Impact of the EU HTA Regulation

Global industry perspective

12 October 2023

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Agenda

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Question 1

Do you feel you are well informed and know enough about the new EU HTA Regulation?

Question 2

Are you clear on how this regulation will affect your organization’s EU HTA operations?

Question 3

Are you facing any obstacles within your organization to plan for the Regulation’s full implementation?

November 2022: does the industry feel prepared?

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ISPOR EU November 2022

Most participants are not sure about the content and impact of the EU HTA Regulation

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Key: HTA, health technology assessment.

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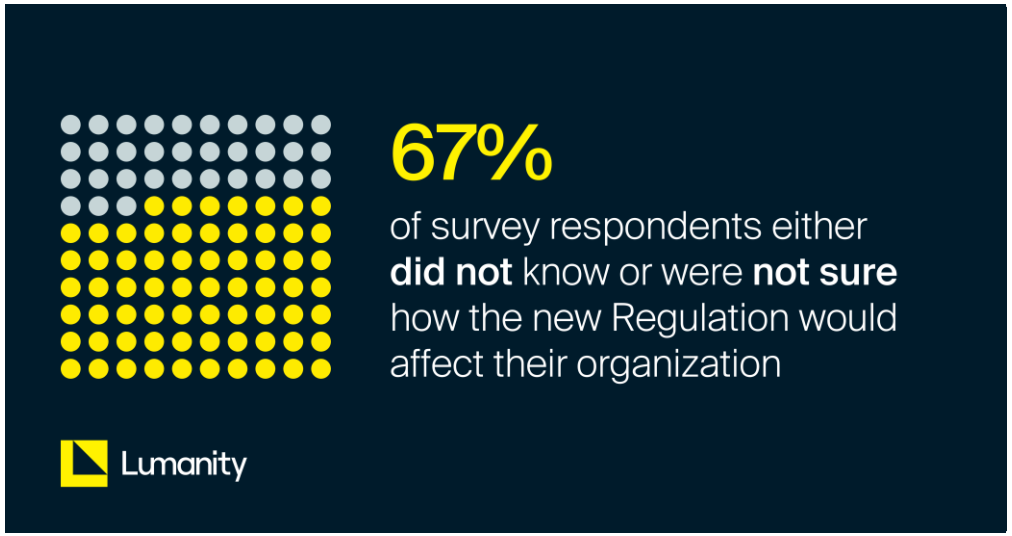

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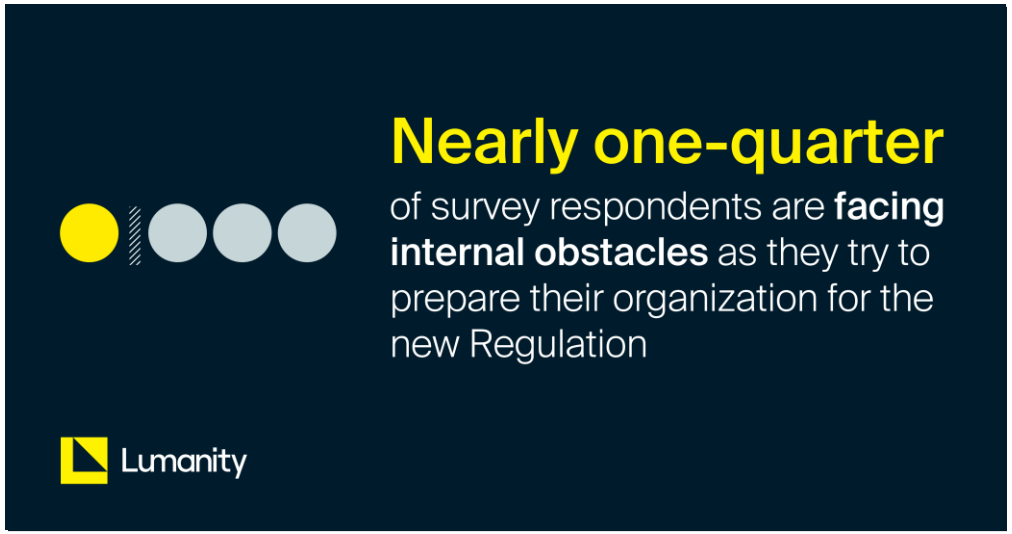

