

Who Loses Health Behind the Average Cost-Effectiveness Ratio? Distributional Opportunity Costs, Financial Risk, and Equity in Medicines Reimbursement

Priya Menon¹, Michael Tan^{2*}, Rania Khalil³

¹Department of Health Economics and Pharmaceutical Policy, Faculty of Pharmacy, Indian Institute of Management Kozhikode, Kozhikode, India.

²Department of Pharmacy Administration and Health Economics, Faculty of Science, National University of Singapore, Singapore.

³Department of Clinical Pharmacy and Health Equity, Faculty of Pharmacy, Cairo University, Cairo, Egypt.

*E-mail ✉ michael.tan@nus.edu.sg

Received: 26 July 2023; Revised: 23 October 2023; Accepted: 27 October 2023

ABSTRACT

Conventional cost-effectiveness analysis identifies whether the incremental health generated by a medicine is sufficient relative to its incremental cost, but an average cost-effectiveness ratio does not identify how those health consequences are distributed. This methodological article develops an approach for making the distribution of recipient health, displaced health, financial-risk protection, and normative equity judgments explicit in medicines reimbursement. The analysis separates five inputs: subgroup-specific recipient health effects and costs; the magnitude and subgroup incidence of health displaced elsewhere by reimbursement expenditure; household financial-risk consequences; baseline health distributions; and explicit equity weights. Qualitative hypothetical reimbursement scenarios are used to examine situations in which interventions have identical average cost-effectiveness but differ in who gains health, who bears opportunity costs, and who receives financial protection. Efficiency, distributional health, and financial protection are retained as analytically distinct outputs before any normative aggregation. An average incremental cost-effectiveness ratio can be compatible with materially different distributions of health gain and health loss. Distributional conclusions depend not only on heterogeneity among recipients but also on assumptions about where displaced health occurs. Financial-risk protection can move independently of health outcomes, while alternative equity weights can alter reimbursement rankings without changing the underlying clinical or cost evidence. The qualitative scenarios therefore illustrate how a reimbursement decision can be unchanged, strengthened, weakened, or reversed once distributional information is introduced. Equity-informative medicines reimbursement requires more than applying an equity weight to the beneficiaries of a new medicine. The distribution of health opportunity costs and financial protection must also be made explicit. Reporting these components separately preserves transparency about efficiency, distribution, uncertainty, and normative judgment while avoiding an unvalidated composite measure of value.

Keywords: Distributional cost-effectiveness analysis, Health opportunity cost, Equity weighting, Financial risk protection, Medicines reimbursement, Health inequalities

How to Cite This Article: Menon P, Tan M, Khalil R. Who Loses Health Behind the Average Cost-Effectiveness Ratio? Distributional Opportunity Costs, Financial Risk, and Equity in Medicines Reimbursement. *Ann Pharm Pract Pharmacother*. 2023;3(2):93-104. <https://doi.org/10.51847/dqWf6slCjv>

Introduction

Cost-effectiveness analysis is designed to compare incremental costs with incremental health effects, yet the resulting average can conceal the distribution of both. Distributional cost-effectiveness analysis extends conventional evaluation by asking how health gains and losses are allocated across equity-relevant groups and how alternative distributions affect social value[1]. This extension matters because funding one intervention in a constrained health system also creates an opportunity cost: resources used for the reimbursed technology cannot

simultaneously produce health elsewhere[2]. The identity of those receiving the new treatment and the identity of those bearing displaced health therefore need not be the same.

The size of that displaced-health burden depends on the relationship among the available budget, the reimbursement rule, and the health produced by existing expenditure[3]. The simplifying assumption that every new technology causes only a marginal change can also become unreliable when a medicine has a large budget impact, because the health forgone may change with the scale of adoption[4]. These considerations mean that the average incremental cost-effectiveness ratio (ICER) is incomplete as a distributional descriptor even when it remains informative about efficiency.

Methods for introducing equity into economic evaluation are already well developed enough to demonstrate feasibility, but their applications vary in subgroup definitions, inequality measures, weighting procedures, and treatment of opportunity costs[5]. Medicines reimbursement adds a particular complication because the price accepted by the payer affects both the surplus generated by the intervention and the health displaced elsewhere in the system[6]. An equity analysis that describes only the distribution of treatment benefits may therefore miss an equally important distributional consequence on the supply side.

The problem also extends beyond health alone. Contemporary value assessment increasingly considers dimensions such as disease severity, risk, insurance value, vulnerability, and other consequences that conventional cost-per-QALY analysis may not fully represent[7]. Stakeholders nevertheless differ in the importance they attach to these elements, including financial-risk protection and benefits accruing to vulnerable groups[8]. The methodological question is consequently not how to manufacture a single enlarged measure of value. It is how to identify, report, and interpret the components that an average ICER leaves unresolved.

This article addresses that question for medicines reimbursement by separating recipient health effects, displaced-health incidence, financial-risk protection, baseline inequality, and explicit normative weighting. The central proposition is conditional: distributional analysis adds decision-relevant information when these components differ across population groups. If the distributions are effectively proportional, the conventional reimbursement conclusion may remain unchanged. The purpose is therefore to make visible the circumstances under which the average conceals consequential differences rather than to presume that every equity analysis must overturn a cost-effectiveness result.

