EMA
EUROPEAN MEDICINES AGENCY

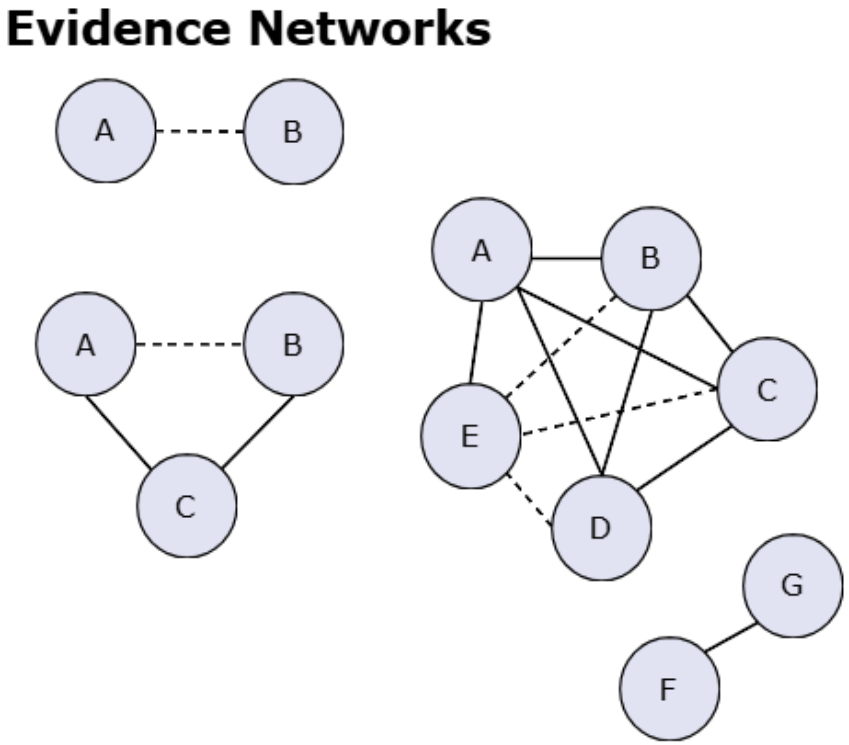
Development of a new guidance for reporting on indirect comparisons

16th Industry Stakeholder Platform on R&D support

Artur Lewandowski & Anouk Neven

Why indirect comparisons?

Recall the third criterion: […] *if such a method already exists, the medicine must be of significant additional benefit*[…].



Potential approaches: Side-by-side, Matched Adjusted Indirect Comparisons (MAIC), Network Meta-Analysis (NMA), …

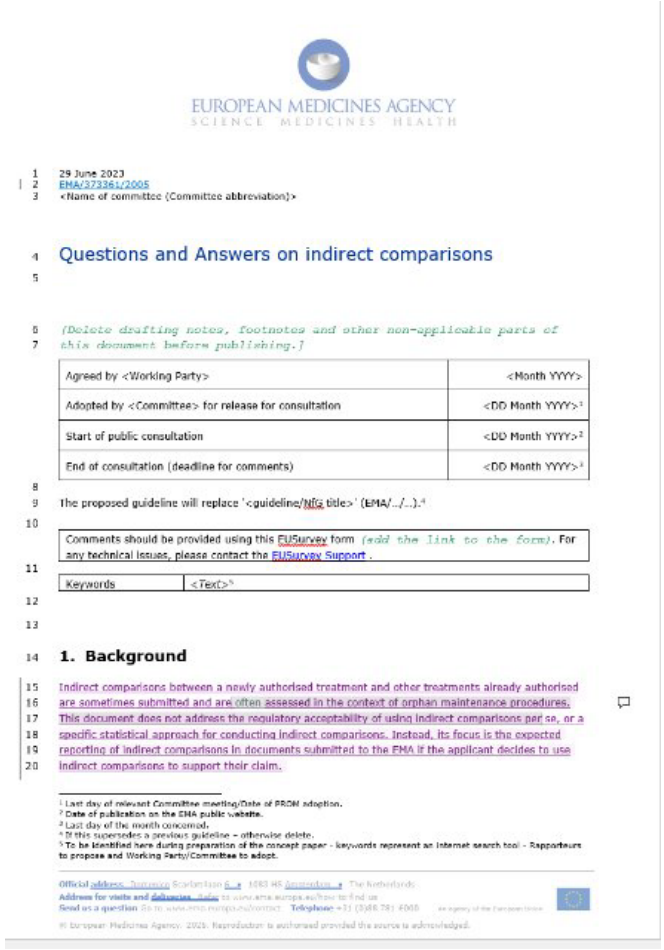
In general, we feel that we see an **increasing use** of quantitative approaches

