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The impact of rarity on oncology health technology assessment (HTA) and funding in Ontario: A review of pCODR recommendations from 2012 - 2017

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Provincial Health Services Authority



Cancer Care Ontario
Action Cancer Ontario



Canadian Cancer Society
Société canadienne du cancer

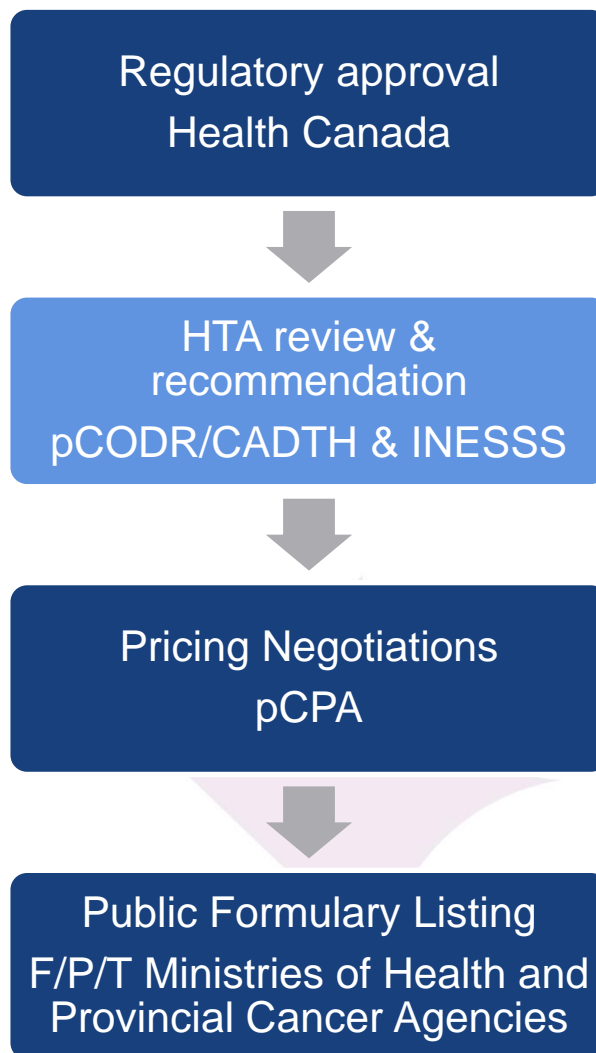
Conflicts of Interests

- We have no conflicts of interests of declare
- The views expressed in this presentation are solely those of the authors and do not reflect the views of Cancer Care Ontario

Overview

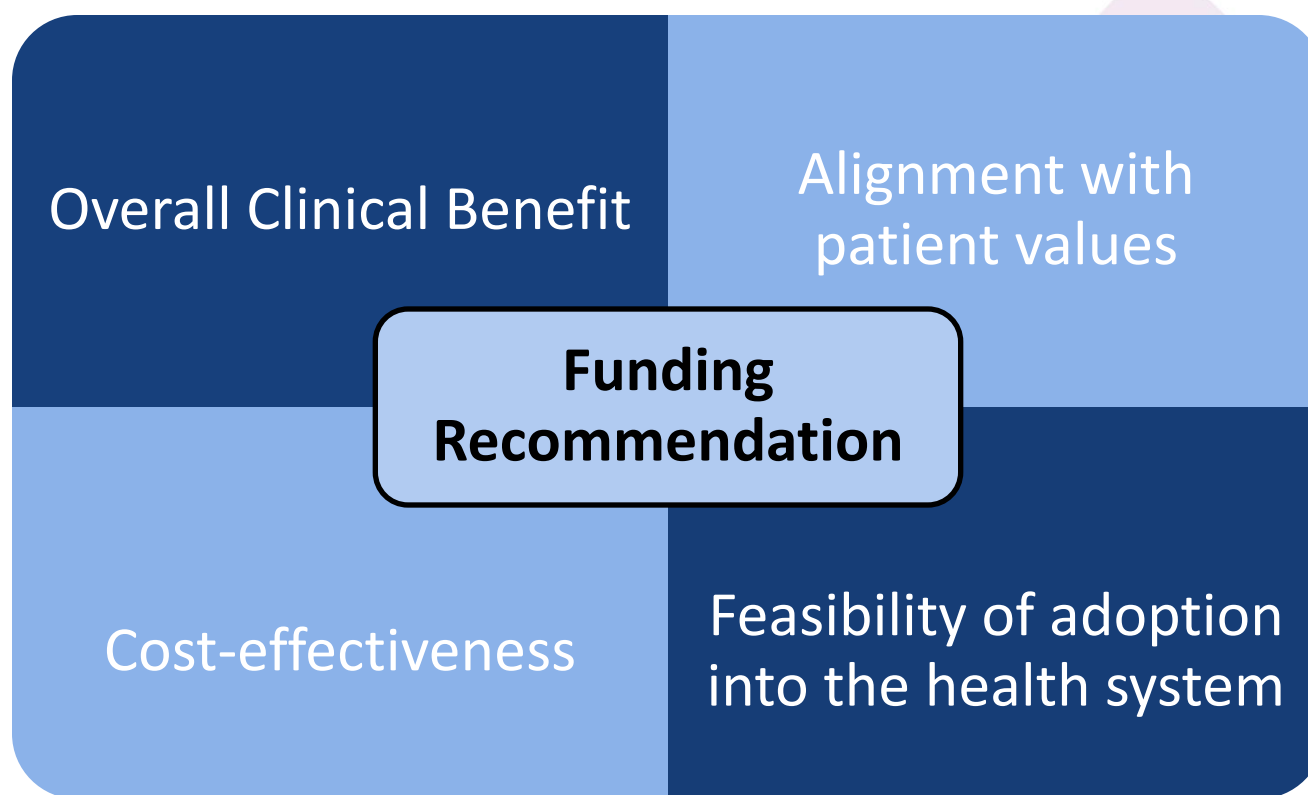
1. Oncology HTA in Canada (pCODR Expert Review Committee framework)
2. What is rarity in cancer?
3. Study objectives
4. Rarity and Canadian HTA/funding in Ontario
5. Conclusions & future directions