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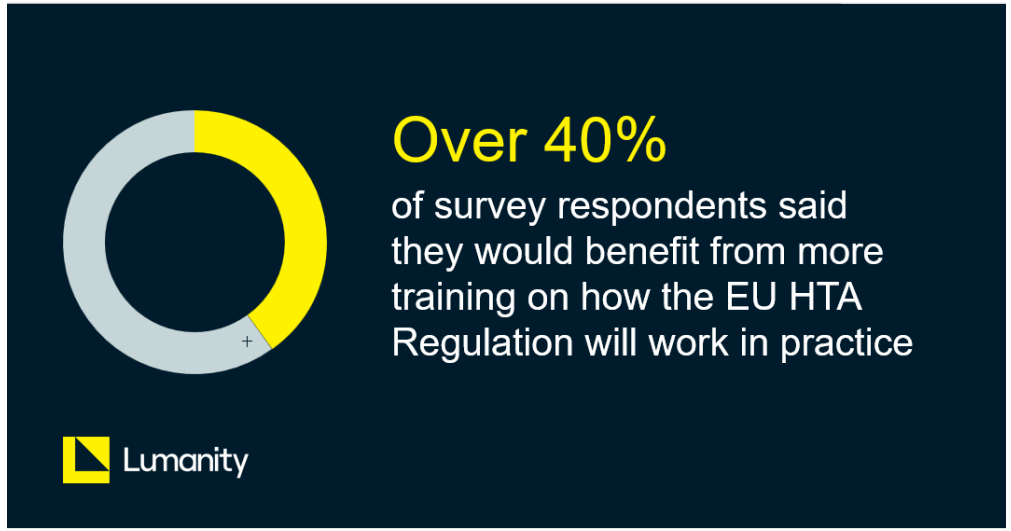

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Key: HTA, health technology assessment.

Expressed concerns

The industry has discussed their main worries in dialogues with HTA bodies

Concerns of the industry focus on feasibility of meeting the dossier requirements under tight timelines and resources

Number of decision problems and **no opportunity to contribute** to the scoping process

The JCA must be inclusive, meaning that all Member States' needs will be taken into account via a survey, but will be converted into as few PICOs as possible. There is no opportunity for companies to contribute to PICO scoping or respond to the JCA's conclusions.

Complexity and **short timeframes**

PICO scoping may result in a multitude of comparators thus requiring a large number of indirect treatment comparisons (ITCs) and a wide range of alternative methods to accommodate the preferences of different member states, adding to the size of the dossier. This could be challenging given the tight timelines, especially for small and mid-size pharmaceutical companies with limited resources.

Risk of **duplication** of work

Since the appraisal decision remains with the Member States, there is a risk of duplication of work at a national level. It remains to be seen how 'due consideration' will play out following the joint work.

Stringent evidence and **methodological requirements**

RCT is the golden standard. Any other design would need to be justified in the JCA and will be criticized.

In the case of non-randomized controlled trials, no methods for comparative efficacy using aggregate data are sufficient. Methods for unanchored comparisons should be based on patient level data (PLD). The possibilities for acquiring such data rely on making early decisions on whether trials can be designed to better address these challenges.

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Key: HTA, health technology assessment; ITC, indirect treatment comparison; JCA, joint clinical assessment; PICO, population, intervention, comparator, outcome; PLD, patient-level data; RCT, randomized controlled trial.

