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CURRENT OPINION

Re-anchoring the Value of Innovative Therapies in NICE Decision Making When Comparators are Cost Ineffective: A Case Study of Late-Onset Pompe Disease

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Abstract

National Institute for Health and Care Excellence (NICE) technology appraisal processes assume that the standard of care (SoC) is itself cost effective. However, many treatments in use in the UK National Health Service (NHS), particularly in rare diseases, were historically commissioned without formal value assessment and are priced without reference to cost-effectiveness thresholds. Cost-ineffective comparators distort how value is ascribed to new technologies, undermining the coherence of NICE's decision-making framework, and imposing substantial opportunity costs on the NHS. Using late-onset Pompe disease (LOPD) as an exemplar, we demonstrate the implications of a cost-ineffective comparator in assessments of innovative therapies. A clinically superior enzyme replacement therapy (ERT) may command a lower value-based price than current ERTs, whilst a hypothetical curative gene therapy is valued at over £4 million against current ERT, but just £629,392 when re-anchored against best supportive care. Here, value is driven by displacement of costs rather than health gain, raising affordability concerns that may limit access to genuine innovation. The 2025 NHS 10-Year Plan grants new NICE statutory powers to withdraw access to cost-ineffective therapies, presenting an opportunity to reform technology appraisal. We propose several policy responses, including comprehensive reassessment of active guidance with decisions made with respect to a standard cost-effectiveness frontier, reviews triggered by new comparators, and use of flexible decision rules within existing frameworks. These changes could allow the evolving value of medicines to be reflected in NHS practice, redefining NICE as a body that takes a dynamic, whole-lifecycle view of value. Deliberative public and stakeholder engagement is essential for success, given the potential consequences for manufacturers and patients.

1 Introduction

Since its formation in 1999, the National Institute for Health and Care Excellence (NICE) has provided evidence-based guidance on health and social care. Through its technology appraisal processes, NICE makes recommendations on new health technologies, acting as both de facto price negotiator and gatekeeper to the National Health Service (NHS). NICE's health technology assessment (HTA) framework systematically links NHS funding to cost-effectiveness analysis (CEA), anchoring decisions to transparent measures of value. New technologies must demonstrate both clinical efficacy and cost effectiveness, ensuring they do not reduce overall population health, given the finite healthcare budget. This embeds a utilitarian logic of resource allocation into decision making, ensuring that only technologies demonstrating clinical value without imposing undue opportunity costs are funded.

Central to NICE's Single Technology Appraisal (STA) process is the principle of incremental evaluation, whereby the value of a new technology is measured relative to the established NHS standard of care (SoC). This approach inherently assumes that the baseline SoC is itself cost effective, tracing back through a chain of prior evaluations to a theoretical 'do nothing' approach. In this way, each generation of treatment iteratively generates net health benefits (NHB) versus not only the existing SoC but also all previous treatments. This means that treating a patient is objectively the correct decision from a healthcare-system perspective. This system breaks down, however, when a profoundly cost-ineffective SoC is used as a reference point. In such cases, this approach generates misleading estimates of cost-effectiveness, distorting incentives for innovation and perpetuating inefficient spending decisions.

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Key Points for Decision Makers

Historical commissioning decisions made outside of conventional value assessment frameworks have allowed highly cost-ineffective technologies to become established in NHS practice. When the standard of care (SoC) is highly cost ineffective in health technology assessment, the valuation of new, innovative therapies can be distorted, undermining the principles of NICE's decision-making processes.

Using late-onset Pompe disease (LOPD) as a case study, we show that a curative gene therapy could be valued at over £4 million per patient when compared against the current enzyme replacement therapy (ERT). However, when 're-anchored' against best supportive care, its maximum economically justifiable price is as low as £629,392, illustrating that value is primarily driven by displacing the unjustified costs of SoC rather than by health gains.

Assessment of new technologies against a cost-ineffective SoC creates perverse incentives, risks limiting patient access to genuinely innovative healthcare technologies due to affordability concerns and perpetuates inequities in resource allocation.

Policy responses empowered by NICE's new statutory powers could allow NICE to dynamically withdraw access to cost-ineffective options from practice, reorientating HTA around a whole-lifecycle view of value and allowing fair assessment of innovative technologies.

