

When simpler isn't better: A case for generalizing cost-effectiveness math to avoid undervaluing medicines

Oversimplified health economics math is jeopardizing future medical progress and risks saddling society with preventable costs and illness.

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Millions of families every year hire financial advisors to help them determine which investments to choose as they plan for retirement. In the world of healthcare, similarly, advisors help governments and insurers figure out which medicines, diagnostics, and procedures are worth their price. These advisors are health economists.

Health economists wield equations that determine which prices are too high much the same way that a financial advisor might tell you which stock prices are too high or bond yields too low to be worth putting into a retirement portfolio. They know that their math helps society think about whether and how much to pay for new medicines. And they know that what we pay for today (and how much we pay for it) helps determine what kinds of medicines we'll get in the future. They talk about having a long-term societal perspective, like how paying off a mortgage doesn't just save you money on rent in the long run, but also allows you to pass your home to your kids or grandkids.

America is considering giving more influence to health economists' calculations, as governments in places like the UK and Canada have done for years. Many insurers and even lawmakers have begun turning to an organization called The Institute for Clinical and Economic Review (ICER) to see if their math says a drug is "worth it."

In a sense, we are each health economists. We weigh our own ailments and health worries and the costs of treating them, or not treating them. Whether to exercise and eat healthy, or not. Whether to buy health insurance in case we get sick or take our chances.

Insurance is worth paying for because there are so many effective procedures and treatments that can restore our health when we get sick but are too expensive to afford without insurance. So insurance has value to us because of the treatments it covers. And since not all insurance plans cover the same treatments, people weigh plans' pros and cons when deciding which one to buy, or even which job to take based on the insurance that's offered. Professional health economists actually write out their math, but all of us amateurs are doing health value calculations in our heads, influencing the market of plans that eventually adjust to our preferences.

A benefit of many people coming together as members of one insurance plan is the collective bargaining strength with which to negotiate lower prices from doctors and drug companies and hospitals. But to truly bargain, you have to be willing to say no, which means having an acceptable alternative. When there are five hospitals in a region and several insurance plans each covering

millions of people, plans have alternatives. Each plan can negotiate with each hospital to get the lowest price possible for its members. If there is only one hospital, or one hospital system, then insurance plans have less leverage. As a result, their members pay higher premiums to cover hospital care for those who need it.

Knowing what's worth paying for, and what's not, is essential and can require some expertise. If a doctor prescribed a drug that wasn't going to work for a patient or caused a nasty side effect that outweighed its benefit, we'd be grateful to our insurance plan for refusing to cover it. If surgeons at one hospital charged more for the same procedure than surgeons at another hospital, we'd want to know if there was any difference in quality. If not, we'd want our insurer to steer us and others in our plan towards the more cost-effective option, which keeps down premiums for everyone in that plan.

So the idea that an insurance plan, a private one or a government-run plan, would listen to health economists about what's worth it and what's not would seem reasonable.

But here's the thing. The kind of math those health economists run is critical to guiding the trade-off between our near-term and long-term well-being and budgets. Some math is really meant to figure out whether a drug offers good value to a health plan this year or over the next few years but not whether the drug offers value to society as a whole for the long run. So what if health economists prioritized making decisions that look smart this year but end up costing everyone dearly in the future?

In search of value

It's easy to see how this might happen. If a finan-

cial advisor told a family they could save money by paying less for one home rather than paying more for another of the same size, quality, and location, it might seem an obvious choice. Who wouldn't want to pay less? But what if that financial advisor failed to point out that the lower cost home is a rental and the more expensive home would be owned by the family when the mortgage was paid off? It's silly to imagine a financial advisor that ignores the difference between paying rent and paying a mortgage. Yet this is just one of the problems that plagues the field of health economics.

“ Some math is really meant to figure out whether a drug offers good value to a health plan this year or over the next few years but not whether the drug offers value to society as a whole for the long run. ”

Consider that most drugs go generic, becoming inexpensive public goods forever, much as a home mortgage gets paid off and the home can benefit future generations.¹ And yet, many health economists base their math only the branded price of a drug, ignoring that it becomes much cheaper once it goes generic. They ignore much more. For example, everyone can agree that an antibiotic has value when it saves someone's life,

