ICER: SIMILARITIES AND DIFFERENCES BETWEEN UK (ENGLAND) AND USA COST-EFFECTIVENESS WATCHDOGS

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INTRODUCTION

As global healthcare budgets become increasingly strained, the role of cost-effectiveness (CE) bodies in providing timely guidance to healthcare decision makers is ever more important. The National Institute for Health and Care Excellence (NICE) was established 20 years ago with the mandate to reduce variation in the availability and quality of National Health System (NHS) treatments and care. The Institute for Clinical and Economic Review (ICER) was founded several years later, in 2006, as an independent organization that objectively evaluates the clinical and economic value of prescription drugs, medical tests, and other health care and health care delivery innovations. Today, NICE is one of the best-known CE health technology agencies (HTA) worldwide, and ICER's visibility has increased in recent years as drug pricing has become a national issue, resulting in ICER being widely known as the USA's independent advisor on drug pricing.

OBJECTIVES

Our research aims to evaluate the similarities and differences between the UK's NICE, and the USA's ICER by comparing both the NICE and ICER review process. Furthermore, to support the comparison, the assessment reports of 2 drugs that have been reviewed by both NICE and ICER were compared. The selected case studies included tisagenlecleucel for the treatment of B-cell acute lymphoblastic leukaemia (ALL), and lumacaftor/ivacaftor combination for the treatment of cystic fibrosis (CF).

METHODS

Our research aims to evaluate the similarities and differences between the UK's NICE, and the USA's ICER by comparing both the NICE and ICER review process. Furthermore, to support the comparison, the assessment reports of 2 drugs that have been reviewed by both NICE and ICER were compared. The selected case studies included tisagenlecleucel for the treatment of B-cell acute lymphoblastic leukaemia (ALL), and lumacaftor/ivacaftor combination for the treatment of cystic fibrosis (CF).

RESULTS

SIMILARITIES AND DIFFERENCES BETWEEN THE NICE & ICER REVIEW PROCESS

TOPIC SELECTION & PRIORITISATION

- Both bodies select topics based on input from independent advisory committees including the National Institute for Health Research Innovation Observatory for NICE, the California Technology Assessment Forum (CTAF) and the New England Comparative Effectiveness Public Advisory Council (CEPAC) for ICER. Furthermore, public recommendations from healthcare professionals, researchers, and patients are also considered when selecting topics. To be appraised by NICE, a product also needs to be referred by the Secretary of State for Health in England, a function of NICE's gatekeeper role to control NHS expenditure.

- Major drivers for topic prioritization include drugs expected to have a significant clinical benefit, financial impact, improvement in system outcomes/value, and high public relevance. Both NICE and ICER are committed to reviewing topics to allow timely guidance publication in anticipation of product launch, with NICE aiming to review topics before UK regulatory approval is granted, and ICER reviewing drugs which are likely to be approved by the FDA within 1 year. Unlike ICER, NICE automatically reviews all new cancer drugs, most likely due to their significant clinical and financial impact.

EVIDENCE REVIEW & METHODS

- Both NICE and ICER engage with clinical experts, patients, patient groups, manufacturers and payers to support the evidence review process. Furthermore, both demonstrate a commitment to limit reviews to publicly available, peer-reviewed literature wherever possible. ICER will consider grey literature, if the evidence base is rapidly evolving, and NICE will accept the use of confidential information, if the findings could have a significant impact on the commercial interests of the company, or for academic in confidence data.

- Both NICE and ICER ensure reviews are based on high quality and robust evidence by assessing the quality of the evidence, through NICE's independent evidence review group (ERG) and ICER's evidence rating matrix.

- Although randomized controlled trials are considered 'gold standard' evidence, both will consider indirect treatment comparisons and network meta-analysis where suitable, with ICER additionally leveraging patient group feedback to identify when real world evidence can be used.