The challenges of assessing value in the context of a cost-ineffective SoC are particularly pronounced in rare diseases, as NICE largely avoided HTA in this area until the introduction of the Highly Specialised Technologies (HST) programme in 2013 [1]. Even then, a formal cost-effectiveness test was not incorporated into the decision-making framework until 2017 [2], at which point the toleration of substantial opportunity costs to realise benefits in rare diseases was codified, with a standard threshold of £100,000 per QALY gained. Until this point, many technologies were commissioned at or near their list price on an ad-hoc basis, often driven by political pressure to address high unmet need rather than through structured evaluation of efficacy and cost. While these precedents have provided immediate support for patients, they also allowed technologies to become established in the healthcare system at prices far exceeding conventional cost-effectiveness thresholds and have become the basis for future comparisons.

A legacy of these decisions continues to affect decision making in rare diseases to this day. A pertinent example is the direct commissioning of enzyme replacement therapies (ERT) for lysosomal storage disorders (LSDs) such as Fabry disease, Pompe disease, and some types of mucopolysaccharidosis. Here we present a case study of late-onset Pompe disease (LOPD), where we explore the implications of assessments against a cost-ineffective, historically commissioned SoC in two recent NICE appraisals [3, 4]. With several gene therapies in development in this area [5–10], we examine the challenges NICE will soon face in evaluating potentially curative health technologies in this context. We consider both the methodological issues of value assessment and the normative considerations around fairness and the broader equity of NHS resource allocation and propose potential policy mechanisms to address these issues.

2 Appraising Innovative Technologies for Late-Onset Pompe Disease—Modelling Case Study

2.1 Background

LOPD is a progressive genetic neuromuscular disorder caused by partial deficiency of the enzyme acid α-glucosidase (GAA), responsible for breaking down glycogen within lysosomes [11, 12]. This reduced enzymatic activity leads to glycogen accumulation and cellular damage, primarily affecting skeletal and respiratory muscles. Typically manifesting in adolescence or adulthood [13], patients experience progressive weakness, initially in the lower limbs and trunk, leading to impaired walking and an increasing reliance on mobility aids. Respiratory insufficiency may also necessitate ventilatory support, such as use of a bilevel-positive airway pressure machine. LOPD is a debilitating condition with significant lifelong morbidity and mortality consequences [14, 15].

In the UK, the SoC treatment for LOPD has long been alglucosidase alfa, an ERT [16]. ERT involves regular intravenous infusions of recombinant GAA enzyme to reduce glycogen accumulation, improving muscle function, respiratory capacity, and overall quality of life. Alglucosidase alfa has been available through the NHS since 2006, following its commissioning as part of the Lysosomal Storage Disorders Service, providing funding through specialist UK centres [17–20]. Alglucosidase alfa has therefore never undergone formal assessment. Recently, two new ERTs, avalglucosidase alfa and cipaglucosidase alfa with miglustat have been recommended by NICE under the STA process [3, 4]. However, these recommendations were based on comparisons with alglucosidase alfa and did not include an evaluation against best supportive care (BSC).

2.2 Analysis

We adapted a published decision model to explore how comparator choice in LOPD affects value-based pricing of new technologies. This model was originally developed to compare current ERTs (cERT) against BSC. A discrete event simulation was used to link changes in 6-minute walk distance (6MWD) and forced vital capacity (FVC) % predicted over time to quality-adjusted life years (QALYs) and care costs related to mobility and ventilatory support needs. Modelling methodology is reported by Walton et al. [21].

The base analysis compares BSC, comprising supportive care only, with cERT, proxied using alglucosidase alfa, as the only product in use with a publicly available acquisition cost. All ERTs demonstrated similar effectiveness in a Bayesian network meta-analysis of the available clinical evidence, as reported by Corbett et al. [22], and an assumption of clinical equivalence had minimal impact on the cost-effectiveness results [21].

