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EE262

Use of Single-arm Trials in CADTH Reviews of Oncology Drugs

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Introduction

- Single-arm trials (SAT) have been increasingly used to support oncology reimbursement submissions worldwide.
- In the absence of relative treatment efficacy directly available from trials, alternative approaches are available to generate indirect evidence using external controls. Experience from past Canadian Agency for Drugs and Technologies in Health (CADTH) submission based on SATs, which necessitate use of external comparator data, could be of interest for future submissions. .
- In a previous study, the authors assessed the use of SAT-based oncology technology appraisals (TAs) by the National Institute for Health and Care Excellence (NICE) from 2017 to 2022, with focus on approaches used to generate comparative evidence, and recommendations from committee reviews.[1]

Objective

- The objective of this study was to assess the use of SATs in CADTH submissions of oncology drugs and compare primary reasons for recommendation with the NICE review.

Methods

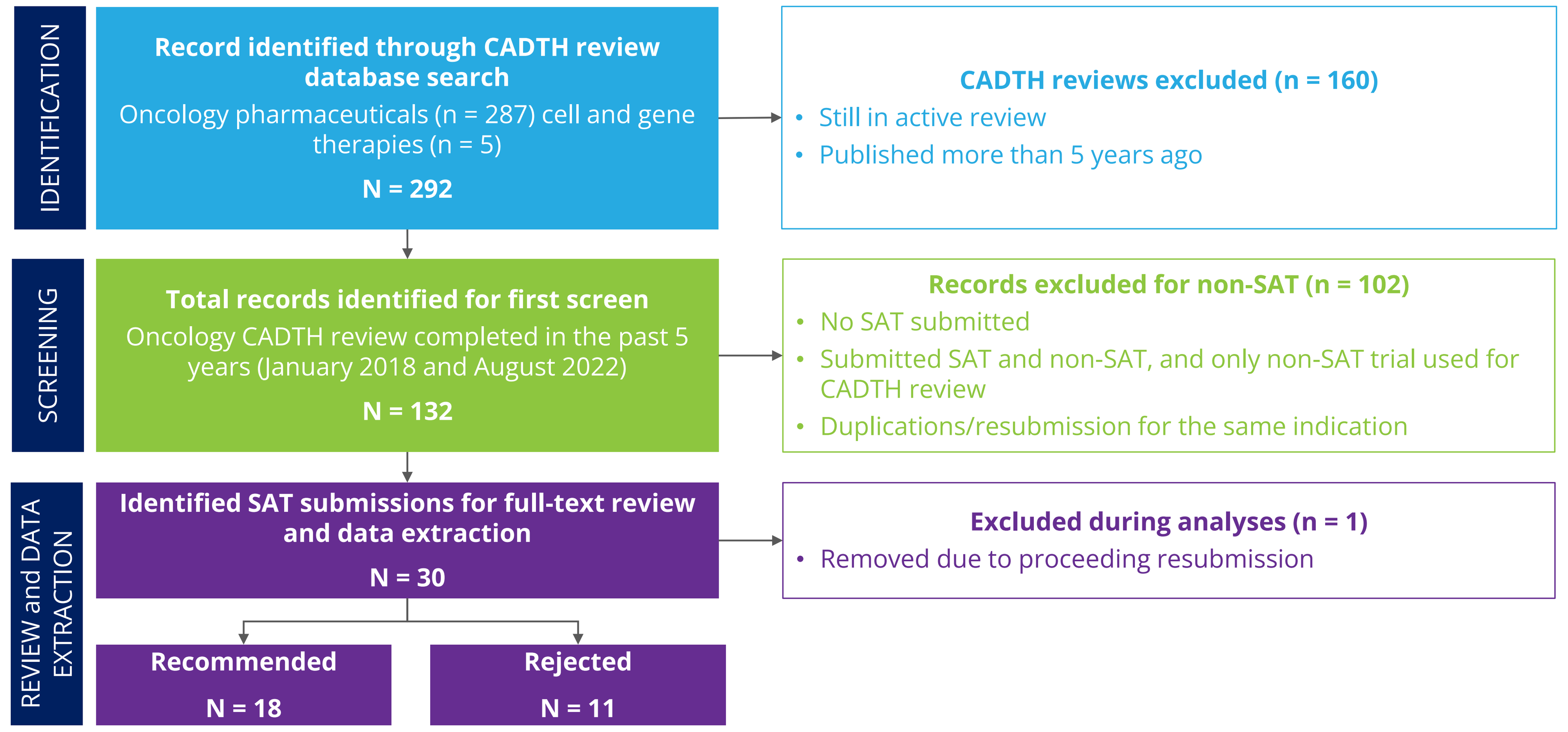
- The same method employed by the NICE review study (Zou 2022)[1] was used; submissions only using SATs as clinical evidence were identified from CADTH reimbursement recommendations published in the past five years (January 2018 to August 2022).
- Final recommendations and clinical/economic guidance reports were independently reviewed by two investigators to extract information on interventions, indications, trial design, external comparator data source, and committee commentaries.
- The final identified CADTH reviews with positive recommendations (n = 18) were compared with NICE TAs with recommendation for routine use (n = 15) or Cancer Drug Fund (CDF) (n = 12) from the previous study. Reasons for recommendations regarding net clinical benefit, cost-effectiveness, and unmet need were extracted for comparison.