The impact of the EU Regulation on the estimation of comparative efficacy

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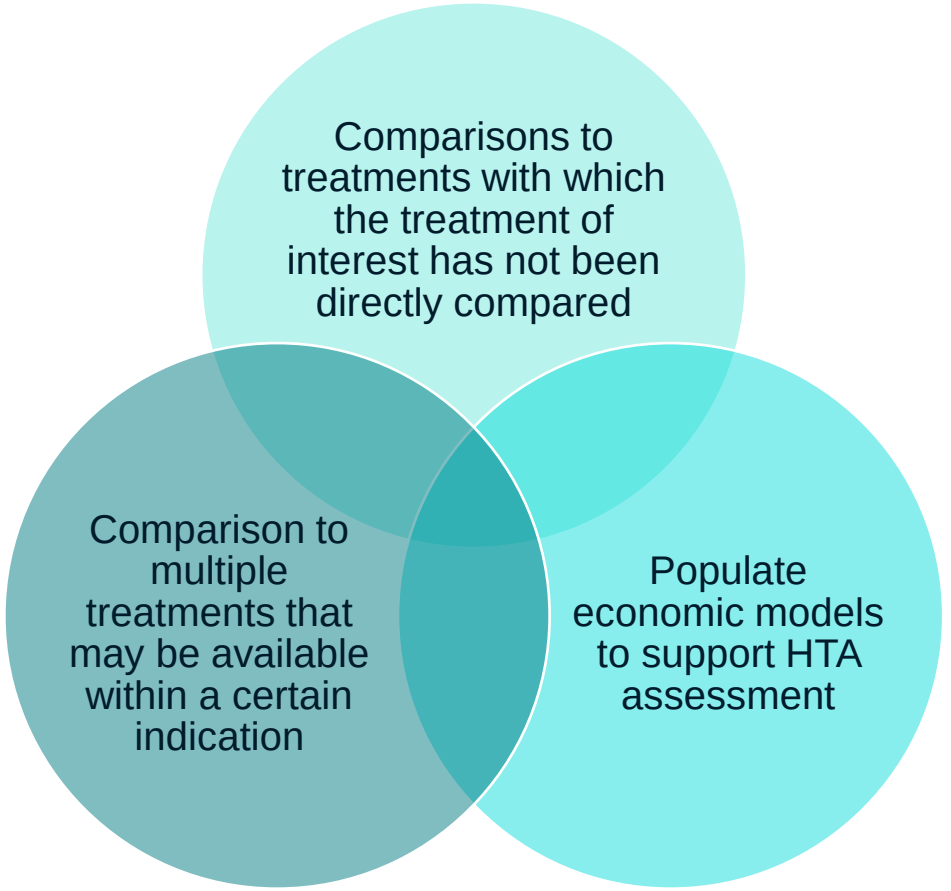
Broader objectives for comparative efficacy increase the demands on ITC

Generally, ITCs are developed for the following goals:



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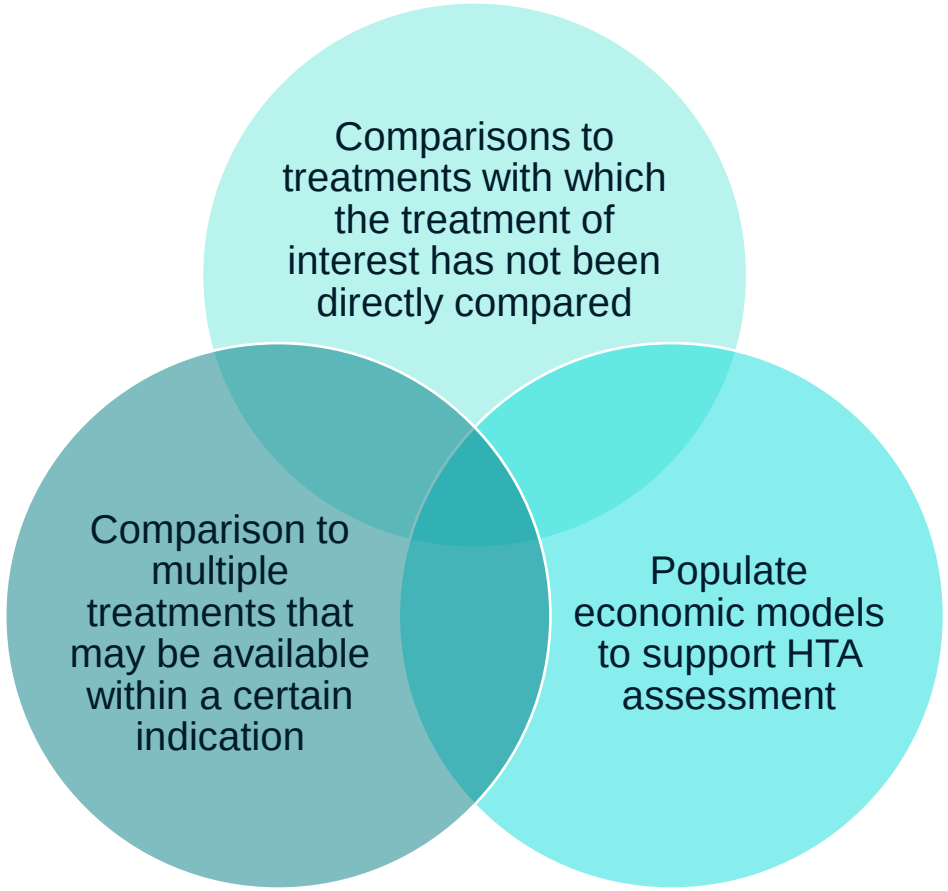
Broader objectives for comparative efficacy increase the demands on ITC



