



# A comparison of reasons for recommendation and rejection in four HTA systems: NICE, SMC, CADTH and PBAC

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# Introduction

- Health technology appraisal (HTA) systems are used in many countries to assess newly licensed drug treatments and devices.
- The HTA bodies typically base their decisions on three main factors:
  - Clinical effectiveness
  - Safety
  - Cost-effectiveness
- However, decisions on whether a particular drug is recommended by the HTA bodies or rejected varies between the bodies.

## Study objective

- Our objective was to identify the reasons underlying recent drug appraisal decisions by four appraising bodies in Australia, Canada, England/Wales and Scotland, where decisions differed between the agencies.

Country	Appraising body
Australia	Pharmaceutical Benefits Advisory Committee (PBAC) <sup>1</sup>
Canada	Canadian Agency for Drugs and Technologies in Health (CADTH) <sup>2</sup>
England	National Institute of Health and Clinical Excellence (NICE) <sup>3</sup>
Scotland	Scottish Medicines Consortium (SMC) <sup>4</sup>

1. [http://www.health.gov.au/internet/main/publishing.nsf/Content/health-pbs-general-outcomes\\_full.htm](http://www.health.gov.au/internet/main/publishing.nsf/Content/health-pbs-general-outcomes_full.htm)
2. <http://cadth.ca//index.php/en/cdr>
3. <http://www.nice.org.uk/>
4. [http://www.scottishmedicines.org.uk/smc/CCC\\_FirstPage.jsp](http://www.scottishmedicines.org.uk/smc/CCC_FirstPage.jsp)

## Methodology - inclusion/exclusion criteria

- Internet searches identified submissions appraised between 1 November 2005 and 31 May 2008.
- Only submissions resulting in opposing outcomes for the same drug and indication, by two or more of the bodies were included.

CADTH	NICE	PBAC	SMC
<b>Submission inclusion criteria</b>			
Initial submissions	STA & MTA submissions	Public summary documents	Full & abbreviated submissions
Resubmissions	Resubmission	Resubmissions	Resubmissions
All indications	All indications	All indications	All indications
<b>Submission exclusion criteria</b>			
Request for advice			Non-submissions
			Limited information available

- Where there was more than one submission to a single HTA body for the same indication, the most recent outcome was included.