References

1. Zou D, et al. *Value Health.* 2022;25(12, Supplement):S117. 2. Canadian Agency for Drugs and Technologies in Health. CADTH Reimbursement Review. Published January 2018 to August 2022. Completed with single-arm trial as clinical evidence. 3. National Institute for Health and Care Excellence. Technology Appraisals. Published May 2017 to May 2022. Completed with single arm trial as clinical evidence.

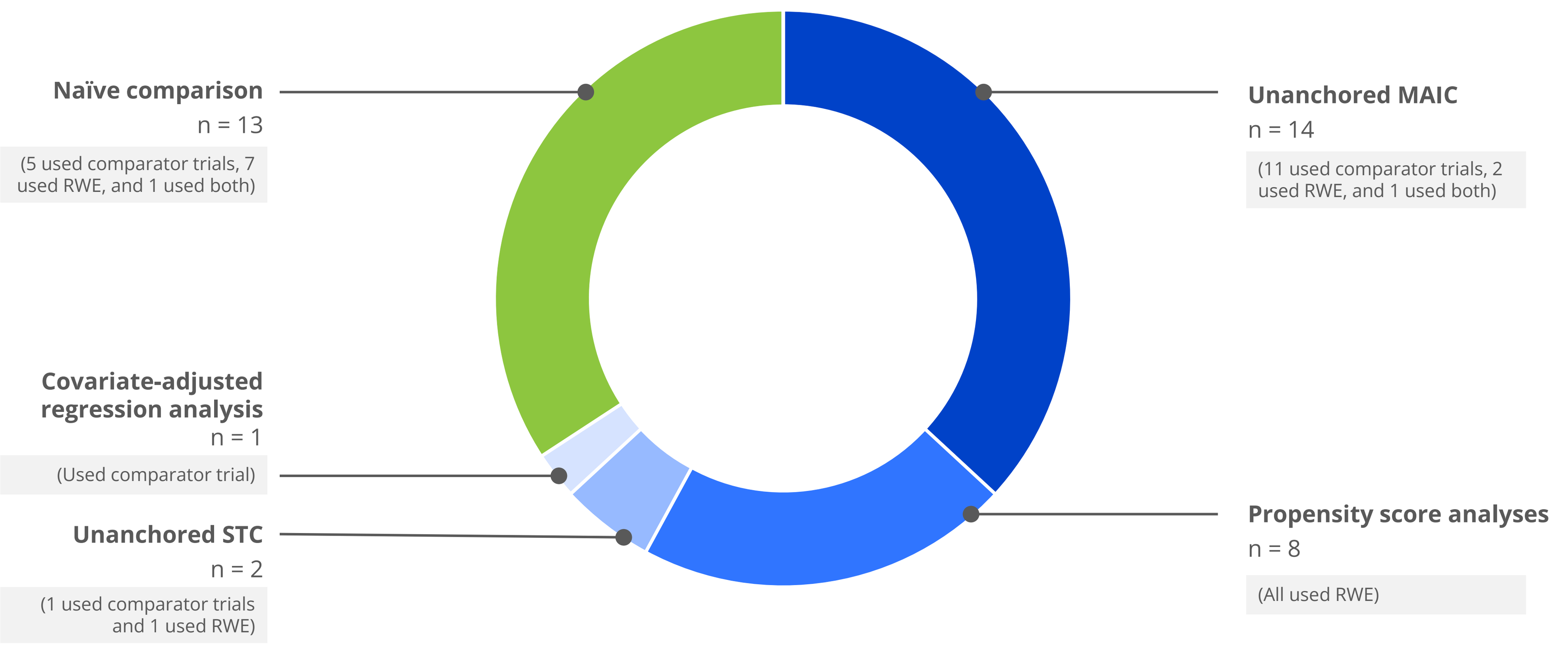
Results

Figure 1. Flow Chart of the Review Process for CADTH Oncology Single-arm Trial



Abbreviations: CADTH = Canadian Agency for Drugs and Technologies in Health; SAT = single-arm trial

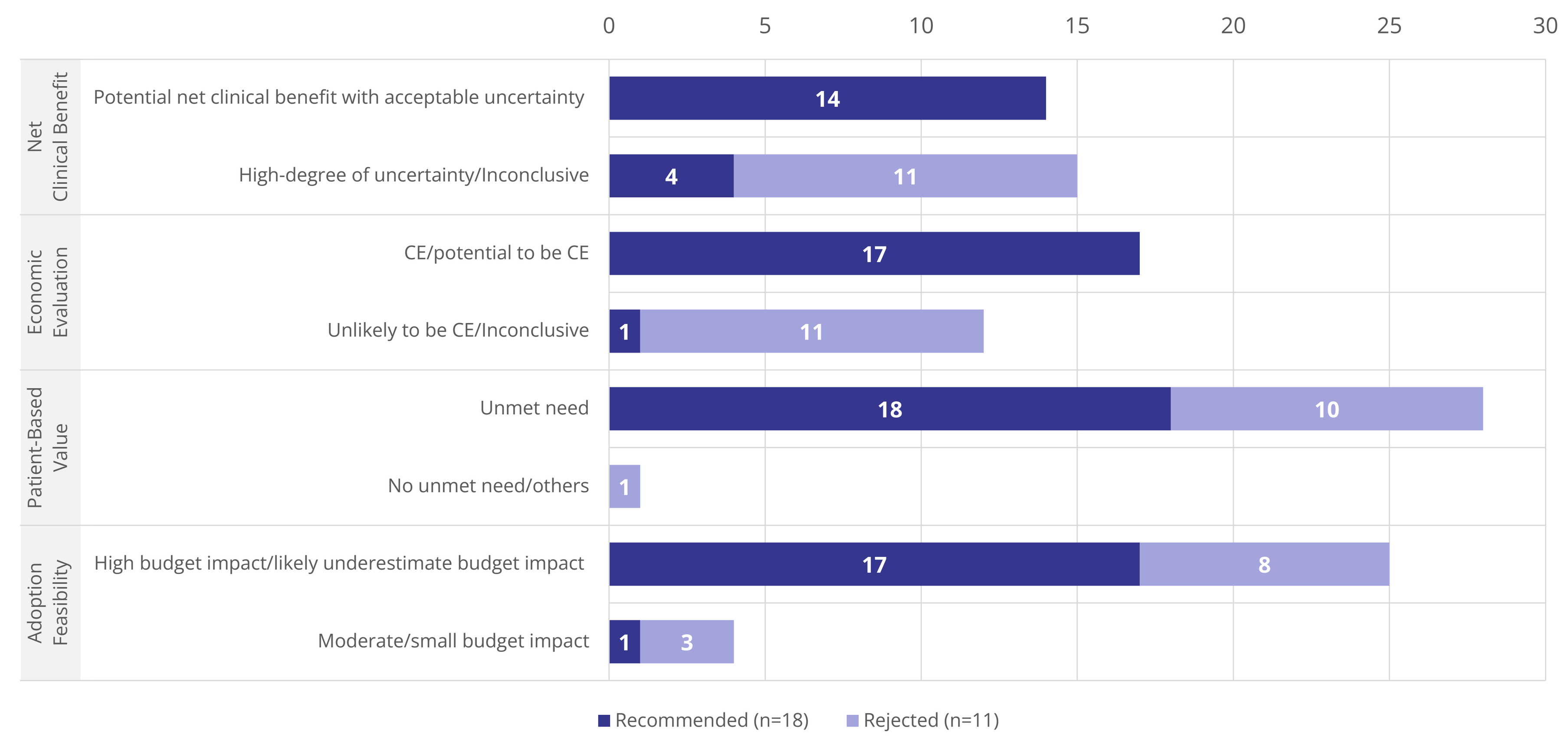
Figure 2. Approaches Used for Generating Comparative Efficacy in the CADTH Submissions for Oncology Single-arm Trial