But…

'**Intransparent**' and '**heterogeneous**' reporting (see next slides)

Guidance development: Q&A on indirect comparisons

- Collaboration across MWP, COMP and CHMP (referenced in MWP workplan Methodology Working Party Workplan 2026-2028 - Adopted)
- No regulatory documents exist; HTAs have guidance (HTA CG link 1, link 2; NICE DSU TSD18)
- Focus on **improving the reporting**, not on evidentiary standards or permissive contexts
- Main use case is significant benefit and the COMP, but can also be of relevance in other assessments (e.g. conditional marketing approval by CHMP)



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29 June 2023
EMA/373361/2005
<Name of committee (Committee abbreviation)>

Questions and Answers on indirect comparisons

(Delete drafting notes, footnotes and other non-applicable parts of this document before publishing.)

Agreed by <Working Party>	<Month YYYY>
Adopted by <Committee> for release for consultation	<DD Month YYYY>[2]
Start of public consultation	<DD Month YYYY>[2]
End of consultation (deadline for comments)	<DD Month YYYY>[3]

The proposed guideline will replace '<guideline/NfG title>' (EMA/.../...).[4]

Comments should be provided using this EUSurvey form *(add the link to the form)*. For any technical issues, please contact the EUSurvey Support .

Keywords	<Text>[5]

1. Background

Indirect comparisons between a newly authorised treatment and other treatments already authorised are sometimes submitted and are often assessed in the context of orphan maintenance procedures. This document does not address the regulatory acceptability of using indirect comparisons per se, or a specific statistical approach for conducting indirect comparisons. Instead, its focus is the expected reporting of indirect comparisons in documents submitted to the EMA if the applicant decides to use indirect comparisons to support their claim.

[1] Last day of relevant Committee meeting/Date of PRAC adoption.
[2] Date of publication on the EMA public website.
[3] Last day of the month concerned.
[4] If this supersedes a previous guideline – otherwise delete.
[5] To be identified here during preparation of the concept paper - keywords represent an internet search tool - Rapporteurs to propose and Working Party/Committee to adopt.

