Beyond EU JCA: The value of early global PICOS mapping to market access of innovative medicines in APAC markets

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Authors Latour, A[1]; Chanda, V[2]

[1]Remap Consulting, Zug, Switzerland; [2]Remap Consulting, Cheshire, United Kingdom

INTRODUCTION

- An EU-focused PICOS (population, intervention, comparator, outcomes or study-type) framework may be insufficient for global HTA evidence generation, as it may not reflect differences in treatment landscapes, reimbursement conditions, or evidence requirements across markets
- APAC decision-making is informed by country-specific standards of care, affordability constraints, treatment sequencing, and local treatment reimbursement and adoption
- Consequently, evidence generated based on EU-relevant PICOS may have limited transferability to APAC HTA and reimbursement contexts

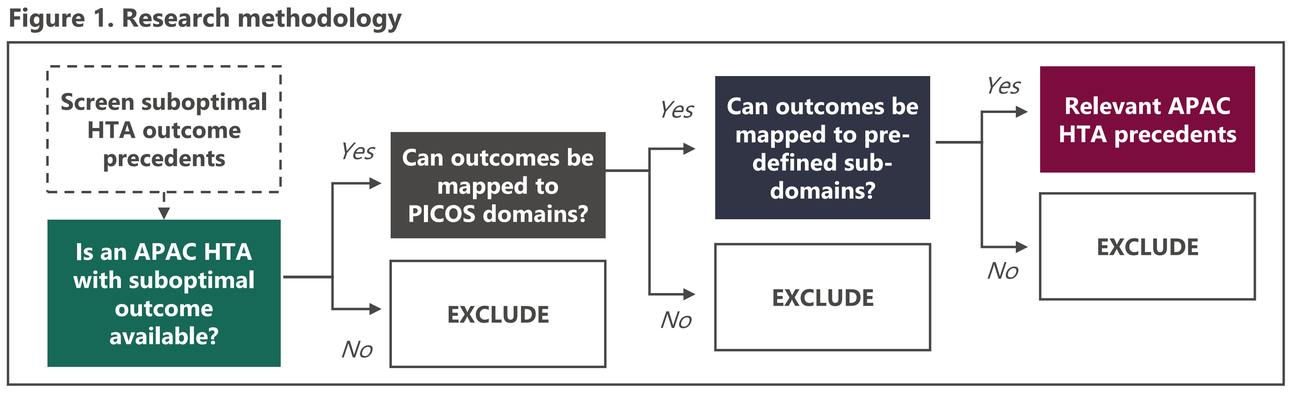
OBJECTIVES

- This analysis aims to evaluate the extent to which PICOS-related issues were a primary driver of suboptimal HTA outcomes, including rejection, deferral, restriction, or price impact
- HTA precedents were used to assess how misalignment between EU-focused PICOS domains and APAC evidence requirements may affect access and pricing opportunities

METHODS

- A targeted literature review of HTA reports and grey literature between 2020 and 2026 was conducted across Japan, S. Korea, Australia, New Zealand, Taiwan and Singapore, to identify HTA precedents where PICOS-related issues were the primary driver of rejection, deferral, restriction or price impact
- Findings were mapped to PICOS domains and pre-defined sub-domains. Primary drivers were selected and qualitatively interpreted to identify APAC-specific evidence and access risks that may not be captured by an EU JCA-focused evidence strategy

Figure 1. Research methodology



RESULTS

- Fifteen APAC precedents were identified via literature review with the primary PICOS drivers of suboptimal HTA outcomes being population (3/15), intervention (2/15), comparator (5/15), outcome measure (3/15) and study-type (2/15)
- **Population** issues led to rejection, deferral, or population restriction due to limited trial generalisability and unclear reimbursement population scope
- **Intervention** issues led to deferral, price reduction, and conditional reimbursement pending evidence generation due to concerns related to treatment line, sequencing, and treatment duration, where evidence did not align with local treatment pathways
- **Comparator** misalignment was the most quoted issue and led to rejection, restriction, or price reduction where comparators did not reflect local standards of care, limiting added benefit quantification
- **Outcome measure** issues resulted in deferral, rejection, or recommendation pending local data due to the use of surrogate endpoints and uncertain country-level utility inputs
- **Study-type** limitations included single-arm trials and immature data, leading to rejection or deferral due to uncertainty around comparative benefit and durability of effect

Figure 2. Number of APAC HTA precedents resulting in suboptimal HTA outcomes segmented by PICOS domain

