An Unresolved Paradox: The Additional Challenge of Demonstrating Cost-Effectiveness for Innovative Treatments Addressing Diseases With High Unmet Need

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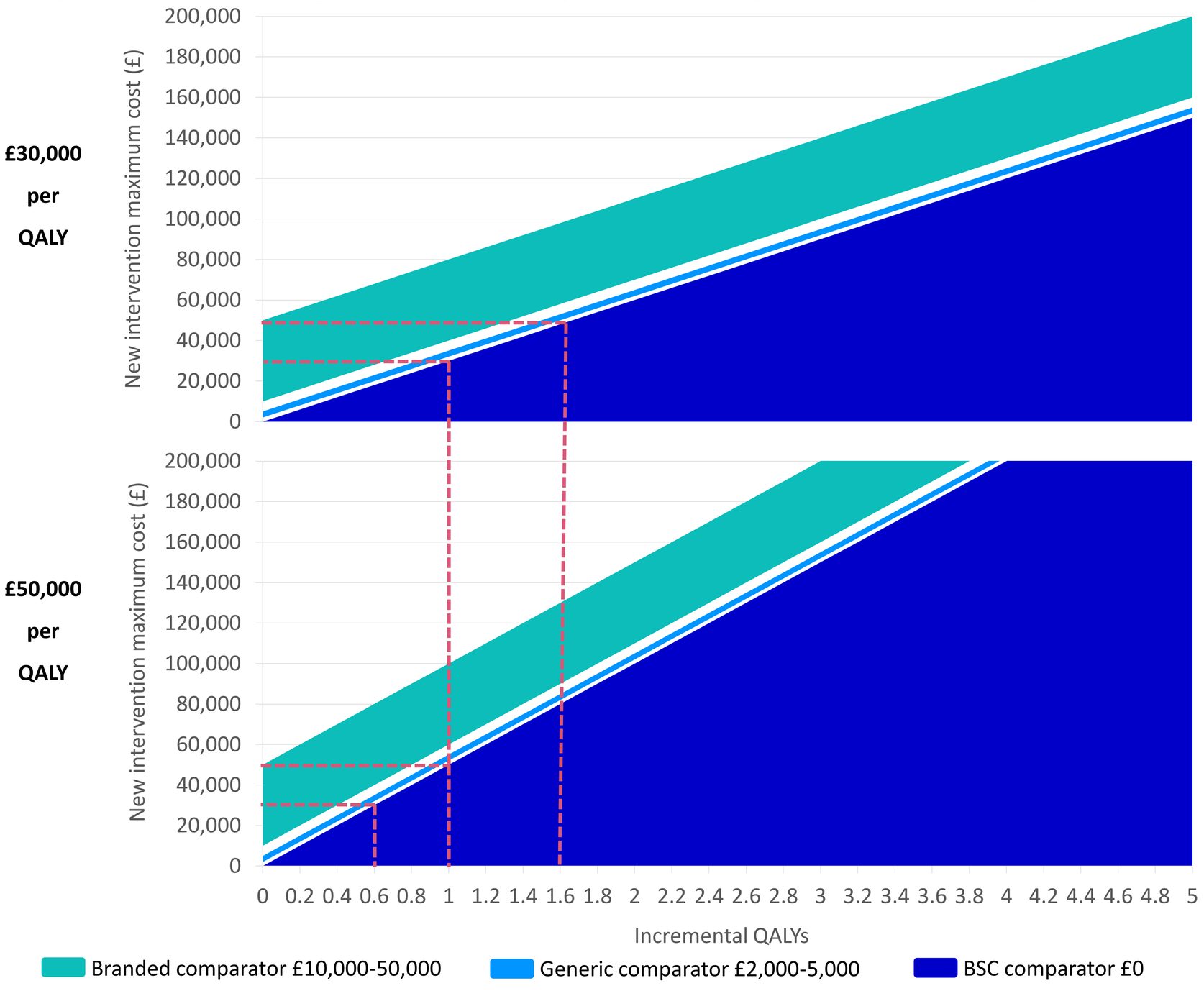
Objectives

NICE evaluates whether a new technology is cost-effective versus an appropriate comparator to make NHS funding decisions. They define an appropriate comparator as "established practice," which may include branded, generic and biosimilar medicines [1] or best supportive care (BSC), representing non-pharmacological therapy.

The research presented builds on a previously described paradox, [2] that it can be harder to make a cost-effectiveness case for innovative treatments in a disease with high unmet need and limited to no treatment advancements, given low-cost comparators and lower baseline quality-adjusted life-years (QALYs).

Figure 1: Maximum price ranges of new intervention by incremental QALY gain at £30,000 and £50,000 per QALY thresholds