Abbreviations: CADTH = Canadian Agency for Drugs and Technologies in Health; ITC = indirect treatment comparison; MAIC = matching-adjusted indirect comparison; RWE = real-world evidence; STC = simulated treatment comparison

Note: Five submissions reported using both unadjusted (naïve comparison) and population-adjusted ITC approaches; one sponsor did not submit any indirect evidence. For the 20 submissions using population-adjusted ITC approaches: one used both STC and MAIC methods, one used both covariate-adjusted analyses and MAIC; three used both MAIC and propensity score analysis.

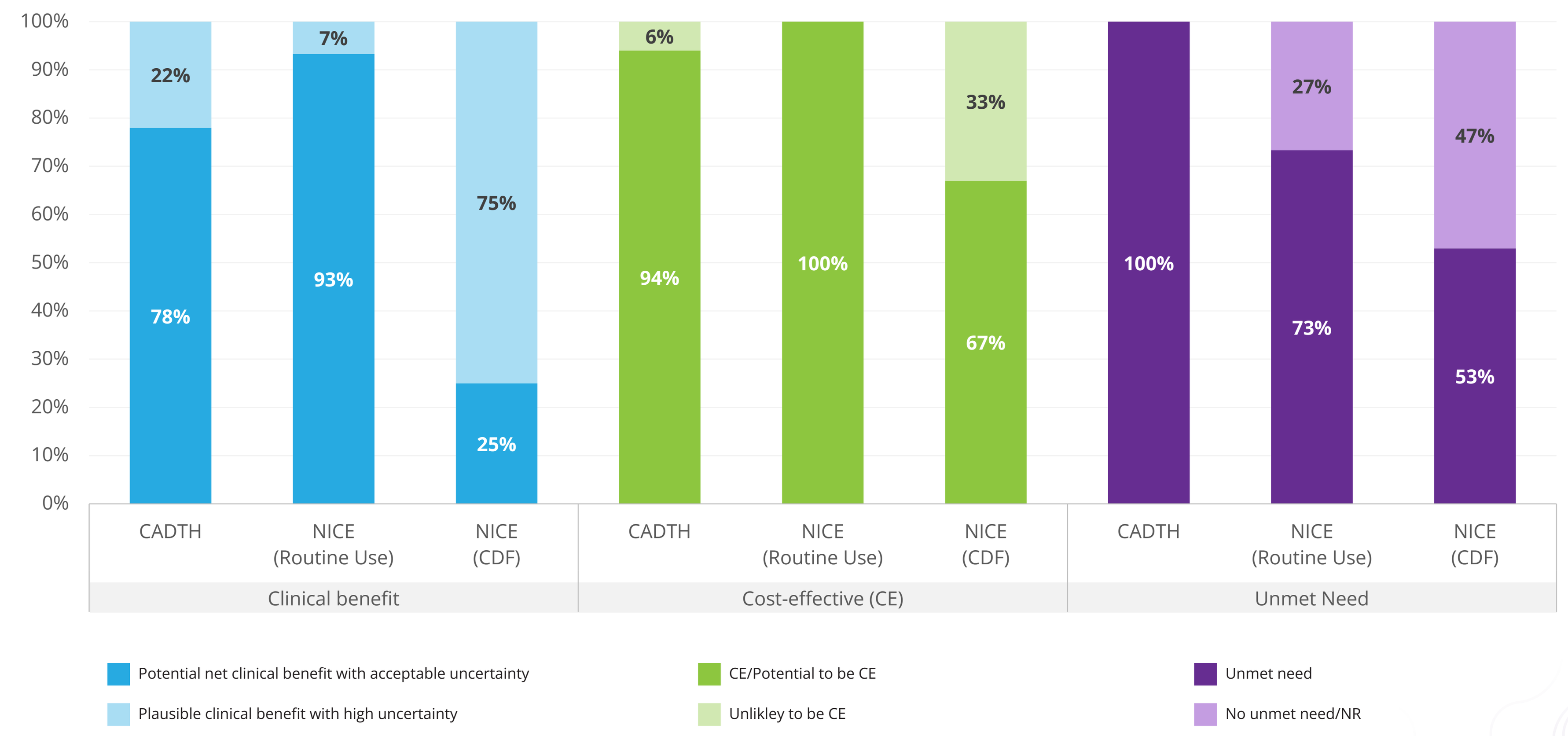
Figure 3. Summary of Reason for Recommendation and Rejection based on pERC's Deliberative Framework



