Patient-Reported Outcomes in Indirect Treatment Comparisons: A Targeted Literature Review

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Background

- Patient-reported outcomes (PRO) and indirect treatment comparisons (ITC) are both useful tools for assessing the value of treatments and facilitating shared treatment decision-making.

- In the oncology literature, comparative effectiveness research has highlighted direct benefits on various clinical outcomes, such as improving overall quality of life, enhancing functioning, and ameliorating specific symptoms.[1,2]

- However, it remains unclear the extent to which PRO data are included in ITC publications. It is important to note that trials that include PRO-based endpoints may not publish PRO findings as frequently or as comprehensively as other outcomes,[3] thus restricting the ability to include these outcomes in ITC analyses.

- As efforts to increase patient centricity in clinical research continue, it is important to understand the intersection of PRO and ITC by evaluating the inclusion of PRO in ITC publications.
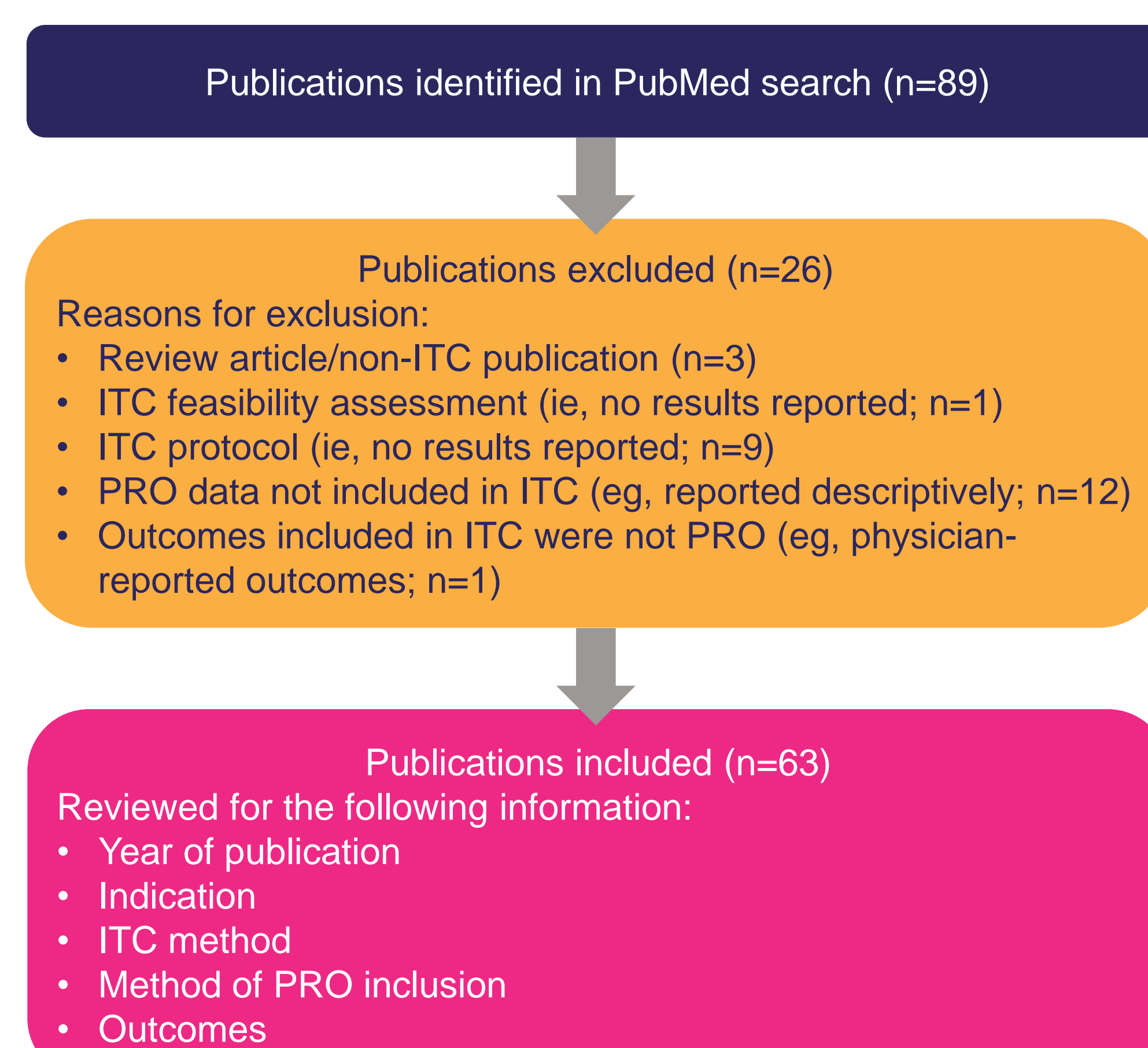
Objectives