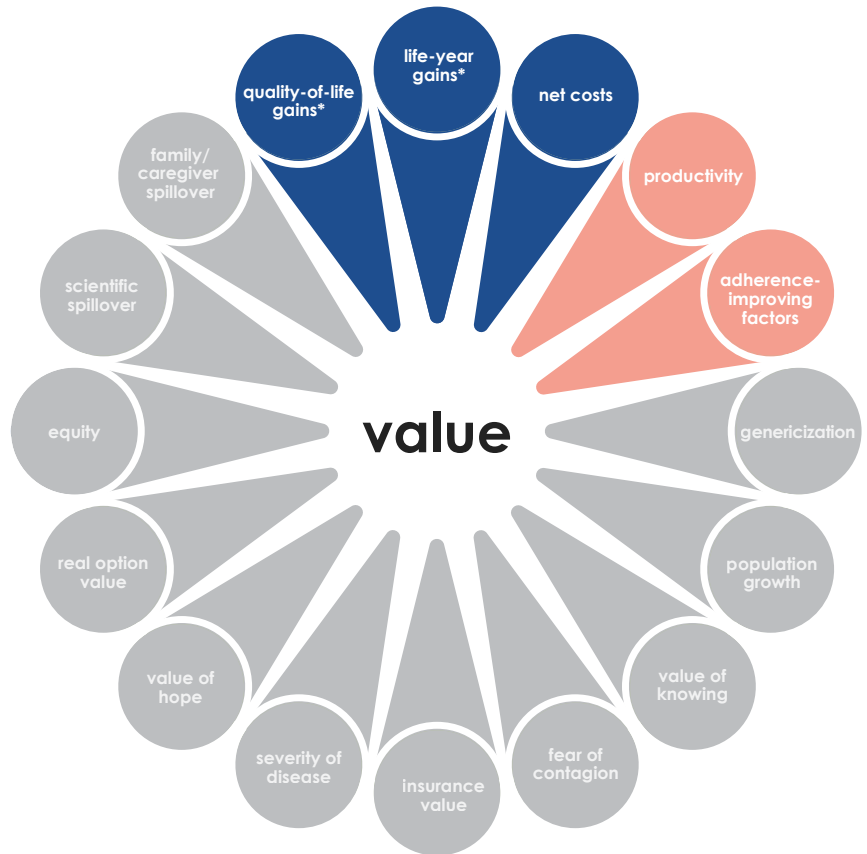
¹ But some drugs don't go generic and become inexpensive after their patents expire because they are hard or impossible to reliably copy, like gene therapies. As in the case of other such natural monopolies (e.g. water utilities, railroads), this market failure can be fixed with regulations that require that companies lower the price of their drugs after the usual 10-15 period of market-based pricing. I have called this regulatory fix Contractual Genericism. Peter Bach and Mark Trusheim have proposed a similar idea called P-Quad (Production Plus Profit Pricing). Fundamentally, these proposals are based on the principle underpinning the patent system that innovation should be rewarded with only temporary exclusivity to allow for temporary rewards, like a finite mortgage.

but what is the value of the joy experienced by the patient's family and friends at not losing someone close to them? What is the value of the reassurance all the rest of us feel that the antibiotic would save our lives if we got a similar infection? Fear of disease has a real cost ... just look at the economic damage wrought by COVID-19 as billions of people retreated from one another into their homes. Vaccines and drugs that make COVID-19 or any disease less scary restore our willingness to socialize and engage with the economy. This creates calculable value that's ignored by conventional health economic math because that math serves the narrow interests of healthcare plans (i.e. will this drug help the people we treat and offset our other healthcare costs this year?), not society as a whole.

If we think even more expansively, let's consider the value of what's called "scientific spillover" from one invention to another. A medicine for one disease might later be combined with another to treat a totally different disease. Or consider that mRNA vaccine technology wasn't created in response to COVID-19, but we are all no doubt grateful that scientists were able to put it to use against the pandemic. Scientific spillover is a real phenomenon and happens constantly. The Apollo project to send astronauts to the moon is credited with sparking innovation that led to the creation of everything from solar panels to polymer fabrics and cordless devices.² So there's good reason to believe that whatever drug a health economist values today will probably lead to more value than we can see or know. But how do you measure that scientific spillover before it happens?

figure 1. the value flower

Adapted from [https://www.valueinhealthjournal.com/article/S1098-3015\(17\)33892-5/fulltext](https://www.valueinhealthjournal.com/article/S1098-3015(17)33892-5/fulltext)



In calculating whether a medicine may be worth its price, **Generalized math** takes into account at least some of the values represented by **grey petals**, while **conventional Special math** focuses on just **blue** and sometimes **orange petals**.

