A PROPOSAL FOR LIFECYCLE VALUE REASSESSMENT

Unlocking biologic therapy value through biosimilar-enabled access and repositioning

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September 2026

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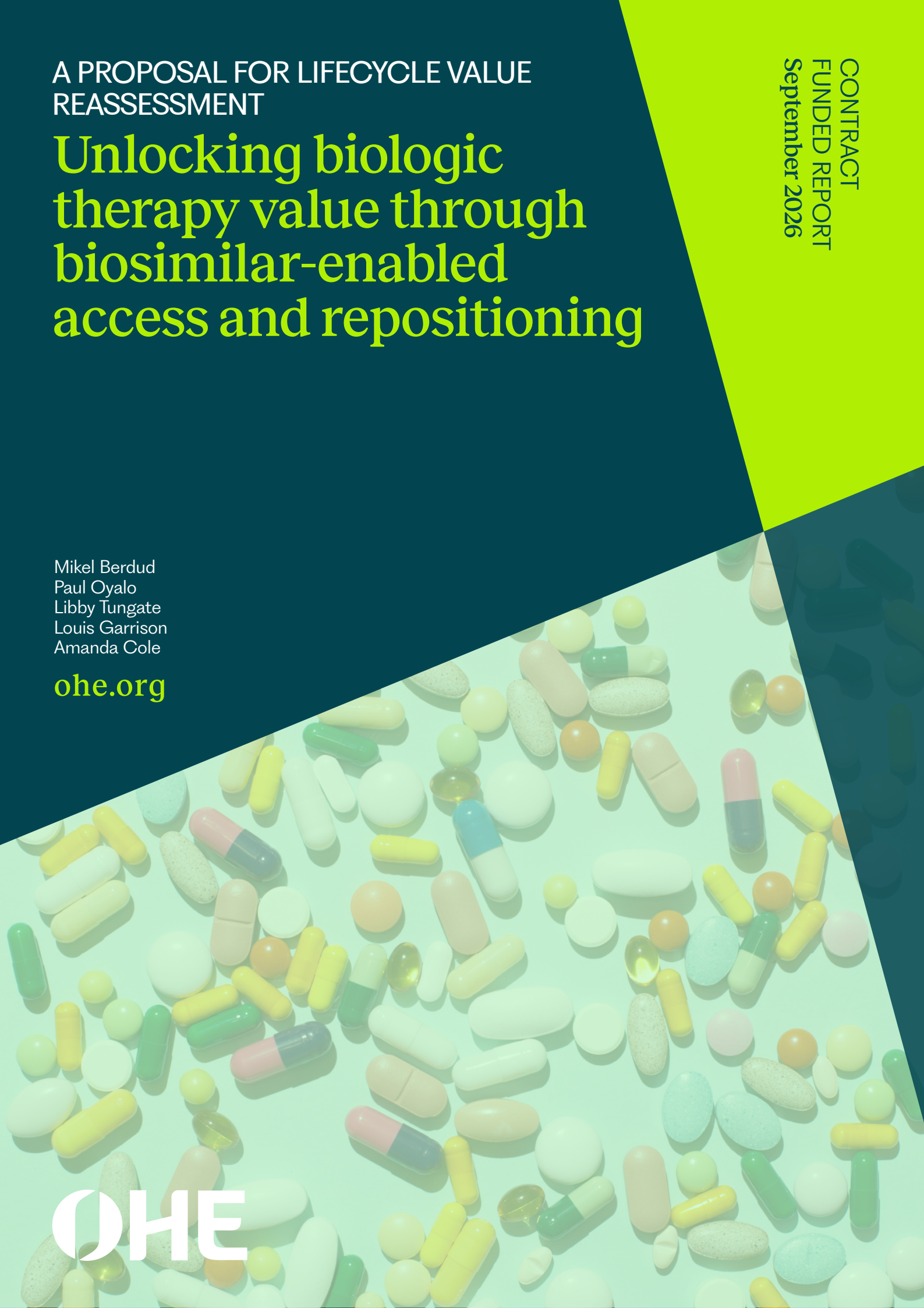

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Key messages

- Biosimilar-Enabled Access and Repositioning (BEAR) can unlock substantial value for patients, health systems and industry — yet it remains overlooked.
- Health systems worldwide already apply BEAR — but in isolation, and through divergent mechanisms.
- While opportunities for repositioning exist globally, mechanisms for unlocking those opportunities vary by system-type.
- BEAR adoption requires overcoming misaligned incentives, free-riding, and limited HTA capacity, while leveraging tailored stakeholder engagement and robust evidence generation, including RWE.
- In order to move from isolated examples into standard practice, it will be necessary to work towards: stakeholder alignment; education and early-dialogue; and robust evidence generation.

Executive summary

Biologic medicines account for over 40% of global pharmaceutical spend. When originator patents expire, biosimilar competition should drive prices down, generating cost-savings, broadening access, and improving outcomes, yet that promise remains largely unrealised. From the first US launch in 2015 up to 2025, biosimilars saved the US health system an estimated $56.2 billion in drug costs, but one analysis estimates that $124.5 billion in savings could be achieved: a $68 billion gap. Supply- and demand-side barriers as well as contracting structures produce low penetration, recurring shortage risk, and a growing 'biosimilar void'. The dominant policy response has been narrow, focusing on biosimilar value as a cost-saving opportunity in already-funded populations. This report argues that this framing misses a larger opportunity: biosimilar competition can also generate clinical benefits by enabling broader and potentially more clinically appropriate use of biologic therapies, for example by reducing economically driven restrictions on eligible populations or treatment positioning. The research thereby addresses an important gap in the prevailing narrative.

When biosimilar competition lowers the cost of a biologic, it can do more than reduce drug expenditures; it can change the therapy's cost-effectiveness profile, potentially bringing it within the acceptable range for populations, indications, and treatment lines previously considered too expensive to fund. This requires lifecycle reassessment and practice updating, revisiting earlier coverage and guideline decisions in light of the new lower price. This report terms that mechanism Biosimilar-Enabled Access and Repositioning (BEAR): a lifecycle perspective that treats cost-effectiveness as open to revision, distinct from and additional to the savings from price competition alone.

The analysis was conducted in three phases: a scoping review of the global literature identifying BEAR cases; in-depth examination of case studies; and a structured workshop with eight independent HTA, policy and academic experts across six countries. First, an analytical framework was developed, describing a recurring sequence from trigger to process to impact through five channels (see Figure 2): severity threshold broadened; treatment line advanced; expansion to new populations or indications; removal of administrative or formulary restrictions; and liberalised prescribing.

Across every BEAR case in the literature, biosimilar entry, and the price reduction it brings, was the enabler. Reassessment by the relevant decision-maker then expanded access, extended use to previously denied indications, advanced the therapy to an earlier line, or removed restrictions. Spanning 11 national health systems and diverse indications, these examples confirm BEAR is widely observed. Yet none acted systematically as every case was reactive or ad hoc. Nonetheless, seven selected cases (boxes 1—7, Appendix C) illustrate all five framework channels across five systems: NICE (England), PHARMAC (New Zealand), PBAC (Australia), TLV (Sweden) and CMS (US).

In-depth modelling of two cases demonstrates the quantitative value of BEAR. For denosumab in the US, modelling across three expanded osteoporosis populations we estimated 492,366 fractures prevented and $22.9 billion in fracture-related cost-offsets — nearly twice the $12.0 billion in drug cost-savings available from only substituting existing patients onto cheaper biosimilars. The post-BEAR ICER of $100,921/QALY sits within the US willingness-to-pay range of $100,000—$150,000/QALY. In total (incorporating the cost offsets as well as the cost of treatment expansion), the BEAR approach would generate ~$10.5Bn in net monetary benefit (NMB) to the health system, calculated at the $150,000/QALY threshold (the upper end of an ICER's WTP range).

In England, bevacizumab had been declined for mCRC three times on cost-effectiveness grounds, largely because of the originator's acquisition price, until NICE reassessed it under its whole lifecycle approach. Biosimilar-driven price erosion brought the therapy

within NICE's £30,000/QALY threshold, opening access to roughly 7,000 previously ineligible patients, with the negotiated net-price discount cutting the ICER to an estimated £20,378/QALY. This delivered a health gain of 2,170 QALYs to mCRC patients, and £20.8 million of NMB over and above the £132 million that biosimilar competition alone saved across bevacizumab's four already-recommended indications. The NMB achieved through BEAR for mCRC alone over three years is equal to 15% of the savings from the other four indications over six years.

How BEAR can be unlocked depends on the system. CEA-driven systems (England, Australia, Canada) are responsive to the ICER and NMB; budget-impact systems (Spain) focus on cost-savings but reward bottom-up engagement with regional HTA, pharmacy, and clinical stakeholders; clinical-value systems (Germany) require demand-side policy — quotas, rebate contracts, automatic substitution — rather than reassessment; and market-based systems (US) require engaging a fragmented set of payers, societies, and guideline developers. NICE's whole lifecycle approach is the closest to systematic, underpinning the England examples; elsewhere opportunities are flagged reactively. CEA-driven systems are best positioned since reassessment may in some cases require no more than revisiting a prior appraisal at the new biosimilar price.

The workshop identified three recurring challenges to systematic BEAR adoption. First, complexity and misaligned incentives complicate the case for reassessment: negotiations often struggle to reconcile the scale of access expansion with fiscal acceptability, free riding discourages investment in supporting evidence, and, in some systems, intermediary incentives can work against expanded access. Second, data and evidence gaps persist because biosimilar regulators and manufacturers typically rely on equivalence data alone, generating no additional evidence to support expanded populations or indications. Third, institutional and systemic constraints vary by country but consistently slow progress. Limited HTA capacity constrains reassessment in Australia, Canada and the UK, while Germany's founding principles restrict the use of economic arguments. Institutional rigidity and a narrow focus on cost-savings limit ambition in Spain and Australia, and fragmentation across decentralised systems, such as Spain's regional structure, further complicates coordinated action.

The workshop's recommendations can be grouped under four themes. They address the key gaps identified across the evidence and are set out by theme in the table below.

HTA, GUIDELINES, PAYERS & REGULATORY ALIGNMENT	Encourage cross-stakeholder collaboration and joint consultations to reduce fragmentation
	Publish studies surfacing misalignment between clinical guidelines and payer policies
	Adopt formal policies for routine post-LoE reassessment of biologic therapies
	Leverage bottom-up approaches in decentralised systems (e.g. Spain, Germany, US)
	Create regulatory incentives to reward evidence generation
EVIDENCE GENERATION	Invest proactively in RWE and novel data (modelling, simulation, Bayesian methods) to support reassessment
	Ensure evidence consistency across sub-national actors in decentralised systems
	Support public-sector incentives to address the free-rider problem in evidence investment
STAKEHOLDER EDUCATION	Raise awareness of BEAR's value among key stakeholders with messaging tailored to system type
	Upskill stakeholders — particularly patient and clinical groups — to engage effectively with formal HTA processes
EARLY DIALOGUE	Embed structured early dialogue between manufacturers, regulators, HTA bodies, and payers on evidence requirements
	Develop proactive horizon scanning and routine lifecycle assessment commitments at post-LoE stage

This report establishes BEAR as a generalisable mechanism, quantifying examples of value generation that goes beyond price-competition savings alone, and identifies the structural reasons this value goes unrealised, alongside recommendations to address them. We recommend that biosimilar entry should trigger a structured review of whether the new price justifies expanded access to new populations, indications and earlier treatment lines. This is timely as a wave of major biologics are approaching loss of exclusivity. Routine reassessment could also address the wider biosimilar market failure: by rewarding the fuller value biosimilars unlock, it could strengthen the commercial case for development and help close the low-penetration and 'biosimilar void' gaps that persist globally, provided incentives and implementation are aligned across health systems.

Biosimilar competition is routinely used only to lower prices. This report shows it can also be a recurring enabler of expanded access, generating value that is comparable to, and in some cases exceeding, procurement savings. That value is real and measurable but not automatic. Embedding systematic lifecycle assessment and BEAR into how health systems manage biologics post-LoE suggests both an immediate opportunity and a need for lasting reform.

1 Introduction

Are biosimilars delivering on their promise?

Biologic medicines are increasingly used: In 2023, they represented over 40% of total pharmaceutical spend globally, in Europe, and in the US (IQVIA, 2024; Muñoz, 2020) — around a 10 percentage-point increase since 2018 (Arnum, 2024). Biosimilars are highly similar versions of their reference biologic counterparts, with no clinically meaningful differences in safety, purity, or potency. Once originator biologics lose exclusivity after patent expiry, they face biosimilar competition, expected to drive prices down toward efficient competitive levels. Biosimilars are therefore expected to generate substantial value globally to systems and patients, while they create headroom for innovation.

Biosimilars were first approved and sold in Europe in 2006, contrasting with the US, where the long-delayed regulatory pathways deferred the first biosimilar approval to 2015 (Scott Morton, Stern and Stern, 2018; Mestre-Ferrandiz, Towse and Berdud, 2016). Since then, significant cost-savings have been reported in both markets. In only 10 years, biosimilars are estimated to have saved the US health system $56.2 billion (AAM, 2025), while realised list-price savings in Europe in just five years between 2016 and 2021 reached €50 billion (Maksabedian Hernandez et al., 2022).

The intuitive expectation — shared by health economists, policymakers and payers alike — is straightforward: given biologics' large share of pharmaceutical expenditure and their high price, biosimilar competition should generate material cost-savings, broaden access, and improve health outcomes. Yet this potential remains largely unrealised. Biosimilar markets are highly variable, often characterised by a limited number of competitors and low, inconsistent uptake relative to the reference product (Car et al., 2023; Böhm, Steiner and Stargardt, 2023; Mulcahy et al., 2022; Carl et al., 2022). Full biosimilar value is therefore not realised; in the US for example, one study estimated drug cost-savings of $38.4 billion between 2021 and 2025 — yet projected that these could reach $124.5 billion under a scenario of increased utilisation and more robust price competition (Mulcahy et al., 2022).

Understanding this gap requires examining the fundamental nature of these products. Unlike small-molecule generics, biosimilars are not identical to their reference biologics. Their development, approval and manufacturing are considerably more complex, creating substantial supply- (e.g., large cost of entry, first-mover advantage) and demand-side barriers (e.g., brand loyalty, prescriber inertia) to entry. These barriers and their competitive effects remain poorly understood by regulators and policymakers, producing policy approaches that leave markets inefficient, unsustainable, and consistently underperforming.

European payers have prioritised stringent cost-containment policies such as tendering, price-linkage, and internal reference pricing to drive down prices and realise savings (Machado et al., 2024). In the US, biosimilar markets are challenged by downstream contracting structures that create barriers to entry and limit competition. Pharmacy benefit managers (PBMs) play a central role: through exclusionary incentives and rebate traps — where originators pay rebates conditional on meeting market share thresholds — they effectively limit biosimilar entry (Arad et al., 2022; Morton and Boller, 2017; Mehr and Brook, 2017). Originator strategies compound the problem further: evergreening (filing patents on minor product modifications to extend exclusivity) delays biosimilar entry, while provider inertia entrenches first-mover advantage and suppresses switching (Mehr and Brook, 2017; Feldman, 2018). Across different policy contexts, unresolved market failures converge on the same outcome globally: low biosimilar penetration, heightened shortage risk as fragile markets deter sustained supply (Napier et al., 2024; Arad et al., 2022; Roth et al., 2025), and lost value for patients and health systems. Consequently, the biosimilar

industry faces diminished investment returns contributing to what has been termed the biosimilar void: a growing gap in which a substantial proportion of originators losing patent protection now and in the coming years have no biosimilar in development (12,13). That void is about entry, whereas the evidence in this report concerns the molecules where entry already happened and the lower price still fails to translate into wider access.

Addressing this requires looking beyond price competition alone (Dutta et al., 2020) — though significant opportunities remain simply from promoting biosimilar entry in originator-dominated markets. Policy discussion has so far centred on price reductions, cost savings and budget impact, paying far less attention to the clinical benefits of broader, more clinically appropriate use of biologics. Where biosimilar competition reduces therapy costs, substantial untapped value may remain in addressing biologic underutilisation: in reassessing prescribing practices, in exploring expanded indications, and in advancing treatment lines (Kvien et al., 2025a; Tam et al., 2025).

Realising this requires recognising that biologic value is dynamic, interdependent, and global. It is dynamic because value evolves across the product lifecycle, from approval through off-patent competition. It is interdependent because opportunities identified and realised in one setting — a new or expanded indication, for example — can be rapidly replicated elsewhere without new development. And it is global because the scale of uptake across settings shapes industry investment and development incentives, while biosimilar approvals for new indications or expanded populations create competitor free-riding risks and misaligned R&D incentives.

Yet current practice rarely reflects this complexity. Static, country-level assessments — typically conducted once at reference product launch — risk locking in decisions that leave significant value on the table and fail to capture opportunities as they emerge across the product lifecycle and across settings. What is missing is a global product lifecycle perspective. Sustainable biosimilar markets and optimal patient access depend on all markets contributing. Continuous local reassessment and repositioning as evidence, prices, and competition evolve represent a significant and largely unexplored dimension of biosimilar value — one that can further help support well-functioning global markets. The next section introduces biosimilar-enabled access and repositioning (BEAR) as the mechanism through which this value can be unlocked.

From one-time access decisions to a lifecycle approach for biologic therapies

Because biologic medicines are costly to manufacture and typically expensive relative to small molecules, their commercial success depends principally on access and uptake in high-income countries. However, the coverage and reimbursement decisions made when a biologic first launches are rarely reopened, even as its price falls. The value of biosimilars, which enter after originator patent expiry, is therefore seen narrowly — limited to cost-savings from price competition in the indications approved at the time of initial regulatory approval — with no reassessment when biosimilars offer a redefined value proposition.

Yet biosimilar price competition can do more than deliver cost-savings. By lowering the cost of biologic therapy, it can improve cost-effectiveness more broadly making these therapies worthwhile across expanded populations and indications — a benefit for both patients and health systems.

Reassessment of value in response to key events or changes in context (of which biosimilar or generic entry is a notable one) represents what has been termed in the literature as well as by leading HTA bodies and scientific societies such as NICE and ISPOR a “whole lifecycle” or “Living HTA” approach. NICE's whole lifecycle approach commits to continuous reassessment of medicines as evidence evolves and prices change, allowing

biosimilar entry to trigger re-evaluation of therapies previously deemed cost-ineffective and expand access accordingly (Storm12, 2026; people and NICE, 2026). This is illustrated by two cases: biosimilar natalizumab prompting expanded NHS eligibility in highly active relapsing-remitting multiple sclerosis (NICE, 2026c), and biosimilar bevacizumab enabling a positive recommendation for metastatic colorectal cancer (NICE, 2026f) — a previously unrecommended indication. Similarly, ISPOR's Living HTA framework reconceptualises HTA as a systematic, ongoing process, continuously incorporating new evidence and real-world data to update recommendations when warranted (ISPOR, 2026; Sarri et al., 2026).

These remain isolated examples though (Kvien et al., 2025a; Tam et al., 2025). No shared framework guides when, how, or by whom reassessment should be triggered, and incentives across payers, clinicians, guideline developers, and HTA bodies remain poorly aligned. The global conversation is also uneven — low- and middle-income countries are largely absent, despite standing to benefit most. The sections that follow draw together an assessment framework, set out the evidence base assembled through real case studies, and translate both into actionable recommendations that align stakeholders and unlock the full value that lifecycle reassessment and repositioning can deliver.

2 Methods

How we built the evidence

The project was organised in three phases: the scoping, evidencing, and translating phases. Across all phases, a project steering committee (SC) of external experts validated methods and reviewed interim outputs. The SC comprised eight independent experts from HTA bodies, policy and academia, representing the United States, the United Kingdom, Australia, Canada, Spain, and Germany. The committee reviewed scoping and evidencing phase methods and outputs through two formal SC meetings. These allowed experts to input on methodologies and analyses, flag additional literature and data sources, and provide updated country-specific policy context. During the translation phase, the committee participated in a workshop to reflect on findings and develop policy-relevant, actionable recommendations.

Scoping

We began by searching and mapping the global evidence base for cases where biosimilar entry led to a change in the therapeutic positioning of a biologic medicine, reflected in an HTA decision, reimbursement policy, clinical guideline, or payer policy change. This was undertaken through a targeted review of scientific and policy literature. Searches for scientific literature covered PubMed, the Cochrane Library, and Google Scholar databases using a block-based Boolean strategy built from four concept groups: biologics and biosimilars; HTA, guideline, and payer decision contexts; language around repositioning and treatment pathway changes; and generics. Policy literature searches covered HTA and reimbursement decision repositories and individual agency websites including NICE, CADTH, IQWiG, HAS, PBAC, and AIFA. We supplemented these searches with sources recommended by the SC.

The review included papers that documented cases in which biosimilar entry led to changes in the therapeutic positioning and that quantified or discussed the impact of such changes on patient outcomes, cost-savings, or system-level effects. Where evidence for biologics was sparse, analogous examples from small-molecule generics were obtained. The review covered publications from 2015 onwards, the year the FDA approved the first US biosimilar. While Europe approved its first biosimilar in 2006, OHE researchers expected most documented experiences of BEAR to fall within the last decade. Data extraction covered the product involved, therapeutic area, type of policy or guideline change, jurisdiction, and reported impacts.

The initial search identified 36 papers, with a further 27 added through targeted follow-up searches and SC recommendations. After screening, 25 met the inclusion criteria, of which 23 were included for data extraction and reviewed in full. The remaining 2 described no specific case study example and were retained only for conceptual framing.

Drawing on the evidence from the literature, we developed an analytical framework (presented in Figure 2 in the next section) that sets out how BEAR proceeds from trigger to impact through different impact channels, which we then used to characterise our case studies.