We extended this analysis to include two hypothetical innovative technologies: a next generation 'superior ERT' (sERT) and a one-off curative gene therapy. Our aim was not to predict the real-world cost effectiveness of any specific emerging technology, but to quantify the distortionary effect of making reimbursement decisions relative to cost-ineffective comparators. For each hypothetical technology, acquisition costs were varied until NHB-neutrality was achieved, that is, the point at which it generated neither net gain nor loss of QALYs, at decision thresholds of £30,000 and £100,000, reflecting the typical upper limits in the STA and HST programmes, respectively. Each analysis comprised 3000 probabilistic iterations, each run over 250 simulated patients for each intervention.

2.2.1 Base Analysis: Current Enzyme Replacement Therapies (cERT) Versus Best Supportive Care (BSC)

In the original model as reported by Walton et al. [21], cERT generated 1.62 additional lifetime QALYs relative to BSC at an incremental cost of £3,263,718. This translates to an incremental cost-effectiveness ratio (ICER) exceeding £2 million per QALY gained, far above any plausible threshold. As a result, cERT was associated with NHBs of − 107.2 QALYs at the NICE approval norm of £30,000 per QALY gained, and − 31.01 QALYs at the HST threshold of £100,000. Based on this analysis, cERT are highly cost-ineffective compared with BSC and likely generate a substantial net health loss for the general NHS population.

2.2.2 Superior Enzyme Replacement Therapy (sERT) Versus cERT

We next considered a hypothetical 'sERT' which substantially slows long-term disease progression relative to current care options, modelled as a 50% reduction in the long-term rate of decline in 6MWD and FVC%. sERT generated an additional 1.04 QALYs relative to cERT. Results assessing cost effectiveness versus cERT (which is in turn compared with BSC) are presented in Table 1 (Scenario 1).

If we assume sERT has an identical unit price to cERT (~£269,400 per year [21]), extended time on treatment (due to improved efficacy) attaches an incremental cost versus cERT of £163,446, producing an NHB of − 4.40 at a £30,000 threshold, and an ICER of £156,623 per QALY gained. To achieve NHB-neutrality relative to cERT, its maximum economically justifiable price would be £259,971 per year. In other words, despite offering superior clinical outcomes, sERT would command a lower value-based price than cERT (and may require discounts to be negotiated) because generating QALY benefits through prolonged survival or delayed progression is structurally cost ineffective, that is, the incremental drug costs during a longer treatment time outweigh the maximum possible value of the QALYs achievable in that same period.

2.2.3 Reframing Comparisons of ERT Against BSC

If instead, we assess the value of each technology incrementally relative to BSC, the maximum economically justifiable annual price for cERT would be £21,011 at a £30,000 threshold, and £29,636 at a £100,000 threshold. These prices represent respective discounts of 92.2 and 89% on the current list price of alglucosidase alfa.

In this analysis, the NHS would be willing to pay up to £30,438 per annum for sERT at a £30,000 per QALY threshold and £44,178 at a £100,000 threshold. When BSC is used as the reference comparator, sERT is valued more due to its greater effectiveness, justifying a higher price. However, the magnitude of the price reductions required to achieve cost effectiveness may render these products economically unviable for manufacturers to develop and produce.

This also illustrates that present pricing cannot be justified under any conventual valuation framework.

2.2.4 Valuing Curative Therapies for Late-Onset Pompe Disease (LOPD)

Finally, we assessed the potential value of a curative gene therapy for LOPD under alternative frameworks. The technology is administered as a one-off treatment at time zero with an upfront acquisition cost. For simplicity, we assume no administration costs and that all patients successfully