Abbreviations: CE = cost-effective; pERC = pan-Canadian Oncology Drug Review Expert Review Committee

Note: Reasons were not mutually exclusive; multiple reasons were commonly cited for reimbursement review.

Figure 4. Summary of Reason for Positive Recommendation for CADTH vs. NICE



Abbreviations: CADTH = Canadian Agency for Drugs and Technologies in Health; CDF = Cancer Drugs Fund; CE = cost-effective; NICE = National Institute for Health and Care Excellence; NR = Not Reported

Note: Reasons were not mutually exclusive; multiple reasons were commonly cited for reimbursement review.

Results (Cont'd)

- Of 132 oncology CADTH reviews identified, 29 (22%) used SATs as primary clinical evidence (**Figure 1**), where comparative evidence was generated from various sources, including 13 comparator trials, 12 real-world evidence studies, and three using both.
- Of 29 submissions, 13 (45%) used unadjusted indirect treatment comparison (ITC) (i.e., naïve comparison) and 20 (69%) used population-adjusted ITC, including 14 (48%) matching-adjusted indirect comparisons, two (7%) simulated treatment comparisons, eight (28%) propensity score analyses, and one (3%) covariate-adjusted regression analysis. Some submissions applied more than one source or approach (**Figure 2**).
- In spite of the uncertainty around treatment benefits generated from SATs, CADTH granted positive recommendations to 62% (18 of 29) of SAT-based submissions. Compared to those rejected, SAT-based submissions that received positive CADTH recommendations were more likely to demonstrate potential net clinical benefit with acceptable uncertainty (14 of 18) and greater potential to be cost-effective (17 of 18). pERC noted therapies evaluated generally addressed patient's unmet need but also posed pressure on healthcare budget (**Figure 3**).
- Compared with NICE recommendations for routine use, CADTH had less frequent recommendations that reported potential net clinical benefit with acceptable uncertainty (78% vs. 93%). High degree of net clinical benefit uncertainty frequently led to negative CADTH recommendations, while in the NICE review, that led to recommendations used within CDF (75%) (**Figure 4**).
- Most CADTH (94%) and NICE (100% for routine use and 67% for CDF) reviews with positive recommendations concluded cost-effective (CE) / potential CE based on the sponsor-submitted economic evaluation or committee's re-analysis. The majority of recommendations acknowledged unmet need for indications in the CADTH (100%) and NICE reviews (73% for routine use) (**Figure 4**).

Conclusions

- For CADTH review, the decisive factors were the convincingness of net clinical benefit and plausible cost-effectiveness, which were determined by trial outcomes and relative treatment effect demonstrated through ITC. Unmet need was also considered. These factors also aligned with NICE review.
- Generally, SAT-based submissions using appropriate unadjusted or adjusted ITC approaches could lead to positive reimbursement decisions.

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