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How Can a Medicine Be Cost-Effective Yet Unaffordable? Reconciling Value, Budget Impact, Cash-Flow Timing, and Health-System Displacement

Lucas Meyer[1]*, Aisha Khan[2], Peter Nagy[3]

[1]Department of Health Economics and Pharmaceutical Policy, Faculty of Pharmacy, University of Amsterdam, Amsterdam, Netherlands.
[2]Department of Pharmacy Administration and Health Economics, Faculty of Pharmacy, Lahore University of Management Sciences, Lahore, Pakistan.
[3]Department of Pharmaceutical Policy and Health Financing, Faculty of Pharmacy, Corvinus University of Budapest, Budapest, Hungary.

***E-mail** ✉ lucas.meyer@uva.nl

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ABSTRACT

A medicine can represent good value for money and still create an adoption problem for a health system. Cost-effectiveness evaluates incremental costs and consequences relative to an alternative, whereas affordability depends on the scale and timing of expenditure, the population eligible for treatment, the resources required to deliver care, and the services displaced when additional resources cannot be obtained immediately. These quantities can move in different directions. A therapy with a favorable lifetime cost-effectiveness profile may require concentrated expenditure before benefits or offsets occur, may create a large aggregate budget impact because many patients are eligible, or may require scarce diagnostic, treatment, monitoring, and administrative capacity. Conversely, a medicine with a high acquisition cost can sometimes be accommodated when eligible volume is small, payment is distributed over time, or additional resources can be mobilized without substantial displacement. This Practical Application separates value, budget impact, cash-flow timing, implementation capacity, and health-system displacement as related but non-equivalent reimbursement quantities. It examines when marginal cost-effectiveness reasoning becomes unreliable for large expenditure changes, how payment arrangements alter financial timing without necessarily reducing total expenditure, and why nonfinancial constraints can remain binding after funding is secured. The practical implication is that reimbursement should identify the source of the affordability problem before selecting a policy response. Cost-effectiveness remains necessary for judging value, but it cannot by itself determine whether adoption is financially and operationally feasible within a particular health system and time horizon.

Keywords: Cost-effectiveness, Affordability, Budget impact, Health opportunity cost, Cash-flow timing, Managed entry agreements

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Introduction

Cost-effectiveness and affordability enter reimbursement decisions because both concern scarce resources, yet they answer different questions. Cost-effectiveness asks whether the incremental health produced by a medicine is worth its incremental cost relative to an appropriate comparator. Affordability asks whether the resulting expenditure can be financed and implemented within the relevant institutional, temporal, and operational constraints. Contemporary value-assessment approaches increasingly acknowledge this separation by considering budget impact alongside conventional assessments of incremental value rather than treating the two quantities as interchangeable [1].

The distinction becomes especially important when the size of the eligible population or the concentration of expenditure changes. A medicine used in a small population may impose a high cost per treated patient but only a limited aggregate financial commitment. A treatment for a prevalent condition may create a much larger fiscal requirement even when its cost-effectiveness is favorable. Potentially curative therapies create another configuration: expenditure can be concentrated near treatment initiation while health gains, avoided complications, and any cost offsets accumulate over much longer periods [2]. Affordability can therefore deteriorate without any corresponding deterioration in the medicine's incremental clinical value.

Large budget changes also challenge the assumption that the health displaced by additional expenditure can always be inferred from a marginal cost-effectiveness threshold. When a new technology absorbs a nonmarginal share of available resources, the services displaced may differ from those represented by a marginal estimate of health-system productivity. The resulting opportunity cost can therefore depend on the scale of the budget change and on how the health system actually adjusts expenditure, capacity, and activity [3]. The relevant issue is not simply whether the new medicine produces sufficient health per unit of cost, but what the system must forego to accommodate adoption at the required scale.

"Affordability" itself must be specified carefully. The literature contains multiple definitions and measurement approaches, including expenditure relative to available budgets, financial sustainability, fiscal impact, and the feasibility of adopting an intervention without unacceptable consequences elsewhere in the system [4]. For this article, affordability is used operationally to mean the ability of a payer and delivery system to finance and implement an intervention for the relevant eligible population over the relevant decision horizon without displacement or operational consequences judged unacceptable within that jurisdiction. This definition deliberately avoids implying a universal monetary cutoff.