Evaluating ITC use in orphan maintenance procedures

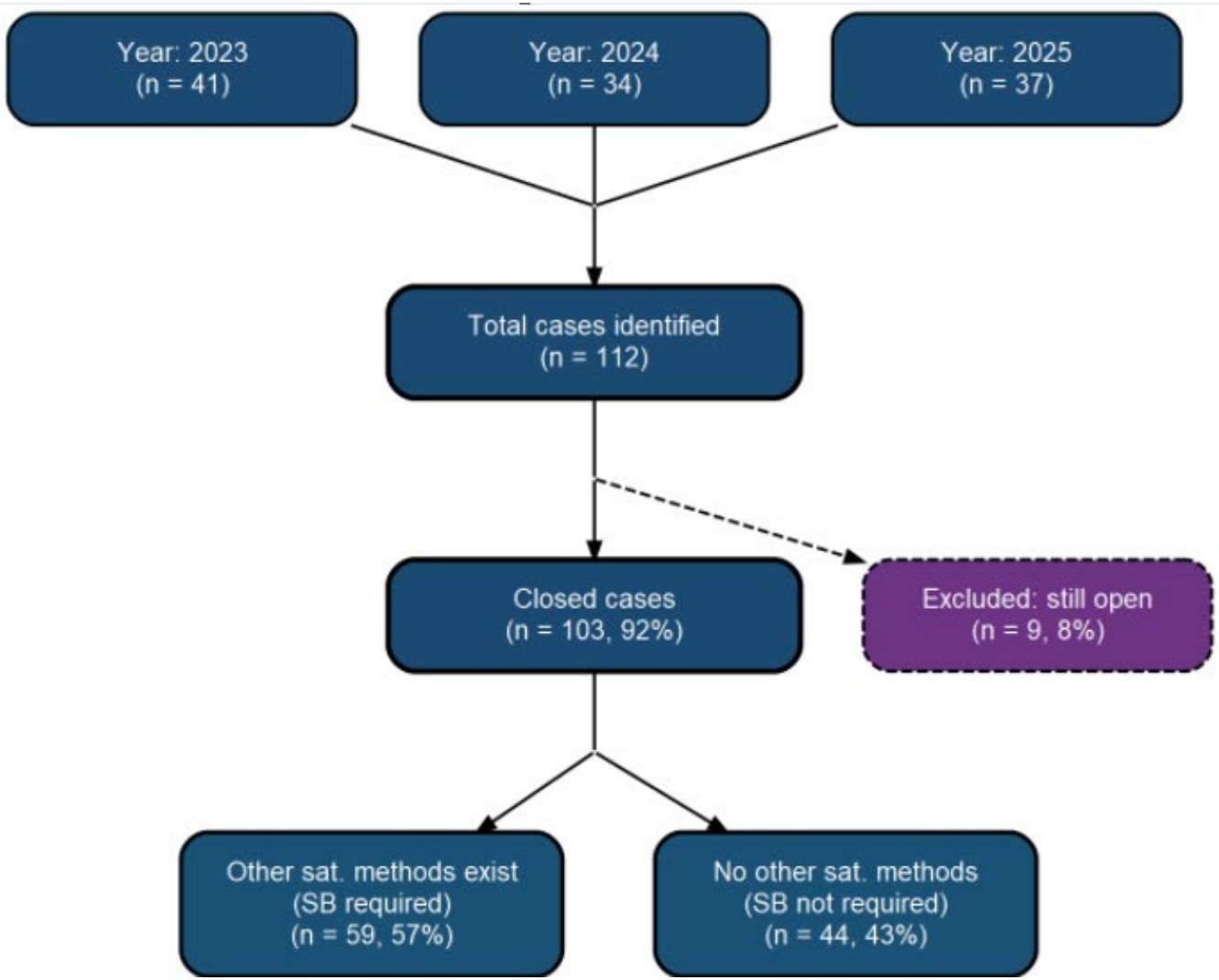
We evaluated **all orphan maintenance procedures** initiated between 2023 to 2025 to analyse ITC use and reporting.

From initial submissions we extracted:

