The PICO definition: the EUnetHTA 21 case study

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JCA production process & relevant HTA Regulation Articles

Initiation Phase

Art. 6 – annual work plan

Art 7 – health technologies subject to JCA

Scoping Phase

Art. 8 – Initiation of JCA & PICO development

Art. 9 – Submission Dossier

Art. 10 – Obligations of HTD

Assessment phase

Art. 10 – Obligations of HTD

Art. 11 – Assessment process

Art. 12 – finalization of JCA

Art. 13 – MS obligations

Art. 14 – updates of JCA

Implementing Acts

Art. 15 –detailed procedural rules JCA

Art. 25 – rules involvement & selection external experts and stakeholder organisations

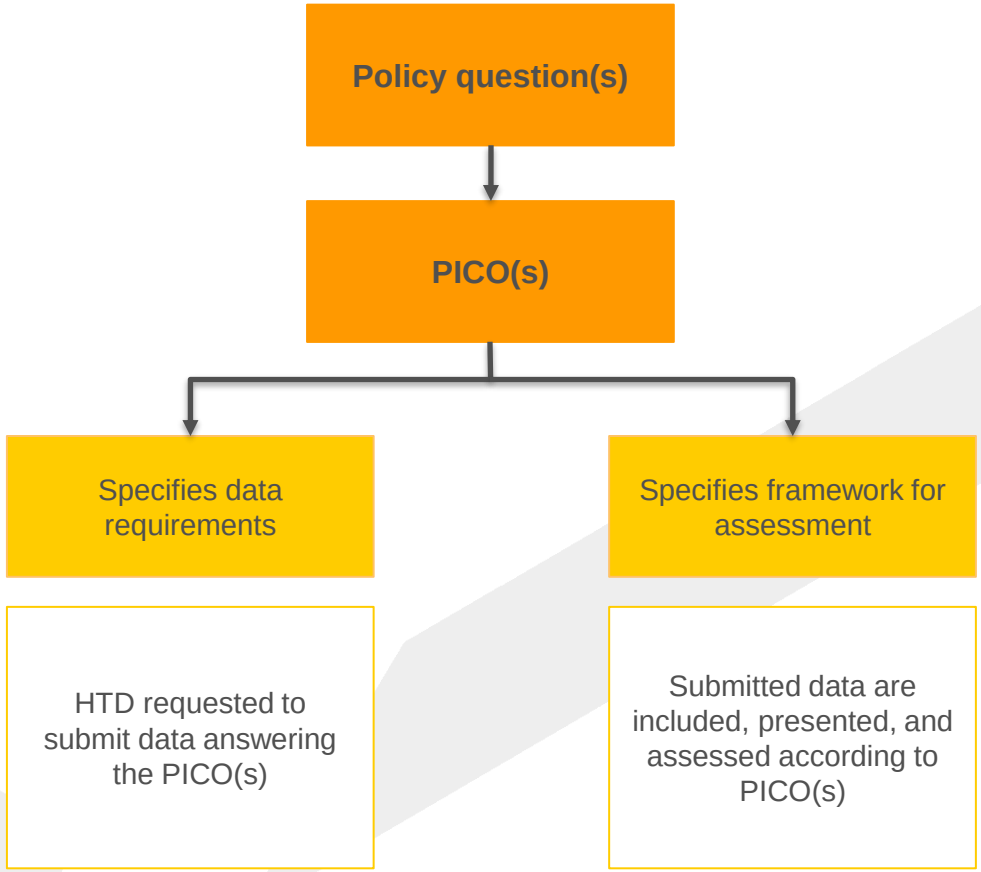
Art. 26 – format & templates of submission dossier & JCA report