Table 1 Cure and superior ERT pricing analysis results

Int.	Total		Incremental		ICER	WTP £100,000		WTP £30,000	
	Costs	QALYs	Costs	QALYs		NHB	CE %	NHB	CE %
Scenario 1: Comparison of ERT with equally priced sERT (slows progression by 50%)									
BSC	£629,442	5.82							
cERT	£3,893,160	7.45	£3,263,718	1.62	£2,010,565	− 31.01	0.00%	− 107.2	0.00%
sERT	£4,056,606	8.49	£163,446	1.04	£156,623	− 0.59	0.00%	− 4.40	0.00%
Scenario 2: Cure list price £3,843,411 (Priced to £30k/QALY threshold vs cERT)									
BSC	£683,864	6.51							
cERT	£3,893,160	7.45	£3,263,718	1.63	£2,002,281	− 31.01	0.00%	− 107.2	0.00%
Cure	£3,980,160	10.35	£87,000	2.90	£30,000	2.03	0.00%	0.00	0.00%
Scenario 3: Cure list price £4,046,411 (Priced to £100k/QALY threshold vs cERT)									
BSC	£683,864	6.51							
cERT	£3,893,160	7.45	£3,263,718	1.63	£2,002,281	− 31.01	0.00%	− 107.2	0.00%
Cure	£4,183,160	10.35	£290,000	2.90	£100,000	0.00	0.00%	− 6.77	0.00%
Scenario 4: Cure list price £629,392 (Priced in fully incremental analysis at £30k/QALY threshold)									
BSC	£683,864	6.51							
Cure	£765,342	10.35	£135,900	4.53	£30,000	3.17	100%	0.00	53.00%
cERT	£3,893,160	7.45	£3,127,818	− 2.90	Dominated	− 34.18	0.00%	− 107.2	0.00%
Scenario 5: Cure list price £945,693 (Priced in fully incremental analysis at £100k/QALY threshold)									
BSC	£683,864	6.51							
Cure	£1,082,442	10.35	£453,000	4.53	£100,000	0.00	54.40%	− 10.57	0.00%
cERT	£3,893,160	7.45	£2,810,718	− 2.90	Dominated	− 31.01	0.00%	− 96.59	0.00%

BSC best supportive care, *CE %* probability of cost effectiveness, *cERT* current ERTs, *ERT* enzyme replacement therapy, *ICER* incremental cost-effectiveness ratio, *Int* intervention, *NHB* net health benefit, *QALY* quality-adjusted life year, *sERT* superior ERT, *WTP* willingness-to-pay

receive the treatment and its effects. It was assumed that the extent to which functional capacity is restored was equivalent to cERT at 12 months. All treated patients are assumed to maintain their peak level of function, achieved at 12 months, indefinitely.

When pricing is based on a pairwise comparison with cERT (see Table 1, BSC shown for reference), the value-based price at which a curative therapy could be justifiably recommended by NICE could be extremely high. At a £30,000 per QALY threshold, a cure would be NHB-neutral at a price of £3,843,411 (Table 1, Scenario 2). This increases to £4,046,411 when considering a £100,000 threshold, as applied in the HST programme (Table 1, Scenario 3).

To contextualise these prices, the most expensive gene therapy currently commissioned by the NHS is Libmeldy® [23], used to treat late-infantile or early-juvenile metachromatic leukodystrophy. Libmeldy has a list price of £2.85 million, though it is available at a discount NHS England describes as 'significant'. Assessment against cERT alone could therefore make a curative therapy in LOPD the most expensive health technology on the NHS.

In a fully incremental analysis including BSC, a curative therapy would need to be priced at £629,392 or less to be the most cost-effective option at a £30,000 per QALY threshold (Table 1, Scenario 4), or £945,693 at a £100,000 threshold (Table 1, Scenario 5). These values illustrate that the value of cure in LOPD is driven not by health benefits associated with cure, but by the substantial acquisition costs displaced through the avoidance of long-term cERT use.

Figure 1 compares these results against alternative cost-effectiveness frontiers applicable when BSC or cERT are used as the baseline comparator. The figure plots incremental costs and QALYs relative to BSC, showing that both cERT and sERT priced equivalent to cERT lie far above the true efficiency frontier, with ICERs exceeding £2,000,000 per QALY gained. Consequently, any technology priced to appear cost effective relative to cERT cannot be considered cost effective under conventional thresholds, and such comparisons produce misleading conclusions from an efficiency perspective. As described above, the acquisition cost of our hypothetical curative therapy must be below £629,392 for it to lie on or below the efficiency frontier and thus represent a cost-effective use of NHS resources at a £30,000 threshold.

3 Discussion

3.1 Implications for the Health System

Our analysis confirms the stark cost ineffectiveness of ERTs for LOPD at current prices, generating an estimated net health loss in excess of 100 QALYs per treated patient at a £30,000 per QALY threshold—an arguably generous benchmark of NHS marginal productivity [24, 25]. Even accounting for unmet need and the rarity of LOPD, it is difficult to justify this commissioning decision from a system-level perspective. Given the modest clinical benefits of ERT, this is less a trade-off between individual and population health than a transfer of NHS resources to manufacturers. The recent NICE appraisals of avalglucosidase alfa and cipaglucosidase alfa with miglustat have further extended the collection of substantial monopoly (duopoly) rents in this indication, ensuring that the economic benefits of the product lifecycle will continue to remain with manufacturers [26].

