HTA79

Comparative Clinical Effectiveness in Skin Cancer: Lessons From HTA Decision Making in EU4, UK, and Australia

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Background

- Comparative clinical evidence is central for health technology assessment (HTA) decision-making, yet head-to-head (H2H) trials in skin cancer are often unfeasible once effective therapies become available, due to ethical and recruitment challenges.[1]
- In the absence of direct evidence, indirect treatment comparisons (ITCs) such as Bucher, matching-adjusted indirect comparison (MAIC), and simulated treatment comparison (STC) are increasingly used to estimate relative effectiveness across trials.[2]
- However, interpretation and acceptance of ITCs varies considerably across settings.

Objectives

1. To investigates how comparative clinical effectiveness approaches have been applied in skin cancer HTA submissions across major agencies (AIFA, AEMPS, G-BA, HAS, NICE, PBAC) between 2019 and 2024.
2. To examine the methodological strategies used, the types of comparative analyses presented, and the appraisal outcomes reported by HTA bodies.
3. To assess how methodological choices and evidentiary quality influence HTA conclusions in the absence of direct H2H trials.

Methods

Step 1: Identification

- **HTA reports** on skin cancer (2019–2024) were retrieved.
- **Included agencies**: AIFA (Italy), AEMPS (Spain), G-BA (Germany), HAS (France), NICE (United Kingdom), and PBAC (Australia).
- **Source**: HTA-Hive database

Step 2: Data Extraction

- **Clinical evidence**: Type of evidence (direct or indirect), comparative methods, and study design.
- **HTA outcomes**: Direction of recommendation and agency appraisal.
- **Methodological concerns**: Key issues around adjustment, bias, and data compatibility.

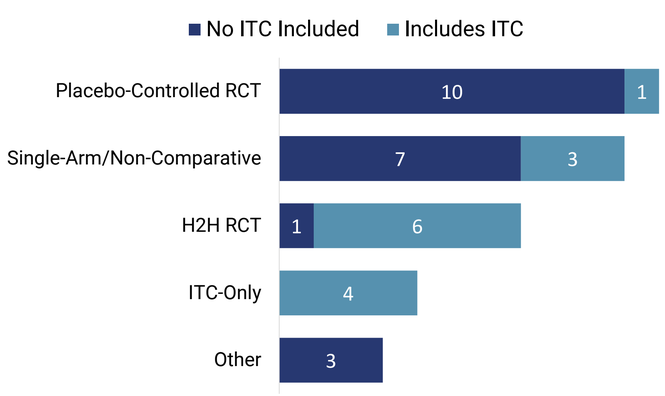
Step 3: Mixed Methods Analyses

- A qualitative review identified key themes across comparative approaches, agency evaluations, and methodological issues.
- Agencies' evaluations of evidence reliability were recorded (acceptable, ambiguous, insufficient).
- A quantitative analysis summarised the distribution of comparative methods and agency assessments, applying descriptive and inferential statistics to explore associations with HTA outcomes.

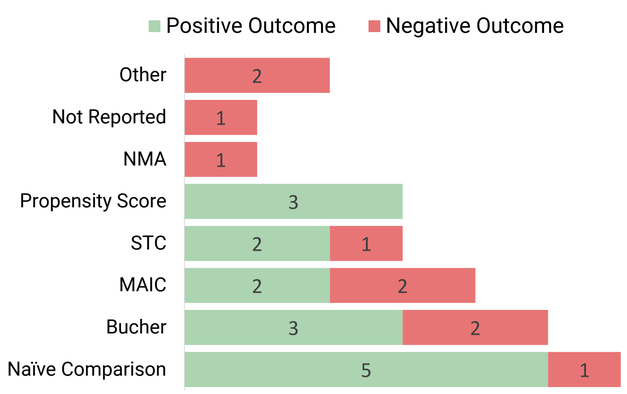
Results

- 40 appraisals were reviewed; 35 included clinical evidence, and five were minor resubmissions without new evidence.
- 60% (n=21) relied on direct or single-airm evidence, while 40% (n=14) incorporated ITCs.
- Study designs included single-arm/non-comparative (n=10), placebo-controlled RCTs (n=11), H2H RCTs (n=7), ITC-only (n=4), and other/mixed designs (n=3).
- ITC methods applied included: Naïve (24%), Bucher (20%), MAIC (16%), STC (12%), propensity-score methods (12%), NMA (4%), other (8%), and unreported (4%).
- Agency evaluations found evidence acceptable/reliable in 43% of cases, ambiguous in 36%, and insufficient in 21%.
- Agencies frequently raised concerns related to ITC methods, particularly adjustment (29%), bias/confounding (27%), data compatibility (29%), and modelling assumptions (15%); transitivity issues were cited less often but noted across several agencies.
- No significant association was observed between the type of comparative method and the HTA outcome ($\chi^2 = 5.42$, $df = 6$, $p = 0.49$). Submissions using ITCs showed a non-significant trend toward more positive outcomes.
- t-test analysis ($t = 1.07$, $df = 23$, $p = 0.30$) found no significant difference in outcomes between submissions using single versus multiple comparative approaches.