Importantly, these goals are tailored by country that each have specific requirements and preferences related to:

- Comparators, endpoints and populations
- Acceptability of alternative ITC methods

The different country preferences and needs can impact the demands of any ITCs related to these factors, including:

- Greater number of relevant comparators
- Focus on different patient population or subgroups
- Potential emphasis on different outcomes
- Willingness to accept different methodologies

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Key: HTA, health technology assessment; ITC, indirect treatment comparison.

Multiple PICOs may be required to meet member state requirements

Potential challenges of covering multiple PICOs

- Dilute the main objective of the ITC into multiple possible objectives
- Create an unwieldy evidence base and large body of resulting evidence that can be difficult to manage, particularly within the timeframes
- Increased likelihood of a large, poorly connected network given the potentially broader range of relevant comparators

A clear understanding of the likely treatment landscape and careful upfront planning for analysis timing will be essential to address these challenges

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Key: ITC, indirect treatment comparison; PICO, population, intervention, comparator, outcome.

What to do when RCTs are not viable

Orphan indications and ATMPs for example

Gold standard not feasible

We must consider other approaches that allow us to estimate comparative efficacy, despite their limitations

Comparative efficacy for a new therapy still needs to be estimated to support HTA submissions, as this will avoid delaying access for patients to potentially life-saving treatments

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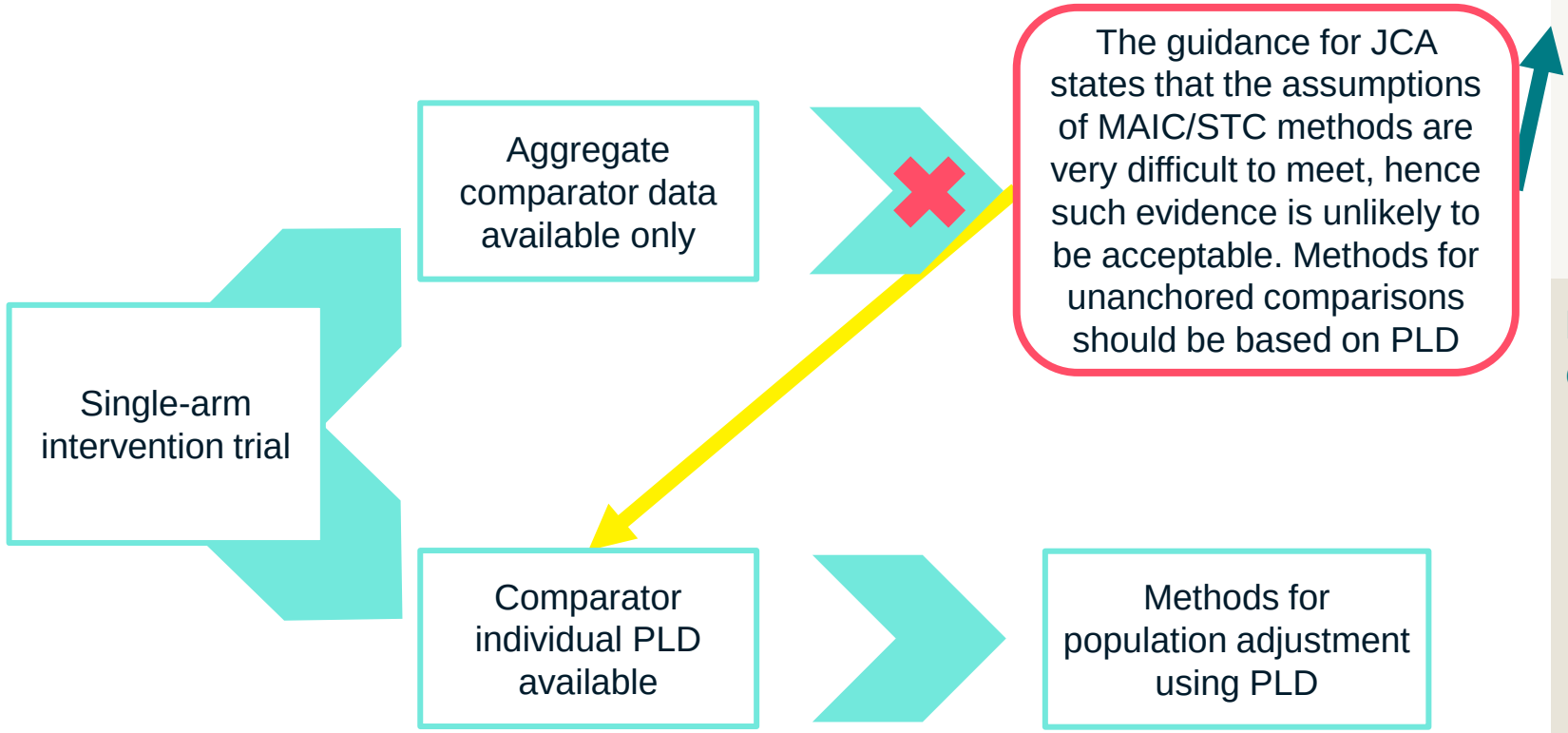
Key: ATMP, advanced therapy medicinal products; HTA, health technology assessment; RCT, randomized controlled trial.