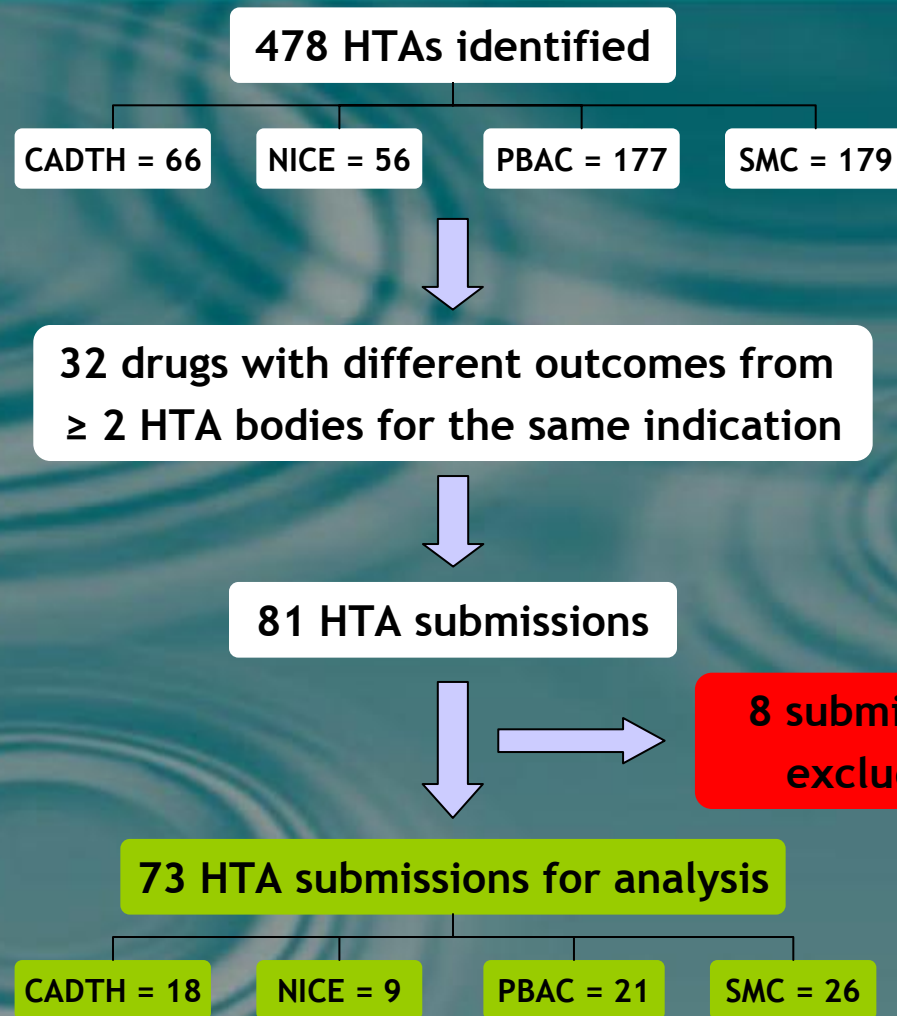
## Methodology - extractions

- All extractions were carried out by two independent reviewers.
- Any discrepancies were reconciled by a third independent reviewer.
- Reasons for guidance were extracted according to pre-defined categories and sub-categories.
- The main categories included reasons relating to:
  - clinical efficacy/safety
  - economic evaluation
  - study population
  - general/other
- In addition to reasons for the guidance, contrasting positive/negative comments were also extracted using the same pre-defined categories.

# Methods - categories of reasons for guidance

	Negative reasons	Positive Reasons
Related to safety and/or efficacy	Not more effective than placebo	More effective than placebo
	Not more effective than comparators	More/At least as effective than comparators
	Failure to use all appropriate comparators in efficacy/safety analyses	Appropriate comparators used for efficacy and safety-analyses
	Uncertainties regarding safety	Less adverse events than with comparators
	More/worse adverse events than with comparators	No associated serious adverse events
	Administration more problematic than comparators	Easier administration than comparators
	Lack of long-term data	-
	Not recommended by clinical specialists	Recommended by clinical specialists
Related to economic evaluation	Not cost-effective	Considered cost-effective
	Concerns/Limitations in economic model presented	Suitable economic model presented
	-	Lower cost negotiated
Related to study population	Study populations did not reflect intended population in clinical practice	-
	Indicated population not specific enough	Study populations reflected intended population
General	Insufficient supporting evidence	-
	Not a clinically meaningful improvement	Considered clinically important
	Criticism of study design	-
	Other	Other