Oncology Drug Funding in Canada



The pERC Deliberative Framework

pCODR expert review committee (pERC) considers 4 criteria when making funding recommendations:



Evaluating Rare Indications

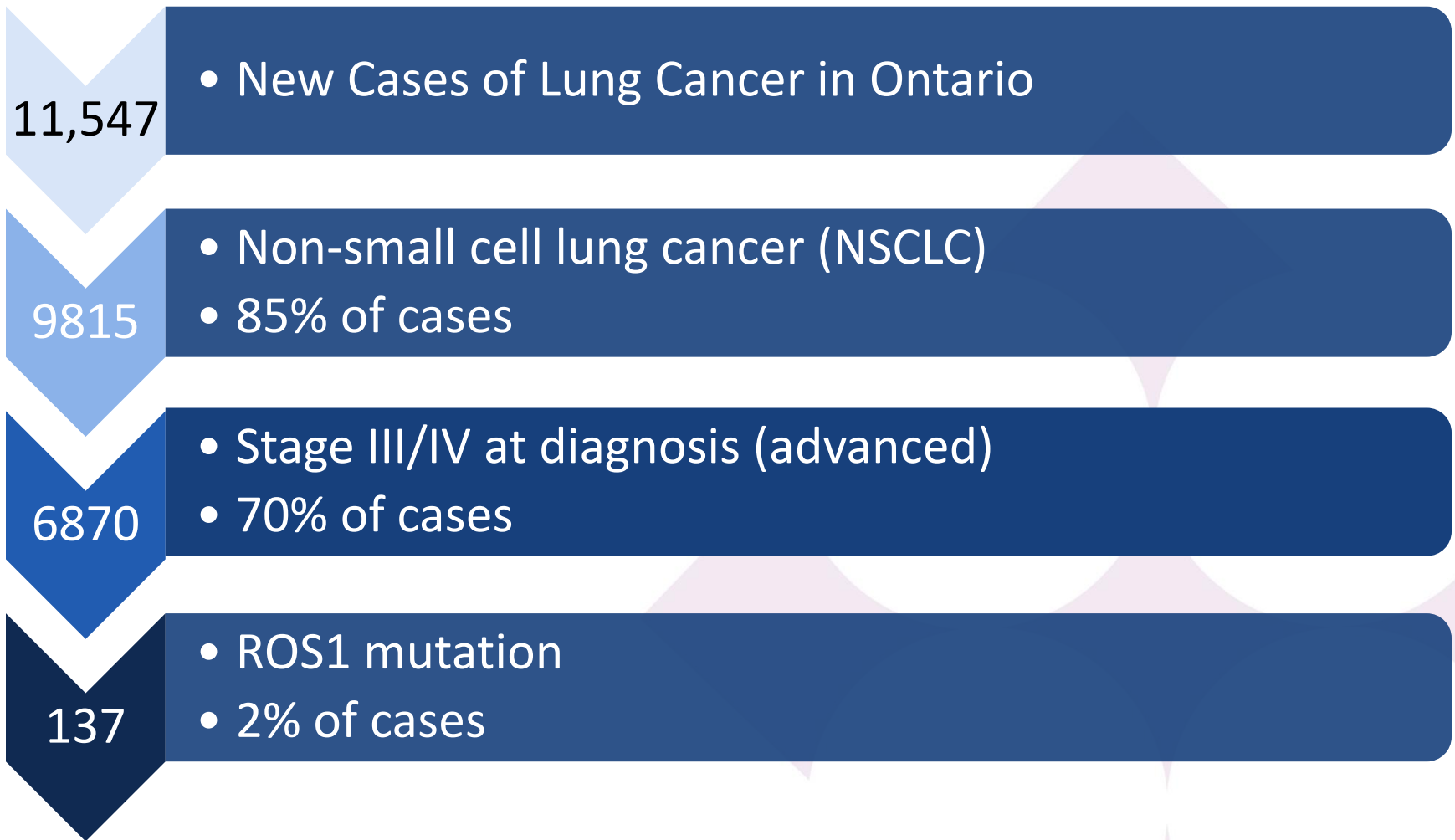
- pERC's framework does not explicitly address rarity
 - Available evidence must suggest drug under review could substantially ↓ morbidity and/or mortality of disease

Significant Unmet Need	
Rarity of Condition	<ul style="list-style-type: none">• Affects small # of patients• Often genetically based• Heavy burden on health system• Difficult to study
Population	<ul style="list-style-type: none">• Need identified on a population basis
Absence of Alternatives	<ul style="list-style-type: none">• Absence of effective alternatives• Substantial morbidity/mortality

Evaluating Rare Indications

- Challenges of evaluating drugs for rare indications include:
 1. High unmet need
 2. Uncertainty in clinical evidence
 - Lack of RCTs and comparative data
 - No appropriate comparator/standard of care
 - Uncertainty in burden of illness
 3. High costs/challenges with pharmacoeconomic evaluations
 4. No universal definition of rarity

What is considered rare in cancer?