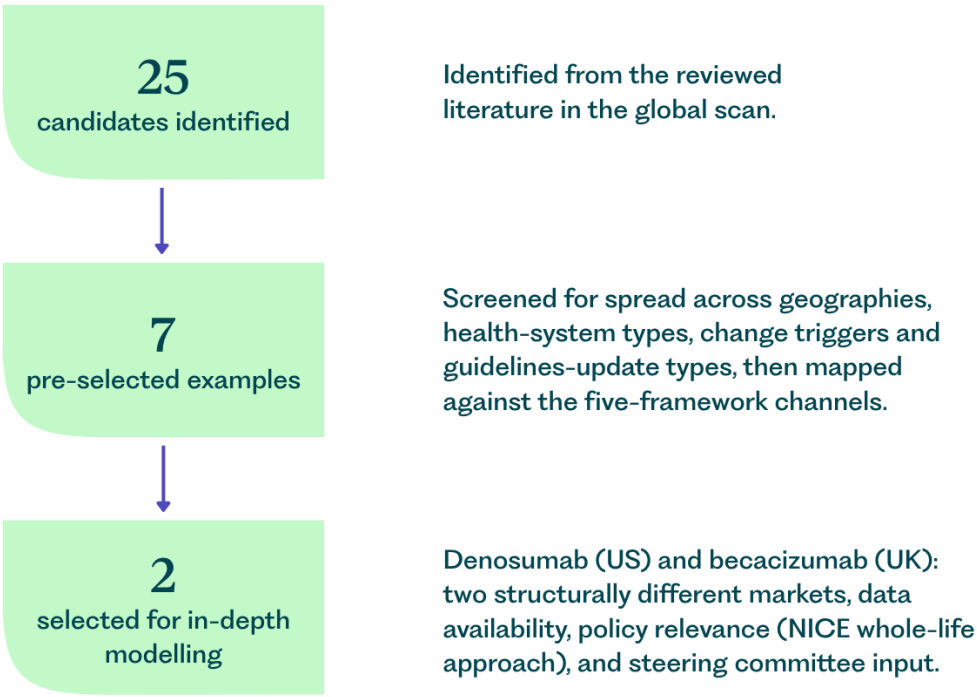
Evidencing

We extracted 25 global case-study candidates from the reviewed literature. These were narrowed to seven pre-selected examples spanning different geographies, health system types, change and repositioning triggers, and guideline update approaches. We mapped

the seven pre-selected examples against the five channels of the analytical framework to confirm that the set captured the range of BEAR mechanisms identified in the literature.

Two of the seven pre-selected cases were then selected for in-depth modelling: denosumab in the United States and bevacizumab in England. The selection was guided by the need to cover two major yet structurally distinct country contexts, data availability, relevance to current policy developments, and input from the second SC meeting. A summary of the selection process is presented in Figure 1 below. A table detailing all identified studies is available in Appendix C.

Figure 1 Case study selection



For the denosumab case study in the US, we modelled adoption of biosimilar denosumab versus oral alendronate across three osteoporosis populations — postmenopausal women (WOP), men (MOP), and glucocorticoid-induced osteoporosis (GIOP) — over a lifetime horizon with annual cycles. Three scenarios were specified: a conservative scenario reflecting current low-uptake trajectories; a base case with gradual adoption peaking at 85% by year six; and an upper-bound scenario assuming immediate and complete switching. For bevacizumab, we modelled the addition of a biosimilar to fluoropyrimidine-based chemotherapy for adults with metastatic colorectal cancer (mCRC) in England, over five years, building on a published Markov model (Tappenden et al., 2007).

Outcomes were reported in several forms so that results would be interpretable by different audiences and system contexts: patients treated, health gains (e.g., QALYs, fractures prevented), cost-offsets from improved outcomes, incremental costs or savings, cost-effectiveness ratios, and net monetary benefit (NMB). Full model specifications, input parameters, and scenario assumptions are available in Appendix A, Table A3.

Translating

The third phase tested the evidence against implementation realities. A structured workshop brought together the SC experts, representing different country, policy, and

health system contexts to examine what it would take for lifecycle BEAR approaches to move from isolated examples to routine practice. We prepared a set of pre-workshop materials and asked SC experts to read them in advance of the workshop. Materials included summaries of findings from previous project phases, clarification of scope and objectives for each workshop discussion, and prompt questions to support discussion.

The workshop covered three main discussions: a final validation and review of project findings; opportunities, barriers and enablers for implementing lifecycle therapy assessments and BEAR; and actionable recommendations for implementation.

3 Results

Impact of lifecycle BEAR approaches

This section presents the evidence generated on the impact of lifecycle BEAR approaches. It examines whether lifecycle assessment and BEAR-based optimisation of biologic therapies deliver value beyond the price reductions and cost-savings associated with biosimilar competition alone. The analysis considers how lower biosimilar acquisition costs can trigger HTA reassessment (e.g., lifecycle assessment) and subsequent changes in guidelines and access policies, leading to expanded access and additional value for patients, health systems, payers, and industry (e.g., BEAR). The evidence is based on two complementary components: a targeted review of published literature on lifecycle assessment and BEAR implementation, and economic modelling of two illustrative case studies to quantify their value impact.

The section first introduces an analytical BEAR framework describing how biosimilar entry can enable reassessment and subsequent changes in clinical guidelines, treatment pathways, and access criteria. It then summarises the global evidence base and presents seven illustrative case studies drawn from different countries and health system settings. Finally, it reports results from the economic modelling of two case studies, quantifying the health and economic impacts of BEAR and drawing out common patterns across the evidence.

3.1 A framework for change

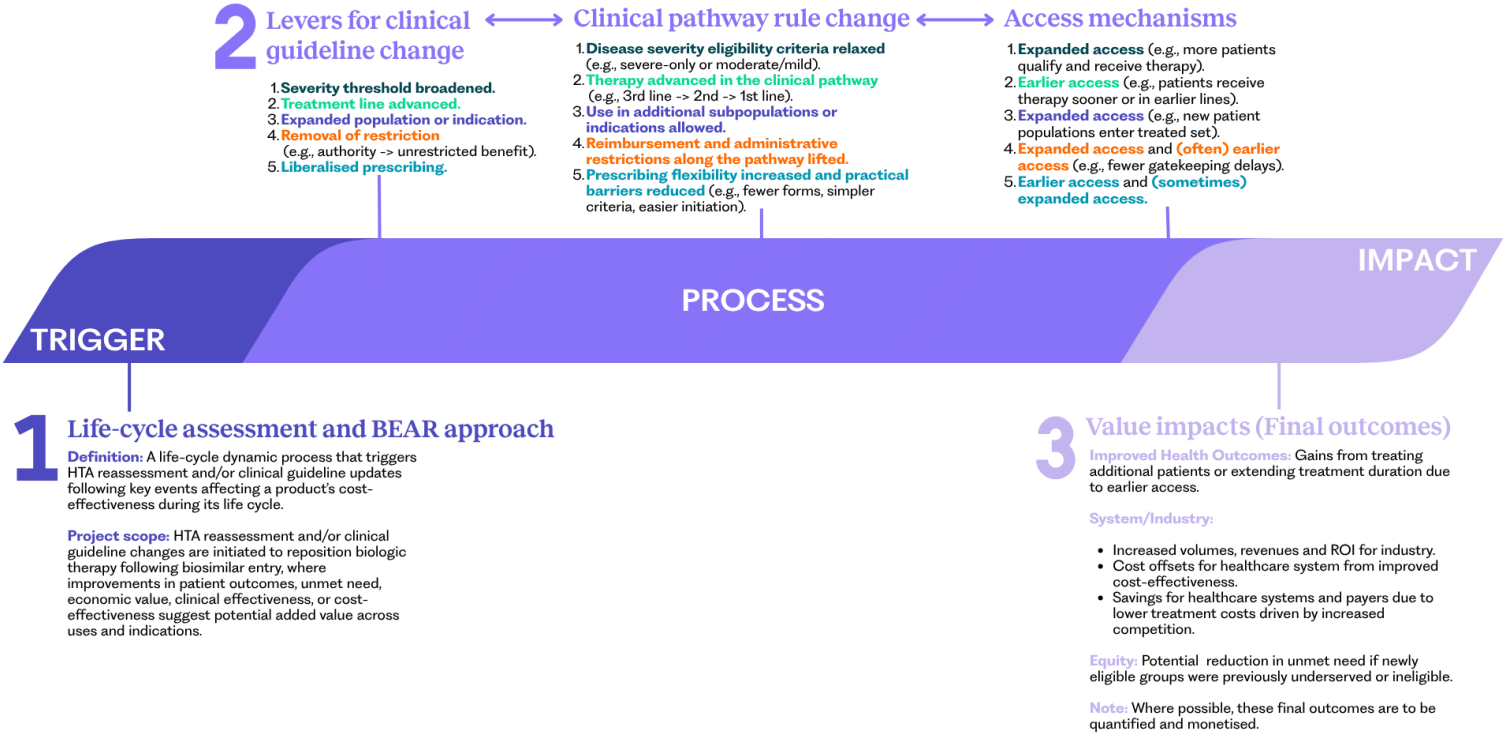
We stated in the introduction section that biosimilar value is dynamic, interdependent, and global, yet assessment practice in most health systems reflects none of these properties. Biologic therapies are typically evaluated once, at originator launch, and those decisions are rarely revisited as prices fall, biosimilar competition enters, and clinical evidence accumulates. Opportunities to expand access to previously restricted populations, to reposition therapies earlier in treatment pathways, or to address underutilisation in indications where biologic use remains low relative to clinical need often go unrecognised as a result.

Closing this gap requires a way of systematically identifying where BEAR opportunities exist, what evidence is needed to support them, and what value they are expected to produce. To fill that gap, we developed an analytical BEAR framework (Figure 2), constructing it inductively from the patterns observed across the literature reviewed. The framework's channels are also consistent with, and arguably grounded in, the logic of how access decisions are structured. The reviewed evidence revealed a recurring sequence: biosimilar entry reduces therapy costs; this cost reduction improves the cost-effectiveness profile of the biologic; improved cost-effectiveness creates the conditions for a change in guidelines, formulary status, or access criteria that expands access through broader patient populations, earlier line use, and/or reimbursement of additional indications.

The framework captures this as a trigger-to-channel-to-impact progression. Biosimilar entry — more specifically the price and cost reduction that follow — is the enabler, with the lifecycle reassessment that follows acting as a trigger. The process captures the different channels and mechanisms through which change occurs, and the impact is the value attributable to that change. Which channel yields the greatest incremental value in a given setting will depend on the product, the indication and the system, and the evidence

base assembled here is not sufficient to rank them; establishing that comparison, most plausibly by product type, should be a priority for future research.

Figure 2 The BEAR framework: trigger, channel and impact



The specific form of the change varied across the reviewed evidence but fell consistently within one of the five channels represented in the process stage of the framework (Figure 2).

These are:

1. *Broadening of the severity thresholds* — eligibility criteria are relaxed, allowing patients with less severe disease to access treatment previously reserved for more severe cases.
2. *Treatment line advancement* — a therapy moves earlier in the treatment pathway allowing eligible patients to receive it earlier. For example, from second-line to first-line therapy in a given indication.
3. *Expansion to new populations or indications* — a therapy becomes available for a disease, indication, or patient group not previously covered by funding or clinical guidelines.
4. *Removal of administrative or formulary restrictions* — non-clinical barriers to access are removed to allow an expanded use.
5. *Liberalised prescribing* — administrative controls governing who may initiate or prescribe a therapy are relaxed to promote an expanded use.

The pre-selected examples in section 3.3 exemplify all the channels in practice.

Using the framework, the ultimate BEAR impacts — including expanded patient access, improved health outcomes, cost-savings, cost-offsets, and equity gains — can be linked to the specific channel through which change occurs. We use these two cost terms

consistently throughout: cost-savings are reductions in drug expenditure arising from price competition, while cost-offsets are avoided downstream medical costs arising from prevented clinical events. Each channel is associated with distinct forms of value expansion, enabling potential reassessment opportunities to be characterised according to the benefits they may generate and subsequently evaluated through detailed modelling. The framework therefore serves not only as an organising structure for the evidence collected, but also as a tool for identifying, assessing, and prioritising BEAR opportunities that health systems have not yet pursued.

3.2 Global evidence base

A consistent finding across all cases identified in the literature was that biosimilar entry, and the associated reduction in acquisition price, acted as the main driver of BEAR. By improving the cost and cost-effectiveness of an established biologic, biosimilar competition created the conditions for lifecycle reassessment of decisions made at the time of product launch. Reassessment by a competent decision-maker then triggers BEAR, broadening patient access, extending use to indications previously denied, advancing the therapy to an earlier line of treatment, or removing use restrictions — all on the basis of a revised cost-effectiveness and value profile.

At the same time, we found little evidence of health systems implementing BEAR through a well-defined, systematic process. The closest example identified was NICE's recent implementation of whole lifecycle approach to HTA, which recognises that technologies may warrant review as evidence and value propositions evolve over time (NICE, 2026g). While this goes some way to building reassessment into the HTA, it does not constitute a dedicated mechanism for systematically identifying all such opportunities.

BEAR examples identified in the literature spanned 11 national healthcare systems with markedly different regulatory, reimbursement, and HTA frameworks, suggesting generalisability in the observed benefits of biosimilar-driven improvements in cost-effectiveness and affordability.

The route by which access was expanded varied across systems. In some cases, a body with a standing remit to revisit cost-effectiveness reopened a formal appraisal once price competition rendered a previously rejected use viable (NICE, 2026c; f). In others, savings from biosimilars were redirected through funding and procurement decisions into broader eligibility, with no fresh economic evaluation undertaken (PHARMAC, 2021b). In a third group, changes to listing status or prescribing rules removed administrative barriers following the fall in price (Department of Health and Aged Care, 2022a; Moorkens et al., 2017). These routes occupied different positions on a spectrum from formal HTA to administrative discretion. The reported outcome was consistent across them: improved health system value and patient outcomes via lower prices and expanded or earlier treatment availability.

The global evidence reinforces the need for an analytical framework to systematise lifecycle assessments and BEAR implementation. To test the utility of the framework and illustrate BEAR impacts, we examined a selected set of illustrative case studies in detail.

3.3 Illustrative case studies

We selected seven illustrative case studies from the global examples identified in the review. These span five health systems (NICE in England, PHARMAC in New Zealand, PBAC in Australia, Centers for Medicare & Medicaid Services (CMS) in the US, and TLV in Sweden), together covering all five channels of the BEAR framework. We summarise all of

them in Appendix C using separate boxes reflecting on their trigger, mechanism of change, the channel through which they were implemented, and documented quantified impact; the accompanying discussion places each within the relevant channel. Two of the seven, bevacizumab (England) and denosumab (US), are fully modelled and analysed in the next section, Modelled Case Studies.

Taken together, the case studies demonstrate that BEAR is not a single policy mechanism but a family of approaches through which health systems translate biosimilar-driven improvements in affordability and cost-effectiveness into additional value. Spanning multiple countries, healthcare systems, and therapeutic areas, the examples show that reassessment of an established biologic's value proposition can lead to meaningful changes in access, treatment positioning, and prescribing practices throughout the product lifecycle.

The case studies also illustrate that opportunities for BEAR can be identified and implemented through different institutional routes. In England, NICE used lifecycle assessment to revisit indications that had previously not met cost-effectiveness thresholds at higher originator prices. In New Zealand, PHARMAC reinvested savings generated through biosimilar competition to expand access to previously uncovered patient populations and indications. Other examples demonstrate how procurement, reimbursement, formulary, guideline, and prescribing decisions can similarly be used to realise value created by biosimilar competition.

The examples therefore provide empirical support for the BEAR framework and demonstrate how its channels operate in practice.

3.4 Modelled case studies

This section reports the results from modelling two case studies: denosumab in the US and bevacizumab in England. These represent structurally distinct systems — one driven by market-based price negotiation (denosumab, US) and the other by cost-effectiveness analysis (bevacizumab, England) — as well as contrasting market contexts. Denosumab covers larger-volume, multiple chronic-use indications with substantial patient populations, while bevacizumab represents a lower-volume oncology indication in a smaller market.

The two modelled case studies are not intended as a comprehensive representation of global impacts but as specific, quantifiable examples of BEAR-driven outcomes across economic, clinical, and effectiveness impacts relevant to global stakeholders and decision-makers. Modelling estimates are therefore illustrative, designed to convey the potential value unlocked through lifecycle assessment and BEAR implementation for biologic therapies.

Each case study quantifies cost and outcome impacts of BEAR, complemented by an illustration of cost-saving estimates from biosimilar price competition alone, to contextualise their scale. Results are presented at both per-patient and aggregate level, using standard metrics including incremental cost-effectiveness ratio (ICER), net monetary benefit (NMB) and quality-adjusted life years (QALY), as well as access measured in patient numbers, health outcomes (e.g., fractures avoided) and health system cost-offsets. Together, these metrics distinguish additional value generated by BEAR from the mere cost-savings realised by biosimilar price competition. In addition, the two cases differ in whether the change in access has already occurred. For bevacizumab, NICE has recommended expanded access in England, and our modelling estimates the value of that actual change. For denosumab, the increase in uptake has not yet occurred; hence, our modelling instead projects the value that could be generated through higher uptake following biosimilar entry.

Denosumab repositioning in United States

The case and modelling

Osteoporosis remains one of the most undertreated conditions in US medicine, despite the availability of effective therapies. Postmenopausal women, men with reduced bone mass, and patients receiving long-term glucocorticoids all face substantial fracture risk, yet many remain untreated. This pattern has persisted despite successive guideline updates and an expanding range of therapeutic options. Although denosumab has been FDA-approved and reimbursed for these populations since 2010, its uptake has remained relatively limited, largely due to its higher acquisition cost (Cromer et al., 2022). Payers and PBMs frequently apply prior authorisation and formulary restrictions to biologic therapies, resulting in lower-cost bisphosphonates being preferred as first-line treatment (AJMC, 2026). Even where denosumab is covered, patient cost-sharing, including co-payments and coinsurance, may contribute to treatment delays, discontinuation, or reduced adherence (Flanigan et al., 2026).

By the end of 2025, the FDA had approved nine denosumab biosimilars. Each is marketed by a different manufacturer under two brand names — one for Prolia (osteoporosis), and one for Xgeva (oncology) — resulting in 18 branded products in total and creating the potential for substantial price competition across all indications (The Center for Biosimilars, 2026). Whether lower prices translate into broader treatment access is less certain. Coverage and formulary decisions are made independently by commercial insurers, PBMs, and public payers, with no mechanism linking savings from biosimilar competition to expanded treatment of eligible patients. As a result, while biosimilar entry may reduce expenditure, it does not automatically alter coverage policies, prescribing patterns, or treatment pathways that limit access.

This case study explores whether biosimilar-driven price reductions could support wider use of denosumab among eligible populations, expanding its value in the United States. We modelled a hypothetical BEAR-driven expansion of denosumab access for patients at high risk of bone fracture currently treated with oral alendronate — the current standard of care (SoC) in osteoporosis — across three eligible indications: WOP (Sarafrazi et al., 2021), MOP (Sarafrazi et al., 2021) and GIOP (Humphrey et al., 2023). A summary of the eligible populations is presented in Appendix D, Table D1. Figures for WOP and MOP are drawn from (Sarafrazi et al., 2021) and those for GIOP from (Humphrey et al., 2023) complemented with supplementary prevalence data. Together, these three patient populations represent approximately 3.18 million eligible patients for treatment in the US. This estimate is based on informed extrapolations using available prevalence data, Medicare fracture data, and payer and clinical definitions of high risk, as no direct epidemiological estimate of the treatment-eligible population was available in the literature or databases (see Table D1, in the Appendix).

For this case study, we assume that biosimilar competition and price erosion improve denosumab therapy's cost-effectiveness, enabling patients to switch from the SoC to a biologic previously restricted by the reference product's high acquisition cost. In other words, the case study illustrates the impact of lifecycle assessment and BEAR through a hypothetical but plausible real-world scenario in the US.

The analysis adopts a US payer, health system perspective over a lifetime horizon and reports fractures prevented, QALY gains, fracture-related cost-offsets, incremental costs, and cost-effectiveness. The analysis does not cover other licensed uses including bone loss in men receiving androgen-deprivation therapy for prostate cancer and women receiving adjuvant aromatase inhibitor therapy for breast cancer. Model structure, assumptions, parameter values, and data sources are set out in Appendix D.

Results are presented for a base case, representing the most plausible scenario, and upper- and lower-bound scenarios. The key assumptions for the three scenarios are:

- Lower-bound: Continuation of current practice, characterised by slow uptake reaching a plateau of 500,000 patients — 16% of the 3.18 million total eligible population — and a less aggressive biosimilar price erosion of 30%. Uptake reflects current US practice, where in some cases originators retain considerable market share for years after biosimilar entry (LaMountain et al., 2024) and reflects a floor scenario, with no BEAR impact at all.

- Base case: Gradual S-shaped uptake curve reaching 85% of the eligible population by year six, with price erosion progressing over the first five years to a maximum reduction of 60% at year five. At peak uptake this corresponds to about 2.7 million of the 3.18 million eligible patients across WOP, MOP and GIOP combined. Patient numbers decrease after year six due to mortality. Detailed patient uptake curves and price erosion trajectory are both available in Appendix D (Table D2).

- Upper-bound: Immediate treatment of the 3.18 million eligible patients from year one at the maximum biosimilar discount of 70%. This reflects a theoretical ceiling.

The lower-bound represents actual denosumab uptake across the three modelled eligible indications under current practice, with a conservative price erosion assumption based on literature (LaMountain et al., 2024). It serves as the benchmark against which the BEAR-driven impact of both the base case and the upper-bound is estimated. The projected increase in denosumab uptake illustrates how far use could rise above current levels. The scenarios span a plausible range of outcomes, and the estimated impacts count only the additional uptake beyond the observed lower bound, which reflects current practice.

Specifically, impacts — fractures prevented, cost-offsets, QALYs — were calculated only for the additional patients in the base case and upper-bound scenarios relative to the lower-bound. For example, the fractures prevented in the base case are

quantified for the additional 2.2 million patients treated beyond the 500,000 patients in the lower-bound, together making up the base case's total of 2.7 million patients.

NMB is calculated by valuing each QALY gained at a willingness-to-pay threshold of $150,000, the upper end of the cost-effectiveness threshold range ($100,000—$150,000 per QALY) used by the US Institute for Clinical and Economic Review (ICER) in its value assessments (ICER, 2023). As there is no single official US cost-effectiveness threshold, results are also assessed against the lower-bound of this range at $100,000 per QALY.

KEY FINDINGS

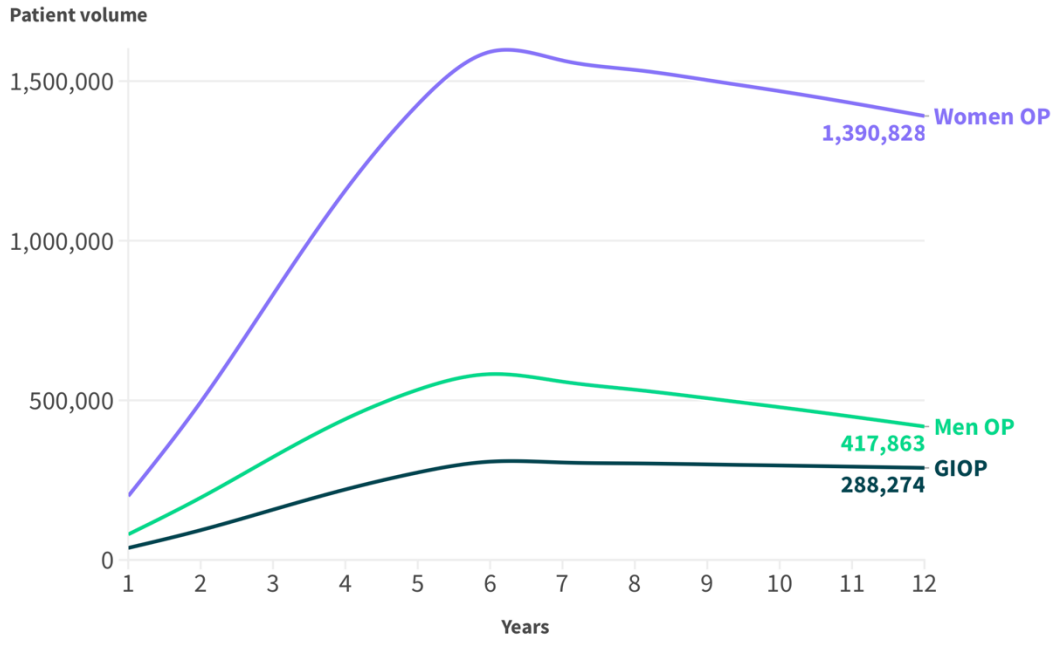
BEAR-driven access expansion

Although denosumab is approved for several indications in the US, originator list prices exceed what payers will fund, leaving many patients who meet the clinical criteria on less effective therapies. Biosimilar entry and the resulting price erosion change this calculus, enabling expansion of the eligible patient population to include those previously excluded at originator pricing.