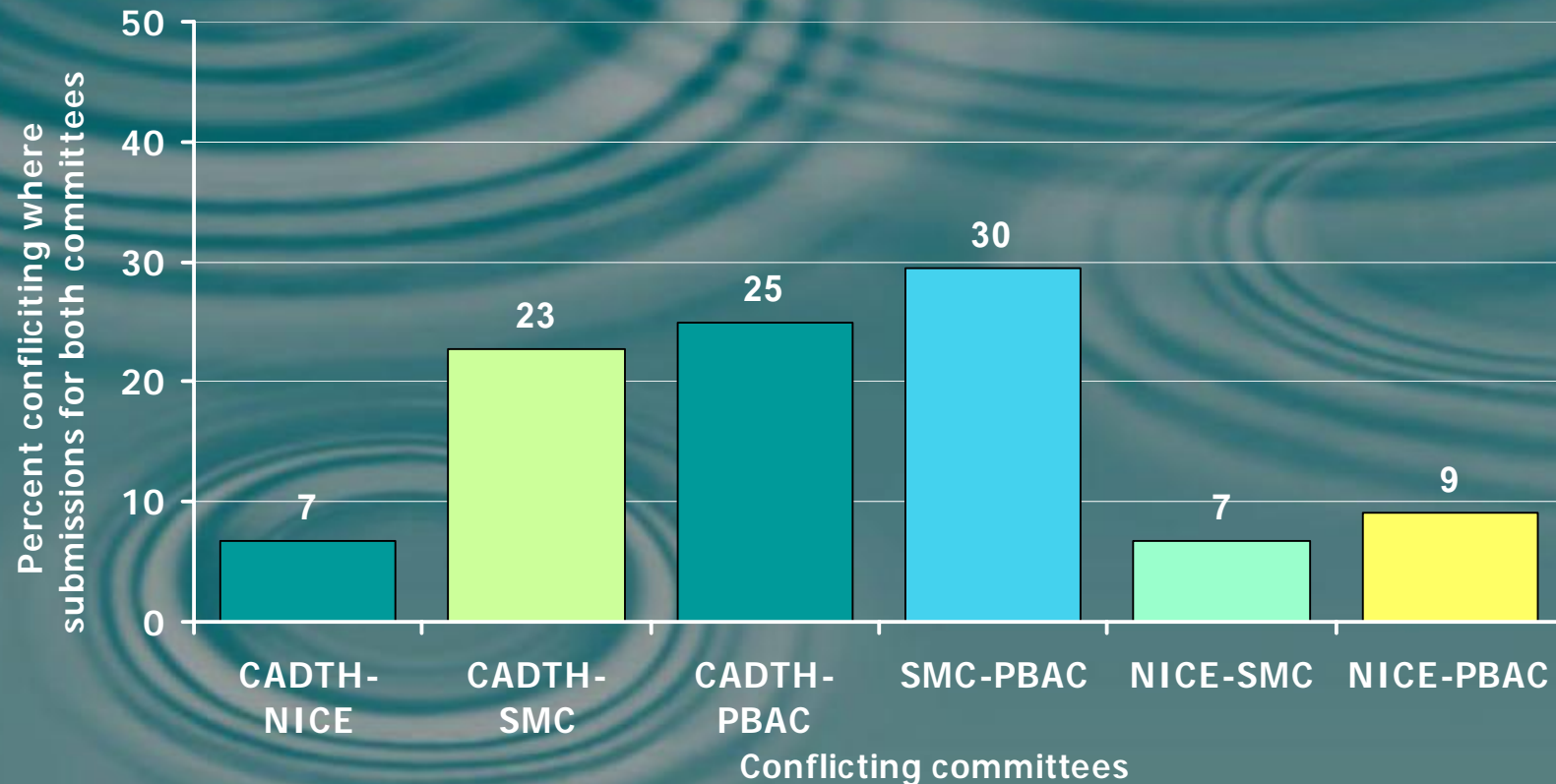
# Results - study flow



# Results - Conflicting Guidance from Committees

44 incidents of conflicting guidance were identified.

A high incidence of conflict was observed between CADTH and the SMC and PBAC. This was also observed between SMC and PBAC.

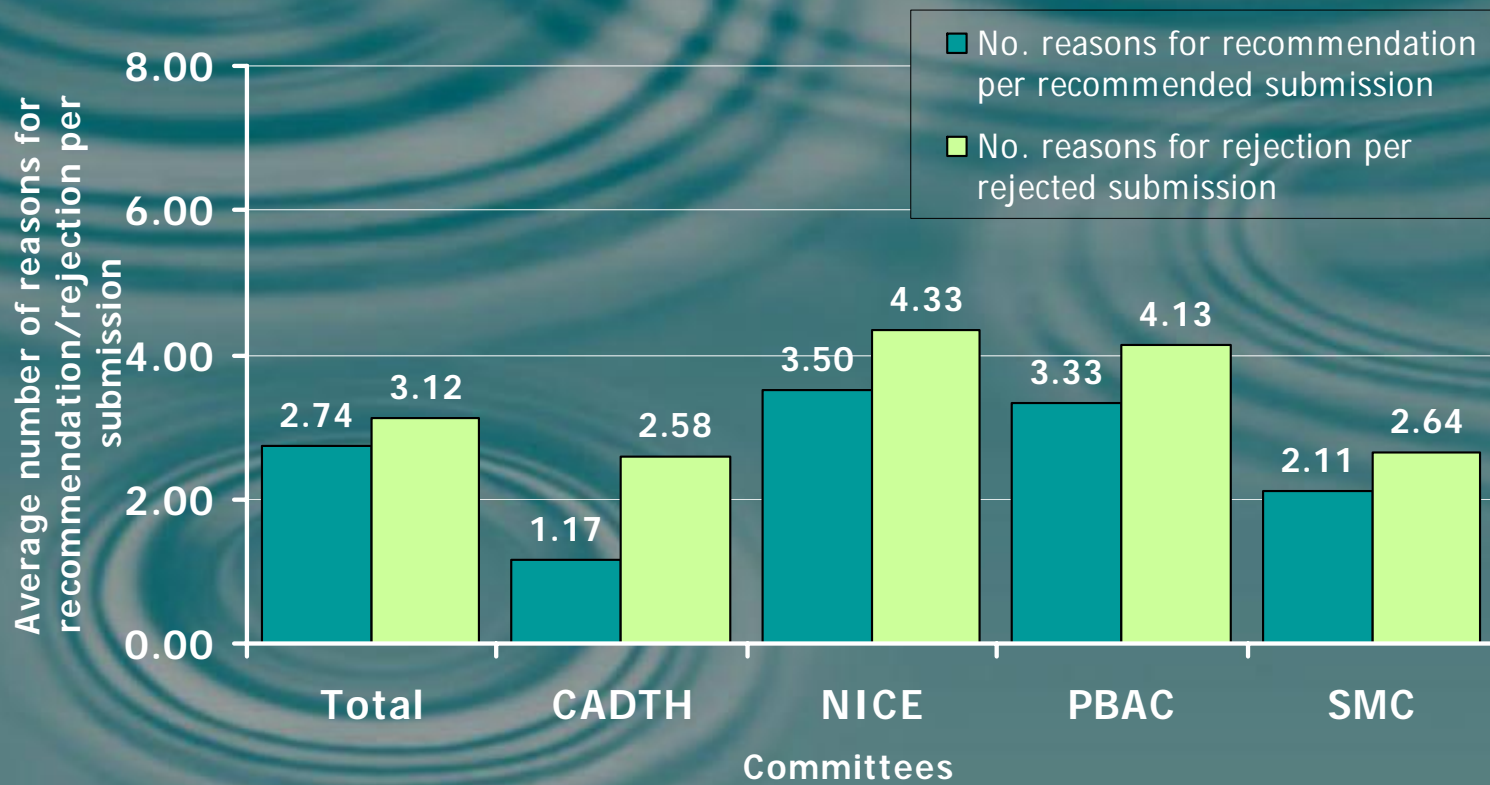


# Results - Number of reasons for recommendation and rejection per submission

73 submissions; 34 were recommended and 39 were rejected.