Research Questions

1. How often are positive funding recommendations made for rare indications by pCODR?
2. How many rare indications are submitted to pCODR with an RCT? In how many instances is conducting an RCT feasible?
3. Are drugs for rare indications less cost-effective (higher ICER)?
4. What is the time to funding for rare indications in Ontario?

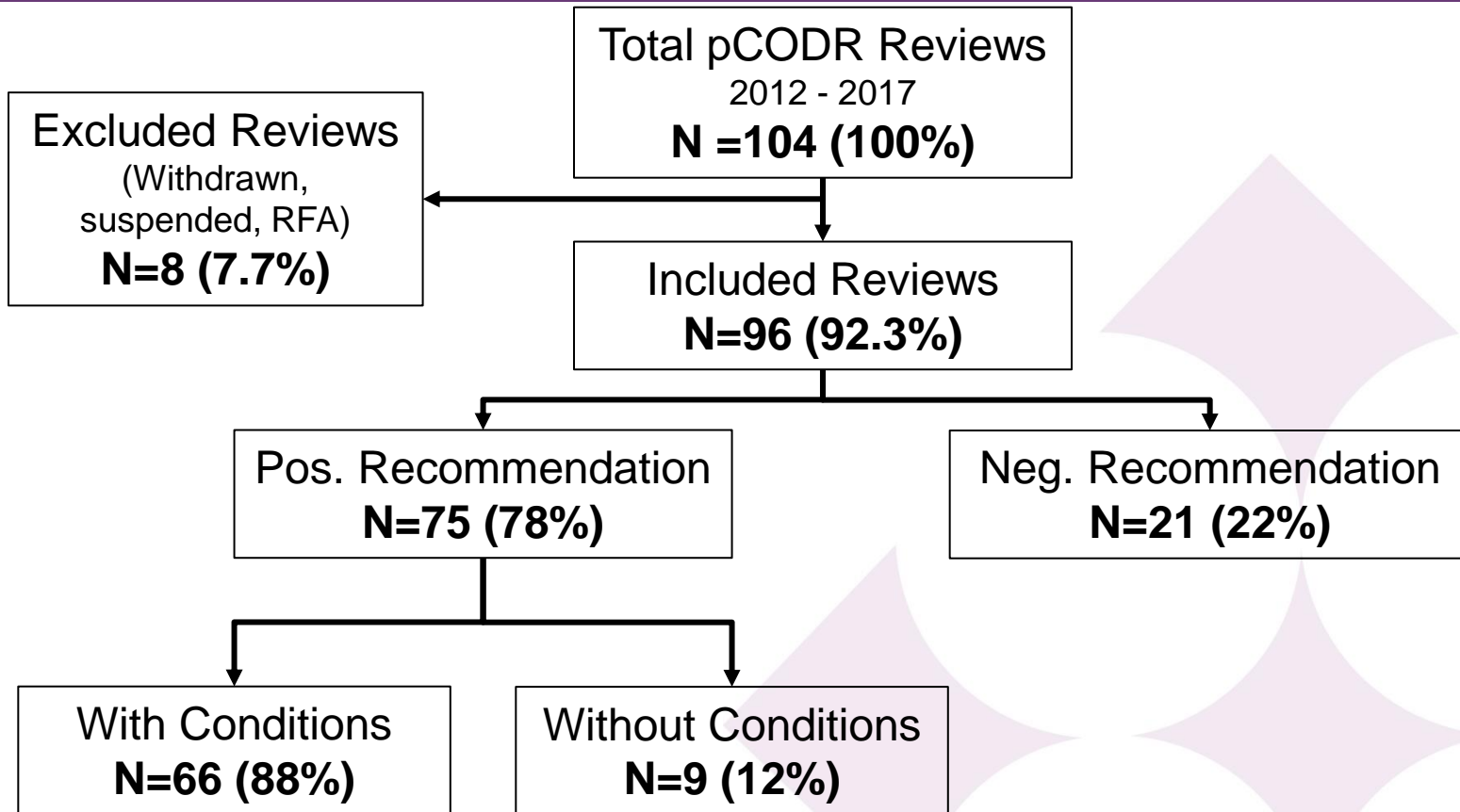
Methods

- No universal definition of rarity
- Incidence is one approach to operationalize rarity
 - Definition 1 (less stringent): Incidence $< 5/10,000$ diagnoses per year
 - Definition 2 (more stringent): Incidence $< 1/100,000$ diagnoses per year

Methods

- pCODR submissions with final recommendations (2012-2017)
 - × 2018/19 recommendations
 - × Submissions that were withdrawn, suspended or requests for advice
- Incidence rates for each indication were extracted from:
 1. pCODR Final Recommendations or Final Clinical Guidance Reports
 2. Canadian Cancer Society Statistics
 3. Pivotal Trials