- To identify publications reporting on ITC analyses that included PRO
- To assess any changes over time in these publications and whether the inclusion of PRO in ITC analyses was more common in specific indications
- To evaluate whether certain methods were more common and if PRO-related benefits were observed

Methods

- PubMed was searched in December 2024 using the following terms: patient-reported, indirect treatment comparison, network meta-analysis, population-adjusted indirect comparison, matching-adjusted indirect comparison, multilevel network meta-regression, and simulated treatment comparison (Figure 1).

Figure 1. Search and review process

Publications identified in PubMed search (n=89)

Publications excluded (n=26)
Reasons for exclusion:
- Review article/non-ITC publication (n=3)
- ITC feasibility assessment (ie, no results reported; n=1)
- ITC protocol (ie, no results reported; n=9)
- PRO data not included in ITC (eg, reported descriptively; n=12)
- Outcomes included in ITC were not PRO (eg, physician-reported outcomes; n=1)

Publications included (n=63)
Reviewed for the following information:
- Year of publication
- Indication
- ITC method
- Method of PRO inclusion
- Outcomes

Abbreviations: ITC, indirect treatment comparison; PRO, patient-reported outcome

Results

- The targeted literature search yielded 63 publications since 2014.

- From 2014 through 2017, 5 (8%) publications included PRO compared with 15 (24%) publications from 2018 through 2021 and 43 (68%) publications from 2022 through 2024 (Figure 2).

Figure 2. ITC publications including PRO data by year
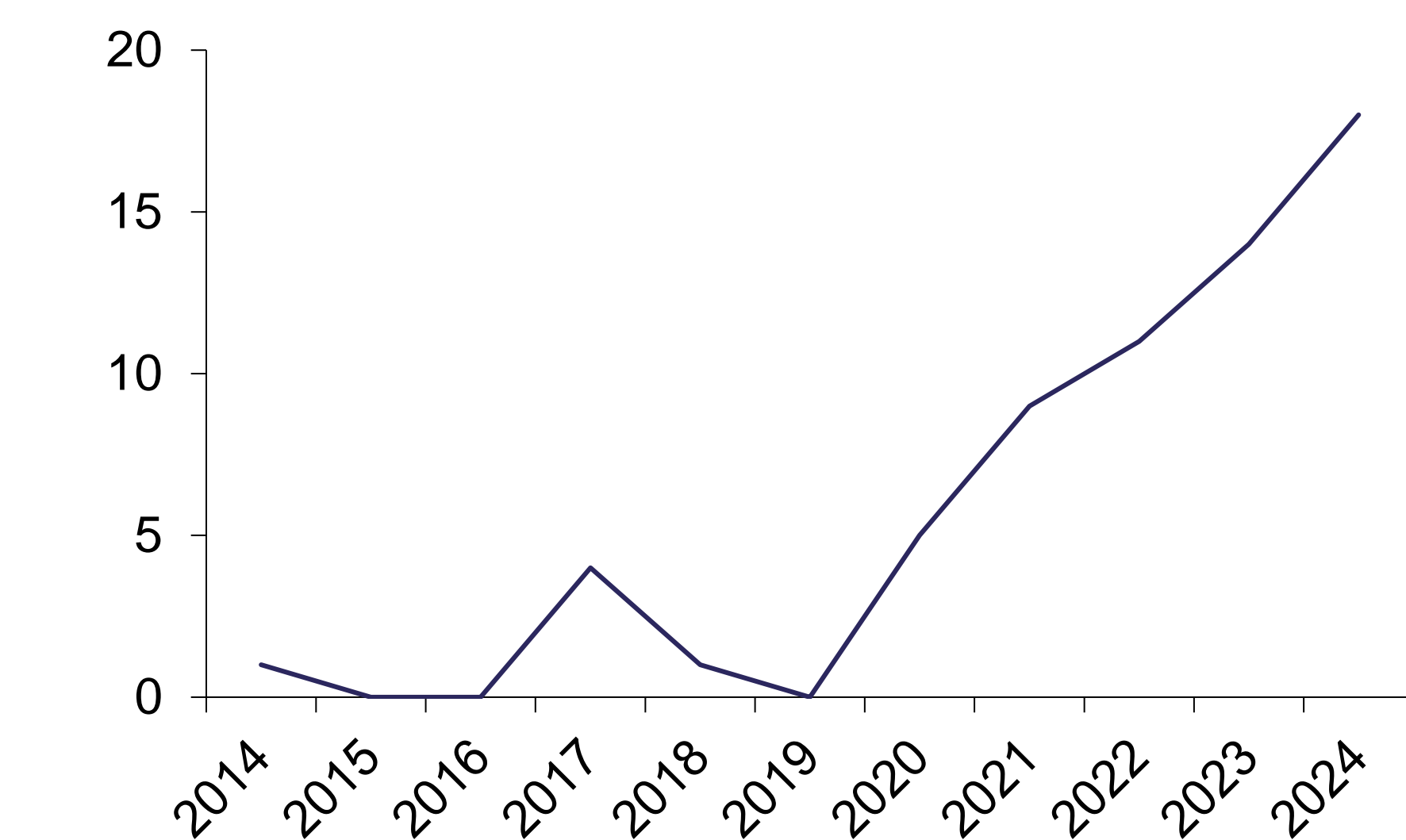
Abbreviations: ITC, indirect treatment comparison; PRO, patient-reported outcome