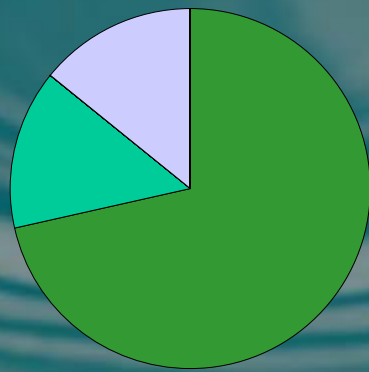
The average number of reasons given for recommendation was 2.74.

The average number of reasons for rejection was 3.12.

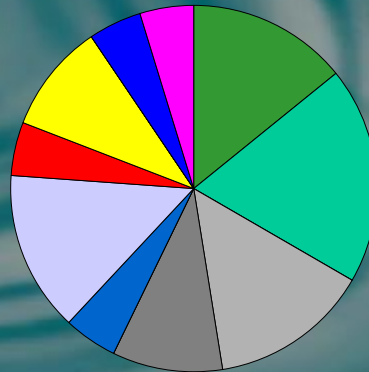


# Results - Reasons for recommendation

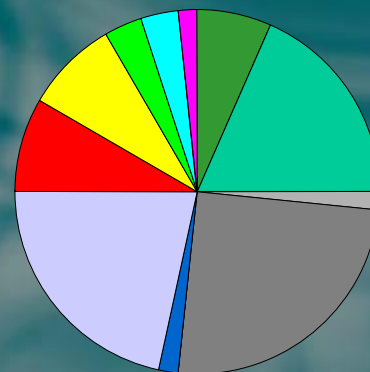
Percentage reported as a reason for recommendation (of the total number of reasons given for each committee).