Actual reimbursement processes reinforce the difference between economic value and budget feasibility. Dutch decision evidence shows that budget impact and cost-effectiveness can perform different functions at different stages of reimbursement assessment [5]. Budget impact can trigger additional scrutiny even when the incremental value case is otherwise favorable, while its relevance can vary according to the decision being made. This makes affordability partly an institutional question: the same projected expenditure may be manageable under one financing arrangement and problematic under another.

Stakeholders likewise do not treat budget impact as a mechanically weighted extension of the cost-effectiveness ratio. Interviews with Dutch decision-makers and pharmaceutical-sector representatives found variation in how budget impact was interpreted and when it was considered relevant [6]. Such variation does not make budget impact arbitrary. It indicates that an affordability judgment combines technical estimates with explicit institutional constraints, including available budgets, timing, authority to redistribute resources, and the consequences of doing so.

Even the interpretation of a cost-effectiveness threshold requires attention to context. Theoretical relations among willingness to pay, health-system productivity, and the value of health depend on assumptions that are not automatically satisfied in routine policy settings [7]. A reimbursement process should therefore avoid turning a cost-effectiveness threshold into a surrogate affordability threshold. The central practical problem is to establish which economic or operational quantity is binding in a particular decision and to preserve the distinction between incremental value and the feasibility of financing adoption.

Value, budget impact, and affordability are non-equivalent decision quantities

Expanding an economic evaluation beyond health effects does not remove opportunity cost; it changes what must be considered displaced. Broader cost-effectiveness approaches that incorporate additional dimensions still require consistency between the benefits counted and the consequences of committing resources to one use rather than another [8]. This is directly relevant to affordability. Financial pressure, implementation resources, and broader consequences cannot be added to a reimbursement judgment as if they were costless decision criteria.

The institutional meaning of a cost-effectiveness threshold is also heterogeneous. Comparative evidence across nine countries shows substantial variation in whether thresholds are formally adopted, how they are used, and whether they function as financing, reimbursement, or pricing criteria [9]. A value judgment derived in one institutional setting therefore does not supply a portable affordability rule for another. Jurisdictions differ in their authority to change budgets, negotiate prices, shift expenditure across sectors, defer implementation, or accept temporary financial pressure.

Observed reimbursement behavior may reveal valuations that are not equivalent to a formally declared incremental cost-effectiveness threshold. Analyses of German pharmaceutical reimbursement under AMNOG illustrate how observed decisions can be examined for implicit willingness-to-pay patterns while remaining embedded in a system that does not operate through a conventional statutory ICER threshold [10]. Such evidence reinforces the need to distinguish the economic concept of value from the institutional rule used to convert evidence into a reimbursement or pricing decision.

Value is also dynamic. Comparators change, competing treatments enter or leave practice, prices evolve, and new evidence modifies estimates of benefits, harms, and resource use. A cost-effectiveness-based price that appears aligned with value at launch may cease to have the same interpretation after those conditions change [11]. Affordability can evolve even faster because eligible population size, uptake, expenditure concentration, and delivery requirements can change before the evidence base supporting lifetime value has materially matured.

Price introduces another distinction. A medicine's price is neither identical to its incremental value nor to the opportunity cost imposed on the health system. Fair-pricing analysis can require simultaneous consideration of supply-side health opportunity cost, demand-side willingness to pay, and incentives for innovation [12]. The existence of these separate quantities makes a single composite "value-and-affordability" score difficult to defend without strong additional assumptions. In practical reimbursement, the more transparent approach is to state which question is being answered and which constraint is being tested.

The principal economic quantities are therefore better retained as analytically separate questions before they are brought together in a final reimbursement judgment.

