Dealing with uncertainty in cost-effectiveness and affordability to inform risk-averse healthcare decision makers

Yunni Yi[1], Anne Meiwald[1], Alex Hirst[1]
[1]Adelphi Values PROVE, Bollington, United Kingdom

ADELPHI VALUES | PROVE Expertise in Access and Value Evidence Outcomes
SA45 ISPOR US 2023

Objectives

- Decision makers are increasingly concerned about both cost-effectiveness and affordability of new health technologies, resulting in the use of willingness to pay (WTP) cost-effectiveness thresholds (CET) and budget impact thresholds (BIT) as one of the criteria for healthcare decision making.[1-2]
- Cost-effectiveness and affordability are typically addressed separately using cost effective analysis (CEA) and budget impact analysis (BIA) respectively. This may produce conflicting conclusions as, although a CEA may show the incremental cost-effectiveness ratio for a new technology is below a CET, it may still be beyond the affordability of a payer.[3]
- Cost-effectiveness acceptability curves (CEAC) have been widely used to summarize uncertain CEA results. However, this method ignores the budgetary resources necessary to fund the technology and assumes risk neutral in valuing uncertain costs and effects.[4-5] Affordability curves (AC) have been used, though less often, to present the probability that an intervention is affordable at different budget levels.[4] However, this ignores whether the technology is deemed cost-effective and assumes an additional budget is available.
- Cost-effectiveness affordability curves (CEAFC) have been proposed to simultaneously consider both cost-effectiveness and affordability, combining CEA and BIA results graphically in a single curve and showing the joint probabilities of an intervention being both cost-effective and affordable at varying CETs and BITs.[4]
- Since 2021, cost-effectiveness risk-aversion curves (CERAC) have been proposed as an additional tool to inform decision making, by estimating the net benefit-to-risk ratio for a wide range of CETs and incorporating a common minimally acceptable net monetary benefit (NMB) as decision markers' preferences over uncertain costs and effects.[5]
- The objectives of this study were to critically review the recent applications of CEAFCs and CERACs in economic evaluations of healthcare technologies/programs and draw implications for future research.

Methods

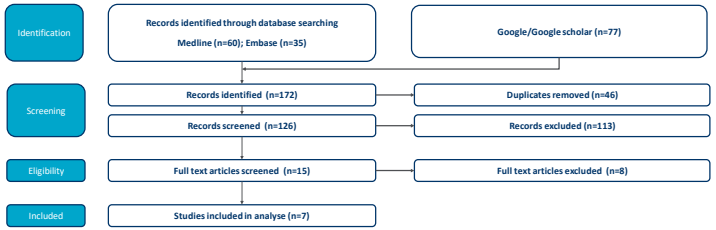
- A targeted literature review was performed to update a previous review on the use of CEAFC in 2017[6] and to review the use of CERAC since 2021.
- The search was conducted in OVID-catalogued databases (Embase and Medline) using predefined search terms, including "cost-effectiveness affordability curve" or "cost-effectiveness risk-aversion curve". A grey-literature search in Google/Google Scholar was also conducted.
  - The search was limited to English studies and covered 1st August 2017 to 10th April 2023.
  - Only economic evaluation studies reporting the use of ACs, CEAFCs and/or CERACs in addition to CEACs to evaluate health care technologies or programs were included.
- A reviewer determined the suitability of abstracts retrieved against the predefined inclusion and exclusion criteria. After initial screening, the full-text of included abstracts were appraised by two reviewers using the same inclusion and exclusion criteria.
- Once the full-text studies were identified, study information, methodology and author conclusions were extracted with use of CEAFC and CERAC were noted for analysis.

Results

Search results

- 126 abstracts were screened, with 113 and 8 studies excluded at abstract and full-text review stage, respectively. Seven studies were included for detailed review; all reported CEACs and ACs, six CEAFCs and two CERACs (**Table 1**).

Figure 1. PRISMA diagram for targeted literature review



Disease areas and interventions

- Four new therapy areas were included (breast cancer, HIV, dengue, and dentistry).
- A mixture of interventions were assessed: treatments (3), vaccinations (2), prevention programme (1), and diagnostic testing (1).

Perspective

- Five countries were reported with three new country settings (UK, Switzerland, The Netherlands) since the 2017 review.
- All studies used either a healthcare system or payer perspective.

