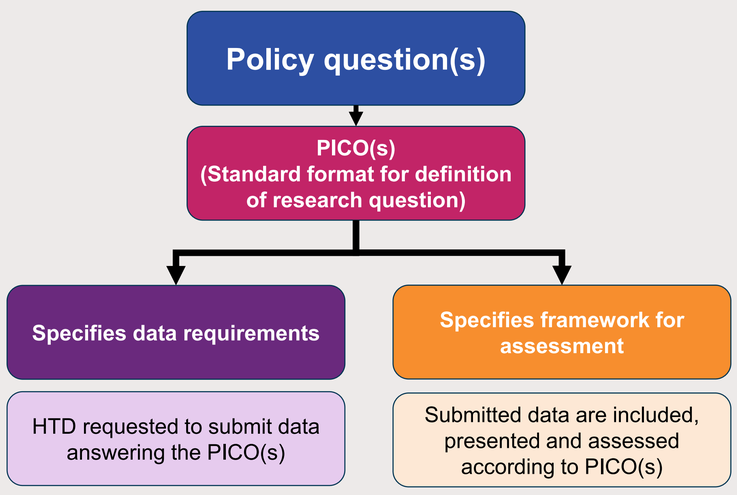
BACKGROUND

- EU HTA Regulation (EU 2021/2282)[1] requires Health Technology Developers (HTDs) to participate in Joint Clinical Assessments (JCAs) from 2025. Anticipating research question(s), prior to the definition of the actual JCA scope, is critical for Health Technology Developers (HTDs) to be able to prepare the JCA submission in a meaningful manner.
- According to the guidance on PICO (Population, Intervention, Comparator, Outcomes) scoping, presented in Figure 1, the "assessment scope is an appropriate translation of national policy questions into research questions". Furthermore, since the scoping is policy-driven, versus evidence-driven, "it may contain PICOs for which no evidence is available."
- This is in contrast to scopes defined by national HTA bodies which are typically evidence driven or informed by the Marketing Authorisation (MA) indication that reflects clinical trial evidence.
- Due to the fact that the JCA process has only been in place since January 2025, there is currently a gap in understanding the perspectives of the stakeholders who are involved in the scoping process.

Approach of the PICO process



HTD: health technology developer; PICO: Population, Intervention, Comparator(s), Outcomes

Figure 1. PICO scoping with policy approach (Guidance on the scoping)[2]

OBJECTIVES

- The objective of this study was to explore clinical and HTA experts' views in defining JCA scope with the HTA Regulation (HTAR) defined policy approach.
- A further objective was to identify implications for HTDs preparing for JCA submissions.

METHODS

- A policy-based PICO prediction for 11 EU Member States was conducted by reviewing clinical guidelines and recent HTA appraisals (2023-2024).
- The identified PICOs were validated via e-survey and semi-structured interviews (n=19) with clinical and HTA experts. Qualitative responses were analysed to identify common themes and potential challenges.
- The interviews focused on the PICO scope that had been developed based on a policy approach, that is, not driven by clinical trial evidence.
- Respondents' perspectives on the policy-driven PICOs were elicited via an online survey.
- Issues related to PICO scoping were further probed to clarify challenges. For example, how the local HTA bodies would approach requesting the JCA scope.

RESULTS

60+ **PICOs identified during scoping using the policy approach**

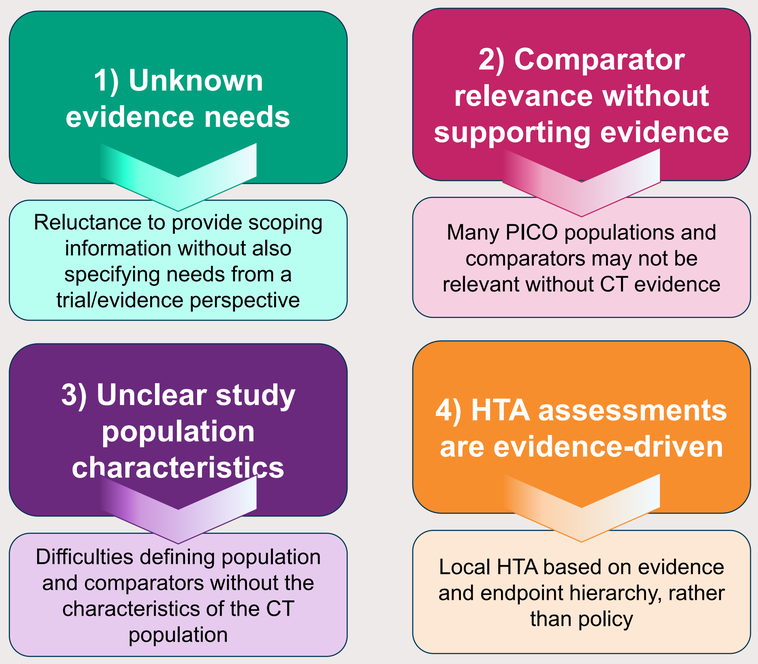
Key drivers

- **Numerous populations and available comparators**
- **Need for individual comparisons versus basket comparisons**

The recurring theme across all interviews was the challenge to define the PICO scope using a policy approach versus an evidence-driven approach

1. HTA experts found it challenging to define the scope **without any clinical trial evidence:** trial data is generally required in several markets to define relevant subgroups, outcomes and comparators.
2. PICO scoping was considered particularly problematic as many populations and comparators may not be considered relevant **without supporting evidence** from clinical trials (e.g., several populations and comparators were marked as "*not required*" due to the lack of evidence).
3. **Missing key information** on pivotal trial design such as **population characteristics** was considered important for scoping.
4. HTA experts anticipated that the local HTA will be **based on evidence and endpoint hierarchy**, rather than policy. The policy-driven approach was not preferred by the majority of the interviewed HTA experts, while clinical experts were able to adapt to a policy-based scope.

