

Reviewing the Use of Matching Adjusted Indirect Comparisons in Health Technology Assessment Submissions

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Background

Indirect comparisons are often utilized in the health technology assessment process, as it is rare to have a single head-to-head study that includes all relevant comparators. Matching adjusted indirect comparisons (MAICs) are used to facilitate population-adjusted indirect treatment comparisons (ITCs) to support health technology assessment submissions. A recent publication (Phillippo 2020, *Statistics in Medicine*) raised serious concerns about MAIC after evaluating the performance of MAIC with an extensive simulation. Based on the results of the simulations, MAIC may be biased in cases of small sample sizes (N<500), large reductions in effective sample size (ESS), and missing effect modifiers.

Objective: Assess MAICs that have been submitted to the Canadian Agency for Drugs and Technologies in Health (CADTH) to identify and summarize features that may impact the validity of the ITC.

Method

Search: Reimbursement reviews reports available from CADTH were reviewed according to the following criteria (<https://www.cadth.ca/reimbursement-review-reports>):

Submission dates: From January 2016 through May 2021

Extraction date: June 15, 2021

Product type: Oncology pharmaceutical

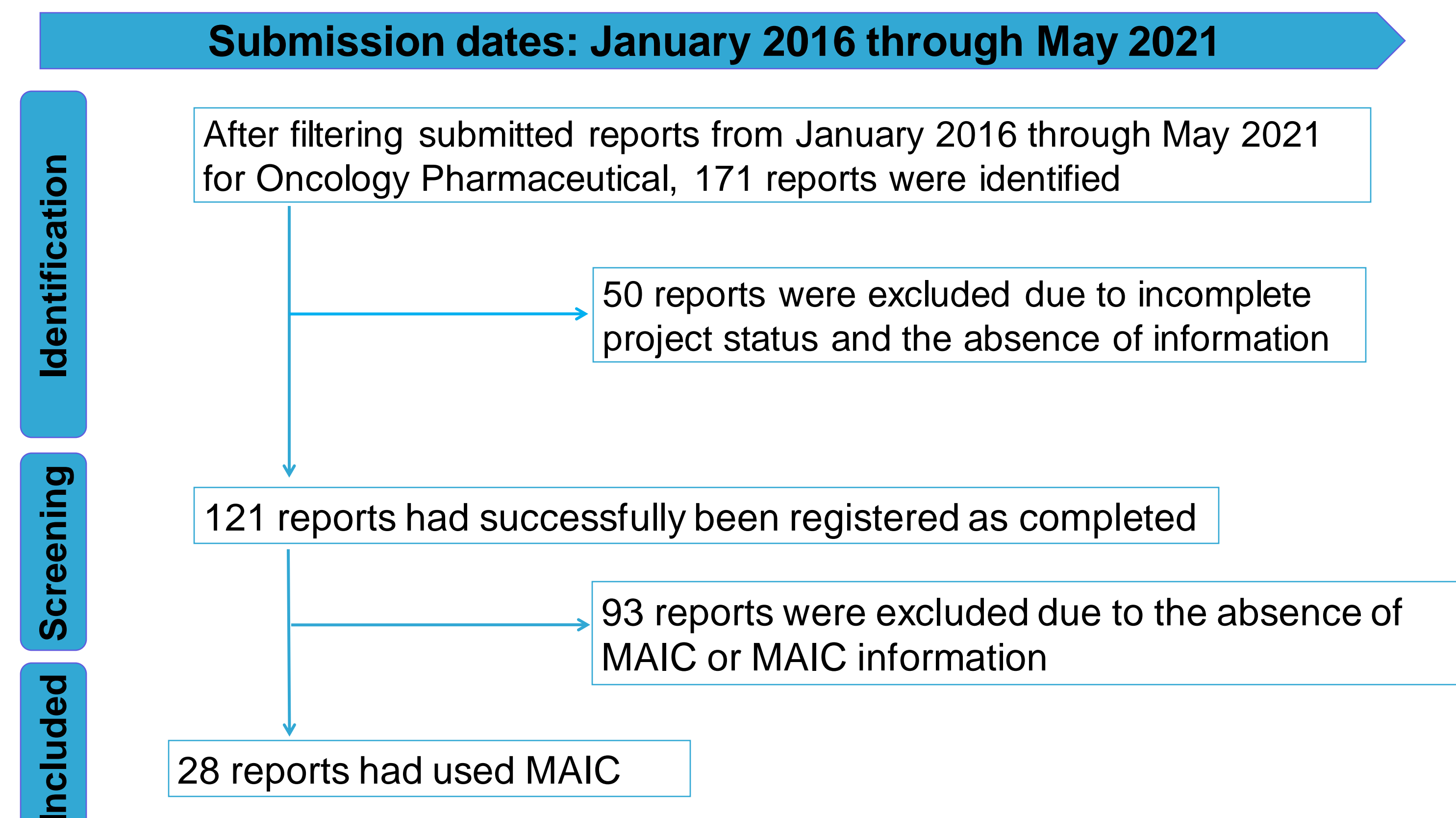
Project status: Complete

Extraction: Factors that may impact the validity of the MAIC were extracted and additional submission details:

- Sample sizes:
 - Reduction in ESS
 - Missing effect modifiers
 - Final determination of clinical benefit and recommendation

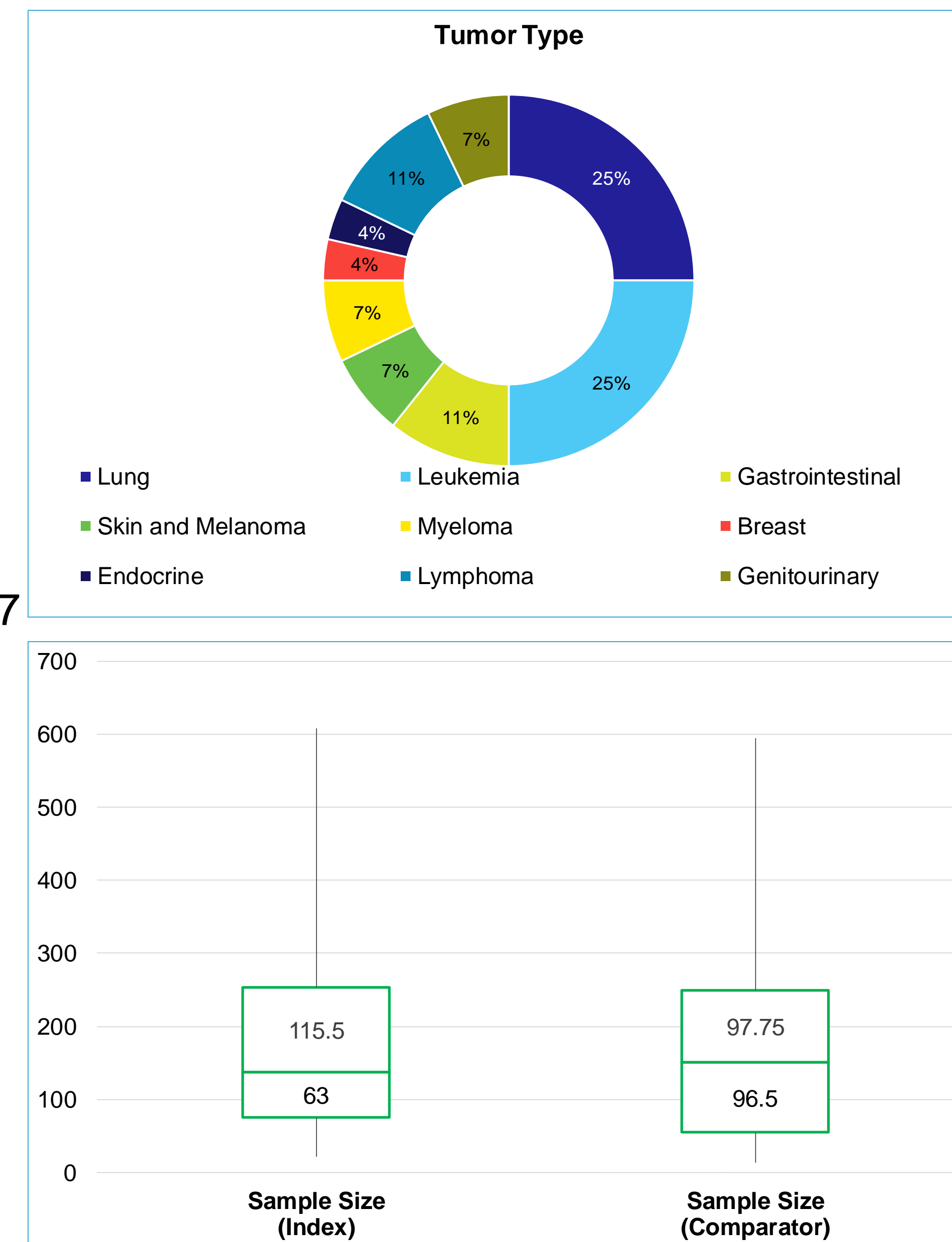
Analysis: Factors were summarized using frequencies and proportions for categorical variables and median/range for continuous variables. (Figure 1)