Table 1. Five economic quantities that can lead to different reimbursement conclusions

Economic quantity	Primary question	Unit of concern	Why a favorable result on another dimension is insufficient	Typical decision sensitivity
Incremental value / cost-effectiveness	Is the additional health or other accepted benefit worth the additional resource use relative to the comparator?	Incremental costs and consequences per treated population or patient	Good value does not specify the total expenditure required for all eligible patients	Comparator, treatment effect, price, horizon, discounting
Budget impact	What additional expenditure or saving will adoption create for the relevant payer over the budget horizon?	Aggregate payer expenditure	A favorable ICER may coexist with a large eligible population or rapid uptake	Population size, uptake, substitution, local prices, budget horizon
Cash-flow timing	When must payments be made, and when do savings or avoided costs occur?	Time profile of expenditure and offsets	Similar lifetime costs can impose very different near-term financing requirements	Upfront payment, installments, outcome contingency, timing of offsets
Affordability	Can the intervention be financed and implemented under the payer's relevant constraints without unacceptable consequences elsewhere?	Jurisdiction-specific fiscal and operational feasibility	Neither cost-effectiveness nor budget impact alone defines what the system can absorb	Available resources, financing flexibility, implementation horizon, institutional rules
Health-system displacement	What health-producing activity is forgone when resources are redirected to adoption?	Foregone services, activity, and resulting health	The same expenditure can displace different activities depending on scale and system response	Marginal versus nonmarginal change, service mix, capacity, ability to expand resources

When budget impact is nonmarginal, displacement cannot be read from the ICER alone

Health opportunity cost can be estimated empirically, but the resulting estimates are characteristics of particular systems, data, and methods rather than universal reimbursement constants. Recent econometric work using Spanish National Health Service data illustrates how estimates of marginal health-system productivity depend on the underlying empirical specification and institutional setting [13]. Such estimates can inform displacement

analysis, but they should not be imported into another payer's affordability decision as though they were transferable financial thresholds.

Even where empirical opportunity-cost estimates exist, their incorporation into routine economic evaluation is uneven. A scoping review of 1,171 cost-effectiveness analyses and protocols across four countries found that relevant empirical estimates were not consistently used to support published conclusions [14]. This gap matters because the conceptual appeal of opportunity-cost reasoning does not guarantee that reimbursement submissions adequately represent what additional expenditure displaces in practice.

Budget impact analysis addresses a different part of this problem by estimating the short-run financial consequences of adoption from a payer perspective. Cost-effectiveness and budget impact can therefore produce apparently discordant results without either analysis being internally inconsistent. An intervention can generate attractive health gains relative to incremental cost while still requiring expenditure that exceeds what can be absorbed over the relevant budget horizon [15]. The discordance is informative because the two analyses are testing different constraints.

Budget impact estimates are themselves uncertain. In a retrospective evaluation of 12 Irish budget-impact models, subsequent medicine utilization was overpredicted in six cases and underpredicted in six [16]. The absence of a uniform direction of error is important. Affordability analysis should not assume that modelled uptake is automatically conservative or automatically optimistic. Eligible population estimates, speed of diffusion, substitution, discontinuation, and prescriber behavior can all change the realized financial burden.

Applied budget-impact studies further demonstrate why local inputs matter. An Argentine analysis of flash continuous glucose monitoring required payer-specific assumptions about the eligible population, adoption, current monitoring practice, and unit costs to estimate financial consequences [17]. The direction or magnitude of such a result cannot simply be transferred to another health system. For affordability purposes, budget impact is a property of a particular intervention–population–payer configuration, not an immutable attribute of the technology itself.

Financial resources are also not the only scarce input. Economic evaluations may face multiple simultaneous constraints, including workforce, infrastructure, diagnostic capacity, administration time, or treatment slots. When such constraints bind, conventional cost-utility analysis alone may not fully represent what is feasible or which services are displaced [18]. A medicine can therefore be funded yet remain difficult to implement at the modeled scale.

Figure 1 shows how incremental value, aggregate budget pressure, and nonfinancial constraints can interact without defining a universal numerical affordability boundary.

