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# ICER's Unsupported Price Increase Report: Unfit for Policymaking



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Since 2019, the Institute for Clinical and Economic Review (ICER) has published an annual Unsupported Price Increase (UPI) Report on its "assessment on drugs that experience significant price hikes without any novel clinical evidence" to guide policy making on prescription drugs. US lawmakers have shown interest in the UPI approach as a potential tool to optimize healthcare resource allocation. As ICER is once again seeking manufacturer participation for the 5th report (covering data for 2022), this whitepaper offers an investigation into UPI protocols and published reports. Our analysis of the UPI approach documents conceptual inconsistencies, procedural inadequacies, and substantial threats to the internal and external research validity. We discuss how the UPI reports' findings are based on a partial product selection, how ICER rejects high-quality evidence and how the report offers healthcare decision makers misleading guidance on the value of the assessed products. We find that significant methodological flaws mar the UPI reports' potential utility. Beyond being a flawed academic exercise, reliance on the UPI approach in coverage and pricing could cause unintended consequences that US healthcare decision makers and patients can ill afford.

## CONTEXT

Prescription drug spending remains a priority for US federal and state lawmakers. While initiatives such as price transparency and drug affordability boards are now law in some states, several jurisdictions are considering regulating price increases.[1] Proposed state legislation would impose taxes or penalties when the list price (i.e., wholesale acquisition cost [WAC]) of a branded medicine increases above a pre-specified threshold and that increase is deemed "unsupported" by clinical evidence.[1,2] As unsupported price increase-based policy proposals are shaped by analyses from private third-party organizations, such as the Institute for Clinical and Economic Review, they should be subject to rigorous standards and open debate.

ICER, a 501(c)(3) non-profit, is a research organization that issues health policy papers and reports on the clinical and cost-effectiveness of pharmaceutical products.[3] ICER's operations are funded through grants, contracts, and unrestricted gifts from donors, the largest being Arnold Ventures LLC.[4] Crediting financial support from Arnold Ventures, ICER launched its annual Unsupported Price Increases Report (UPI Report) in 2019 to "advance the public debate on drug price increases." Its most recent edition (published on December 6, 2022) covers the year 2021. As decision makers consider using the report to define health policy and to affect resource allocation, the quality and objectivity of the analysis, methodology, interpretation of the findings, and its implications require critical review.

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## ICER'S UPI RESEARCH PREMISE

When assessing the quality of any social science research program, a foundational consideration is whether the research design offers precisely defined terms and avoids logical fallacies regarding measuring causations, relationships, or associations.[5]

The report's title and study variable of interest – "unsupported price increases" – suggests that the market price increases analyzed were unjustified by clinical evidence and should therefore be subject to enhanced scrutiny by healthcare decision makers. If price is a market dynamic between supply and demand, then such framing is misleading in that it implies that market pricing dynamics rest solely on recently published clinical trial data. However, the US pharmaceutical pricing process reaches beyond the data ICER deems sufficient. Prices result from a competitive and negotiated process between multiple actors involving rebates, channel concessions, volume agreements, and utilization restrictions, among other factors.[6,7] ICER's assessments acknowledge the importance of domains such as utilization management and formulary tiering given their direct association with net pricing yet ignore these same domains in its UPI Report.[8]

Acknowledging the ambiguity around an ill-defined research question, the UPI report states as a limitation that the methodology "cannot determine whether a price increase for a drug is fully justified by new clinical evidence ".[3] The degree to which the UPI analysis offers only a partial view of a price change justification remains unaddressed, and it is forgotten in the headline.[3] The approach rests on a logical fallacy. ICER's finding of a lack of literature does not necessarily mean a price change is unsupported. Other factors, including the perceived value of the drug, may explain observed price changes. Ignoring other explanatory variables simply threatens the internal validity of the research.

ICER's blurred research construct can be restated more simply. Conclusions of the UPI Report are based on ICER's categorical determination of clinical evidence meeting its own expectations. The presence or lack of clinical evidence meeting ICER criteria is then erroneously interpreted as the sole legitimate foundation for pricing dynamics, a misconstruction of drug reimbursement realities without economic, strategic pricing, or health economic rationale.

