Uptake of Early Health Technology Assessment in the United Kingdom: A Literature Review of Empirical Studies

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Background

- Traditional health technology assessments (HTAs) assess the cost-effectiveness of a product (e.g., medical device, diagnostic test, or pharmacological therapy) at the end of the development process, meaning that manufacturers have already invested considerable resources before finding out whether their product will be reimbursed by government payers.
- Early HTA is a valuable tool that informs decision-making at early stages of development, facilitating go/no-go decisions and providing developers with key information on drivers of cost-effectiveness that can improve the economic viability of their products.
- One proposed definition of early HTA is, *"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]
- Early HTA differs from traditional HTA in that it takes place before the product is licensed, which allows for the product development process to be informed by the results of early HTA, thereby increasing the probability of achieving support from decision-makers in public health systems.

Objective

- The objective of this research was to provide an update on current developments in early HTAs conducted in the United Kingdom (UK). Several published reviews have covered developments until 2016;[1-4] therefore, we focused on literature published since 2017.

Methods

- A literature review was conducted to identify empirical studies that reported on the implementation of early HTA for any product from the UK perspective. Searches were run in Embase and Medline in June 2023, with a filter to identify English language literature published since 2017. Hand-searching of reference lists of included literature reviews was also conducted to supplement the database searches.

Results

Search results

- The literature searches identified 413 records, of which 84 were selected for full text screening. Eighteen articles[5-22] reporting findings of 18 empirical studies met the criteria for inclusion; two of which discussed early HTA in the context of European cross-country analysis, including the UK.

Choice of early HTA tools

- The included articles reported data related to 16 technologies being assessed (**Table 1**).
- Early economic models were utilized in 17 studies, including headroom and/or value-of-information analyses in eight of them, while multicriteria decision analyses were conducted in the last study[6] (**Table 1**).

Early HTA findings

- Six early HTA studies were funded by manufacturers involved in the production of the technology being assessed. In five of these studies, early economic modelling was used, and in all those cases, the experimental technology was found to be cost-effective or cost-saving.
- All early HTA studies investigating devices, diagnostic tests, and prevention programmes concluded that the experimental technology had the potential to be cost-effective or cost-saving.
- On the other hand, none of the pharmacological therapies assessed with early HTA were found to be cost-effective. In three of these studies, the cost-effectiveness of the therapies in development was found to have a high degree of uncertainty, mainly attributed to lack of data on treatment effects, and therefore further investigations were suggested by the authors.[17,19,20]
- Of note, although acalabrutinib was not cost-effective compared to ibrutinib according to early HTA when phase 1/2 data were used in cost-utility analyses,[15] it is now recommended for the treatment of patients with relapsed chronic lymphocytic leukaemia in guidance issued by the National Institute for Health and Care Excellence (NICE)[23] under a commercial arrangement. The manufacturer submitted a cost-minimisation analysis with the assumption that acalabrutinib is as effective as ibrutinib for this population; considering that the early HTA study did not receive funding from the manufacturer, we cannot conclude that the findings from the early HTA might have influenced the company's strategy for reimbursement of this drug.