- The predominant CE modelling method for NICE and ICER is cost utility analysis. NICE acknowledge that where an estimate of QALYs gained cannot be made, alternative methods such as life years gained, cases averted, or a disease specific outcome can be considered. Approaches including decision trees, markov cohort modelling, or simulation methods are used by both NICE and ICER to model CE, with the choice of method dependent on the drug's expected health outcomes. Both NICE and ICER conduct sensitivity analyses of CE models and show a preference for probabilistic sensitivity analysis for estimating uncertainty. Productivity costs and costs borne by patients and carers that are not reimbursed by the NHS or social services are not normally included in NICE analyses, which contrasts with ICER, where productivity losses, caregiver burden, and other indirect costs are considered in analyses.

REVIEW TIMELINES & CE / BI THRESHOLDS

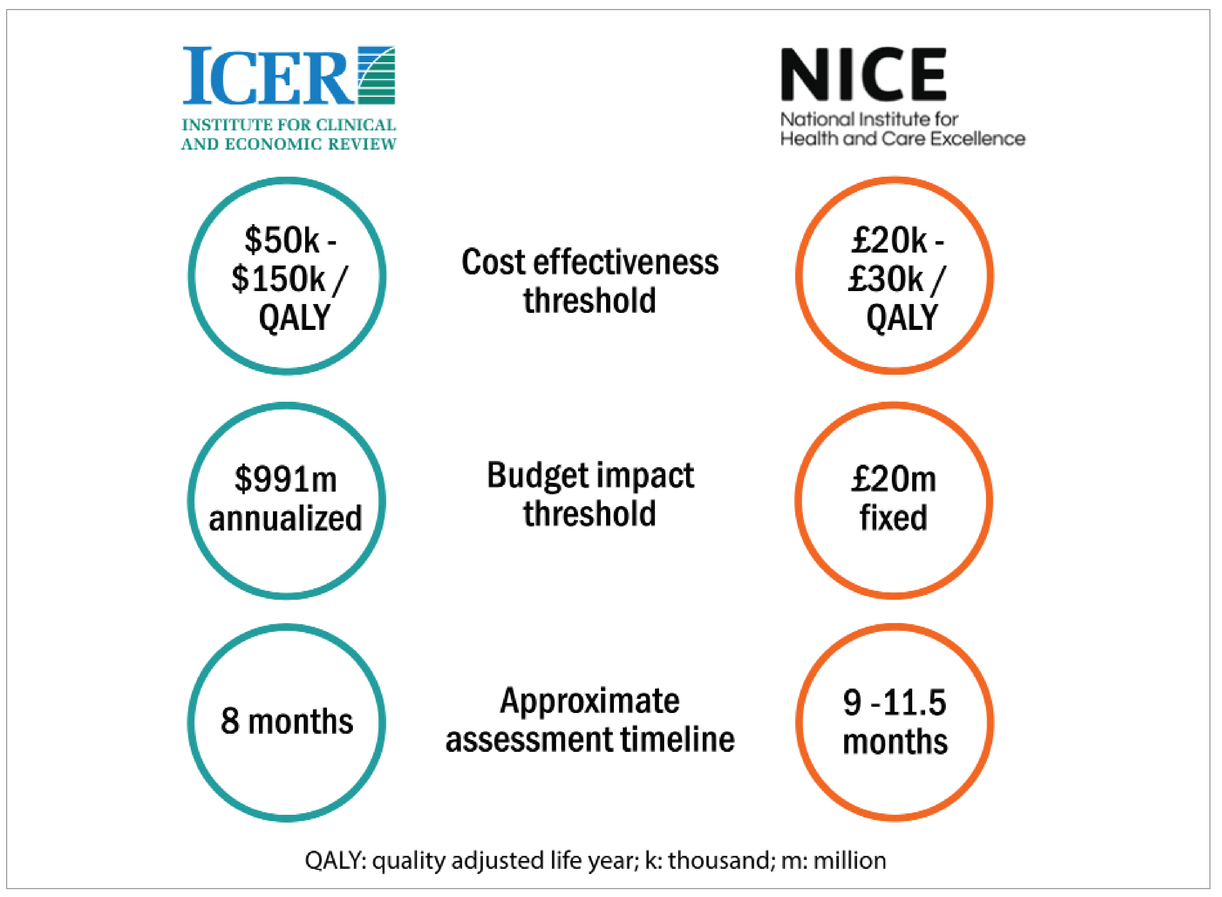
- NICE and ICER review timelines are broadly similar, with a time period of ~ 9 – 11.5 months from topic selection to final appraisal determination or appraisal consultation document respectively for NICE, and ~ 8 months from topic selection to final evidence report publication for ICER (Figure 1).