> *"Conclusions of the UPI Report are based on ICER's categorical determination of clinical evidence meeting its own expectations."*

## THE UPI APPROACH

Our review finds that ICER's UPI methodology lacks substantiation in the health economics literature. It can be best described as a set of sequential analytical steps to rank products.

1. Net sales estimates are obtained from a proprietary approximation by SSR Health LLC to determine 250 medicines with the highest net revenues.[9]
2. Changes in the average WAC are calculated for the selected 250 products, and those with an increase exceeding the medical consumer price index by 2% qualify for further examination.[9] In the most recent UPI Report for 2020 data, 32 drugs exceeded this threshold.
3. For those 32 products, ICER again utilizes SSR Health estimates to calculate net price changes, gauging net sales and expected budget changes due to the change in net price. ICER then excludes drugs from consideration based on a "lack of face validity" if the net price is higher than the WAC price. In the most recent report, 11 of the 32 drugs— more than one-third–were excluded due to this inconsistency.[10]
4. ICER arbitrarily adds three products meeting certain subjective criteria, undermining their primary selection methodology and raising questions about the impartiality of drug selection. For example, the addition of "drugs whose price increases raise concerns about the fairness of the price increases" is particularly problematic and open to interpretation.[9]
5. Manufacturers of the 15 highest ranked products are then notified that their drugs will potentially be reviewed for price justification. The manufacturers are granted three weeks to clarify the calculated estimates of average price changes or budget impact. Disputes must include either the effect of net price changes on change in revenue, or average net prices and total sales volumes for the evidence review period.
6. Finally, after disputes are resolved, the top 10 drugs remaining on the list are evaluated further. ICER determines all indications that account for at least 10% of the utilization of each drug. For the indications above the 10% threshold, ICER assesses the quality of the clinical evidence drawing on the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) scale.[11] If ICER analysts rate evidence as "moderate or high quality" according to the GRADE scale, the net benefit is estimated using the ICER Evidence Rating Matrix.[12] Products without new "moderate or high quality" evidence of benefit are categorized as having unsupported price increases.

Importantly, the UPI Report lacks rationale why certain rankings were made and by whom, nor does it fully explain the application of their evidence rating matrix or many of its findings. We also found no reference to the level of inter-rater reliability among the ICER assessors to gauge the reproducibility of the results.

## PROCEDURAL INADEQUACIES

The described analytical procedure presents both internal and external research validity challenges. The most concerning inadequacy is that the UPI Report doesn't make any effort to assess the clinical and economic value of the listed medications. It assesses only a partial context of price changes while ignoring the empirical economic realities and market factors that govern pricing in the US pharmaceutical supply chain.

ICER also lacks a systematic method of data collection. From a research quality perspective, consideration of evidence for "justifiable" price changes is based on each manufacturer's interpretation of the report criteria, which may result in a vastly dissimilar evidence base for each assessed product.[3] As manufacturer participation is optional, ICER conducts its own independent systematic review of evidence only on products when it cannot rely on manufacturer submissions. However, that review is limited to published data from randomized controlled trials (RCTs). ICER thereby ignores other crucial types of research, including real-world analyses, meta-analyses, and observational data. This data selection process yields a highly fragmented and uneven evidence pool inappropriate to support comparative analysis.

By using a narrow definition of "substantial new evidence," the UPI Report does not capture the clinical value of a drug. In the UPI Report on 2020 data for example, of the 286 pieces of evidence reviewed, only 21 (7%) were considered "moderate to high quality" and used in the final analysis; 137 of the 286 (48%) submissions ICER dismissed as "studies not meeting criteria for new moderate-to-high quality evidence," despite having been peer-reviewed and presented at established conferences and published in scientific journals such as *The Journal of the American Medical Association* (JAMA),[13] *The New England Journal of Medicine*,[14] and *The Lancet* (**Table 1**).[15]

Would clinical experts in the disease states addressed by the evidence show a similar level of rejections? Without transparency on the review process and evidence ratings, questions about the reproducibility and generalizability of the report's findings are heightened.

