

From Real-World Evidence to Subsidy Decisions: Insights from Health Technology Assessments by the Agency for Care Effectiveness

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Objective

To examine how real-world evidence has been considered in recent health technology assessments (HTAs) by the Agency for Care Effectiveness (ACE) in Singapore, focusing on its role in estimating treatment effects, addressing evidence gaps and informing subsidy recommendations.

Background

- In January 2026, the ACE released a position statement on the use of real-world data/evidence (RWD/RWE) to support HTA,¹ underscoring its increasing relevance in Singapore subsidy decisions.
- This study examined how RWE has been considered in recent ACE appraisals, following the release of the RWE position statement by ACE, and how it may have influenced subsidy decision-making.

Methods

- ACE appraisals published between January 2024 and April 2026 were identified.² Indication reviews, withdrawn appraisals and documents that did not report committee discussion were excluded.
- Included appraisals were reviewed to determine the role of RWE in HTA assessment, limitations of RWE noted by ACE, and subsidy recommendation outcomes.

Results

Appraisal Characteristics and RWE Use

- Of 54 appraisals reviewed, eight appraisals evaluating nine regimens incorporated RWE to estimate treatment effects where trial-based evidence was absent or insufficient.
 - The disease areas of the eight appraisals are summarised in **Figure 1**; all four cancer appraisals were company-led submissions.
- The types of RWE incorporated comprised observational studies, long-term extensions, natural history cohorts, overseas registry data and post-marketing safety data (**Figure 2**).
- RWE addressed limitations including lack of comparative trials, trials not reflecting local populations, small sample size in trials, and/or insufficient long-term data (**Figure 2**).
- Five appraisals incorporated RWE into indirect treatment comparisons (ITCs), including matching-adjusted indirect comparisons (n=3), propensity score-matched analysis (n=1), meta-analysis (n=1) and naive comparison (n=1).

Impact on Subsidy Recommendations

- Overall, 5/9 regimens received subsidy recommendations, including two on first assessment and three after price negotiations (**Figure 3**).
 - Among recommended regimens, clinical superiority was established for 3/5 regimens via ITCs that incorporated RWE. This was despite the RWE-ITCs being associated with limitations, such as residual confounding, small effective sample size and local applicability.
 - For the remaining 2/5 recommended regimens, RWE reinforced trial evidence to support superiority, despite limitations such as lack of pre-specified analyses and lack of control arms.
- Of the 4/9 regimens not recommended, the reasons cited by ACE are illustrated in **Figure 3**.

Conclusion

RWE was valuable in establishing clinical effectiveness and informing HTA decision-making in Singapore when trial-based evidence was absent, insufficient or poorly aligned with local practice. Although methodological limitations were commonly noted, ACE appeared willing to consider RWE where it addressed important evidence gaps and supported clinically plausible conclusions. Nonetheless, subsidy decision-making also depends on other factors, including price.