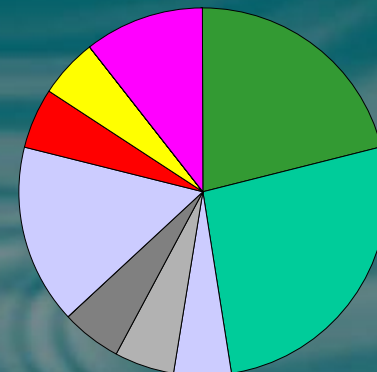
CADTH



NICE



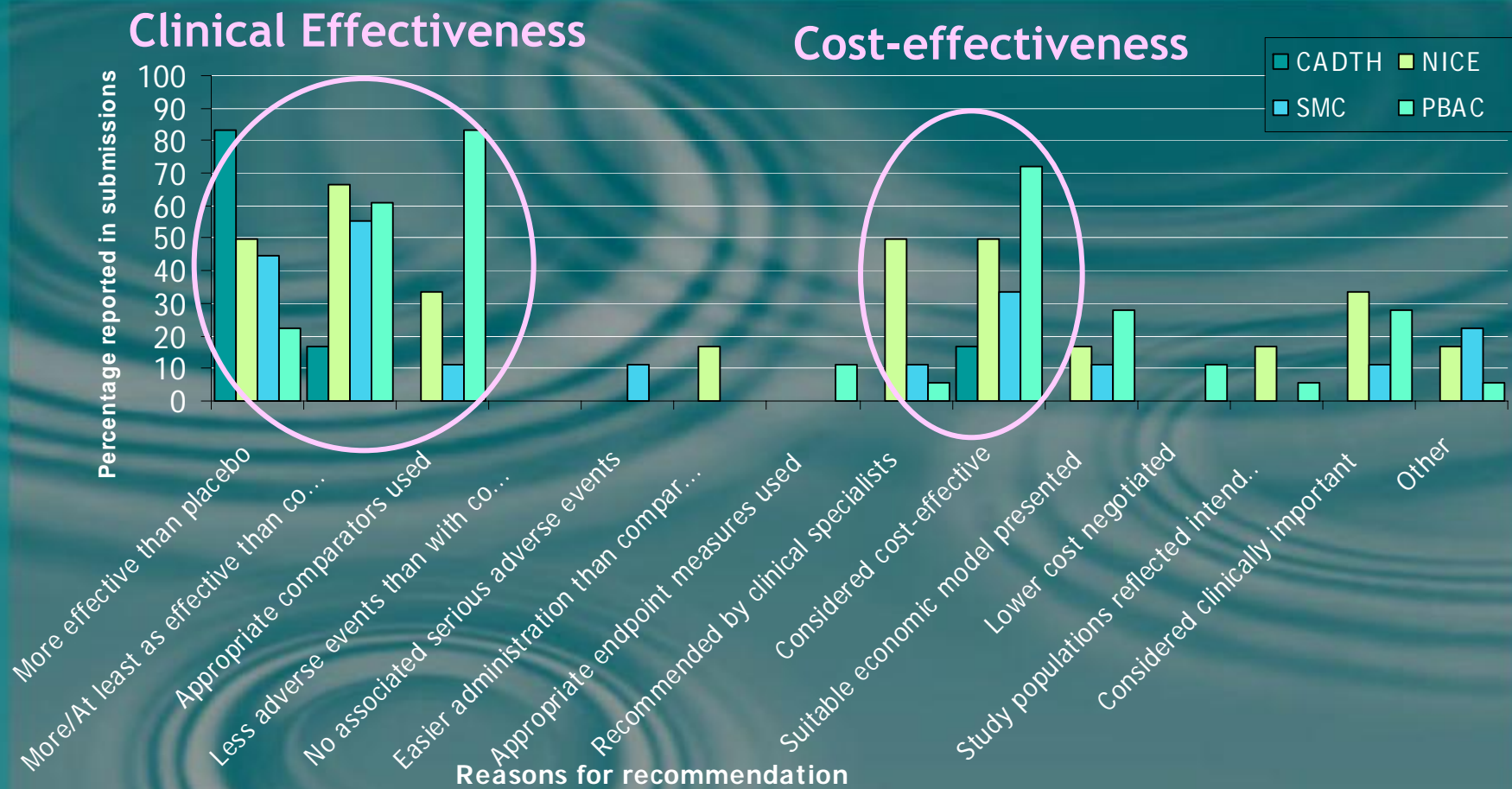
PBAC



SMC

- More effective than placebo in intended population
- More effective than comparators
- No associated serious adverse events
- Recommended by clinical specialists
- Appropriate comparators used
- Less adverse events than with comparators
- Study populations reflected intended population for clinical practice
- Considered cost-effective
- Suitable economic model presented
- Considered clinically important
- Lower cost negotiated
- Appropriate endpoint measures used
- Easier administration than comparators
- Other

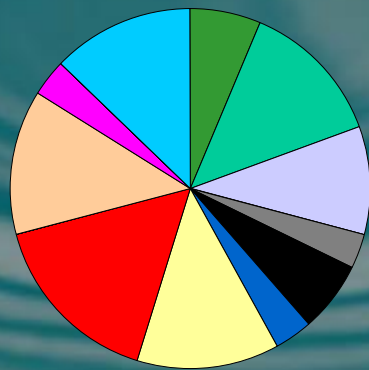
# Results - Reasons for recommendation



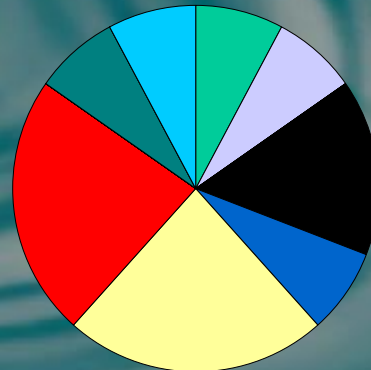
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# Results - Reasons for rejection

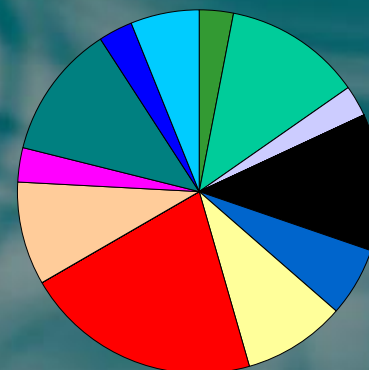
Percentage reported as a reason for rejection (of the total number of reasons given for each committee).



