Uptake of Early Health Technology Assessment in the United States (US): A Literature Review of Empirical Studies HTA57

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Background

- Traditional health technology assessments (HTAs) evaluate the cost-effectiveness of a product after its development process is completed, implying that manufacturers have already committed significant resources before determining if their product will be covered by government payers.
- Over the past few decades, there has been an increasing focus on utilizing early-stage models to inform product development, market access, and pricing strategies.
- As early-stage health economic modeling has been employed for some time, various interpretations of early HTAs have surfaced. Generally, they encompass "*all methods used to inform industry and other stakeholders about the potential value of new medical products in development, including methods to quantify and manage uncertainty*."[1]
- An advantage of early HTAs is that their results can offer crucial insights to companies regarding the expected benefits, risks, and uncertainties linked with novel healthcare technologies. This information can assist in making informed decisions on whether to persist in allocating resources for additional development or cease efforts if economic viability seems unlikely.
- In the United States (US), HTAs are conducted by various organizations such as the Agency for Healthcare Research and Quality (AHRQ) and the Institute for Clinical and Economic Review (ICER).

Objective

- The aim of this research was to offer a recent overview of ongoing advancements in early HTAs carried out in the US. While previous reviews have addressed progress up to 2016,[1-4] our focus was on literature published from 2017 onwards.

Methods

- A comprehensive literature review was conducted to identify empirical studies that reported on the implementation of early HTAs for any product from the US perspective. Searches were run in Embase and Medline in December 2023, with a filter to identify English language literature published since 2017. Other sources included hand-searching reference lists of relevant literature reviews.

Results

Search results

- The literature searches identified 454 records, of which 98 were selected for full-text screening. Seven articles reporting findings of early HTAs for 7 technologies from the US perspective met the criteria for inclusion.[5-11]

Results (cont.)

Choice of early HTA tools

- The included articles reported cost-effectiveness data related to 7 technologies: 4 medical devices, 2 drugs, and 1 gene therapy (**Table 1**).
- Compared to traditional HTAs, the included early HTAs did not use efficacy data generated from clinical trials. Instead, they depended heavily on evidence published from previous studies via literature reviews, as well as clinical expertise.
- Early economic models were utilized in all included studies, but only 1 included value-of-information analyses.[6] Markov state transition models were the most common modeling approach (n=4), followed by simulation models (n=2) and decision-analytic models (n=1) (**Table 1**).
- All models were validated by experts in the area.

Early HTA findings

- Over half of the early HTA studies were funded by manufacturers involved in the production of the technology being assessed (n=4).
- All early HTAs reported economic evaluation results that favored the technology under investigation; 4 early HTAs found the technologies to be potentially cost-effective at relatively high willingness-to-pay (WTP) thresholds (>$50,000), while 3 early HTAs concluded that the uptake of those new technologies may lead to cost-savings (**Table 1**).

Limitations of early HTA as reported in the literature

- Overall, there is a lack of good quality evidence regarding costs and benefits of the assessed technologies, especially for rare genetic diseases[9] or conditions that require medical devices.[5,7,10,11]

Addressing uncertainty

- Given the frequently restricted evidence base in early HTA, it is essential to perform thorough sensitivity analyses to assess uncertainties when solid clinical effect estimates and definitive pricing guidelines are lacking.
- The evaluation of uncertainties was conducted through deterministic or probabilistic sensitivity analysis, as well as univariate and multivariate sensitivity analyses across all early HTAs. In these investigations, variations were made in the effectiveness of the new technology and/or its financial costs to determine whether the technology surpasses or falls short of different WTP thresholds (**Table 1**).