Study and model types

- CEAFCs were used in either CEA alone (4) or combined CEA/BIA (3) while CERACs were only used in CEAs.
- Decision trees (4) and Markov models (2) were used and one study was trial based without a model.

Results (continued)

Analyses

- All identified studies reported results on the probability of cost-effectiveness based on CEACs and separately the results on the probability of affordability based on ACs.
- Six studies reported the joint probability of cost-effectiveness and affordability based on CEAFCs with only two studies including a CERAC to help inform risk-averse decision makers.

Results and conclusions

- Three studies found consistent results on cost effectiveness and affordability including one study found better benefit to risk of the intervention as an additional information.
- Four studies found some conflicts between cost-effectiveness, affordability and risk-adjusted benefit to risk of interventions.
- Authors stated that their aim of using ACs, CEACs and CERACs was to help facilitate more informed decisions for decision makers.

Conclusions

- The current review may not identify all relevant studies but it shows the use of CEAFC has recently extended from mainly for public health interventions in developing countries, as previously reported, to cancer and dentistry treatment in developed countries.
- Decision makers' risk attitudes toward uncertain costs and outcomes play an important role in coverage and reimbursement decisions of new technologies. The CERAC is a relatively new method in health economics literature to assist risk-averse decision makers. CERACs can be constructed using different approaches, each with strengths and weakness.[15] Further empirical studies are needed to identify the best approach.
- CEAC, CEAFC and CERAC can be jointly used in model based CEA alone, or combined CEA with BIM, and even trial based CEA without model to provide more comprehensive information required by risk-averse healthcare decision makers.
- Increased use of these methods in areas with potential conflicts between cost-effectiveness and affordability, such as gene therapies with a high one-off cost, rare disease treatments with very high costs for a small number of patients, or cancer treatments with high costs and large numbers of patients or even preventive interventions with a low cost but an enormous number of participants, may be useful to inform healthcare decision makers who are generally risk averse towards uncertain costs and/or health benefits.

Table 1. Economic analyses which used the CEAFC and CERAC method since August 2017

Reference	Country	Study type	Therapy area	Type of intervention	Perspective	Model type; Time horizon	Data used	Analysis	CEAC	AC	CEAFC	CERAC	Results/conclusions	Funding source
†Yi et al. 2019[7]	UK	CEA and BIA	Breast cancer	Treatment	Payer	Markov model; Lifetime	Data from published models	PSA using Monte Carlo simulation	Yes	Yes	Yes	NA	The intervention was not cost-effective at list price with 0% joint probability of being both cost-effective and affordable.	Claimed no conflict of interest
‡Huang et al. 2020[8]	China	CEA	HIV	Diagnostics testing	Health service providers	Decision Tree; NC	Test results, cost	One-way SA; PSA	Yes	Yes	NC	NA	The intervention was cost-effective at the WTP used and is affordable.	NC
Matthys et al. 2020[9]	The Netherlands	CEA	Dentistry	Treatment	Patient or healthcare insurance	Trial based, no model; 5 years	Health effect, cost	PSA using bootstrapping analysis	Yes	Yes	Yes	NA	The intervention had a high probability of being both cost effective and affordable.	Research collaboration with industry
Suwantika et al. 2020[10]	Indonesia	CEA and BIA	Dengue	Vaccination + intervention program/heath education	Health care (for BIA only) and payer	Decision tree; 10 years	Epidemiology, Vaccine efficacy, QALY loss, costs	Univariate SA; PSA using Monte Carlo simulation	Yes	Yes	Yes	NA	Vaccination +/- a Wolbachia program was the cost-effective but the additional budgetary requirement would be challenging.	Academia
Suwantika et al. 2021[11]	Indonesia	CEA and BIA	Dengue	Vaccination + screening	Health care and payer	Decision tree; 10 years	Vaccine coverage, efficacy, screening accuracy, costs	Univariate SA; PSA using Monte Carlo simulation	Yes	Yes	Yes	NA	Implementing dengue vaccination and pre-vaccination screening in Indonesia would be cost-effective but unaffordable.	Academia
Sendi et al. 2021[12-13]	Switzerland	CEA	Breast cancer	Treatment	Healthcare	Markov model; Lifetime	Data from a published model	PSA using Monte Carlo simulation	Yes	Yes	Yes	Yes	Without a budget constraints, the CEAFC corresponded to the CEAC; With budget constraints, the CEAFCs were lower than the CEAC; CERACs indicated preferences over interventions may change at varying WTP thresholds.	Academia
Victory et al. 2022[14]	UK	CEA	Dentistry	Prevention programme	Payer	Decision tree; 2 years	Health outcome, utility, cost	Univariate SA; PSA using Monte-Carlo simulation	Yes	Yes	Yes	Yes	The intervention was cost effective, cost-saving and provided better benefit to risk.	Independent research funded by NIHR

