Utility of Early Evidence Synthesis in Market Access: Building a Compelling Evidence Base

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Aim

The aim of the present review was to investigate the potential utility of adopting evidence synthesis approaches earlier in drug development. Our objective was to identify instances where evidence synthesis approaches could have been used pre-emptively to strengthen submissions to health technology assessment (HTA) bodies beyond the standard approach of compiling clinical, economic, and quality-of-life data. Our review focused on National Institute for Health and Care Excellence (NICE) Highly Specialised Technology (HST) evaluations, and considered evidence across 7 domains: population, comparators, trial outcomes, subgroup analyses, health states and/or transition probabilities, health state utilities, and resource use and/or costs.

"Evidence synthesis approaches have utility beyond late-stage preparation for HTA submissions"

Methods

Final evaluation documents for all NICE HST submissions published up to March 2024 were reviewed by a single researcher to identify gaps in supporting evidence noted by the evidence review group (ERG) and/or committee. For each submission, the domains were rated as not present, minimal impact, moderate impact, or major impact, based on whether evidence gaps were identified in the original submission, whether additional evidence was sourced by the company/ERG, and the impact of any additional evidence on the model and recommendations.

Findings

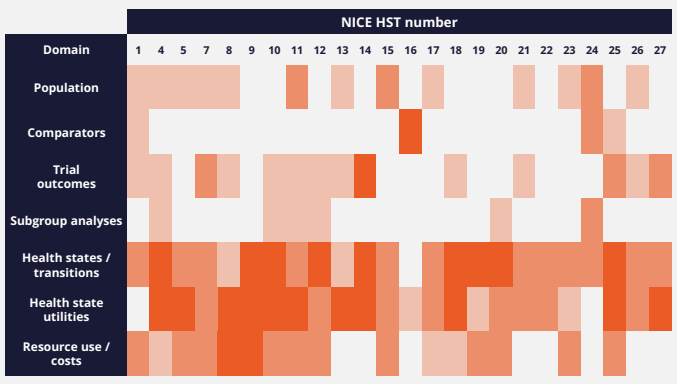

***Figure 1**. Impact of gaps in supporting evidence across 24 HST submissions*

- *Not present* — *No gaps pertaining to supporting evidence identified by ERG or committee*
- *Minimal impact* — *Gaps identified but submitted evidence deemed sufficient for decision-making*
- *Moderate impact* — *Additional evidence incorporated in model somewhat altered results*
- *Major impact* — *Additional evidence substantially altered model results and recommendation*

Background

The HTA review process can be time-consuming, resource-intensive, and costly—and, ultimately, it may not lead to a positive reimbursement recommendation:

- In 2020, the average time from acquiring marketing authorisation to intervention availability across European countries was 511 days for all products and 636 days for orphan medicines [1].
- More than half of all new drugs assessed by HTAs from 2015–2019 were rejected or recommended with access restrictions [2] and decisions varied considerably across Europe, Australia, and Canada.

Evidence synthesis methodologies (e.g., systematic, targeted, scoping, mapping, and umbrella reviews) can be used to generate robust evidence that can be used to strengthen HTA submissions. However, these approaches are often used late in the market access pathway and to a limited degree—typically only to fulfil mandatory HTA requirements. Given the resource and cost implications of undergoing a protracted or unsuccessful HTA evaluation, identifying how evidence gaps in previous submissions impacted recommendations is critical.

Findings

Of the 24 NICE HST evaluations reviewed, 4 were re-evaluations (HST19, HST22–24). In all but one (HST27), the intervention was ultimately recommended. The presence and impact of gaps relating to supporting evidence is shown by domain in Figure 1 and summarised below:

- **Population:** it was not clear that the clinical effectiveness data could be generalised in 13 evaluations, but in most cases (77%) this had a minimal impact, and data were deemed suitable for decision-making.
- **Comparators:** in 4 evaluations, key comparators were not included in the clinical evidence and/or model; in only one case, the company was required to submit a revised model with an alternative comparator.
- **Trial outcomes:** evidence to support the study outcomes was lacking in 14 evaluations but in most cases (72%), the impact was minimal. However, in 4 evaluations, alternative outcomes sourced by the ERG or company were used to inform the final economic model.
- **Subgroup analyses:** in 6 evaluations there was insufficient evidence to support the inclusion/non-inclusion of subgroup analyses. In only one (17%), stratified analyses performed by the ERG were preferred.
- **Health states / transitions:** 23 evaluations lacked evidence to support these model inputs. This had a major impact in 39% of cases, where inputs informed by alternative data altered the model results.
- **Health state utilities:** in 22 evaluations there was insufficient evidence to support the utility/disutility values, which often had a moderate (36%) or major (50%) impact. In one case, concerns related to disutilities contributed to the intervention not being recommended.
- **Resource use / costs:** inappropriate or missing costs were noted in 16 evaluations. Alternative values sourced by the ERG/company had a moderate or major impact in 69% and 13% of cases, respectively.

Discussion

Conclusion: Evidence provided in company HST submissions is often lacking, which can ultimately impact the final recommendation.

Implications for research: Evidence synthesis approaches have diverse applications and can be used pragmatically and pre-emptively to generate evidence that can strengthen company HST submissions.

Implications for practice: Manufacturers should consider using evidence synthesis methodologies at an earlier stage in drug development to capitalise on benefits. This is particularly important for identifying suitable model inputs for health states and transition probabilities, and for sourcing utility/disutility values, given that evidence gaps pertaining to these domains can have a major impact on final recommendations.

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References

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2. Newton M, et al. European Federation of Pharmaceutical Industries and Association (EFPIA) Waiting to Access Innovative Therapies (W.A.I.T.) Indicator Survey. Jun 2024. https://efpia.eu/media/vtapbere/efpia-patient-wait-indicator-2024.pdf

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