Patient volumes (see

Figure 3), adjusted for mortality, expand across all three populations, WOP, MOP, and GIOP, as lower biosimilar prices are assumed to bring newly eligible patients into treatment over successive annual cycles. Volumes rise until uptake peaks in year six, following a progressive biosimilar price erosion that reaches its lower price at year five. After peaking in year six, uptake gradually declines, as no new patients enter the model beyond that point and assumed mortality reduces the treated patient pool (see Appendix D for modelling details and assumptions). This patient expansion is the main route through which BEAR generates value, as each additional patient receives a more effective therapy.

Figure 3 **Expansion in patient volumes on denosumab over time, by population**



We estimate that approximately 2.7 million additional patients across the three indications receive denosumab under the base-case scenario (indication breakdown provided in Table 1). This expansion is the consequence of biosimilar entry-led reassessment and BEAR.

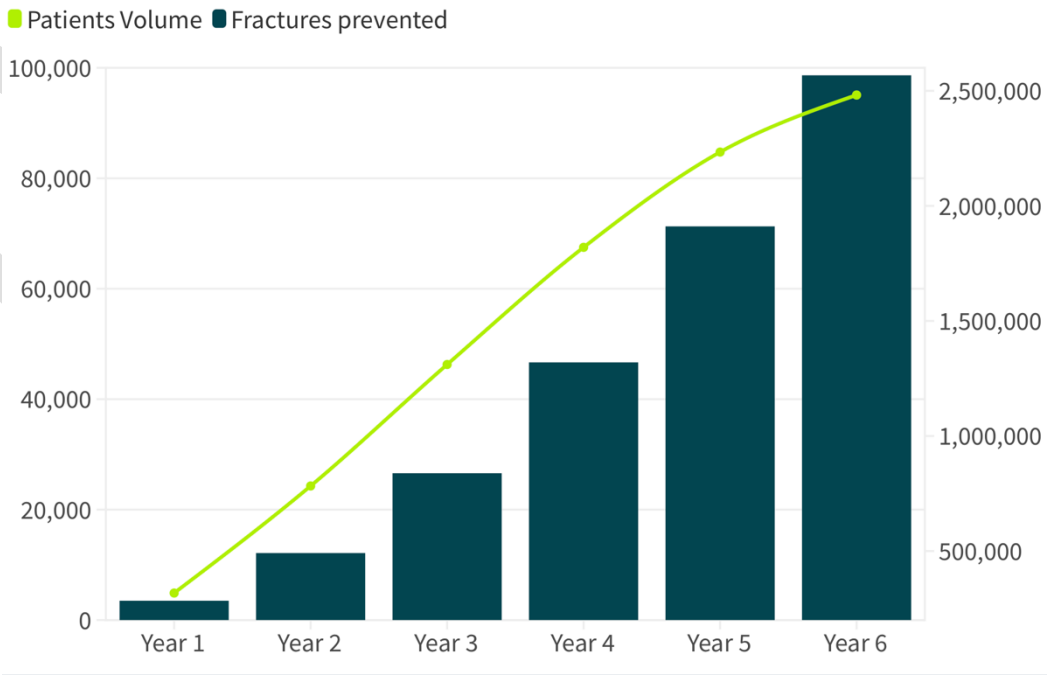
Table 1 Additional patients treated in the base case

POPULATION	ADDITIONAL PATIENTS TREATED
WOP	1,700,000
MOP	680,000
GIOP	318,750
Total	**2,698,750**

BEAR-driven value

We illustrate the volume-value link of BEAR by relating access expansion — which occurs up to year six, when uptake reaches its peak in the model — to the resulting health and economic impacts. Figure 4 shows this link between volume expansion and fracture-related cost-offsets in the base case scenario. Each additional patient treated with denosumab has a reduced fracture risk, which translates into a number of fractures prevented per patient. Annual patient increases (shown on the right-hand y-axis) are converted into accumulated fractures prevented by multiplying per annum increase in patients by the fractures prevented per patient. These prevented fractures are then multiplied by the cost-offset per prevented fracture, drawn from literature (Yeh, Saeedian and Badaracco, 2025), to generate the total health system cost-offsets attributable to the expanded access to a more effective treatment — enabled by biosimilar competition, as assumed in BEAR.

Figure 4 Cost-offsets due to access expansion and fractures prevented



At the base case uptake, we estimated 492,366 fractures prevented over the lifetime horizon. WOP patients account for about two-thirds aligning with their larger population expansion (Table 2). The total number of fractures prevented generated an estimate of $22.9 billion in direct fracture-related healthcare cost-offsets, equivalent to approximately $656.1 million annually. This represents a BEAR-driven effect beyond savings from a more favourable acquisition cost of denosumab biosimilar compared to the originator. These figures represent the projected potential impact under the uptake scenarios described above.

Table 2

Base-case fractures prevented and cost-offsets by population

POPULATION	FRACTURES PREVENTED	COST-OFFSETS	ANNUALISED AVOIDED COST
WOP	324,843	$15.1B	$432.4M
MOP	86,889	$4.1B	$115.7M
GIOP	80,634	$3.7B	$108.0M
Combined	**492,366**	**$22.9B**	**$656.1M**

BEAR-driven cost-effectiveness impact

The lower acquisition cost of denosumab biosimilar brings the modelled ICER of the three osteoporosis populations within the cost-effectiveness threshold in the base case scenario, which justifies the reassessment and BEAR. We estimated a combined base-case ICER of $100,921 per QALY across the three indications, which was considered cost-effective at willingness-to-pay threshold of $150,000 per QALY, the upper end of the $100,000-$150,000 range used by ICER in its US value assessments (39). This finding is consistent with recent US economic evaluations of denosumab versus generic oral bisphosphonates (Yeh, Saeedian and Badaracco, 2025). At this threshold, the expanded population generated a total positive NMB of $10.5 billion over the covered period, and total combined QALY gains of 214,033.

Table 3 provides the indication-specific breakdown of QALY gains, NMB and the ICERs, alongside the aggregate estimates.

Table 3

METRIC	WOP	MOP	GIOP	COMBINED
QALYs gained	141,749	38,587	33,697	214,033
Net monetary benefit[1]	$7.1bn	$1.5bn	$1.9bn	$10.5bn
ICER	$100,122	$110,145	$93,719	$100,921

METRIC WOP MOP GIOP COMBINED
QALYs gained 141,749 38,587 33,697 214,033
ICER $100,122 $110,145 $93,719 $100,921
Net monetary benefit[1] $7.1bn $1.5bn $1.9bn $10.5bn

Base case ICER, QALY gains, and NMB[1] by indication

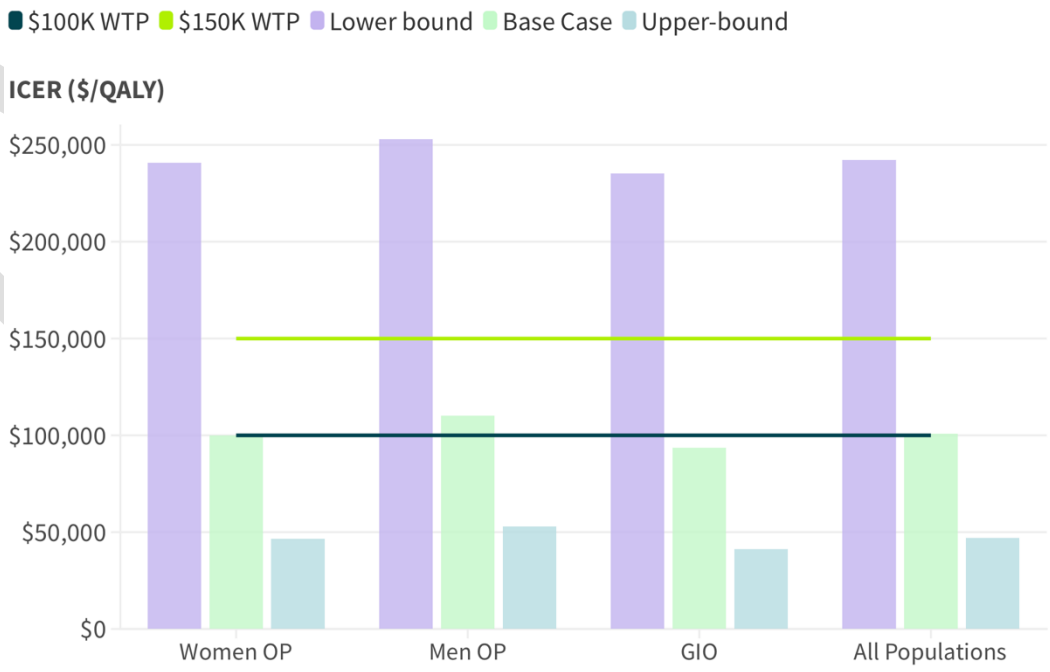
Calculation integrates cost-offsets from prevented fractures reported in Table 2.

[1] NMB calculated at $150,000/QALY WTP threshold

The results are highly sensitive to assumptions regarding biosimilar uptake and price erosion (Figure). We compare the base case scenario with the lower-bound scenario, which assumes a slower adoption and less aggressive price erosion and with the upper-bound scenario, which assumes maximum uptake and price erosion from year 1. Figure shows this comparison.

Under the lower-bound scenario, denosumab was not cost-effective in any indication, with ICERs ranging from $235,385 to $253,032 per QALY and a negative NMB of –$3.8 billion. This suggests that substantial price reduction from biosimilar competition is needed to generate positive value (or NMB) for the health system value. However, although ICERs remain well above the cost-effectiveness threshold, the magnitude of the negative NMB is comparatively limited. This reflects the lower volume expansion assumed in the lower-bound scenario, which contains the loss of value to the system and highlights expanded access as a key driver of the overall effect.

Figure 5 ICER by population and scenario at the $100,000 and $150,000 WTP thresholds



In contrast, under the upper-bound scenario, ICERs fall to $41,250—$53,032 per QALY and NMB increases to $31.1 billion. This increase in NMB is large relative to the reduction in ICERs, suggesting that expanded access substantially amplifies the total value generated.

The roughly $35 billion difference between the two bounds highlights how sensitive cost-effectiveness and BEAR-driven value are to uptake and price erosion.

Contextualising the value of BEAR

Traditionally, biosimilar value has been equated to cost-savings generated through price competition, realised solely in patient populations and indications already covered by the originator. In the denosumab case, this saving is real and immediate: holding uptake constant at current levels, we estimated that biosimilar entry can reduce cumulative denosumab spending from $21.75 billion at originator Wholesale Acquisition Price (WAC) to $9.73 billion under the base-case pricing assumption — a saving of $12.02 billion. This requires no change to coverage, guidelines, or the number of patients treated, meaning that US payers are already positioned to realise these savings without BEAR.

Our analysis shows that a lifecycle assessment of the therapy at biosimilar entry followed by a BEAR approach could expand the value of denosumab substantially beyond that cost-saving estimate. The BEAR-driven access expansion would result in total estimated fracture-related cost-offsets of $22.9 billion, nearly twice as large as the $12.02 billion price-competition savings. The NMB tells the same story in potential value delivered to system: estimated at $10.5 billion, it represents a value-added figure as large as the price-competition savings.

Additional value through BEAR is substantial and comparable to savings from price competition but is only realised when lifecycle assessment is triggered following biosimilar entry, requiring a more proactive role for HTA bodies or decision-makers than has been seen to date. In the decentralised US system, where reimbursement policy, formulary design, and clinical guidelines are not routinely revisited in response to price changes, this value remains available but unrealised. The denosumab case illustrates how much value is missed when reassessment does not follow biosimilar entry. Realising that value also depends on biosimilar competition remaining commercially viable: if price erosion does not leave competing manufacturers with a sustainable margin, entry and sustained supply are put at risk, the potential value of BEAR goes unrealised, and the resulting signal discourages investment in future biosimilar development.

Bevacizumab reassessment in England

Following biosimilar entry, NICE undertook a reassessment of bevacizumab as an add-on therapy in combination with fluoropyrimidine-based chemotherapy for mCRC under its whole lifecycle approach, recommending it for the first time in both first- and second-line treatment (NICE, 2026f), having previously declined to do so on cost-effectiveness grounds in three prior appraisals (NICE, 2012, 2007). While no new efficacy data informed the reassessment, biosimilar-driven price erosion brought bevacizumab within NICE's cost-effectiveness threshold, leading to a positive recommendation.

This case maps directly to the BEAR framework. Biosimilar entry and price erosion enabled the lifecycle assessment leading to an expanded, earlier access to treatment of mCRC patients with capacity to generate additional value in the form of improved outcomes and QALYs for patients, additional cost-savings generated in already funded bevacizumab indications, and a positive NMB for the health system.

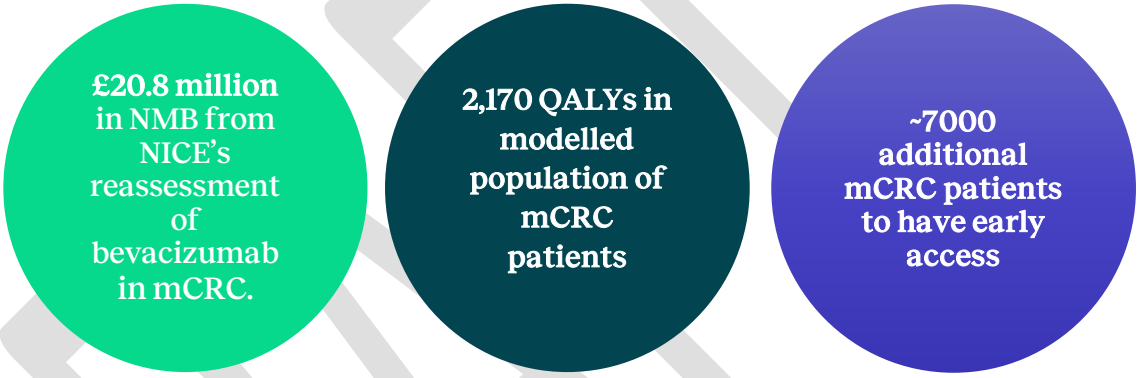
The case and modelling approach

To estimate this additional value of bevacizumab attributable to BEAR, we developed a simple model drawing on inputs from NICE's technology appraisal for bevacizumab for mCRC. Efficacy of bevacizumab was taken as already established in the technology appraisal. The estimated eligible first-line mCRC population in England (approximately

7,000 patients) was drawn from the appraisal. The appraisal also informed the total uptake estimate, recognising that not all eligible patients receive bevacizumab because of safety considerations or other clinical factors.

Our model compared bevacizumab plus fluoropyrimidine-based chemotherapy with chemotherapy alone across three pricing scenarios: the originator list price, the biosimilar list price, and an estimated NHS net price reflecting confidential discounts. The originator and biosimilar prices were sourced from the BNF (NICE, 2026a) (see Table D4 in the Appendix for the list prices). We estimated total QALY gains ICER and NMB for the first-line use of bevacizumab in the mCRC population under the three alternative pricing scenarios. A supplementary analysis estimated total cost-savings from biosimilar price erosion alone, across indications where bevacizumab was already reimbursed in England, independent of any additional value from BEAR.

KEY FINDINGS



BEAR driven access expansion

BEVACIZUMAB PRICE LEVELS	NMB1	QALY GAINS
Originator at list price	-£22.8 million	
Biosimilar at list price	-£14.8 million	2,170 QALYs
Biosimilar at NHS confidential pricing	£20.8 million	

Bevacizumab had previously been rejected three times on cost-effectiveness grounds, largely owing to the originator's price (NICE, 2012, 2007, 2010). The lower net price following biosimilar competition triggered an automatic reassessment, drawing on the evidence and modelling from previous appraisals, that brought bevacizumab below NICE's £30,000 per QALY threshold, opening access to approximately 7,000 mCRC patients in England.

Assuming an uptake trajectory estimated by NICE (NICE, 2026i) and illustrated in Figure ,

Table 4 summarises the health gains and NMB for the newly treated mCRC patients at originator, biosimilar list, and biosimilar net prices.

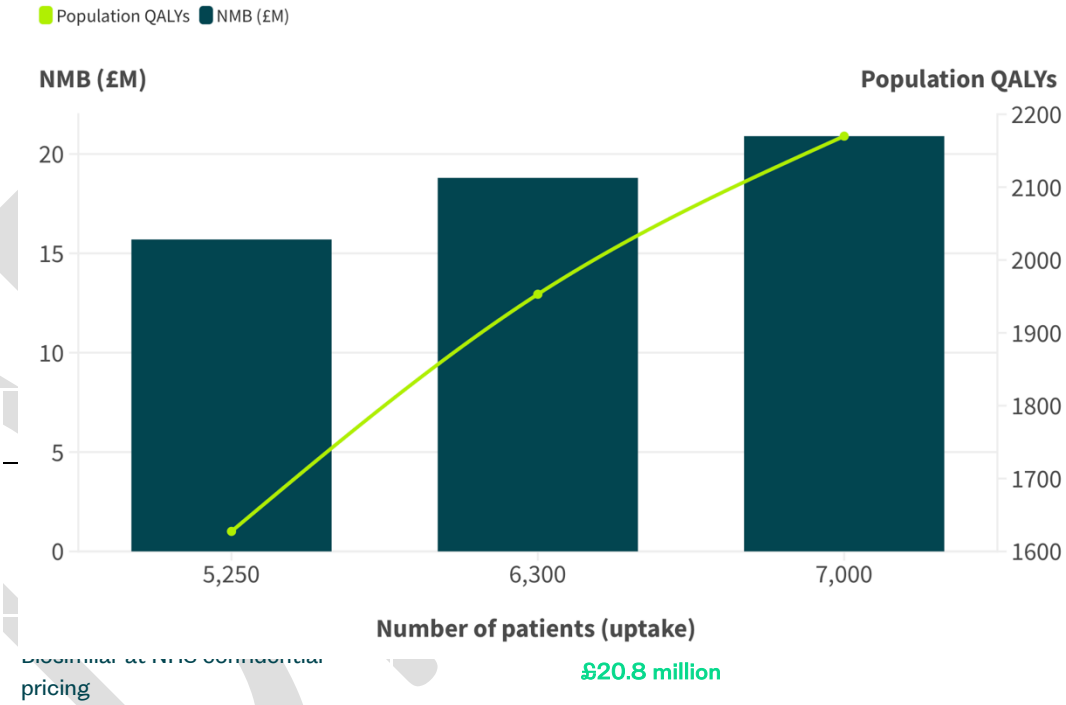
Table 4 Bevacizumab NMB and QALY gains across price scenarios

[1]NMB for the eligible population of 7,000 patients and calculated using the £30,000/QALY.

BEAR driven Value

Over the modelled period, earlier first- and second-line treatment of the eligible mCRC population produces an estimated 2,170 QALYs. The value grows with treated volume: Figure shows the relationship between uptake, QALY gains and the NMB applying the negotiated net price.

Figure 6 Bevacizumab uptake and QALY gains



pricing

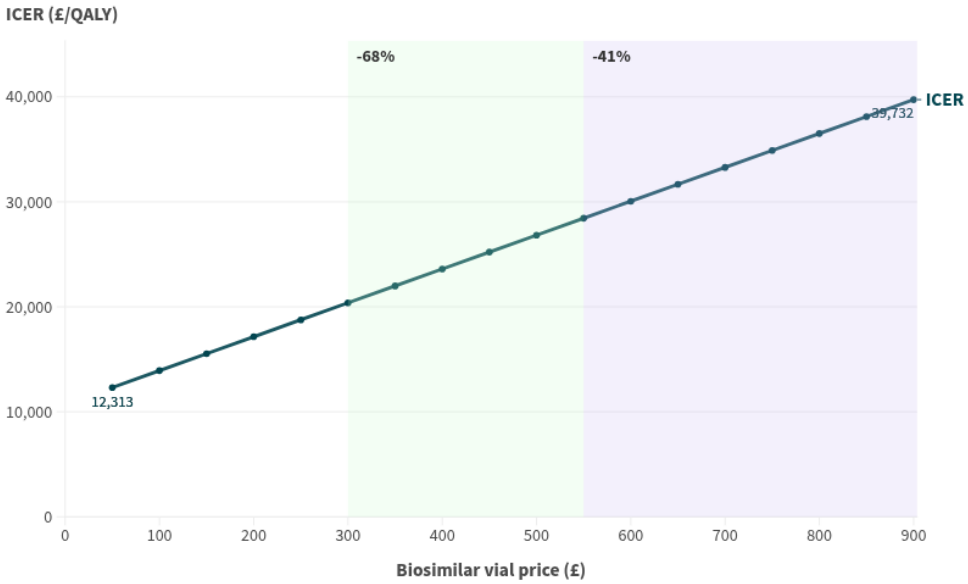
£20.8 million

BEAR-driven cost-effectiveness

Biosimilar competition enabled the reassessment that expanded access for mCRC patients; the value of that expansion is estimated below. At the originator list price of £924 per vial, the ICER was £40,520 per QALY — well above NICE's £30,000 per QALY threshold. The biosimilar list price of £810 per vial, just 12% lower and in line with the 10-15% reductions typically seen at biosimilar entry, brought bevacizumab's ICER down to £36,829 per QALY — still above the threshold. Only at the deeper NHS negotiated net price did the ICER fall to £20,378 per QALY, bringing bevacizumab within the cost-effective range for mCRC.

Figure shows the price-ICER sensitivity, identifying the minimum price discount required to bring bevacizumab within the £30,000 per QALY threshold at £550 per vial, representing a 41% reduction from the originator list price. The final negotiated discount, estimated at 68%, further reduced the price and generated additional value for the health system, as shown in the figure.

Figure 7 Bevacizumab price-ICER sensitivity against the £30,000 per QALY threshold



The resulting NMB quantifies the value of BEAR-driven access to bevacizumab by mCRC patients, the single indication reassessed under TA1136, for the health system. It captures the monetary value of QALY gains and cost-offsets, net of the incremental medicine cost, measured against the comparator. We estimated the NMB at £20.8 million: a significant net value gain for mCRC patients and the health system.