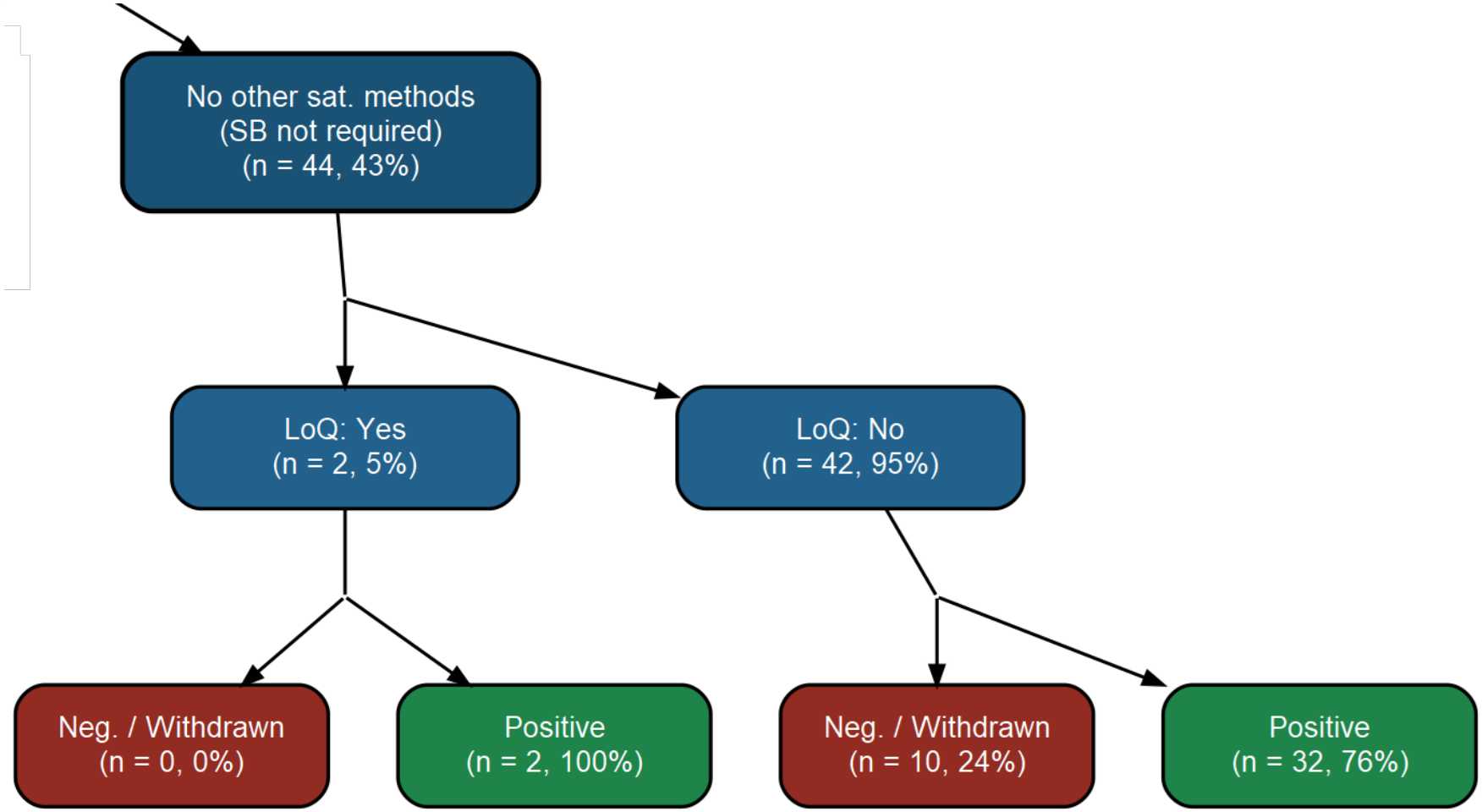
- Type of ITC method used
- Presence of ITC-specific reporting elements
- Issuance of List of Questions (LoQ)
- Procedural outcome

The goal was to review current practices and reporting by sponsors and to identify potential areas of improvement.

