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Policy Analysis

Justice in the Distribution of Gene Therapies for Rare Diseases

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ABSTRACT

Gene therapies for rare diseases combine unprecedented clinical promise with list prices that break the actuarial assumptions underlying conventional health insurance, since a durable, often lifelong benefit is billed as a single upfront cost.

This policy analysis surveys the ethical and economic literature on how these therapies are priced, the financing innovations -- outcomes-based contracts, annuity-style installments, and pooled or supranational funds -- proposed to make that pricing tractable, and the deeper equity gap separating health systems that can experiment with these mechanisms from the much larger population of eligible patients in low- and middle-income countries.

It examines the evidentiary uncertainty underlying value-based pricing claims at launch, the practical obstacles to implementing outcomes-based and risk-pooling arrangements, and the upstream diagnostic and delivery infrastructure gaps that limit access even where financing is resolved.

It then considers competing justice frameworks -- rule-of-rescue intuitions, prioritarian weighting of the worst-off, and fair-innovation arguments -- that inform how health systems reason about coverage decisions for identifiable, severely affected patients.

We argue that financing innovation, diagnostic infrastructure, and global differential pricing must be treated as a single connected policy problem, since addressing any one in isolation risks reproducing the same distributive inequities in a new form.

Keywords: gene therapy; rare disease; distributive justice; health policy; global health equity

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INTRODUCTION

A single infusion of onasemnogene abeparvovec for

spinal muscular atrophy, or a one-time course of an approved sickle-cell gene-editing therapy, can carry a list price well into seven figures. These are not

incremental improvements on existing drugs; in many cases they are the first treatment of any kind for the condition, and in several they plausibly cure it outright. That combination -- extraordinary clinical promise attached to a price tag that no ordinary insurance premium was designed to absorb -- has turned gene therapy pricing from a niche health-economics question into one of the more pressing distributive-justice problems in contemporary medicine [1].

The problem is not simply that these therapies are expensive. Orphan drugs have always commanded premium prices, and health systems have lived with that tension for decades. What is different about gene therapy is the payment structure it demands: a durable, potentially lifelong benefit is billed as a single upfront cost, which breaks the actuarial logic that health insurance and public payers rely on to spread risk over time [2]. A therapy that might genuinely be worth its price over a patient's lifetime can still bankrupt the payer who has to write the check in year one, particularly if that patient later changes insurers or the health system is not built to amortize the expense.

This paper surveys the ethical and policy literature on how gene therapies for rare diseases are priced, financed, and allocated, and asks what a defensible account of distributive justice would require of the systems now being built around them. It considers three interacting problems: the pricing logic manufacturers use to justify current list prices, the financing innovations -- outcomes-based contracts, reinsurance, and disease-specific funds -- being proposed to make those prices tractable for payers, and the deeper equity gap between health systems that can experiment with these mechanisms and the much larger number of patients, concentrated in low- and middle-income countries, for whom none of them are realistically on offer [3].

THE PRICE OF A CURE: HOW GENE THERAPIES ARE PRICED AND WHY

Manufacturers typically justify gene therapy list prices with a value-based argument: the price reflects the discounted lifetime cost of the conventional treatments, hospitalizations, and lost productivity the therapy is expected to avert, not simply the cost of manufacturing the product [4]. For a handful of therapies with strong long-term efficacy data, that argument has real force. But the argument depends on evidence that is, almost by construction, incomplete at launch. Rare-disease trials are small, often single-arm, and rarely followed for the decades over which the "lifetime savings" are supposed to accrue, so a manufacturer's value claim at approval is necessarily a projection rather than a demonstrated fact [5].

This evidentiary thinness matters ethically because it shifts the risk of being wrong onto payers and, indirectly, onto other patients whose care is funded

from the same finite pool. A national health system or insurer that accepts a manufacturer's value-based price is effectively betting a large sum on durability data that will not fully mature for years. Analyses of gene-targeted therapy development have argued that the field cannot resolve this by pricing alone -- diagnosis capacity, newborn screening infrastructure, and the specialized centers needed to actually deliver a gene therapy all have to scale alongside the drug itself, or "equitable access" becomes a slogan attached to a product most eligible patients cannot physically reach even where it is nominally covered [6].

There is also a genuine market-structure problem beneath the ethical one. Diseases rare enough to qualify for orphan designation may have patient populations too small to support the kind of price competition that disciplines conventional drug markets, and several therapies approved for very small populations have struggled commercially regardless of price, prompting manufacturers themselves to withdraw products for ultra-rare indications when the economics did not work even at high list prices [7]. Justice arguments about gene therapy pricing therefore cannot only be about restraining manufacturers; they also have to grapple with the possibility that some ultra-rare conditions are not commercially viable to treat under any pricing model built on per-patient revenue.