Contextualising the value of BEAR

Where a reference biologic is already recommended in a given indication, lower prices from biosimilar competition deliver value through cost-savings. We estimated total cost-savings across already recommended bevacizumab's indications and compared these with the additional value generated in mCRC through BEAR, to contextualise and quantify relative value added.

We estimated savings as the difference between the originator and biosimilar prices, using the erosion rate implied by the net price in the mCRC example. Multiplying these by the eligible population in each existing indication, drawn from NICE resource impact templates, gave the total saving per indication. These are presented in Table 5.

Table 5 Medicine cost-savings from biosimilar competition in existing bevacizumab indications

INDICATION	ELIGIBLE PATIENTS	COST-SAVINGS (6 YRS)
TA946: High-grade ovarian, fallopian or primary peritoneal cancer	3,062	£1.39M
TA939: Metastatic cervical cancer	5,655	£2.57M
TA666: Advanced or unresectable hepatocellular carcinoma	10,458	£4.75M
TA1022: Wet age-related macular degeneration	271,085	£123.2M
All indications combined	**290,261**	**£132M**

Across the four indications where bevacizumab was already recommended, biosimilar competition is estimated to have delivered £132 million in cost-savings over six years — value payers realise automatically, without reassessment. BEAR delivered an estimated additional value in mCRC alone of £20.8 million in NMB over three years from a single indication, representing roughly 15% of total savings across all four established indications. Under the current focus on price erosion alone, this value risks being unrealised. Treating biosimilar entry as a procurement event only secures the cost-savings but leaves BEAR-driven access gains unrealised.

Beyond the single case: towards systematic reassessment

The bevacizumab reassessment illustrates how cost-effectiveness-driven systems are well positioned to operationalise BEAR where prior appraisal decisions already exist. In such settings, earlier negative or restricted recommendations can be revisited using an existing economic model, updated with new net prices. Where acquisition costs have fallen sufficiently, the ICER for the reassessed indication moves within the cost-effectiveness threshold and its NMB turns positive, making guidance revision a natural next step.

In principle, this creates a relatively straightforward policy opportunity. Where prior appraisals exist and the clinical evidence base is stable, BEAR opportunities could be identified and routinely implemented following price renegotiation. The critical gap is institutional: there is no consistent mechanism for identifying when biosimilar entry and price competition justify reassessment, nor clarity on who is responsible for initiating review, how candidates are prioritised, and how revised recommendations are operationalised into guidance and commissioning practice. A structured BEAR process would address this by introducing formal opportunity scanning around loss of exclusivity. Where opportunities are identified and reassessed, this will trigger price renegotiation and formal guidance revision.

The approach is considerably less straightforward in settings where the original appraisal did not establish a stable and transferable evidence base — for example, in new indications, new patient populations, or previously non-appraised earlier-line uses of the product. In these cases, BEAR would require earlier alignment between regulators, HTA bodies, and manufacturers, alongside prospective evidence generation and clearer incentives for investment in post-launch data collection. More systematic BEAR approaches, with agreed evidence requirements and defined reassessment triggers, could help address these challenges, streamlining the path to reassessment when biosimilar entry occurs.

3.5 What does the evidence tell us?

Taken together the framework, the global evidence base, and both illustrative and modelled case studies tell a consistent story: biosimilar competition can generate substantial value beyond price-competition cost-savings alone. By reducing the price of biologic therapy, biosimilars can improve cost-effectiveness, affordability, and procurement economics to the point where expanded use becomes highly valuable across populations, indications, and treatment lines previously not reimbursed at originator prices.

The expanded use of biologic therapy materialised through the five alternative channels the framework sets out: broadening of severity thresholds, advancement to earlier treatment lines, extension to new populations and indications, removal of prescribing restrictions, and liberalised prescribing. These channels all unlock the same value — more patients treated or earlier, less restricted access, better health outcomes, and cost-offsets — but which channel each health system uses depends on its institutional design, not on the underlying economics. Where formal cost-effectiveness assessments dictate reimbursement, the lower biosimilar price can bring the ICER within the accepted threshold allowing the HTA body to issue a revised recommendation for a population or indication expansion or an earlier use, in a more advanced line of treatment, as in the cases of bevacizumab and natalizumab in England. Where procurement leads, the savings from biosimilar supply agreements can be reinvested directly to wider eligibility as PHARMAC did with adalimumab in New Zealand. Where the binding constraint is administrative, price erosion can prompt a reclassification or relaxation of prescribing controls, as observed with rituximab in Australia and filgrastim in Sweden. Finally, where no route is standardised — as in the case of the United States, where neither guideline-driven repositioning nor formulary redesign automatically follows biosimilar entry — the value of expanded access remains largely unrealised unless payers actively revisit therapeutic positioning.

The decision criterion through which the BEAR gains in access, outcomes, and efficiency are recognised differs by system: a CEA-driven system responds to ICERs and NMB; a budget-impact-driven system to cost-offsets and expenditure forecasts; and a clinical-value-driven system to evidence of improved patient outcomes and reduced unmet need.

Different BEAR channels also affect stakeholders in different ways. Payers will want to know whether expanded use increases or reduces the net cost to the system, and over what time horizon. Patients and their representatives will care most about whether a more effective treatment becomes accessible. From a health system perspective, the question is whether expanded biologic use improves resource use efficiency, reducing pressure on downstream services. Pharmaceutical manufacturers — of both originators and biosimilars — will consider how reassessment enlarges the market through access expansion across new populations, indications, and treatment lines, strengthening the incentive to invest in biosimilar development, manufacturing, and launch. The evidence from analysed case studies suggests these incentives are real: where systems have acted on biosimilar-driven price reductions to widen access, total patient volumes have grown, increasing the market size and value.

Our analysis of the evidence shows that in every instance where expanded access was realised, a relevant authority — a payer, clinical society, or HTA body — actively recognised and took advantage of the opportunity created by lower price with a BEAR approach; expanded access did not occur without a deliberate intervention.

Two questions follow from this. The first is when reassessment for BEAR should be initiated: the evidence shows it happens reactively and at varying points after biosimilar entry, rather than at a defined, anticipated moment in the product lifecycle. The second is how it should be institutionalised: across the cases reviewed we found no health system operating a systematic approach for identifying and acting on these opportunities. The scale of what is forgone when systems do not act is not trivial, as the modelled cases show. Turning these ad hoc, after-the-fact responses into a systematic and anticipatory

approach could unlock substantial value. We address this implementation challenge in the next section.

4 Implementation

From case-by-case evidence to systematic adoption

The case studies in section 3 demonstrate that reassessment and repositioning can unlock significant biosimilar value. Yet across most health systems they remain isolated exceptions rather than routine practice. Evidence of what BEAR can deliver is necessary but not sufficient: reassessment requires triggers to initiate it, processes to carry it through, and stakeholders with both the mandate and the incentive to act.

To understand what would change that, an expert workshop was convened with leading academics, HTA experts, and payers from across the Steering Group countries. This section draws on its insights, anchored in the case-study evidence, to set out the opportunities, challenges, and recommendations shaping potential lifecycle BEAR approaches and the pathways most likely to move systems from isolated examples to systematic adoption.

Although all health systems are driven (implicitly or explicitly) by clinical value and economic considerations, their decision-making frameworks differ considerably. Who decides, what counts as value in practice, the weight assigned to different value elements, how utilisation is steered, and whether assessment processes are systematically triggered all vary. Together, these differences shape how BEAR approaches can be integrated.

Table 6 sets out a high-level cross-country pricing and reimbursement (P&R) and HTA typology. This provides the lens through which the opportunities, challenges, and recommendations captured in the expert workshop are interpreted.

Table 6 Cross-country HTA and P&R typologies

CEA-DRIVEN SYSTEMS	NON-CEA DRIVEN SYSTEMS				
	Clinical added value/ additional therapeutic benefit	Clinical added value with additional CEA	Budgetary impact weighted against therapeutic value	Multi-criteria: added therapeutic value and budgetary impact prioritised	Market-based price negotiations
					

At the broadest level, we have classified systems into cost-effectiveness analysis (CEA)-driven and non-CEA-driven systems (Katsikostas-Michopoulos et al., 2022). A CEA-driven system is one in which CEA serves as a key determinant of value assessments leading to reimbursement decisions. In contrast, non-CEA-driven systems rely on alternative criteria, which can be a subset of CEA elements themselves (e.g., price and effectiveness) or related variables (e.g., budget impact, therapeutic value). The non-CEA-driven category has subsequently been grouped into five sub-types to accommodate the range of countries and system types considered in the analysis:

- Clinical added value/additional therapeutic benefit: Systems are based on the analysis of relative effectiveness, evaluating medicines in comparison with therapeutic alternatives to prove an added benefit (Kilwing and Dintsios, 2026).
- Clinical added value with additional CEA: Clinical added value remains the primary criterion, with CEA providing complementary input to inform decision making.
- Budgetary impact weighted against therapeutic value: Estimation of the fiscal consequences of adopting a new technology or intervention plays a major role in decision-making, with the possibility of specific thresholds being established (Jamshidi, Foroutan and Salamzadeh, 2014).
- Multi-criteria weighting incorporating therapeutic value and budgetary impact: Pricing and reimbursement negotiation relies on a multi-criteria approach, including both therapeutic value and budgetary impact, as well as other factors such as disease burden and unmet need (Garau and Jommi, 2023)
- Market-based price negotiations: Reimbursement decisions follow decentralised, multi-payer price negotiations across public (e.g., Medicare and Medicaid) and private insurers, with pharmacy benefit managers (PBM) acting as key intermediaries managing rebates, formularies, and access in the absence of centralised price regulation (Levitt, 2024).

The countries included in the typology reflect those represented by country-specific experts at the workshop (Australia, Canada, Germany, Spain, the UK, and the US). France and Italy were added to illustrate how HTA and reimbursement frameworks vary even within them.

The typology therefore serves as a reference framework for the workshop analysis, enabling country-specific insights to be contextualised within broader system types and, with appropriate caveats, transferred to countries with similar characteristics. It also serves to identify the key stakeholders and their incentives within each system type.

4.1 Framing the workshop analysis

Stakeholders' utilisation incentives

Within CEA-driven systems, removing restrictions or expanding indications depends on demonstrating value against formal cost-effectiveness benchmarks.

The lower competitive price that follows biosimilar entry is the primary enabler for BEAR in these systems, bringing the ICER within cost-effectiveness threshold and allowing the health system to realise net value while improving patient health. In some CEA-driven settings though, budget impact also plays an important role, particularly in some countries

like Australia where decision-makers expect biosimilars to reduce total treatment cost, i.e. focusing narrowly on the cost-saving potential of biosimilars while overlooking BEAR-driven value expansion.

Incentives to activate lifecycle assessment and BEAR approaches differ across non-CEA systems. In budget-impact systems, evidence of cost-savings driven by price discounts is the primary incentive. In Spain, for example, these savings are the focus of the Ministry of Health (MoH). Regions — through HTA, pharmacy management departments, or hospitals — can trigger BEAR locally based on a product's redefined value proposition, which can then be raised to the MoH for central reassessment. Although these systems prioritise the cost-saving and cost-offset opportunities of biosimilars, systems may differ in how stakeholders within the ecosystem recognise BEAR's value beyond these and are positioned to trigger reassessment. In multi-criteria systems, such as Italy, this means finding who in the decision-making ecosystem can best recognise BEAR's value, at the right level of the health system.

In clinically driven, non-CEA systems, incentives centre on demonstrated clinical added value and outcomes. At the extreme, these systems do not restrict access to clinically superior therapies, so the originator may already be used wherever it adds therapeutic value, reducing the need for BEAR. Germany is the clearest example: access is recommended based solely on its added therapeutic value. In this context, unlocking greater biosimilar value through BEAR depends less on the price than on designing the right demand-side incentives and policies to drive biosimilar uptake: optimising prescriber behaviour, supporting patient and prescriber education, and establishing prescription quotas, automatic substitution, and interchangeability frameworks. France follows the same typology to a lesser extent: since 2013, pharmaceutical and medical-device companies also submit CEAs to Haute Autorité de santé (HAS) for presumed-innovative products, under submission criteria updated in 2022 (Doghri et al., 2023).

The utilisation incentives described above interact with existing uptake and prescription policies across all system types. Demand-side incentives for biosimilars — such as interchangeability, automatic substitution, prescription quotas, and benefit-sharing schemes — are central to overcoming the barriers to uptake created by originator, prescriber, and patient behaviour (Tam et al., 2025). Their effect can be substantial: mandatory switching drove a sharp rise in infliximab biosimilar uptake in Canada (Zhang, 2021), and prescription quotas in Belgium achieved greater uptake than in France, which has no equivalent policy (Barcina Lacosta et al., 2022). How far these incentives enable biosimilar competition directly shapes their role in BEAR, and this dynamic plays out differently across system types. In CEA and budget-impact systems, they act as preconditions that enable or impede implementation: interchangeability, for instance, can support expansion on cost-effectiveness grounds, while quotas may constrain the contracting flexibility that requires. They become the primary lever for expanding BEAR value — a point already illustrated in the German and French cases above.

A second barrier to BEAR implementation lies in perverse economic incentives. The clearest example is the US, where PBMs, wholesalers, and other intermediaries use their market power not only to offer financial incentives (such as formulary rebates) but also to maintain pricing structures that limit the scope for competition and make biosimilar entry harder. Together, these practices discourage substitution and effective competition, creating significant obstacles to BEAR approaches. In the US setting, biosimilar adoption is shaped by the buy-and-bill reimbursement structure. Recent evidence from ~1,500 US hospitals shows that between 2020 and 2024, biosimilar acquisition prices fell 60—72% while reimbursement prices fell only 32—36%, allowing hospital margins to widen substantially even as biosimilar adoption reached 84—93% of relevant use (Robinson, Kosorukov and Whaley, 2026). Robinson and colleagues (2026) frame this as an implicit gainsharing arrangement that has helped drive adoption. In the accompanying editorial, Sachs and colleagues argue that biosimilar adoption remains far slower than typical generic adoption, and that the buy-and-bill structure captures a substantial share of achievable savings before they reach patients or premiums (Sachs, Dusetzina and Mitchell,

2026). This literature concerns transmission of price competition to price within existing utilisation — a distinct question from the reassessment-and-repositioning value that is the subject of this report — but the two failures co-exist: even the direct price-competition savings that BEAR is intended to complement are, on current evidence, only partially transmitted.

Overall, both demand-side and perverse economic incentives highlight that issues arising from existing incentives need to be revisited and redesigned in alignment with BEAR approaches, whether this means using them as a target for BEAR expansion or as a first level of market structure reform.

Key stakeholders

Across systems, BEAR engages a diverse range of stakeholders, each motivated by differing outcomes based on their role and the system context. The key stakeholders identified by the steering group included payers, policymakers, HTA bodies, alongside clinical guideline developers and clinical societies at both the local (e.g. the British Society for Rheumatology) and global (e.g. the European Society for Medical Oncology, ESMO) level. Hospitals, budget holders, clinicians, pharmacy management, and patients were also noted, operating at different levels of the healthcare system and with varying degrees of decision-making authority and influence across countries and systems.

Payers, policymakers, budget holders, and pharmacy management are primarily focused on the financial and fiscal impact of BEAR. HTA bodies, using CEA to inform decision-making, instead focus on value that can be measured, assessed, and compared using established CEA methodologies. For clinical guideline developers, clinical societies, clinicians, and patients, focus is on clinical value and outcomes. Hospitals occupy a middle ground, balancing budgetary pressure whilst in some cases undertaking their own CEA.

Manufacturers are stakeholders too, with systematically opposed incentives. As exclusivity is lost, the originator defends the reference product's franchise while the entrant seeks to expand appropriate use and build volume at a lower price. This asymmetry is one reason the market does not self-correct towards BEAR outcomes. The party with the strongest incentive to argue for reassessment is the entrant, which has the least standing before payers, HTA bodies, and guideline developers, while those with that standing may have less reason to advocate for expanded use at a lower price. Furthermore, incentives rest on biosimilar and price competition remaining commercially viable, with margins that encourage entry and ensure sustainable supply.

The relative importance of each stakeholder type and their associated motivations differ across countries and systems. In the US context, there is a case to incentivise payers to re-evaluate biologic therapy based on biosimilar competition. Most payers in the US cover biosimilars on parity with the reference product. Both public (CMS) and private (formulary decision-makers such as PBMs) payers are important in this context. Guideline developers such as NIH are also key stakeholders, as are clinical societies like the American Society of Clinical Oncology (ASCO). In the US, oncology coverage tends to follow the National Comprehensive Cancer Network (NCCN) Compendium. When NCCN raises a therapy's evidence category, CMS and most commercial payers follow. That makes a compendium listing one of the most direct BEAR routes for indications like those in our bevacizumab case. Notably, most guideline developers focus on clinical outcomes, with ACC/AHA being a notable exception in explicitly embracing CEA.

Payers are also key stakeholders in the Australian context, which operates a CEA-based system. Convincing Australian payers to expand utilisation of a post-loss of exclusivity (LoE) medicine would, at minimum, require assurance that it would not increase financial risk to taxpayers: treating more patients for the same cost may be more acceptable than a

net cost increase, although clinical stakeholders may be able to influence and encourage adoption for new indications or populations where this is value-driven. There have been precedents of clinical/patient groups pushing for indication expansions, but this has been on a case-by-case basis.

The role and influence of payers is less decisive in the UK. Decisions lie primarily with HTA (NICE) following CEA. This represents an extreme case of a CEA-driven system whereby the HTA decision is binding. The key stakeholder for BEAR implementation is therefore the HTA body. Patients are also considered to be relevant stakeholders, for example, contributing actively to the natalizumab repositioning example for treating highly active relapsing—remitting multiple sclerosis after disease-modifying therapy (NICE, 2025a, 2026c).

As of June 2019, Canada's Drug Agency (CDA) stopped reviewing biosimilar submissions through the Common Drug Review (CDR) or the pan-Canadian Oncology Drug Review (pCODR), with submissions instead to be filed directly with provincial jurisdictions and the pan-Canadian Pharmaceutical Alliance (pCPA) (50). Under this streamlined process, biosimilars are assumed equally effective to originators and thus require no further assessment for approval. However, this neglects the value of BEAR. A bottom-up approach may therefore be needed due to the fragmented nature of decision-making across provinces, potentially starting with clinical societies and patients.

In Germany, a system driven by added therapeutic value, the key stakeholders are neither HTA agencies nor guideline developers, but rather physicians (for awareness) and sick funds (for quota and contract preparation). The focus should therefore be on considering barriers to entry and incentives to switch across stakeholders (e.g. prescribers, pharmacists, sick funds, statutory insurance, GBA). In particular, the biosimilar quotas and statutory doctors' associations' promotion of biosimilar prescribing are the existing channels through which the case should be made. The former are able to raise the topic to the GBA level and trigger broader system responses, whilst the latter are instead partners for quota setting and physician awareness.

In Spain, BEAR is most likely considered as an approach at the decentralised level. As a result, the key stakeholders are predominantly regional: regional HTA, hospitals, clinical societies, and regional pharmacy portfolio managers or departments (often embedded within regional HTA bodies or in Departments of Health). Clinical societies are particularly important given that they develop guidelines and exert significant influence on decision-makers by providing relevant clinical evidence and real-world practice experience. They represent the first step in triggering change through a bottom-up approach. The central stakeholder is the MoH, which can update guidelines centrally if provided with consistent evidence across regions.

4.2 The workshop

The workshop facilitated discussion surrounding opportunities, challenges, and recommendations for BEAR implementation by stakeholder group and health system context. Experts provided input related to how relevant decision-makers could identify opportunities for lifecycle HTA assessment and guideline updates leading to BEAR; how these opportunities could be anticipated; and how stakeholder collaboration could be used to leverage these opportunities.

Opportunities

Revisiting past decisions can identify opportunities for BEAR.

Opportunities for reassessment arise when there are restrictions (second/third line use, populations etc.), as lower priced biosimilars may be able to demonstrate cost-effectiveness or added value and remove restrictions placed on biologic use. Identifying these opportunities requires HTA bodies and decision-makers to review current guidelines, in particular patient populations, treatment lines, and indications, to understand where there are restrictions of use in place. CEA-driven systems are best positioned to lead this, given their established HTA frameworks. In cases where a biologic is already recommended in first-line use, reassessment may not be necessary nor add value; in this case, focus would instead be on leveraging policy levers (i.e. mandatory therapeutic substitution) or incentives (i.e. benefit sharing) to promote biosimilar uptake relative to the reference biologic where doing so would lead to cost-savings.

Timing is important for spotting, scanning and assessing opportunities.

LoE gives a time point where positioning can be reviewed. A period of 18-24 months pre-LoE may be optimal to start scanning BEAR opportunities: new indications may be sufficiently attractive to the sponsor of the reference biologic to prompt an HTA or coverage submission, and if not, that may provide some momentum for a biosimilar sponsor to apply. However, this period is indicative and could be even longer when evidence generation for a new indication approval is required, unless RWE-based approaches are recognised and accepted. Reality is substantially different, though, with payers generally not proactively scanning for opportunities to expand indications and/or populations of post-LoE medicines, instead relying on proactive companies sensing a commercial opportunity or a clinical or patient group pushing for expanded access. While NICE's whole lifecycle approach moves towards a more proactive model, it is early days with only a few examples so far, all of which were able to leverage indication-level evidence from previous technology appraisals.

Stakeholder engagement is needed to identify and leverage BEAR opportunities.

Engagement with key stakeholders is vital for creating BEAR opportunities, but the approach must be tailored based on system type. In the US, this should involve redesigning how evidence is communicated to payers. A streamlined, biosimilar-specific dossier is currently in development (AMCP, 2026) — a step that could expand opportunities and the scope for BEAR while establishing lifecycle therapy assessment as a more routine practice for US payers. In Spain, engagement with regional HTA agencies, pharmacy management departments, hospitals, and medical societies could offer opportunities for BEAR. In Australia, the PBAC's Drug Utilisation Subcommittee (DUSC) provides highly influential advice to PBAC and would be pivotal to any horizon scanning function for biosimilars. Opportunities could be identified proactively through two complementary mechanisms: the PBAC's minor amendment (MA), which offers a streamlined pathway for lower-risk listing extensions, and DUSC's Predicted versus Actual (PvA) utilisation reviews, which monitor real-world uptake post-listing and can engage clinical and patient stakeholders to surface BEAR opportunities following LoE.

Designing policies and incentives where access is already guaranteed.

For clinical added value driven systems, where, in theory, an originator biologic demonstrating added therapeutic value faces no restrictions on access, focus should be on encouraging biosimilar entry, price competition, and sustainable biosimilar markets.

Challenges

Complexity and misaligned incentives

Ambitious forms of BEAR leave the government and sponsoring company with conflicting financial objectives that are difficult to reconcile.