Our analyses illustrate how the use of a highly cost-ineffective SoC can distort the logic of the decision-making process. The negative NHB generated by sERT, relative to cERT, despite being more clinically effective than cERT but priced equally, is a clear illustration of how NICE's decision rules can break down under such conditions. This example highlights how a cost-ineffective comparator can reverse incentives, perversely rewarding less effective therapies. Taken to its logical extreme, this could imply that the NHS would fund interventions that harm patients if doing so generates sufficient cost savings, although such technologies would, of course, never receive marketing authorisation. Our results also show that despite placing a lower value on sERT, NICE's current decision-making framework would still result in the NHS overpaying for such a treatment, perpetuating the distortionary effect of previous commissioning decisions.

Moreover, the entrenched costs of ERT risk discouraging investment in genuinely innovative technologies. A curative gene therapy could appear cost effective at a price exceeding £4,000,000 per patient—not due to its intrinsic clinical value (i.e., health generation) but simply because it displaces vast lifelong treatment costs. This distorts how value should be ascribed to health technologies within NICE's decision-making framework and should not serve as a basis for decision making.

Unless cost effectiveness is re-anchored against BSC, the immediate budget impact of a recommended curative technology could exceed £1 billion for this small population. This may mean patients are denied access, as the NHS possesses few levers to contain such large costs beyond delaying implementation. With six gene therapies in development for LOPD, this poses an imminent challenge to NICE, who must also consider that manufacturers may deprioritise the UK