Methods

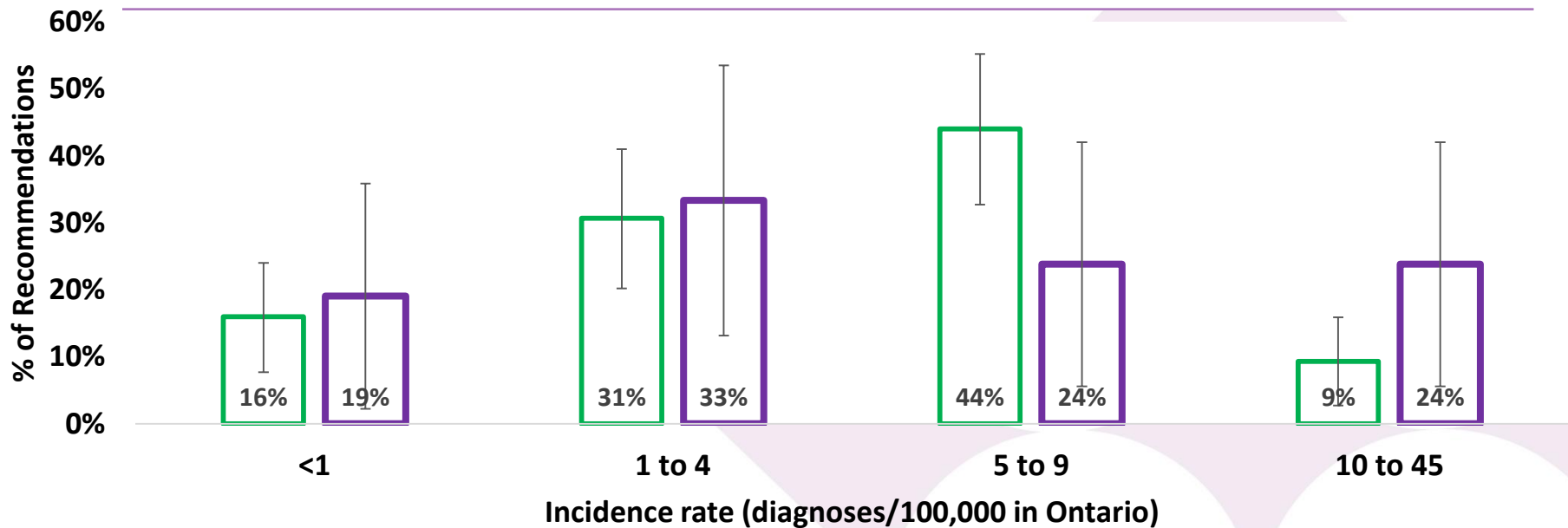


Definition 1: Incidence < 5/10,000
All recommendations (positive and negative) were rare

How often are positive recommendations made for rare and non-rare indications (definition 2)?

	Rare (<1/100,000)	Non Rare (>1/100,000)
Positive Recommendation (n = 75)	12 (75%)	63 (78.8%)
Negative Recommendation (n = 21)	4 (25%)	17 (21.2%)