FIGURE 1

Disease areas of appraisals that incorporated RWE

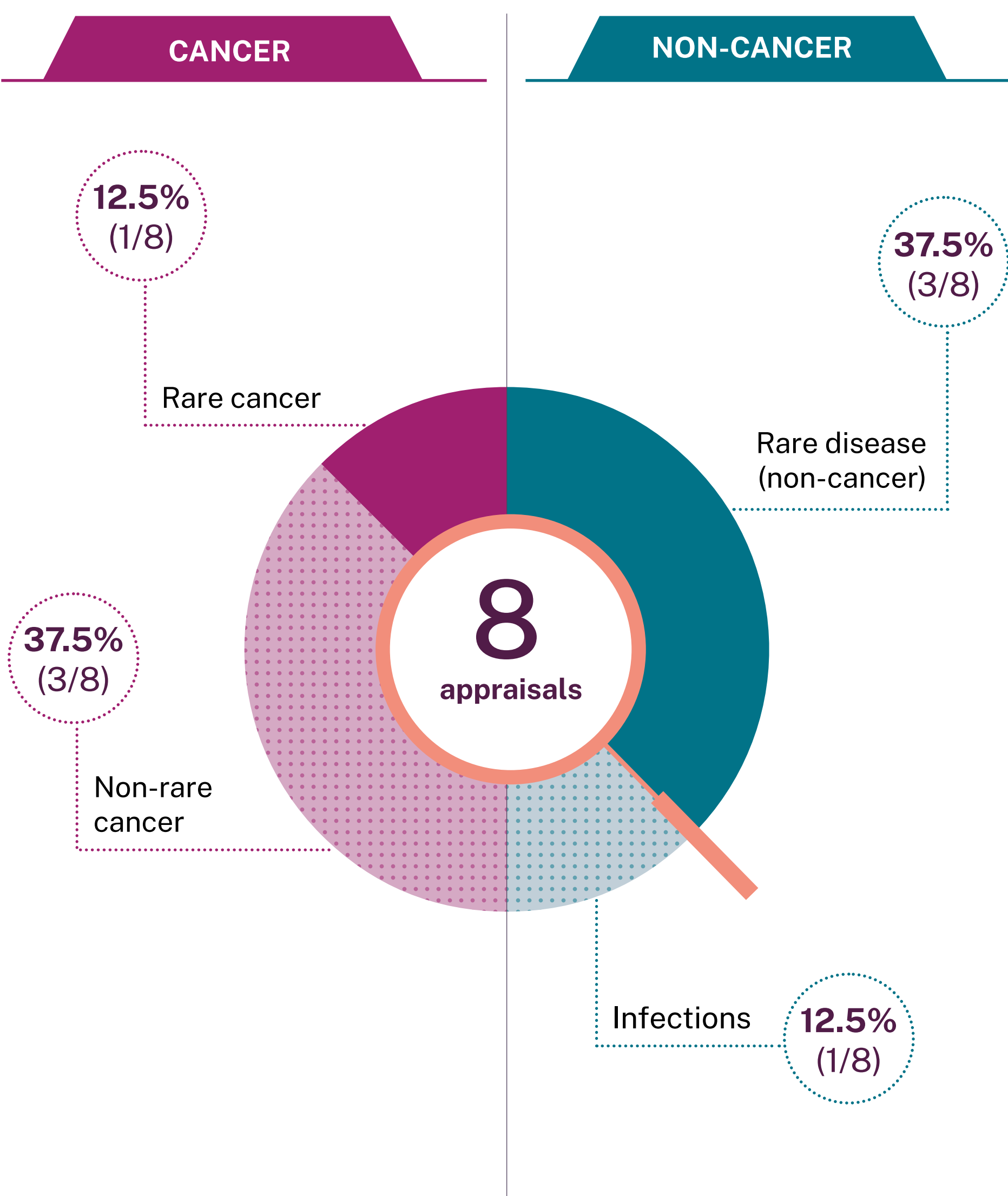


FIGURE 2

Types of RWE incorporated in ACE appraisals

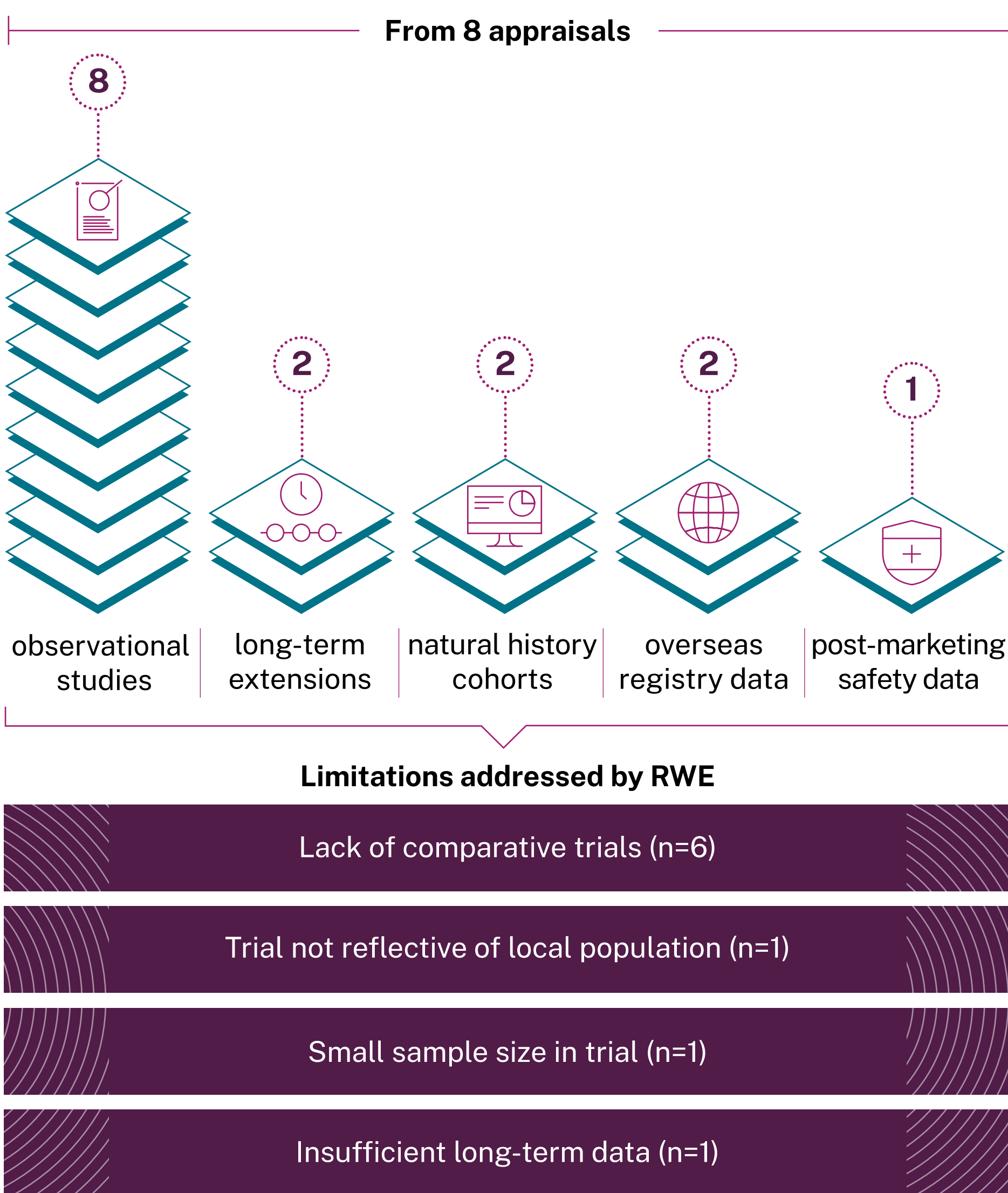
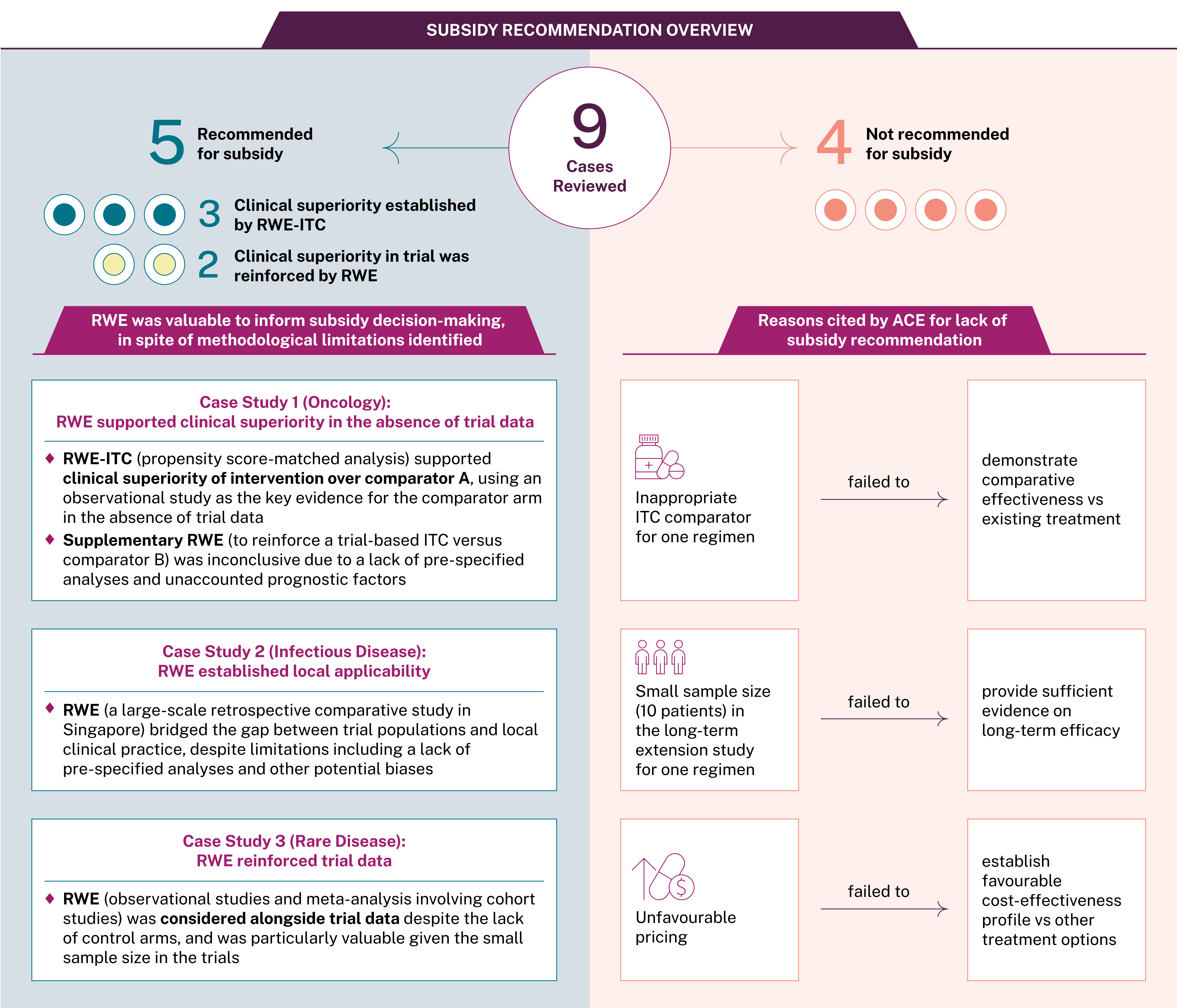


FIGURE 3

Impact of RWE on subsidy recommendations



Abbreviations: ACE: Agency for Care Effectiveness; HTA: health technology assessment; ITC: indirect treatment comparison; RWD: real-world data; RWE: real-world evidence.

References: ¹Agency for Care Effectiveness. Position statement on the use of real-world data/evidence to support health technology assessment. 2026; ²Agency for Care Effectiveness. Published technology guidance appraisals, January 2024–April 2026. Acknowledgements: The authors thank Henny Zhan, Costello Medical, for graphic design assistance.