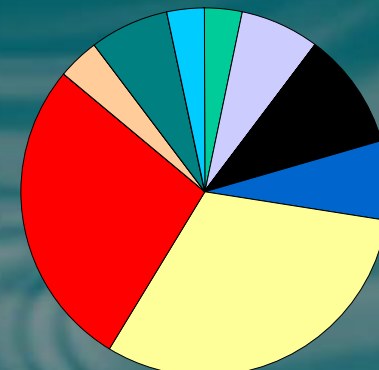
CADTH



NICE



PBAC

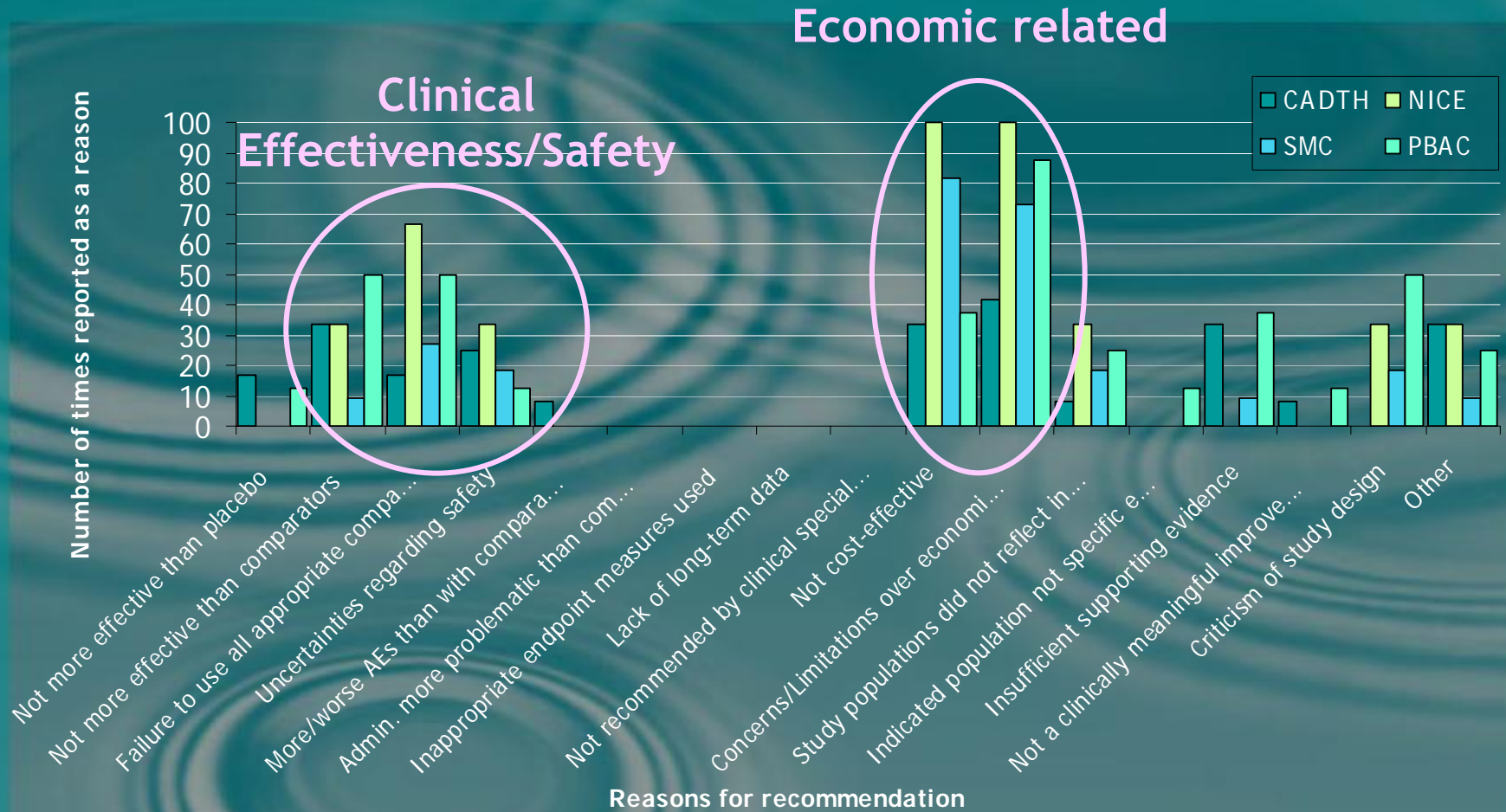


SMC

- Not more effective than placebo in intended population
- Not more effective than comparators
- Uncertainties regarding safety
- Not recommended by clinical specialists
- More/worse adverse events than with comparators
- Failure to use all appropriate comparators
- Study populations did not reflect intended population in clinical practice
- Not cost-effective

- Concerns over (or limitations identified in) economic model presented
- Inappropriate endpoint measures used
- Administration more problematic than comparators
- Lack of long-term data
- Insufficient supporting evidence
- Not a clinically meaningful improvement
- Criticism of study design
- Indicated population not specific enough
- Other