What to do when RCTs are not viable

Orphan indications and ATMPs for example



Early considerations for trial design

- Ensures that relevant outcomes are collected
- Consider early on in the process how treatment comparisons will be made, what the most appropriate comparator is, whether an RCT is viable?

Proactive RWE data collection/generation

- Can comparator IPD be accessed or collected
- Preferred ITC methodologies can be used in the case of single-arm trials
- Analyses can be more flexible (possibly)

However, generating/gaining access to IPD to sufficiently address a potentially broader PICOs remains challenging

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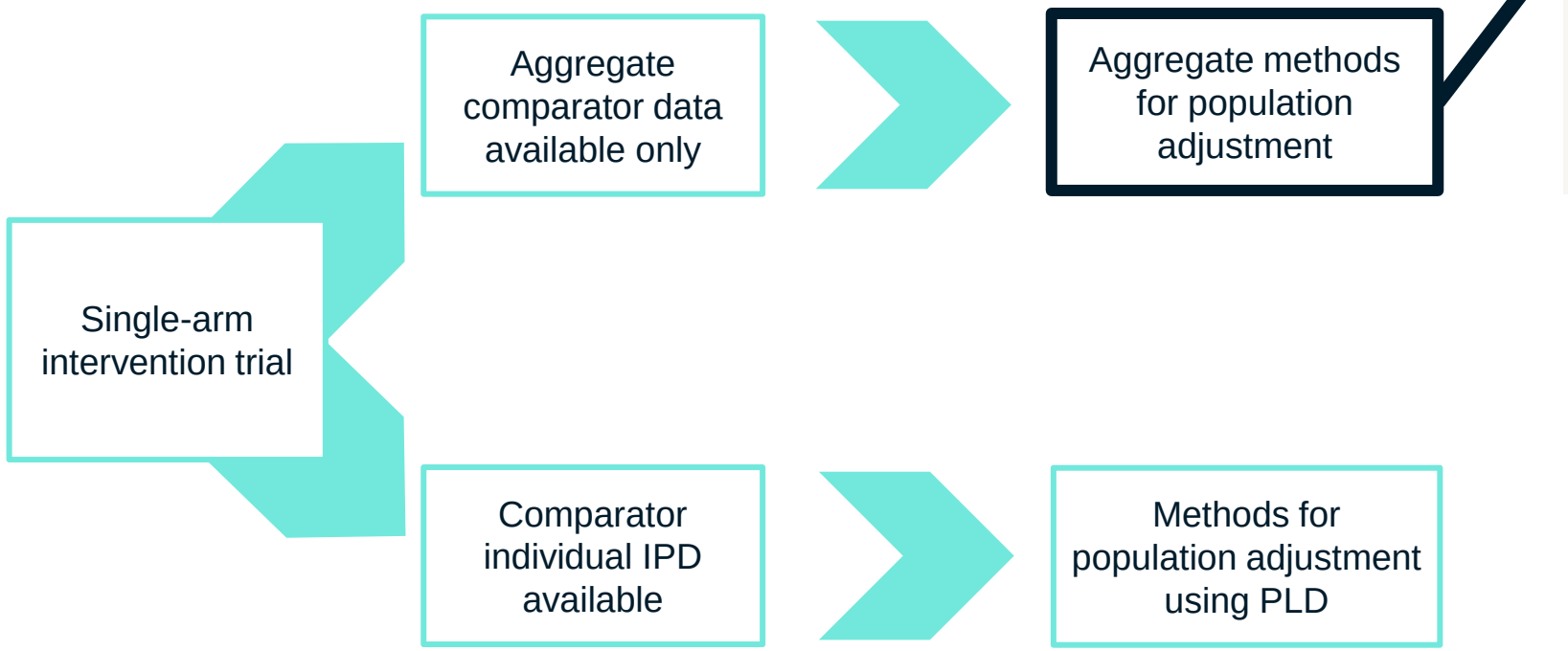
Key: ATMP, advanced therapy medicinal products; ITC, indirect treatment comparison; IPD, individual patient data; JCA, joint clinical assessment; MAIC, matching-adjusted indirect comparison; PLD, patient-level data; RCT, randomized controlled trial; RWE, real-world evidence; STC, simulated treatment comparison.

