

Perspective Mismatch and Static Assumptions: Re-Thinking How Drug Prices Are Specified in U.S. Economic Analyses

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Background

- Economic analyses are decision-relevant only when costs reflect opportunity costs (i.e., value of resources in their next-best use) [1-3]
- In U.S. pharmaceutical markets:
 - Pricing is decentralized and negotiated across multiple actors; different payers (and even plans within payers) have different terms
 - Stakeholders transact at different “prices” for the same product, reflecting distinct transactions across the supply and payment chain and aligning with different analytic perspectives
 - Many relevant price measures are not directly observable, and perspective-consistent price metrics must often be approximated using available data
 - Drug prices evolve over the product lifecycle:
 - After loss of exclusivity (LOE; i.e., price erosion following generic or biosimilar entry) [4-6]
 - During exclusivity (e.g., competition, rebates, and new clinical evidence) [7-9]
- As a result, no single observed U.S. drug price corresponds to opportunity costs across all analytic perspectives or over time; price metrics must be constructed to match the decision context
- Two common departures from opportunity cost-consistent pricing in U.S. economic analyses:
 - Use of price metrics that are not aligned with the analytic perspective: analyses often rely on price proxies that do not reflect the opportunity costs relevant to the decision maker [10]
 - Static treatment of drug prices over time: prices are commonly assumed to be constant despite predictable changes over the product lifecycle [10]

→ These choices can introduce systematic bias in estimates of cost and value (e.g., cost-effectiveness analysis [CEA], budget impact analysis, and business forecasting)

Research objectives

- To clarify how U.S. drug price measures map to analytic perspectives and the opportunity costs they are intended to represent
- To review and classify approaches for incorporating drug price dynamics in economic analyses over the product lifecycle

Methods

- Targeted review of U.S. methodologic guidance, as well as empirical and conceptual literature on pharmaceutical pricing
- Analytical approach
 - Mapped commonly used price measures to analytic perspectives, positions in the supply and payment chain, and key considerations for their use as perspective-consistent price metrics
 - Classified approaches for modeling drug price dynamics over the product lifecycle

Results

Price Measures and Analytic Perspective

- We mapped commonly used U.S. drug price measures to analytic perspectives based on their position in the supply and payment chain and identified key considerations for economic analysis (**Table 1**)
- It is important to distinguish between:
 - Pricing benchmarks**, which are institutionally defined reference prices used in reimbursement, contracting, and policy (e.g., wholesale acquisition cost [WAC], average wholesale price [AWP], and National Average Drug Acquisition Cost [NADAC])
 - Price metrics**, which are constructs that are aligned with analytic perspectives (e.g., manufacturer net revenue, payer net liability, patient out-of-pocket payments, and system-level cost)
 - Note: some price measures may function as both benchmarks and metrics (e.g., NADAC) depending on how they are used and what they are intended to represent
- Empirical evidence indicates that CEAs often rely on readily available, but potentially inaccurate, pricing benchmarks [10]
 - Approximately two-thirds of a sample of U.S. CEAs used list-based pricing benchmarks (e.g., WAC, AWP, and hybrids of both), which do not reflect realized transaction prices
 - An additional 8% used manufacturer net prices, even though these reflect manufacturer revenues (and the manufacturer perspective) and may overstate payer or system costs substantially [11, 12]
- Commonly used price inputs do not correspond to the costs that are relevant to a given analytic perspective because they reflect payments across the supply and payment chain rather than the underlying cost of resources (see **Box 1**)
 - Resource costs** reflect the use of the real economic resources required to produce, distribute, and deliver drugs (e.g., manufacturing, distribution, dispensing, and administration)
 - Financial transfers** redistribute payments across stakeholders without changing underlying resource use; classification depends on analytic perspective (e.g., rebates, discounts, and fees for the societal perspective)
- Because no single price metric corresponds to opportunity costs across perspectives, any given price may be informative for one perspective but misleading for another**

Box 1. Example: Mismatches Between Price and Societal Perspective

- From a societal perspective, opportunity costs reflect the real resources used to develop, produce, and deliver a drug to patients, yet analysts commonly use two measures that diverge from the true economic cost:
 - Manufacturer list price:** a “sticker” price, which is rarely an actual transaction price; it does not reflect rebates and discounts and, for provider-administered drugs, does not reflect provider price mark-ups
 - Manufacturer net price:** what manufacturers retain after rebates and discounts; it understates societal opportunity costs by excluding an estimate of the value of other resources needed to provide the drug to the patient

