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WHY DOES THE U.S. PAY THE HIGHEST PRICES IN THE WORLD FOR PRESCRIPTION DRUGS?

HEARING

BEFORE THE

SUBCOMMITTEE ON PRIMARY HEALTH AND RETIREMENT SECURITY

OF THE

COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS

UNITED STATES SENATE

ONE HUNDRED SEVENTEENTH CONGRESS

FIRST SESSION

ON

EXAMINING WHY THE U.S. PAYS THE HIGHEST PRICES IN THE WORLD FOR PRESCRIPTION DRUGS

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C O N T E N T S

STATEMENTS

TUESDAY, MARCH 23, 2021

WHY DOES THE U.S. PAY THE HIGHEST PRICES IN THE WORLD FOR PRESCRIPTION DRUGS?

Tuesday, March 23, 2021

U.S. SENATE,
SUBCOMMITTEE ON PRIMARY HEALTH AND RETIREMENT SECURITY,
COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS,
Washington, DC.

The Subcommittee met, pursuant to notice, at 10:03 a.m., in room 430, Dirksen Senate Office Building, Hon. Bernie Sanders, Chairman of the Subcommittee, presiding.

Present: Senators Sanders [presiding], Casey, Baldwin, Murphy, Kaine, Hassan, Rosen, Collins, Murkowski, Marshall, Cassidy, and Braun.

OPENING STATEMENT OF SENATOR SANDERS

The CHAIRMAN. Let me call this hearing to order.

Let me thank Senator Collins and her staff for helping to put on this hearing, and thank all of the Subcommittee Members who will be participating, and the panelists who will be with us virtually in a few minutes.

There is an interesting debate among the people of this Country about which powerful special interest has the most clout on Capitol Hill. Some people think it may be Wall Street. Some people may think it's the military-industrial complex. Some people think it's the fossil fuel industry.

I myself may be wrong, but I would give the nod to the pharmaceutical industry, an industry which charges the American people, by far, the highest prices in the world for prescription drugs and has managed to create a situation where they can raise their prices to any level they want any day of the week.

Today, people are walking into a drug store, walking into a pharmacy, the pharmacist is telling them, "Sorry, the price of your medicine has substantially gone up." That's what the drug companies have done.

Drug companies are an industry which year after year make huge profits, and they pay their CEOs incredibly large compensation packages. It is an industry which is significantly responsible for the fact that in the United States we pay the highest prices in the world for health care, almost double what any other country pays. It is an industry which has an incredibly opaque pricing system which charges one branch of government a very different price

than it charges another for the same drug, the same exact drug. Medicare will pay a price, Medicaid will pay a price, the Veterans' Administration will pay a price, community health centers will pay a different price, all for the same exact drug, and that's true for hospitals, for nursing homes, and for individuals. It's very hard to know what they are charging anybody else.

This is an industry that has paid $32 billion in fines for a variety of illegal actions over the last 20 years, including price fixing, overcharging Federal, state, and local governments for their products, bribery, collusion, fraud, and deception. And yet, this is an industry which keeps going on its merry way virtually untouchable, year after year after year.

Now, how do they get away with that? And it is not hard to understand. During the last 23 years, the drug companies have spent $7.6 billion on lobbyists, $7.6 billion over the last 23 years, including the former leadership of the Democratic and Republican parties. They have more than 1,500 lobbyists here in Washington. There are 435 Members of the House and Senate. They have 1,500 lobbyists here in Washington, as well as lobbyists in virtually every state capital in this Country. Since 1990 they have spent nearly $730 million on campaign contributions which have gone to many, many hundreds of Members of Congress, including both political parties.

Let's be clear: the pharmaceutical industry is not particularly sympathetic to the Democratic Party or the Republican Party. They try to buy both parties. In fact, I think it's fair to say that it is not Congress which regulates the drug companies but the drug companies which regulate Congress, and that has got to change. Congress finally, after years and years and years of talk, finally has got to summon up the courage to take on the drug companies and lower prescription drug prices in America. That is what the American people want, and that is what we need to do.

Last year, one out of five Americans could not afford to buy the medicine prescribed by their doctor. How crazy is that? Walking into a doctor's office, getting a diagnosis, getting a prescription drug, but you can't afford to fill it.

Meanwhile, while Americans are dying or getting sicker than they should because they cannot afford the medications they need, nine large drug companies made over $58 billion in profits last year, $58 billion in profits, nine companies, while just six pharmaceutical industry CEOs made $564 million in total compensation over the past 3 years, not too shabby.

Every day in my office, and I'm sure every congressional office, we hear stories from Americans unable to afford the prescription drugs they need. Today we will hear from Ms. Elia Spates from Derby, Vermont, who will tell us how the outrageously high price of insulin in America has impacted her life. And, of course, she is not alone. In 2018, one out of every four Americans with Type 1 diabetes were forced to ration insulin because they could not afford it. Do you believe that? One out of four Americans with diabetes forced to ration insulin.

Let's be clear: insulin is not a new drug. It was invented nearly 100 years ago by Canadian scientists who sold the patent rights for insulin for just $3.00, because they believed it should be accessible

to everyone who needed it. And yet over the past decade, the price of insulin has gone up by over 300 percent.

Yet, 50 miles from my home in Vermont, you can purchase insulin in Canada at about one-tenth the price that we pay in this Country. And let's be clear: prescription drug prices in Canada are also high compared to other countries around the world. According to a recent study by Rand, a standard unit of insulin costs $98 in the United States, $12 in Canada, $11 in Germany, $9 in France, $7.52 in the U.K., and $6.94 in Australia. And it's not just insulin. A one-month prescription of Entocort to treat Crohn's disease costs $830 in the U.S., $81 in Canada. One asthma inhaler, Flovent Diskus, costs $242 in the U.S., $27 in Canada. Two EpiPens cost $686 in the United States, $278 in Canada. And on and on and on it goes, the same medications manufactured by the same companies in the same factories, all available in countries around the world at a far, far lower price than here in the United States.

In my view, we can no longer tolerate a system that allows the former CEO of Gilead to become a billionaire by charging $1,000 for a hepatitis C drug called Sovaldi that costs just one dollar to manufacture and can be purchased in India for $4. We can no longer tolerate a system that allows the Chairman of Mylan, Robert Coury, to receive $164 million compensation package in 2016 after his company jacked up the price of EpiPen by 550 percent over a nine-year period.

All over this Country the American people are asking a simple question: How many people need to die, how many people need to get unnecessarily sicker before Congress is prepared to take on the greed of the pharmaceutical industry? The American people are demanding that Congress listen to their concerns and not cower before the power of the pharmaceutical companies.

In order to begin to address this issue, I have introduced three bills with many of my colleagues in the Senate and the House that would substantially reduce prescription drug prices in this Country and also save the Federal Government significant sums of money.

The first bill is the Prescription Drug Price Relief Act, which would cut prescription drug prices in half by pegging the price of medicine in the United States to the median price in five major countries—Canada, the United Kingdom, France, Germany, and Japan.

The second bill is the Medicare Drug Price Negotiation Act, which would direct the Secretary of Health and Human Services to negotiate lower prices for prescription drugs under Medicare Part D. Every other major country on earth, in one form or another, negotiates drug prices, and the time is long overdue for Medicare to do that as well. According to a recent study, if this bill became law, the U.S. Government could save more than $345 billion over the next decade.

The third bill, the Affordable and Safe Prescription Drug Importation Act, would allow patients, pharmacists, and wholesalers to legally purchase safe, low-cost medicine from Canada and other major countries. We import all kinds of stuff, food and everything else. There's no reason why we cannot safely reimport prescription drugs.

With that, the bottom line is we have been talking about this issue for decades. It is time to act.

Senator Collins.

OPENING STATEMENT OF SENATOR COLLINS

Senator COLLINS. Thank you, Mr. Chairman, for holding our very first Subcommittee hearing on an issue where I hope that Democrats and Republicans can find common ground, and that is improving the affordability of prescription drugs.

When a doctor prescribes a needed medication, an insurmountable barrier to taking it should not be its cost. More than half of Americans and an overwhelming majority of our seniors take at least one prescription drug each month. For many, access to these medicines not only is critical to their well-being but also can literally be a matter of life or death.

During my recent tenure as Chairman of the Senate Aging Committee, one of my top priorities was to uncover the reasons for spikes in pharmaceutical drug prices and to help make medicines more affordable for more Americans. I led a bipartisan investigation with then-Senator Claire McCaskill of Missouri on sudden price spikes of off-patent drugs and the manipulation of the market by people like the infamous Martin Shkreli.

I also worked with Senator Bob Casey to investigate various entities in the opaque market for pricing of prescription drugs such as pharmacy benefit managers.

Our committee also held hearings on the price of insulin and drugs to treat rheumatoid arthritis, listening closely to patients and other witnesses.

The answers that the Aging Committee received from its inquiries, investigations, and hearings resulted in several bills being signed into law. For example, the Making Pharmaceutical Markets More Competitive Act provides more transparent and open application process for generics. It expedites the timeline for FDA to review and approve applications.

Since enactment of this law, not only are we seeing more applications, but approvals are up considerably, with 28 priority generics and 35 competitive generic therapies approved in Fiscal Year 2020 alone.

The Patient Right to Know Drug Prices Act and the Know the Lowest Price Act banned pharmacy gag clauses. They prohibited pharmacists from telling their customers if their prescription would cost less if they actually paid for it out-of-pocket rather than using their insurance plans. This legislation also required the disclosure of settlements reached between biologic and biosimilar developers to the Federal Trade Commission. This has been required of generic drug developers since 2003.

At the end of 2019, Congress passed legislation that will improve and streamline the FDA approval process for new forms of insulin, which should usher in more competition into a category that has seen huge and unwarranted price increases.

At an Aging Committee hearing on the cost of insulin in 2018, a father from New Gloucester, Maine, testified that insulin for his 13-year-old son with Type 1 had tripled in price, forcing him to

purchase from Canada at a lower cost, very similar to what the Chairman has described.

The cost of insulin is among the most prominent examples, and I'm grateful that a constituent of the Chairman is here today to share her own story.

As co-chairs of the Senate Diabetes Caucus, which I founded in 1998, Senator Jeanne Shaheen and I introduced legislation in the last Congress to create a new pricing model for insulin, which, as the Chairman pointed out, was first isolated a century ago in Canada and yet has soared in price in recent years. Recently, we have seen some nascent steps on insulin affordability. More than 1,700 Part D and Medicare Advantage plans have agreed to cap monthly co-pays for insulin at $35 this year. Additionally, manufacturers are adding more affordable options such as Eli Lilly's $35 co-pay program, which has been available during the pandemic.

These are good first steps, but I hope we can do much more.