* Although conventional cost-effectiveness math combines Quality-of-life and Life-Year gains into Quality-Adjusted Life-Years (QALYs), we have split the two measures in recognition of the growing awareness that a QALY undervalues the lives of people whose quality of life is reduced by disabilities. Using QALYs would result in a conclusion that extending the life of someone living in a wheelchair is less worthwhile than extending the life of someone who is otherwise healthier. By splitting the QALY into its constituent parts, it becomes possible to value life extension equally for everyone.

² https://www.nasa.gov/sites/default/files/80660main_ApolloFS.pdf

Some of these values are impossible to calculate accurately, others are just hard to estimate. And yet, that doesn't make those values any less real. Ignoring them entirely will naturally cause the math to undervalue the very thing we're trying to value.

Yet health economists have split into two camps. There are those who choose the simpler math that only includes values they can measure (just the blue and sometimes orange petals of the value flower in [Figure 1](#).) – let's call them the Specialist health economists. And then there are those that acknowledge all the other values, attempt to calculate them, and point out the dangers of just ignoring them. Let's call those Generalists.

You might think that Special is better. Who doesn't want to be Special? But in math, Special actually means that an equation is simplified to deal with a "special case." Special is narrower and less useful, though it might be much more memorable.

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For example, Einstein's Theory of General Relativity uses a set of 10 equations to explain the relationship of mass, energy, velocity, and gravity in ways that guide the function of everything from our global navigation systems to nuclear reactors.

But gravity turns out to be a really hard thing to take into account, so if we were to just ignore it, the math becomes simpler. Einstein did just that when he worked out his simpler, gravity-free theory of relativity, calling it Special Relativity. When you further simplify Special Relativity to where velocity is assumed to be the speed of light (c), it becomes familiar, something we all learn as kids: $E=mc^2$. A huge amount of mathematics boils down to those five characters if we just ignore gravity and pick a conveniently simple speed value. That one simple equation is still useful. It approximates the energy output of a nuclear reactor given a certain amount of nuclear fuel, for example.

But it's not as useful as General Relativity. Einstein's General math encompasses all the various Special cases you can think of. Not just something moving at the speed of light but a satellite moving in orbit around the earth, its internal clock running a little bit faster due to weaker gravity relative to our clocks on Earth, by an increment we can calculate and compensate for thanks to Einstein's Theory of General Relativity and absolutely no thanks to his Special one.

Consider that if Einstein had settled for just keeping things simpler with Special Relativity, we wouldn't have GPS. It's good that he didn't say "Gravity is hard so let's pretend it doesn't exist," because wishing that doesn't actually make it true. Thankfully, Einstein persevered and derived the more comprehensive, complex, and useful theory of General Relativity. What Special Relativity would say is impossible, General Relativity reveals as possible.

So what's more useful? Math that tells us we shouldn't be able to do something we are already doing? Or math that describes how we're actually able to do it and could help us figure out what else we can actually do?

So who should we listen to?

Just as Special Relativity ignores gravity, Special Health Economic formulas, what might also be called “conventional cost-effectiveness analyses,” ignore all the grey petals in the value flower.

The result is that even when American insurance is paying for a particular medicine, Specialist health economists in Europe will often declare “That doesn't make sense. You shouldn't want to pay that price for that medicine based on our calculations of its cost-effectiveness. It's not worth that!” Sometimes those countries are willing to not use that drug at all, even though their patients could benefit from it. In those cases, drug companies usually simply lower what they charge in those countries, since making some money in those markets is better than making no money. And as long as the US remains willing to pay enough, then investors and innovators continue to invest in R&D to bring more drugs to market, knowing that much of the reward will come from the US and other countries will pitch in a little here and there.

But what if those European countries were to hire Generalist health economists to do the hard work of factoring in the value that the Specialists ignore? What they would be more likely to hear is “I see why the US finds this product to be well worth its price and so should you.” Of course this is not what European health agencies want to hear when they are looking for an excuse to demand discounts from drug companies.

It's not surprising that a buyer who wants to negotiate down the price of a product will try to argue that it's not worth what the seller is trying to charge. But cynical math tactics employed by some to get a good deal should not be mistaken for actual measures of a novel product's value to society.

Yet lawmakers and insurance plans in the United States are also increasingly interested in assessing whether new drugs are “worth it.” So we're approaching a crossroads where the Specialist and Generalist health economists stand, offering very different advice and conclusions.

“Cynical math tactics employed by some to get a good deal should not be mistaken for actual measures of a novel product's value to society.”