### Table 1. References Considered Versus Accepted by ICER

| Evidence References | 2018 | 2019 | 2020 | 2021 | All years |
|---|---|---|---|---|---|
| **Total considered** | 1393 | 264 | 286 | 137 | 2,080 |
| **Total accepted by ICER** | 3 | 9 | 21 | 9 | 42 |
| **Percentage accepted** | 0.22% | 3.41% | 7.34% | 6.57% | 2.02% |

## ICER CRITERIA DISREGARD CERTAIN INDICATIONS AND CRITICAL EVIDENCE

The UPI Report utilizes explicit exclusion criteria that further limit the ability to assess clinical evidence, such as rejecting clinical evidence for indications that account for less than 10% of drug utilization and excluding confirmatory studies that strengthen certainty of clinical impact.

ICER rejected 17 submissions of clinical evidence in the UPI Report on 2020 data on these grounds.[3] By excluding clinical evidence for less-common indications such as underserved populations, including those with rare or pediatric conditions – regardless of potential quality or impact – the UPI Report appears to discount the voices of patients who may already be overlooked in the healthcare system, and it disincentivizes research in underserved populations for marketed therapies.

The exclusion of confirmatory studies is particularly perplexing. Confirmatory trials strengthen the certainty around a treatment. ICER acknowledged the critical importance of such studies in its policy paper on the US Food and Drug Administration (FDA) Accelerated Approvals pathway This type of evidence also plays a crucial, validating role in evidence-based medicine and is used by professional societies to determine clinical guidance with a higher degree of confidence.[16, 17]

> *"ICER has rejected a total of 98% of the evidence"*

> *"ICER has assessed a total of 2,080 references and accepted only 42"*

A conspicuous omission is the failure to capture observational data and real-world evidence. ICER declares, "most high-quality comparative observational studies generate only low-quality evidence using GRADE for the comparison being assessed".[3] It is misleading to suggest types of research other than RCTs do not inform clinical care, or to imply that the GRADE methodology supports ignoring non-RCT evidence. Not a single real-world evidence study was considered moderate-to-high quality by ICER in its 2020 report.[3] The reductionist approach to evidence is not supported by established scientific methodology, and it could discourage continued research in this critical area.[18] Such a restrictive approach also breaks ranks with the FDA, which now considers these evidence types as meaningful endpoints even for drug approval. [18] In addition, key healthcare stakeholders including patients, payers, and providers are using real-world research to improve evidence-based care (including ICER, who uses this type of data when conducting its value assessments).

By limiting its attention to RCTs alone, the UPI Report deviates from scientific methodology accepted and encouraged by the FDA and omits crucial high-quality peer-reviewed data that examines the impact of the drug on outcomes in real world settings. The UPI Report further validates criticisms of patient associations that have challenged ICER on its perceived lack of interest in incorporating patient perspectives in its findings. [19]