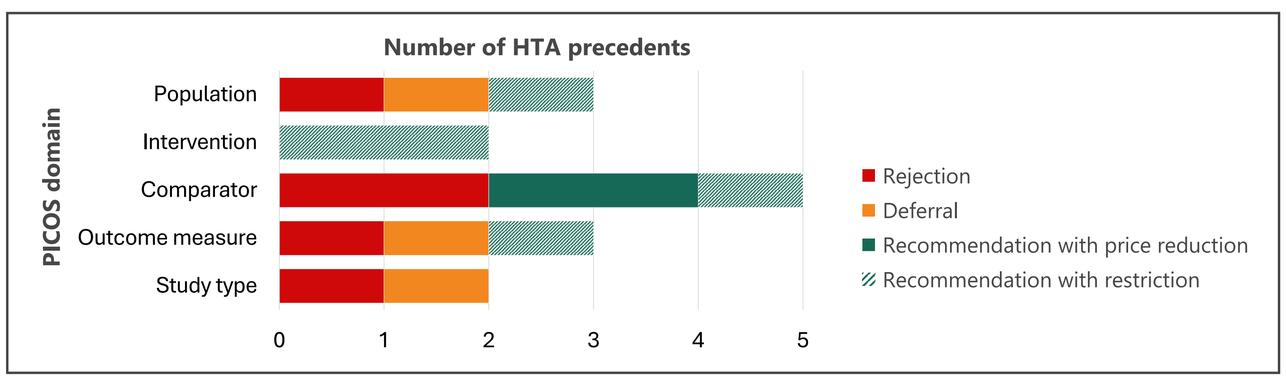


Table 1. APAC HTA precedents demonstrating suboptimal outcomes mapped to PICOS domains and sub-domains

PICOS domain	PICOS sub-domain	Outcome	Description	Country (HTA body)
Population	Clinical trial population	**Rejection**	Trial evidence was considered not generalisable to the local population due to limited ethnic subgroup data	New Zealand (PTAC)
		Recommendation with restriction: population	Initial reimbursement population was unclear; eligibility was narrowed to prioritise patients with severe or life-threatening disease	South Korea (HIRA)
	Scope	**Deferral**	Reimbursement scope was insufficiently defined, limiting the proportion of submissions receiving approved scope	Taiwan (CDE/NHIA)
Intervention	Treatment line	**Recommendation** with restriction: line of therapy	Reimbursement was restricted to later-line use where the available evidence best matched the treated population	Singapore (ACE)
	Dosing / treatment duration	**Recommendation** with restriction: evidence development	Recommendation was conditional on further evidence development due to uncertainty around treatment duration and stopping rules	Taiwan (CDE/NHIA)
Comparator	Local SoC	**Rejection**	Selected comparator was not accepted as it did not reflect the local treatment pathway or reimbursed standard of care	Australia (PBAC)
		Recommendation with restriction: line of therapy	Chemotherapy comparator does not reflect Taiwan's local SoC; reimbursement was restricted to align with locally relevant comparators and treatment pathways	Taiwan (CDE/NHIA)
		Recommendation with price reduction	Lack of evidence against relevant comparator resulted in no additional benefit non-inferiority via cost-minimisation	Japan (C2H)
	Comparator relevance	**Rejection**	PBAC considered that relevant comparators differed by biomarker subgroup, which were not presented in the initial submission; a later resubmission addressed comparator sequencing more directly, but the resubmission is noted to be partially addressed/uncertain	Australia (PBAC)
		Recommendation with price reduction	Non-locally relevant comparator choice reduced applicability of the evidence, contributing to a lower accepted benefit estimate and price reduction	Japan (C2H)
Outcome measure	Surrogate endpoints	**Deferral**	Reliance on surrogate endpoints, without significant OS or QoL benefit, introduced uncertainty and led to deferral	New Zealand (PTAC)
		Rejection	An analysis of HTA submissions for cancer drugs between 2012-2022 that relied on a surrogate outcome in lieu of overall survival or if the surrogate outcome was relied on for PBAC decision found a 44% rejection rate, reflecting uncertainty in clinical benefit	Australia (PBAC)
	Country-level inputs	**Recommendation** with restriction: pending local data	Use of non-local HRQoL inputs was criticised; assessment required adjustment using Japanese correction factors in the model	Japan (C2H)
Study-type	Single-arm trial	**Rejection**	Single-arm evidence was criticised due to non-comparative design and small sample size, limiting interpretation of clinical benefit	Singapore (ACE)
	Immature evidence	**Deferral**	PTAC considered evidence to be immature, and focused on dose-determination with placebo comparators, rather than safety and efficacy	New Zealand (PTAC)

CONCLUSIONS AND LIMITATIONS

Our analysis suggests that PICOS misalignment may directly influence APAC HTA outcomes, with PICOS issues resulting in rejection, deferral, restriction, or price reduction. However, the analysis was exploratory and hypothesis-generating; the small sample size and absence of a comparator set of positive HTA outcomes limited the ability to demonstrate a causal association between PICOS misalignment and suboptimal HTA outcomes. Further research should include a full systematic literature review and controlled analysis comparing positive and suboptimal HTA outcomes to quantify the relative contribution of PICOS-related factors to reimbursement decisions across APAC markets

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Abbreviations: APAC: Asia-Pacific; ACE: Agency for Care Effectiveness; C2H: Center for Outcomes Research and Economic Evaluation for Health; CDE/NHIA: Center for Drug Evaluation / National Health Insurance Administration; EU: European Union; HIRA: Health Insurance Review and Assessment Service; HRQoL: Health-related quality of life; HTA: Health technology assessment; JCA: Joint Clinical Assessment; NMA: Network meta-analysis; OS: Overall survival; PBAC: Pharmaceutical Benefits Advisory Committee; PICO: Population, intervention, comparator and outcomes; PICOS: Population, intervention, comparator, outcomes and study-type; PTAC: Pharmacology and Therapeutics Advisory Committee; QoL: Quality of life; SoC: Standard of care