As with everything, we ought to listen to the people who take more facts and reality into account. We should seek the counsel of those who are intellectually curious enough to consistently look for what they might have missed. Indeed, intellectual curiosity is essential, because any economic equations, including health economic math, are often far-from-accurate proxies for humanity's actual lived values.

For example, if you're wondering whether to buy an electric car or a standard one that runs on gasoline, a Specialist might consider the electric car's higher upfront cost, lower maintenance and fuel costs, and subsidies, and still tell you that the electric car isn't worth it. And yet, despite what seems like pretty comprehensive math, you might feel drawn to the electric car. A Specialist would tell you to follow the math and buy the standard car. A Generalist would ask “Why do you still want to buy it when the math says it's overpriced?”

Perhaps you care about the environment and climate and would feel better by helping the world transition away from fossil fuels. A Specialist would tell you to ignore your climate concerns because they aren't represented in his math and are hard to calculate. A Generalist would tell you that your concern for the environment is very real to you, hopefully point out that it's a legitimate concern, and even help quantify the impact of carbon emissions to show why your desire to buy the elec-

tric car could very well be mathematically rational.

If economists might overlook the value people place on protecting the environment, then it's not hard to imagine that they might fail to appreciate the values we place on health and life itself.

So, we should listen to the health economists who take a more generalized, objective approach, who acknowledge that the math is too imprecise to dictate our decisions but can help us appreciate why we value some things more than others. We need to be skeptical of those who urge policy makers to trust their Special math to unquestioningly override people's preferences.

Specialist health economists in the UK (NICE), Canada (CADTH), and Australia (PBAC) and other countries are deploying simplified math to argue that drugs are not nearly worth the prices companies are charging for them and those countries are making their purchasing decisions based on the math. Led by ICER, Specialists are trying to

gain influence in the US to impose price controls on new medicines here as well (instead of urging insurance reform to make medicines affordable to those who need them). If fewer such medicines end up being invented because rewards are cut, then Specialist health economists think that's OK, because there's no sense in incentivizing the development of medicines that, according to their calculations, aren't worth it.

Meanwhile, the Generalists, out of favor with those who need evidence that medicines are overpriced, have been somewhat quieter, unfortunately. They teach behind the scenes, urging caution. Anyone who has bothered to listen to Generalists has heard them say that many new medicines are more valuable than Specialists acknowledge.^{3 4} They counsel that we would be shooting ourselves in the foot if we reduce incentives for the continued invention of these products and consequently got fewer of them. (See **Table 1.**)

Table 1. Examples of generalized cost-effectiveness scholarship

Paper	Authors	Publication	Insight
The Social Value Of Vaccination Programs: Beyond Cost-Effectiveness	Jeroen Luyten, Philippe Beutels	Health Affairs	Vaccines have more societal value due to herd immunity and other commonly overlooked factors.
Health Technology Assessment with Risk Aversion in Health	Darius Lakdawalla, Charles Phelps	Journal of Health Economics	Drugs for severe diseases are worth more than conventional CE assumes.
The Insurance Value of Medical Innovation	Darius Lakdawalla, Anup Malani, Julian Reif	Journal of Public Economics	Conventional CE meaningfully understates the value of historical health gains and disproportionately undervalues treatments for the most severe illnesses.
Do Cost-Effectiveness Analyses Account for Drug "Genericization"? A Literature Review and Assessment of Implications	Meghan Podolsky, Peter Neumann, Anirban Basu, Daniel Ollendorf, Joshua Cohen	ISPOR	The omission of assumptions about genericization means that cost-effectiveness analyses may be misrepresenting the opportunity costs of drugs in the long run.

3 [https://www.valueinhealthjournal.com/article/S1098-3015\(10\)60387-7/pdf](https://www.valueinhealthjournal.com/article/S1098-3015(10)60387-7/pdf)

4 <https://www.sciencedirect.com/science/article/abs/pii/S0167629619309208>



Good Research Practices for Measuring Drug Costs in Cost-Effectiveness Analyses: A Societal Perspective: The ISPOR Drug Cost Task Force Report—Part II	Louis Garrison, Edward Mansley, Thomas Abbott, Brian Bresnahan, Joel Hay, James Smeeding	Value in Health	Very few, if any, published CE analyses have taken a societal perspective in measuring the value of medicines (through inclusion of time costs, opportunity costs, or community preferences), though many claim to do so.
Health Technology Assessment With Diminishing Returns to Health: The Generalized Risk-Adjusted Cost-Effectiveness (GRACE) Approach	Darius Lakdawalla, Charles Phelps	Value in Health	Our Generalized Risk-Adjusted Cost-Effectiveness (GRACE) approach helps align HTA practice with realistic preferences for health and risk.
Reconsidering the Economic Value of Multiple Sclerosis Therapies	Tiffany Shih, Craig Wakeford, Dennis Meletiche, Jesse Sussell, Adrienne Chung, Yanmei Liu, Jin Joo Shim, Darius Lakdawalla	American Journal of Managed Care	A large majority of the significant social value generated by MS drugs accrues to consumers, in particular through “peace of mind” value to the healthy. Future economic valuations of medical technology should consider both the potential value to the healthy and the effects of insurance.