- Orthopedic publications were most common (orthopedic=35%; dermatology=11%; autoimmune=11%; oncology=10%; CNS=10%; other=24%) (Figure 3).

- Other indications included respiratory, gastrointestinal, periodontics/dentistry, disability, rare disease, urology/gynecology, ophthalmology, surgical, cardiovascular, vein, and sinus.
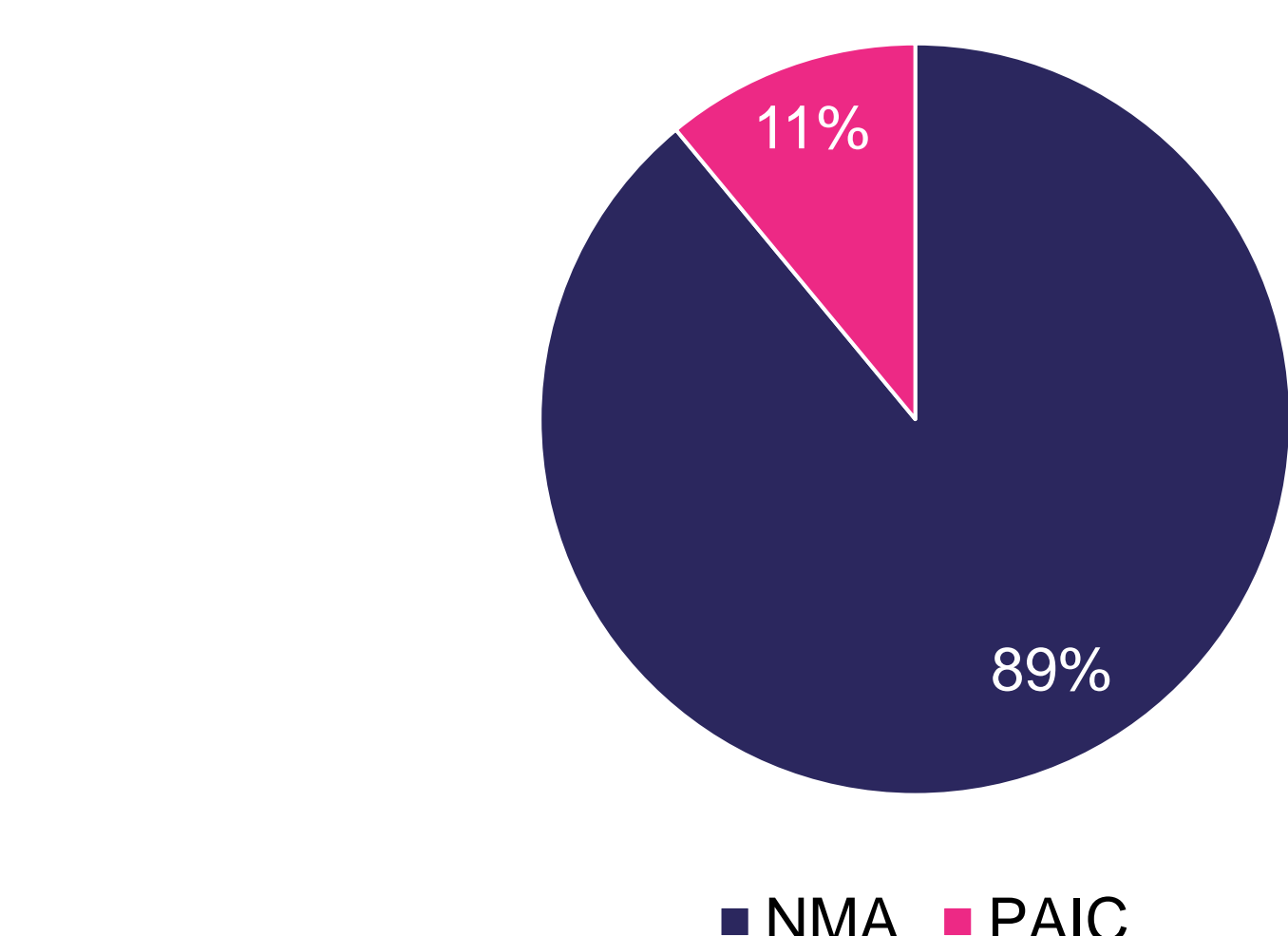
Figure 3. Indications