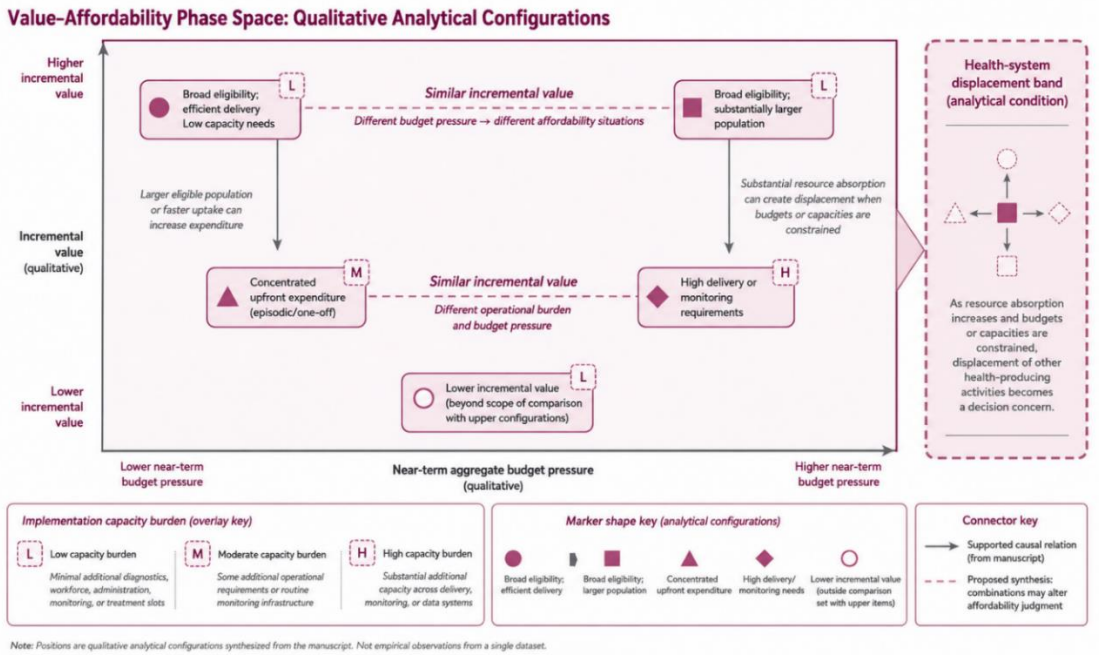

Figure 1. Similar incremental value can coexist with different affordability consequences

Cash-flow timing can diverge from lifetime economic value

Pricing structure changes the fiscal consequences of treatment even when the underlying clinical evidence is unchanged. Analyses of indication-specific and weighted-average value-based pricing in oncology demonstrate that different pricing rules can change modeled prices and aggregate expenditure across indications [19]. Such evidence is relevant to affordability because expenditure depends on the interaction among price, indication mix, eligible population, and uptake rather than on incremental value alone.

The temporal profile becomes especially important for therapies with large initial expenditure and benefits expected to persist over many years. Economic evaluations of RPE65-mediated inherited retinal disease have shown substantial sensitivity to assumptions concerning durability, utilities, discounting, and model structure [20]. A favorable lifetime estimate therefore need not imply that the payer's near-term expenditure profile is easy to accommodate. Lifetime economic value and annual cash requirement are different objects.

Alternative financing arrangements can modify the latter without necessarily changing the former. Modeling of gene therapy for sickle cell disease shows that financing mechanisms do not automatically eliminate substantial budget impact when the underlying price and eligible treatment volume remain high [21]. This provides an important counterexample to the assumption that payment spreading is itself an affordability solution. If the binding problem is the concentration of expenditure in the first budget period, spreading may help. If the binding problem is the total amount that must ultimately be financed, redistributing payment dates may leave the core problem largely intact.

Outcome-contingent arrangements add another dimension by changing when payments occur and whether some payments depend on observed outcomes. Modeling of payment arrangements for atidarsagene autotemcel illustrates how alternative contract structures can generate different payer financial profiles under different response assumptions [22]. Such arrangements can redistribute timing and risk, but a change in payment profile does not by itself establish a reduction in total nominal expenditure; economic burden also depends on discounting, financing costs, and the resources needed to administer the arrangement.

The suitability of a managed-entry agreement consequently depends on the problem it is intended to solve. A structured assessment for high-cost one-off therapies emphasizes that different agreements address different combinations of evidence uncertainty, financial exposure, and payment timing [23]. Complexity has a cost: monitoring, contract administration, outcome definition, adjudication, and data collection can themselves require resources.

The diversity of existing pricing and payment schemes reinforces this point. A recent scoping review identified 70 distinct scheme types across 68 records and classified them according to objectives and design characteristics [24]. The existence of many contractual mechanisms should not be interpreted as evidence that each improves affordability. Scheme names can obscure the more important questions: whether price changes, whether payment is delayed or conditional, who bears uncertainty, what evidence must be collected, and what administrative capability is required.

