Predicting PICOs Through Machine-Learning-Powered Information Compression and Statistical Ranking

MSR:170

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Objective

To evaluate whether an AI-driven tool **(PICO+)** can accurately and efficiently identify likely PICO criteria for oncology and advanced therapy medicinal products (ATMP) to prepare for the EU Joint Clinical Assessment. Outputs of the tool are assessed against published European Union Health Technology Assessment Coordination Group (HTA CG) PICO exercises.

Introduction

Changing requirements for EU JCA

With the introduction of the Joint Clinical Assessment (JCA) as part of EU Health Technology Assessment Regulation (Regulation (EU) 2021/2282), early preparation has become crucial for assessing potential Population, Intervention, Comparator & Outcome (PICO) criteria requested by Member States as part of the JCA process.[1]

Multiple data points and sources

This is typically a labour-intensive process and requires synthesising information across multiple diverse sources such as health technology assessment reports and clinical guidelines from across Europe.

An AI powered solution

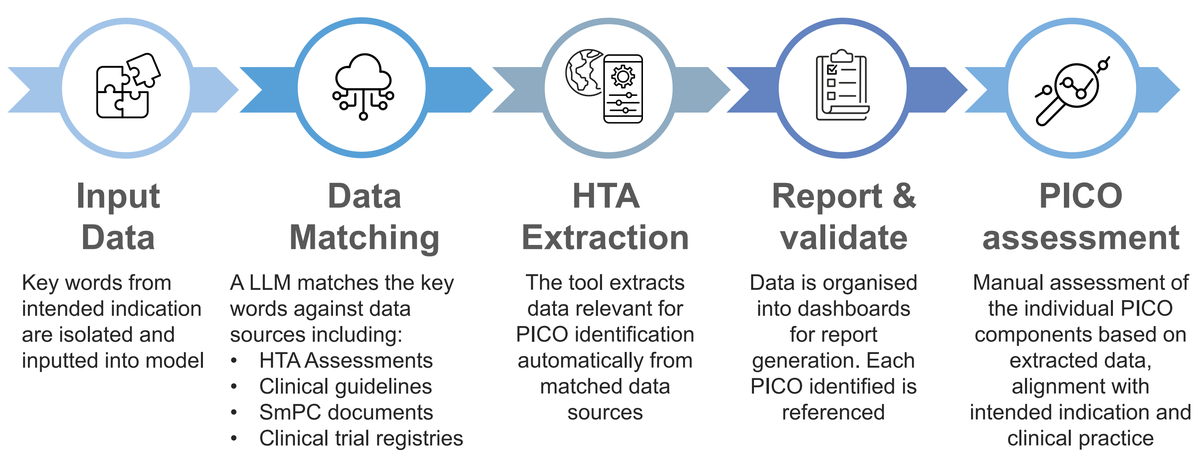
Efficient methods of data navigation to estimate likely PICOs for a given product are thus needed. We introduce PICO+ as a tool to identify and synthesise potential PICOs in oncology.

Methods

Tool design

A proprietary, AI-driven simulation & analysis tool was designed to support early HTA planning by identifying PICOs based on precedent HTA assessments, clinical guidelines, and trials from select EU member states (Czechia, France, Germany, Italy, Portugal, Spain, Sweden) (Figure 1).

Figure 1. Tool Schematic



Assessment against HTA Coordination Group PICO exercises

- The indication descriptions for three HTA Coordination Group PICO exercises were inputted into PICO+:
  - Advanced or unresectable hepatocellular carcinoma (HCC) in the first line[2]
  - KRAS G12C mutated non-small cell lung cancer (NSCLC) after at least one prior systemic therapy[3]
  - Severe and moderately severe Haemophilia B (congenital Factor IX deficiency) in adult patients without a history of Factor IX inhibitors[4]
- PICO+ identified 89 precedent HTA reports and clinical guidelines from which to extract relevant PICO information using natural language processing
- These elements were manually assessed for context and semantic variation then ranked using a rules-based algorithm to identify likely PICOs. Ranking was based on date of publication, HTA appraisal outcome, population matching and applicability across markets
- These PICOs were then compared against those identified in the HTA Coordination Group exercises for alignment of unique populations, comparators and outcomes[2–4]

Results

Advanced / unresectable HCC

- For advanced or unresectable HCC in the first line, 13 discrete PICOs were identified by the JCA SG following a manual PICO survey aligned with EU HTA methodology
- This comprised of one full population, six sub-populations, seven discrete comparators or comparator combinations and seven sets of outcomes
- PICO+ instantly identified 100% of the populations & comparators and 93% of unique outcomes that were requested in the JCA SG scoping exercise (Figure 2)