Price Dynamics Over the Product Lifecycle

- We identified five distinct approaches in the literature for incorporating drug price dynamics over the product lifecycle (**Table 2**). These approaches differ in how price changes are represented, the data required for implementation, and considerations for economic analyses
 - Discrete reductions at LOE** [16, 17]: applies fixed or staged price drops following generic or biosimilar entry. Requires assumptions on timing, uptake, and magnitude of price change. Simple and transparent, but does not capture pre-LOE dynamics and may therefore misrepresent price evolution
 - Time-varying erosion curves**: uses empirical data on observed price trajectories to parameterize functional forms that model gradual pre- and/or post-LOE price changes toward a long-run floor. Requires assumptions on decline rates, time to floor, and terminal price. More realistic and flexible, but sensitive to structural assumptions about price trajectories
 - Analog-based forecasts**: uses lifecycle price trajectories of comparable products to inform expected price evolution. Requires selection and justification of appropriate analogs and alignment of their price trajectories to the product of interest over the relevant time horizon. Best suited for early-stage analyses (e.g., at launch) and for other instances when direct data are limited, but less reliable for unique products and following policy changes that impact pricing behavior
 - Structural/dynamic industrial organization models**: simulates pricing behavior under competition and explicitly links price dynamics to demand, costs, and market structure. Requires detailed data on prices, quantities, and assumptions about market conditions. Data-intensive, but allows for internally consistent projections since they are based on the fundamental tenets of economic theory
 - Cost-based pricing floors**: defines the lower bounds for long-run prices based on production costs (e.g., cost of goods sold [COGS] plus some margin). Requires estimates of manufacturing costs and mark-ups. Useful for benchmarking price floors, but may not reflect observed market prices. Estimation is challenged by the proprietary nature of COGS
- Key implications:
 - Approaches vary substantially in data requirements, from simple class-level assumptions to detailed market data
 - Most focus on post-LOE dynamics, while price changes during exclusivity are less frequently incorporated
 - The choice of approach can materially affect cost-effectiveness and budget impact estimates (particularly in long-horizon analyses) and introduce structural uncertainty related to timing and the magnitude of price changes

Table 1. Examples of U.S. Drug Price Measures: Perspectives and Key Considerations

Price measure	Transaction (buyer → seller)	Key considerations for economic analyses
Published list price benchmarks (WAC, AWP)	Wholesaler or direct purchaser → manufacturer	Administrative benchmark; excludes rebates and discounts; not a realized transaction price; sometimes used in benefit design (e.g., to calculate patient cost sharing)
Manufacturer net price (price net of rebates, chargebacks, discounts, and fees)	Wholesaler or direct purchaser → manufacturer	Net revenue per sale; typically confidential; proprietary estimates available; excludes downstream margins and costs
Retail pharmacy acquisition prices (NADAC, AAC, invoice prices)	Retail pharmacy → wholesaler (or manufacturer)	Retail community pharmacy acquisition costs; may exclude off-invoice concessions (e.g., bulk discounts)
Provider acquisition/“buy-and-bill” pricing measures (ASP)	Provider (e.g., hospital, physician practice) → wholesaler (or manufacturer)	Highly variable across sites and contracts; confidential; ASP-based reimbursement is common; imperfect proxy for provider acquisition cost in medical-benefit settings
Federal and statutory acquisition prices (FSS, FCP)	Federal purchaser (e.g., VA, DoD) → manufacturer	Derived from statutory pricing rules and federal contracting frameworks; observable
340B-covered entity acquisition prices	340B-covered entity → manufacturer	Applies only to eligible entities; governed by statutory program rules; discounts typically mediated via wholesaler chargebacks; may differ substantially from non-340B acquisition prices [13]
Post-discount payer net liability	Insurer or self-insured employer (plan sponsor) → pharmacy or provider	Constructed net spending measure; combines adjudicated claims payments with estimated rebates, fees (e.g., DIR), and other off-claims financial transfers (e.g., PBM administrative fees) [14, 15]
Patient-facing prices	Patient → pharmacy or provider	Determined by benefit design (e.g., deductibles, copays, coinsurance, and maximizer and accumulator programs); varies across plans and over time
Systemwide net expenditures (SNE)	Healthcare sector as a consolidated buyer → the supply chain as a consolidated seller	Does not correspond to a single buyer-seller transaction; requires estimation of payments and retained margins across the entire supply chain; relevant for both the healthcare sector and societal perspectives; SNE has been estimated for insulin [11]

340B, 340B Drug Pricing Program; AAC, actual acquisition cost; ASP, average sales price; AWP, average wholesale price; DIR, direct and indirect remuneration; DoD, Department of Defense; FCP, federal ceiling price; FSS, federal supply schedule; NADAC, National Average Drug Acquisition Cost; PBM, pharmacy benefit manager; SNE, systemwide net expenditure; VA, Department of Veterans Affairs; WAC, wholesale acquisition cost.