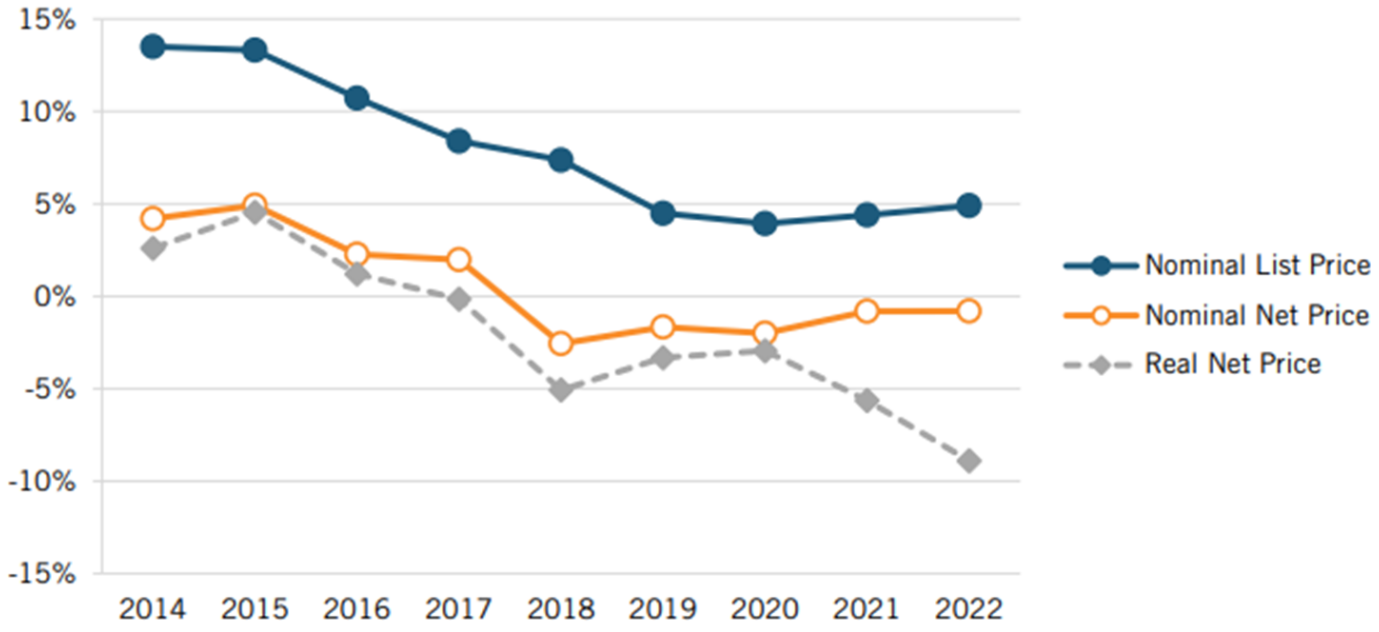
Consistent with previous years, ICER rejected all comments and most references submitted by manufacturers in the report on 2020 data. Based on our analysis ICER has rejected a total of 98% of the evidence submitted by manufacturers and found by ICER in its own searches, dismissing a large volume of peer-reviewed scientific literature. To date in its UPI report series, ICER has assessed a total of 2,080 references and accepted only 42.[3, 10, 20, 21] This biased methodological exclusion of peer-reviewed clinical and other high-quality data greatly diminishes the chance the UPI Report can find new evidence potentially in support of a price increase (Table 1).

## THE UPI APPROACH VS. EMPIRICAL REALITIES

By not discussing the value of therapies, the UPI approach ignores the important clinical judgement providers exercise every day on behalf of patients, the choice of health plans who place therapies on their formularies, and the overall value these therapies provide to the entire healthcare system. Price regulation approaches that ignore these realities and regulate prices based on the subjective rejection of medical evidence offer an unsound policy foundation. Specifically, the UPI approach fails to acknowledge that pharmaceutical pricing is subject to the negotiation between manufacturers and various economic actors like payers, pharmacy benefit managers (PBMs), wholesalers, and distributors .[22] In analyzing the results of this process, multiple independent reports show that broader medicine uptake is the major driver of increases in drug spending, not perceived drug price increase.[22, 23] As case in point, the Congressional Budget Office (CBO) confirmed that the average net price of a prescription "fell from $57 in 2009 to $50 in 2018 in the Medicare Part D program and from $63 to $48 in the Medicaid program".[25]

Figure 1.

**Change in average list and net prices of brand-name drugs, 2014-2021 [26]**




> *The ICER UPI approach produces arbitrary findings that may create unintended market distortions.*

Scientific innovation in areas of unmet need shifts spending to novel therapies and drug classes, but due to effective genericization and declining brand net prices (Figure 1),[26] manufacturer revenues after discounts and rebates grew by only $56 per capita in the decade after 2010. [24] Looking at the overall budget impact, the CBO confirms that "nationwide per capita spending on prescription drugs has generally held steady or declined since the mid-2000s —other than the increase from 2013 to 2015". [25] Thus, an incomplete focus only on perceived price changes in a selection of branded products as proposed by the UPI approach, entirely misses accounting for data on the consistently moderating effect of generics and new generic entries, including biosimilars.