Role of PICO into JCA

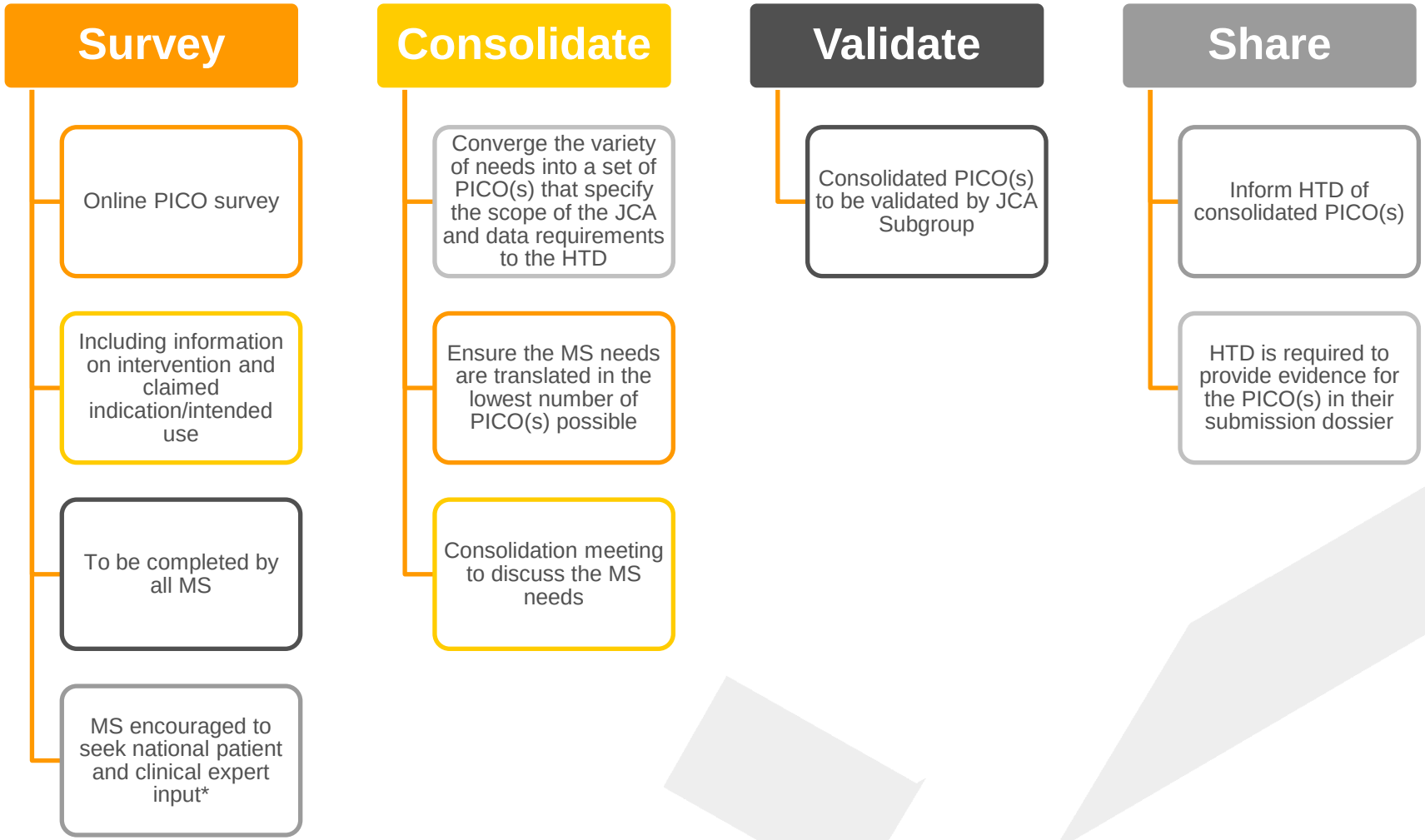
More information on: https://www.eunethta.eu/d4-2/