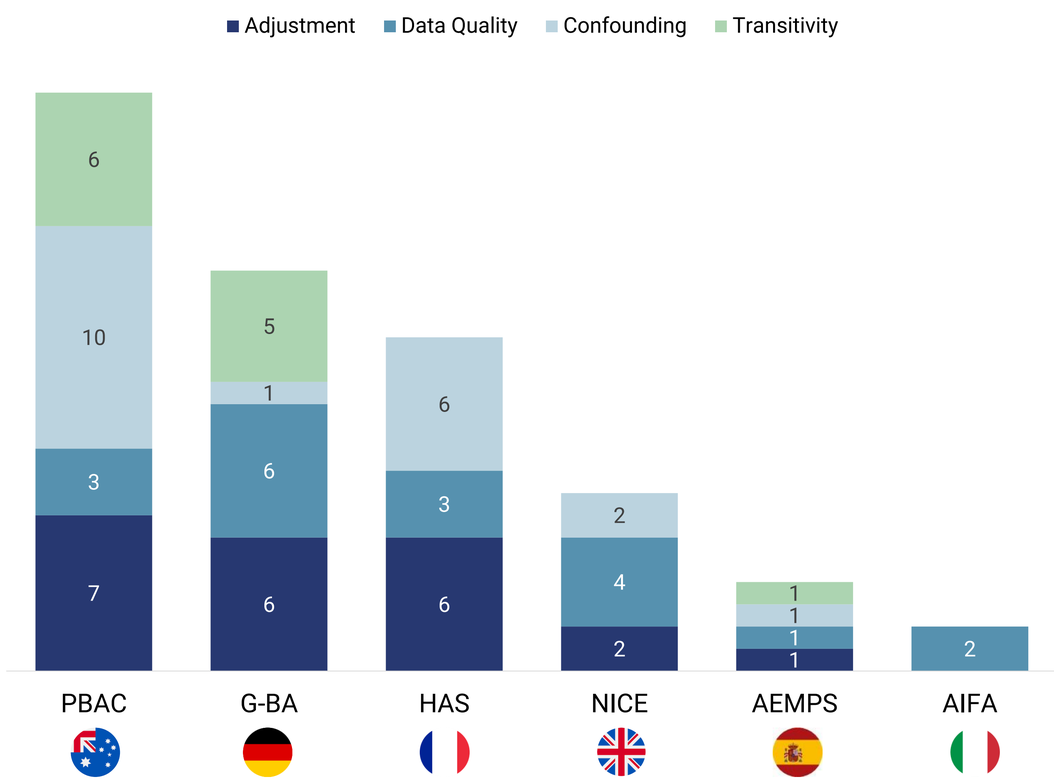
Study Designs and Use of ITC in Skin Cancer Submissions



Distribution of HTA Outcome by ITC Method Used



Methodological Concerns Identified Across HTA Agencies



Conclusions

- Comparative evidence for skin cancer therapies often relied on single-arm or placebo-controlled trials, limiting the strength of clinical comparisons.
- When direct evidence is limited, ITCs can help bridge evidence gaps and support decision-making; however, their acceptance varies by agency.
- Methodological concerns, including adjustment quality, data compatibility, and bias/confounding, frequently undermine confidence in ITC findings.
- Despite these limitations, 43% of submissions were judged acceptable, highlighting the potential value of ITCs when applied transparently and within robust methodological frameworks.
- Clearer cross-agency guidance on acceptable comparative approaches could improve consistency, rigor, and confidence in indirect comparative evidence and streamline future evaluations.

References

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2. Phillippo, D. M., Ades, A. E., Dias, S., Palmer, S., Abrams, K. R., & Welton, N. J. (2018). *Methods for population-adjusted indirect comparisons in health technology appraisal.* Medical Decision Making, 38(2), 200–211. https://doi.org/10.1177/0272989X17725740

Abbreviations

AEMPS, Agencia Española de Medicamentos y Productos Sanitarios; AIFA, Agenzia Italiana del Farmaco; G-BA, Gemeinsamer Bundesausschuss (Federal Joint Committee, Germany); HAS, Haute Autorité de Santé (French National Authority for Health); HTA, Health Technology Assessment; H2H, Head-to-head (trial); ITC, Indirect Treatment Comparison; MAIC, Matching-Adjusted Indirect Comparison; NICE, National Institute for Health and Care Excellence; NMA, Network Meta-Analysis; PBAC, Pharmaceutical Benefits Advisory Committee (Australia); STC, Simulated Treatment Comparison.

Contact Information

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