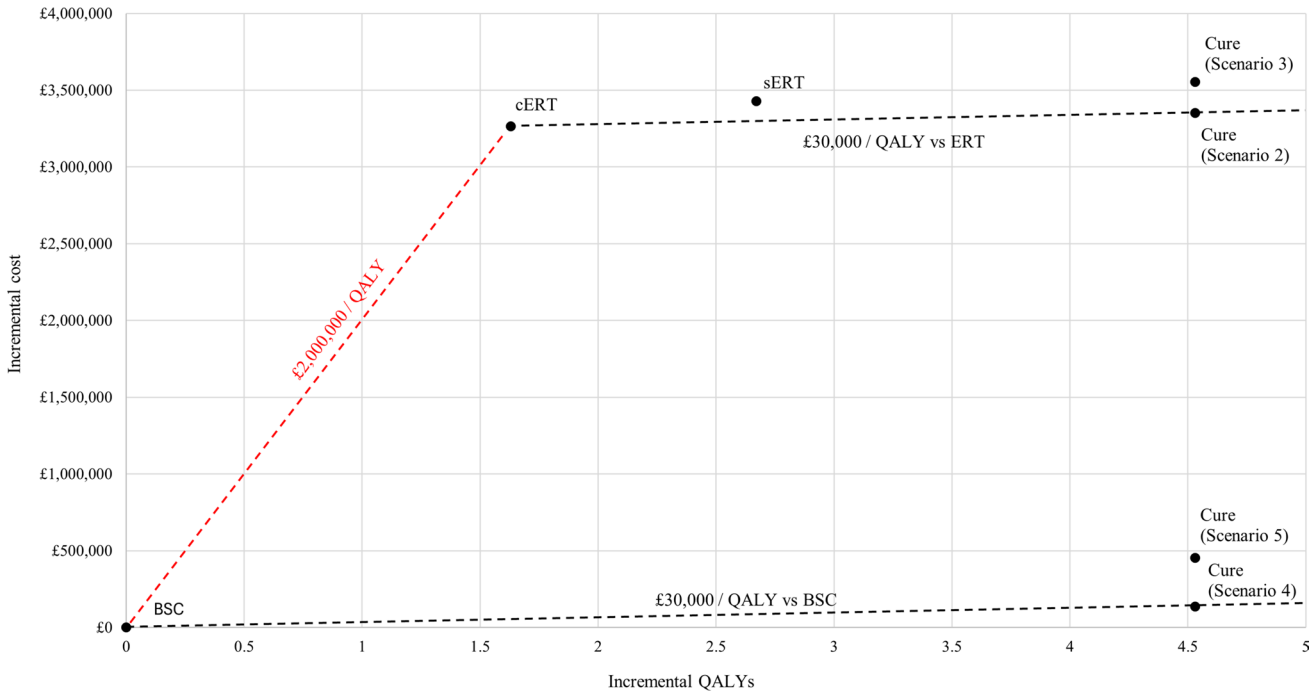

Fig. 1 Cost-effectiveness frontier: cERT vs BSC as baseline comparator. *BSC* best supportive care, *cERT* current enzyme replacement therapies, *QALY* quality-adjusted life year, *sERT* superior enzyme replacement therapy

market if list prices have a ceiling as low as £629,392 in a fully incremental value assessment.

A further concern is the perpetuation of stark spending inequities across arbitrarily selected conditions caused by historical precedent. This has allowed new expensive technologies to be approved that otherwise would struggle to demonstrate cost effectiveness. These areas thus continue to receive preferential treatment even where unmet need has been addressed. It is unfair that patients with comparable clinical needs are denied access to therapies held to stricter tests of cost effectiveness. For example, the highly effective olipudase alfa was not recommended for acid sphingomyelinase deficiency, as the manufacturer could not provide a sufficiently large discount in the context of cheap BSC [27].

This highlights the more fundamental question of whether limited NHS resources should be used to fund expensive, marginally effective therapies for small patient groups, or be allocated more equitably across the healthcare system. Special provisions have historically been made for rare diseases without reference to a robust value framework or—in the case of the HST programme—operating well beyond a grounding of marginal productivity. The prioritisation of rarity in resource allocation decisions has itself long been controversial and may lack public support [28].

While addressing the needs of patients with rare diseases is politically and socially sensitive, continued investment in high-cost, low-value technologies undermines NICE's goals of allocative efficiency and health equity. Without a mechanism for disinvestment or reassessment of cost-ineffective therapies, the wider NHS population will continue to bear the burden of these inefficiencies, compromising not only future innovation but also the fundamental fairness of resource allocation in a single-payer healthcare system.

3.2 Policy Measures—What Can Be Done?

The LOPD case study illustrates how NICE's HTA processes can break down when comparators are approved outside of a consistent value assessment framework, leading to suboptimal reimbursement decisions which may harm individual patients and the wider health system. This issue is not unique to LOPD. Historical commissioning decisions similarly affect conditions such as Fabry disease and the mucopolysaccharidoses amongst the LSDs alone. Recent examples in the NICE TA programme of value propositions based on the displacement of cost-ineffective SoC treatments include efanesoctocog alfa for haemophilia A [29], efgartigimod for generalised myasthenia gravis [29], and evinacumab for homozygous familial hypercholesterolaemia [30]. This issue therefore affects a broad range of conditions and must be addressed systematically by NICE.

The July 2025 NHS 10-Year Plan signals a major policy shift, granting NICE new statutory powers to withdraw access to cost-ineffective technologies in order to improve the efficiency of resource allocation [31]. While this removes a longstanding political barrier to disinvestment, substantial uncertainty remains regarding how these powers will be implemented. The proposed approach is described as 'retiring' recommendations through 'surveillance reviews'—a process which may in practice mean that only medicines towards the end of their life cycle are likely to be phased out. It is also unclear whether indications lacking an alternative, similarly effective treatment option for patients to switch to could be targeted. Ultimately, the scope and ambition of any new reassessment framework will determine its potential to improve the efficiency of spending on pharmaceuticals in the NHS.

We outline three alternative frameworks for operationalising NICE's new mandate. These approaches vary in terms of resource intensity, stakeholder acceptability, and the speed and scale at which they could reduce opportunity costs.