Another focus area is biosimilar competition. Later this spring, along with my colleague Senator Tim Kaine, I will reintroduce the Biologic Patent Transparency Act to prevent drug manufacturers from gaming the patent system. Time is money when it comes to abusing the patent system to thwart competition. There are reports that AbbVie, the manufacturer of Humira, filed 247 patent applications for this drug, and one patent that could have protected the medicine for up to 39 years from any competition from a biosimilar. In fact, the price of Humira in the United States increased by an additional 6.2 percent in January 2019 to offset price reductions from biosimilar competition overseas.

Mr. Chairman, in the last Congress three committees—the HELP Committee, the Finance Committee, and the Judiciary Committee—all advanced bipartisan bills to reform our broken drug pricing system. I was a co-sponsor of the Grassley-Widen bill the last Congress, as were several Members of this Subcommittee. HHS Secretary Becerra and I spoke about drug prices at length during his nomination process.

Let's bring this bill to the Senate floor as separate legislation so that we can have full and open debate and amendment to come up with the best solutions. We want new medicines to reach consumers and for pharmaceutical companies that invest in the research and take the risks necessary to develop these drugs to see a fair return on their investment. But we must do more to ensure that these essential medicines are more affordable and their prices transparent. I hope that today's hearing will help us craft policies to strike that balance.

Thank you, Mr. Chairman.

The CHAIRMAN. Thank you, Senator Collins.

We have an outstanding group of panelists. Let me begin by welcoming our first panelist, Dr. Aaron Kesselheim, who is a Professor of Medicine at Harvard Medical School and a faculty member in the Division of Pharmacoepidemiology and Pharmacoeconomics in the Department of Medicine at Brigham and Women's Hospital.

Dr. Kesselheim created and leads the program on regulation and more, an interdisciplinary research program focusing on prescription drugs and medical devices, patient health outcomes, and regu-

latory practices and the law. He has authored over 450 publications in peer-reviewed medical and health policy literature.

Mr. Kesselheim, thanks very much for being with us.

STATEMENT OF AARON KESSELHEIM, M.D., JD, MPH, PROFESSOR OF MEDICINE, BRIGHAM AND WOMEN'S HOSPITAL AND HARVARD MEDICAL SCHOOL, BOSTON, MA

Dr. KESSELHEIM. Thank you, Chairman Sanders, Ranking Member Collins, and Members of the Committee. We're here today because the U.S. spends far more on drugs per capita than any other industrialized nation, over $1,200 in 2018, while the OECD average was less than $600.

U.S. prices are primarily driven by spending on brand-name drugs, most of which have been on the market for many years, during which time they're subject to astonishing price increases. We compared drugs that accounted for the highest Medicare Part B spending with Japan, Germany, Switzerland, and the U.K., and found prices 46 to 60 percent lower in those places.

How is this possible? I want to focus on three reasons and their solutions.

First, the U.S. allows drug makers to set prices after FDA approval at any level they want, and then require Medicare and Medicaid to pay no matter what the drug's clinical utility.

Second, we allow manufacturers to raise those prices each year beyond inflation.

Third, manufacturers extend their patent-protected market exclusivity by building a thicket of dozens or even hundreds of patents to delay generic entry. Other industrialized nations, even some states and payers in the U.S., have strategies that address these issues.

The first step to address excessive drug prices would be to evaluate and negotiate. The Defense Department isn't forced to buy every new weapon at the price Raytheon conceives of. It determines the usefulness and negotiates. The approach in other countries begins after regulatory approval with a process known as health technology assessment, in which independent organizations help determine a fair price based on how well the new drug performs against other available treatments. Only if a drug provides more benefit to patients should it cost more than other options. The U.S. needs to establish a publicly funded body that would determine a price for a drug based on its clinical benefit.

In Germany, drug evaluation and negotiation occurs during a drug's first year when a non-profit, non-governmental research organization assesses its therapeutic benefits. In review of outcomes in that market, we found that no drugs providing important benefit left the German market, while cancer drug prices substantially declined and were more closely aligned with clinical benefit. States like New York and Massachusetts have now initiated such a review process for their Medicaid programs.

My second major recommendation is to limit drug price increases. In the U.S., Gleevec was introduced in 2001 for a list price of $26,000 a year and increased to more than $120,000 by 2016. Many brand-name drugs provide rebates to commercial payers and Medicare Part D plans, but those only offset some of these price in-

creases. By contrast, in other countries, agreements between the government or payers and manufacturers restrict price increases. We found that spending per unit for the cancer drug lenalidomide in the U.S. increased from 2010 to 2018 from about $400 a unit to nearly $700 a unit, while during that same period of time the drug in France decreased from $239 a unit to $202 a unit. One model would be to extend the drug price inflation rebate penalty currently in place for Medicaid. Bills were introduced in the prior Congress with bipartisan support for this plan, as Ranking Member Collins mentioned.

A final component would be to arrange for more efficient transition to a competitive market. Generic or biosimilar entry is often delayed in the U.S. because of patent thickets covering trivial attributes of the drug. Here again, lessons on how to improve the experience in the U.S. can come from other countries. Results from foreign patent offices suggest that the U.S. Patent Office could reduce the number of wrongly issued patents by allocating greater resources to ensure patent quality. In addition, we could leverage the Patent Trial Appeals Board set up by the 2001 America Invents Act to weed out invalid patents before they get caught up in litigation by reviewing patents listed by the FDA.

There is my prescription, informed by successful policy initiatives in other countries and U.S. states. Independent therapeutic evaluation leading to price negotiation, limits on price increases, and efficient generic entry at the end of market exclusivity.

The industry may contend that any drug pricing reform will have reduced innovation, but meaningful innovation need not decline. Large pharmaceutical manufacturers invest only about 10 to 20 percent of their revenues in R&D. To ensure new therapeutic insights, we must augment support of the NIH since transformative drug innovation often emerges from publicly funded research and development, as it recently did for COVID–19 treatments and vaccines.

In reality, these policies are likely to actually improve meaningful innovation. In the last decade, only one-third of new drugs in the U.S. were rated by one of these international independent organizations as having even moderate therapeutic benefit. If drug prices more adequately reflected the clinical benefits that they offer to patients, this would incentivize more meaningful pharmaceutical innovation and there would be less investment in making trivial changes to existing products and more investment in meeting unmet medical needs. Generous rewards would still be provided for creating important new medicines.

Most importantly, with the changes I've proposed, policymakers can rest assured that more patients will be able to access these vital products at an affordable price.

Thank you very much.

[The prepared statement of Dr. Kesselheim follows:]

PREPARED STATEMENT OF AARON KESSELHEIM

Chairman Sanders, Ranking Member Collins, and Members of the Committee:

My name is Aaron Kesselheim. I am an internal medicine physician, lawyer, and health policy researcher and a Professor of Medicine at Harvard Medical School in the Division of Pharmacoepidemiology and Pharmacoeconomics of the Department of Medicine at Brigham and Women's Hospital in Boston, one of the main Harvard

teaching hospitals. I lead its Program On Regulation, Therapeutics, And Law (PORTAL), an interdisciplinary research group that studies the intersections between prescription drug affordability and use, laws and regulations related to medications, and the development and cost of drugs. PORTAL is one of the largest and most prolific non-industry funded research centers in the country that focuses on pharmaceutical law, use, and economics. I am honored to have been invited today to talk to you about brand-name drug prices in the U.S.: both why they are so high and what you can actually do about it.

I will start by reviewing the problem of high drug prices, touching on why prices are so high in the U.S. and what the implications are of high drug prices for patients and the health care system. I will then describe a three-pronged approach to ensuring that U.S. patients pay fair prices for new therapeutics: negotiating with brand-name drug manufacturers, ensuring that prices cannot rise excessively over time, and ensuring a timely and efficient transition to generic competition at the end of the market exclusivity period. For each of these major categories, I will compare the U.S. approach to other industrialized countries (and some cutting-edge U.S. states) to provide points of contrast and pathways forward for policymaking by Congress. Finally, I will address some important counter-arguments that are sometimes made in opposing plans to address high U.S. drug prices. I will conclude by explaining the problems with these arguments, and suggest how they can be addressed in any policy changes that are made.

I. The Problem of High Drug Prices

The U.S. spends far more on prescription drug prices per capita than any other industrialized nation. Total prescription drug spending here jumped from $427 billion in 2015 to $511 billion in 2019.[1] According to the World Health Organization, the U.S. spent $1,011 per capita on retail pharmaceuticals in 2015, which increased to $1,229 in 2018, far outpacing all other OECD countries: the next highest, Switzerland, came in at $894, and the OECD average was far lower, at $562.[2] One government report estimated that about 17 percent of the U.S. health care spending goes to prescription drugs, although some payors have reported that pharmaceuticals account for closer to 25 percent of spending overall.

High U.S. drug prices are primarily driven by spending on brand-name drugs, which make up only about 10 percent of prescriptions, but account for about 75 percent of spending. Most of this spending is not for the newest drugs approved in the last year or two, but from brand-name drugs that have been on the market for many years, during which time they have been subject to substantial promotion to physicians and direct-to-consumer advertising. Many of them have been subjected to astonishing price increases from year to year, even with no changes in the drug itself. For example, in 2019, Medicare Part D—the Federal Government's outpatient prescription drug insurance program for patients over age 65—topped its list of greatest spending with three drugs: the anticoagulants apixaban (Eliquis), which has been on the market for 8 years, and rivaroxaban (Xarelto), on the market for 10 years, and the cancer treatment lenalidomide (Revlimid), which has been on the market for 15 years. These three drugs accounted for about $16 billion in gross spending for Medicare Part D alone just in 2019 (or approximately $10 billion in net spending). In Medicare Part B—which covers hospital-or physician-administered drugs for older patients—top-spending drugs in 2019 included the ophthalmologic drugs aflibercept (Eylea, $2.9 billion total spending, 9 years on market) the anticancer drug rituximab (Rituxan, $1.7 billion, 23 years), and the pegfilgrastim (Neulasta, $1.2 billion, 19 years). High spending and prices are not indicators of innovation reaching patients but of a system that allows manufacturers to freely set and raise prices while preventing effective competition.

Among the most concerning examples of high drug prices relate to drugs that have been available for multiple decades, including products like insulin, the opioid reversal agent naloxone, and epinephrine for potentially fatal allergic reactions. In a study led by Dr. William Feldman in our group, we studied data on Medicare Part D drug spending to examine injectable insulin products. We found that in 2017, Medicare Part D spent about $7.8 billion (even after assuming large rebates) on 31

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[1] Tichy EM, Schumock GT, Hoffman JM, et al. National trends in prescription drug expenditures and projections for 2020. American journal of health-system pharmacy. 2020;77(15):1213–1230.