What to do when RCTs are not viable

Orphan indications and ATMPs for example



Generate estimates of comparative efficacy using aggregates despite issues. Ensure **clear justification** and a comprehensive suite of **scenarios** are developed to explore the known limitations of these methods

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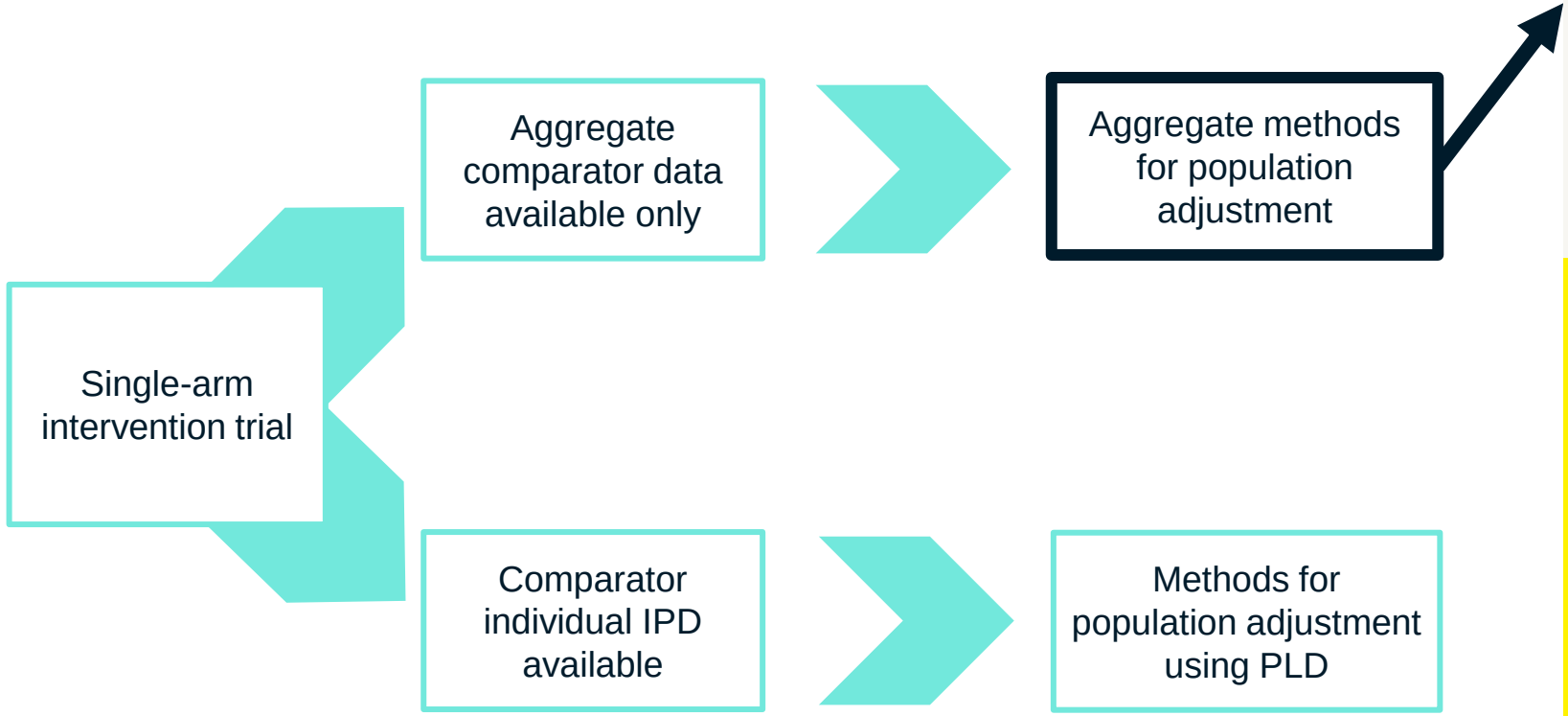