Odds Ratio = 0.67 (95% CI: 0.19, 2.4); P-value = 0.5*

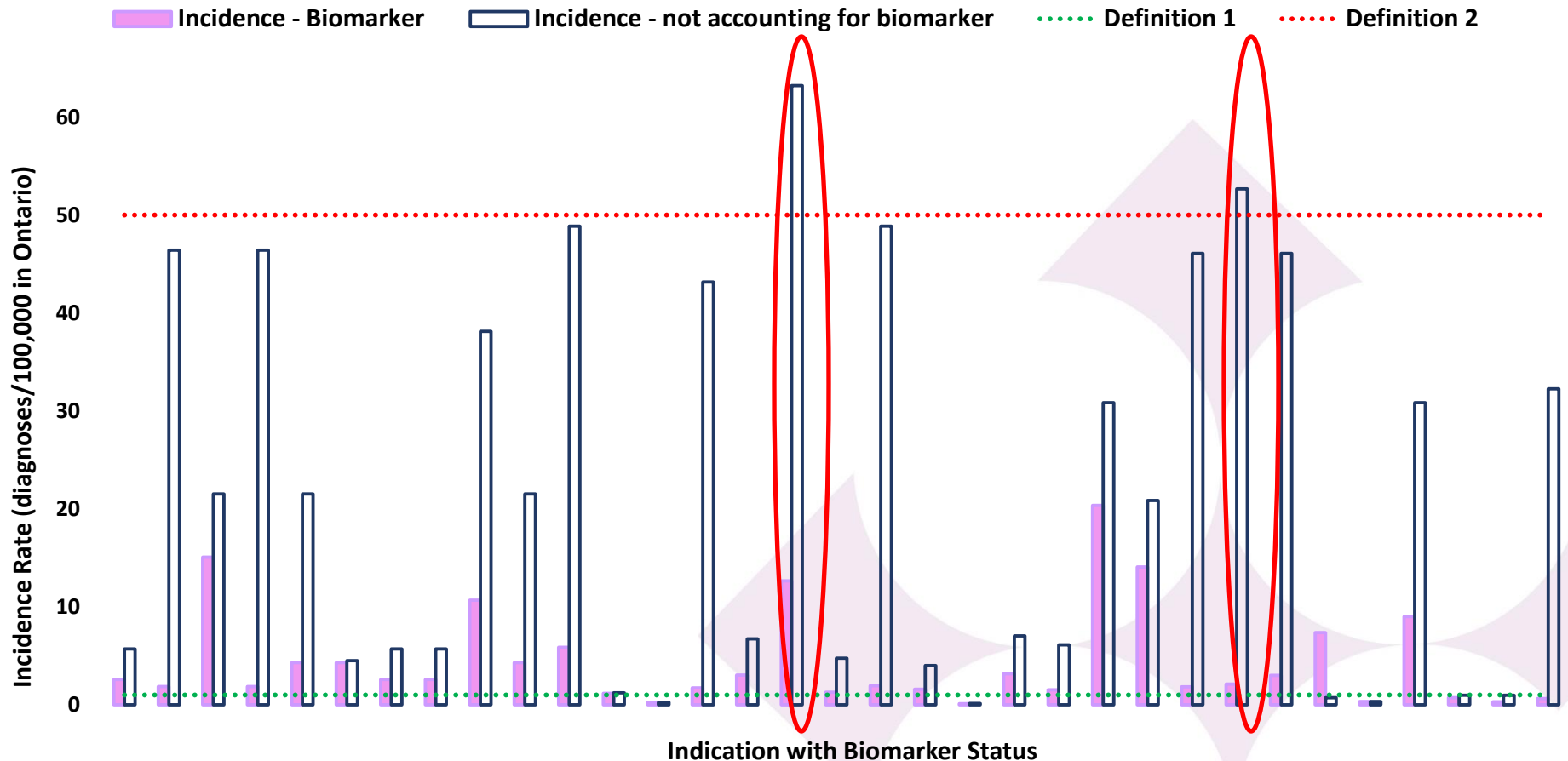


The frequency of positive recommendations for rare and non-rare indications were similar (75% vs 78.8%; p-value = 0.5).

*Fischer's Exact Test

Source: pCODR Website - Find a Review; <https://www.cadth.ca/pcodr/find-a-review>

Does Biomarker Status affect the definition of rarity?

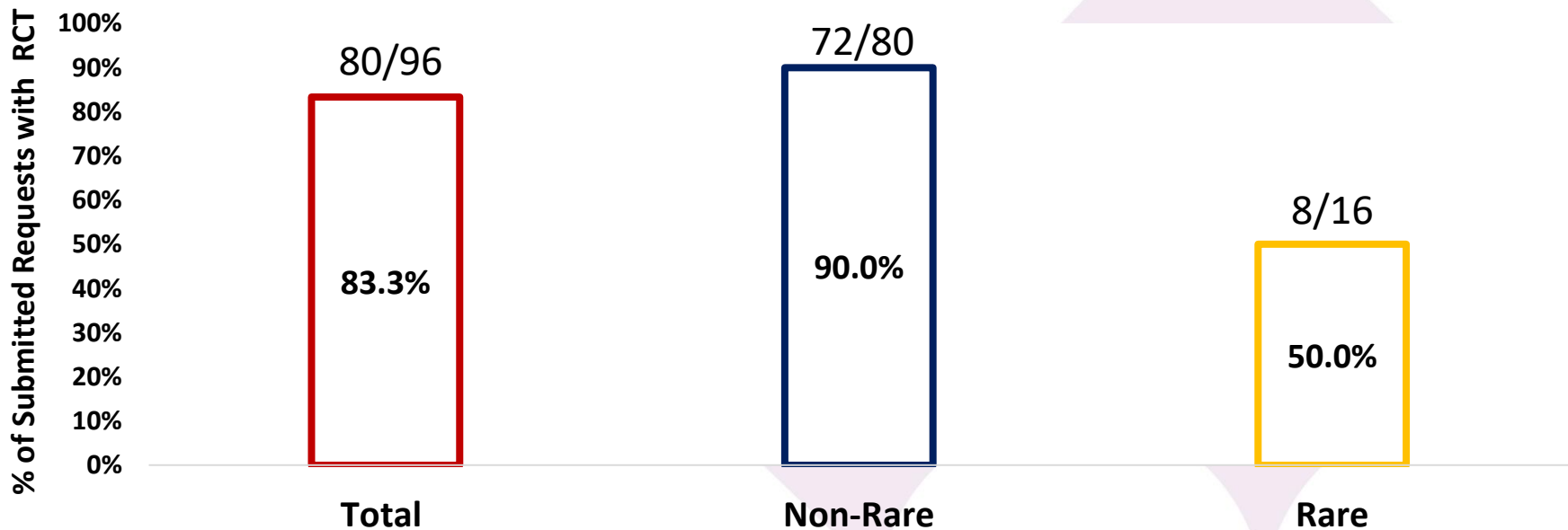


**2 indications changed from rare → non rare using definition 1 (<5/10,000).
There were no changes in rarity status for definition 2 (<1/100,000).**

How many rare indications are submitted to pCODR with a RCT?