[2] Kesselheim AS, Hwang TJ, Avorn J. Paying for Prescription Drugs in the New Administration. JAMA 2021;325(9):819–820.

different insulin products.[3] Unfortunately, the availability of multiple brand-name products does not consistently lead to substantial reductions in prices, as might be expected, because they are not interchangeable, reducing the possibility of price competition.[4]

The prices paid for these same brand-name drugs are much lower in other industrialized countries than they are in the U.S.. In one study led by Thomas Hwang in our group, we evaluated the prices of 75 brand-name drugs that accounted for the highest Part B expenditures in fee-for-service Medicare beneficiaries in 2016, compared to the prices for the same drugs in four comparator high-income countries: Japan, Germany, Switzerland, and the UK. In virtually all cases, the U.S. paid more for these drugs than the median of prices in comparator high-income countries. Overall, drug prices in high-income countries were 46–60 percent lower than those in Part B, taking rebates into account.[5]

Brand-name prescription drug prices are so high in the U.S., and much higher than in other comparable countries, because in the U.S. we allow brand-name pharmaceutical manufacturers to charge whatever they want during their periods of government-granted market exclusivity—a condition not seen in any other developed nation. At the same time, numerous laws and rules require coverage of many high-priced drugs by government or private payors. As a result, brand-name manufacturers set drug prices in the U.S. at levels far exceeding prices for the same drugs made by the same companies for use in other high-income countries around the world, because they can, and then raise those prices each year at rates much higher than the rate of inflation.[6] As a final step, manufacturers also take numerous steps to extend their market exclusivity periods as long as possible by building a "thicket" of patents designed to delay generic entry.[7]

These high prices have important implications for patients. Americans struggle to afford their prescriptions, and three in ten report not taking a medication as prescribed by their doctor because of the cost.[8] Non-adherence to important medications can lead to increased patient mortality.[9] Drug costs passed on to consumers and patients through insurance premium increases make such insurance less affordable, and can force people off of their insurance plans. High drug prices have spillover implications for other aspects of health care and social spending, since public and private spending on prescription drugs is not available to meet other needs. Medicaid programs, for example, have had to respond to expanding drug budgets by cutting coverage for other services and limiting access to drugs.[10]

I am optimistic that this hearing, among the first held by the HELP Committee, indicates a new commitment by the new leadership in the Senate to make progress on the issue of unaffordable drug prices and their harmful effect on patients and the U.S. economy. Progress on excessive drug prices in the U.S. has been stymied before by the pharmaceutical industry and its well-funded and powerful lobbying clout. In the past, both Republicans and Democrats have responded to that pressure by staying away from taking evidence-based and enforceable steps to bring pharmaceutical spending in line with other industrialized nations. In the last 4 years, the Trump Administration continued this tradition by doing little to address drug prices

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[3] Feldman WB, Rome BN, Lehman LS, Kesselheim AS. Estimation of Medicare Part D spending on insulin for patients with diabetes using negotiated prices and a defined formulary. JAMA Internal Medicine 2020;180(4):597–601.

[4] Sarpatwari A, DiBello J, Zakarian M, Najafzadeh M, Kesselheim AS. Competition and price among brand-name drugs in the same class: a systematic review of the evidence. PLoS Medicine 2019;16(7): e1002872. See also Luo J, Avorn J, Kesselheim AS. Trends in Medicaid Reimbursements for Insulin From 1991 through 2014. JAMA Internal Medicine 2015;175 (10):1681–1686.

[5] Hwang TJ, Jain N, Lauffenburger JC, Vokinger KN, Kesselheim AS. Analysis of proposed Medicare Part B to Part D shift with associated changes in total spending and patient cost-sharing for prescription drugs. JAMA Internal Medicine 2019;179(3):374–380.

[6] Kesselheim AS, Avorn J, Sarpatwari A. The high cost of prescription drugs in the United States: origins and prospects for reform. JAMA 2016;316(8):858–871; Ways and Means Committee Staff. A Painful Pill to Swallow: U.S. vs. International Prescription Drug Prices. Washington, DC September 2019.

[7] Vokinger KN, Kesselheim AS, Avorn J, Sarpatwari A. Strategies that delay market entry of generic drugs. JAMA Internal Medicine 2017;177(11):1665–1669.

[8] "Three in ten of all adults (29 percent) also report not taking their medicines as prescribed at some point in the past year because of the cost." Kirzinger A, Munana C, Wu B, Brodie M. Data Note: Americans' Challenges with Health Care Costs. KFF. 2019. *https://www.kff.org/health-costs/issue-brief/data-note-americans-challenges-health-care-costs/*. 11 June 2020.

[9] Gagne JJ, Choudhry NK, Kesselheim AS, Polinski JM, Hutchins D, Matlin OS, Brennan TA, Avorn J, Shrank WH. Comparative effectiveness of generic and brand-name statins on patient outcomes. Annals of Internal Medicine 2014;161:400–407.

[10] Galewitz P. States Cut Medicaid Drug Benefits to Save Money. Kaiser Health News July 24 2012. *https://khn.org/news/Medicaid-cuts-sidebar/*.

in a meaningful way. However, I believe bold action now will be rewarded at the polls. There is clear evidence that most Americans favor action to help them with the high drug prices faced by them and their family. In a national survey leading up to the 2020 election, the second-ranked domestic priority for Democrats and Republicans alike was lowering the cost of prescription drugs, following just behind access to affordable health care. [11]

Below, I describe a three-pronged practical approach that Congress could implement to address high drug prices, drawing on lessons from other countries—and from a few states that have begun to enact such thoughtful reforms.

II. A Three-Pronged Solution to Ensure Fair Prices in the U.S.

A comprehensive approach to address high U.S. brand-name drug prices must account for the several major components of the U.S. market that sustain those high prices: (1) brand-name manufacturers can freely set prices for new drugs at the time of FDA approval at any level they wish, unlike what is seen in other countries, and important payors such as Medicare are required to accept those prices and to cover nearly all such products, whether they represent an increase in patient benefit or not; (2) brand-name manufacturers are permitted to freely raise prices to any level they choose during government-protected market exclusivity periods; and (3) these companies can use patents and other government-enforced tools to delay effective generic or biosimilar competition as long as possible.

A multi-pronged solution to ensure fair prices is therefore grounded in negotiating fair prices for brand-name drugs, ensuring that brand-name manufacturers cannot raise prices over time beyond inflation unless they make meaningful improvements to their drugs, and providing an efficient transition to a competitive generic market after exclusivity periods ends. Most other industrialized nations already have strategies that address each of these components.

A. *Negotiating Prices of Brand-Name Drugs*

While other countries have implemented a variety of effective price negotiation and review tools, U.S. legislators have not directly addressed drug prices and instead allow manufacturers to freely set prices while enforcing purchases by public sector programs and allowing for prolonged extension of government-granted monopolies. This situation is different from the purchase of nearly all other goods and services in our free-enterprise marketplace economy. The markets for prescription drugs are served by a patchwork of public and private payors that are unable in many cases to negotiate effectively, and/or are prohibited from declining to cover drugs that do not add anything meaningful to available treatment options. Medicare is forbidden by law from negotiating prices with drug manufacturers, despite the fact that it negotiates or sets the price for every other medical service it covers. Medicare Part B pays for all drugs at their average sales price (plus an additional percentage that acts as a dispensing fee), while the individual plans that offer coverage through Medicare Part D are forced to buy all drugs in several "protected" classes and cannot exclude any from their formularies, whether or not they add benefit or are severely overpriced. This situation—uniquely different from nearly all other Federal procurements—limits their ability to negotiate effectively. Medicaid programs receive a guarantee that they will get the best price being offered in the commercial market, but generally cannot negotiate any further since they are required to list virtually all FDA-approved drugs on their formularies.

In the private sector free from Medicare restrictions, commercial insurers can refuse to pay for particular costly drugs that have equivalent less expensive alternatives; they may also impose high co-payments to discourage patient demand for such lower-value medications. Unfortunately, such negotiation may not necessarily be based on the clinical benefit of the drug but on the extent of rebates, the financial goals of the pharmaceutical benefit manager (PBM) that often controls the negotiation, and other arrangements the PBM may have with it. Manufacturers, through PBMs, do negotiate prices but these other issues are central to the negotiation, rather than the extent of clinical benefit. The approach is also counteracted by manufacturer coupons to patients and patient assistance programs, as well as state laws that require coverage of certain drug products.

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[11] Harvard T.H. Chan School of Public Health & Politico, Americans' Domestic Priorities for President Trump and Congress in the Months Leading Up to the 2020 Election (Feb. 2020), *https://cdn1.sph.harvard.edu/wp-content/uploads/sites/94/2020/02/PoliticoFeb2020.pdf*.

One most direct way to address excessive drug prices would be for the government to negotiate the price of drugs for taxpayer-supported drug benefit programs, just as the Defense Department negotiates the prices of armaments it purchases. The prevailing approach to negotiating brand-name drug prices in other industrialized countries begins after regulatory approval with a process known as Health Technology Assessment (HTA). Numerous other countries have health technology assessment organizations that assess a newly approved drug's actual clinical benefit and help determine a fair price based on how well the new drug is expected to perform against other available treatments. These publicly funded organizations conduct assessments of the effectiveness, safety, and cost of new drugs compared with other interventions to evaluate what price the payor should agree to reimburse.

Germany, for example, launched a major drug pricing reform law in 2011 (Arzneimittelmarktneuordnungsgesetz, or AMNOG) to align prices and reimbursement more closely with expected treatment benefits. Under this law, called AMNOG, the manufacturer sets prices freely during a drug's first year on the market. During this time, the Institute for Quality and Efficiency in Health Care (IQWiG), a nonprofit, nongovernmental research organization, assesses its possible additional therapeutic benefits relative to existing standards of care (rating drugs as having: major, considerable, minor, or no or not quantified benefit). For drugs without sufficient clinical evidence of therapeutic benefit that surpasses the standard of care, payors will not reimburse prices higher than the existing standard of care. A 2018 analysis showed that of 139 drugs reviewed in the clinical benefit pricing procedure, only 22 were later withdrawn by the manufacturer from the market, and of those 22 all but one had received a rating of no additional clinical benefit; the remaining drug had a non-quantifiable benefit and was withdrawn from all European markets. [12]

In France, the Economic Committee for Health Products (CEPS) primarily judges the value of a new prescription drug based on the added clinical benefit that a drug provides to patients in comparison to available alternatives. This added benefit is classified as major (I), substantial (II), moderate (III), mild (IV), or absent (V). CEPS is composed of representatives from the health and finance ministries, the country's national health insurer, and private insurers. It negotiates drug prices with manufacturers on that basis. Drugs with major, substantial, or moderate added benefit are guaranteed to have a list price similar to those in the United Kingdom, Germany, Spain, and Italy. [13]

As these examples show, in Germany and France—as well as in other countries like Australia, Japan, and Canada—the primary tool for leveraging lower drug prices is to rigorously assess the clinical benefit of new drugs against pre-existing therapies or comparators. If a new drug does not have clinical evidence to show it is more effective than other drugs already available to treat a condition, then payors should not pay more for it than they do for those pre-existing drugs, a mainstay of all market-based transactions. [14] The basic logic is that if a drug costs more than other options, it should provide more benefit to patients. Benefit is usually evaluated with patient-relevant outcomes, including evidence of effectiveness on life-extension, improvements in quality of life, and/or other clinical outcomes. Additional benefit can be translated into health economic terms and cost-effectiveness to determine whether a proposed price is defensible. Alternatively, clinical benefit can be

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[12] Spuleucel-T (Provenge) received a benefit rating of "not quantifiable" and was scheduled to be re-reviewed but was withdrawn from European markets before then. Staab TR, Walter M, Mariotti Nesurini S, et al. "Market withdrawals" of medicines in Germany after AMNOG: a comparison of HTA ratings and clinical guideline recommendations. Health Economic Review 2018;8(1):23.