A systematic review of financing and reimbursement approaches for personalized medicine likewise found substantial heterogeneity across models and technologies [25]. No single approach emerged as a universally dominant solution. For practical reimbursement, the relevant distinction is therefore between a mechanism that changes total expected expenditure and one that mainly changes the timing or contingency of payment.

Table 2 illustrates hypothetical nominal payment profiles. The indexed amounts do not include discounting, financing costs, administrative costs, or clinical consequences.

Table 2. Hypothetical payment-timing scenarios showing why cash-flow relief is not equivalent to lower total expenditure

Scenario	Total indexed payment if contractual conditions are fully met	Year 1 payment	Later payment pattern	What changes economically	What does not automatically change
A. Full upfront payment	100	100	None	None; expenditure is concentrated at treatment initiation	Total expected expenditure; clinical value
B. Five-period equal installments	100	20	20 units in each of four later periods	Cash-flow concentration is reduced	Total nominal payment if all installments occur

C. Deferred second tranche	100	50	Remaining 50 paid later	Part of expenditure moves beyond the first budget period	Total payment if no price reduction or cancellation occurs
D. Outcome-contingent balance	Up to 100	50	Remaining amount depends on the defined contractual outcome	Timing and payer risk become conditional on observed performance	A lower total payment is not guaranteed
E. Upfront price reduction	80	80	None	Total expected expenditure is lower than in the 100-unit scenarios	Expenditure remains concentrated in the initial period

The timing mismatch becomes most consequential when payments, health gains, cost offsets, and displaced services occur on different schedules.

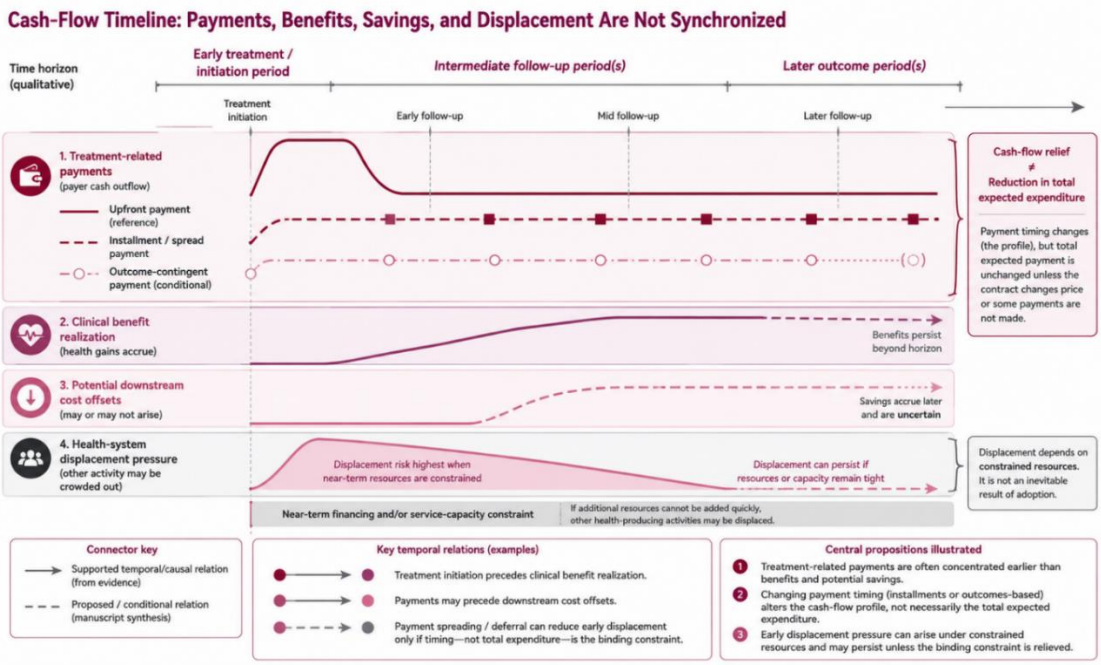

Figure 2. The timing mismatch between upfront expenditure, later benefits, and displaced services

A payment arrangement can improve the payer's cash-flow profile without eliminating the period in which other services are displaced, particularly when expenditure precedes realized health gains or offsets (**Figure 2**).