- Orthopedic 35%
- Oncology 10%
- Dermatology 11%
- Autoimmune 11%
- CNS 10%
- Other 24%
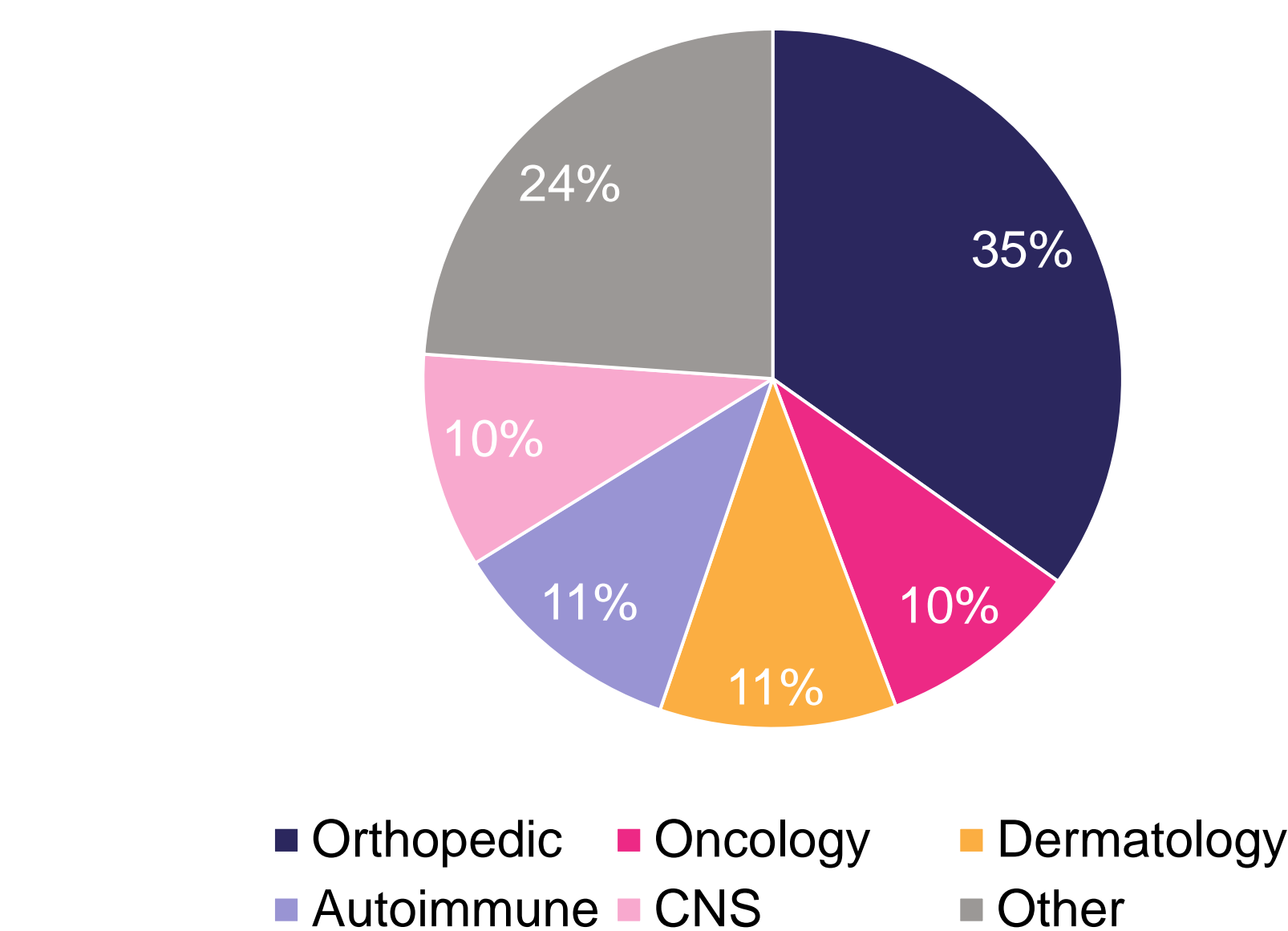
Abbreviations: CNS, central nervous system