Table 1. Details from included early HTAs

Technology type	Author, year	Type of early HTA (model approach)	Technology being assessed	Target population	Impact of varying the ranges of costs and effects	Cost-effective?
Gene therapy	Klimchak, 2023	Early economic model (model structure with 5 health states)	Delandistrogene moxeparvovec (SRP-9001) plus standard care vs standard care alone	Patients aged 4 years with DMD	• WTP varied at $150,000 , $250,000, $500,000 • Costs were discounted at 3% and benefits at either 3%, 1.5%, or 0% • Similar variations in the ICER when using different measures of benefits: – Scenario A, IQR when using QALY: $128,844-$180,574 – Scenario B, IQR when using evLYG: $129,990-$169,642	Potentially at a WTP threshold of $500,000/evLYG
Medical device	Terjesen, 2017	Early economic model (decision analytic model)	Single-use flexible video bronchoscopes vs reusable flexible video bronchoscopes	Patients at intensive care units requiring video bronchoscopes	• Average cost of current reusable technology: $424 (0.7% infection rate) • Cost of new single-use technology varied at $100, $200, $300, $400, or $500 • Infection rates with current reusable technology varied at 10%, 15%, 20%, 25%, 30%, 35%, or 40% • Compared to new single-use technology at $305 (0% infection rates), only a cost of $100 could make the reusable technology more cost-effective	Cost-saving
Medical device	Gibson, 2022	Early economic model (semi-Markov structure with 15 health states)	Light-based, at-home antiviral treatment (EmitBio, RD-X19) vs standard practice	Average adult individuals with mild to moderate COVID-19	• Scenario analyses varied the proportion of eligible infected individuals receiving intervention (5%, 10% [base case], and 25%) alongside alternative intervention clinical benefit scenarios where the time to no or mild symptoms was assumed to be 50% above (3.6 days [150%]) and 50% below (1.2 days [50%]) the base case of 2.4 days (100%) • Adoption of the intervention resulted in cost savings per person treated for all combinations, with results ranging from a low of $997 (5%; 1.2 days) to a high of $3,969 (25%; 3.6 days) • In a deterministic sensitivity analysis, variations of the interventional efficacy (reduction in symptomatic days), proportion of the total population over the age of 18 years, and proportion of confirmed COVID-19 infections were shown to drive the greatest changes in cost savings per person receiving the intervention	Cost-saving
Medical device	Yeroushalmi, 2022	Early economic model (Markov structure with 4 health states)	Robotic-assisted UKA	Patients with mean age of 65 years with single-compartment end-stage knee osteoarthritis	• All ICER estimates remained under $50,000 per revision avoided when the following parameters were varied: discount rate (0%-5%), cost of r-UKA robot ($400,000-$900,000), revision probability, and r-UKA effectiveness. • Varying the number of cases seen per center had a substantial impact on the ICER: – 10 r-UKAs per year: $187,362 per revision avoided – 200 r-UKAs per year $5,147 per revision avoided	Yes, at a WTP threshold of $50,000 per revision avoided
Medical device	Namin, 2019	Multicriteria decision analysis (system dynamics model)	CIM knee implants	Patients requiring knee replacement	• Nine effectiveness parameters were changed by ±50% under 90% insurance coverage for CIM implants at the same time and varying at year 1, 2, and 3 • The parameters of multiplication of *off-the-shelf product cost for the price of CIM implant* and *time to make decision (surgeons to adopt)* were the most sensitive for total cost per patient within 3 years, with changes between 3% and 9%	Results show an adoption rate of 90% for CIM implants leads to 62% and 39% reductions in readmissions and revision surgeries, respectively, and reduced cumulative healthcare costs of $38 billion
Pharmacotherapy	Alrawashdh, 2022	Early economic model and expected value of perfect information analysis (Markov model with 2 health states)	BTKIs: ibrutinib, acalabrutinib, and zanubrutinib	Patients with relapsed or refractory mantle cell lymphoma and at least 1 prior line of treatment	• Medication costs for the 3 BTKIs were the most critical variables in terms of impact on the cost-effectiveness estimates • ICURs for both acalabrutinib and zanubrutinib were highly sensitive to the WAC of ibrutinib, especially when the ibrutinib WAC decreased, which resulted in increased ICURs – For instance, if the cost of ibrutinib was decreased by 15% ($1,945), the ICUR for acalabrutinib would exceed the $150,000/PFQALYg threshold and ibrutinib would prevail over acalabrutinib in cost-effectiveness – A 30% reduction ($3,890) in the ibrutinib WAC would yield an ICUR exceeding $240,000/PFQALYg – Both the 15% and 30% reductions in the ibrutinib WAC would make it impossible for zanubrutinib to be cost-effective – Conversely, reducing the cost of acalabrutinib (and zanubrutinib), independently or in conjunction with reductions in the price of ibrutinib, might place both acalabrutinib and zanubrutinib within the $150,000 WTP threshold	Yes, at a WTP threshold of $150,000/PFQALYg
Pharmacotherapy	Javanbakht, 2023	Early economic model (Markov model structure with 2 submodels)	Resmetirom	Patients with mean age of 50 years with nonalcoholic steatohepatitis	• Threshold analyses at $50,000, $100,000, and $150,000 WTP thresholds were performed probabilistically to determine the daily price at which resmetirom would still be considered cost-effective • Results indicate that resmetirom would be cost-effective at a daily price of $50.35 ($50,000 WTP threshold), $72.00 ($100,000 WTP threshold), and $93.64 ($150,000 WTP threshold), depending on the selected WTP threshold • Scenario analysis based on varying cardiovascular risk had little impact on the results (ICER $51,862-$67,300 compared to base case ICER $53,929)	Yes, at a WTP threshold of $100,000/QALY

Key: BTKI – Bruton's tyrosine kinase inhibitor; CIM – customized individually made; DMD – Duchenne muscular dystrophy; evLYG – equal value of life-years gained; HTA – health technology assessment; ICER – incremental cost-effectiveness ratio; ICUR – incremental cost-utility ratio; IRQ – interquartile range; PFQALYg – progression-free survival quality-adjusted life-year gained; QALY – quality-adjusted life-year; r-UKA – robotic-assisted unicondylar knee arthroplasty; UKA – unicondylar knee arthroplasty; WAC – wholesale acquisition cost; WTP – willingness to pay.

Conclusions

- We previously reported the findings of 18 United Kingdom (UK)-based early HTAs using similar methodology.[12] Compared to our findings from the UK, we noted that very few early HTAs have been published in the US healthcare setting.
- Early economic modeling stands out as the primary tool employed to advise medical technology manufacturers when making investment decisions. Conversely, implementing early HTA for pharmacotherapies appears challenging, primarily due to uncertainties surrounding the therapy's effectiveness in the initial stages of development.
- There is a scarcity of guidance on performing early HTA, and there remains a lack of consensus regarding the most suitable theoretical framework, while robust methods for early HTA are still being developed.
- One limitation of the current research is the absence of Medical Subject Headings (MeSH) and clearly defined keywords in the field of early HTA, potentially resulting in the oversight of relevant published literature.
- Finally, manufacturers of health technologies might be conducting early HTAs without disclosing the outcomes, especially if they are unfavorable to the new technology. This introduces a risk of publication bias in studies focusing on early HTA.

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