Governments may require a substantial price reduction to ensure that expanded use is fiscally sustainable. However, this may be commercially unsustainable for biosimilar manufacturers, particularly those launching in small markets and facing high manufacturing costs and complex processes. With no mechanism to compel agreement, both parties could be left too far apart to reach a mutually acceptable compromise. The case of Australia, where the PBAC attempted to initiate an evaluation for an indication expansion of rituximab against a company's unwillingness, was raised during the workshop discussion.

Free riding erodes commercial incentives for companies to generate evidence for indication or population expansion post-LoE.

Biosimilar companies typically rely on the evidence required for marketing authorisation (i.e. equivalence studies) where the originator is already approved and do not generate additional data for expanded populations or additional indications. Therefore, when a BEAR approach seeks to extend access beyond what has been approved, the original evidence base may not be fully applicable. For example, with a different patient population, clinical outcomes, and the product's benefit-risk profile may differ, thus altering its cost-effectiveness.

However, any investment in evidence generation for indication or population expansion by biosimilar manufacturers is unprotected: competitors can enter the market without incurring the same substantial costs, free riding on the evidence. Therefore, there may be little incentive for the originator to expand use since the return on the investment could be undermined. This represents a crucial market failure whereby the free-rider problem creates a socially inefficient outcome in which valuable indications and populations may never be pursued through private investment alone.

Attempts to address this through market protection incentives are also difficult due to risk of competition distortion and the substantial monitoring costs. Alternative routes to address the issue may lie in leveraging more systematic RWE approaches, or in guaranteeing sufficient rewards to the data generation lead through pull incentives such as priority review vouchers (PRV) — a regulatory incentive awarded to manufacturers that can be redeemed to accelerate the regulatory review of a future product, or sold to another company (Olliaro and Torreele, 2024). Relatedly, Article 48 of the EU's new pharmaceutical legislation allows not-for-profit entities to submit evidence to the EMA for new therapeutic indications of an authorised generic or biosimilar addressing an unmet medical need; if the opinion is positive, marketing authorisation holders must update the label (Scholte et al., n.d.).

In market-based price negotiation systems, the market structure, incentives, and behaviours work as a barrier to BEAR.

The US experience illustrates how these barriers can emerge through multiple pathways. Firstly, as outlined in section 4.1 of this report, PBMs and other intermediaries may leverage their market power, distort pricing, and offer financial incentives to discourage substitution and biosimilar competition. Besides, originator biologics have strong incentives to protect their franchise as biosimilars approach (Conti, 2017), and evergreening tactics operating through PBM rebate structures have been a documented barrier to biosimilar uptake in the US (Barrenho et al., 2025). Secondly, BEAR approaches rely heavily on influencing key stakeholders through education and engagement, rather than on structured, automatic assessments. This dependency is further compounded by the limited use of CEA by professional societies, which hinders automatic lifecycle assessment and undermines the conditions under which BEAR adoption could be more readily achieved. This has led to inertia taking hold and disincentivising rapid biosimilar uptake, prompting calls for more centralised price-setting mechanisms to overcome the barriers associated with the current market design (Phengsitthy, 2025; Rome, Bhaskar and Kesselheim, 2026).

Institutional, regulatory and system constraints

Resource constraints for HTA and intensive lifecycle assessments hinder BEAR.

Implementing BEAR approaches through lifecycle assessment places additional burden on HTA agencies regardless of whether their primary decision-making framework is CEA or other criteria. When HTA agencies lack the resource to absorb this work, BEAR approaches will be challenged irrespective of their expected merit.

This can be exemplified using the Australian context where HTA capacity is already squeezed: each year, the PBAC considers up to 200 separate agenda items across six meetings with 20-30 individuals from the Department of Health and contracted evaluation groups. There is no room to take on additional proactive work, which is also compounded by staffing caps in the Australian Public Service. These sorts of institutional constraints are relevant across all health system and country contexts.

Institutional rigidity and myopic perspectives are present in budgetary-driven systems.

An excessive focus on budgetary impact means that access expansions driven by value-based improvements are often overlooked. This is most pronounced in budget-impact-driven systems but can also emerge in CEA systems where budgetary impact serves as a complementary decision-making criterion. Spain's MoH exemplifies the former: decision-making is based predominantly on price-erosion savings, and the few economic evaluations conducted at national level focus exclusively on costs and cost savings. Australia illustrates the latter: despite being CEA-driven, payers are strongly influenced by budgetary impact when making reimbursement decisions for post-LoE medicines. In both cases, decision-makers risk overlooking the value-adding potential of BEAR, precisely because it may involve higher initial spend on a disease area — a concept largely foreign to post-LoE markets — even when that spend represents a sound value-for-money decision.

Decentralisation and regional variation create fragmented reassessment pathways.

Implementing BEAR is difficult in systems where there is regional variation in decision-making structures and infrastructure, as it requires tailored approaches to trigger reassessment and consistency across regions. This is the case in Spain where biosimilar uptake varies across regions due to fundamental differences in HTA and decision-making (Espin, Špacírová and García-Mochón, 2026). For example, Andalucia has centralised decision-making, whereas in Castilla y León or Castilla-La Mancha it is largely hospital-driven. In other regions such as Galicia or Basque Country, pharmacy management departments oversee medicine access and procurement.

Recommendations

HTA, guidelines, payer and regulatory alignment

Encouraging global stakeholder collaboration and joint consultations to reduce fragmentation.

Three key recommendations emerge from the fragmented state of stakeholder collaboration and use of global joint consultations to overcome fragmentation. First, HTA bodies should engage more systematically with the guideline development community. Beyond them, patients, clinicians, and clinical societies are key enablers, offering insight into patients' lived experience and how a medicine addresses their needs. Engagement with this group of stakeholders is best framed around clinical value rather than economic arguments. Second, where restrictions on a biologic's use are driven by non-clinical factors (e.g. cost-effectiveness or rationing considerations), countries should streamline the HTA or decision-making process to expedite BEAR, focusing mainly on price negotiation and targeted policy levers to maximise the benefits of biosimilar competition. Third, the introduction of EU Joint Clinical Assessments (JCA) in 2030 (European Commission, 2024) presents both an opportunity and a risk for biosimilars seeking approval for new indications or expanded populations. A streamlined or accelerated review pathway for biosimilars within the JCA framework could be considered, though this is currently out of remit; where this is not feasible, biosimilar developers should be encouraged to engage with early scientific advice, ensuring the required evidence is in place ahead of formal assessment and avoiding delays, or iterative back-and-forth.

Highlighting misalignment between clinical guidelines and payer policies.

Particularly in fragmented systems, publishing studies that surface misalignment between clinical guidelines and payer policies would make such disconnects visible and highlight BEAR opportunities. For example, in the US, clinical guidelines tend to focus solely on clinical aspects, with no explicit incorporation of cost-effectiveness or other economic considerations into their recommendations. While HTA plays a smaller role, some US-based payers do consider it when formulating their coverage policies (Enright et al., 2025). A more targeted strategy may be needed to identify payers whose policies are misaligned with clinical guidelines and represent opportunities to reposition biologic use.

Within the Spanish context, where HTA is applied unevenly across regions, the same logic operates: studies surfacing inconsistencies between regional practice and national clinical guidelines would make BEAR opportunities visible. In Germany, because economic factors are not relevant, studies could instead target which incentives need revisiting, redesigning,

or implementing to align behaviours with a greater use of biosimilars in already adopted indications or populations.

Implementing formal policies supporting routine reassessment of post-LoE medicines

Governments should adopt policies supporting routine assessment of post-LoE medicines to identify populations that were excluded at initial listing due to cost-effectiveness and/or budget impact concerns, but which may now be eligible for treatment at reduced biosimilar prices. In the absence of such policies, updates to listings for post-LoE medicines will remain a case-by-case prospect — the case in most countries studied. Policies enabling routine assessments are therefore generally required.

Leveraging bottom-up approaches to promote BEAR in decentralised health systems

Top-down approaches may be insufficient to drive BEAR in these systems. Engaging stakeholders at a more localised level — particularly where they hold independent decision-making authority — and building upwards from there is more likely to gain traction. In Spain, this means starting with clinical society guidelines and regional HTA bodies, before the Ministry of Health considers reassessment. In Germany, regional sick funds are the natural entry point ahead of biosimilar market entry, from where the topic can be raised to the GBA to trigger a broader system-level response. In the US, by contrast, the more fragmented payer landscape calls for payment reform and greater centralisation of pricing and reimbursement, for example, using Medicare as the lead payer.

Harnessing incentives to reward regulatory and HTA data generation for reassessment.

Responsive lifecycle assessment and BEAR approaches would require setting incentives rewarding the company that generates the regulatory and HTA data. However, granting a period of data or market exclusivity for the first company to register and reimburse a new indication for a multi-brand market seems unfeasible, as this would involve convincing governments to adopt a temporarily anti-competitive approach, and having the capacity to track use of the protected market leader within the BEAR indication only. Options that accelerate assessment and reimbursement decision processes, such as PRVs or other similar system-specific mechanisms, would be more palatable than options that could slow down competitive entry. Where such mechanisms already exist, they offer a lower-barrier route to reward data generation without new legislation. Extending or replicating such mechanisms elsewhere may offer a more immediately actionable incentive for evidence generation. These incentives, however, would need to be globally coordinated to effectively incentivise biosimilar R&D and global market launch. Incentives would be especially important in the US market as the lead global funder for pharmaceutical R&D and manufacturing investments.

Evidence generation

Collecting evidence to support reassessment

Biosimilar manufacturers should invest proactively in generating the evidence needed to support lifecycle assessment and BEAR — for example, by anticipating opportunities to demonstrate cost-effectiveness in wider populations or additional indications. However, given the free-rider problem, this cannot rely on private investment alone; public-sector support through incentives and targeted policy intervention is essential. In decentralised

systems where BEAR follows a bottom-up approach, consistency in evidence across sub-national actors is critical — as illustrated by the requirement for Spanish regions to present aligned evidence to the MoH when seeking national adoption.

Considering use of novel data and analytical approaches

Biosimilar companies and HTA agencies evaluating biosimilars in other lines of therapy should consider using broader types of evidence beyond trials. There has been exploration from regulators and HTA agencies (e.g., NICE and the HTA Innovation Laboratory) to consider the use of novel types of data (e.g., modelling, simulation, pre-clinical data) and how it can be used to extrapolate to populations not covered in the clinical trials. Leveraging more RWE, outcomes and cost-effectiveness data can also represent an opportunity for BEAR. New statistical approaches already validated by FDA, such as Bayesian methods, which streamline evidence generation by drawing on existing knowledge (Niazi, 2026a; b) offer a further avenue. Collectively, these novel data types and analytical approaches warrant policy-makers assessment to better enable BEAR and maximise value of biosimilars. Data generated through outcomes-based payment models, using registries or other real-world data collection systems, can also serve as a push for broader BEAR implementation, beyond its use for specific adoption issues, when evidence is not robust or uncertainties remain. Such agreements have, however, been used sparingly and become less applicable after loss of exclusivity, when eroded prices leave little margin to place at risk. At that stage, the more practical source of evidence may be collective specialty learning, whereby clinical societies and specialist networks pool routine practice experience in newly treated populations, which avoids relying on any single manufacturer.

Stakeholder education

Raising stakeholder awareness of the value of BEAR

In order to inspire action, stakeholders must be convinced of the value of BEAR. Our case studies and modelling suggest that biologic medicines hold considerable potential to deliver value across existing and new indications, once price goes down after LoE. Realising this potential depends on engaging the key stakeholders within a given country's decision-making framework. In the US, for example, payer education is a key priority to highlight BEAR's potential to unlock value and trigger the lifecycle assessments, particularly given the nature of the US system. Awareness could be raised through platforms such as the meetings of AMCP, which attract broad payer participation.

Upskilling stakeholders to communicate with each other.

Awareness alone is not enough. Stakeholders must also have the capacity and the channels to engage meaningfully with one another. In Australia, for example, both clinical and patient groups could be better supported to raise biosimilar opportunities more systematically, including developing skills to communicate their views in ways that resonate with formal HTA processes. At the same time the PBAC could do better in being transparent in plain language about its processes and approaches. In practice, patient and clinical groups may be able to upskill faster than HTA bodies are to develop effective two-way communication channels. The broader principle applies beyond Australia: where willingness exists but capability is lacking, targeted upskilling is the lever that converts intent into action.

Early dialogue

Structured dialogue and ongoing review mechanisms

It is important to embed structured dialogue into governance frameworks to ensure that review and reassessment become routine rather than reactive. For HTA agencies, providing early dialogue with industry and regulators on case preparation and data requirements would clarify the scope of the lifecycle assessment to perform and whether the population, indication, or line-advancement expansion is appropriate. Acknowledging these requirements early on could enable efficient investment in evidence generation and more predictable BEAR initiatives.

At post-LoE stage, implementing a routine lifecycle assessment commitment — followed by a BEAR where supported — would replace the current reactive model, in which opportunities to expand access are only pursued when a suitably informed stakeholder happens to raise them. In Australia, for example, this could be embedded within the upcoming 5-year Australian Strategic Agreement between the government and the Generic and Biosimilar Medicines Association, or in similar strategic plans in other countries where relevant.

Proactive horizon scanning and stakeholder engagement.

Health systems should engage early, and more systematically, in spotting opportunities for BEAR in order to realise its full potential. In Germany, for example, supporting proactive biosimilar quota setting at the regional level (through the 17 statutory doctors' associations) would enable early engagement and ensure that quota targets reflect the new competitive landscape, rather than lagging behind on historical prescription data. In Spain, earlier horizon scanning, value-based processes at both regional and central level should be developed and implemented. This would enable anticipation of areas of greater value added by biosimilars and trigger the BEAR process in advance. The MoH would need to step forward in recognising value beyond budget impact, a process that may be ongoing as per the recently approved Royal Decree on HTA (Lamas, 2026) and the one on pricing and reimbursement under political debate for passing (Ministerio de Sanidad, 2024).

Table 7 presents the recommendations discussed above and outlines the key stakeholders for each. Recommendations in the table are made at general level, for ease of interpretation, with country-specific and system-specific nuances detailed within the section above.

Table 7 Recommendations

RECOMMENDATIONS		STAKEHOLDERS						
	Subtheme	Regulators	Payers: private and public	HTA	Providers & NHS	Clinical guideline developers	Patient & public	Industry
HTA, GUIDELINES, PAYERS AND REGULATORY ALIGNMENT	Encouraging global stakeholder collaboration and joint consultations	✓	✓	✓		✓		✓
	Highlighting misalignment between clinical guidelines and payer policies		✓			✓		
	Formal policies supporting routine reassessment of post-LoE medicines		✓	✓				
	Leveraging bottom-up approaches in decentralised health systems		✓	✓	✓	✓		
	Regulatory incentives to reward regulatory and HTA data generation	✓						✓
EVIDENCE GENERATION	Collecting evidence to support reassessment	✓		✓				✓
	Considering use of novel data (i.e. modelling, simulation, pre-clinical data)	✓		✓				
STAKEHOLDER EDUCATION	Raising stakeholder awareness of the value of BEAR		✓	✓	✓	✓	✓	
	Upskilling stakeholders to communicate with each other	✓		✓		✓	✓	✓
EARLY DIALOGUE	Structured dialogue and ongoing review mechanisms	✓		✓				✓
	Proactive horizon scanning and stakeholder engagement	✓	✓	✓				✓

5 Discussion

What does this evidence change about how we should consider biosimilar value?

This section situates the findings within the existing literature, highlights the value added, and draws out implications for decision-makers. The central finding is clear: biosimilar entry does more than lower prices. It can act as an enabler for broadening access, expanding indications, and advancing treatment lines: what this report has termed BEAR. Yet no health system today realises this value systematically, leaving large potential gains untapped, as our modelling illustrates. The imperative for decision-makers is therefore to leverage opportunities to reassess and expand a product's use under its redefined value profile following biosimilar entry, which should be actively and routinely pursued.

These opportunities also apply to small molecules and generics. The underlying logic is the same: when a medicine's lower cost post-LoE redefines its cost-effectiveness, decision-makers and guideline developers should recognise this and act to realise the resulting value. Given the scale of value at stake, these opportunities should be systematically scanned, identified, and realised through dynamic lifecycle reassessment and therapy repositioning.

This report focuses on biosimilars, however. While we recognise the value of post-LoE reassessment and repositioning more broadly, three reasons justify this focus. First, biologics are typically more expensive and more prone to use restrictions than small molecules, creating greater scope for BEAR. Second, biosimilar value remains comparatively untapped: some areas and classes of innovation are approaching LoE without an established biosimilar pipeline (i.e., the “biosimilar void”), meaning they stand to benefit disproportionately from a dynamic reassessment and repositioning approach that could help incentivise investment in those areas. Third, biologics are more commonly multi-indication therapies, increasing their potential for access expansion through reassessment.

England has come closest to developing a systematic approach. Recent NICE initiatives — the collaborative Biosimilar Taskforce (NICE, 2026b) and the Whole Lifecycle Approach programme (NICE, 2026d) — show that institutional capacity can be mobilised around biosimilar entry, though they remain focused on facilitating entry and uptake in low-challenge cases rather than routinely reassessing eligibility, positioning, or target populations. The denosumab and bevacizumab case studies illustrate the value that could be unlocked when reassessment is performed and prior restrictions reconsidered. Across the case studies, the common enabling condition was price erosion, which relaxed budget constraints previously tied to the reference product’s price and created scope to revise prior decisions (NICE, 2026h) and expand eligibility. The institutional pathways differ across settings. NICE in England revisited bevacizumab in mCRC once biosimilar pricing brought it within the cost-effectiveness threshold, while PHARMAC in New Zealand reinvested biosimilar savings in removing use restrictions. However, the underlying logic was the same: biosimilar competition changed the economic case for broader use, and reassessment determined whether the opportunity was realised.

While the bevacizumab case in England demonstrates how extra value can be realised by extending use, the denosumab case illustrates value left on the table when lower prices are not followed by guideline reassessment — substantial cost-offsets and fractures avoided remain unrealised, alongside a missed opportunity for clinicians and a weakened commercial signal to manufacturers. Critically, the magnitude of value scales with the size

of access expansion: a sufficient price reduction is the necessary enabler, but the gain — in health, cost-offsets, or NMB — grows with the newly eligible population. We estimated that where expansion is leveraged to reach millions, the cost-offsets could run to billions, nearly doubling the savings from price reduction alone in the case of denosumab. Systematic BEAR frameworks are therefore essential to realise this value consistently and at scale.

Building those frameworks requires deliberate change across four areas that target the triggers for effective BEAR implementation. Each area was identified as a key recommendation through the expert workshop and supported by the case studies, which generated supporting value estimates based on modelling. First, HTA, guideline, payer, and regulatory alignment. This addresses fragmentation across stakeholders and the lack of a systematic, consistent trigger for reassessment. Second, evidence generation. Strengthening the evidence base needed for reassessment, for example through real-world evidence and other novel data to support extrapolation into new populations or indications, will be important but will require public-sector support and targeted incentives, with early anticipation of evidence generation needs. Third, stakeholder education. Improving awareness of BEAR's value among key stakeholders and upskilling them to communicate with one another, so that they can act as effective lifecycle assessment triggers for BEAR opportunities. Fourth, early dialogue. Structured, proactive engagement to ensure timely opportunity scanning, reassessment, and implementation. Together, these are the levers that turn biosimilar price erosion into enhanced value, realised access, and health gain.

These recommendations respond to a clear gap in the evidence. The biosimilar literature concentrates on uptake and price competition, with less attention to whether lower prices translate into broader patient access and value expansion; the value forgone when lifecycle assessment and BEAR opportunities are not actively sought has neither been systematically examined nor quantified in the literature. The cases identified and reviewed in this research help to address that gap, illustrating the value potential of BEAR using real examples. They show that, although biosimilar-driven price reductions can weaken the rationale for earlier coverage restrictions, access and value only expand where those restrictions are actively revisited. This is particularly evident when BEAR implementation is straightforward, such as in previously appraised but unfunded uses of the therapy. This was the case in the UK for natalizumab whereby the trigger for NICE reassessment was biosimilar entry allowing price competition (24) as well as the case in New Zealand, whereby biosimilar competition prompted PHARMAC to actively revisit Special Authority criteria and reinvest procurement savings to widen eligibility across multiple indications (30).

The modelled case studies quantified the potential value of repositioning, which was corroborated by the expert elicitation exercise. Contributors recognised value beyond price reduction while confirming that post-LoE reassessment remains ad hoc rather than routine. Canada illustrates the drift, moving from HTA review of biosimilars towards direct price negotiation (CDA-AMC, 2019); Spain was described as reactive at regional level with central decision-making authorities insensitive to BEAR-driven value (Río-Álvarez and Cruz-Martos, 2024), and the US as fragmented, with limited payer attention to countervailing incentives from intermediates (i.e. PBMs) in the supply chain. Bodies generating clinical guidelines such as the NCCN Compendium and ESMO may offer a more tractable route, with their guidance also used by clinicians internationally.

Where and how BEAR works depend on the system. In CEA-driven systems, implementation is generally smoother, owing to an explicit decision rule. This is clearest in the UK, where HTA decisions are binding. In budget-impact systems, it rests on identifying stakeholders who recognise BEAR's value beyond cost-savings and can initiate reassessment. This stakeholder mobilisation is equally critical in multi-criteria systems such as Italy and in decentralised or fragmented systems such as the US. In clinical-value-added systems such as Germany, where therapeutic added value is the sole decision criterion, BEAR must instead be built into uptake policy, with demand-side incentives

shaping prescriber and patient behaviour given that access is already unrestricted. This behavioural dimension also conditions CEA-driven and budget-impact systems acting as a set of preconditions that can enable or impede BEAR implementation. In market-based price-negotiation systems, it manifests as the perverse incentives of intermediaries such as US PBMs, who can use market power to limit biosimilar competition and uptake. Policy reform should therefore be considered where needed to create conditions conducive to lifecycle assessment and BEAR. Throughout, country-specific factors mean these conclusions are tendencies, not universal rules. For example, embedding BEAR within HTA may not apply in Canada, where HTA is bypassed, or in Australia, where budgetary considerations dominate for post-LoE products, shifting the focus to decision-maker cost-saving myopia.

BEAR's potential value also reaches beyond the payer, engaging stakeholders motivated by different outcomes. HTA bodies using CEA focus on whether biosimilar-driven cost reductions bring a therapy within the decision threshold and generate positive NMB; payers, policymakers and budget holders focus on financial and fiscal impact; providers weigh both, with an added interest in pathway simplicity; and guideline developers, clinicians, and patients focus on clinical value. The value of BEAR may therefore resonate differently across stakeholders. In the US denosumab case, payers are the primary audience, making the potential $22.9bn in cost-offsets most compelling, while guideline developers, patients, and clinicians may be more interested by the 492,366 fractures that could be prevented; with no national HTA body and payers not bound by HTA, ICER and NMB messaging is of limited relevance. By contrast, the bevacizumab reassessment in England sat within a binding CEA-driven system, where NMB and the ICER's sensitivity to price carried the decisive weight, even as patients and clinicians remained focused on access and health gains.