Special health economics is expensive

Let's revisit the financial advisor analogy. Imagine that a family is living in a cramped rented apartment paying \$2000/month far from their jobs and having to spend another \$1000/month in transportation costs to get to work each month. Now imagine that they could buy a larger house much closer to their jobs for \$3000/month in mortgage payments for 15 years. If they went for the house, transportation costs would drop to \$600/month so they would pay \$3600/month for 15 years, and then only \$600/month thereafter. But if they stay in the apartment, they will pay \$3000/month on rent and transportation forever.

This isn't a poor family for whom the extra \$600/month is unaffordable, but they want to make a prudent decision, so they consult two financial advisors.

The Specialist financial advisor ignores the difference between mortgage payments and rent. He ignores the value of the extra time the parents spend commuting instead of with their kids. And he ignores that the family is considering having another child that their current rental couldn't accommodate. “Although the house is nicer and bigger, the extra \$600/month you'll be paying isn't worth it. You shouldn't buy the house,” he says.

But the Generalist financial advisor sees the bigger picture and more of the house's benefits. “You'll have a lot more time for each other, you'll enjoy the house more than the apartment, and then you'll save a lot in the long run, especially if we consider that having another child means you would have to move to a larger and more expensive rental if you don't buy this house.” The Generalist advisor notes that the mortgage payments are finite, that rent on their current or future apartment may go up, and so may transportation costs. He also notes that their children would be able to inherit the home, which leaves them more financially secure, something the parents care about. “I'm not telling you what you should do,” the Generalist says, “but even if the house cost you \$4000/month in mortgage payments, it would be mathematically rational to prefer it over your rental.”

Why would the house only cost \$3000/month if the math suggests it's worth \$4000/month? Because the value of a product doesn't dictate its price. If there are enough builders out there competing for business and materials are not too expensive, then the market price for building a home might be well below the value of that home. That difference between the value of the home to the family and what it pays for the home is called the

“consumer surplus.” In other words, buying the home is not only worth it, but the family will come out far ahead. It would be irrational for the family to stay in its rental apartment provided it can afford the higher payments in the near term.

In this analogy, the rental apartment is expensive hospital care. You see, hospitals don't go generic. What we pay for them will only grow, like rent, along with costs of labor and land. Like the family above, our population is growing and aging, which means that we'll need to spend a lot of money on building and running more hospitals unless we come up with ways to stay out of them. The US spends over three times more on surgery than branded drugs, and surgery doesn't go generic.⁵ Diseases without treatments, like Alzheimer's, condemn us all to fear terrible endings to our lives and paying the tremendous and growing costs of providing long-term care to all patients. The costs related to Alzheimer's in the US alone are projected to be over \$1T/year by 2050.⁶ That's a hell of a burden to live with ourselves and to pass on to our children and grandchildren. But if we were to offer mortgage payments to the biomedical innovation community, signaling that new medicines would be rewarded with temporarily high prices, then we would commission the “building” of medicines to avert at least some of that spending and suffering (i.e. let us move out of the rented apartment). What we pay for medicines is indeed a mortgage because drugs go generic, becoming comparatively inexpensive, like a paid-off home. All the extra joy and savings that society would enjoy from preventing Alzheimer's progression would be our consumer surplus.

Investing together

Unfortunately, the Specialist health economists don't think this way and overlook many real values of medicines. Yet they are the ones that lawmak-

ers are listening to, and Generalists remain back-stage. Like a parent seeking the wrong financial counsel, our lawmakers are being urged to save money by foregoing mortgage payments to fund innovation, condemning all of us to accept the pain and costs of diseases like Alzheimer's as our and our children's destiny.

To some, the costs of a new drug may seem unaffordable. But that's an illusion. All the branded drugs Americans have today cost about 1.4% of US GDP and represent less than 8% of our overall healthcare spending.⁷ When we look at the world, all branded drug spending is <0.7% of Global GDP.⁸ We could afford them, collectively, via insurance.