[13] Rodwin MA. Pharmaceutical Price and Spending Controls in France: Lessons for the United States. International Journal of Health Sciences. 2020;50(2):156–165.

[14] Pharmaceutical Benefits Advisory Committee. Guidelines for preparing a submission to the Pharmaceutical Benefits Advisory Committee. September 2016; IQWiG. General Methods. Köln 10 July 2017. *https://www.iqwig.de/en/about-us/methods/methods-paper/*; Shiroiwa T, Fukuda T, Ikeda S, Takura T. New decision-making processes for the pricing of health technologies in Japan: The fiscal year 2016/2017 pilot phase for the introduction of economic evaluations. Health Policy. 2017;121(8):836–841; *https://www.canada.ca/content/dam/pmprb-cepmb/documents/consultations/draft-guidelines/2020/PMPRB-Guidelines2020-en.pdf*. The French Haute Autorité de Santé, its national health authority, rates drugs on two scales: first, whether the new drug provides clinical benefit, which determines whether it will be reimbursed. The second, is whether the new drug provides additional benefit compared to available therapies, and the amount or degree of additional benefit determines the extent to which its price may be higher than comparator therapies. Haute Autorité de Santé. Pricing & Reimbursement of drugs and HTA policies in France. Haute Autorité de Santé. *https://www.has-sante.fr/jcms/c-1729421/en/transparency-committee*. Published 2015. Updated 29 January 2021.

plotted as an "efficiency frontier" to determine whether a price is in line with the degree of benefit, an approach which does not set any values of cost-effectiveness.[15] These evaluations inform an anchor price for negotiations with manufacturers.[16] Other countries have either a government or independent agency that reviews the manufacturer's evidence of clinical effectiveness and the proposed list price.[17] This process does not occur in the U.S., making it difficult for value-based assessments to drive medication use and cost. Currently, several smaller public and private entities, like the Institute for Clinical and Economic Review, take on this role on a voluntary basis.

Thus, my first recommendation is for the U.S. to establish similar publicly funded body that would determine a verifiable, evidence-based price for a drug based primarily on the clinical benefits it would provide. This effort should start with some of the brand-name or single-source drugs that account for the greatest spending or have the highest prices. Eventually, this body would be charged with reviewing all new drugs within the first year after approval; until then, manufacturers could be permitted to charge the price they believe is appropriate. This approach is analogous to the Drug Efficacy Study Implementation (DESI), a program that Congress mandated in the 1960's through the 1980's, to assess existing drugs for evidence of efficacy once that became a requirement for marketing. In determining a rational price, this body could also consider information about the cost of development, cost of failure, overall health care budget, extent of government funding in its development, and other relevant factors. Drugs that do not show benefits over other products would be offered the same price as the pre-existing alternatives. The advantages of such a reference pricing system are two-fold: first, at market entry, the prices for new drugs will be more consistent with their clinical benefits, and second, it incentivizes manufacturers to invest in research and development that will bring new drugs to market that meaningfully improve upon pre-existing therapeutics or address unmet needs. Manufacturers would also be incentivized to conduct the research needed to demonstrate comparative effectiveness. This system does provide extra rewards to drugs that offer no or minimal improvements on pre-existing therapies.

Past legislative efforts to establish such a body in the U.S. to review drugs' clinical benefits and determine their cost-effectiveness have been derailed by the political process. At different points, the Office of Technology Assessment, the Agency for Healthcare Research and Quality, and the Patient-Centered Outcomes Research Institute have all been proposed as the centers of such an effort. More recently, a few states have successfully initiated such review boards. For example, the New York legislature delegated the new authority for drug assessments and negotiation to an existing agency within the state Department of Health to review the cost-effectiveness and clinical benefit of prescription drugs that the state's Medicaid program purchases.[18] The board primarily relies on third-party organizations, such as the Institute for Clinical and Economic Review, and evaluates the following factors: publicly available pricing information, information supplied by the state Department of Health, value-based pricing analyses provided by third parties, the severity and prevalence of the treated condition, utilization data, the effectiveness of the drug,

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[15] For example, the Australian and Canadian health technology assessment bodies (PBAC and CADTH, respectively) translate clinical benefit into health economic measures of cost-effectiveness. By contrast, the German health technology assessment body (IQWiG) plots an efficiency frontier using the most significant clinical outcome or a combination of net health benefits and extrapolates an appropriate price from this. Pharmaceutical Benefits Advisory Committee. Guidelines for preparing a submission to the Pharmaceutical Benefits Advisory Committee, version 5.0; CADTH. Guidelines for the Economic Evaluation of Health Technologies: Canada. Ottawa March 2017. IQWiG. General Methods. Köln 10 July 2017. *https://www.iqwig.de/en/about-us/methods/methods-paper/*.

[16] See e.g., Patented Medicines Prices Review Board *https://www.canada.ca/content/dam/pmprb-cepmb/documents/consultations/draft-guidelines/2020/PMPRB-Guidelines2020-en.pdf*; Pharmaceutical Reimbursement and Pricing in Germany. June 2018. *https://www.oecd.org/health/health-systems/Pharmaceutical-Reimbursement-and-Pricing-in-Germany.pdf*; Transparency Committee. Principles of medicinal product assessments and appraisal for reimbursement purposes. 2 December 2020.

[17] Emanuel EJ, Zhang C, Glickman A, Gudbranson E, DiMagno SSP, Urwin JW. Drug Reimbursement Regulation in 6 Peer Countries. JAMA Internal Medicine 2020; See also Rand LZ, Kesselheim AS. An International Review of Health Technology Assessment Approaches to Prescription Drugs and Their Ethical Principles. Journal of Law Medicine, and Ethics 2020;48(3):583–594.

[18] For a full description of the New York process, as well as processes created in Massachusetts and other states, see Bendicksen L, Rome BN, Avorn J, Kesselheim AS. Pursuing value-based prices for drugs: a comprehensive comparison of state prescription drug pricing boards. Milbank Quarterly 2021 [in press].

the extent to which the drug improves patient health or quality of life, the likelihood that use of the drug will reduce patients' utilization of other medical services, the post-rebate cost of the drug to Medicaid, the availability of therapeutic alternatives, the number of manufacturers that produce the drug (in the case of generics), and information supplied confidentially by the manufacturer to the board. After the board agrees on a fair, value-based price for the drug, New York's Medicaid program uses this price as a benchmark in negotiations with the drug's manufacturer for additional supplemental rebates. The board has completed three full reviews to date and successfully exacted additional discounts for at least two reviewed drugs. Such an effort would not be excessively costly. Though a New York-specific fiscal analysis is not available, the Maryland prescription drug affordability board is expected to fully fund its activities by assessing $1,000 fees on the approximately 1,400 corporations in the prescription drug supply chain in Maryland (generating a yearly operating budget of $1.4 million).

Such value-based price negotiations can be effective at reducing prices. In France, the government takes clinical benefit into account in pricing negotiations and additional factors, such as the price of alternatives that treat the same or similar conditions, and the number of people eligible to use the drug: products that treat conditions that affect more people are priced lower because manufacturers can make the same profits with lower margins given increased volume. The French system has been very effective; in the 1970's and 1980's, the U.S. and France were among the OECD countries with the highest spending on pharmaceuticals, but in France, the rate of spending began to slow with implementation of new regulations, and was only $638 per capita in 2018—half the amount the U.S. spent per person ($1,229).[19] The House's Elijah E. Cummings Lower Drug Costs Now Act (H.R. 3), introduced in 2019, included a provision for direct negotiation of drug prices in Medicare and was expected to save $448 billion in direct Medicare spending.[20]

It is important that the price identified and negotiated through this process be offered to the private market too. The U.S. has a fragmented health system with many different payors, each of whom is responsible for securing drugs. By contrast, in other countries, a single entity is responsible for negotiating the list price for the country. This leverages the full market power of the country's payors. In some countries, such as the UK, France, and Japan, a government department of health carries out negotiations with manufacturers to secure a price for a national health insurance system. Within this framework in Europe, drug price negotiations can be centralized and involve both public and private insurance plans: in Germany, centralized negotiations are carried out by a body called the Federal Joint Committee and representing more than 100 insurance plans.[21] Prescription drug pricing defaults to reference pricing to comparators, but if there is evidence of additional benefit, then the Federal Joint Committee negotiates with drug manufacturers to determine a list price that will be paid by all the insurers.[22] If negotiations fail in Germany, a price is set by arbitration. In a study we conducted with Prof. Ariel Stern at Harvard Business School using data on 57 anticancer drugs launched in Germany from 2002 to 2017, we found that implementation of these negotiations was associated with drug prices being more closely aligned with clinical benefit and a 24.5 percent decrease in negotiated prices relative to launch prices.[23] Another study found that prior to the introduction of these centralized negotiations, U.S. prices in Medicare Part B were 29 percent higher than German prices for the same drugs. Following the introduction of the centralized negotiations and assessment of clinical benefit in Germany, German prices became lower than U.S. prices by a further 29 percent.[24]

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[19] Raimond VC, Feldman WB, Rome BN, Kesselheim AS. Why France spends less than the United States on drugs: a comparative study of drug pricing and pricing regulation. Milbank Quarterly 2021 [in press]

[20] Congressional Budget Office. 2019. Budgetary Effects of H.R. 3, the Elijah E. Cummings Lower Drug Costs Now Act. Washington, DC: Congressional Budget Office.