Figure 1. Search strategy



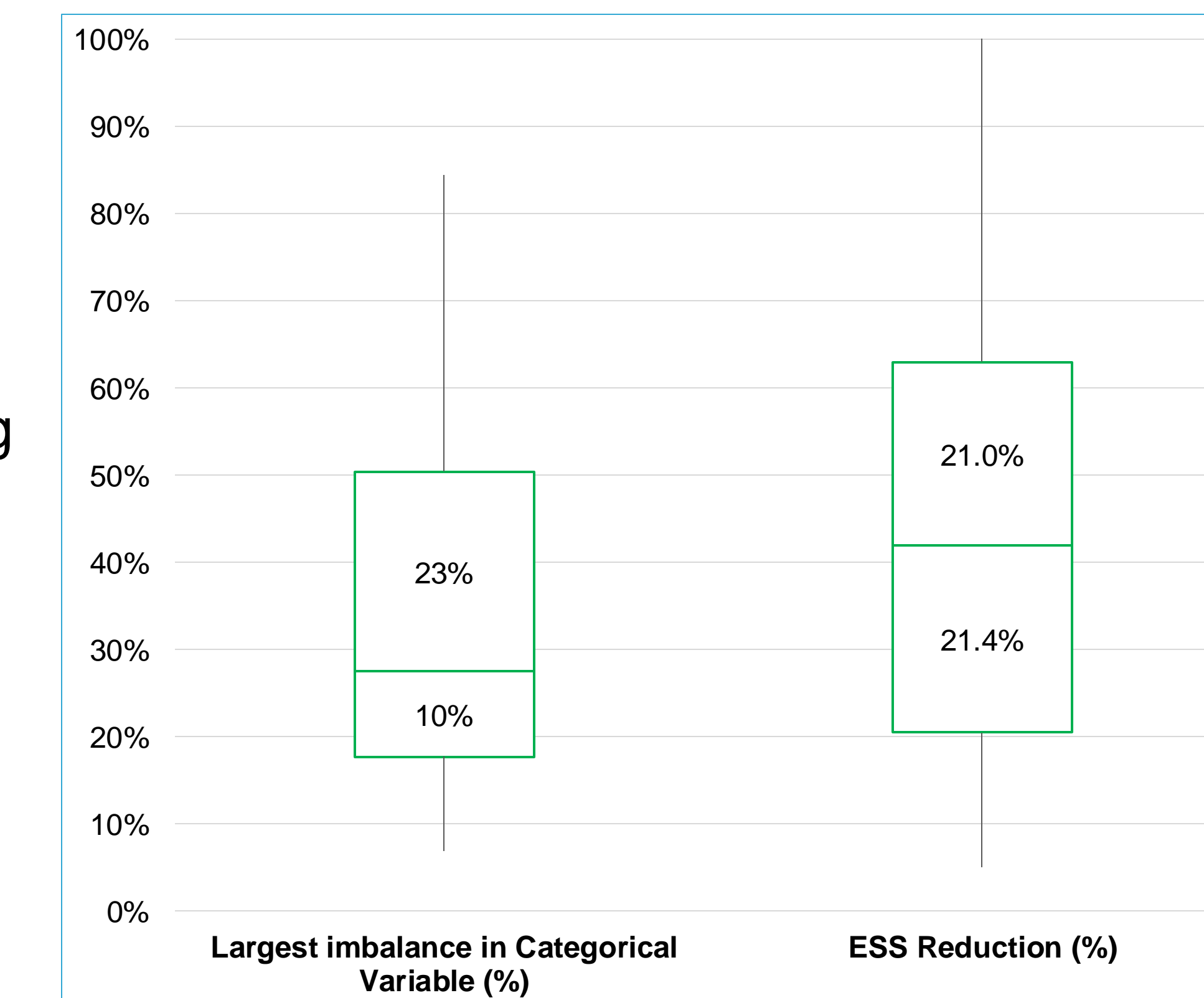
Results

- The review identified 28 submissions that included an MAIC, 23 of which reported detailed methodological summaries
- Among 28 submissions, lung tumors and leukemia accounted for 50% of the indications
- Within the 23 submissions, median sample sizes were 117 (range: 21-470) in the index trial and 137 (range: 14-444) in the comparator trial



Results

- ESS was reported in 14/23 trials (61%), with a median 36.8% reduction (range: 5.1%-75.6%).
- The ITCs included a median of 8 (range: 3-14) effect modifiers, and 7/23 (30%) submissions reported missing effect modifiers.
- Furthermore, CADTH noted limitations with respect to the representativeness of the target population in 7/28 (25%) submissions.
- Ultimately, 21/28 (75%) submissions had a positive clinical benefit determination resulting in a reimbursement recommendation.



Limitations and conclusions

This study was limited in several ways:

- The analysis was based on clinical summary reports; several key variables such as reduction in effective sample sizes, number of effect modifiers, and whether effect modifiers were missing were not consistently available.
- Furthermore, access to clinical summary reports was limited to publicly available submissions. Therefore, features of studies with redacted information could not be included.

Conclusion:

Several features that may impact the validity of MAICs were present in submissions to CADTH. Given the prevalence of these methodological issues, the use of MAICs as the population-adjustment technique of choice should be discouraged.

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Abbreviations: CADTH, Canadian Agency for Drugs and Technologies in Health; ESS, effective sample size; ITC, indirect treatment comparisons; MAIC, matching adjusted indirect comparisons.