Materials and Methods

Analytical perspective, decision estimands, and reimbursement unit

The analytical unit is a medicines reimbursement decision made under a constrained healthcare budget. The starting efficiency estimand remains incremental cost relative to incremental health generated by the intervention. Distributional analysis adds a vector of subgroup-specific consequences rather than replacing that aggregate quantity.

A first requirement is to distinguish the total health opportunity cost from its incidence. Empirical work on expenditure and health production indicates that the health generated by changes in healthcare spending can be socially patterned because disease burden, service use, and the health productivity of expenditure vary across groups[9]. Supply-side cost-effectiveness thresholds are themselves estimates requiring careful interpretation; different empirical approaches can represent different underlying concepts, populations, and margins of expenditure[10]. Accordingly, the method treats both the magnitude and the distribution of displaced health as uncertain inputs.

Scale also matters. When the budget impact of reimbursement is substantial, optimal implementation and displaced health can differ from those implied by a purely marginal analysis[11]. Timing can matter independently of discounted expenditure totals because alternative expenditure profiles can impose different health opportunity costs across periods[12]. The methodological specification therefore requires the reimbursement unit to state the eligible population, implementation scale, expenditure profile, and assumed supply-side opportunity-cost process before distributional conclusions are interpreted.

Distribution of recipient health effects and costs

Recipient-side distribution begins with the health and cost consequences among the groups eligible for the medicine. Baseline health must be represented separately from incremental treatment effects because the same incremental gain can have different implications for inequality depending on starting health[13]. Applied

distributional analyses further show that the result depends on assumptions concerning both the treatment effect and the population distribution of the associated opportunity cost[14].

The method therefore permits subgroup heterogeneity in disease prevalence, treatment eligibility, access, uptake, adherence, effectiveness, adverse consequences, costs, and baseline health. Patient-level and population-level inequality need not move in the same direction when treatment access and downstream population effects differ[15]. Simulation evidence also shows that distributional direction can become difficult to predict when treatment-effect modification is weak or multiple disease and treatment characteristics interact[16].

This prevents the analysis from treating “disadvantaged patients” as a single homogeneous category. High-cost therapies can generate large health gains while still producing different equity interpretations under alternative social preferences or prices[17]. Conversely, interventions targeted toward disadvantaged populations can sometimes increase both total health and equity, demonstrating that an efficiency–equity trade-off is not inevitable[18]. Recipient heterogeneity is consequently represented before normative weighting rather than being inferred from group labels.

Incidence of displaced health under constrained budgets

Displaced health is assigned independently of recipient health. For each reimbursement scenario, total expected health opportunity cost is first defined from the relevant supply-side assumption. The analysis then specifies a distribution of that displaced health across equity-relevant groups.

Three forms of incidence can be examined. A proportional specification allocates displaced health according to a defined population or healthcare-use distribution. An empirically informed specification uses available evidence on the social patterning of healthcare expenditure and health production. A sensitivity specification deliberately varies the incidence to determine whether the reimbursement interpretation depends on who is assumed to lose health.

This separation is essential because identical treatment benefits can have different population consequences when the displaced-health distribution changes. It also prevents baseline disadvantage from being used as a surrogate for supply-side incidence. A group can have poorer baseline health without necessarily bearing a disproportionate share of the opportunity cost, and the reverse is also possible. Where incidence data are weak, the appropriate output is sensitivity analysis rather than a precise distributional estimate.

Financial-risk protection and household exposure

Health benefits and financial-risk protection (FRP) are represented as different consequences. Economic evaluations that explicitly incorporate FRP demonstrate that interventions or financing policies can produce one distribution of health gains and another distribution of protection from out-of-pocket expenditure[19]. Proposed approaches that place greater priority on financially protective interventions can consequently change resource-allocation rankings[20].

For medicines reimbursement, the relevant FRP variables may include changes in household out-of-pocket expenditure, exposure to catastrophic expenditure, or other explicitly defined financial consequences attributable to coverage. Extended cost-effectiveness analyses show that the health and financial consequences of public financing can vary across wealth groups[21]. Similar modeling indicates that access-oriented financing can generate distributions that differ by both income and sex[22].

The present method therefore does not convert FRP automatically into QALYs or embed it within the ICER. Instead, FRP is reported alongside health outcomes so that a decision maker can see whether reimbursement generates concordant or discordant consequences across the two domains.

Equity weights, subgroup definitions, and normative assumptions

Equity weights enter only after the underlying distributions have been specified. Stated-preference evidence indicates that the value assigned to health gains can vary with characteristics such as severity and age[23]. However, systematic evidence from the United States shows substantial heterogeneity in public preferences concerning equity and efficiency[24]. A broader methodological review likewise finds large variation across elicitation methods, countries, samples, and framing choices[25].

Equity weighting is therefore treated as a normative sensitivity parameter rather than an empirically fixed constant. Alternative methods can produce different weights even when directed toward the same socioeconomic gradient[26]. Subgroup definition must also be explicit: possible classifications include socioeconomic position,

race or ethnicity, geography, disease severity, age, sex, or another characteristic justified by the reimbursement question. The analysis distinguishes these normative choices from empirical treatment-effect heterogeneity. The methodological components that must be specified before synthetic reimbursement analysis are summarized below.