Affordability can be constrained by capacity as well as money

Financing does not guarantee deliverability. A systematic review of economic evaluations in precision medicine found that capacity constraints were discussed in only a minority of the underlying studies and quantified in still fewer, despite the potential importance of diagnostic, laboratory, workforce, and service limitations [26]. This omission matters because modeled uptake can exceed the number of patients a system can identify, initiate, administer, or monitor within the same period. In such circumstances, a payer may have authorized expenditure while the delivery system remains unable to realize the modeled treatment pathway.

Capacity constraints also arise from the reimbursement mechanism itself. Outcomes-based managed-entry agreements for complex therapies require defined outcomes, reliable follow-up, data capture, governance, contract administration, and mechanisms for reassessment or financial reconciliation. Experience with treatments such as nusinersen and tisagenlecleucel shows that these requirements can be substantial [27]. The same policy intended to manage financial or evidentiary uncertainty can therefore create additional administrative demand.

For affordability analysis, capacity should consequently be treated as a separate resource constraint rather than hidden inside a monetary budget. Scarce treatment slots, specialist time, diagnostic throughput, infusion capacity, monitoring infrastructure, registries, or contract-management capability can determine the feasible pace of

adoption. Capacity may sometimes be expanded through additional expenditure, but expansion may take time or draw on resources that are scarce for reasons other than money. The resulting restriction on uptake is analytically different from a conclusion that the medicine provides insufficient incremental value.

This distinction also changes the interpretation of displacement. When a service operates near capacity, accommodating a new treatment can displace other activity even if the drug budget itself has been increased. Conversely, a therapy with a large acquisition cost may be operationally manageable if treatment volume is small and the required infrastructure already exists. Reimbursement therefore needs to identify whether the binding constraint is the amount of money available, the timing of that money, or the system's ability to convert funding into treatment. Those problems can coexist, but they require different responses.

Payment and managed-entry arrangements solve different problems

Commercial and reimbursement arrangements should be selected according to the problem they are intended to modify. This becomes particularly important when a medicine has multiple indications. Modeling of pembrolizumab in the Netherlands showed that a common market-entry arrangement could coexist with materially different cost-effectiveness relationships across five indications [28]. A product-level agreement can therefore conceal indication-level differences in incremental value and expenditure. Broadening access may change the composition of treated patients, aggregate spending, and the relationship between price and value even when the contractual terms themselves remain unchanged.

Evidence from cancer-medicine reimbursement across several countries similarly suggests that managed-entry arrangements arise in response to different combinations of clinical, economic, and evidentiary uncertainty [29]. This does not establish that a particular agreement caused better affordability or better health outcomes. It indicates that the rationale for an agreement matters. A payer confronting uncertainty about long-term effectiveness faces a different problem from one confronting a known but unaffordable aggregate expenditure, and both differ from a payer whose principal difficulty is a concentrated first-year payment.

Real-world financial performance also cautions against interpreting the existence of an agreement as evidence that affordability has been solved. Italian experience with managed-entry agreements generated identifiable financial paybacks, but those recoveries represented only a limited share of overall pharmaceutical expenditure [30]. Financial agreements can therefore recover expenditure without materially altering the system-wide scale of the budget problem. The relevant comparison is between the magnitude of the financial mechanism and the magnitude of the expenditure constraint it is expected to relieve.

Contract performance can also change when assumptions derived from clinical or published evidence are replaced with payer-specific utilization data. Medicaid-based modeling of cell and gene therapy showed that real-world eligibility and utilization assumptions changed expected break-even performance compared with estimates derived from published evidence [31]. This reinforces a broader principle: an agreement that appears financially attractive under one population, persistence pattern, or utilization assumption should not be presumed to perform similarly in another payer.

Outcomes-based agreements are consequently most defensible when the outcome can be measured reliably, the uncertainty is material to the reimbursement decision, and the administrative burden is proportionate to the problem being managed. European policy recommendations emphasize that implementation requirements can be substantial and that simpler arrangements should remain credible alternatives where they can address the same problem [32]. Complexity is therefore a cost that must itself be justified.