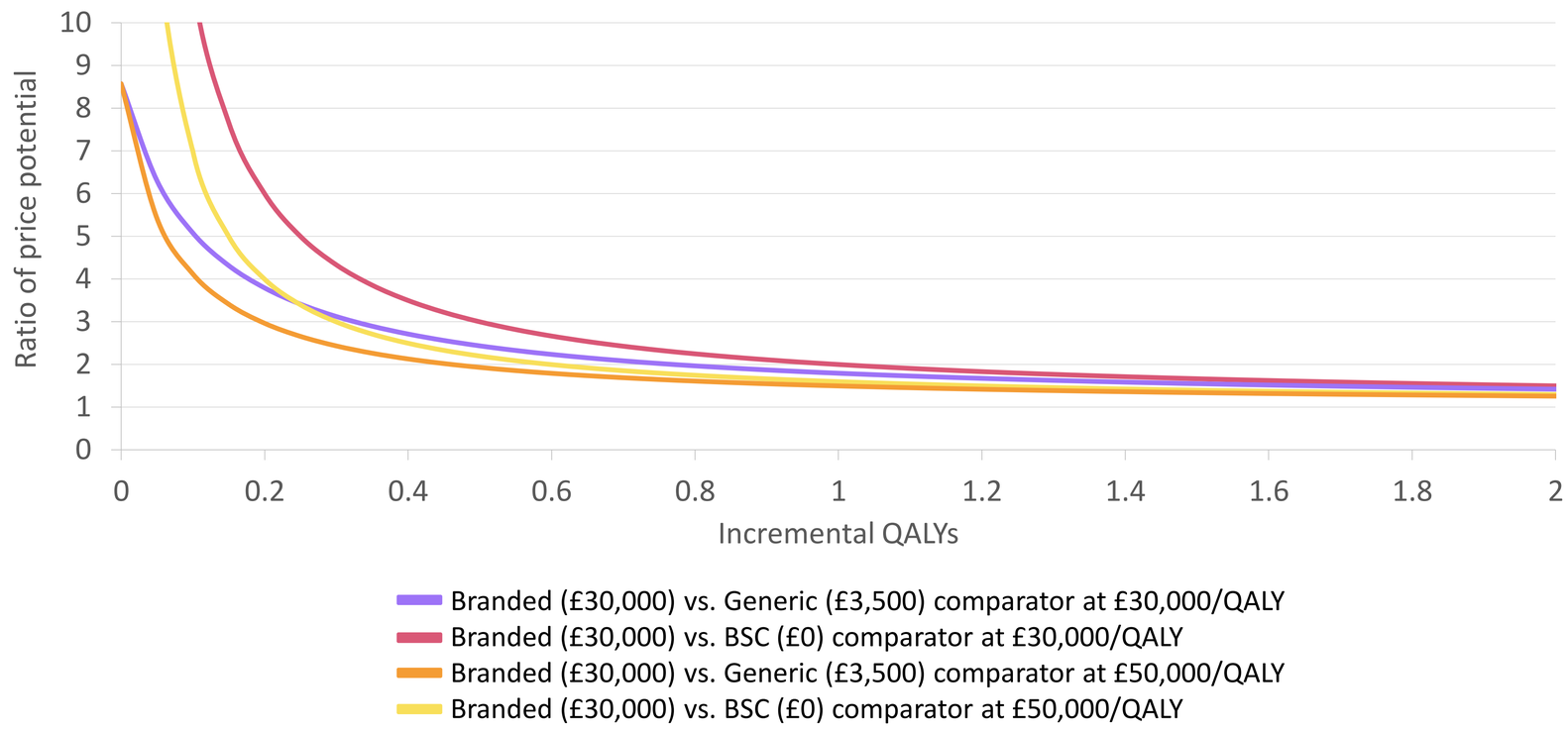
Methods

Hypothetical examples are explored, based on the mathematical relationship between key inputs in the incremental cost-effectiveness ratio (ICER) equation, to understand the additional costs that can be justified for a new intervention versus a branded, generic/biosimilar medicine or BSC. Indicative costs per annum are considered: £10,000 – £50,000, £2,000 – £5,000 and £0 respectively (mid-point base-case), and the impact of varying QALY gains (0–2, 0.2 increments) and ICER thresholds (£30,000 and £50,000).

Results

For a new intervention offering 1 QALY gain, the justifiable costs comparing to a branded medicine versus a generic/BSC (at £30,000/QALY) are 1.8/2.0-fold higher (Figure 2). Perversely, this differential further increases with reduced QALY gains, which may represent diseases with limited innovation. For example, a 0.4 QALY gain (which could represent a doubling in survival where baseline survival is low), there is a 3.5-fold differential for a branded vs BSC comparator (Figure 2).

Figure 2: Ratio of price potential with branded comparator vs. generic or BSC comparator



The differentials between comparisons reduce as the threshold increases to £50,000/QALY.

As an alternative example (Figure 1 – red), a new intervention offering no QALY gain entering an established market of branded comparators could charge an equivalent price (for example £30,000-£50,000). However, if a new highly innovative product entered an unestablished market (likely to have patient with a higher unmet need with poor outcomes and no active comparator) versus BSC they would need to provide 1.0-1.6 additional QALYs to reach an equivalent price but only 0.6-1.0 additional QALY at a £50,000/QALY.

Conclusion

Comparators have a marked impact on additional costs justified within cost-effectiveness analysis. This paradox may have perverse impacts on investment decisions and access to novel treatments for diseases with limited innovation, especially where there are low baseline QALYs.

To reduce inequity NICE should consider additional analysis comparing interventions with a common baseline comparator to highlight potential biases. Increasing the QALY threshold could also help to mitigate this paradox.

Reference

1. NICE health technology evaluations: the manual (2022) https://www.nice.org.uk/process/pmg36/resources/nice-health-technology-evaluations-the-manual-pdf-72286779244741
2. Sacristán JA, Abellán-Perpiñán JM, Dilla T, Soto J, Oliva J. Some reflections on the use of inappropriate comparators in CEA. Cost Eff Resour Alloc. 2020 Aug 27;18:29. doi: 10.1186/s12962-020-00226-8. PMID: 32874138; PMCID: PMC7457280.