The trouble is that America's insurance is designed with high out-of-pocket costs intended to discourage people from accessing the very medicines their doctors and even insurance plans agree are right for them. When they first signed up for insurance, people thought, rightly, their insurance would pay for these medicines. For those with high-enough incomes to afford their out-of-pocket costs, insurance is indeed good enough. But for about 20% of Americans who either aren't insured or can't afford the out-of-pocket costs imposed by their insurance, healthcare isn't affordable. They can show up at the ER and, if they don't accidentally sign the wrong form, they can get free care (if they sign the form, they can be bankrupted by the bills). But they can't afford most branded medicines and even many generic ones, often relying on charities or support directly from the medicine's manufacturer, or else just going without.

High out-of-pocket costs give lawmakers the impression that drug prices are too high. They find evidence for that in the simplified Special math run by the Specialist health economists. So lawmakers around the world try to get their countries

5 <https://www.cms.gov/research-statistics-data-and-systems/statistics-trends-and-reports/nationalhealthexpenddata/downloads/highlights.pdf>

6 <https://www.alz.org/alzheimers-dementia/facts-figures>

7 <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/NHE-Fact-Sheet>

8 <https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/global-medicines-use-in-2020>



to pay less for drugs, failing to realize that a patient without insurance or a patient with a \$5,000 deductible she can't afford still won't be able to afford a \$60,000 cancer medicine even after it's been price-controlled down to \$20,000. And then, failing to realize that it's precisely society's willingness to pay a high price for a new medicine that spurs investment in research to solve our remaining healthcare unmet needs, lawmakers' wrong-headed approach to saving patients money will only cost us all more down the road.

The US is making four mistakes. 1) We're not properly insuring patients, leaving what should be societal investment decisions to rest too heavily on patients. 2) Even when we consider the societal value of medicines, we're hiring Specialist health economists instead of Generalists to value them; even drug companies make this mistake when evaluating their own drugs. 3) We're increasingly letting over-simplified Special cost-effectiveness math dictate how little society (via insurance) will pay for medicines instead of listening to the marketplace of patients, physicians, insurance plans, and employers. 4) We're failing to convince other countries, via diplomacy, to contribute to funding innovation by paying more for branded medicines that they too will eventually enjoy as inexpensive generics.

Drug prices are market-based and must remain so

There is a false notion among lawmakers, the public, the media, and even Specialist health economists that there is no real drug pricing market (which some say therefore justifies price controls). They argue that because patients don't actually pay the real prices of drugs, drug companies therefore can just charge what they want.

But there is a market. Insurance plans compete for customers, and one plan could try to win more members by lowering its premiums by simply not covering branded drugs for rheumatoid arthritis, migraines, or rare genetic disorders. But it turns out that's not the kind of insurance that employers and patients want to buy. Such a plan would be

pretty heartless, and the savings are not worth the negative publicity, so plans choose to cover those drugs. Employers could encourage insurance plans to design drug formularies that only covered generic drugs for their employees, but employers are competing for workers. They know that such skimpy health coverage would give them a bad reputation and they wouldn't be able to hire workers, even if spending less on health insurance would let the employer pay workers more or generate higher profits. That's not to say that insurance plans don't exclude some drugs from coverage. They say "no" all the time and manage to remain in business. So insurance plans are capable of being discerning, balancing their customers' preferences for both paying as little as possible while also getting access to important medicines.

There are lots of other examples of consumers buying into a group "plan" and then not directly controlling what that plan spends money on to keep their members happy. For example, Netflix.

Netflix could charge less per month for subscriptions if it didn't spend billions generating new content. But it knows that people would rather pay more and get new content than pay less and be stuck watching the same old shows. So while no one person is paying for any one show on Netflix, Netflix is like an insurance plan that spreads the cost of both reruns and "innovation" across all its members.

Consumers don't have to directly pay for a show or a drug to convey collectively through a "plan" like Netflix or health insurance that they value access to those things. The people running those plans know their customers' preferences and make decisions for them; if they make a wrong move, they lose customers. Those consumer preferences, even when conveyed indirectly through a group plan's actions, signal to innovators and investors what products to risk their time and money on. When they fail, they don't get paid. When they succeed, they get paid enough to have made their risks and efforts worthwhile. And just as some shows compete with one another for an audience (e.g. most people only watch one news

station at a time), similarly drug companies that make patented medicines can still end up competing with one another with similar medicines. For example, there are multiple insulins, multiple hepatitis C cures, and multiple drugs to treat asthma, thereby giving insurance plans leverage to negotiate discounts (really rebates), saving their members money.