- Key principles:
  - Inclusiveness
  - Independence

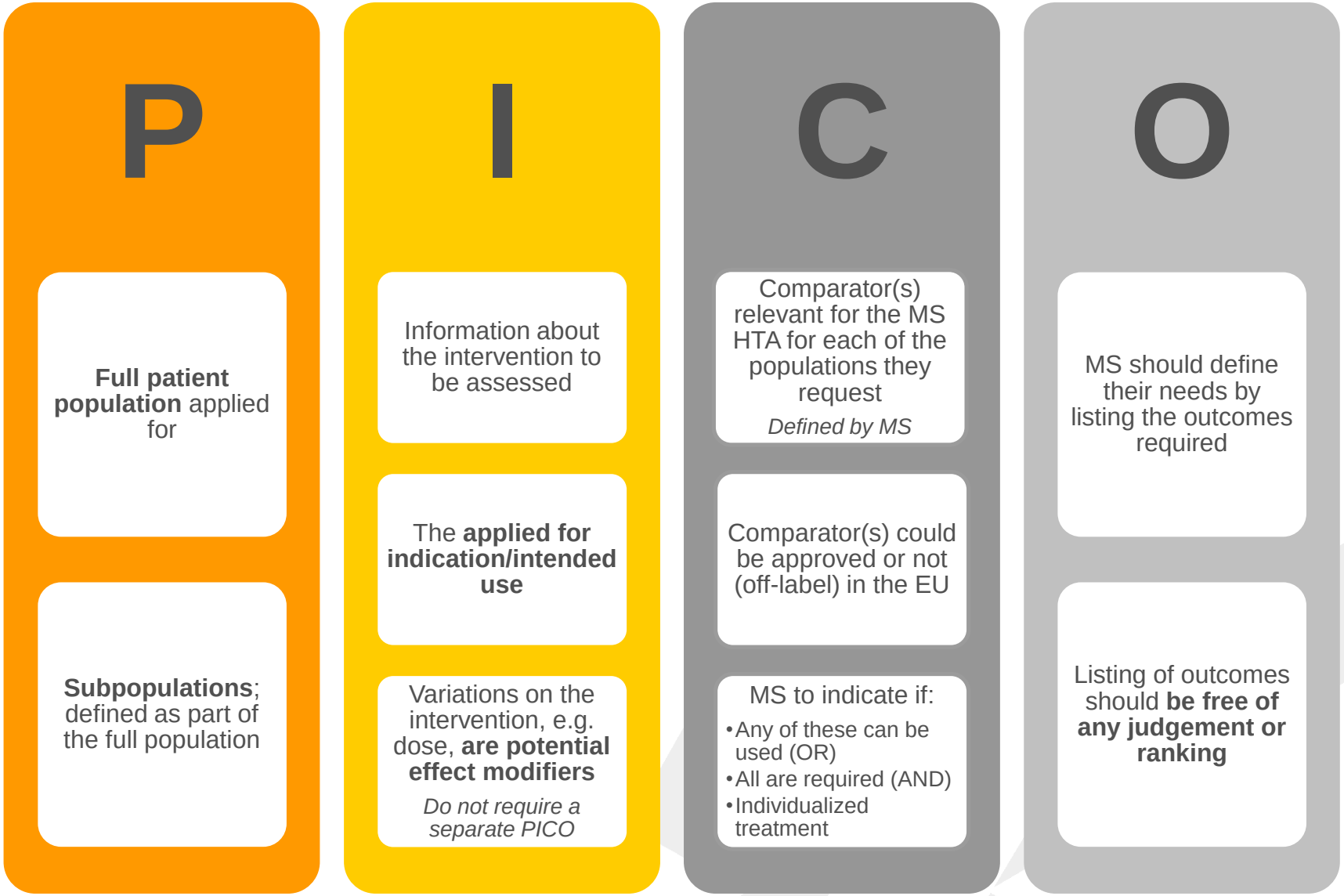
- PICO should **not be data** driven, but based on policy needs
- Should reflect all Member States' needs (HTAR Art. 8)
  - MS receive information on
    - The intervention to be assessed and claimed indication/intended use in EU is provided
    - Any Joint Scientific Consultation that might have taken place.
      - However, the JCA PICO should be generated under the conditions existing at the time of the survey.



PICO development process



*this process flow does not show the EU level patient and HCP input.