Unlocking BEAR is ultimately a matter of evidence. Where the required clinical evidence already exists, application is straightforward and needs only economic reassessment. The challenge is greater when BEAR extends to populations or indications for which evidence has not been generated. Originators have limited incentives to develop evidence for lower-value indications, and after LoE neither originators nor biosimilar manufacturers are likely to invest due to free-riding risk. As a result, the incentive structure may prevent these opportunities from being realised. Addressing this means leveraging validated alternative evidence frameworks, such as real-world evidence and registries, digital outcomes data, and AI-, in-silico- or simulation-based models.

We see examples of this pursued through NICE's HTA Innovation Laboratory (NICE, n.d.), the FDA's validation of Bayesian methods (Niazi, 2026a; b) and AMCP's streamlined biosimilar dossier, coupled with proactive horizon scanning. In the EU, the JCA framework could be an enabler of streamlined or accelerated clinical evidence generation and review pathways for biosimilars. The moment is opportune: multiple blockbuster biologics are losing protection (IQVIA, 2023), and the depth of accumulated real-world experience means newer biosimilars enter the market with a well-characterised safety and efficacy record, warranting more streamlined pathways (Simoens, Lockhart and Courmier, 2025; Cohen et al., 2023). Further, changes such as those proposed by the FDA in October 2025 to reduce the need for comparative effectiveness studies for many biosimilars could reduce development costs and further increase the number and timeliness of biosimilars entering the market (FDA, 2025).

These mechanisms operate within a wider structural context that this report does not seek to resolve. Lifecycle reassessment and BEAR can strengthen incentives for biosimilar development by creating additional market opportunities but cannot resolve the broader failure of biosimilar markets. That failure is visible in two symptoms: a shrinking pipeline for branded biologics approaching loss of exclusivity, sometimes termed the "biosimilar void" (IQVIA, 2024, 2023), and recurring supply shortages (Napier et al., 2024; Dranitsaris et al., 2017; Napier et al., 2025). In the US, fragmentation, anti-competitive practices, and misaligned supply-chain incentives have undermined effective competition; in Europe and

elsewhere, cost-containment policies adapted from generic medicines have prioritised short-term price erosion over long-term sustainability.

On the US medical-benefit side, recent evidence documents that even the direct price-competition savings from biosimilar entry are only partially transmitted from manufacturer to system, with buy-and-bill reimbursement structures allowing a substantial share to be retained as hospital margin (Robinson, Kosorukov and Whaley, 2026; Sachs, Dusetzina and Mitchell, 2026). MedPAC-proposed reforms — blended volume-weighted ASP and capped add-on payments — illustrate concrete competition-mechanism instruments that could improve transmission. These reforms address a different mechanism failure from BEAR, but the two are complementary: fixing transmission without unlocking repositioning still leaves a large share of biosimilar value unrealised, and vice versa.

Because global R&D is disproportionately financed through high-income markets, and the United States in particular, market-design failures affecting biosimilar competition in the US carry consequences beyond it, for the sustainability of the biosimilar sector globally and, through it, for access in other jurisdictions. Therefore, addressing this requires market-design reform globally: the US should lead by reducing fragmentation and restoring a credible investment signal. It should also carefully manage the effects of policies such as the Inflation Reduction Act and Most Favoured Nation-style pricing proposals on incentives for biologic and biosimilar development (Verrilli, Vargas and Junghahn, 2024; Jeremias, 2024); Europe must redesign procurement to support uptake while preserving sustainable competition; and lower- and middle-income countries stand to gain most from a stronger global pipeline. Across settings, the guiding principle should be to reward biosimilar development both in already covered indications and populations and through expanded access under BEAR — securing sufficient returns, ensuring multiple viable suppliers, and preventing market power from concentrating at any point in the supply chain.

A strength of this analysis is that it combines four complementary sources of evidence to examine the policy logic underpinning the BEAR framework: a targeted review, illustrative case studies, quantitative modelling, and structured expert workshop, each addressing a different aspect of the same question. The review explains how biosimilar price erosion creates opportunities for reassessment, the case studies illustrate how BEAR-led expanded access may be realised through different institutional pathways, the modelling estimates the potential impacts and value added from broader treatment, and the workshop considers whether the framework is feasible within real-world decision-making environments. We note, however, that these evidence streams were designed to be complementary rather than independent, and their agreement should therefore be interpreted as evidence of a coherent framework rather than as four independent tests of it.

A further strength of the analysis is the deliberately conservative scope of the quantitative modelling. Restricting the denosumab analysis to osteoporosis indications increases confidence in the estimates because the eligible population and treatment gap can be characterised with reasonable certainty. A limitation of this approach is that other indications, in which denosumab is indicated and reimbursed, were not modelled although they represent comparable opportunities for BEAR. Similarly, the bevacizumab analysis is confined to a single lifecycle HTA assessment context within one jurisdiction. The reported estimates should therefore be interpreted as illustrating that BEAR can generate measurable additional value rather than as estimates of the full opportunity. The case studies show what BEAR delivered where it occurred and, for denosumab, what it could deliver, but they do not indicate how often such opportunities arise or how much potential benefit is missed overall. Answering these questions would require systematically tracking biosimilar entries and the reassessments that follow.

The SC provided an opportunity to examine whether the proposed framework reflects the practical realities of reimbursement and implementation that cannot be assessed through

the literature or modelling alone. Participants from the United States, United Kingdom, Australia, Germany, Canada, and Spain contributed perspectives from academia, HTA organisations, public bodies, and related policy settings.

A limitation of the SC's composition is its coverage. The systems represented were all mature ones with established reimbursement processes, but France and Italy were not included, nor were healthcare systems in Latin America, Asia-Pacific, or Africa. A second limitation is the absence of practising clinicians. The expert discussions pointed to their role in turning expanded access into actual uptake, and in some systems, Germany among them, uptake decisions rest heavily with them. Without that perspective, we have less insight into prescribing behaviour, switching practices, and physician- and patient-level barriers to implementation.

These limitations mainly affect the transferability of the findings rather than the validity of the BEAR framework. The opportunity identified here may exist in many healthcare systems, but the mechanisms through which reassessment occurs are likely to differ. We therefore interpret these findings as establishing the principle of BEAR and illustrating the value it can generate, while not quantifying the full scale of that opportunity. The analysis of the expert workshop using a healthcare system typology partially addresses the broader range of systems not captured in the modelled cases. By organising findings across system archetypes and mapping relevant stakeholders within each, opportunities, challenges, and recommendations could be contextualised at a level of generality applicable across comparable systems. Nevertheless, findings were drawn from a defined set of countries and direct input was not available for all system types such as multi-criteria systems and hybrid therapeutic value and cost-effectiveness systems. Consequently, whilst recommendations are applicable at a high level, country-specific operationalisation would require dedicated input from national stakeholders.

6 Conclusion

Where biosimilar competition reduces therapy costs, our analysis suggests substantial untapped value remains in addressing biologic underutilisation across restricted populations, expanded indications, and advanced treatment lines. BEAR offers a mechanism through which this value can be unlocked. It operationalises a global product lifecycle perspective, reassessing biologic therapies in anticipation of and in response to key lifecycle events, in particular reference product loss of exclusivity and biosimilar entry.

This report has developed a BEAR framework inductively from patterns observed across the literature, examined the global evidence base across products, indications, and systems, and used illustrative and modelled case studies to quantify the potential scale of value that lifecycle assessment and BEAR can generate. Taken together, these findings tell a consistent story: lifecycle assessment and BEAR are already applied across different settings, generating substantial value to patients, health systems, and industry beyond price-competition cost-savings alone. However, its routine and systematic adoption remains a key policy gap.

Lifecycle reassessment should move from exception to standard practice in HTA, guideline-setting and adoption incentives design, with shared frameworks that travel globally across system types and income levels. The expert workshop identified the opportunities and challenges associated with this shift, organised within a system typology spanning across CEA-driven systems, budget-impact-driven systems, clinical-value-added systems, and fragmented payer markets. Across systems, understanding key stakeholders and their incentives, raising awareness of BEAR-driven value, and promoting early engagement and collaboration are vital for unlocking biosimilar value through lifecycle assessment and BEAR.

Payers and HTA bodies should embed systematic lifecycle assessment triggers into their processes so that biosimilar entry automatically prompts structured review of whether the new price context justifies expanded access. This would shift reassessment from a reactive and inconsistent process to one that is anticipated, scheduled, and resourced. Clinical societies and guideline developers should treat biosimilar entry as a standing moment to revisit therapy's place in care. This means asking whether therapies previously excluded on cost grounds now warrant recommendation, and identifying areas where biologic therapy could be expanded, including in populations or indications not previously assessed. Guidance should then be updated accordingly. This is a timely opportunity: a wave of major biologics is approaching loss of exclusivity, and embedding systematic lifecycle assessment now would allow health systems to realise this value as soon as it becomes available at loss of exclusivity, rather than leaving it to be picked up years later, if at all.

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Appendix

Appendix A: Targeted Literature Review

Approach and objectives

We developed the evidence base for this report through a targeted review of peer-reviewed, grey, and policy literature undertaken during the project scoping phase. We selected a targeted review because it provides a systematic approach to identifying evidence while applying focused search criteria. We considered this approach appropriate because our research question centred on a recurring pattern of institutional decision-making across multiple products and healthcare systems, rather than on a single clinical or comparative intervention. The review had two complementary purposes: first to identify relevant case studies, and second to inform the inductive development of the analytical framework presented in this report. Specifically, the review focused on:

- Identifying examples where biosimilar market entry was associated with changes in the therapeutic positioning of a biologic medicine, as reflected in HTA decisions, reimbursement or coverage policies, clinical guidelines, or payer policies.
- Identifying and synthesising evidence describing the value and impact of these changes, including effects on patient outcomes, healthcare costs, system efficiency, access to care, equity, and service capacity.

Search strategy and sources

We searched peer-reviewed bibliographic databases, grey and policy literature, and the websites of HTA agencies, payers, and regulators to identify relevant evidence. We supplemented these searches with Google Scholar to identify additional reports and citations and searched the Tufts Medical Center Cost-Effectiveness Analysis Registry for published cost-effectiveness studies and utility estimates. Project Steering Committee members also recommended relevant publications and supplementary sources. Table A1 summarises the sources included in the review.

Table A1 Databases and sources searched

SOURCE	CATEGORY
Medline / PubMed	Peer-reviewed
Embase	Peer-reviewed
Cochrane Library of systematic reviews	Peer-reviewed
EconLit	Peer-reviewed (economics)
HEED (Health Economic Evaluations Database)	Grey literature
INAHTA HTA reports database	Grey literature
HTA agency websites	Policy literature
Payer and regulatory websites	Policy literature

Google Scholar	Peer and grey literature
Tufts CEA Registry	Grey literature

The search strategy combined three primary concept blocks:

- Biologic and biosimilar medicines.
- HTA, reimbursement, guideline, and payer decision-making contexts.
- Therapeutic repositioning, treatment sequencing, eligibility criteria, and changes in patient access.

Table A2 Boolean search strategy

BLOCK	QUERY
Block 1 Biologics and biosimilars	("biosimilar" OR "biosimilars" OR biosimilar* OR "biologic" OR "biologics" OR biologic* OR "biological medicine*" OR "biological product*" OR "monoclonal antibody" OR "monoclonal antibodies" OR "mAb" OR "mAbs")
Block 2 HTA, guideline and payer decision contexts	("health technology assessment" OR "health technology assessments" OR HTA OR "technology appraisal" OR "technology appraisals" OR "reimbursement" OR "reimbursement decision*" OR "coverage decision*" OR "coverage polic*" OR "funding decision*" OR "funding polic*" OR "commissioning" OR "commissioning polic*" OR "clinical guideline" OR "clinical guidelines" OR "practice guideline*" OR "treatment guideline*" OR "treatment recommendation*" OR "position statement*" OR "consensus statement*" OR "formulary decision*" OR "formulary polic*" OR "NICE" OR "National Institute for Health and Care Excellence" OR "NHS" OR "National Health Service" OR "CADTH" OR "IQWiG" OR "HAS" OR "PBAC" OR "AIFA")
Block 3 Repositioning, line of therapy, criteria and pathway changes	("therapeutic reposition*" OR "drug reposition*" OR "drug repurpos*" OR "treatment line" OR "treatment lines" OR "line of therapy" OR "lines of therapy" OR "treatment sequence" OR "treatment sequences" OR "treatment sequencing" OR "step therap*" OR "stepwise therap*" OR "step-wise therap*" OR "treatment pathway" OR "treatment pathways" OR "indication expansion" OR "expanded indication*" OR "indication extension" OR "indication extensions" OR "expanded access" OR "access criteria" OR "access restriction*" OR "eligibility criteria" OR "eligibility restriction*" OR "restriction* relaxed" OR "restriction* removed" OR "restriction* broadened" OR "utilization management" OR "utilisation management")
Block 4 Generics and analogues	("biosimilar" OR "biosimilars" OR biosimilar* OR "biologic" OR "biologics" OR biologic* OR "biological medicine*" OR "biological product*" OR "monoclonal antibody" OR "monoclonal antibodies" OR "mAb" OR "mAbs" OR "generic drug" OR "generic drugs" OR "generic medicine*" OR "generic product*" OR generic*)

Inclusion and exclusion criteria

We assessed records against two inclusion criteria. For repositioning, we included publications that described a case in which biosimilar market entry led to a change in the therapeutic positioning of a biologic medicine, as reflected in an HTA recommendation, reimbursement or formulary policy, clinical guideline, or payer policy. For impact, we

included publications that reported or discussed the consequences of this repositioning, including patient outcomes, cost-savings, healthcare resource use, and broader system-level effects such as improved access, equity, or service capacity.

We excluded records that met none of these criteria. We retained a small number of publications we deemed relevant for the conceptual framing and discussion section of the report, although we did not include these in the formal evidence extraction, as they did not describe specific case examples.

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Case Study screening and selection

Figure A1, adapted from the PRISMA 2020 flow diagram, summarises the screening and study selection process. Table A3 lists all publications that met the inclusion criteria. Of the publications assessed, we carried 23 forward into detailed data extraction and retained a further 2 to inform the introduction and discussion

From the initial set of 23 publications included in data extraction, seven case studies were identified as meeting the inclusion criteria and were used as illustrative examples of BEAR. They are explained in detail in the Appendix C of this report.

Figure A1 PRISMA Flow Diagram for Case Study Selection

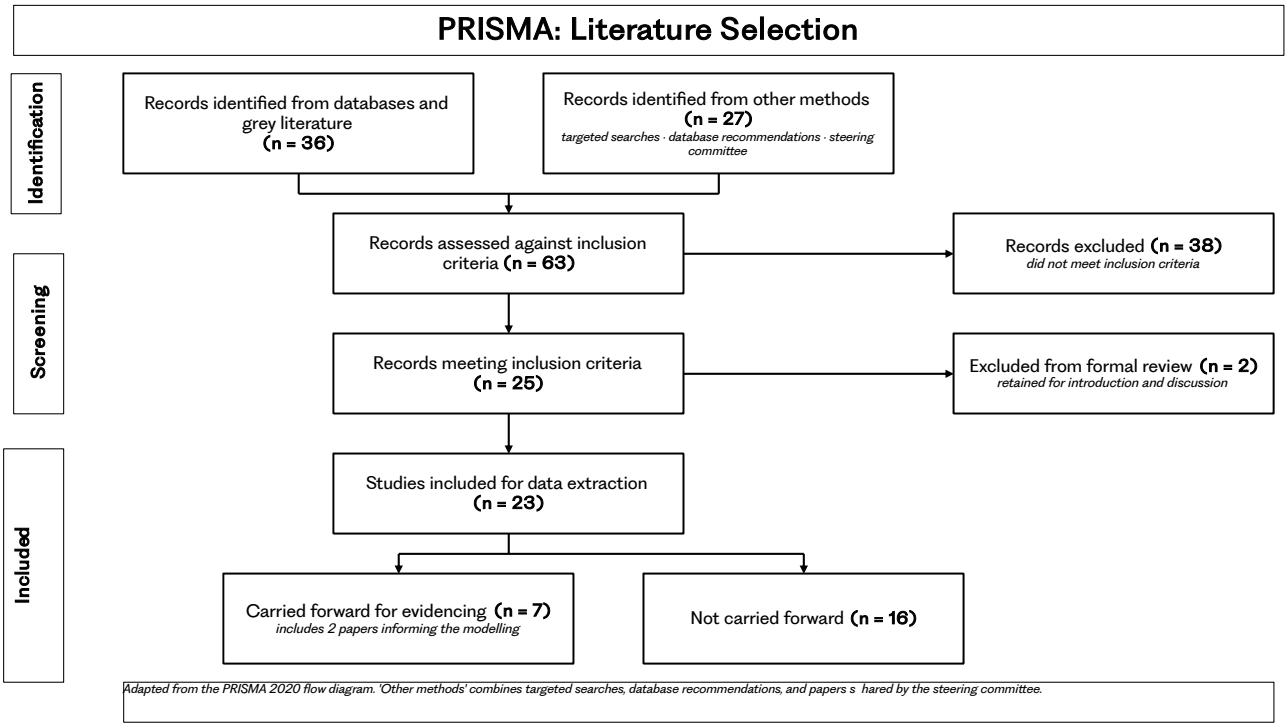


Table A3 Records included as per inclusion criteria

REFERENCE	YEAR	TITLE
(Goll and Kvien, 2023)	2023	Improving patient access to biosimilar tumor necrosis factor inhibitors in immune-mediated inflammatory disease: lessons learned from Norway
(Hörbrand et al., 2023)	2023	PHARAO-Studie: Arzneimittelversorgung entzündlich rheumatischer Erkrankungen (PHARAO study: drug treatment of inflammatory rheumatic diseases)
(Jensen et al., 2020)	2019	for the quick and safe implementation of infliximab and etanercept biosimilars
(Kvien et al., 2025b)	2025	Beyond Cost: Observations on Clinical and Patient Benefits of Biosimilars in Real-World Settings
(Barcina Lacosta et al., 2022)	2022	Qualitative Analysis of the Design and NICE recommend biologics Implementation of Benefit-Sharing Programs for Biologics Across Europe
(Maksabedian Hernandez et al., 2022)	2022	Estimating the impact of biosimilar entry on prices and expenditures in rheumatoid arthritis: a case study of targeted immune modulators
(Moorkens et al., 2023)	2023	A Systematic Literature Review of Gaps and Challenges in Value Assessment of Biosimilars: An ISPOR Special Interest Group Report (scientific, marked as exceptional inclusion)
(Robinson, 2021)	2021	'Milestone' as in moderate rheumatoid arthritis for the first time
(Ruiz-Villaverde and Galán-Gutierrez, 2021)	2020	Biosimilars in psoriasis: what should your positioning be?
(Tam et al., 2025)	2025	Biosimilar Policies and Their Impact on Market Penetration of Adalimumab, Etanercept and Infliximab: A Policy Synthesis and Descriptive Analysis in 13 OECD Countries
(Tan et al., 2024)	2025	Impact of Value-Driven Healthcare Strategies for Biosimilar Adoption: The Singapore Story
(Zhang, 2021)	2021	Biosimilars in Canada: Building momentum in the wake of recent switching policies
(NICE, 2021a)	2021	Adalimumab, etanercept, infliximab and abatacept for treating moderate rheumatoid arthritis after conventional DMARDs have failed
(NICE, 2025b)	2025	Thousands more people with advanced bowel cancer to benefit as NICE approves bevacizumab biosimilars
(NICE, 2025a)	2026	Natalizumab (originator and biosimilar) for treating highly active relapsing—remitting multiple sclerosis after disease-modifying therapy

(PBAC, 2021)	2021	Pharmaceutical Benefits Scheme (PBS)
(PBAC, 2024)	2024	Pharmaceutical Benefits Advisory Committee (PBAC) Meeting Outcomes December 2024
(Department of Health and Aged Care, 2022b)	2022	Pharmaceutical Benefits Scheme — Biosimilar Rituximab
(PHARMAC, 2021b)	2020	Decision To Widen Access to Rituximab and Award Sole Supply
(PHARMAC, 2021d)	2021	Decision to widen access to rituximab for treatment of membranous nephropathy
(PHARMAC, 2021c)	2021	Decision to widen access to rituximab for people with B-cell acute lymphoblastic leukaemia/lymphoma
(PHARMAC, 2021a)	2021	Widened access Special Authority criteria Adalimumab
(PHARMAC, 2021b)	2021	Decision to widen access to adalimumab and award Principal Supply
(PHARMAC, 2022)	2022	Decisions to widen access to rituximab and zoledronic acid
(PHARMAC, 2023)	2023	Decision to fund rituximab for IgG4-related disease

Data extraction and synthesis

For each study included for data extraction, we recorded the biologic product; the country or healthcare system; the biosimilar entry event that triggered the change; the HTA, reimbursement, or guideline decision; affected indications; the framework channel through which repositioning occurred; and the reported impacts for patients, the health system, and payers. The extracted evidence informed the inductive development of the analytical framework set out in Appendix C.

Appendix B: Steering Committee

Role, Composition and Engagement

As part of the evidence generation process, we developed the analysis with input from, and validation by, a steering committee of external experts who contributed across all phases of the project. The committee provided independent methodological oversight by validating the research approach at each stage and reviewing intermediate outputs, including the analytical framework, case-study selection, model assumptions, and preliminary findings.

The committee comprised eight external experts, alongside representation from OHE. We selected experts based on their expertise in health technology assessment, clinical guideline development, and health economics, their capacity to provide methodological oversight, and their geographic diversity. Collectively, they represented six countries: Australia, Canada, Germany, Spain, the United Kingdom, and the United States, providing a range of healthcare system perspectives. Consistent with the approach taken throughout the report, we present the committee's input as part of the study findings rather than attributing contributions to individuals.

We structured engagement around three phases aligned with the scoping, evidencing, and translating stages of the project. We supported these phases through two steering committee meetings and one expert workshop, supplemented by structured written follow-up.

- Scoping phase: We convened a steering committee meeting to validate the scoping approach for the literature review and the development of the analytical framework and to confirm the overall review methodology.
- Evidencing phase: We held a second steering committee meeting to validate the case-study selection and modelling approach, review intermediate outputs, and advise on the application of the analytical framework to assess the identified case studies.
- Translating phase: We conducted an expert workshop to validate findings, contextualise results across HTA and payer systems, gather country-specific perspectives on potential BEAR implementation — including barriers and enablers — and co-develop recommendations.

For SC meetings in scoping and translating phases, we circulated pre-read materials outlining the methodology and inputs under review. In the translation phase, we provided the draft synthesis of findings and structured discussion topics to guide both the workshop discussion and the subsequent written follow-up. Following each meeting and the workshop, we circulated minutes and follow-up queries, enabling experts to confirm the record and address any outstanding questions.