Innovators and the investors who back them base their willingness-to-invest in R&D to create new medicines based on society's willingness-to-pay for the medicines we have today. Higher prices today encourage greater investment into riskier projects yielding further progress in the treatment of diseases. In other words, the relationship between price and R&D is shifted by one development cycle.

This may sound obvious. After all, it's how innovation works in just about every sector. For example, higher oil and gas prices prompted research into how to extract more oil and gas from harder-to-reach places. When consumers demonstrated that they were willing to spend more on mobile phones, they progressively got more and more modern smart phones loaded with advanced features such as GPS, water-resistance, multiple high-resolution cameras and displays, and crack-resistant screens.

Yet a mistake many industry critics make is thinking that the price of a drug should reflect its own, specific development costs and risks. But high R&D costs don't entitle a company to charge a high price for whatever product they create just like high production costs don't entitle a Hollywood studio to make a lot of money on a movie – lots of projects in many industries fail to recover their cost of development. A society that has a high enough willingness-to-pay for a product can expect to innovators and investors to make an effort to meet that need. Basically, the market works on the premise that what we pay for novel products today isn't a reward for past work but an incentive

to keep working on more such products. By being willing to pay a high price, we reveal our preferences. And what insurance plans pay conveys our collective preference.

Some observers express surprise that companies would dare to set prices based on society's willingness-to-pay, unconstrained by what critics see as the immorality of charging a lot even if the product cost little to make. Some call for more transparency into each drug's cost of development and justification for its price. And yet, for all of the drug industry's presumed pricing power, what's little appreciated is how low its collective profit margins are. When factoring in all branded drug revenues and all expenses to make and market those drugs as well as develop new ones, the industry's net profit margins are only about 10% (lower certainly than the impression that many have when they selectively focus on just the companies that are most successful at any one time).⁹ These modest profits are an indicator that the market is functioning and that buyers have sufficient leverage in their negotiations with sellers.

The market isn't always rational just as a crowd isn't always wise. It can make some very counter-productive decisions. For example, we don't have an effective model for paying adequately for new antibiotics, so we get few of them. So price controls that lower rewards for novel medicines would simply risk doing for other areas of biomedical innovation what other market failures have done for antibiotics.

But the market is always open to new information, including the fact that its reward mechanisms for antibiotics are insufficient. That has prompted society to discuss ways of correcting the problem.¹⁰ And when innovators and investors find promises of greater rewards credible, they will increase their investment in antibiotic R&D, increasing our chances of getting new antibiotics.

The danger of price controls is that they aim to set prices below society's willingness-to-pay and

⁹ <https://www.linkedin.com/pulse/wbpi-2-impact-international-reference-pricing-world-inc-ravi-mehrotra?articleId=6701125395334410240>

¹⁰ <https://www.pewtrusts.org/en/research-and-analysis/articles/2020/11/11/new-bill-aims-to-jump-start-development-of-urgently-needed-antibiotics>

override society's signals of its willingness-to-pay, yet at the same time their proponents claim that price controls won't interfere with patients getting truly valuable new medicines. So once price controls become law and fewer medicines come to market, price control defenders will insist that they have not created a market failure but have simply encouraged more efficient allocation of society's resources. In other words, the drugs we won't get because of price controls are drugs that wouldn't have been worth what companies would have wanted to charge. "Don't worry," they will say, "our math shows we didn't miss out on anything worthwhile."

“ To avoid making the mistake of falling for price controls based on self-justifying Special math, we need Generalized math that takes into account demonstrable properties of medicines, like the fact that they do go generic. ”

And no matter how patients protested saying that they wanted new medicines for cancer, Alzheimer's, and other diseases, Specialist health economists will show them over-simplified math saying that their wants are irrational. Politicians used to voters asking for all kinds of irrational things seemingly without regard for cost might place more faith in the judgment of seemingly unbiased health economists, especially when their math is

convincingly precise, down to the dollar.

To avoid making the mistake of falling for price controls based on self-justifying Special math, we need Generalized math that takes into account demonstrable properties of medicines, like the fact that they do go generic. The purpose of Generalized math wouldn't be to set better prices but to serve as confirmation of whether the existing market-based approach is still generating value for society. In other words, is the willingness-to-pay we all express through the insurance plans we purchase rational?