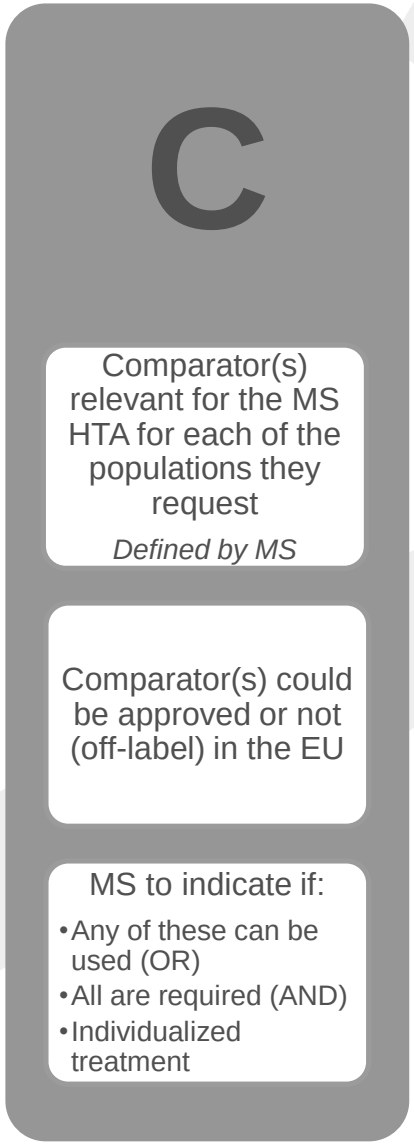

P
Full patient population applied for
Subpopulations; defined as part of the full population
I
Information about the intervention to be assessed
The applied for indication/intended use
Variations on the intervention, e.g. dose, are potential effect modifiers
Do not require a separate PICO
C
Comparator(s) relevant for the MS HTA for each of the populations they request
Defined by MS
Comparator(s) could be approved or not (off-label) in the EU
MS to indicate if:
•Any of these can be used (OR)
•All are required (AND)
•Individualized treatment
O
MS should define their needs by listing the outcomes required
Listing of outcomes should be free of any judgement or ranking

Comparators – different scenario's

- AND scenario
  - All the listed comparators are required for the comparison
  - Seperate PICO required for each of the comparators, so only 1 C per PICO

- OR scenario
  - All comparators are equally suitable for the population
  - The comparator(s) meeting most MS requirements can be selected/combined in consolidation

- Individualized treatment scenario
  - If comparator does not applly to all patients in the population
  - Treatment is chosen for an individual patient by the physician, from multiple available options
    - All are considered standard of care depending on patient characteristics
    - Choice is based on individual patient characteristics for treatment decision
    - e.g. pre-treatment, localisation of tumor



Learnings from EUnetHTA 21 PICO exercises

EUnetHTA 21 PICO exercises	Pluvicto®	Ebvallo®	Pombiliti®
CHMP opinion	13 Oct 2022	16 Dec 2022	15 Dec 2022
Therapeutic area	Oncology	ATMP; orphan	Orphan
Indication	Metastatic castration resistant prostate cancer	Epstein-Barr virus positive post-transplant lymphoproliferative disease	Late-onset Pompe disease
MS (associated HTAb participation)*	8 (n/a)	10 (3)	10 (4)
# PICOs	6	5	9
# Populations	5	4	3
# Comparators	6	5	4
# Outcomes/*****	18	22	18

Source: EUnetHTA 21. D.5.4 JCA without HTD submission https://www.eunethta.eu/d5-4/ (date accessed: 14/9/23)
*The first survey on was only sent to EUnetHTA 21 members, the other two were send to more organisations. MS were asked to give one answer per country. **When different outcomes were mentioned in one line these were counted separately (e.g., radiological tumour assessment, including ORR and DoR was counted as 2 outcomes). ***Outcomes were not consolidated

Key take-aways

- Based on products with positive CHMP opinion
- In the first therapeutic areas in scope under the HTAR
- Through consolidation the number of PICOs were reduced significantly
  - The number of PICOs ranged from 5 to 9; these PICOs were consolidated across 8-10 MS only
  - All case studies included full population as per EMA label, with PICOs for up to 4 subpopulations
  - Comparators: included physician's choice and individualised therapy
- Only the consolidated PICO at EU level will be published (not the individual MS level PICOs)
- Learnings and revisions made
  - Two weeks is short for MS to return the survey
  - PICO survey 2 and 3 based on proposal by assessor
  - Incorporation of glossary to standardize terminology used
  - Recommendations for a PICO Working Group to standardize consolidation process