Appendix C Framework and Case Studies

We selected cases in three stages using the framework. First, we narrowed the 25 publications meeting the inclusion criteria to seven illustrative case studies, selecting cases that collectively represented the range of reassessment triggers, repositioning mechanisms, and access pathways the framework captures. Second, we mapped the seven cases against the framework to demonstrate coverage of different BEAR channels identified. Third, we selected two cases for in-depth analysis.

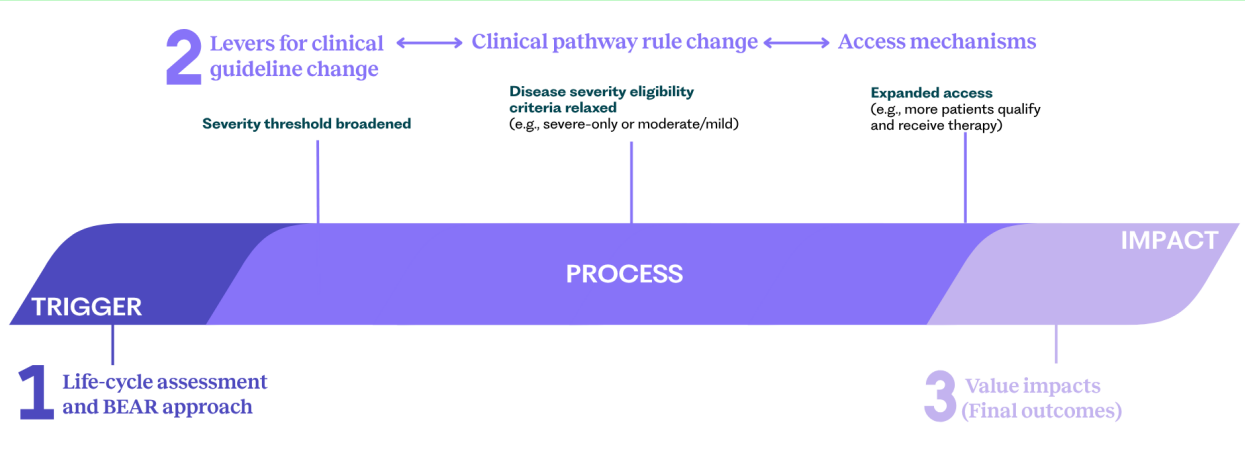
We present detailed descriptions of the seven illustrative case studies in this section.

Natalizumab (England)

Broadening a severity threshold allowed NICE to extend access to natalizumab to a less severe population in England. Biosimilar competition enabled a further (confidential) price discount bringing the therapy within NICE's accepted cost-effectiveness range for its use at lower disease severity. Consequently, patient eligibility moved from rapidly evolving severe to highly active relapsing-remitting multiple sclerosis (RRMS) (Box 1). The price reduction reopened the existing appraisal, so the expansion proceeded through a formal HTA reassessment by NICE, enabled by the biosimilar price discount (NICE, 2021b).

Box 1 Natalizumab (SC originator, IV biosimilar) — England (NICE, 2026c)

	CHANNEL: SEVERITY THRESHOLD BROADENED
System	NICE (England, UK) ·
Indication	Highly active RRMS, in adults who have had at least one prior disease-modifying therapy and at least one documented relapse, and for whom cladribine is unsuitable.
Trigger	England's NICE whole-lifecycle reassessment of a previously unfunded application, enabled by biosimilar price competition and patient demand.
Mechanism of change	Whole lifecycle HTA approach; EAG-built economic model, with cost-effectiveness assessed by incremental NMB; Conditional NICE recommendation at an agreed maximum price via simple commercial contract.
Channel	The severity threshold was broadened: severity eligibility criteria were relaxed, expanding access to a wider patient population.
Impact	Thousands of newly eligible patients gained access to natalizumab, a more effective therapy, following the lowering of the eligibility threshold from rapidly evolving severe to highly active RRMS — within a pool of around 43,000 people with RRMS (NICE, 2026e).



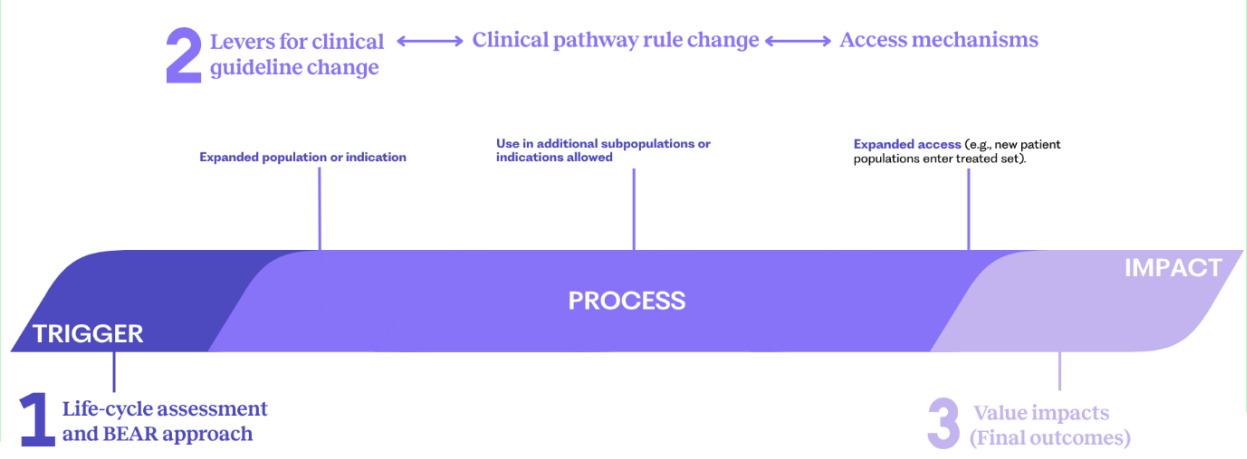
Adalimumab (New Zealand)

Patient population expansion drove a widening of funded access to adalimumab in New Zealand. PHARMAC reinvested the savings from competitive biosimilar pricing into broader eligibility, adding indications that were previously not funded and easing the criteria on existing ones (Box 2). The expansion was not contingent on a new cost-effectiveness appraisal of each indication. Instead, PHARMAC's advisory committee assessed biosimilar equivalence and the safety of switching, while the access changes were implemented through the principal supply award and revised Special Authority criteria, funded from the procurement savings (PHARMAC, 2021b).

Box 2 Adalimumab — New Zealand (PHARMAC, 2021b)

	CHANNEL: EXPANDED POPULATION OR INDICATION
System	PHARMAC (New Zealand)
Indication	Multiple immune-mediated conditions rheumatology, gastrointestinal, dermatological, and other autoimmune conditions.
Trigger	PHARMAC's selection of the biosimilar Amgevita as Principal Supply[1]; biosimilar entry followed by commercial competition.
Mechanism of change	Revised Special Authority criteria, with procurement savings reinvested in widened eligibility across multiple indications. No new cost-effectiveness appraisal of each indication; PHARMAC's advisory committee assessed biosimilar equivalence and switching safety.
Channel	Access was expanded to new populations and indications: previously unfunded indications were added and the criteria on existing ones were eased, expanding and bringing forward access.
Impact	• More than 700 additional patients in the first year, on a base of around 6,400 (PHARMAC, 2021b). • In the first year, expanded access was expected to benefit approximately 130 patients with ulcerative colitis, 340 patients requiring dose escalation for Crohn's disease, and 60 patients with IBD-associated arthritis (PHARMAC, 2021e).

[1]*Principal Supply* is the main funded brand of a medicine in New Zealand. It is awarded by PHARMAC through competitive tender and guaranteed the large majority of the funded market for a set period

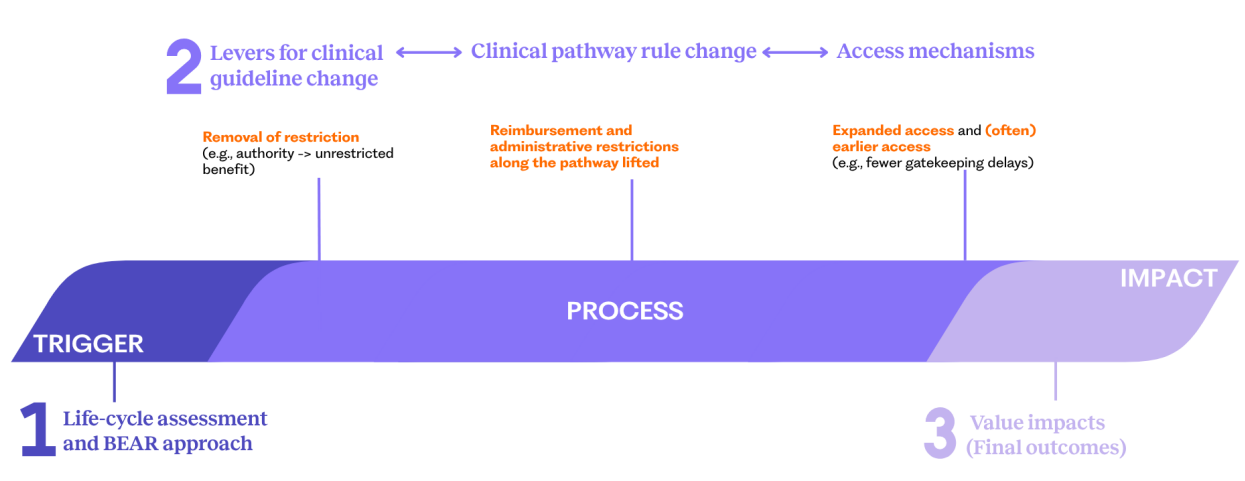


Rituximab (Australia)

Removing a formulary restriction opened subsidised access to rituximab in Australia (Box 3). Biosimilar price erosion and the originator's withdrawal from the Pharmaceutical Benefits Scheme (PBS) allowed PBAC to move all brands to unrestricted benefit, dropping the prior-approval step at initiation (Department of Health and Aged Care, 2022a).

Box 3 Rituximab (all products) — Australia (Department of Health and Aged Care, 2022a)

CHANNEL: REMOVAL OF RESTRICTIONS



System	PBAC (Australia)
Indication	Autoimmune and haematological conditions.

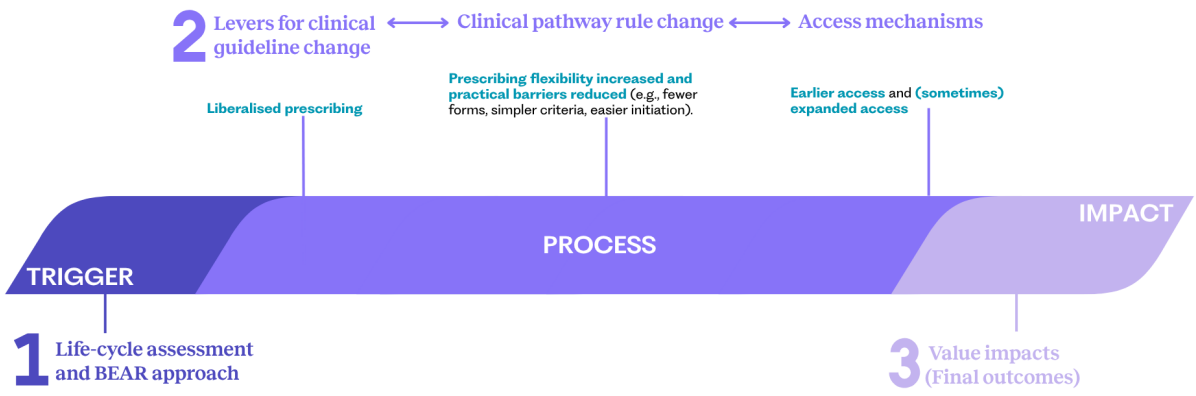
Trigger	PBAC decision to move all rituximab products to unrestricted benefit. Enabled by biosimilar price erosion and the manufacturer's withdrawal of the originator from the PBS.
Mechanism of change	All rituximab products moved from authority required to unrestricted benefit, removing the authority-required step at initiation. The expanded use was judged cost-effective at the reduced price.
Channel	The administrative restriction was lifted, removing the prior-approval step at initiation. Access expanded with fewer gatekeeping delays, allowing more patients to be treated.
Impact	• Opens funded access for ANCA-associated vasculitis, neuromyelitis optica, pemphigus vulgaris, immune thrombocytopenic purpura, and systemic lupus erythematosus (Bray, 2021). • These patients had previously relied on compassionate, hospital or private access only, involving either delayed treatment, or less effective treatment, or higher treatment cost for patients (Bray, 2021). • The expanded use was judged cost-effective at the reduced price (PBAC, 2021).

Filgrastim (Sweden)

Liberalising prescribing redefined who could initiate filgrastim in Sweden's Southern Healthcare Region (Skåne Region), prompted by biosimilar entry and the concomitant price reduction. A multi-physician approval process gave way to streamlined single-physician decisions, and use of granulocyte colony-stimulating factor (G-CSF) rose substantially once that step was removed (Box 4). The clinical case was unchanged but rather the price competition led to the removal of an administrative barrier, that had otherwise delayed access to the therapy (Kvien et al., 2025a).

Box 4 Filgrastim — Sweden (20)

CHANNEL: LIBERALISED PRESCRIBING



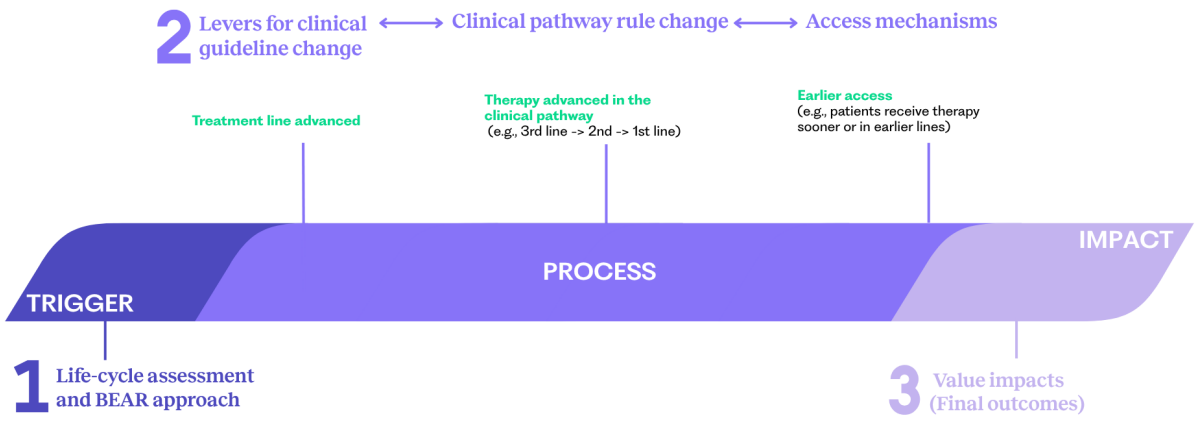
System	TLV / Dental and Pharmaceutical Benefits Agency Skåne Region; Southern Healthcare Region in Sweden
Indication	Neutropenia supportive care.
Trigger	The Southern Healthcare Region's decision to liberalise prescribing controls on G-CSF, enabled by biosimilar filgrastim entry and price competition.
Mechanism of change	Multi-physician approval process replaced by standard single-physician decision-making.
Channel	Prescribing was liberalised: practical barriers to initiation were reduced, giving expanded and earlier access as more patients could receive prophylaxis without separate authorisation
Impact	• Daily use of G-CSF in the region increased approximately fivefold following the relaxation of prescribing restrictions (Kvien et al., 2025a; Cornes and Krendyukov, 2019). • Despite that rise in usage, the region recorded net savings of about €2 million, roughly 4-5% of its total medicine budget in one year alone (Cornes and Krendyukov, 2019). • More patients received prophylaxis, with no separate authorisation required.

Tocilizumab (United States)

The case of tocilizumab in the US illustrates BEAR operating across two channels simultaneously, advancing the treatment line and widening the eligible population. While the clinical rationale for repositioning pre-dated biosimilar competition — driven by high rates of tumour necrosis factor inhibitor (TNFi) therapy failure and safety concerns associated with Janus kinase (JAK) inhibitors — biosimilar-driven price erosion was instrumental in enabling the change. By improving the cost-effectiveness of tocilizumab, lower prices strengthened the economic case for reassessment and helped translate an emerging clinical preference into broader access and earlier use (Box 5).

Box 5 Tocilizumab after TNF inhibitor failure — US (Fraenkel et al., 2021)

CHANNELS: LINE ADVANCEMENT AND EXPANDED POPULATION



System	CMS, US
Indication	Rheumatoid arthritis after failure of TNF inhibitor therapy; giant cell arteritis; juvenile idiopathic arthritis; cytokine release syndrome following CAR-T cell therapy.
Trigger	American College of Rheumatology guideline updates favouring tocilizumab after inadequate response to DMARDs including TNF inhibitors. Biosimilar price erosion was the enabler, improving cost-effectiveness and payer acceptance and translating the clinical preference into broader access.
Mechanism of change	Guideline-driven repositioning from TNFi cycling toward mechanism-of-action switching, supported by lower biosimilar prices. The shift operated through ACR clinical guidance and payer coverage rather than a formal reassessment.
Channel	The treatment line was advanced, with tocilizumab moving to earlier use after first TNFi failure, giving earlier access. The eligible population was widened to include patients in whom JAK inhibitors are avoided, giving expanded access.
Impact	• 1.3 million adults with rheumatoid arthritis in the US; around 52 per cent discontinue their first TNFi(Luozzo et al., 2025).

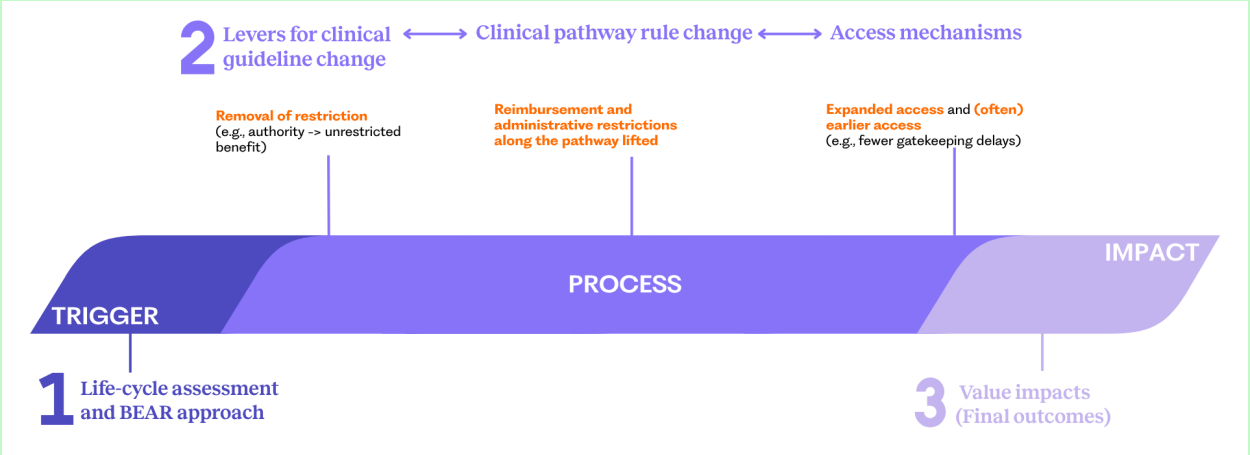
- Improved affordability strengthened the value proposition of tocilizumab relative to TNFi cycling and JAK inhibitors(Luozzo et al., 2025)

Denosumab (United States)

The US FDA's approval of the first interchangeable denosumab biosimilars in 2024 created the conditions for formulary expansion and reduced cost barriers to treatment (Box 6) (FDA, 2024). Within the framework, this represents the removal of access restrictions, with uptake expected to increase through incentivised provider adoption and the extension of prescribing from specialist to primary care settings. Where treatment rates remain low among patients at high risk of fracture, lower treatment costs could improve access and increase uptake within an expanded eligible population — preventing a significant number of fractures and producing substantial improvements in patient outcomes.

Box 6 Denosumab — US (Research, 2024)

CHANNEL: REMOVAL OF RESTRICTION	
System	(CMS), US.
Indication(s)	High-fracture-risk osteoporosis: postmenopausal women, men, glucocorticoid-induced bone loss, and androgen-deprivation-therapy-related bone loss in prostate cancer.
Trigger	US payers are substituting existing patients onto the cheaper biosimilar without widening eligibility to the broader patient population. Biosimilars represent a therapy improvement over the standard of care (SoC) for eligible indications and patients, realising better outcomes and cost-offsets — but because no single body is positioned to reassess coverage and change formulary decisions, this BEAR value remains projected rather than realised. FDA approval of the first interchangeable denosumab biosimilars, delivering price competition, represents the main enabler for potential therapy repositioning.
Mechanism of change	US FDA approval of interchangeable denosumab biosimilars in 2024, leading to formulary expansion. Access widened through incentivised provider adoption and the extension of use from specialty to primary care (FDA, 2024).



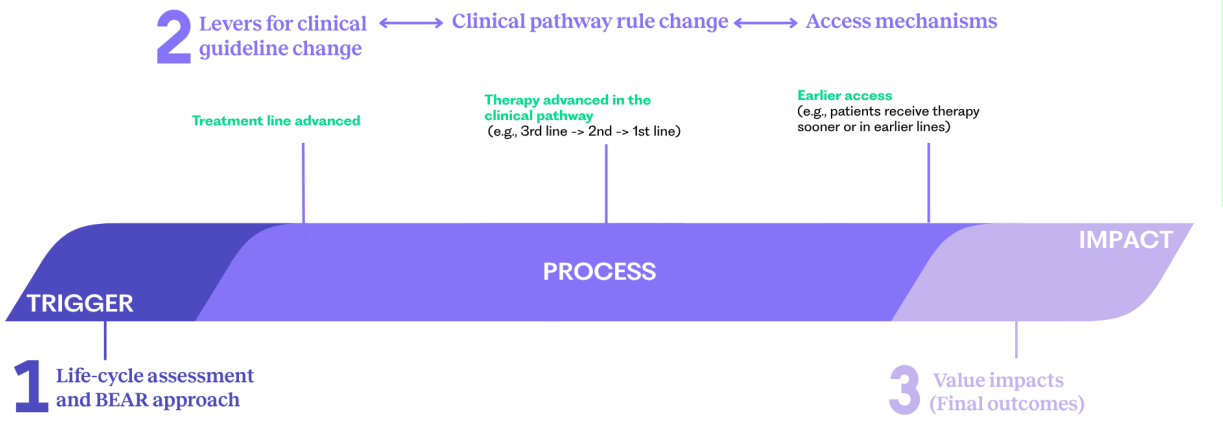
Channel	Removal of restriction: lower cost would relax barriers to treatment, expanding access among high-fracture-risk patients where treatment rates remain low.
Impact	Projected under potential BEAR application: • An eligible pool of around 3.18 million osteoporosis patients across WOP, MOP and GIOP. • Substantial number of prevented fractures, patient outcomes improvement and QALY gains, and cut downstream health-system costs from avoided fractures.