Table 1. Summary of findings

Technology	Author, year	Type of early HTA	Technology being assessed	Target population	Impact of varying the ranges of costs and effects	Cost-effective?
Devices	Federici, 2021[8]	Early economic model and headroom analysis	A fall-prevention wearable device	Elderly patients with an increased risk of falling	Varied cost of device (£130/15 years, £230/10 years, £300/6 years): Device was not cost-effective over £230/10 years	Yes
	Manetti, 2020[12]	Early economic model, VOI and headroom analysis	Robotic exoskeletons to prevent falls that can result in hip fractures	High-risk patients with dementia or with CVD	- Varied leasing costs of intervention (£3,000, £4,000, £5,000, and £6,000): Leasing at £6,000 was only likely to be cost-effective in younger patients (65–74 years) - Varied purchase costs of intervention (£12,500, £15,000, £17,500, and £20,000): Purchasing at any cost was unlikely to be cost-effective	Yes
Pharmacotherapies	Angelis, 2020[6]	MCDA	Hypothetical product profile was assessed against three compounds under development	Patients with NASH in fibrosis stages F2–F3	Not reported	Not reported
	Landry, 2022[19]	Early economic model and headroom analysis	Hypothetical regenerative therapy for hearing loss	Patients aged over 50 years with age-related hearing loss	Not reported	Likely to be cost-effective
	Mandavia, 2020[20]	Early economic model and headroom analysis	Novel hearing therapeutics	Patients with unilateral idiopathic sudden sensorineural hearing loss	Not reported	Likely to be cost-effective
	Vreman, 2019[15]	Early economic model	BTK inhibitor acalabrutinib	Patients with relapsed chronic lymphocytic leukaemia	Not reported	No
	Willems, 2020[16]	Early economic model and headroom analysis	Hypothetical potential future treatment	Adults with moderate to severe hidradenitis suppurativa	10%, 30%, and 50% price premium of hypothetical treatment relative to SOC did not change conclusion except if dosage was reduced from weekly to Q4W	No
	Williams, 2022[17]	Early economic model and VOI analysis	Addition of tranexamic acid to usual care	Older adults experiencing mild traumatic brain injury in the pre-hospital setting prior to CT scanning	Not reported	Likely to be cost-effective
Prevention	Frempong, 2022[9]	Early economic model, VOI, and headroom analysis	Intervention to improve Prevention Programme uptake	Individuals identified as pre-diabetic through GP patient registers and NHS Health Checks in primary care	For each uptake level examined, VOI analysis was conducted for the maximum price estimated at that uptake level	Yes
	Malcolm, 2022[21]	Early economic model	Vision-based patient monitoring and management system	Older adults in mental health hospitals with dementia and adults on acute mental health wards	Not reported	Cost-saving
	Malcolm, 2022[11]	Early economic model	Vision-based patient monitoring and management	Patients in psychiatric intensive care units	Not reported	Cost-saving
Surgical techniques	Nherera, 2020[13]	Early economic model	Non-CT r-UKA	Patients undergoing UKA at high-volume orthopaedic centres	Not reported	Yes
Tests	Abel, 2019[5]	Early economic model and headroom analysis	Test-guided treatment for patients with COPD managed in primary care who are experiencing an exacerbation	Patients managed in primary care who are experiencing an exacerbation	Not reported	Yes
	Bajre, 2022[7]	Early economic model	Multiparametric magnetic resonance	Patients with autoimmune hepatitis in secondary care	Not reported	Cost-saving
	Gray, 2021[10]	Early economic model	Spectroscopic liquid biopsy for the detection of brain cancer	Suspected brain tumour patients with or without the availability of a triage blood test in primary or secondary care settings	Varied cost serum spectroscopy (£50, £75, £100, and £200): The intervention is not cost-effective at cost ≥£100	Yes
	Moloney, 2019[22]	Early economic model	PCR-based diagnostic testing strategy to identify CPE carriers upon admission to hospitals	Patients admitted to hospital who were considered to be at high risk of colonisation with CPE	Not reported	Cost-saving
	van Leeuwen, 2021[14]	Early economic model	AI software to aid the detection of intracranial large vessel occlusions in stroke in comparison to standard care	Patients who received computed tomography angiography in the diagnostic work-up of acute stroke	Varied prices for the AI tool per analysis ($0–$200) and % of reduction of missed diagnoses (0%–100%): Intervention was not cost-saving when cost was ≥$200 (assuming 50% reduction in missed diagnoses) or when cost was ≥$100 (assuming 20% reduction in missed diagnoses)	Yes
	Zakiyah, 2022[18]	Early economic model	Novel predictive blood test using metabolomic biomarkers	Healthy, first-time mothers with a singleton pregnancy	Not reported	Cost saving

Key: AI – artificial intelligence; BTK – Bruton tyrosine kinase; COPD – chronic obstructive pulmonary disease; CPE – carbapenemase-producing *Enterobacteriaceae*; CT – computerised tomography; CVD – cardiovascular disease; GP – general practitioner; HTA – health technology assessment; MCDA – multi-criteria decision analysis; NASH – non-alcoholic steatohepatitis; NHS – National Health Service; PCR – polymerase chain reaction; Q4W – every 4 weeks; r-UKA – robot-assisted unicompartmental knee arthroplasty; SOC – standard of care; VOI – value-of-information analysis.

Results (cont.)

Addressing uncertainty

- As early HTA utilizes an often-limited evidence base, comprehensive sensitivity analyses ought to be conducted to quantify uncertainties in the absence of solid clinical effect estimates and final pricing guidelines. The impact of uncertainties was assessed with deterministic or probabilistic sensitivity analysis in 13 early HTAs; in those studies, the efficacy of the experimental technology and/or the monetary cost were varied to test if the technology is over or under the willingness-to-pay threshold (**Table 1**).

Limitations of early HTA as reported in the literature

- Limitations reported in early HTAs included the following:
  - Models for hypothetical regenerative therapies for hearing loss assumed perfect effectiveness and perfect safety, and therefore the models are likely to overestimate the potential added value of the intervention.[19,20]
  - Including only direct costs in the model can lead to an underestimate of the costs that should be considered by decision-makers (indirect costs).[19]

Conclusions

- Early HTA in the UK healthcare setting encompasses a range of approaches to the economic evaluation of health technologies that are in early development. Our findings support the conclusions of other reviews published on the topic. Early economic modelling is still the most commonly used tool to inform manufacturers during times when investment decisions are made, and it seems that early HTA is difficult to implement on pharmacotherapies, mainly due to uncertainties related to the effectiveness of a therapy in early stages of development.
- Guidance on conducting early HTA is lacking, and consensus has yet to be reached regarding the most appropriate theoretical framework while robust early HTA methods are still in development.
- One limitation of the current research is that no Medical Subject Headings and well-defined keywords exist in the field of early HTA; therefore, our searches might not have identified all published literature in this topic.
- Finally, manufacturers of health technologies may be conducting early HTAs without publishing the results, particularly if the findings are not favourable to the experimental technology, which means that there is some risk of publication bias in our study.

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