- Most publications utilized a network meta-analysis (NMA) approach (n=56; 89%) (Figure 4).

**Figure 4. ITC methods**

- NMA 89%
- PAIC 11%

Abbreviations: ITC, indirect treatment comparison; NMA, network meta-analysis; PAIC, population-adjusted indirect comparison

- Although PRO data were incorporated into ITC analyses in various ways, use of change from baseline results was most common (n=44; 70%) (Figure 5; note that the sum of percentages exceeds 100% because some publications employed multiple approaches to including PRO data in the ITC analyses).

- In addition to minimal clinically important difference (MCID) thresholds, other types of predefined thresholds using PRO data included response, treatment success, satisfaction, and remission.

- Beyond change from baseline and achieving predefined thresholds, other methods included the percentage of patients reporting a specific outcome, the probability of improvement or response, score(s) at specific timepoint(s), and deterioration/non-deterioration endpoints.

- In 11 publications (17%), additional PRO measures could not be included in the ITC analyses due to insufficient data.

Figure 5. Methods of PRO data inclusion

- CFB 70%
- Threshold 14%
- NR 13%
- Other 16%
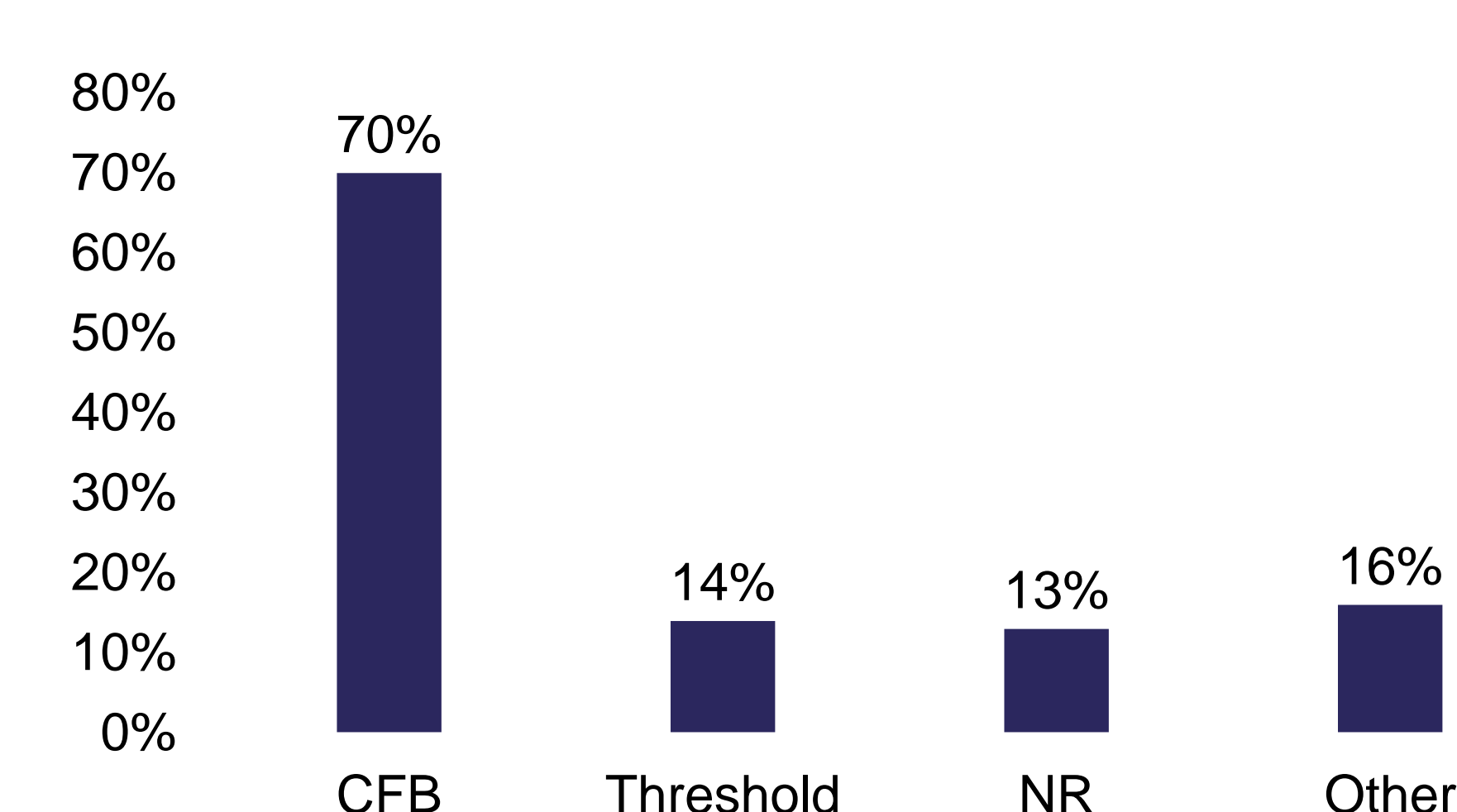
Abbreviations: CFB, change from baseline; NR, not reported
Note: The sum of percentages exceeds 100% because some publications employed multiple approaches to including PRO data in the ITC analyses.

- About 35% of publications included PRO data only, whereas 65% included a combination of PRO data and other outcomes.

- The most common conclusion across publications was that one or more interventions were superior in terms of PRO data (Figure 6).

- However, many publications noted that clinical significance could not be assumed based on the results.