Bevacizumab (England)

Advancing the line of treatment moved bevacizumab earlier in the English treatment pathway for patients with metastatic colorectal cancer (mCRC) (Box 7). Biosimilar pricing brought bevacizumab within NICE's cost-effectiveness threshold as a first- and second-line treatment option for mCRC, securing a positive recommendation the originator product had not achieved at launch owing to its high cost (NICE, 2026h). This resulted in a treatment line advancement for bevacizumab in the NHS England pathway for mCRC, making treatment accessible to 7,000 additional patients who were previously ineligible.

Box 7 Bevacizumab — England (NICE, 2026f)

CHANNEL: TREATMENT LINE ADVANCEMENT	
System	NICE (England, UK) ·
Indication	Adults with mCRC, first- or second-line, where other options are unsuitable.
Trigger	NICE whole-lifecycle reassessment, enabled by biosimilar price competition and patient demand.
Mechanism of change	Whole-lifecycle reassessment under a simplified process, with cost-effectiveness improving on lower biosimilar prices without new clinical evidence. Cost-effectiveness was achieved through the confidential commercial pricing discount rather than at list price.
Channels	Bevacizumab with chemotherapy became available to patients as a first- or second-line option where it had not previously been recommended, advancing the treatment line so more patients gain access and reach it earlier in the pathway.
Impact	More than 7,000 additional patients gained access to bevacizumab in mCRC (NICE, 2026f).



	Treatment available at an earlier line than previous guidance, where other options are unsuitable.

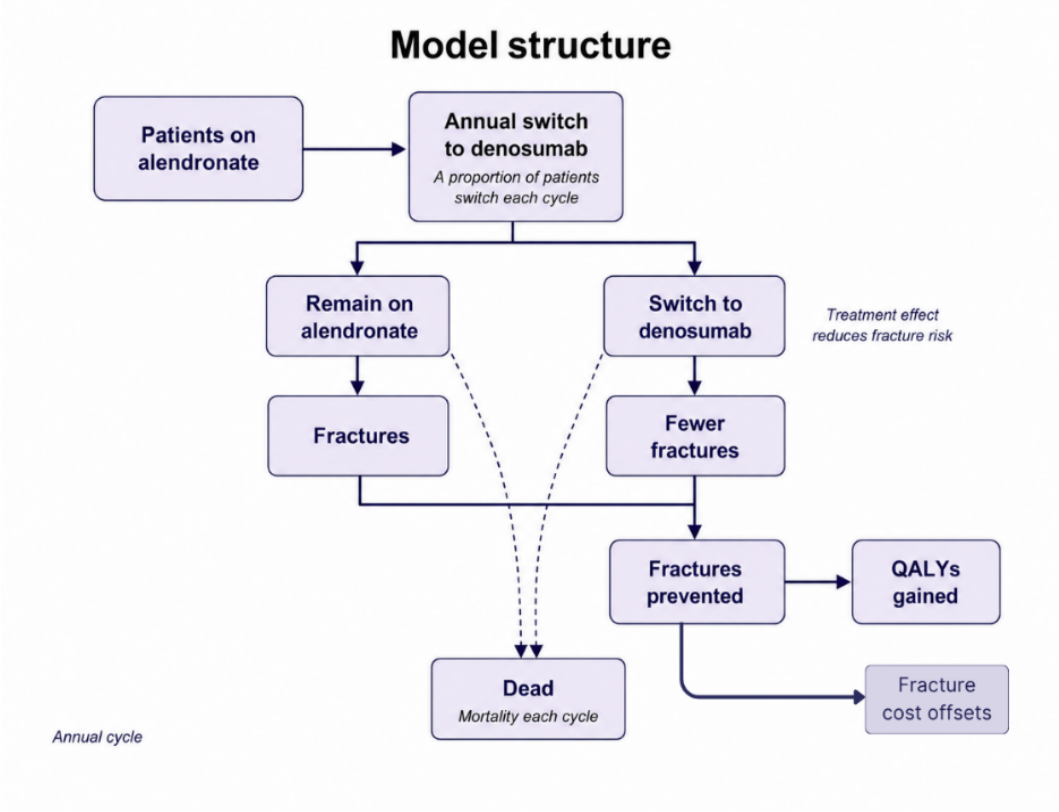
We took two of the seven cases forward for in-depth modelling. We prioritised cases drawn from major pharmaceutical markets in the United States and Europe, across highly differentiated healthcare systems, including one case reflecting cost-effectiveness-driven HTA and ensuring robust and complete data availability. On this basis, we selected bevacizumab in England (NICE) and denosumab in the US (CMS). We describe the detailed modelling approach followed for the two cases in Appendix D.

Appendix D: Modelled Case Studies

Denosumab Case Study

We model the adoption of biosimilar denosumab in place of oral alendronate among eligible high-risk osteoporosis populations in the United States to quantify the value of therapy repositioning after biosimilar entry. Three populations at high-risk of fracture are modelled separately: postmenopausal women over 65 with osteoporosis, men over 70 with osteoporosis, and patients over 55 with glucocorticoid-induced osteoporosis. The analysis takes a US payer perspective over a lifetime horizon, with patients progressing through annual cycles. The model structure is represented in Figure D1.

Figure D1 Denosumab model structure



Calculating the cost-effectiveness of denosumab

For each population, fractures are estimated from an untreated baseline rate adjusted for treatment effect, and costs are accrued for medicine acquisition, administration, the fractures that occur, and other healthcare resource use. Health gains are measured in quality-adjusted life years (QALYs) using published incremental QALY gain estimates for denosumab relative to alendronate. Costs and QALYs are discounted at 3% per year.

Cost-effectiveness is expressed as an incremental cost-effectiveness ratio (ICER): the net incremental cost divided by the incremental QALY gain of denosumab relative to alendronate.

Fracture incidence

Fracture incidence is estimated in two stages. We first apply the relative risk reduction (RRR) for alendronate compared with no treatment to the untreated fracture rate. We then apply the RRR for denosumab compared with alendronate. The difference between treatment arms gives the number of fractures prevented.

$$Alendronate\ rate = Untreated\ rate \times (1 - RRR, alendronate\ vs\ untreated)$$

$$Denosumab\ rate = Alendronate\ rate \times (1 - RRR, denosumab\ vs\ alendronate)$$

$$Fractures\ prevented = (Alendronate\ rate - denosumab\ rate) \times Treated\ population$$

Costs and cost-offsets

The incremental treatment cost per patient is the difference in annual medicine and administration cost between denosumab and alendronate. Preventing a fracture avoids its treatment cost, so the fractures prevented are valued at the cost per event and netted off. Net incremental cost is the incremental treatment cost less these fracture cost-offsets, together with any other healthcare resource use.

$$Incrementaltreatmentcost = (Denosumab\ drug + administration) - (Alendronate\ drug + administration)$$

$$Fracture\ costoffset = \Sigma[Fractures\ prevented \times Cost\ per\ fracture]$$

Accounting for Second fracture

Patients who sustain an initial fracture are at increased risk of a subsequent fracture. Preventing an initial fracture therefore also reduces the likelihood of future fractures. To realise this additional benefit, the model includes a second-fracture module that is applied from year 10 onwards, after the primary-fracture module has captured the direct impact of the treatment on the risk of first fractures(Ha et al., 2025). This timing reflects the point at which a meaningful proportion of the cohort is at risk of a second fracture. Within this module, patients switched to denosumab are assumed to have a lower rate of second fractures than those remaining on alendronate. The reduction is based on the relative risk reported in the post hoc analysis of (2019) and is applied uniformly across hip, vertebral, and non-vertebral fractures. The difference in second fractures between the treatment arms represents additional fractures avoided with denosumab, with each fracture avoided contributing the corresponding cost-savings and QALY gains(Johnson et al., 2021).

Cost-effectiveness

We compare the ICER with willingness-to-pay thresholds of US ranging within $100,000-$150,000 per QALY (ICER, 2023). We also report the NMB at both thresholds.

Model inputs

The parameters entering the calculation, with their values and sources, are set out in Tables D1

Table D1 Model inputs

	PARAMETER	VALUE	SOURCE
COHORT AND TIME HORIZON	Treatment horizon	Lifetime	Model parameter
	Cycle length	1 year	(Yeh, Saeedian and Badaracco, 2025)
	Perspective	US payer	Model parameter
	Discount rate (costs and QALYs)	3% per year	Model parameter
	Cost-effectiveness benchmark	$100,000—$150,000 per QALY	(ICER, 2023)
ELIGIBLE POPULATIONS	Women with OP (over 65, high risk)	2,000,000	(Sarafrazi et al., 2021; Milliman, 2021)a
	Men with OP (over 70, high risk)	800,000	(Sarafrazi et al., 2021; Milliman, 2021)b
	GIOP (over 55, treatment-eligible)	375,000	(Humphrey et al., 2023)c
	Combined total	3,175,000	(Milliman, 2021)d
UNTREATED FRACTURE RATES (PER PATIENT-YEAR)	Women OP — Hip	0.01	(Lewiecki et al., 2020)
	Women OP — Vertebral	0.02	(Lewiecki et al., 2020)
	Women OP — Non-vertebral	0.02	(Lewiecki et al., 2020)
	Men OP — Hip	0.01	(Lewiecki et al., 2020)
	Men OP — Vertebral	0.01	(Lewiecki et al., 2020)
	Men OP — Non-vertebral	0.02	(Lewiecki et al., 2020)
	GIOP — Hip	0.01	(Humphrey et al., 2023)

	GIOP — Vertebral	0.03	(Humphrey et al., 2023)
	GIOP — Non-vertebral	0.02	(Humphrey et al., 2023)
FRACTURE RISK REDUCTIONS (RRR)	Alendronate vs untreated — Hip	38%	(Wells et al., 2025)
	Alendronate vs untreated — Vertebral	47%	(Wells et al., 2025)
	Alendronate vs untreated — Non-vertebral	20%	(Wells et al., 2025)
	Denosumab vs alendronate — Hip	60%	(Yeh, Saeedian and Badaracco, 2025)
	Denosumab vs alendronate — Vertebral	68%	(Yeh, Saeedian and Badaracco, 2025)
	Denosumab vs alendronate — Non-vertebral	45%	(Yeh, Saeedian and Badaracco, 2025)
QALY INPUTS	Lifetime incremental QALYs — Women OP	0.058	(Yeh, Saeedian and Badaracco, 2025)
	Lifetime incremental QALYs — Men OP	0.052	(Silverman et al., 2015)
	QALY gain per second fracture avoided (annualised)	0.0018	(Johnson et al., 2021)
MEDICINE AND ADMINISTRATION COSTS (ANNUAL PER PATIENT)	Biosimilar denosumab, WAC (before erosion)	$3,300/year	(Medi-Span, 2026)
	Denosumab administration	$207/year	(Yeh, Saeedian and Badaracco, 2025)
	Alendronate	$44/year	(Yeh, Saeedian and Badaracco, 2025)
	Alendronate administration	$110/year	(Yeh, Saeedian and Badaracco, 2025)
FRACTURE COSTS (PER EVENT)	Hip	$51,760	(Yeh, Saeedian and Badaracco, 2025)
	Vertebral	$47,898	(Yeh, Saeedian and Badaracco, 2025)
	Non-vertebral	$43,462	(Yeh, Saeedian and Badaracco, 2025)

SECOND-FRACTURE MODULE	Second-fracture rate, alendronate arm	10.10 per 100 pt-yrs	(Kendler et al., 2019)
	Second-fracture rate, denosumab arm	5.80 per 100 pt-yrs	(Kendler et al., 2019)
	Second-fracture RRR (denosumab vs alendronate)	43% (HR 0.57)	(Kendler et al., 2019)
	Year second fractures begin	Year 10	(Johansson et al., 2017)
	RRR applied across fracture types	Hip, vertebral, non-vertebral	
MORTALITY	Mortality source	US Life Tables 2022	(NCHS, 2025)

[a]*Postmenopausal women aged ≥65 at high risk of fracture. The age- and sex-specific osteoporosis prevalence reported by Sarafrazi et al. (2021) from NHANES 2017–2018 was applied to the US resident female population aged ≥65 and narrowed to the high-risk, treatment-eligible subgroup using Medicare osteoporotic-fracture data (Milliman, 2021) and payer and clinical definitions of high fracture risk (prior fragility fracture, femoral-neck or spine T-score ≤ −2.5, or multiple clinical risk factors). Sarafrazi et al. (2021) reports prevalence rates only; the absolute figure is an Organon extrapolation*

[b]*Men aged ≥70 at high risk of fracture. Derived on the same basis, applying the male osteoporosis prevalence in adults aged ≥65 reported by Sarafrazi et al. (2021) to the US resident male population aged ≥70 and restricting to the high-risk, treatment-eligible subgroup using Medicare osteoporotic-fracture data (Milliman, 2021) and payer and clinical high-risk criteria. The absolute figure is an Organon extrapolation from the prevalence rates reported by Sarafrazi et al. (2021).*

[c]*Patients aged ≥55 with glucocorticoid-induced osteoporosis eligible for treatment. Based on the long-term systemic glucocorticoid-exposure and treatment-eligibility framework in Humphrey et al. (2023) (2022 ACR GIOP guideline: ~1% of the US population on long-term glucocorticoids; treatment threshold ≥2.5 mg/day prednisone-equivalent for >3 months), applied to the US population aged ≥55 and complemented with supplementary prevalence data on osteoporosis among chronic glucocorticoid users. Humphrey et al. (2023) does not report an absolute count; the figure is an Organon extrapolation.*

[d]*WOP + MOP + GIOP = 3,175,000 (≈3.18 million) eligible patients, reflecting informed extrapolations from published prevalence data, Medicare osteoporotic-fracture data (Milliman, 2021), and payer and clinical definitions of high risk, as no direct epidemiological estimate of the treatment-eligible population was available in the literature or databases.*

Estimating net monetary benefit and population impact

Net monetary benefit (NMB) restates health and economic value of an intervention in monetary terms. It monetises the incremental QALYs at the cost-effectiveness benchmark and subtracts the incremental cost. A positive NMB indicates that the monetary value of health gain outweighs the additional cost at the benchmark.

$$NMB = (Incremental\ QALYs \times CostEffectivenessThreshold) - IncrementalCost$$

Population outcomes scale the per-patient results by the number of patients treated, derived by applying a scenario-specific switching trajectory to the eligible population in each year. Patients who switch to denosumab are assumed to remain on it for the remainder of the horizon.

$$Treated\ patients(year\ t) = Eligible\ population \times Cumulative\ switching\ rate(year\ t)$$

Additional patients treated, the fractures prevented and the QALYs gained are all derived from the treated population. The switching trajectories are summarised in Table D2.

Scenarios modelled

We model biosimilar entry under three scenarios, each pairing an adoption speed with a level of price erosion, so the results span the plausible range of market outcomes. A patient who starts denosumab stays on treatment to the end of the horizon in every scenario. Under the base case, uptake rises along an S-curve (see Table D2) and the price falls to about 60% below the originator WAC by year five (Beinfeld et al., 2024).

Table D2 Scenario assumptions

SCENARIO	UPTAKE / SWITCHING	PRICE EROSION (OFF WAC)
Lower bound	Minimal adoption; cumulative plateau of 8—15% (WOP), 10—18% (MOP), 12—20% (GIOP)	30% from year 1
Base case	S-shaped: 10% (Year 1), 25% (year 2), 42.5% (Year 3), 60% (Year 4), 75% (Year 5), 85% (Year 6)	35% (Year 1), 48% (Year 2), 52% (Y3), 56% (Year 4), 60% (Year 5)
Upper-bound	100% from year 1	70% from year 1

Cost-savings from price competition

To isolate the saving attributable to price competition alone, we compare denosumab medicine costs under current-practice uptake at the originator WAC against the same population at the base-case biosimilar discount, holding the treated population constant at the lower bound scenario uptake level. The difference is the medicine cost-saving generated purely by price erosion, with no reassessment or guideline change. It is estimated from a health system perspective, discounted over the model horizon and adjusted for all-cause mortality.

Bevacizumab Case Study

Approach to Modelling

We use a simple incremental cost-effectiveness approach, isolating medicine acquisition cost as the only variable that changes across NICE's reassessment of bevacizumab in metastatic colorectal cancer (mCRC) at biosimilar entry. Clinical efficacy is held constant across all scenarios on the basis that the biosimilar and originator are therapeutically equivalent. This ensures that any change in the ICER is driven solely by price variation and, therefore, a consequence of biosimilar competition. The ICER is calculated as the incremental cost of adding bevacizumab to chemotherapy divided by the incremental QALY gain.

The Incremental costs comprise medicine and non-medicine components. Medicine costs are calculated as the price per vial multiplied by the number of 400 mg vials required per cycle and the number of treatment cycles, with rounding to whole vials due to an assumption of non-shareability. Non-medicine costs include incremental administration and monitoring costs per cycle relative to chemotherapy alone, summed across all cycles, plus an assumed one-off cost for managing bevacizumab-related adverse events.

Each calculated ICER is compared against NICE's £30,000 per QALY threshold to assess cost-effectiveness at the modelled price. We hold efficacy constant across all price scenarios in line with NICE's approach, reflecting therapeutic equivalence between the biosimilar and the originator. The base-case incremental QALY gain is 0.31 QALYs (Botrel et al., 2016), and we apply this in the ICER denominator.

Medicine Pricing, Dosing, and Cost Inputs

The NHS net acquisition price for the biosimilar is not publicly reported in NICE guidance, as it reflects confidential commercial discounts, meaning the actual net price is not observable. NICE reports the cost-effectiveness outcomes after reassessment based on these confidential arrangements but does not disclose the underlying NHS acquisition price. We therefore estimated a plausible price range using the literature on price erosion following biosimilar entry (Lee et al., 2024), together with inferences drawn from appraisal records indicating that cost-effectiveness is achieved under confidential discounts below the published British national formulary (BNF) list prices for both the originator and biosimilars.

We take the BNF list prices for the originator and the lowest-cost biosimilar and use the model to derive the threshold biosimilar price at which treatment becomes cost-effective. Cost inputs are summarised in Table D3, and list prices are reported in Table D4.

Table D3 Model inputs and sources

PARAMETER	VALUE	SOURCE
Patient weight	70 kg	Modelling assumption
Dose	5 mg/kg	(NHS, 2020)
Vial size	400 mg (1 vial/cycle after rounding)	(NHS, 2020)
Cycle length	2 weeks	(NHS, 2020)
Treatment course	10 cycles	(NHS, 2020)
Administration cost	£286.71 per cycle	(NICE, 2026f)
Monitoring cost	£25.00 per cycle	(NICE, 2026f)
Adverse-event management	£200.00 one-off	(NICE, 2026f)
Originator price	BNF list price	(NICE, 2026f; a)
Biosimilar list price	Lowest published list price	(NICE, 2026f; a)
Biosimilar net price	Estimated	Authors' estimation

For dosing, we assume an average patient weight of 70 kg and a dose of 5 mg/kg, giving a 350 mg dose per cycle. This requires one 400 mg vial per cycle after rounding, as vials cannot be shared between patients.

NMB and population impact

Alongside the ICER, we calculate the NMB per patient. The incremental QALY gain is held constant (Section D.2) and valued at the NICE cost-effectiveness threshold. The incremental cost is netted off in the calculation.

$$NMB = (incremental\ QALY\ gain \times threshold) - incremental\ cost$$

Because the health gain is fixed, NMB varies only with price, so it measures whether the modelled price delivers value for money at the threshold. Per-patient NMB is then scaled to the treated population (annual eligible cohort × uptake) to give the aggregate monetary value of the health gain in each year.

Price sensitivity analysis

We assess whether acquisition cost is the binding constraint on cost-effectiveness by varying the biosimilar vial price from £50 to £900 in £50 increments and recomputing the ICER at each price while holding all other parameters constant. We calculate the originator ICER in parallel as a fixed reference and we record the implied discount relative to the originator at each price point. This approach identifies the break-even price, defined as the highest vial price at which the ICER remains at or below £30,000 per QALY. We also report the percentage price erosion required from the originator price to reach this break-even point following biosimilar entry.

Biosimilar competition cost-savings in other indications

We estimated savings from biosimilar competition for each previously approved indication by multiplying the treated indication population by the per-patient cost-saving, defined as the difference between the originator price and the estimated biosimilar price, and summing across indications.

$$Cost\ saving\ per\ patient = Originator\ price - (Launch\ list\ price \times Erosion\ rate)$$

$$Total\ cost\ saving = Cost\ saving\ per\ patient \times Treated\ population\ (other\ indications)$$

Treated populations are taken from NICE resource impact templates for TA946 (olaparib plus bevacizumab; ovarian, fallopian and peritoneal cancer), TA939 (pembrolizumab plus chemotherapy with or without bevacizumab; cervical cancer), TA666 (atezolizumab plus bevacizumab; hepatocellular carcinoma), and TA1022 (bevacizumab gamma; wet age-related macular degeneration).

Population estimates are applied according to the structure reported in each template. For TA946 and TA939, NICE reports the expected treated population, which already incorporates uptake, and we use these values directly. For TA666 and TA1022, NICE reports only the eligible population; we therefore assume For TA666 and TA1022, NICE reports only the eligible population, so we assume 100% uptake in line with the NHS commercial framework, which likely overestimates savings for these indications. Where no resource impact template was available, the eligible population was taken from the corresponding NICE appraisal, which reports a single year of data; this was extrapolated over five further years at 1% annual growth, a conservative proxy for underlying incidence growth chosen to avoid overstating later-year patient volumes. We apply the competitive biosimilar price uniformly across all biosimilars and hold it constant over a six-year time horizon. This counterfactual assumes no HTA reassessment occurs, thereby isolating savings attributable to biosimilar price competition alone, meaning cost-savings from mCRC indication are not accounted.

Table D4 NHS Indicative prices of Bevacizumab originator and biosimilars as of February 2026 (NICE, 2026a)

BRAND	MANUFACTURER	TYPE	NHS INDICATIVE PRICE (£/VIAL)
Avastin	Roche Products Ltd	Originator	924.40
Versavo	Dr Reddy's Laboratories (UK) Ltd	Biosimilar	924.40
Zirabev	Pfizer Ltd	Biosimilar	902.70
Oyavas	Thornton & Ross Ltd	Biosimilar	877.80
Alymsys	Zentiva Pharma UK Ltd	Biosimilar	810.10
Abevmy	Biosimilar Collaborations Ireland Ltd	Biosimilar	810.00
Bevqolva	CuraTeQ Biologics s.r.o.	Biosimilar	810.00
Vegzelma	Celltrion Healthcare UK Ltd	Biosimilar	810.00

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