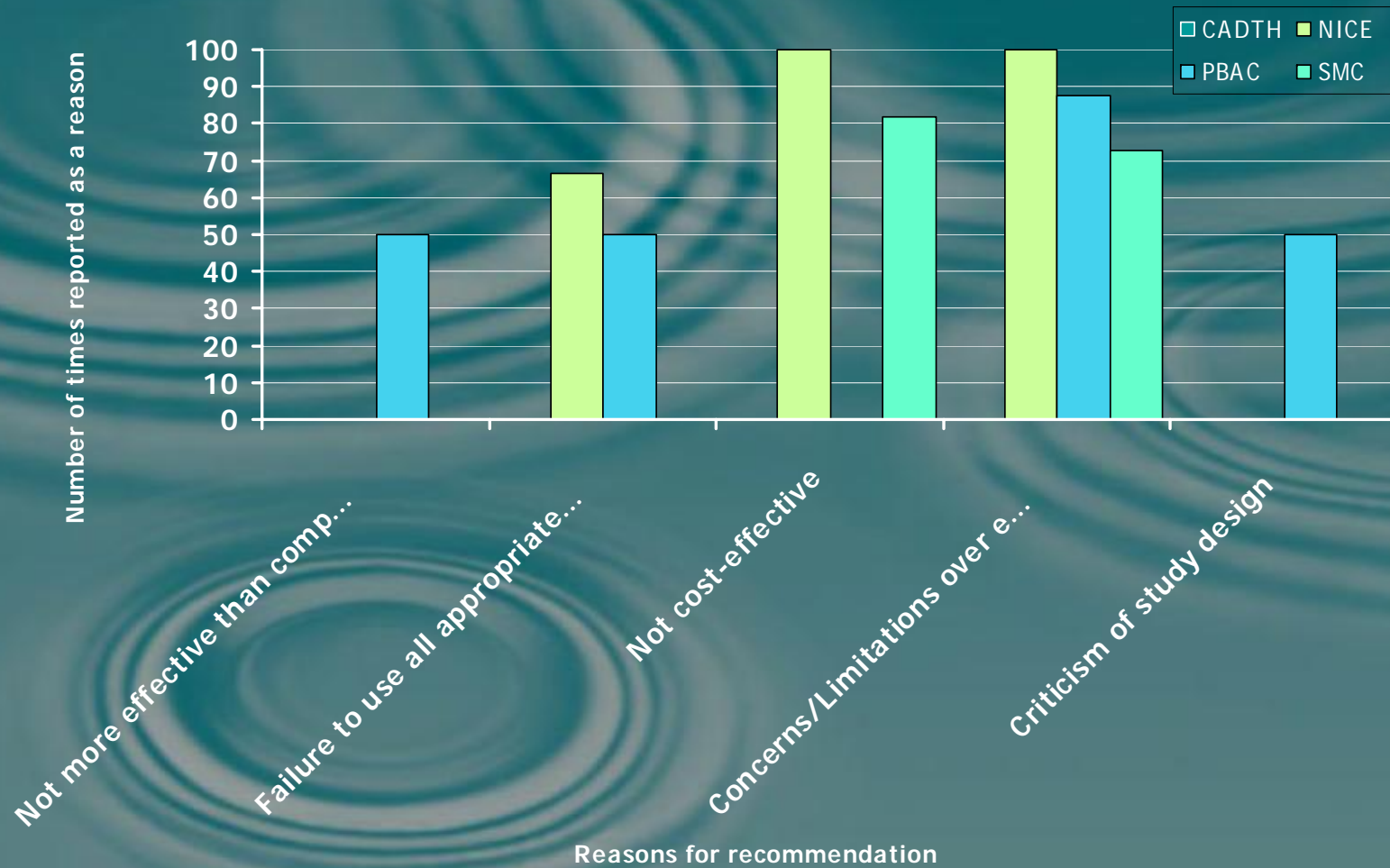
# Results - Reasons for rejection



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# Results - Reasons for rejection