[21] Gemeinsamer Bundesausschuss (G-Ba), or Federal Joint Committee *https://www.g-ba.de/english/*.

[22] *https://www.g-ba.de/english/benefitassessment/*.

[23] Lauenroth VD, Kesselheim AS, Sarpatwari A, Stern AD, Lessons from the impact of price regulation on the pricing of anticancer drugs in Germany. Health Affairs 2020;39(7):1185–1193.

[24] For new drugs authorized between 2004–2018, the average price ratio between U.S., Medicare Part B and German prices before 2011 was 29.2 percent. After the introduction of the German AMNOG law, which established the Federal Joint Committee and introduced clinical benefit as the basis for price negotiation, the difference between Medicare Part B and German prices rose another 28.9 percent. Berkemeier F, Whaley C, Robinson JC. Increasing Divergence in Drug Prices Between the United States and Germany After Implementation of Comparative

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An alternative approach is to implement price limits and allow public and private plans to each negotiate their own prices with manufacturers. In Canada, the Patented Medicine Prices Review Board (PMPRB) is a quasi-judicial, independent body that was created in 1987 to protect consumers from excessive prices during brand-name drug exclusivity periods. When a patent-holder applies to sell a drug in Canada, it must submit information on the labeling of the drug, price, information from benefit analyses undertaken, and estimated use by the population to the PMPRB. The PMPRB then reviews the proposed price, taking into account information that includes reference pricing to comparator therapies, market size for the drug, consumer price index, and prices charged in other countries. Through this process, the Board first establishes an "Interim Maximum List Price", which is followed by a "Maximum List Price" as more information about the drug becomes available. If a manufacturer is found to have excessively priced a drug, the Board can require that the drug price be lowered and introduce clawbacks.[25] In the Canadian example, an independent body protects patients and plans from excessive pricing, and payors then have the option to negotiate discounts with manufacturers.[26]

In summary, experience from other countries (and a few U.S. states) shows that brand-name drug prices can effectively be lowered by first assessing the clinical benefits of a drug and then engaging in effective negotiation on that basis, without the artificial limits currently placed on U.S. public and private payors. For drugs that offer substantial clinical value to patients, this system may lead to paying high prices commensurate with the benefit the drug provides. But most drugs do not have such high value; in fact, one review we conducted of drugs the FDA approved in 2017 found that of those reviewed by international health technology assessment organizations only one-third were rated as offering more than minor benefit over currently available treatments.[27] Another recent review found that of 122 "ultra-expensive" drugs in Medicare, those with annual spending greater than GDP per capita or $63,000, up to 85 percent were rated as having no or low additional value by international health technology assessment organizations.[28] In the U.S., we will be able to better afford paying high prices for truly meaningful improvements because we will pay far less for drugs that do not offer clear clinical benefits.

Importantly, the U.S. is already implementing an approach with some of these features in the Veterans Affairs Health System. Unlike Medicare and Medicaid, the VA is allowed to determine which drugs it will cover, and can negotiate process with manufacturers on this basis. Because of this, prices paid by the VA are substantially lower than those in all other U.S. government-financed systems. We have already developed this approach to a large extent, and it is working very well, so it should not be seen as some kind of exotic "foreign import."

Addressing Price Increases During Market Exclusivity

In the U.S., drug manufacturers are free to raise the price of a drug each year, and often do so, far beyond the cost of inflation. Imatinib (Gleevec), a treatment for numerous rare cancers, was introduced in 2001 for a list price of $26,400 per year,

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Effectiveness Analysis and Collective Price Negotiations. J Manag Care Spec Pharm. 2019;25(12):1310–1317.

[25] 25 *https://www.canada.ca/content/dam/pmprb-cepmb/documents/consultations/draft-guidelines/2020/PMPRB-Guidelines2020-en.pdf* The PMPRB is currently updating its guidelines. Following a court challenge, the new guidelines, which are cited here, took effect on January 1, 2021.

[26] Prescription drugs administered in hospitals are at no cost to patients, but for outpatient drugs, plans are responsible. Provincial and territorial governments have their own public plans, while many Canadians are covered through private plans, such as employer-based coverage. (*https://www.canada.ca/en/health-canada/services/health-care-system/pharmaceuticals/access-insurance-coverage-prescription-medicines.html*) Public and Federal plans in Canada formed the pan-Canadian Pharmaceutical Alliance (as it is now called) in 2010 with the objective of combining negotiating powers to achieve greater value for publicly funded drug programs and patients. The pCPA takes into account health technology assessment (HTA) reports from the two Canadian HTA organizations, budget impact analysis and affordability, the therapeutic landscape and gaps, and other considerations when negotiating with manufacturers. *https://www.pcpacanada.ca/negotiation-process*.

[27] Frank RG, Avorn J, Kesselheim AS. What do high drug prices buy us? Health Affairs Blog. April 29, 2020.

[28] Prices based on 2018 GDP per capita. Average annual spending per beneficiary was $174,699 and of these drugs, Germany rated 29 percent as having no additional value and France rated 31 percent as having no additional value. Overall a majority of drugs were rated as having low or no additional value: 85 percent in France, 74 percent in Germany, and 73 percent in Canada. DiStefano MJ, Kang SY, Yehia F, Morales C, Anderson GF. Assessing the Added Therapeutic Benefit of Ultra-Expensive Drugs. Value in Health 2021;24(3):397–403.

a price which increased to more than $120,000 by 2016.[29] One study found that price inflation of existing brand-name oral drugs rather than market entry of new drugs accounts for 87.3 percent of average weighted costs.[30] Many brand-name drugs provide rebates to commercial payors and Medicare Part D plans that offset some of the list price increases, and while drug-level rebates are confidential, estimates of those rebates indicate that they do not keep pace with list price increases. One review of list and estimated rebates from 2007–2018 on branded pharmaceutical products found that list prices increased by 159 percent—or 9.1 percent per year—but net prices increased by 60 percent overall, with discounts offsetting only 62 percent of increases in list prices for drugs.[31]

Excessive annual price increases are reflected in higher prices to patients. Over 10 percent of people in the U.S. have no drug insurance, and often must pay the full list price. One recent study found that list prices for the 14 top-selling drugs doubled from 2010 to 2016 while median patients' out-of-pocket costs increased by 53 percent.[32] A recent review led by Dr. Benjamin Rome in our group found that patients with insurance who pay deductibles or co-insurance are particularly at risk and are likely to experience substantial increases in out-of-pocket spending when drug list prices rise.[33]

By contrast, in other countries, agreements between the government or payors and manufacturers keep price increases in check. In France and the UK, manufacturers agree to spending caps, essentially growth caps on drug sales, which if exceeded require a portion of excess profit to be rebated.[34] As a result, drug prices in France do not increase routinely over time. If France's Transparency Committee lowers a drug's effectiveness rating, the price for that drug decreases. For example, the rating for insulin glargine was changed from "moderate improvement" to "minor improvement" and then to "no improvement" as new safety data were documented and market competitors emerged.[35] In one study comparing the six highest spending drugs in Medicare between the U.S. and France, we found that the spending per unit for lenalidomide in the U.S. increased from 2010 to 2018 from about $400 per unit to nearly $700 per unit, while during that same period the price of the drug in France decreased from $239 to $202 per unit.[36]

Other countries, including Australia, even require statutory price decreases. On the Australian formulary, brand-name drugs that have no comparator therapies take a 5 percent price cut after five years. This arrangement is part of a five-year agreement made with the drug trade group Medicines Australia.[37] Like using clinical benefit as the basis of price negotiations, the Australian plan is intended to incentivize the development of new drugs that offer improvements or address areas

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[29] Johnson CY. This drug is defying a rare form of leukemia—and it keeps getting pricier. Washington Post. March 9 2016.

[30] Hernandez I, Good CB, Cutler DM, Gellad WF, Parekh N, Shrank WH. The Contribution of New Product Entry Versus Existing Product Inflation in the Rising Costs of Drugs. Health Affairs 2019;38(1):76–83.

[31] Hernandez I, San-Juan-Rodriguez A, Good CB, Gellad WF. Changes in list prices, net prices, and discounts for branded drugs in the U.S., 2007–2018. JAMA 2020;323(9):854–862.

[32] Yang EJ, Galan E, Thombley R, et al. Changes in Drug List Prices and Amounts Paid by Patients and Insurers. JAMA Network Open 2020;3(12):e2028510.

[33] Rome BN, Feldman WB, Desai RJ, Kesselheim AS. Correlation between Changes in Select Brand-Name Drug Prices and Patient Out-of-Pocket Costs, 2015–2017. JAMA Network Open 2021 [in press].

[34] Rodwin MA. Pharmaceutical Price and Spending Controls in France: Lessons for the United States. International Journal of Health Services 2020;50(2):156–165; The 2019 Voluntary Scheme for Branded Medicines Pricing and Access (2018) *https://www.gov.uk/government/publications/voluntary-scheme-for-branded-medicines-pricing-and-access*.

[35] Raimond VC, Feldman WB, Rome BN, Kesselheim AS. Why France spends less than the United States on drugs: a comparative study of drug pricing and pricing regulation. Milbank Quarterly 2021 [in press].

[36] Id.

[37] "PBS medicines are divided into two categories for pricing purposes. Formulary 1 (F1) is for single brand (generally patented) medicines and Formulary 2 (F2) is for medicines (generally off-patent) that have multiple brands listed on the PBS. Medicines on F1 currently take a five per cent cut in the price paid by the Government after five years on the PBS. When a second brand of a medicine is listed on the PBS, the medicine moves to F2 and takes a 16 per cent price cut. Under this budget measure, F1 medicines will continue to take a five per cent price cut after five years on the PBS (extended to 2022), but will also take further price cuts of 10 per cent after 10 years and five per cent after 15 years. When a medicine moves to F2, the price cut will increase from 16 to 25 per cent. Legislation will be required to implement the price cuts." Grove A. Pharmaceutical Benefits Scheme. Parliament of Australia. *https://www.aph.gov.au/About-Parliament/Parliamentary-Departments/Parliamentary-Library/pubs/rp/BudgetReview201718/PBS*.

of unmet need. Japan uses a different approach and reviews list prices every two years, decreasing them if the actual market price paid is lower than the list price.[38]