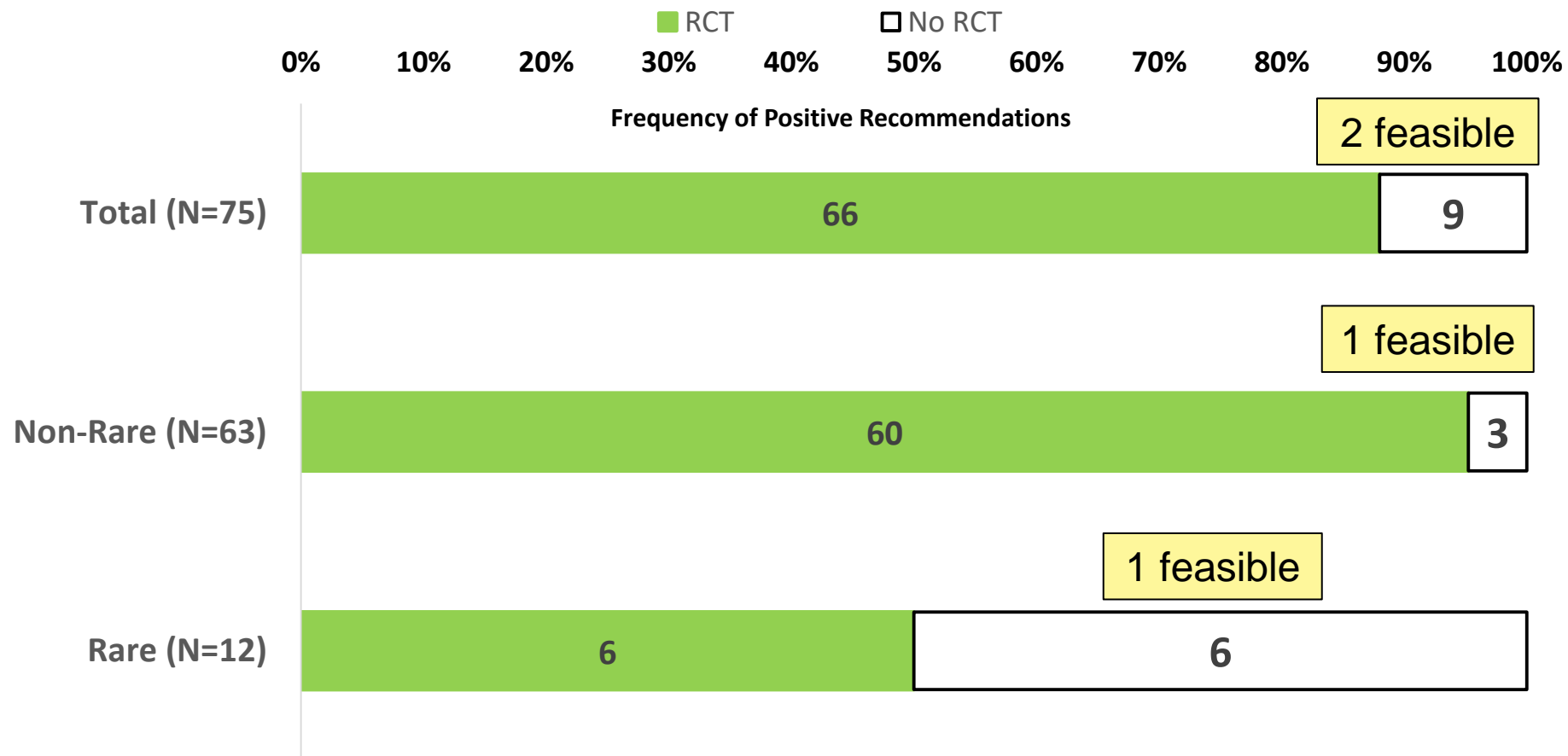
	Rare (<1/100,000)	Non Rare (>1/100,000)
No RCT Conducted (n = 16)	8 (50%)	8 (50%)
RCT Conducted (n = 80)	8 (10%)	72 (90%)

Relative Risk = 5 (95% CI: 2.2, 11.35); Odds Ratio = 9 (95% CI: 2.7, 30.6); P-value <0.01



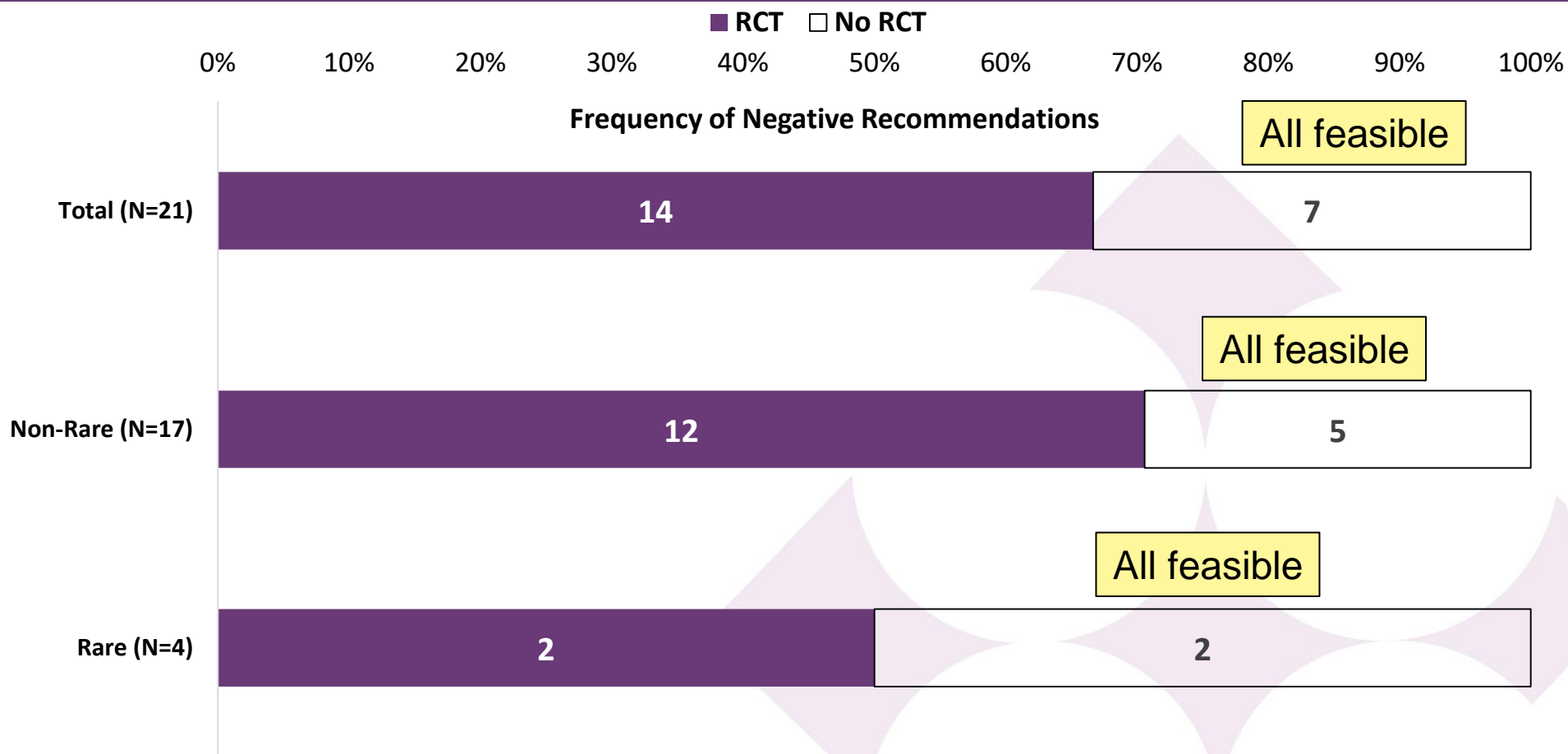
Rare indications appear to have fewer submissions with RCTs conducted