Table 1. Components required to make distributional medicines reimbursement analytically explicit

Component	Quantity specified	Distribution required	Main uncertainty to expose	Role in reimbursement interpretation
Recipient health	Incremental health generated by the medicine	Across eligible or treated subgroups	Effect heterogeneity, uptake, access, baseline risk	Identifies who receives health gains
Recipient cost	Incremental reimbursement expenditure	Across treatment groups and implementation scale	Price, uptake, duration, timing	Determines budget claim generated by adoption
Health opportunity cost	Health forgone because resources are displaced	Across populations bearing reduced health production	Supply-side threshold, scale, timing, incidence	Identifies who loses health elsewhere
Baseline health	Health status before reimbursement effects	Across equity-relevant groups	Measurement and subgroup definition	Locates gains and losses within existing inequality
Financial-risk protection	Change in household financial exposure	Across income or other relevant groups	Coverage design, out-of-pocket liability	Identifies financial protection distinct from health
Equity assumption	Relative social value assigned to specified outcomes or groups	Across explicitly defined characteristics	Preference method and normative parameter	Tests sensitivity of social valuation
Decision uncertainty	Uncertainty surrounding each component	Across plausible scenarios	Data quality, transportability, model structure	Distinguishes robust from assumption-sensitive conclusions

Synthetic reimbursement scenarios and sensitivity analysis

The Results use synthetic scenarios rather than an empirical reimbursement dataset. Each scenario is constructed so that its average cost-effectiveness conclusion can be held constant while one or more distributional components vary. No scenario represents observed patient data, a real medicine price, an estimated payer threshold, or a claimed policy outcome.

The sequence of analysis is: define aggregate incremental health and cost; distribute recipient effects; allocate displaced health; describe FRP; characterize baseline health; then apply alternative equity assumptions if required. Sensitivity analysis varies each uncertain component independently where possible. This permits identification of whether a distributional conclusion is driven primarily by clinical heterogeneity, access, opportunity-cost incidence, financial exposure, or normative weighting.

Results and Discussion

Information lost in the average ICER

The first synthetic demonstration considers reimbursement alternatives that satisfy the same aggregate cost-effectiveness condition. Population-level distributional modeling in Alzheimer disease illustrates why treatment access, recipient benefit, baseline inequality, and opportunity costs can interact even when an intervention is conventionally cost-effective[27]. In the synthetic analysis here, the aggregate ICER identifies neither the subgroup receiving incremental health nor the subgroup losing health through displacement.

If recipient gains and displaced losses are proportional across groups, baseline health is similar, and valuation does not differ between groups, distributional analysis may leave the aggregate decision unchanged. Once either distribution becomes asymmetric, however, the same ICER is compatible with different effects on population health inequality. The missing information is therefore not an additional property of the ratio itself; it is the subgroup incidence of the quantities summarized by that ratio.

Equal mean cost-effectiveness with unequal recipient distributions

A second demonstration holds average cost-effectiveness constant while changing the location of treatment benefits. Severity modifiers already used in health technology assessment show one formal way in which decision rules can value the same health increment differently according to characteristics of the population experiencing it[28]. The synthetic scenarios extend the issue by separating the empirical distribution of gains from the later normative valuation of those gains.

These qualitative scenarios compare distributional configurations without assigning numerical costs, QALYs, patient counts or thresholds.

Table 2. Synthetic reimbursement configurations compatible with the same average cost-effectiveness conclusion

Synthetic configuration	Recipient health pattern	Baseline location of recipients	Displaced-health incidence	Financial-risk protection	Distributional implication
Distributionally proportional	Health gains spread in proportion to the relevant population	Similar across groups	Losses distributed proportionally	Similar across groups	Little additional distributional information beyond the aggregate result
Concentrated recipient gain	Health gains concentrated in a worse-off group	Lower baseline health	Losses broadly distributed	Similar across groups	Potential reduction in health inequality without changing mean cost-effectiveness
Concentrated opportunity cost	Recipient gains broadly distributed	Mixed	Health losses concentrated in a worse-off group	Similar across groups	Distributional interpretation can deteriorate despite unchanged recipient-side efficiency
Opposing health and financial patterns	Health gains concentrated in a relatively better-off group	Higher baseline health	Losses broadly distributed	Financial protection concentrated in a worse-off group	Health-distribution and FRP conclusions point in different directions
Normatively sensitive	Empirical health distributions unchanged	Unequal baseline health	Displacement unchanged	Unchanged	Decision ordering depends on the explicit equity assumption rather than new clinical evidence

The scenarios demonstrate why “equity impact” cannot be inferred from the recipients alone. A reimbursement policy can appear pro-equity on the treatment side and less favorable after displacement is allocated, or the reverse.

Opportunity-cost incidence and distributional reversals

The third demonstration varies only the incidence of displaced health. Formal analyses of value under a fixed healthcare budget show that additional objectives remain constrained by resources; recognizing another valued outcome does not remove the opportunity cost generated by spending[29]. The distributional consequence therefore depends partly on where that opportunity cost is borne.

Consider two otherwise identical synthetic reimbursement cases. Both generate the same recipient health, incremental expenditure, and aggregate opportunity cost. In the first, displaced health is distributed proportionally across the population. In the second, the same total displaced health is concentrated among a group with worse baseline health. Aggregate cost-effectiveness is unchanged, but the equity interpretation is not. Under a valuation that gives greater priority to those with worse baseline health, the second case has a less favorable distributional interpretation because the location of health loss differs.