In each of these countries, the government secures agreement between payors and manufacturers: once a price has been negotiated between payors and manufacturer, it cannot be raised without re-reviewing the clinical and economic evidence. By contrast, the U.S. government grants drug manufacturers a monopoly through patents and FDA exclusivity periods, during which time they can freely set prices, including raising list prices. Therefore, my second major recommendation is to limit the rate of drug price increases, so that the government-granted monopoly does not exploit the patients who rely on these medicines. One model for how this would work would be to implement the drug price inflation rebate penalty currently in place for Medicaid, which contains exorbitant annual increases by requiring a higher rebate if drug price increases exceed inflation. Bills were introduced in the prior Congress with bipartisan support for extending the Medicaid inflation penalty to Medicare Part D: a version of this policy was included in the House Elijah E. Cummings Lower Drug Costs Now Act (H.R. 3) and the Senate Prescription Drug Pricing Reduction Act (S. 2543). According to the Congressional Budget Office, for drugs covered under Medicare Parts B and D, limiting annual price increases to the rate of inflation is expected to save $36 billion over ten years.[39]

C. *Ensuring Effective Transition to a Competitive Market*

A final approach to move toward fairer drug pricing is to arrange for an efficient transition to a competitive market at the end of a brand-name drug's period of market exclusivity. The government provides about 6–7 years of guaranteed generic-free marketing periods for new brand-name drugs via the Hatch-Waxman Act of 1984. (This has been expanded to about 12 years for qualified antibiotics or biologic drugs.) Additionally, a drug it is usually protected by numerous patents, each lasting up to 20 years, that have started accumulating since the drug was originally synthesized or discovered. A study led by Dr. Rome in our research group found that patents actually provide 13–17 years of market exclusivity for new brand-name small-molecule drugs, and even more for biologic products, keeping generic manufacturers from the market long after the exclusivity period ends.[40]

Patents perform a very important role in enabling innovators to profit from their discoveries for a finite amount of time, and rewarding that creativity. But this system has become subject to many abuses, with two distinct patent-related problems contributing to unjustifiably high drug prices. First, pharmaceutical manufacturers can obtain multiple patents—occasionally even hundreds—covering their drugs, even for attributes that reflect no meaningful innovation. The legal and scientific complexity of drug patent applications, combined with the heavy demands on patent assessors who are often not expert in the issues at stake, means that personnel in the U.S. Patent and Trademark Office (USPTO) sometimes issue patents in error. The fact that a patent was improperly granted generally becomes evident only following litigation, long after the patent has issued, when far greater resources are devoted to their evaluation.[41] By this time, however, the delay in generic competition caused by patents that should never have issued can contribute to substantial excess expenditures on brand-name drugs by public and private sector payors, and by patients.[42] This ″thicket″ of additional patents makes it possible for brand-name manufacturers to introduce new versions of their products that provide longer exclusivity with little or no clinical benefit for patients.[43] In one study of drugs approved in 2002, we found that 9 (53%) were introduced in patentable new formulations in the subsequent 15 years, with many of these changes clinically trivial.[44] In another study, we found that the proportion of patents listed with the FDA that cover drug-

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[38] Shiroiwa T, Fukuda T, Ikeda S, Takura T. New decision-making processes for the pricing of health technologies in Japan: The fiscal year 2016/2017 pilot phase for the introduction of economic evaluations. Health Policy 2017;121(8):836–841.

[39] Congressional Budget Office. 2019. Budgetary Effects of H.R. 3, the Elijah E. Cummings Lower Drug Costs Now Act. Washington, DC: Congressional Budget Office.

[40] Rome BN, Lee CC, Kesselheim AS. Market exclusivity length for drugs with new generic or biosimilar competition, 2012–2018. Clinical Pharmacology and Therapeutics 2020 July 12.

[41] Hemphill CS, Sampat B. Drug patents at the Supreme Court. Science 2013;339:1386–1387.

[42] Dave C, Sinha MS, Beall RF, Kesselheim AS. Estimating the cost of delayed generic entry to Medicaid. Health Affairs 2020;39(6):1011–1017.

[43] Amin T, Kesselheim AS. Secondary patenting of branded pharmaceuticals: a case study of how patents on two HIV drugs could be extended for decades. Health Affairs. 2012;31(10):2286–2294. doi:10.1377/hlthaff.2012.0107.

[44] Beall RF, Kesselheim AS, Sarpatwari A. New drug formulations and their respective generic entry dates. Journal of Managed Care and Specialty Pharmacy 2019;25(2):218–224.

related devices tripled between 2000 and 2016 (from 3% to 9% of all drug-related patents).[45] These device patents extend exclusivity periods even though the patent on the drug itself has lapsed. It is important to ensure that such invalid patents are not mistakenly issued, because manufacturers can extract substantial revenues from patented changes. In a recent study, we found that a manufacturer introduced a version of the multiple sclerosis drug glatiramer (Copaxone) that could be taken 3 times per week instead of daily, providing benefits that were tiny in comparison to the $6.5 billion in the resulting additional drug expenditures that the U.S. spent on the new formulation instead of generics.[46] A federal appeals court ultimately held that the patents protecting the new version of glatiramer were invalid, but the payments had already occurred.

Here again, lessons on how to improve experience in the U.S. can come from analyzing how other countries handle patents. Results from foreign patent offices suggest the USPTO could reduce the number of erroneously issued patents by allocating greater resources to ensure patent quality. The European Patent Office (EPO) and Japan Patent Office (JPO) issue fewer, higher-quality patents despite applying a similar legal standard as the USPTO.[47] The EPO and JPO do this in part by spending more time and resources scrutinizing patents, retaining high-quality examiners, and having their employees work in teams.[48] In one study, a 50 percent increase in examination time was associated with a 10 percent decrease in invalid patents.[49] As Doni Bloomfield and I recounted in a recent Washington Post article, "The problem of weak drug patents has worsened under the Trump administration. In the past two years, the PTO has made it even more difficult for examiners to reject patent applications. The office issued directives that increase the amount of work examiners must do to reject certain applications, such as those that seek to patent a process found in nature. Predictably, these directives decreased examiners' rejections for such ineligibility by more than 25 percent." Predictably, these directives decreased examiners' rejections for such ineligibility by more than 25 percent."Predictably, these directives decreased examiners' rejections for such ineligibility by more than 25 percent."[50]

Thus, my third major recommendation is to closely scrutinize the process for issuing drug patents and enforcing them against generic manufacturers. This can be accomplished at a number of different levels. Without even requiring legislation, the USPTO would benefit from greater resources; better agency regulation can give examiners more time and administrative leeway to reject ineligible applications, reflecting current practices in some patent offices around the world. In addition, we could better leverage the U.S. Patent Trial and Appeals Board (PTAB), set up by the 2011 America Invents Act. The PTAB could help weed out invalid patents before they get caught up in litigation if it had the authority to review all patents as soon as they are listed with the FDA by a manufacturer. If steps cannot be taken to clear out the thicket of patents that threatens transitions to an effective competitive market, then we might need to consider automatic price reductions for brand-name drugs after a reasonable period of time on the market;[51] one recent analysis of applying this concept to biologic drugs predicted potential cost-savings over the next five years of $265 billion when compared to the current model of biosimilar competition.[52] At the level of the pharmacy, we could allow closely similar drugs to be more easily substituted with each other by pharmacists even if they have patentable differences, if the FDA judges those drugs to be therapeutically interchangeable. Such

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[45] Beall RF, Kesselheim AS. Tertiary patenting on drug-device combination products in the United States. Nature Biotechnology 2018;36:142–144.

[46] Rome BN, Tessema FA, Kesselheim AS. U.S. spending associated with transition from daily to three-times-weekly glatiramer acetate. JAMA Internal Medicine 2020;180(9):1165–1172.

[47] Picard PM, Bruno VPDLP. Patent office governance and patent examination quality. Journal of Public Economics 2013;104:14–25; Chien CV. Comparative Patent Quality. Arizona State Law Journal; 2018; 50:71–140; Lemley MA, Sampat B. Examiner Characteristics and Patent Office Outcomes. Review of Economics and Statistics 2012;94:817–827; Lei Z, Brian DW. Why Weak Patents? Testing the Examiner Ignorance Hypothesis. Journal of Public Economics 2017;148:43–56.

[48] Id.

[49] Frakes MD, Wasserman MF. Investing in ex ante regulation: evidence from pharmaceutical patent examination. Cambridge, MA: National Bureau of Economic Research; July 2020 (*https://www.nber.org/papers/w27579*).

[50] Bloomfield B and Kesselheim AS. Biden can lower drug prices without Congress doing anything. Washington Post Jan 5 2021.

[51] Dudzinski DM and Kesselheim AS. Scientific and legal viability of follow-on protein drugs. New England Journal of Medicine 2008;358:843–849.

[52] Bach PB and Trusheim MR. The drugs at the heart of our pricing crisis. NY Times. March 15 2021.

a move would broaden competitive markets and require manufacturers seeking to introduce a slightly changed version of a product to ensure that the product really offers important benefits to patients.

III. Common Counter-Arguments and Responses

The greatest challenge in enacting these changes will be the political strength of the pharmaceutical industry lobby, one of the largest in Washington, which will charge that any drug pricing reform will reduce innovation. This is a false assertion; much evidence indicates that meaningful innovation need not decline. Large pharmaceutical manufacturers invest only about 10–20 percent of their revenues in research and development, so providing exceedingly high profit margins to such manufacturers does not directly translate to substantial investment in innovation. A substantial amount of work from our research group has documented how transformative drug innovation often emerges in large part from publicly funded research and development, even though this is rarely reflected in the pricing of the resulting drugs, or in commensurate "payback" to the funding agencies that made them possible.[53] As long as Congress continues funding for the National Institutes of Health, then we can be assured that the next generation of important new therapeutics will be in the pipeline. This view is bolstered by experiences in other countries. In recent work focused on Germany led by my colleague Ariel Stern, we found that for drugs found to provide important new patient benefits, none of them left the German market, despite price negotiations.[54] If concern arises about insufficient support to bring certain types or classes products through clinical testing and regulatory approval—the roles dominated in the current system by venture capital and private industry funding—the recent evolution of Covid–19 treatments and vaccines has shown that public funding and partnerships can help advance highly promising new treatments.

These changes are likely to actually improve meaningful innovation. The current system in which brand-name manufacturers are rewarded with high U.S. prices for new drugs that have limited clinical advantages may even reduce the pressure for them to develop medications that truly add clinical value. It is notable that less than one-third of new drugs approved in the past decade were rated as providing high clinical value compared to existing alternatives, although this has not led to lower prices.[55] If drug prices more adequately reflected the clinical benefits they offer to patients, this would incentivize more meaningful pharmaceutical innovation, and there would be less investment in making trivial changes to existing products and more investment in meeting unmet medical needs. If reference pricing and clinical benefit assessment formed the basis for price negotiations, new drugs that offer improved outcomes to patients would be rewarded with higher prices than available options, creating a powerful incentive for manufacturers to invest their resources in bringing to market drugs that will achieve this price premium rather than products that can be priced high but will not offer patients more health.[56]

Finally, as described above, more data-driven policies on drug pricing need not reduce prices equally across the board; pricing based on a product's actual clinical benefits could still lead to substantial manufacturer revenue and thus offer a strong incentive for private investment in research and development.[57] Payor drug budgets would better be able to account for these situations without being burdened by payments for non-innovative expensive drugs and high-priced drugs for which competitive generic or biosimilar entry is delayed. Particular attention may need to be provided for the rare but clinically ideal scenario of an extremely effective drug with

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[53] See e.g., Kesselheim AS, Tan YT, Avorn J. The roles of academia, rare diseases, and repurposing in the development of the most transformative drugs. Health Affairs 2015;34:286–294; Nayak RK, Avorn J, Kesselheim AS. Public support for late-stage new drug discovery; cohort study. BMJ 2019;367:l5766.