% of Positive Recommendations with RCTs



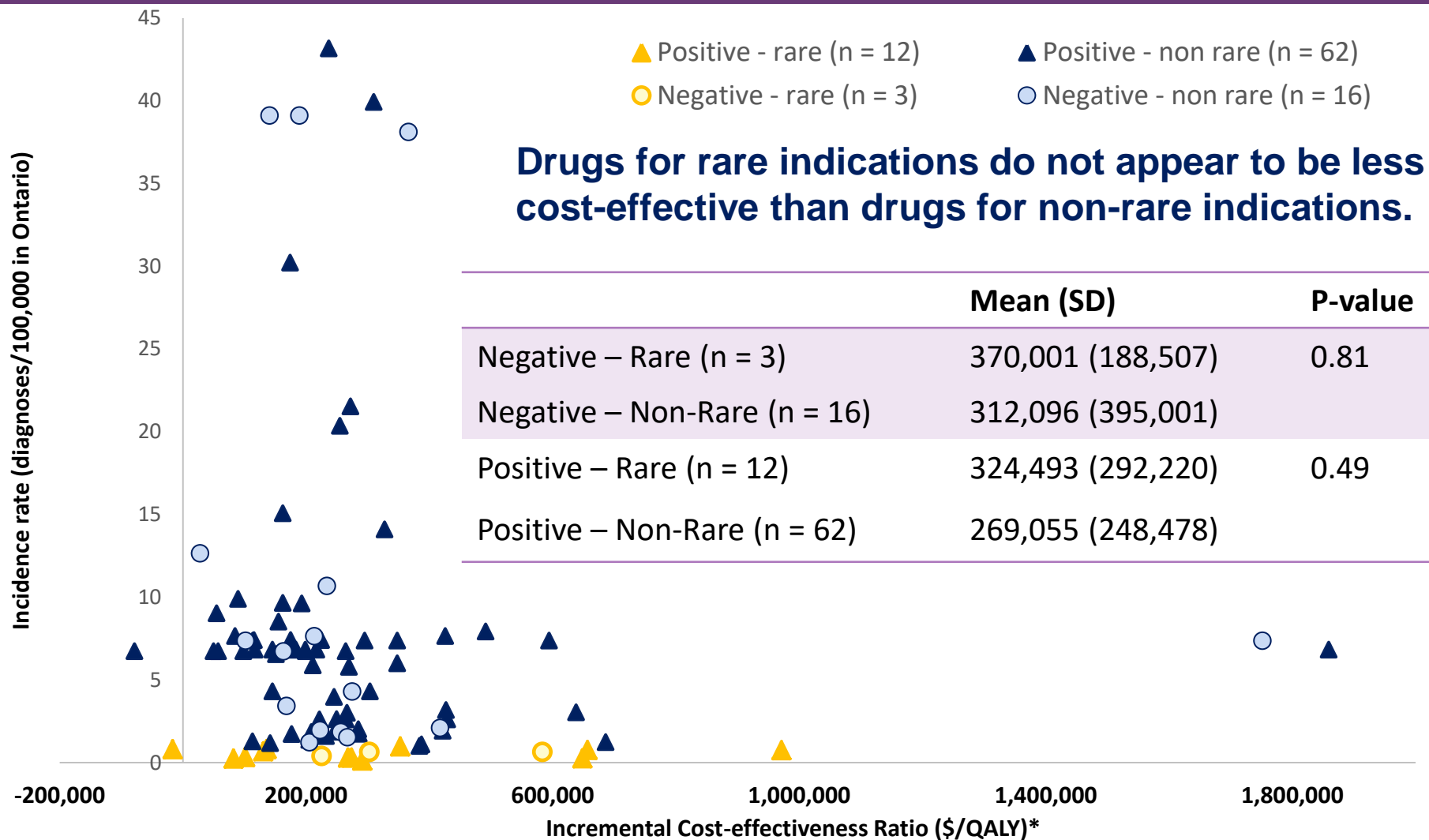
For positive recommendations without an RCT, pERC did not consider future RCT trials to be feasible for majority of the indications.