This logic also works in the opposite direction. If displaced health falls disproportionately on groups with relatively better baseline health while recipient gains accrue to worse-off groups, the reimbursement decision can become more favorable under an inequality-sensitive analysis. These are not empirical claims about the incidence

of displacement in any particular system. They are methodological demonstrations showing that opportunity-cost incidence is an independent determinant of distributional interpretation.

Figure 1 represents the population distributions of recipient gains and displaced losses that an average ICER leaves unresolved.

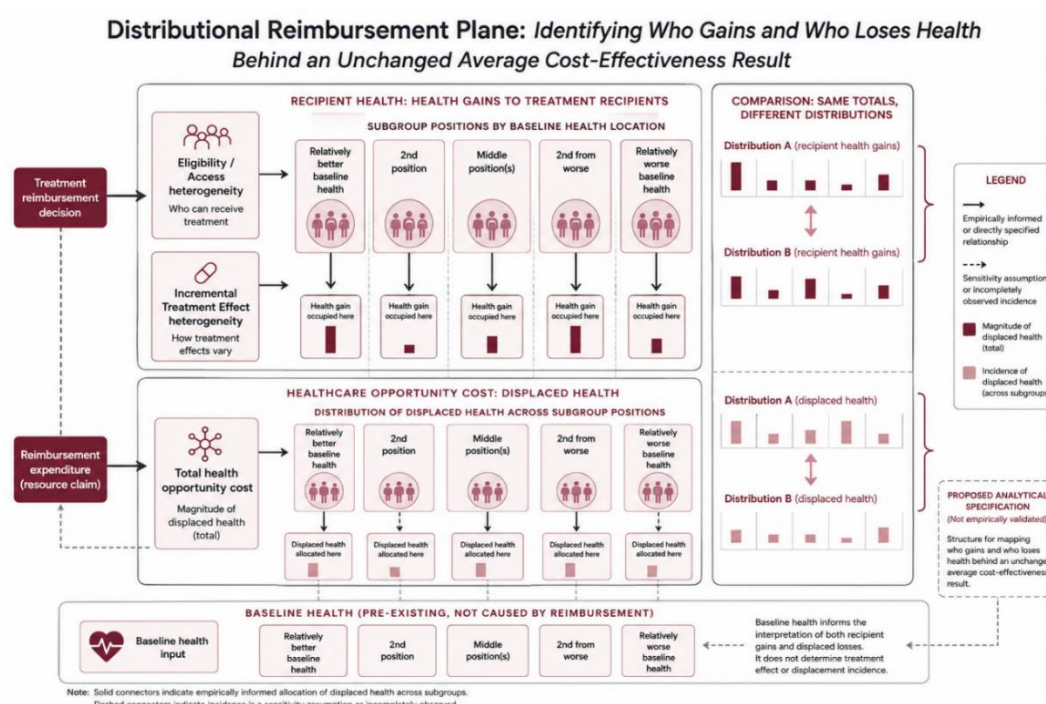


Figure 1. Population location of recipient health gains and reimbursement-related displaced health

Financial protection when health gains move in a different direction

The fourth synthetic demonstration holds the health distribution constant while varying financial protection. Alternative health-objective functions have been proposed to address perceived limitations of conventional QALY maximization, but formal analysis shows that some proposed metrics can generate internally inconsistent rankings under particular choice structures[30]. Earlier work proposing health-years-in-total illustrates the broader methodological point that modifying the objective function can change how outcomes are valued[31]. Taken together, these studies support caution before translating every additional social concern into a new composite metric.

The FRP demonstration therefore reports financial consequences alongside health rather than transforming them into a common score. A scenario can produce greater health benefit among relatively better-off patients while providing substantial protection from treatment-related expenditure among lower-income households. Another can generate favorable health distribution with little additional FRP because the medicine was already publicly financed. Neither pattern is contradictory. Health and financial exposure are different outcomes and may move independently.

Equity weighting and ranking sensitivity

The fifth demonstration introduces alternative equity assumptions only after recipient health, displaced health, and FRP have been defined. Empirical case studies of broader value elements show that adding such elements can move cost-effectiveness results in different directions across interventions[32]. Aggregate distributional cost-effectiveness analysis also demonstrates that health inequality effects can sometimes be estimated with routinely available data, although the lower data burden comes with stronger assumptions than a fully disaggregated analysis[33].

Three interpretive states follow. A reimbursement decision is distributionally robust when plausible equity weights preserve the same ordering. It is normatively sensitive when reasonable weights change the preferred option. It is data sensitive when the direction changes primarily because subgroup health, access, or opportunity-

cost incidence is uncertain. Separating these states prevents normative disagreement from being described as empirical uncertainty and prevents weak subgroup data from being disguised by precise equity weights.

Separating efficiency, health distribution, and financial protection in decision output

The final demonstration considers the output shown to a reimbursement committee. Empirical evidence indicates that equity and efficiency do not always form a fixed trade-off: improvements in system performance can sometimes increase both population health and equity[34]. Applied aggregate DCEA also shows that distributional consequences depend on disease characteristics, treatment features, population patterns, and modeling assumptions rather than following a universal direction[35].