The ICER UPI approach produces arbitrary findings that may create unintended market distortions.

Prioritizing a process by sales volume means that widely used therapies (which are more widely used because of their clinical value) could be marked as having "unsupported" price increases, while lesser used treatments in the same class with similar or greater price changes would not be flagged, even though the aggregate impact in dollar terms for the budget holder could well be greater.

## THE UTILITY OF UPI APPROACH IN DECISION MAKING

Economic research focuses on elucidating relative value for money, misaligned incentives, or market failures. The UPI Reports ignore these dimensions. Yet, the report's findings are being utilized to advance price control policies by state governments.[2] Recent survey research also suggests that over 6 in 10 commercial payers now consider the results of ICER's UPI Report in formulary decision making. [27]

Analyses of drug spending have their place in budgetary decision making. However, one cannot determine the net benefit of drug spending controls by examining the existence of "substantial new clinical evidence," as narrowly defined by ICER. Visible cost savings for high volume (and arguably more valuable) treatments may be completely offset by implicit market distortions

created by the UPI approach. Policymaking based on UPI Reports which fail to consider other costs and benefits could create substantial downsides for allocative efficiency and spending overall. The partial UPI analysis could divert payers from actions that may have greater impact on their budgets and fewer unintended consequences.

Using the UPI report findings could result in unfair, uneven, or systematically biased price controls, while opening the process to legal challenges.[28] The fundamental methodological flaws in the ICER process go beyond a mere failure of research design or misguided signals to policymakers and may result in serious consequences for patient access and outcomes.

Unfortunately, albeit with minor amendments and despite claims its protocol is the outcome of engagement with manufacturers and stakeholders, the most recent analysis protocol just published addresses none of the inadequacies discussed above.

## CONCLUSION: ICER'S UPI REPORT IS ADVOCACY PRESENTED AS EVIDENCE

Bridging scientific research to health policymaking can be challenging. Effectively shaping evidence-based policy requires deliberate persuasion, intentional positioning, and emotional appeal that allows for abstract models to impact decision makers.[29] Organizations such as ICER straddle difficult territory in their quest to shape policy outcomes. However, where the dividing line between advocacy and research gets thin, a critical distinction emerges. In our analysis, ICER's research process excludes countervailing results to steer policymaking in a specific direction. Given the fundamental methodological flaws, the UPI report is advocacy presented as research, which aligns with the report donor's openly stated mission to motivate drug price reductions.[30, 31]

In times of polarized policy debates, rigorous health policy analysis is important for both long-term scientific credibility and dependable policymaking. Policymakers are responsible for making decisions that impact the people's overall health and thus need to prioritize patient-centricity. Our analysis demonstrates how the UPI Report's methods may result in partial product selection, feature an incomplete analysis of the evidence, and deliver potentially misleading conclusions regarding growth drivers in healthcare spending.

Were we to GRADE the evidence set used by ICER to reach its product-specific conclusions, the rating most applicable is "very low–the true effect is probably markedly different from the estimated effect." In a report aspiring to leverage the authority of objective scientific analysis to inform policy choices, such major methodological failings mar its utility.

In addition to flawed methodology, the UPI report diverts attention away from true drivers of healthcare spending. A 2022 IQVIA report found that the cost of medicines after all discounts and rebates declined 2.9% in 2020, continuing a downward trend over the past five years.[24] Of the more than 20,000 prescription drugs approved for marketing in the US, the UPI Report examining 2020 data highlighted 12 drugs with a meaningful impact on spending due to price changes, of which only eight were deemed to have had unsupported net price increases. Furthermore, one of those eight caused 85% of the identified drug spending increases.[10]

**For budget-constrained payers, the UPI Report provides no policy guidance as to the value of any of the selected therapies, no view on the market efficiency within the drug classes, or important impacts on population health. It is a blunt tool to rally against market price dynamics for a subset of drugs, but caution is advised. Partial and flawed analyses such as the UPI Report may cause unintended consequences healthcare decision makers and patients can ill afford.**