FINANCING INNOVATIONS: OUTCOMES-BASED CONTRACTS AND RISK POOLING

Because the "pay once, benefit for decades" structure is what breaks conventional financing, most of the policy energy in this space has gone into re-engineering how payment is spread out and conditioned on results, rather than into price controls as such. Outcomes-based agreements tie some portion of payment to whether the therapy actually delivers the clinical benefit it was priced on, with rebates or installment reductions if it does not [8]. In principle this reallocates risk more fairly, since the payer is no longer betting blind on durability data that did not exist at approval. In practice, outcomes-based contracts have proven difficult to implement: they require long-term outcome tracking infrastructure that many health systems lack, they raise thorny questions about which endpoints count as "failure," and patient mobility between insurers undermines the multi-year tracking the model depends on [9].

A related approach spreads payment over time through annuity or "mortgage" style installments rather than tying it to outcomes, addressing the cash-flow problem even without resolving the durability-risk problem. The U.S. Centers for Medicare & Medicaid Services' Cell and Gene Therapy Access Model is one attempt to operationalize this kind of arrangement at a state-Medicaid scale, coordinating outcomes-based

agreements for sickle cell disease gene therapies across participating states rather than leaving each payer to negotiate separately [10]. Reinsurance and risk-pooling proposals go a step further, arguing that no single payer, however large, should have to absorb the full tail risk of a handful of extremely expensive patients arriving in the same year, and that pooling that risk across payers is itself a matter of fairness to the specific insurer or health system unlucky enough to have several eligible patients in its covered population at once [11].

Table 1. Financing mechanisms proposed for gene therapies, the distributive problem each targets, and its principal limitation.

Mechanism	Distributive problem addressed	Principal limitation	Typical scope
List price / value-based pricing	Links price to projected lifetime benefit	Depends on immature long-term durability data at launch	Single payer/manufacturer
Outcomes-based contract	Shifts durability risk from payer to manufacturer	Requires long-term tracking infrastructure; patient mobility undermines follow-up	Single payer, per therapy
Annuity / installment financing	Spreads upfront cost over time to ease cash-flow	Does not resolve underlying durability-risk uncertainty	Single payer or state program
Pooled / supranational fund	Gives small payers negotiating leverage; spreads rare-event risk	Requires cross-jurisdiction political coordination	Regional bloc or multi-state program

Figure 1. Schematic comparison of payer risk reduction and administrative/data burden across four financing mechanisms discussed in this review (illustrative, not derived from a single empirical study).

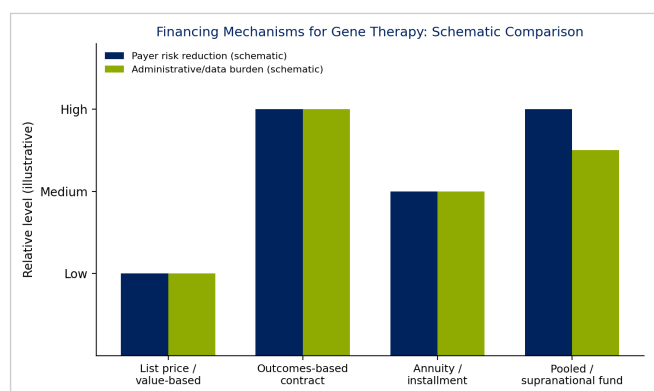


Table 1 summarizes the main financing mechanisms discussed in this literature, the distributive problem each is designed to address, and its principal limitation. Figure 1 places the same mechanisms on a schematic axis of how much they reduce payer risk against how much administrative and data infrastructure they require to operate -- illustrating why the mechanisms that reduce risk most are also, not

coincidentally, the ones health systems have found hardest to actually implement.

A disease-specific or pooled fund model, proposed for the European context as an "Orphan Genomic Therapies Fund," represents a different logic again: rather than each payer negotiating its own outcomes contract, a supranational fund would negotiate collectively and disburse across member states, explicitly framing the arrangement as a solidarity mechanism rather than a purely actuarial one [12]. Proponents argue this addresses a fairness problem the payer-by-payer models cannot: a small country with only one or two eligible patients per year has essentially no negotiating leverage on its own, and pooling changes that.

GLOBAL INEQUITY: ACCESS BEYOND HIGH-INCOME HEALTH SYSTEMS

Nearly all of the financing innovations above assume a health system sophisticated enough to negotiate outcomes-based contracts, track long-term outcomes, and deliver the therapy through specialized infrastructure in the first place. That assumption fails for most of the world's population. Comparative work examining gene therapy access in Brazil, South Africa, and India found that even where a national health system has the will to pursue access, it typically lacks the regulatory pathways, reimbursement mechanisms, and specialized delivery centers that wealthy-country payers take for granted, so the barrier is not solely price [3].