- The cost-effectiveness (CE) threshold for NICE is £20k-£30k/QALY and $50k-$150k/QALY for ICER. ICER, also assess a drug's value against a value-based price benchmark, reflecting the prices that would be needed to achieve ICER's thresholds of $100k-$150k/QALY. Whilst there is limited clarity on how NICE derived its CE threshold, ICER's is based on World Health Organization (WHO) guidance, which indicates a range of 1-3 times the per capita GDP of the country, per additional QALY.

- Both NICE and ICER relax the CE threshold for rare disease drugs, to accommodate the challenges of generating high quality evidence in smaller patient populations, and the likely higher unmet need for these difficult to treat patient populations. Under NICE's highly specialized technology appraisal route, the maximum limit of the CE threshold increases from £20k-£30k/QALY to £100k/QALY, and NICE will also consider analysis that explores a QALY weighting that is different from the reference case. The maximum limit of ICER's CE threshold increases from $150k /QALY to $500k/QALY, although the value-based price benchmark remains the same at $150k/QALY. ICER are currently requesting stakeholder input on the CE thresholds for both common and rare diseases for the ICER 2020 value assessment framework, therefore it is possible that these thresholds may change with the finalization of the updated value framework. NICE also relaxes the CE threshold to £50,000 for drugs which meet end of life criteria. The end of life criteria specifically focuses on treatments that are indicated for patients with a short life expectancy, normally less than 24 months, and where there is sufficient evidence to indicate that the treatment can offer an extension to life, normally a mean value of at least an additional 3 months compared with a current NHS treatment.

- Both NICE and ICER evaluate net budget impact. NICE's fixed budget impact threshold is set at £20M, and if a drugs budget impact exceeds £20M in any of the first 3 years, NHS England may engage in commercial discussions with the manufacturer to mitigate the impact that funding the drug would have on the rest of the NHS. ICER's variable 5-year annualized budget impact threshold is currently set at $991M, and is calculated over a 5-year timeframe in order to account for clinical benefits and cost offsets provided by new treatments. ICER's budget impact threshold is linked to the growth in the overall US economy, and if a new treatment's estimated budget impact exceeds the 5-year annualized threshold, this is a signal to stakeholders and policymakers that the amount of added healthcare costs associated with this new treatment may be difficult for the health system to absorb over the short term without displacing other needed services, or contributing to rapid growth in insurance costs that threaten sustainable access to high-value care for patients.

FIGURE 1: COMPARISON OF COST EFFECTIVENESS THRESHOLDS, BUDGET IMPACT THRESHOLDS, AND ESTIMATED ASSESSMENT TIMELINES FOR ICER & NICE