The most direct solution would involve a structured and systematic programme of reassessment across all NICE's recommendations, whereby all active technology appraisal guidance for a given condition is reviewed in a single analysis. This approach could enable the NHS to identify and disinvest from technologies which are no longer (or were never) cost effective. This might repurpose NICE's multiple technology appraisal (MTA) process to periodically re-evaluate all technologies within an indication in a comprehensive guideline and recommend reimbursement for one or more options based on contemporary incremental NHB, thereby disinvesting from technologies which lie above a consistent cost-effectiveness frontier. This shares similarities with the dynamic model of HTA proposed by Woods and colleagues [32], in which reassessments could be triggered by emerging clinical evidence or changing market conditions. This would allow the evolving value of individual medicines to be fully reflected in NICE guidance and NHS practice, redefining NICE's role as a body which takes a dynamic whole-lifecycle view of product value.

While most impactful, identifying cost-ineffective technologies would be resource intensive given the large volume of active NICE recommendations and the widespread use of unassessed health technologies used in clinical practice. This style of reassessment would also be substantially more expensive and complex than a standard appraisal. However, prioritising high opportunity cost topics could yield substantial long-term savings and may simplify future assessments as new technologies emerge and are added into existing guidance. Clarity will be required to determine whether restrictions would apply to patients currently receiving a technology or only to new prescribing. This would produce only a gradual tapering of spending on lifelong conditions as the treated population discontinues over time, which may dilute the benefits of disinvestment whilst creating inequities

between the incident and prevalent populations. There is also a risk that manufacturers may be discouraged from launching new technologies if companies are wary of the potential loss of market access for their established products. These challenges underscore the importance of deliberative public and stakeholder engagement in designing any future framework.

A more passive model would involve reassessing cost-ineffective technologies only when new alternatives are licenced. Emergent technologies would trigger an MTA, with decisions based on a fully incremental analysis of all available alternatives, allowing new innovation to be introduced whilst simultaneously phasing out cost-ineffective medicines. Whilst less resource-intensive, this approach could leave many cost-ineffective technologies such as ERTs in LOPD in place for many years. It would also continue to generate misleading value signals for prospective new market entrants and may similarly reduce incentives for manufacturers to bring forward new therapies if market access for existing products is at risk.

A third option, though one that does not necessarily make use of the new powers provided by the NHS 10-year plan, is for NICE to make use of its existing powers to adjust decision thresholds when comparators are demonstrably cost ineffective. The 2022 NICE methods guide explicitly permits committees to exercise discretion around choice of comparator in such circumstances. In these cases, new technologies could also be required to deliver substantial cost savings or recommend that the least costly, clinically effective option is used first. This would preserve some flexibility to reward innovation without an explicit disinvestment mandate and achieve meaningful cost savings for the NHS. However, this would not address financial barriers to the adoption of innovative therapies with high upfront costs. In practice, new technologies could be systematically rejected on economic grounds, leaving expensive SoCs in place. Additionally, it is unclear how thresholds and decision rules could be sensibly defined or theoretically grounded in opportunity cost in this context.

4 Conclusions

This analysis explores how legacy commissioning decisions can distort current HTA processes. Using LOPD as an exemplar, we demonstrate how comparisons with a highly cost-ineffective SoC undermine the conceptual foundation of incremental decision making, creating perverse incentive structures which only favour clinically superior alternatives if they are significantly cheaper than current options, while artificially inflating valuations of curative therapies. Such extreme value-based pricing risks limiting the adoption of genuinely transformative therapies in order to protect NHS budgets.

NICE's new powers to withdraw access to cost-ineffective technologies presents a timely opportunity to address these historical anomalies and improve the efficiency of NHS spending on pharmaceuticals. With the political barrier to disinvestment now removed, attention must shift to the design and implementation of reassessment mechanisms which maintain acceptability to stakeholders. It is important that these powers are used to their fullest extent if maximal benefits are to be realised.

Policy options range from comprehensive reassessment across all indications to a more structured approach to the application of Appraisal Committee discretion around selection of comparators and threshold adjustment to better reflect opportunity cost. Each approach presents trade-offs and will require carefully building stakeholder and public assent through a process of deliberative engagement. Only by re-anchoring future decision making to real-world cost effectiveness can NICE reassert a normative foundation for equitable and efficient resource allocation whilst preserving incentives for innovation.

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Declarations

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Availability of data and material All data contributing to this work were derived from a systematic review of published studies, which can be found in Corbett et al. [22]

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