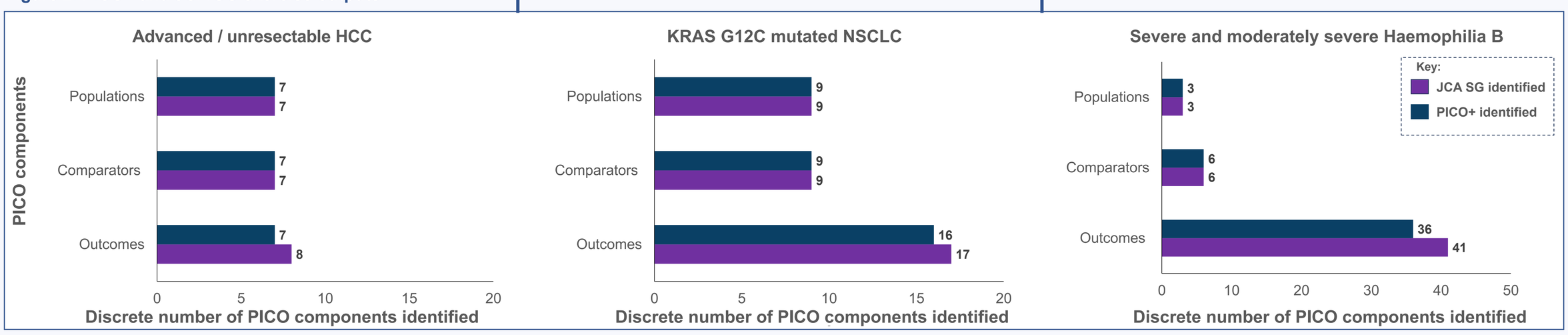
KRAS G12C mutated NSCLC

- For KRAS G12C mutated NSCLC after at least one prior systemic therapy, 13 discrete PICOs were identified following manual review by the JCA SG
- This comprised of five PICOs for the full population, eight subpopulations & nine comparators or comparators combinations
- Outcomes requested were broadly aligned across PICOs. Three PICOs requested sub-analysis based on stratification by prior treatment experience
- PICO+ identified 100% of the comparators, 100% of the populations, 93% of unique outcomes and 92% of populations and comparator combinations identified in the JCA SG exercise (Figure 2)

Severe and moderately severe Haemophilia B

- For adult patients with severe or moderately-severe haemophilia B (congenital Factor IX deficiency) and no history of Factor IX inhibitors, seven discrete PICOs were identified following manual review by the JCA SG
- This comprised of five PICOs for the full population and 2 PICOs for sub-populations (those on prophylaxis; and those not on prophylaxis)
- Three PICOs requested subgroup analyses based on stratification by severity (severe vs moderately severe) and by presence/absence of pre-existing anti-AAV5 neutralising antibodies
- PICO+ identified 100% of the comparators, 100% of the populations, 88% (36/41) of all clinical and safety outcomes, which included 100% of safety outcomes, identified in the JCA SG exercise (Figure 2)

Figure 2. PICO+ and JCA SG exercise outputs



Conclusion

- An AI-powered methodology can accurately identify likely PICOs for given oncology and haemophilia populations instantly, enabling a more rapid and efficient PICO preparation process
- The tool does not seek to simulate what PICOs may be identified in a scoping process, rather it identifies the likely PICO components based on published data sources. This reduces the opportunity of hallucinations in outputs as human interpretation of the identified components is required
- PICO+ successfully identified the component populations, interventions, comparators, and outcomes included in the JCA SG exercises; however, subgroup stratifications (e.g., by disease severity) were not clearly attributable to specific PICOs, which may reflect ambiguity in how populations and subgroups were defined during the JCA SG exercise
- This exercise was based on a focused HTA extraction from seven markets which may indicate the influence these markets have in shaping the clinical landscape or the homogeneity of the clinical landscape across markets in the indications assessed

References

1. EU health Technology Regulation – Regulation (EU) 2021/2282
2. JCA Subgroup Exercise 01 - Durvalumab (Imfinzi®) (Feb 3, 2025)
3. JCA Subgroup Exercise 03 - Adagrasib (Krazati®) (Feb 3, 2025)
4. JCA Subgroup Exercise 05 - Etranacogene dezaparvovec (Hemgenix®) (Feb 3, 2025)

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