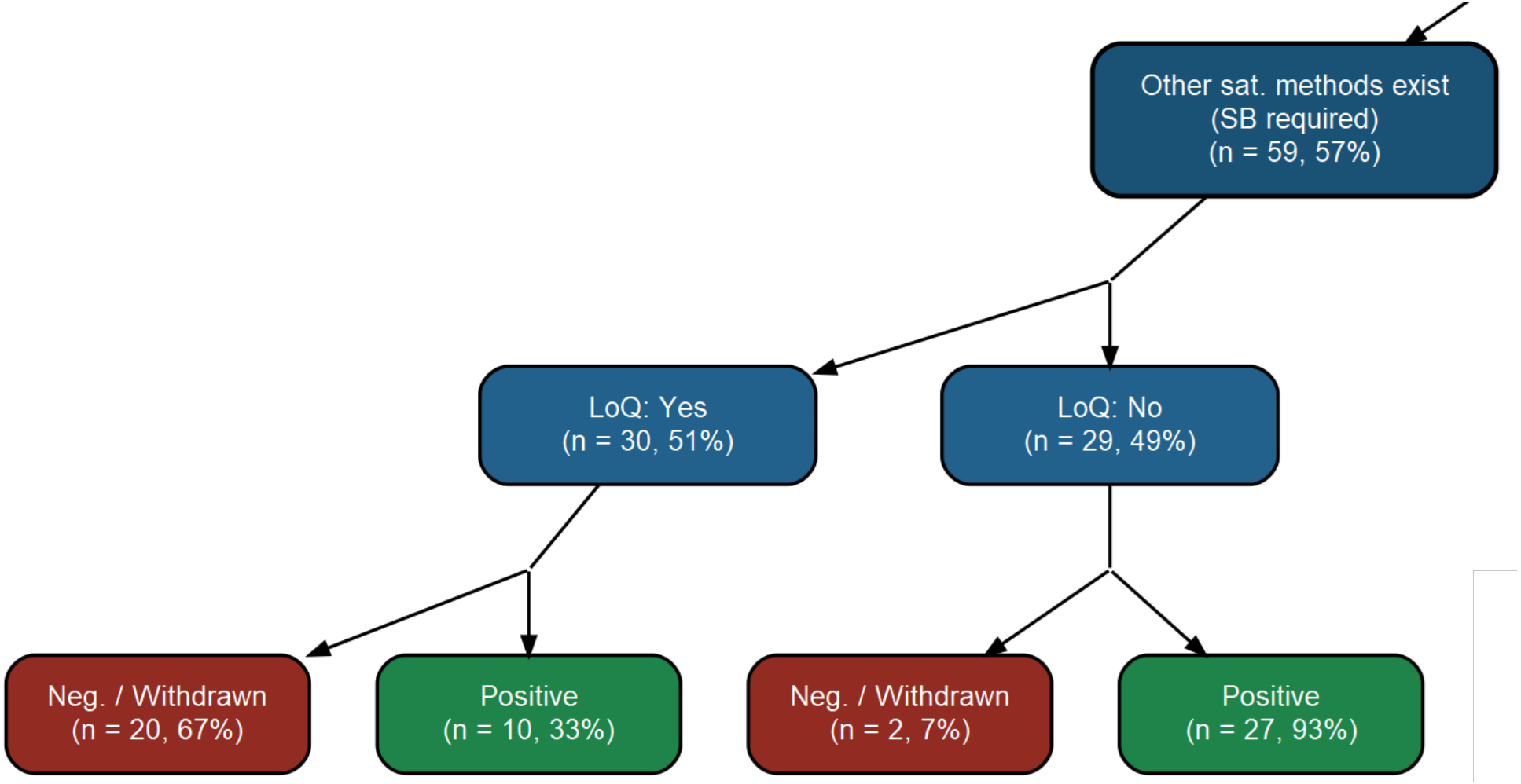
Flowchart (1)