Where price is the barrier, it is a severe one: comparative pricing analyses across low- and middle-income countries have found that orphan drug prices are frequently set at levels that consume many multiples of per-capita health expenditure, sometimes with little or no differential pricing relative to high-income markets despite vast differences in ability to pay [13]. Advocacy organizations working on global vaccine and therapeutic access have argued that gene therapy risks repeating, on a compressed timeline, the access gap that took roughly a decade to substantially narrow for antiretroviral therapy -- unless tiered pricing, technology transfer, or manufacturing capacity building are pursued deliberately rather than left to follow market incentives on their own schedule [14].

A less obvious equity problem sits upstream of treatment access altogether: diagnosis. Many rare genetic conditions eligible for gene therapy require early, often neonatal, identification for the therapy to be effective at all, and newborn screening infrastructure is itself unevenly distributed globally, meaning that even a hypothetically free therapy would still reach patients unevenly if screening programs are not extended alongside it [15]. A recent synthesis on rare-disease drug development has argued for building patient-centricity and equity into trial design and regulatory pathways from the outset, rather than

treating global access as a downstream commercialization problem to be solved after approval in wealthy markets [16]. Reviews of the ethical literature on orphan drug policy more broadly have converged on a similar diagnosis: affordability, innovation incentives, and access are usually discussed as a three-way trade-off, but that framing can obscure how much of the current imbalance reflects deliberate policy choices about where R&D investment and regulatory priority are directed, not an unavoidable technical constraint [17].

JUSTICE FRAMEWORKS: RULE OF RESCUE, PRIORITARIANISM, AND FAIR INNOVATION

Underneath these policy debates sit competing accounts of what justice actually requires when a small number of identifiable, often pediatric, patients face a fatal or severely disabling condition that a single treatment can address. The "rule of rescue" -- the strong, largely pre-theoretical pull toward saving an identified life in front of us, even at a cost that would be judged excessive if spent preventing statistically equivalent harm to an unidentified population -- captures why gene therapy funding decisions provoke such visceral public reaction when a health system declines to cover a named child's treatment [18]. Critics of allowing the rule of rescue to drive coverage policy point out that every dollar spent on one visible, expensive case is a dollar not spent on less visible but equally real health needs elsewhere in the same budget, and that policy built on identified-victim intuitions systematically disadvantages the larger number of people whose suffering is statistical rather than individually named.

Prioritarian and capability-based frameworks offer an alternative that tries to take rarity and severity seriously without collapsing into pure rule-of-rescue reasoning: they weight benefits to the worst-off more heavily, which can justify some premium for treating a severe, otherwise-untreatable rare disease, but only up to a point bounded by opportunity cost, not without limit [2]. Recent regulatory-policy commentary on gene therapies for rare diseases has argued that credible ethical frameworks for this class of product need to be built into evidentiary and reimbursement standards proactively -- addressing evidentiary uncertainty, post-market surveillance duties, and equitable access commitments as conditions attached to approval and pricing -- rather than being improvised health-system by health-system after each therapy reaches the market [19].

None of these frameworks, on their own, resolves the tension the introduction opened with. Rule-of-rescue intuitions explain why gene therapy access campaigns succeed politically; prioritarian reasoning explains why health economists remain uneasy about extending that logic without limit; and global equity analysis makes clear that both debates, as usually conducted, are

conversations among wealthy health systems about how to divide a burden that most of the world's eligible patients are not even positioned to enter.

CONCLUSION

Gene therapy for rare disease sits at an unusually sharp intersection of clinical promise, financing incoherence, and global inequity, and none of the mechanisms surveyed here resolves all three at once. Outcomes-based contracts and installment financing address the actuarial mismatch between upfront cost and durable benefit reasonably well within health systems sophisticated enough to implement them, but do nothing for the diagnosis and delivery infrastructure gaps that keep most of the world's eligible patients out of the conversation entirely. Pooled or supranational funds address the negotiating-leverage problem facing small payers but have so far been proposed mainly within wealthy regional blocs. And the underlying ethical debate about how much a health system owes an identified, treatable patient, weighed against everyone else drawing on the same budget, remains as unsettled as it has ever been -- gene therapy has simply raised the financial stakes of getting that answer wrong. A defensible path forward likely requires treating financing innovation, diagnostic and delivery infrastructure, and global differential pricing as a single connected policy problem rather than three separate ones, since progress on any one alone will keep reproducing the same inequities in a new form.

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Conflict of Interest

The authors declare no conflicts of interest relevant to this work.

Author Contributions

Carla Marques conceived the review, synthesized the literature on pricing and financing mechanisms, and drafted the initial manuscript. Sylvie Peeters developed the sections on global access inequity and diagnostic infrastructure and critically revised the manuscript. Rui Nowak contributed the analysis of justice frameworks, coordinated reference verification, and gave final approval of the submitted version. All authors read and approved the final manuscript.

Ethics Statement

As a literature review synthesizing previously published, publicly available research and policy

analysis, this article did not involve new data collection from human or animal subjects and did not require institutional ethics committee approval.

Data Availability

No new data were generated or analyzed for this review. All sources discussed are cited in the reference list and are publicly available through their respective publishers.

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