% of Negative Recommendations with RCTs



For negative recommendations without an RCT, pERC deemed it feasible to conduct an RCT for all indications.

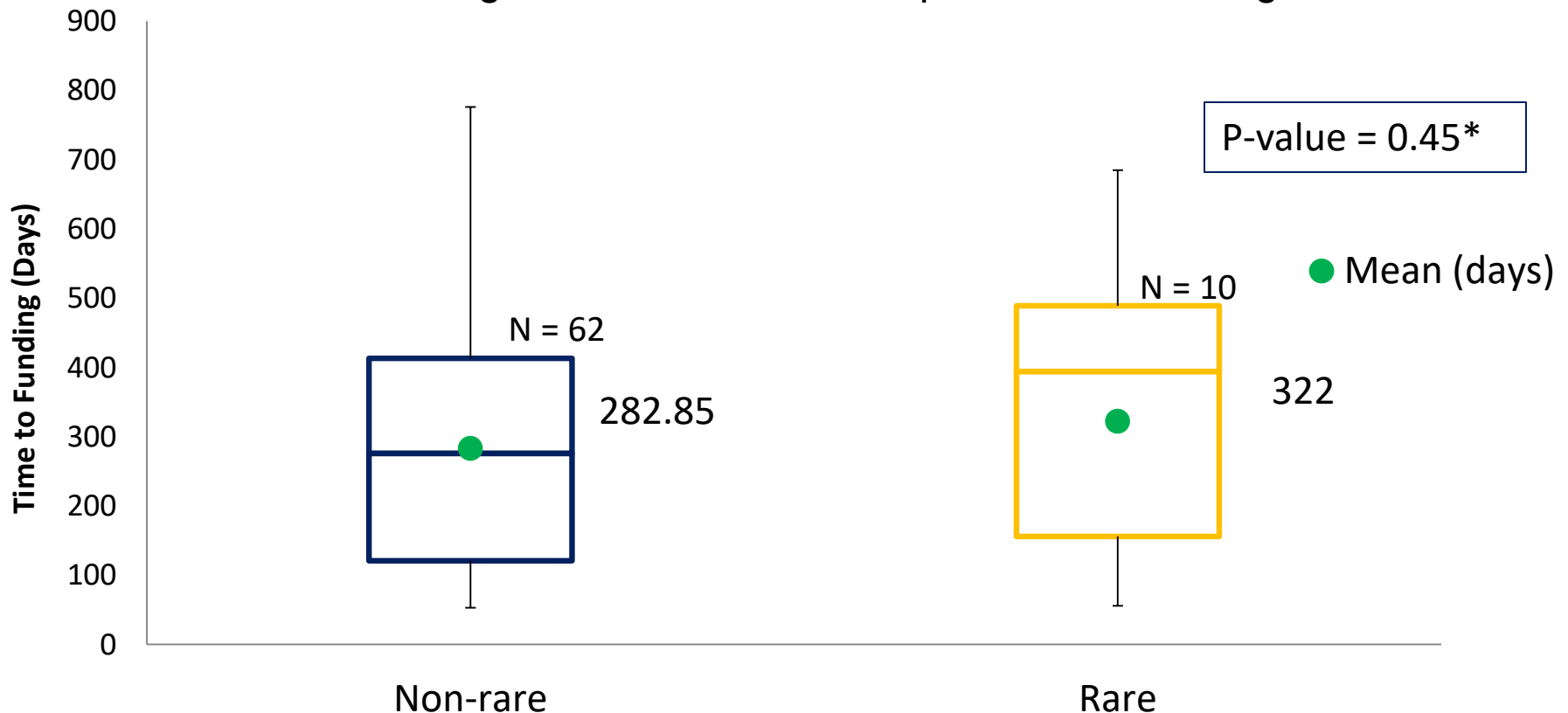
Are drugs for rare indications less cost-effective?



*The upper range of the ICER was plotted for submissions where the range of ICER was provided;
 Note: Two submissions without ICERs reported were excluded; One submission with the ICER upper range of ~4 million was excluded
 Source: pCODR Economic Guidance Panel Report;

Time to Funding in Ontario

Time to Funding = Date of Notice of Implement to Funding Date



There appears to be no significant differences in time to funding between rare and non-rare indications.

*Calculated from Wilcoxon-Mann-Whitney test

**3 reviews were excluded from the analysis as they were not funded at the time of data extraction

Source: pCODR Website - Find a Review; <https://www.cadth.ca/pcodr/find-a-review>

Limitations

1. Line of therapy or previous treatment(s) not factored in to incidence calculation
2. Limited number of rare indications submitted to pCODR
3. No universal definition of rarity
4. Incidence calculated from multiple data sources and often using best estimates
5. Did not control for multiple factors contributing to funding recommendations and decisions

Conclusions

1. Rarity does not significantly impact positive or negative funding recommendations
2. Rare indications appear to have fewer submissions with RCTs conducted
3. Drugs for rare indications do not appear to be less cost-effective than drugs for non-rare indications
4. There appears to be no significant differences in time to funding between rare and non-rare indications.

Future Directions

- Evaluate real-world utilization/public expenditures on drugs for rare oncology indications
- Conduct a sensitivity analysis for the limitations described in our incidence calculations
- Further examine how rarity should be incorporated into oncology HTA in Canada

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