Generate estimates of comparative efficacy using aggregates despite issues. Ensure **clear justification** and a comprehensive suite of **scenarios** are developed to explore the known limitations of these methods

This approach could be:

- *Vital* – we have no other option that does not delay access to patients
- *Necessary* given we are unlikely to have access to IPD for all possible comparators
- *Required* if countries request specific analyses
- The *best way* to make the most of the data that are available

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Closing remarks

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Impact of the regulation by scenario

Challenges affect different indications in different ways

Challenges related to study design and statistical analyses create more difficulties for ATMP and orphan diseases

Multiple PICOs are more challenging for large disease areas, e.g. oncology

In either case, these methods make best use of the empirical data that are available.

When considering these methods, it will be important to acknowledge their limitations and comprehensively explore the impact of these limitations

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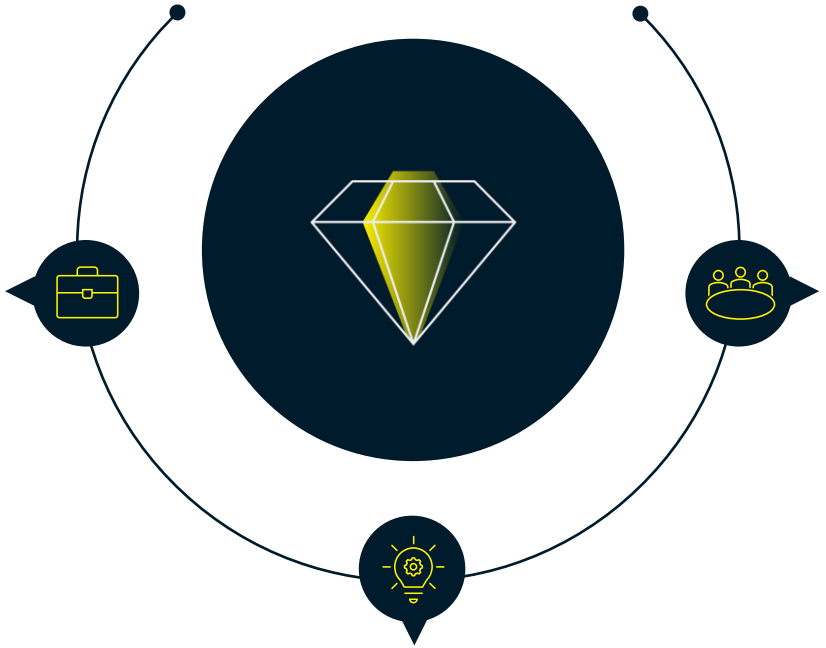
Key: ATMP, advanced therapy medicinal products; ITC, indirect treatment comparison; JCA, joint clinical assessment; PICO, population, intervention, comparator, outcome.

Preparation is key

Proactive planning will be crucial for success

Landscaping

Exploration of PICOs across member states to anticipate the scope of the JCA



Internal preparation

- Awareness of requirements
- Evaluation of internal processes and consideration of operational and infrastructure changes to ensure global and local affiliates will be ready for the regulation

Evidence generation plan

Careful planning of clinical trial design and comparative efficacy strategy, including statistical analysis plan

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Key: JCA, joint clinical assessment; PICO, population, intervention, comparator, outcome.

Thank you

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