[54] Stern AD, Pietrulla F, Herr A, Kesselheim AS, Sarpatwari A. The impact of price regulation on the availability of new drugs in Germany. Health Affairs 2019;38(7):1182–1187. The oncology drug regorafenib (Stivarga) was withdrawn from the market; it received an early positive assessment, but was later reassessed by the Federal Joint Committee, which failed to confirm its prior positive benefit assessment.

[55] Hwang TJ, Vokinger KN, Ross JS, Kesselheim AS. Association between FDA and EMA expedited approval programs and therapeutic value of new medicines. BMJ 2020;371:m3434.

[56] Fojo T, Mailankody S, Lo A. Unintended Consequences of Expensive Cancer Therapeutics—The Pursuit of Marginal Indications and a Me-Too Mentality that Stifles Innovation and Creativity: The John Conley Lecture. JAMA Otolaryngology—Head & Neck Surgery. 2014;140(12):1225–1236.

[57] Kesselheim AS, Hwang TJ, Avorn J. Paying for prescription drugs in the new administration. JAMA 2021;325(9):819–820.

tremendous long-term clinical benefits, similar to the direct-acting antiviral hepatitis C virus drugs when they were introduced in 2015. In that case, the high price set by the manufacturer was ultimately cost-effective, but too expensive for many payors, particularly Medicaid programs, in the short-term. In these situations, Congress could support Medicaid with support for payments over time assuming ongoing clinical benefits, or create a special high-risk pool of Federal dollars separate from a patient's insurance, similar to the way in which Medicare pays for the medical expenditures of all dialysis patients.

IV. Conclusion

The high drug prices faced by U.S. patients directly result from existing Federal policies that have helped shape the organization of the pharmaceutical market in the U.S., in which brand-name manufacturers are given years-long government-granted market exclusivity periods and near-total freedom to establish prices—with nearly half of that expenditure paid by government programs such as Medicare and Medicaid. Compounding this situation, the lattice of public and private payors in the U.S. are limited by their inability to negotiate (as for Medicare Part B) or restrictions that require them to cover any FDA-approved drug no matter how useful it is (as for Medicaid and Medicare Part D "protected drug classes").

To effectively lower prices, policymakers can adopt three important principles currently in place in other industrialized countries to better ensure that we are paying prices commensurate with the utility offered by new drugs. First, the U.S. needs to set up a system to evaluate the clinical benefits of brand-name drugs and help determine the basis for reasonable pricing given those benefits. Health technology assessment organizations that conduct this work are operating effectively in many other countries. The U.S. then needs to empower negotiation of prices based on that clinical evaluation process and offer negotiated prices to the private market. Second, the U.S. must ensure, as other countries do, that brand-name drug prices are not increased exorbitantly beyond inflation during a drug's market exclusivity period unless the manufacturer makes clinically meaningful improvements to the drug. Third, the U.S. needs to provide a rapid, efficient transition to a competitive generic market after a product's government-enforced monopoly expires. Currently, brand-name manufacturers can delay generic entry by obtaining numerous patents, many of them for trivial changes, and then leverage them to introduce new formulations with only minor clinical effects that can forestall direct competition. If the USPTO adopted approaches similar to those used by its counterparts in Europe or Japan, protecting drugs with invalid or otherwise problematic patents would happen less often.

Congress can take up this model secure in the knowledge that the drug industry's charges that their effects on innovation are overblown. Enhanced investment in public funding for research will continue to provide the insights needed to develop transformative products, as it has done for numerous important drugs and Covid–19 vaccines. Fair and even generous rewards would still be provided to drugmakers who create important new medications—just not for those that add little or nothing to what we can offer patients. With the changes proposed above, policymakers can rest reassured that more patients will be able to access these vital products at an affordable price that accords with a drug's value and cost of development. In fact, better aligning U.S. drug prices with their clinical benefits will reward and promote innovation because it will better incentivize manufacturers to invest in helping develop new treatments that meet unmet medical needs or offer meaningful clinical benefits to U.S. patients.

[SUMMARY STATEMENT OF AARON S. KESSELHEIM]

- The U.S. spends far more on prescription drug prices per capita than any other industrialized nation—about double that of many wealthy countries. Overall prescription drug spending jumped from $427 billion in 2015 to $511 billion in 2019. Even though brand-name drugs account for only 10 percent of prescriptions, they are responsible for about 75 percent of drug spending.
- U.S. prices for the same drugs, made by the same companies, are far higher in the U.S. than in other comparable countries. For example, some drugs covered by the Medicare program cost 40–60 percent less than the prices paid for those same drugs in four other high-income countries.

- Government-granted monopolies in the form of patents allow companies to freely set prices at any level they wish—a situation not seen in any other countries.
- Reforming the U.S. drug pricing system should be based on a three-pronged approach:

  1. The government should engage in direct price negotiation with manufacturers over the medications it purchases (e.g., in the Medicare program), based on the additional clinical benefit that a new drug provides to patients. Other countries evaluate how much additional benefit a new drug offers above existing alternatives; products that provide little or no additional benefit are reimbursed at the same price as the existing therapeutics. Several states are implementing review boards to evaluate evidence to inform such negotiation, but this should be carried out by a centralized body to leverage the market power of the U.S.. Experience in other countries shows that successful, evidence-based negotiations can be conducted by the government or non-governmental bodies representing private payors.

  2. In the U.S., manufacturers often raise the list prices of brand-name drugs each year well beyond inflation, placing new financial strains on patients and insurers in the public and private sectors. The Federal Government should prevent price increases well beyond inflation that are not justified by new clinical evidence of improved effectiveness by limiting such increases to the rate of inflation, as is already done in Medicaid. Again, the U.S. is an outlier in allowing these increases, and in most countries they are either prohibited by law or tightly limited.

  3. It will be vital to ensure a competitive market once a drug's basic period of patent-provided exclusivity ends. Drug companies often obtain numerous extra patents to extend their monopoly powers for years longer than originally expected, often for clinically trivial changes. This allows them to move market share to their newer product formulations even if these offer limited or no clinical advantages but can be sold at a high prices. The U.S. Patent and Trademark Office has been undermined in its ability to ensure that all patents issued are legitimate, resulting in lengthy legal battles and delays to the availability of more affordable generic versions as patents are challenged in court.

- The pharmaceutical lobby is large and well-funded and will argue that any reduction in revenues will harm innovation. But most drugs approved each year are not truly innovative and in a review of 2017 new approvals, only a minority of those reviewed by independent expert bodies offered more than minimal clinical advantages over available treatments. In addition, only 10–20 percent of large pharmaceutical manufacturer revenues go to research and development of new drugs, and public funding often plays a key role in financing research that leads to the most innovative new drugs.
- By contrast, these three proposals will actually increase innovation by providing greater incentive to discover truly important medications, an improvement over the current system that incentivizes manufacturers to profit by extending patent life beyond its original duration and developing drugs that offer little clinical benefits but can be priced freely. Negotiations based on additional patient benefit, limited price increases, and stronger patent scrutiny incentivizes what matters most: the development of drugs providing important new benefits to patients and addressing unmet need.

The CHAIRMAN. Dr. Kesselheim, thank you very, very much.

Our next witness is Dr. Nav Persaud, who is the Canada Research Chair in Health Justice and Associate Professor at the University of Toronto. He is a staff physician and scientist at St. Michael's Hospital and Unity Health Toronto, where he provides care to patients and leads studies as part of the MAP Center for Urban Health Solutions.

Dr. Persaud, thanks so much for being with us.

STATEMENT OF NAV PERSAUD, M.D., MA, CANADA RESEARCH CHAIR IN HEALTH JUSTICE, UNIVERSITY OF TORONTO, ON, CANADA

Dr. PERSAUD. Thank you and good morning.

In Canada, per capita drug spending is $879, versus over $1,200 in the United States. Per capita spending is about 40 percent higher in the United States largely because of the regulation of patented drug prices by the Canadian Patented Medicines Prices Review Board. Posted prices for patented medicines are approximately three times lower in Canada. The Patented Medicines Prices Review Board is slated in July to drop the United States from its list of comparative countries used to set price ceilings because prices are shockingly high in the United States compared with other high-income countries, including the United Kingdom.

The marketing of a raft of patented medicines during the 1990's boosted per capita spending disproportionately in the United States. The larger rise in spending during the 1990's was partially due to patented opioid products such as OxyContin that was illegally marketed by Purdue Pharma on the lie that these medicines were safer than less expensive alternatives. Pharmaceutical companies continue to profit from the opioid crisis that killed approximately 80,000 Americans in the twelve-month period ending in May 2020.

Pressure and lobbying by pharmaceutical companies have undermined reforms in both Canada and the United States. Multiple government reports over decades have recommended including medicines in Canada's publicly funded single-payer system to improve fair access and to save billions each year, but this has not happened. So we continue to pay high prices relative to comparable countries such as Norway and Australia, and inequities persist in Canada.

America is a superpower, a superpower that has not shown its strength in standing up to pharmaceutical companies that rip off Americans, as driven by the price differences for patented medicines across our border. My colleagues and I have conducted a randomized control trial of distributing essential medicines, as per international guidance from the World Health Organization, to people who report not being able to afford them.

We found improvements in the control of blood pressure and diabetes, fewer missed medical appointments, and total health care savings that average more than $1,000 per patient per year. The biggest benefit was in the ability to make ends meet or afford basic necessities such as rent and food. Only 29 percent in the usual access or control group could make ends meet, but 86 percent of those who did not have to pay out of pocket for medicines could afford necessities. A farmer in our study, for example, was better able to grow food when he had his asthma puffers.

Would publicly funding a list of essential medicines work in the United States? It already is working at the United States Veterans' Administration. Since its creation in 1997, the VA's national formulary has led to improvements in care, and its negotiating power has led to impressive price reductions.

The VA's approach of creating a rational list of medicines and then using proven methods to negotiate prices accords with inter-

national guidance. It's a model that could be adapted to an even larger scale in the United States.

There are three key elements of government action to reduce drug spending while promoting access and equitable care.