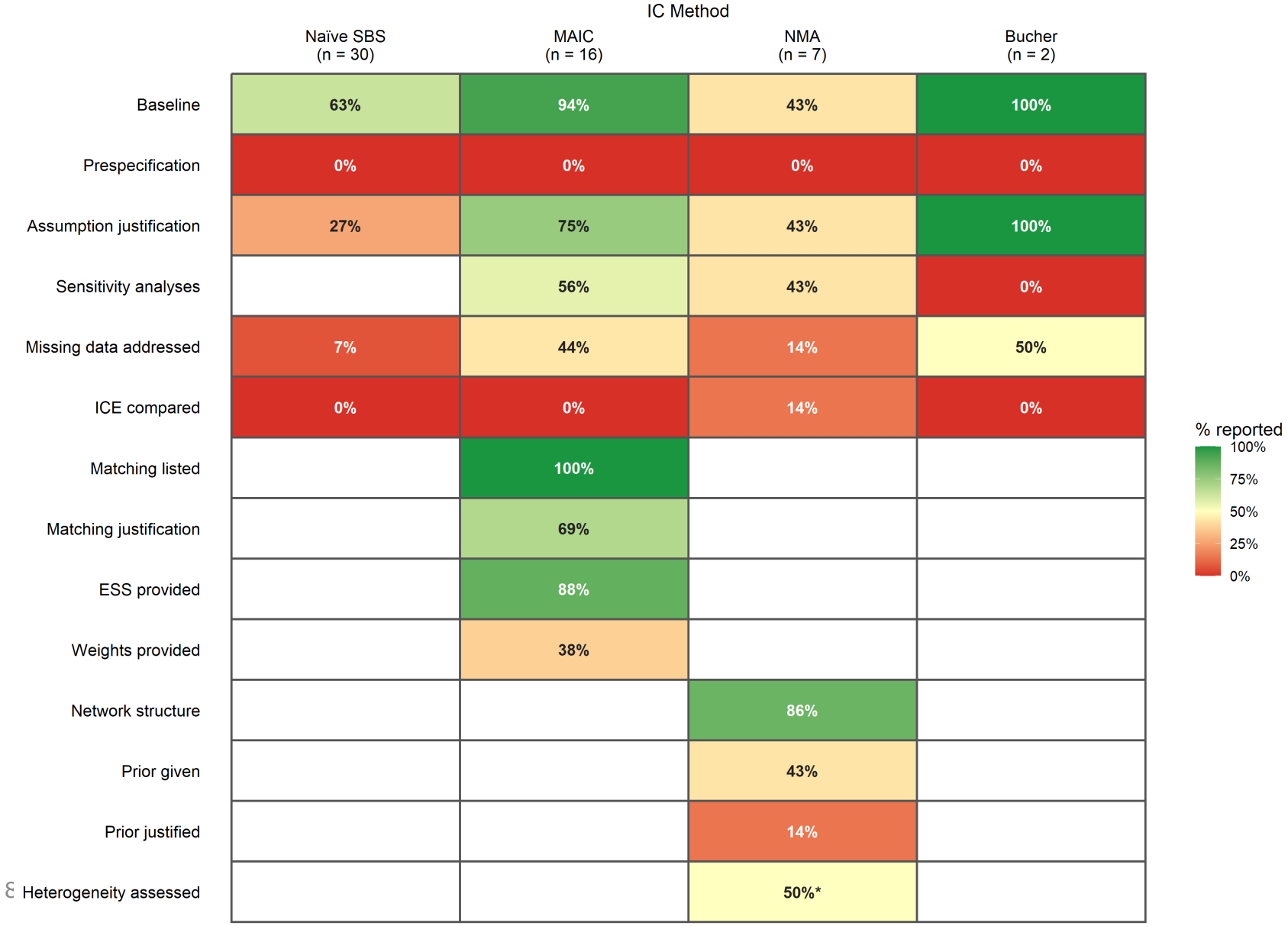
Flowchart (2)



Flowchart (3)