The decision output should therefore retain three primary consequences: efficiency, distributional health, and FRP. Normative weights may subsequently influence deliberation, but their effect should remain identifiable. The same approach applies to uncertainty: clinical uncertainty, opportunity-cost uncertainty, subgroup-incidence uncertainty, and normative uncertainty should not be collapsed into a single confidence label.

Table 3. Interpretation of distributional reimbursement outputs without compulsory aggregation

Decision dimension	Primary question	Evidence-bearing input	What can change the conclusion	Appropriate interpretation
Efficiency	Does reimbursement generate sufficient health relative to its resource claim?	Incremental cost, incremental health, opportunity-cost estimate	Clinical effect, cost, price, supply-side health productivity	Conventional cost-effectiveness conclusion
Recipient distribution	Which groups receive the treatment-related health gain?	Eligibility, access, uptake, effect heterogeneity, baseline health	Differential access or treatment effect	Distribution of direct benefit
Opportunity-cost distribution	Which groups bear health displaced elsewhere?	Total displaced health and subgroup incidence	Budget scale, expenditure profile, incidence assumption	Distribution of indirect health loss
Net health distribution	How are recipient gains and displaced losses jointly located?	Recipient and opportunity-cost distributions	Either side of the distributional accounting	Population health-inequality consequence
Financial-risk protection	Who receives protection from household financial burden?	Coverage and out-of-pocket exposure	Benefit design, household income, prior financing	Distinct financial consequence
Normative weighting	How much relative social value is assigned to specified gains or losses?	Explicit equity parameter or decision rule	Severity, subgroup definition, preference method	Normative sensitivity, not new clinical evidence
Uncertainty	Which conclusion depends on weak evidence or assumptions?	Parameter, structural, incidence, and normative uncertainty	Data quality and scenario choice	Robust, data-sensitive, or normatively sensitive decision

The resulting methodological output does not dictate that reimbursement committees must optimize several objectives simultaneously. It makes explicit which conclusion follows from efficiency evidence, which follows from the distribution of health, which follows from financial protection, and which depends on normative judgment. An average ICER can remain the central efficiency statistic while ceasing to function as a complete description of who benefits and who bears the consequences of reimbursement.

Reimbursement consequences of making opportunity-cost incidence explicit

The methodological demonstrations indicate that medicines reimbursement can have distributional consequences on two sides of the decision. Recipient-side analysis identifies who receives the health generated by the medicine, whereas supply-side analysis identifies who bears health losses associated with displaced healthcare.

Conventional opportunity-cost reasoning establishes why the second quantity exists[2], but socially disaggregated expenditure analysis shows why its incidence cannot always be assumed to be uniform[9].

This distinction becomes consequential when recipient and displaced-health distributions differ materially. If a medicine principally benefits a population with worse baseline health while displaced health is widely distributed, equity-sensitive interpretation may strengthen the reimbursement case. If the same recipient gains are financed through health losses concentrated in another disadvantaged population, the conclusion can weaken or reverse. These possibilities do not imply that distributional analysis routinely changes reimbursement decisions. Applied work demonstrates that distributional effects depend on treatment access, disease characteristics, effect heterogeneity, baseline health, and model assumptions[16]. The additional analysis is most valuable when those factors produce asymmetry that an aggregate ICER cannot describe.

Making incidence explicit also clarifies the relationship between affordability and equity. Nonmarginal budget impacts can alter the amount of health displaced as adoption expands[4], but the distributional question remains distinct: once the health opportunity cost has been estimated, which population groups bear it? A reimbursement analysis can therefore be sophisticated about budget impact while remaining distributionally incomplete if it represents displaced health only as an aggregate quantity.

For medicines with large eligible populations, high prices, prolonged treatment duration, or rapid uptake, this separation may be particularly important because the scale and timing of expenditure can affect opportunity costs[12]. Yet the method should not presume that these characteristics necessarily create adverse equity effects. The empirical question concerns the actual or plausibly modeled location of gains and losses.

Policy use without collapsing plural objectives into one score

Efficiency, distributional health, and financial-risk protection should initially be presented as distinct decision outputs. The broader-value literature supports the relevance of consequences beyond conventional health gain[7], while FRP methods demonstrate that protection from household financial burden can have a distribution different from the distribution of health benefits[19]. Treating these outputs separately preserves the information required for deliberation.

Normative aggregation remains possible when a decision maker has a defensible social-welfare function, equity parameter, or explicitly adopted weighting rule. The methodological concern is not aggregation itself but opacity. Equity-preference studies show substantial variation across elicitation methods and populations[25], meaning that a weighted result can be sensitive to normative assumptions even when the underlying clinical and economic evidence is unchanged. A reimbursement recommendation should therefore identify whether its distributional conclusion is driven by observed subgroup effects, assumptions about displaced-health incidence, financial-risk consequences, or the social weights attached to those outcomes.

Severity modifiers used in health technology assessment provide one example of explicit normative adjustment[28]. Their advantage for transparency is that the valuation rule can be stated and interrogated. By contrast, combining heterogeneous value elements into an undocumented composite risks obscuring which judgment altered the decision. Formal criticisms of alternative health-objective functions further show that new metrics require validation of their logical properties before being treated as replacements for established measures[30].