Key challenges defining PICO scope using policy approach

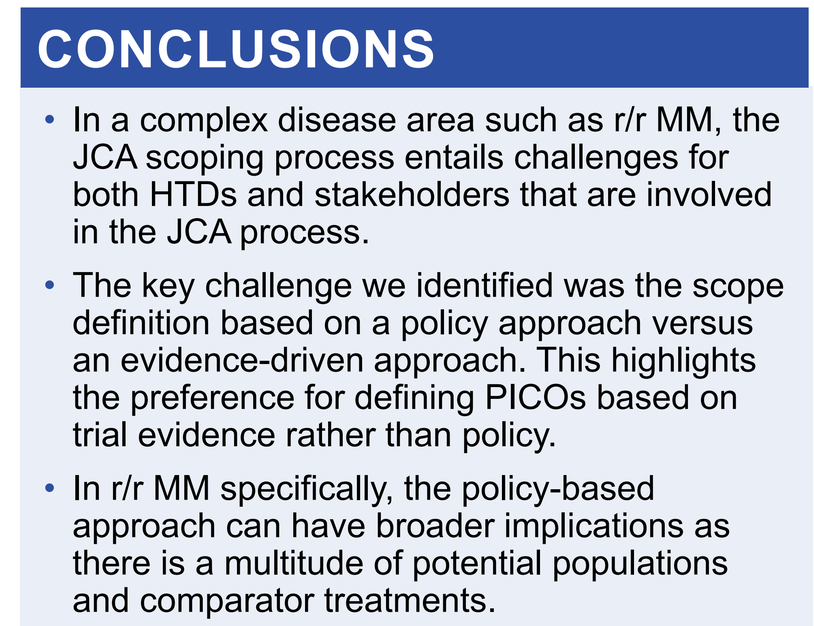


CT: clinical trial HTA: health technology assessment; PICO: Population, Intervention, Comparator(s), Outcomes

Figure 2. Key challenges identified in the interviews

Additional challenges identified

- The **local HTA will consider the EMA indication**, not other populations that could be identified through a policy-based PICO approach.
- Respondents noted that **knowledge of local HTA process requirements** impacts the critical view on the policy approach for scoping.
- It was unclear **whether upcoming therapies would be included in future JCA scope**. There had been no local appraisals yet, and HTA bodies depend on such appraisals to establish relevant comparators.
- Experts **called for a comparison versus all relevant therapies** based on individual physician's choice.



IPT: Informe de Posicionamiento Terapéutico, Therapeutic Positioning Report

Figure 3. Supportive quotes on recurring themes

CONCLUSIONS

- In a complex disease area such as r/r MM, the JCA scoping process entails challenges for both HTDs and stakeholders that are involved in the JCA process.
- The key challenge we identified was the scope definition based on a policy approach versus an evidence-driven approach. This highlights the preference for defining PICOs based on trial evidence rather than policy.
- In r/r MM specifically, the policy-based approach can have broader implications as there is a multitude of potential populations and comparator treatments.
- The extensive number of PICOs we identified does not seem feasible to develop responses for, nor is it a meaningful use of resources for the JCA assessors. Also, protocols and pre-defined statistical analyses of pivotal trials may not cover policy-driven PICOs which leads to deviation from original study planning and post hoc analyses to be presented in the JCA.
- **An unintentional consequence of the policy-based approach may be that HTDs cannot adequately respond to requested scope or only sparse evidence is presented. This in turn may result in further requests at the national level and a duplication of work that was intended to be removed with the EU HTAR and the JCA.**
- **The implication for HTDs based on the findings of this study, is to develop adaptive strategies for evidence generation and invest in early planning for PICO scope prediction and external validation. As the JCA process has now started, it is critical to monitor the progress of the JCA guidance and interpretation of the guidelines for scoping.**

REFERENCES

1. 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.
2. Member State Coordination Group on Health Technology Assessment. (2024). Guidance on the scoping process (V1.0).

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DISCLOSURES

Kaisa Miikkulainen is an employee of Gilead Sciences Sweden AB. Damla Kilic and Brett Doble are employees of Kite, a Gilead Company. Caroline Delaitre-Bonnin, Almudena Olid Gonzalez, Milon Waththuhewa and Aleksandra Zapala-Szufel are employees of Thermo Fischer Scientific which receives consulting fees from Kite, a Gilead Company. Benedikte Lensberg is an employee of Avilon AS, which receives consulting fees from Kite, a Gilead Company.

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