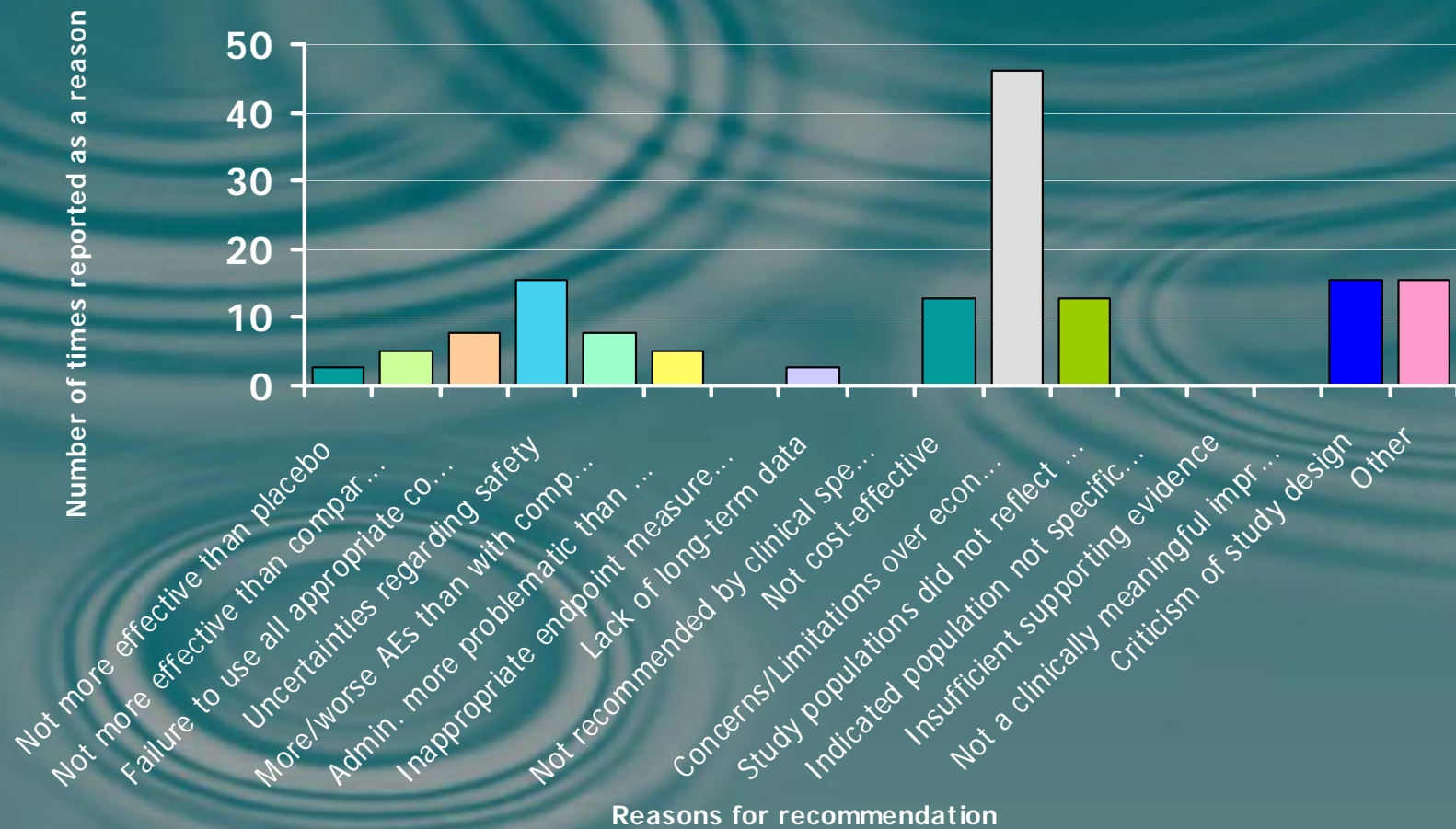
Reasons for rejection in at least 50% of submissions for each body.



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# Results - negative comments despite recommendation

Common negative comments, which have not however resulted in the submission being rejected.



## Results

- Alongside the reasons for rejection, positive comments on aspects of the submission are given. These were compared with reasons for recommendation in recommended submissions.
- Only one area of overlap:
- It was found that in submissions that were rejected, bodies duly noted that the intervention was either more effective than placebo and/or comparators, however despite this rejected the submission.
- “More/at least as effective as comparators” and “More effective than placebo” were common reasons for acceptance.
- This suggests that the main area of conflict between HTA bodies decisions relates to the economic analysis.
- Further research is required to address this observation/idea.

## Summary of results and conclusion

73 HTA submissions were analysed.

44 incidents of conflicting guidance between appraising bodies were identified

Many of which were between the SMC and PBAC (30% of 44 conflicts).

This was closely followed by conflicts between CADTH and the SMC and PBAC.

The average number of reasons for rejection/recommendation were approximately 3.

NICE and PBAC exceeded these averages, particularly the reasons for rejection.

## Summary of results and conclusion continued

CADTH gave the least variety of reasons for recommendation.

- Key reasons identified for positive guidance included
  - superior/non-inferior efficacy compared to placebo and/or comparators
  - robust economic case/cost-effectiveness demonstrated

Variety of reasons for rejection given for all bodies.

The focus was again around efficacy and cost-effectiveness.

PBAC and NICE also commonly cited the reason for rejection as the failure to use all appropriate comparators.

It was commonly observed that submissions were recommended despite the HTA bodies noting concerns in the economic analysis/model.

Further research is required to address the observation that the main area of conflict between HTA bodies' decisions relates to the economic analysis.

# References

1. [http://www.health.gov.au/internet/main/publishing.nsf/Content/health-pbs-general-outcomes\\_full.htm](http://www.health.gov.au/internet/main/publishing.nsf/Content/health-pbs-general-outcomes_full.htm)
2. <http://cadth.ca//index.php/en/cdr>
3. <http://www.nice.org.uk/>
4. [http://www.scottishmedicines.org.uk/smc/CCC\\_FirstPage.jsp](http://www.scottishmedicines.org.uk/smc/CCC_FirstPage.jsp)