Reporting elements completeness per ITC method



□ White cell = Element not applicable for this IC method

Reporting elements completeness per ITC method

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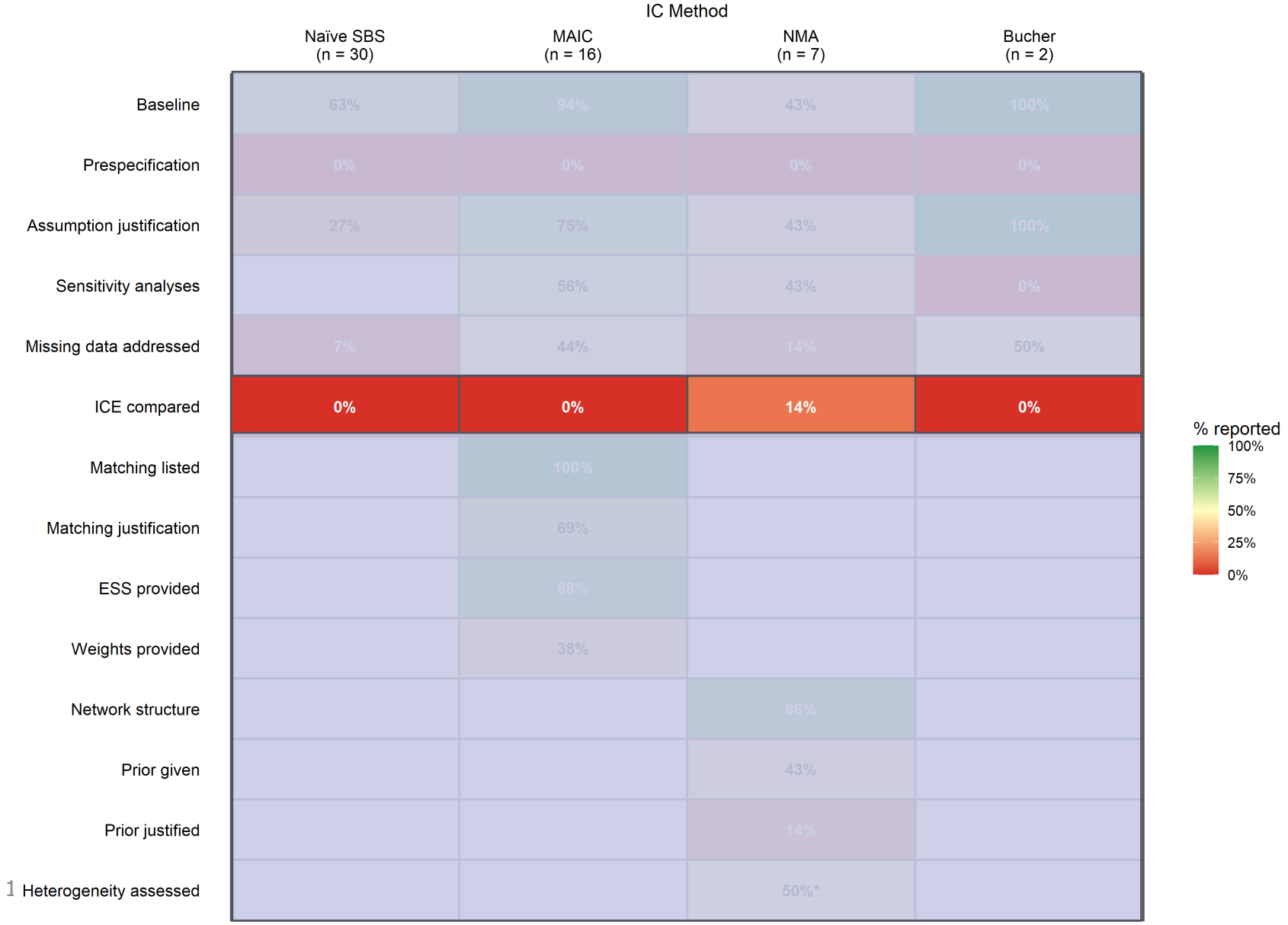
Reporting elements completeness per ITC method



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Reporting elements completeness per ITC method