Some problems are better addressed through reassessment than through payment redesign. Highly specialized technologies can enter practice with immature evidence on durability, long-term outcomes, comparative effectiveness, or resource use. Living health technology assessment has been proposed as a means of updating decisions as evidence evolves [33]. Reassessment can reduce evidentiary uncertainty, but it does not by itself lower a price, expand a budget, or create delivery capacity. It should therefore be distinguished from interventions directed at fiscal affordability.

Finally, improving the speed or procedural quality of health technology assessment does not guarantee that affordability improves in parallel. European Delphi evidence suggests that HTA characteristics may affect different dimensions of medicines access in different ways, with affordability effects less consistently predictable than some other access outcomes [34]. Sustainable access therefore requires the payer to identify the specific constraint before choosing the mechanism intended to address it.

Results and Discussion

A practical reimbursement decision can begin by identifying which quantity is actually binding. Incremental value, aggregate budget impact, near-term cash flow, operational capacity, and health-system displacement are related, but none is a reliable proxy for all the others. Cost-effectiveness analysis remains the appropriate instrument for asking whether incremental health gains justify incremental resource use [1]. Budget impact contributes a different question concerning the scale of financial commitment, and its institutional importance can vary across decision stages [5]. Where diagnostic, workforce, treatment, monitoring, or administrative resources are scarce, the decision must additionally recognize nonfinancial constraints [18].

This distinction prevents a high acquisition cost from being treated automatically as an affordability failure. A high-cost medicine may be financially manageable when the eligible population is small, expenditure is predictable, sufficient implementation capacity exists, and adoption causes little consequential displacement. Conversely, a medicine with a favorable ICER and moderate per-patient price may create substantial aggregate pressure when the eligible population is large or uptake is rapid. Cost-effective and affordable outcomes can therefore coincide; unaffordability is a possible configuration, not an inevitable property of innovative medicines.

The next step is to distinguish a total-expenditure problem from a timing problem. If total price multiplied by eligible treatment volume creates expenditure that the payer considers unsustainable, changing payment dates alone cannot be assumed to correct the underlying constraint. Modeling of sickle-cell gene-therapy financing demonstrates that alternative financing arrangements may leave substantial budget impact when price and treatment volume remain unchanged [21]. Price negotiation or indication-sensitive pricing can change expected expenditure. Prioritization and staged adoption may reduce expenditure within the decision horizon, but deferred treatment need not reduce longer-term spending and may delay health gains. These effects should be distinguished from installment financing.

Where expenditure is acceptable over the longer horizon but excessively concentrated in the near term, payment timing becomes more directly relevant. Installments, deferred tranches, or outcome-contingent payments can redistribute cash requirements, although the diversity of existing schemes means their labels reveal relatively little about their actual economic effect [24]. A payer should therefore specify whether a proposed agreement changes price, timing, risk allocation, evidence generation, or some combination of these before attributing an affordability benefit to it.

Real-world financial experience provides a further safeguard against overclaim. The Italian experience shows that contractual paybacks can be genuine while remaining modest relative to aggregate pharmaceutical expenditure [30]. A policy should therefore be judged against the scale of the problem it was selected to address. A mechanism that recovers a small fraction of expenditure may still be administratively worthwhile, but it should not be described as resolving a system-level affordability problem unless the resulting financial effect is sufficient for that purpose.

Contractual complexity also requires comparison with simpler alternatives. Outcomes-based agreements can be appropriate where clinically important uncertainty is resolvable through measurable post-launch outcomes, but European recommendations emphasize their data and implementation requirements [32]. If an equivalent affordability objective can be achieved through a transparent price agreement or an adjusted payment schedule, adding outcome measurement may create administrative burden without addressing an additional binding constraint.

The proposed practical sequence is therefore diagnostic rather than formulaic. First, determine whether the medicine provides sufficient incremental value under the jurisdiction’s accepted economic methods. Second, estimate aggregate budget consequences under plausible uptake rather than assuming that cost-effectiveness determines total expenditure. Third, examine when payments occur relative to benefits and potential offsets. Fourth, identify whether implementation requires scarce capacity that cannot be expanded immediately. Fifth, determine what activity or health is likely to be displaced if new resources are not available. Only after these questions are separated should a reimbursement or payment response be selected.

The relationship between the diagnosed problem and the possible policy response is summarized below.