Figure 2 decomposes the reimbursement problem without requiring a new universal value score.

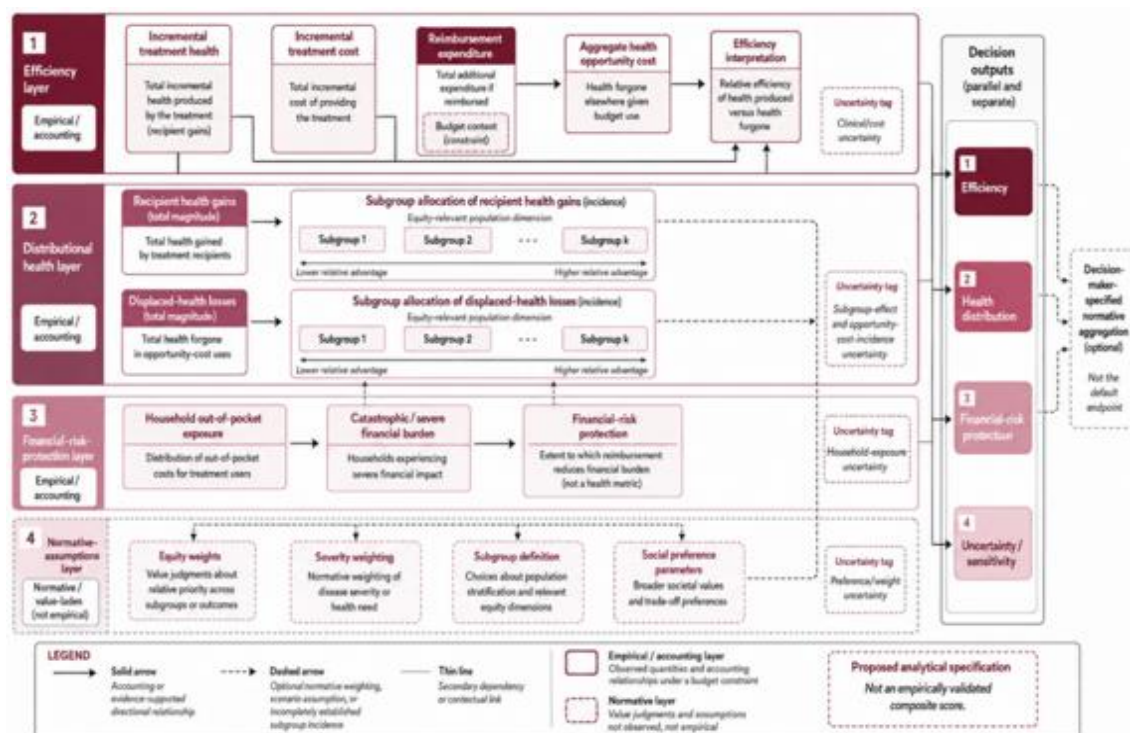


Figure 2. Decomposition of reimbursement value into efficiency, health distribution, financial protection, and normative judgment

Data, implementation, and transferability limits

The principal limitation of the method is its data requirement. Reliable distributional analysis needs information on baseline health, treatment eligibility, access, treatment effects, healthcare use, and the social distribution of health opportunity costs. Baseline health distributions can be estimated for multiple equity dimensions[13], but the quality and availability of equivalent data vary substantially across health systems.

Opportunity-cost incidence is especially challenging. Aggregate distributional methods can reduce the data burden by linking routinely available disease-area information to social groups[33], although their convenience is obtained through assumptions that may not hold in every reimbursement setting. When empirical incidence is unavailable, sensitivity analysis should span distributions that are both substantively plausible and sufficiently different to reveal whether the reimbursement conclusion is dependent on the assumption.

Transferability is limited further by differences in financing arrangements. FRP is likely to be more decision-relevant where households face substantial out-of-pocket exposure than where comprehensive public coverage already protects patients from medicine costs. Similarly, equity weights elicited in one population should not be treated as transportable social preferences when preference studies show substantial methodological and geographic heterogeneity[24].

Model precision should therefore reflect evidence precision. A distributional reimbursement analysis should not display finely resolved subgroup results when treatment-effect heterogeneity, displacement incidence, or preference parameters are poorly identified.

Disconfirming cases and priorities for methodological validation

The value of the proposed specification can be tested through cases in which it should add little information. If treatment benefits and displaced-health losses are proportionally distributed across relevant groups, financial protection is equivalent across alternatives, and no differential equity weighting is applied, distributional analysis should converge toward the conventional efficiency ordering. A method that nevertheless produces a substantial equity effect under those conditions would require methodological justification.

A second test concerns robustness to opportunity-cost incidence. If materially different but plausible incidence assumptions produce the same reimbursement conclusion, the distributional interpretation is robust to this uncertainty. If the conclusion reverses repeatedly, the decision should be reported as incidence-sensitive rather than as an established equity result.

A third test concerns normative assumptions. Equity-weight elicitation is heterogeneous[25], so reimbursement conclusions that change only after alternative social weights are imposed should be identified as normatively sensitive. That sensitivity is decision-relevant, but it is not new empirical evidence about the medicine.