Shifting camps

You might think that over time the Specialists who ignore that drugs go generic would eventually have to acknowledge that they do, because many hundreds of drugs already have. For example, even when your Specialist financial advisor chastises you for paying more for a house, ignoring the Generalist's explanations about mortgage payments being finite and all the other reasons why paying more now is worth it, the Specialist will be forced to acknowledge his mistake when eventually you pay off your mortgage.

And yet, you don't see most Specialist health economists revising their old Special math models for drugs like Lipitor now that there is incontrovertible evidence that this medicine continues to be valuable to millions long after it's gone generic and costs pennies per pill.¹¹ No, they just use the same flawed math to undervalue other drugs that will someday also go generic. Some specialists therefore seem dug in, actively closing themselves off against evidence that drugs offer more value than Special math credits them for. Why might that be?

It's possible that the most dug-in Specialists know that it is only by lending their imprimatur to claims that many branded drugs are over-priced that they remain useful to policy makers and insurance

¹¹ <https://pubmed.ncbi.nlm.nih.gov/23048109/>

plans that want to justify spending less on these medicines. The most common excuse they make is that many of the petals of the value flower are hard or impossible to calculate with any accuracy. And yet, as we discussed before, ignoring those values doesn't make the math any more accurate. It just makes it more precise. Indeed, many people seem to mistake precision for accuracy.

But not all Specialists are dug in. Some are shifting their views in terms of how much of the value flower to take into account and taking on the challenging work of making explicit the calculus that reflects a market based on the preferences of hundreds of millions of people. As more of these values are reasonably approximated, the math consistently shows that branded drugs have a greater societal value than is captured in market-based prices. Their work offers further reassurance that the market, and not price control committees wielding Special math, should continue to assign rewards for innovation. Some have even changed camps, leaving organizations like ICER, for example, that are loud proponents of Special math. They have gone on to work with other organizations, including academic groups, that are studying more Generalized health economic approaches to valuing drugs. Some of these economists might, quite generously, not even see it as changing camps. They might say that they always followed the evidence wherever it led them, which suggests that the Specialist colleagues they left behind remain immune to new evidence.

In any case, what we can say is that there are a growing number of Generalist health economists who do not yet have the ear of policy makers, the media, or even the drug industry. It's time that changed.

Drug makers submit cost-effectiveness dossiers to various regulatory agencies around the world (for now, mostly outside the US). At the very least, these companies should be consulting Generalist health economists on how to do more comprehensive math. There's no sense in undervaluing one's own invention. And even if those agencies

demand that cost-effectiveness be done narrowly using Special math, that approach's limitations (and the results of taking an alternative Generalist approach) could be included in the customary discussion section in which authors are supposed to call out their methodology's shortcomings. Asserting objections to Special math might not let the drug companies win higher reimbursement in other countries, but, akin to how a defense attorney objects in the moment to an inappropriate statement by prosecution, it could preserve the right to appeal the verdict in the future, at least with policy makers and even the court of public opinion, which has proven to be influential.

“ There's no sense in undervaluing one's own invention. ”

Policy makers in the US appear increasingly willing to indict the value of new medicines, declaring them over-priced, based on how much less Europe and other countries have been paying for them. And so citing a long history of consistent objections on the basis of Generalized math in the published literature and even in commentary in cost-effectiveness dossiers would be useful. We don't have a history of Generalized math yet. But if we get started now, in a few years when the drug pricing debate will still be raging, we will. That means drug companies should be consulting Generalists, measuring things like disease risk-aversion and the reassurance value a drug offers, modeling population growth, estimating when their drugs will go generic, and estimating the price of those generics. These tasks are achievable and will demonstrate that new medicines have far more value than Specialists acknowledge. It will probably shift many drugs that were deemed to be over-priced to being considered well-worth their price.



These valuations needn't be precise to be compelling. They just need to show that under a wide range of plausible assumptions, drugs offer consumer surpluses. In other words, that their value is at least as great and likely greater than their prices.

Generalized math cannot help patients struggling to afford the medicines they need today. Only insurance can do that. We must reform insurance so that everyone is insured with plans that charge low out-of-pocket costs on drugs physicians prescribe and that plans acknowledge are appropriate for patients. In that way, the cost of paying for innovation would be spread broadly and made affordable for everyone.

And whenever we have doubts as to whether the market price of a drug we want is worth having our insurance plans pay for it, let's turn to Generalist health economists to do generalized cost-effectiveness math to better understand the value that drug offers us and our children. Making that effort might save us from making short-sighted investment decisions that jeopardize all our futures.

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