†Conference poster; ‡Abstract in English, full-text in Chinese; AC: Affordability curve; BIA, Budget impact analysis; CEA, Cost-effectiveness analysis; CEAC, Cost-effectiveness acceptability curve; CEAFC, Cost-effectiveness affordability curve; CERAC, Cost-effectiveness risk-aversion curve; NC, Not clear; NIHR, National Institute for Health Research; NA, Not applicable; NR, Not reported; PSA, Probabilistic sensitivity analysis; SA, Sensitivity analysis; WTP, willingness to pay.

References:
1. Lomas JRS. Incorporating affordability concerns within cost-effectiveness analysis for health technology assessment. VALUE HEALTH. 2019; 22(8):898–905; **2.** Flume M, Bardou M, Capri S, et al. Approaches to manage 'affordability' of high budget impact medicines in key EU countries, Journal of Market Access & Health Policy, 2018; 6:1, 1478539.; **3.** Bilinski A, Neumann P, Cohen J, Thorat T, McDaniel K, Salomon JA. When cost-effective interventions are unaffordable: Integrating cost-effectiveness and budget impact in priority setting for global health programs. PLoS Med. 2017;14(10):e1002397.; **4.** Sendi PP, Briggs AH. Affordability and cost-effectiveness: decision-making on the cost-effectiveness plane. Health Econ 2001;10:675-80.; **5.** Sendi P, Dealing with bad risk in cost-effectiveness analysis: The cost-effectiveness risk-aversion curve, PharmacoEconomics, 2021; 39:161-169; **6.** Yi Y, Luchenki S, Bellanca L, Heron L. Assessing the joint probability of cost-effectiveness and affordability in decision making. PRM123. Value in Health 2017; 20: A753.; **7.** Yi Y, Luchenki S. Use of cost-effectiveness affordability curves in evaluating cancer drugs in England. Value Health 2019, 22, S462. **8.** Huang SZ, Dai WC, Li XF, Jiang XH, Tang WM, Zhou Y, Cost-effectiveness of HIV self-testing strategy in men who have sex with men: Zhonghua Liu Xing Bing Xue Za Zhi. [Article in Chinese] 2020; 41(5):753-757.; **9.** Matthys C, De Vijlder W, Besselerj, Gilbert M, De Bruyn H, Cost-effectiveness analysis of two attachment systems for mandibular overdenture, Clin Oral Impl Res. 2020;31:615–624; **10.** Suwantika AA, Kautsar AP, Supadmi W, Zakiyah N, Abdullah R, Ali M, Postma MJ. Cost-Effectiveness of Dengue Vaccination in Indonesia: Considering Integrated Programs with Wolbachia-Infected Mosquitos and Health Education. Int J Environ Res Public Health. 2020;17(12):4217.; **11.** Suwantika AA, Supadmi W, Ali M, Abdulah R (2021) Cost-effectiveness and budget impact analyses of dengue vaccination in Indonesia. PLoS Negl Trop Dis 15(8): e0009664.; **12.** Sendi P, Matter-Walstra K and Schwenkglenks M. Handling uncertainty in cost-effectiveness analysis: Budget impact and risk aversion, Healthcare 2021, 9, 1419.; **13.** Sendi P, Matter-Walstra K, Schwenkglenks M. Spotting the Differences: The CEAC vs. CEAFC vs. CERAC. 2021. Preprints (www.preprints.org). DOI:10.20944/preprints202109.0055.v1; **14.** Victory E, Rhiannon ET, Girvan B, Pauline A, Cynthia PM. Cost-effectiveness Analysis of the Dental RECUR Pragmatic Randomised Controlled Trial: Evaluating a Goal-oriented Talking Intervention to Prevent Reoccurrence of Dental Caries in Children. Appl Health Econ Health Policy. 2022;20(3):431-445.; **15.** Elbasha EH, Cost-Effectiveness Risk-Aversion Curves: Comparison of Risk-Adjusted Performance Measures and Expected-Utility Approaches. PharmacoEconomics 2022; 40:497–507