Figure 6. PRO-related conclusions of ITC analyses

- Superiority observed 65%
- Similar results observed 25%
- Mixed results 10%
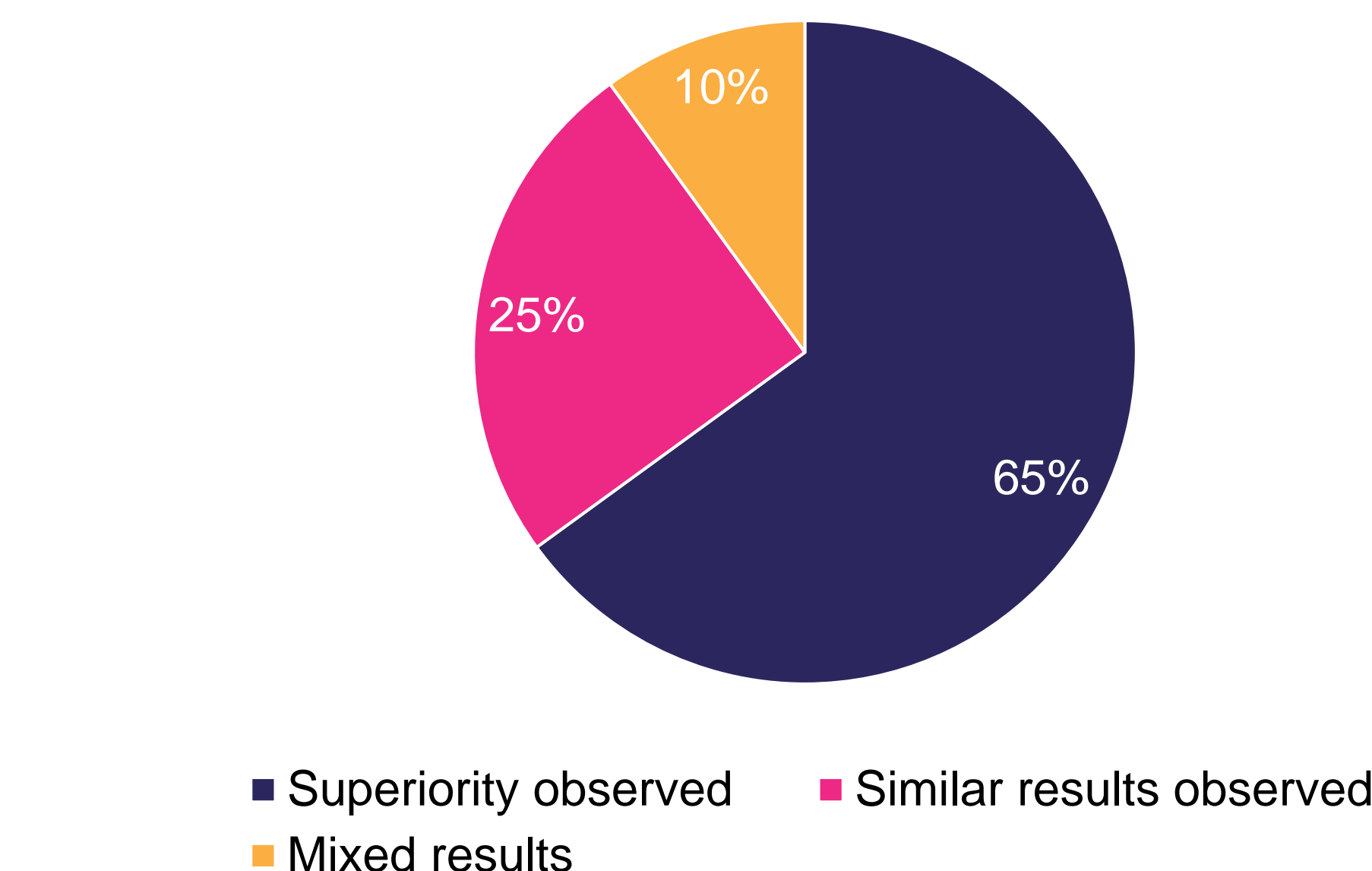
Abbreviations: ITC, indirect treatment comparison; PRO, patient-reported outcome

- An example demonstrating the added value of including PRO data in ITC analyses is a publication that evaluated wound closure methods following surgery. Specifically, although staples decrease closure time, according to PRO data, other methods, such as adhesives and subcuticular suture, are preferable.[4]

- PRO measures included in more than one publication are presented in Table 1.

- Visual analog scales were used most frequently. Although primarily utilized to assess pain, these scales were also used to measure satisfaction and eye dryness in some studies.

- Additionally, various disease-specific PRO measures were used.

Table 1. PRO measures

PRO measures	Publications (n)
Generic measures	
Visual analog scale	21
SF-36	7
EQ-5D	4
Health Assessment Questionnaire – Disability Index	3
Fatigue Severity Scale	2
Disease-specific measures	
Constant-Murley Score	5
Disabilities of the Arm, Shoulder, and Hand	5
EORTC QLQ-C30	5
Western Ontario and McMaster Universities Osteoarthritis Index	5
Dermatology Life Quality Index	4
International Knee Documentation Committee	4
Knee Injury and Osteoarthritis Outcome Score	4
Oxford Knee Score	4
American Shoulder and Elbow Surgeons Score	3
EORTC QLQ-BR23	3
Lysholm Scale	3
Peak Pruritus Numerical Rating Scale	3
St. George's Respiratory Questionnaire	3
Tegner Activity Scale	3
Inflammatory Bowel Disease Questionnaire	2
Knee Society Score	2
Patient-Oriented Eczema Measure	2
Shoulder Pain and Disability Index	2
Victorian Institute of Sport Assessment	2

Abbreviations: EORTC, European Organisation for the Research and Treatment of Cancer; PRO, patient-reported outcome

Conclusions

- PRO data were included most often in orthopedic ITC publications, which aligns with PRO measures being essential in indications that rely on non-externally observable outcomes (eg, pain).[5]

- The large proportion of studies using NMA methodology is consistent with the overall ITC literature.[6]

- As efforts like CONSORT-PRO aim to improve the quality of PRO reporting,[7] PRO inclusion in ITC publications may increase further, thereby providing payers, providers, and patients with valuable information.

References
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