Finally, distributional methods require prospective validation against richer empirical data. Applied analyses show that distributional direction can depend strongly on disease and treatment characteristics[35]. Future methodological work should therefore compare aggregate and fully disaggregated approaches, test alternative methods for estimating the social incidence of displaced health, and evaluate whether distributional information actually changes reimbursement deliberation when decision makers are presented with efficiency, health distribution, financial protection, and normative assumptions separately.

Conclusion

An average cost-effectiveness ratio can establish an efficiency relationship without revealing the population distribution that produced it. Medicines reimbursement can generate health for treated patients while displacing health elsewhere, and the people bearing that opportunity cost may differ from the people receiving the medicine. Equity-informative reimbursement therefore requires explicit representation of both sides of the health accounting. Baseline health, recipient heterogeneity, financial-risk protection, and normative equity weights add further dimensions, but these should remain identifiable rather than disappearing into an unvalidated composite score.

The distributional extension is most consequential when health gains, health losses, or financial protection are unevenly allocated. When those distributions are effectively proportional, conventional cost-effectiveness may already provide the same practical ordering. The methodological contribution is thus conditional: make distribution visible where it contains decision-relevant information, make normative judgments explicit where they alter interpretation, and preserve the distinction between empirical evidence and social valuation.

Acknowledgments: None

Conflict of Interest: None

Financial Support: None

Ethics Statement: None

References

1. Cookson R, Mirelman AJ, Griffin S, Asaria M, Dawkins B, Norheim OF, et al. Using cost-effectiveness analysis to address health equity concerns. *Value Health*. 2017;20(2):206-12. doi:10.1016/j.jval.2016.11.027
2. Sculpher M, Claxton K, Pearson SD. Developing a value framework: The need to reflect the opportunity costs of funding decisions. *Value Health*. 2017;20(2):234-9. doi:10.1016/j.jval.2016.11.021
3. Danzon PM, Drummond MF, Towse A, Pauly MV. Objectives, budgets, thresholds, and opportunity costs—a health economics approach: An ISPOR Special Task Force Report [4]. *Value Health*. 2018;21(2):140-5. doi:10.1016/j.jval.2017.12.008
4. Lomas J, Claxton K, Martin S, Soares M. Resolving the “cost-effective but unaffordable” paradox: Estimating the health opportunity costs of nonmarginal budget impacts. *Value Health*. 2018;21(3):266-75. doi:10.1016/j.jval.2017.10.006
5. Avanceña ALV, Prosser LA. Examining equity effects of health interventions in cost-effectiveness analysis: A systematic review. *Value Health*. 2021;24(1):136-43. doi:10.1016/j.jval.2020.10.010
6. Paulden M. A framework for the fair pricing of medicines. *Pharmacoeconomics*. 2024;42(2):145-64. doi:10.1007/s40273-023-01325-z
7. Neumann PJ, Garrison LP, Willke RJ. The history and future of the “ISPOR value flower”: Addressing limitations of conventional cost-effectiveness analysis. *Value Health*. 2022;25(4):558-65. doi:10.1016/j.jval.2022.01.010