QALY: quality adjusted life year; k: thousand; m: million

FIGURE 2: CASE STUDY COMPARISON OF THE EVIDENCE REVIEW, COST-EFFECTIVENESS

TOPIC	NICE / ICER SIMILARITY	COMMENTARY
	TISAGENLECLEUCEL (ACUTE LYMPHOBLASTIC LEUKEMIA)	
EVIDENCE REVIEW	Aligned	•**Both** ICER and NICE **reviewed pooled data** from **3 single-arm trials**, and noted the lack of comparative data, short median follow-up, and small patient numbers, resulted in an uncertain clinical benefit
COST-EFFECTIVENESS MODELLING	Mixed	•The **nature** of the **economic models** reviewed by NICE and ICER were **similar** (partitioned survival model with decision tree element) •Economic **comparators differed** for NICE (blinatumomab and salvage chemotherapy) and ICER (clofarabine), given the **differences** in **clinical practice** in the UK and USA •**ICER** considered **productivity losses** in the economic scenario analysis, whereas NICE did not •The **cure point range** was **different** by economic body, with NICE estimating between 3 and 5 years, and ICER between 5 and 7 years
CONCLUSIONS & RECOMMENDATIONS	Divergent	• Whilst **ICER** concluded that tisagenlecleucel **met** the established **CE threshold of < $150k / QALY**, **NICE** concluded that the most plausible ICER **exceeded the CE threshold of £30k / QALY** •Tisagenlecleucel was **recommended** for funding through the **cancer drugs fund** by NICE, with **additional evidence generation requirements** (OS data) to enable identification of the assets **curative nature** •**ICER** noted **additional policy implications** for manufacturers, insurers, and providers including the need for early stakeholder dialogue, innovative payment models, and additional evidence generation
	LUMACAFTOR / IVACAFTOR (CYSTIC FIBROSIS)	
EVIDENCE REVIEW	Aligned	• **Both** ICER and NICE **reviewed** data from **3 randomized controlled trials**, and **1 long-term open-label extension study**
COST-EFFECTIVENESS MODELLING	Mixed	•The **nature** of the **economic models** reviewed by NICE and ICER were **similar** (microsimulation model over a lifetime time horizon) •**ICER** considered **productivity losses** in the economic scenario analysis, and **other benefits** and **contextual considerations** including reduction in caregiver burden, novelty of mechanism of action, impact on patient productivity, disease severity and illness burden
CONCLUSIONS & RECOMMENDATIONS	Mixed	•**Both** ICER and NICE **concluded** that lumacaftor / ivacaftor **did not meet** the **established CE thresholds**, with **ICER** additionally noting a **discount of 71%-75%** from the annual WAC price would be **required** to meet the **$100k / QALY - $150k / QALY** threshold •**ICER** noted **additional policy implications** for manufacturers, payers, patient organizations, and professional societies including the need for the manufacturer to engage in **responsible pricing** approaches, and payers to adopt approaches to **moderate** the impact of **monopolistic pricing**

RECOMMENDATIONS / CONCLUSIONS

- NICE conclusions primarily focus on funding implications, with 1 of 5 funding outcomes possible (recommended, optimized, recommended for use within the cancer drugs fund, only recommended in research, and not recommended). Furthermore, whilst ICER publish discounts required to meet CE thresholds, such information remains confidential in NICE appraisals. By contrast, ICER conclusions focus on the application of findings to policy and practice, including recommended actions for participating stakeholders, including patients, clinicians and researchers, purchasers and insurers, and manufacturers.

CONCLUSION

- Whilst the frameworks, modelling methods, and evidence supporting the CE evaluation demonstrate similarities across both bodies, key differences exist in the financial thresholds, the consideration of patient and caregiver productivity losses within the economic model, the framing of conclusions, and the transparency of required actions to meet CE thresholds, which can be explained by ICER's independent consultative role, and NICE's public funding gatekeeper role.

- As the role of CE becomes ever more important globally in supporting market access and affordability decision making, manufacturers would benefit from understanding how CE bodies differ in their evidence requirements and approach, and the impact that this may have on a manufacturers evidence generation and stakeholder engagement strategy. Furthermore, whilst NICE's scientific advice services can support manufacturers in the development of high-quality evidence generation plans, ICER does not currently offer such a service, although ICER has recently discussed the option of providing a service similar to NICE's scientific advice service.

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