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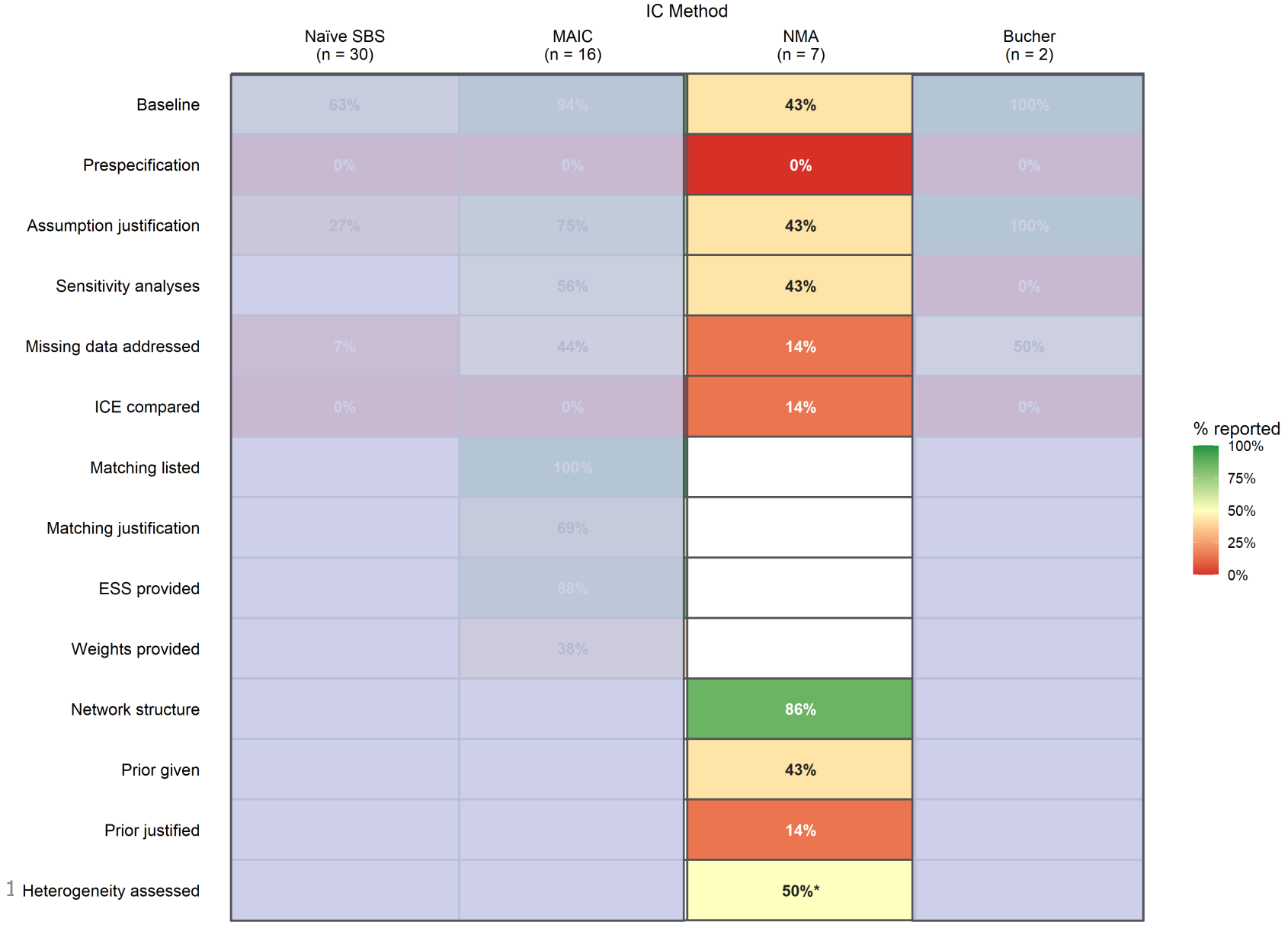
Reporting elements completeness per ITC method



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Conclusions

- The reporting standards are heterogenous. Reports range from a single paragraph with a point estimate (and CI) to 100+ page ITC reports done by contractors.

- Procedures requiring evidence of significant benefit are commonly associated with issuance of LoQ, mostly driven by lack of transparency and incomplete reporting.

- The Q&A on indirect comparisons and the upcoming publication on ITC use in orphan maintenance procedures will strive to improve the current practices.

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Thank you

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Back-up slide (ESS and MAICs)