8. McQueen RB, Inotai A, Zemplyeni A, Mendola N, Németh B, Kalo Z. Multistakeholder perceptions of additional value elements for United States value assessment of health interventions. *Value Health*. 2024;27(1):15-25. doi:10.1016/j.jval.2023.09.2910
9. Love-Koh J, Cookson R, Claxton K, Griffin S. Estimating social variation in the health effects of changes in health care expenditure. *Med Decis Making*. 2020;40(2):170-82. doi:10.1177/0272989X20904360
10. Sampson C, Zamora B, Watson S, Cairns J, Chalkidou K, Cubi-Molla P, et al. Supply-side cost-effectiveness thresholds: Questions for evidence-based policy. *Appl Health Econ Health Policy*. 2022;20(5):651-67. doi:10.1007/s40258-022-00730-3
11. Howdon DDH, Lomas JRS, Paulden M. Implications of nonmarginal budgetary impacts in health technology assessment: A conceptual model. *Value Health*. 2019;22(8):891-7. doi:10.1016/j.jval.2019.04.001
12. Lomas JRS. Incorporating affordability concerns within cost-effectiveness analysis for health technology assessment. *Value Health*. 2019;22(8):898-905. doi:10.1016/j.jval.2019.05.003
13. Kowal S, Ng CD, Schuldt R, Sheinson D, Jinnett K, Basu A. Estimating the US baseline distribution of health inequalities across race, ethnicity, and geography for equity-informative cost-effectiveness analysis. *Value Health*. 2023;26(10):1485-93. doi:10.1016/j.jval.2023.06.015
14. Kowal S, Ng CD, Schuldt R, Sheinson D, Cookson R. The impact of funding inpatient treatments for COVID-19 on health equity in the United States: A distributional cost-effectiveness analysis. *Value Health*. 2023;26(2):216-25. doi:10.1016/j.jval.2022.08.010
15. Jansen JP, Ragavan MV, Chen C, Douglas MP, Phillips KA. The health inequality impact of liquid biopsy to inform first-line treatment of advanced non-small cell lung cancer: A distributional cost-effectiveness analysis. *Value Health*. 2023;26(12):1697-710. doi:10.1016/j.jval.2023.08.010
16. Jansen JP, Brewer IP, Chung S, Sullivan P, Díaz Espinosa O, Partridge Grossman J. The health inequality impact of a new cancer therapy given treatment and disease characteristics. *Value Health*. 2024;27(2):143-52. doi:10.1016/j.jval.2023.11.001
17. Goshua G, Calhoun C, Ito S, James LP, Luviano A, Krishnamurti L, et al. Distributional cost-effectiveness of equity-enhancing gene therapy in sickle cell disease in the United States. *Ann Intern Med*. 2023;176(6):779-87. doi:10.7326/M22-3272
18. Quan AML, Mah C, Krebs E, Zang X, Chen S, Althoff K, et al. Improving health equity and ending the HIV epidemic in the USA: A distributional cost-effectiveness analysis in six cities. *Lancet HIV*. 2021;8(9):e581-90. doi:10.1016/S2352-3018(21)00147-8
19. Verguet S, Norheim OF. Estimating and comparing health and financial risk protection outcomes in economic evaluations. *Value Health*. 2022;25(2):238-46. doi:10.1016/j.jval.2021.08.004
20. Hendrix N, Bolongaita S, Villano D, Memirie ST, Tolla MT, Verguet S. Equitable prioritization of health interventions by incorporating financial risk protection weights into economic evaluations. *Value Health*. 2023;26(3):411-7. doi:10.1016/j.jval.2022.09.007
21. Mao W, Watkins D, Sabin ML, Huang K, Langlois E, Ogundeji Y, et al. Effects of public financing of essential maternal and child health interventions across wealth quintiles in Nigeria: An extended cost-effectiveness analysis. *Lancet Glob Health*. 2023;11(4):e597-605. doi:10.1016/S2214-109X(23)00056-6
22. Fraser HL, Feldhaus I, Edoka IP, Wade AN, Kohli-Lynch CN, Hofman K, et al. Extended cost-effectiveness analysis of interventions to improve uptake of diabetes services in South Africa. *Health Policy Plan*. 2024;39(3):253-67. doi:10.1093/heapol/czae001
23. Reckers-Droog V, van Exel J, Brouwer W. Willingness to pay for health-related quality of life gains in relation to disease severity and the age of patients. *Value Health*. 2021;24(8):1182-92. doi:10.1016/j.jval.2021.01.012
24. Khor S, Elsiszi ZA, Carlson JJ. How much does the US public value equity in health? A systematic review. *Value Health*. 2023;26(3):418-26. doi:10.1016/j.jval.2022.08.009
25. Cadham CJ, Prosser LA. Eliciting trade-offs between equity and efficiency: A methodological scoping review. *Value Health*. 2023;26(6):943-52. doi:10.1016/j.jval.2023.02.006
26. Lal A, Mohebi M, Sweeney R, Moodie M, Peeters A, Carter R. Equity weights for socioeconomic position: Two methods—survey of stated preferences and epidemiological data. *Value Health*. 2019;22(2):247-53. doi:10.1016/j.jval.2018.07.006

27. Synnott PG, Majda T, Lin PJ, Ollendorf DA, Zhu Y, Kowal S. Modeling the population equity of Alzheimer disease treatments in the US. *JAMA Netw Open*. 2024;7(10):e2442353. doi:10.1001/jamanetworkopen.2024.42353
28. Njoroge MW, Walton M, Hodgson R. Understanding the National Institute for Health and Care Excellence severity premium: Exploring its implementation and the implications for decision making and patient access. *Value Health*. 2024;27(6):730-6. doi:10.1016/j.jval.2024.02.013
29. Phelps CE. Values beyond “health” in budget-constrained healthcare systems. *Value Health*. 2024;27(7):830-6. doi:10.1016/j.jval.2024.02.005
30. Paulden M, Sampson C, O'Mahony JF, Spackman E, McCabe C, Round J, et al. Logical inconsistencies in the health years in total and equal value of life-years gained. *Value Health*. 2024;27(3):356-66. doi:10.1016/j.jval.2023.11.009
31. Basu A, Carlson J, Veenstra D. Health years in total: A new health objective function for cost-effectiveness analysis. *Value Health*. 2020;23(1):96-103. doi:10.1016/j.jval.2019.10.014
32. Ma S, Olchanski N, Cohen JT, Ollendorf DA, Neumann PJ, Kim DD. The impact of broader value elements on cost-effectiveness analysis: Two case studies. *Value Health*. 2022;25(8):1336-43. doi:10.1016/j.jval.2022.01.025
33. Love-Koh J, Cookson R, Gutacker N, Patton T, Griffin S. Aggregate distributional cost-effectiveness analysis of health technologies. *Value Health*. 2019;22(5):518-26. doi:10.1016/j.jval.2019.03.006
34. Sandiford P, Vivas Consuelo D, Rouse P, Bramley D. The trade-off between equity and efficiency in population health gain: Making it real. *Soc Sci Med*. 2018;212:136-44. doi:10.1016/j.socscimed.2018.07.005
35. Meunier A, Longworth L, Gomes M, Ramagopalan S, Garrison LP, Popat S. Distributional cost-effectiveness analysis of treatments for non-small cell lung cancer: An illustration of an aggregate analysis and its key drivers. *Pharmacoeconomics*. 2023;41(8):1011-25. doi:10.1007/s40273-023-01281-8