Table 2. Approaches to Modeling Drug Price Dynamics in CEA

Approach (recent examples)	Description	Key data requirements	Key considerations
One-time price reductions at LOE [16, 17]	Apply discrete price reductions at or after generic/biosimilar entry, sometimes phased in over a short period	LOE timing; assumptions on entry, uptake, and magnitude of price reduction	Most common approach; simple and transparent; does not capture pre-LOE dynamics; sensitive to assumptions on timing, magnitude, and occurrence of generic/biosimilar entry and resulting price reductions
Time-varying erosion curves [18-21]	Model post-LOE price evolution using specified functional form (e.g., linear, exponential, or piecewise), usually with assumed long-run floor price	Baseline price; assumptions on data on the timing and rate of price change over time; floor price	Flexible; can capture gradual, time-dependent dynamics; sensitive to assumed trajectory shape and long-run price; requires structural assumptions about price evolution
Analog-based forecasts [22, 23]	Use observed price trajectories of comparable (“analog”) products to project future prices	Selection of appropriate analogs; alignment of price levels and timing (e.g., launch, LOE); scaling assumptions	Useful when direct data are limited (e.g., early-stage analyses); validity depends on comparability of products, markets, and policy environments; may be misleading for novel therapies or changing market conditions; requires justification
Structural/dynamic IO models [24, 25]	Model pricing using economic theory that is relevant for the specific market structure (e.g., oligopolistic competition); link price dynamics to competition, demand, and market structure over time	Price and quantity data; assumptions about demand, costs, competition, and market rules	Grounding in economic theory provides internally consistent predictions and facilitates simulation of responses to competition and policy changes; can be data intensive
Cost-based pricing floors [26]	Define lower bounds for long-run post-LOE prices based on production costs (e.g., COGS plus mark-up)	Estimates of COGS; mark-up assumptions	Useful for bounding long-run prices in competitive scenarios; may not reflect observed market prices in settings with significant intermediary margins or limited competition; uncertainty in COGS estimates owing to the proprietary and evolving nature of manufacturer cost data

CEA, cost-effectiveness analysis; COGS, cost of goods sold; IO, industrial organization; LOE, loss of exclusivity.

Discussion

- Delivering a drug from the manufacturer to the patient in the U.S. involves many different transactions between different stakeholders, each occurring at different transaction prices (as well as at different points in time)
- Common simplifying assumptions about prices can materially impact results in systematic and predictable ways
 - Using price metrics that are misaligned with analytic perspectives will bias estimates of costs [8, 11, 27]
 - Assuming static prices (despite predictable pre-LOE price dynamics and generic/biosimilar entry in the U.S.) will misstate costs over the product lifecycle [16-18, 28, 29] and can therefore potentially reverse value conclusions informed by CEAs [16, 17, 29], misstate budget impact, and distort other types of economic analyses
- These distortions are most consequential when drug costs are key drivers of results
 - The impact of pricing assumptions is greatest when drug spending constitutes a large share of total costs, treatment duration is long, or the timing of price changes differs across alternatives (e.g., different LOE dates)
- Structured approaches can improve the alignment of price inputs with opportunity costs
 - Emerging literature proposes methods to estimate perspective-consistent price metrics and model price dynamics [16-26]
 - Key considerations for tailoring price metrics and trajectories to the needs of each analysis should include institutional features (e.g., statutory rules and patent system), market behavior (e.g., extent of competition within and across drug classes), and data availability (e.g., confidentiality)
- Well-specified analyses remain approximations of true opportunity costs
 - U.S. drug prices reflect negotiated transactions, financial transfers, and institutional rules rather than direct measures of resource opportunity costs
- Explicit price justifications are needed to guide analyses and interpretation
 - Analysts should justify price inputs in relation to analytic perspectives and explore alternative price trajectories
 - Decision makers should interpret results with appropriate caution

Conclusions

- Specification of drug price inputs can materially influence the interpretation of economic analyses, especially when drug costs are significant drivers of results
- Assumptions about price dynamics and analytic perspectives must be carefully aligned with the decision context to avoid misestimating true opportunity costs
- Estimates of opportunity costs are inherently approximations due to the structure of the U.S. drug development, manufacturing, and distribution system, which involves numerous negotiated transactions and institutional rules that are not static
- Analysts should explicitly justify price inputs and consider alternative price trajectories
- Reviewers and decision makers must interpret results cautiously and avoid overgeneralizing across settings or perspectives
- Continued methodological progress and empirical work is needed to support the use of price metrics that better approximate opportunity costs in U.S. economic analyses

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