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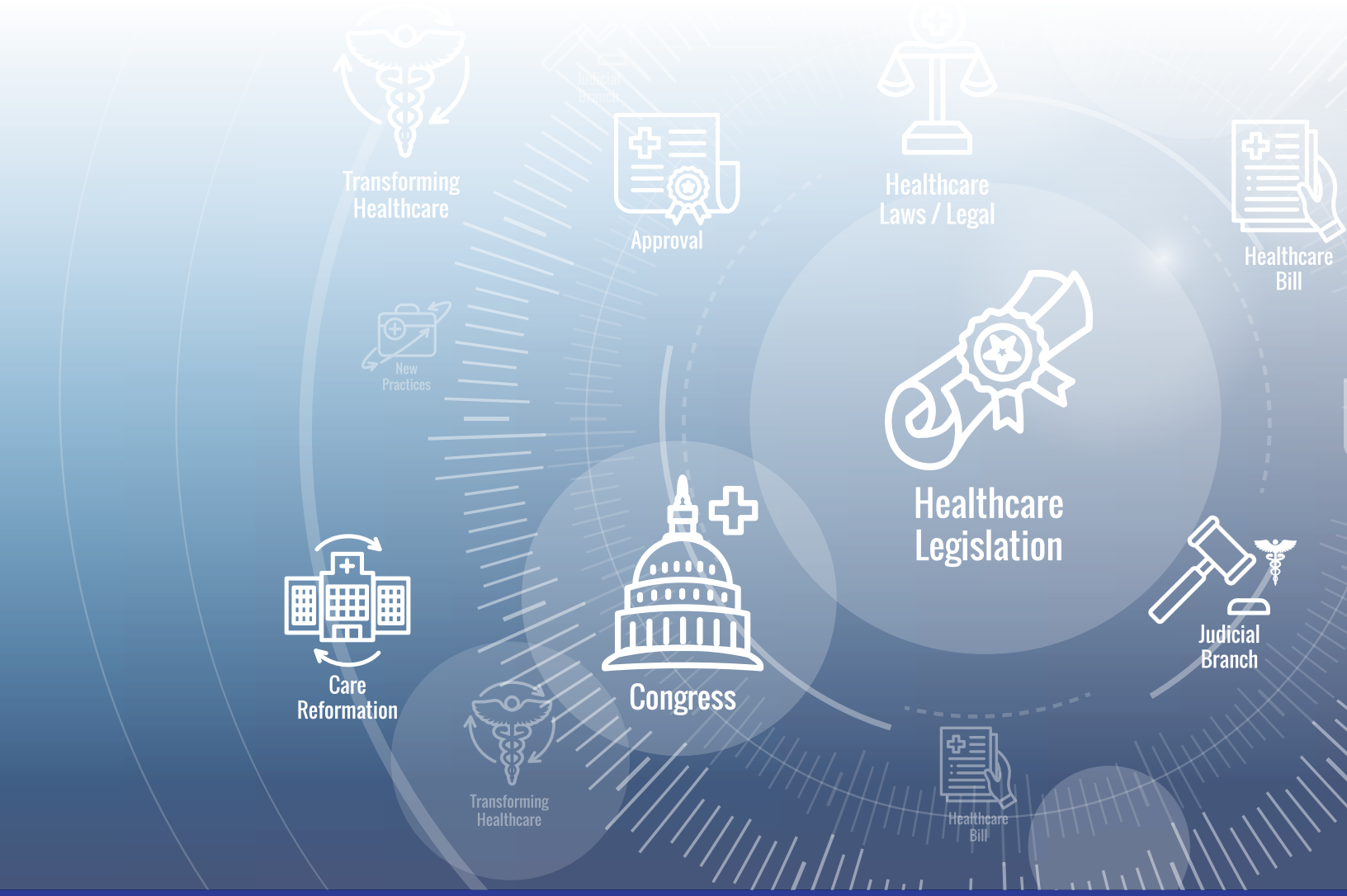


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