Table 3. Matching the source of reimbursement pressure to the policy mechanism it can plausibly modify

Binding reimbursement problem	Diagnostic signal	Potential response class	What the response can plausibly change	What remains unresolved unless addressed separately
Incremental value is insufficient at the proposed price	Expected incremental benefit is not commensurate with incremental resource use under the jurisdiction's decision rules	Price negotiation; indication-sensitive pricing; narrower eligible population	Incremental cost relative to expected benefit	Delivery capacity, cash-flow concentration, evidence uncertainty
Aggregate budget impact is excessive despite acceptable incremental value	Net expenditure, accounting for price, eligible volume, uptake, displaced treatment costs, and other relevant costs or offsets, exceeds the payer's feasible commitment	Price reduction; staged uptake; prioritization; indication-specific access; expenditure caps where appropriate	Total or near-term aggregate expenditure	Clinical uncertainty and implementation capacity unless separately managed
Expenditure is acceptable overall but concentrated too early	Large initial payment precedes later benefits, savings, or budget replenishment	Installments; deferred tranches; payment spreading	Timing of cash outflow	Total expected expenditure if price and volume are unchanged
Important reimbursement uncertainty is measurable after launch	Decision materially depends on durability, response, or another observable outcome	Outcome-contingent agreement; coverage linked to evidence development; reassessment	Allocation of evidentiary or financial risk; future decision information	Affordability if expected expenditure remains excessive
Delivery capacity is the limiting resource	Treatment slots, diagnostics, specialist workforce, monitoring, data systems, or administration constrain feasible uptake	Staged implementation; capacity expansion; service redesign; prioritization	Pace or feasibility of implementation	Underlying value and total expenditure
Common price or agreement obscures heterogeneous indication value	Incremental value varies materially across indications or populations	Indication-specific or weighted pricing; indication-specific eligibility or reassessment	Alignment between price and indication-level value	Aggregate expenditure if eligible volume remains large
Adoption produces substantial residual displacement	Funding or capacity must be withdrawn from other health-producing activity	Additional resources; reduced price; slower uptake; explicit prioritization	Magnitude or timing of displaced activity	Distribution of lost health unless separately analyzed

The final reimbursement judgment remains jurisdiction-specific. Decision-makers differ in available budgets, budget flexibility, authority to transfer resources, service capacity, tolerance of financial risk, and the social opportunity cost of displaced activity. Qualitative evidence already shows that the weight attached to budget impact varies by institutional stage and stakeholder perspective [6]. European HTA evidence likewise indicates that improvements in access processes do not necessarily produce uniform affordability effects [34]. A practical application should therefore report the residual constraint after the proposed policy response, rather than implying that adoption becomes sustainable merely because a financing or managed-entry mechanism has been attached to the medicine.

This approach also protects the distinction between aggregate displacement and distributional equity. The present analysis asks whether adoption displaces health-producing resources at the system level and whether the magnitude or timing of that displacement affects affordability. It does not determine which social groups bear that health loss, how equity weights should be applied, or how financial risk should be distributed across populations. Those are additional normative questions requiring their own evidence and methods.

The strongest implication is consequently procedural. Reimbursement should not begin with the question, "Which innovative payment model should be used?" It should begin with the economic and operational diagnosis. A payment mechanism is useful only to the extent that it changes the quantity creating the constraint. When the diagnosis is incorrect, sophisticated contracting can redistribute accounting entries while leaving the substantive affordability problem intact.

Conclusion

A medicine can be cost-effective yet unaffordable because cost-effectiveness and affordability describe different consequences of adoption. Incremental value concerns what is gained for additional resource use relative to a comparator. Affordability depends on how much must be financed in aggregate, when expenditure occurs, whether the delivery system can implement treatment at the intended scale, and what other health-producing activity is displaced.

The distinction is conditional rather than absolute. Cost-effective medicines can also be affordable when eligible volume, expenditure timing, capacity requirements, and displacement are manageable. Where affordability is problematic, the appropriate response depends on its source. Price changes address different problems from payment spreading; outcome-contingent agreements address different problems from capacity expansion; and reassessment addresses different problems from additional financing. Sustainable reimbursement therefore requires the payer to identify the binding constraint before selecting the policy mechanism intended to relieve it.

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