One, punish abusive pricing of patented medicines by creating a new bureau. Create a new bureau to set price ceilings for patented medicines. Give that bureau the resources and teeth to keep prices low, and empower that bureau to issue compulsory licenses when companies price patented medicines unreasonably. The new bureau should be able to cut annual drug spending by at least $100 billion.

Two, use negotiating power and open tendering processes to secure low prices on a defined set of essential medicines as per international guidance. Negotiating power can help to ensure equitable access to needed medicines, including off-patent or generic medicines.

Three, use existing legislation, and additional political will, to discipline the companies currently bloated by high medicine prices that illegally market products.

There is a need for urgent action. Americans are getting ripped off by more than $100 billion per year, and this money in the wrong hands is used to illegally market medicines that kill Americans.

Thank you.

[The prepared statement of Dr. Persaud follows:]

PREPARED STATEMENT OF NAV PERSAUD

Canada Regulates the Price of Patented Medicines and Pays Less for the Same Medicines

In Canada, per capita drug spending is $879 versus over $1,229 in the United States.[1] Per capita drug spending is about 40 percent higher in the United States largely because of the regulation of patented drug prices by the Canadian Patented Medicine Prices Review Board.

Posted prices for patented medicines are approximately 3 times lower in Canada.[2] The Patented Medicines Prices Review Board is slated, in July, to drop the United States from its list of comparator countries used to set "price ceilings", because prices are shockingly high in the United States compared with other high-income countries including the United Kingdom.[3]

The marketing of a raft of patented medicines during the 1990's boosted per capita drug spending more in the United States.[4] The large rise in drug spending during the 1990's was partly due to patented opioid products such as OxyContin that was illegally marketed by Purdue Pharma on the lie that these medicines were safer than less expensive alternatives.[5] Pharmaceutical companies continue to profit from the opioid crisis that killed approximately 80,000 Americans in the 12 month period ending in May 2020.[6]

Change is Possible With Political Will

Pressure and lobbying by the pharmaceutical companies (and private insurers) have undermined reforms in both Canada and the United States. Multiple government reports over decades have recommended including medicines in Canada's pub-

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[1] *https://data.oecd.org/healthres/pharmaceutical-spending.htm*.

[2] *https://www.canada.ca/en/patented-medicine-prices-review/services/reports-studies/annual-report-2018.html*.

[3] *https://www.canada.ca/en/patented-medicine-prices-review/services/legislation/about-guidelines/guidelines.html*.

[4] *https://www.commonwealthfund.org/sites/default/files/documents/-media-files-publications-issue-brief-2017-oct-sarnak-paying-for-rx-ib-v2.pdf*.

[5] *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2622774/*.

[6] *https://www.cdc.gov/media/releases/2020/p1218-overdose-deaths-covid-19.html*.

lic single-payer system to improve fair access and to save billions each year.[7] But this has not happened, so we continue to pay higher prices than comparable countries such as New Zealand and Australia and inequities persist. America is a superpower that has not shown its strength in standing up to pharmaceutical companies that rip off Americans, as proven by the price differences for patented medicines across our border.

My colleagues and I have conducted a randomized controlled trial of distributing essential medicines, as per international guidance from the World Health Organization, to people who report not being able to afford them. We found improvements in the control of blood pressure and diabetes, fewer missed medical appointments, and total healthcare savings that averaged more than a thousand dollars per patient per year.[8] The biggest benefit was in the ability to "make ends meet" or afford basic necessities such as rent and food: only 29 percent in the usual access or control group could make ends meet, but 86 percent of those who did not have to pay out-of-pocket for life-saving medicines could afford necessities. A farmer in our study, for example, was better able to grow food when he had asthma puffers.

Could public funding for a list of essential medicines work in the United States? It already is working at the United State's Veteran's Administration. Since its creation in 1997, the VA's national formulary has led to improvements in care and its negotiating power has led to impressive reductions in prices.[9] The VA's approach of creating a rational list of medicines and then using proven methods to negotiate prices accords with international guidance. It's a model that could be adapted to an even larger scale in the United States.

Three Ways America—The Superpower—Can Lower Drug Prices

There are three key elements of government action to reduce drug spending while promoting access and equitable care:

(1) Punish abusive pricing of patented medicines by creating a new Bureau. Create a new Bureau to set price ceilings for patented medicines,[10] give that Bureau the resources and teeth to keep prices low, and empower that Bureau to issue compulsory licenses when companies price patented medicines unreasonably.[11] The new Bureau should be able to cut annual drug spending by at least $100 billion.

(2) Use negotiating power and open tendering processes to secure low prices on a defined set of essential medicines as per international guidance.[12] Negotiating power can help to ensure equitable access to needed medicines including off-patent or generic medicines.

(3) Use existing legislation, and additional political will, to discipline the companies currently bloated by high medicine prices that illegally market products. There is a need for urgent action—Americans are getting ripped off by more than $100 billion each year and, in the wrong hands, this money is used to illegally market medicines in ways that kill Americans.

(1) Punish abusive pricing of patented medicines.

The Canadian Patented Medicine Prices Review Board was created in 1987 through an amendment of the Patent Act. The Patented Medicine Prices Review Board sets a "price ceiling" for patented products based in part on the prices paid in comparator countries. Companies forgo revenues from excessive pricing. The Patented Medicine Prices Review Board is revising its guidelines for setting price ceilings including the list of comparator countries and plans to stop using the United States (as well as Switzerland) in its list of comparator countries.

The United States Federal Government can create a new Bureau empowered to fine companies that sell patented products at excessive prices. This Bureau could define abusive pricing based on comparator countries that currently pay lower prices for patented medicines including Canada and the United Kingdom. Since the purpose of medicines is to promote health and save lives (as opposed to supporting a

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[7] *https://www.canada.ca/en/health-canada/corporate/about-health-canada/public-engagement/external-advisory-bodies/implementation-national-pharmacare.html*.

[8] *https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2752366&cleanmeds.ca*.

[9] *https://www.pbm.va.gov/nationalformulary.asp*.

[10] *http://pmprb-cepmb.gc.ca/home*.

[11] *https://www.healthaffairs.org/doi/10.1377/hlthaff.2015.1120*.

[12] *https://www.who.int/medicines/technical-briefing/tbs/ndp-rdg-prs/en/*.

specific industry or "the economy"), prices that prevent people from accessing needed medicines should prompt action.

Patented medicine prices are approximately three times higher in the United States compared with Canada (Average Foreign-to-Canadian Price Ratios was 3.36 in 2017 for patented products for the United States; for comparison it was 1.08 for generic medicines for the United States and 0.94 for patented medicines in the United Kingdom in 2017).[13] If per capita pharmaceutical spending in the United States equalled that in Canada, there would be savings of over $100 billion per year in the United States and this would represent more than 30 percent of drug spending. The budget of the Canadian Patented Medicine Prices Review Board is approximately $15 million annually. The new Bureau in the United States should be adequately funded and insulated from political influence and lobbying so it can take on large multinational pharmaceutical companies.

The new Bureau should be empowered to issue compulsory licenses for patented products sold at unreasonable prices. This power will reassure Americans that they will not be priced out of life-saving treatments and also ensure that patentees respect the Bureau.

(2) Use negotiating power and open tendering processes to secure low prices on a defined set of essential medicines as per international guidance.[14] The World Health Organization recommends that countries create an essential medicines list that includes the medicines people need. Essential medicines meet the priority needs of a population. Twenty-one high-income countries, including Portugal and Sweden, have registered essential medicines lists with the World Health Organization. Essential medicines lists typically include around 300 medicines that include treatments for cardiovascular disease, cancer, infectious diseases, respiratory diseases, joint conditions, mental health conditions and other conditions.[15] There is a procedure for adding medicines to the list and a committee usually reviews relevant evidence before making a recommendation or decision about whether a medicine should be added. My colleagues and I have surveyed 127 national essential medicines lists and we have created a data base of lists in collaboration with the World Health Organization and it is available at: *essentialmeds.org*.

A national essential medicines list is one important component of national medicines policies, and the list should be used in conjunction with other policies to ensure access and appropriate use of medicines while controlling costs.[16] Transparency is vital to procurement processes to ensure all potential medicine suppliers are treated fairly and to maintain confidence in procurement processes. Secretive deals between manufacturers and purchasers should be avoided regardless of what "special" considerations might be offered by companies in exchange for secrecy. After a list of needed medicines is established, open tendering processes should be used to secure the best prices for high-quality medicines. While the main way to curb drug spending is to lower prices, a national essential medicines list can also support rational medicine selection, for example, toward biosimilar medicines.[17]

Medicines are excluded from Canada's publicly funded single-payer healthcare system. The Canadian Parliamentary Budget Office has estimated that including medicines in our single-payer publicly funded healthcare system would save approximately $4.2 billion while improving access.[18] We know from experiences in the province of Quebec that the answer to excessive drug costs is not expanding or mandating private insurance plans. This has predictably fuelled an increase in drug spending with minimal improvements in access and no measured improvement in health (8.8 percent cost-related non-adherence in Quebec versus 10.7 percent for Canada and 6 percent in comparator countries).[19] Some are paying into private insurance plans that they do not access due to the deductibles. While Canada is doing better than the United States and reigning in the prices of patented products by regulating price ceilings, Canada spends more on drugs per person than comparable high-income countries such as the United Kingdom, Australia and Sweden. Although essential health care services are included in our single-payer publicly funded health care system, medications are excluded and instead covered by a loose

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[13] *https://www.pmprb-cepmb.gc.ca/CMFiles/Publications/Annual%20Reports/2018/2017-Annual-Report-Final-EN.pdf*.
[14] *https://www.who.int/medicines/technical-briefing/tbs/ndp-rdg-prs/en/*.
[15] *https://www.who.int/bulletin/volumes/97/6/18-222448/en/*.
[16] *https://www.who.int/medicines/technical-briefing/tbs/ndp-rdg-prs/en/*.
[17] *http://www.pmprb-cepmb.gc.ca/view.asp?ccid=1456*.
[18] *https://www.pbo-dpb.gc.ca/web/default/files/Documents/Reports/2017/Pharmacare/Pharmacare-EN-2017-11-07.pdf*.
[19] *https://www.cmaj.ca/content/189/40/E1259*.

patch work of private and public plans that leaves out millions of Canadians. Private spending represents the majority of total drug spending in Canada and private employer-based drug insurance plans welcome high drug prices because private insurance companies take a percentage of each claim. While Canadians pay less, in general, for patented products compared with Americans, we pay similar or higher prices for generic products compared with Americans and those in most other high-income countries. Attempts to reduce generic prices have largely failed. When, generic companies were faced with the prospect of an open tender process in Canada in 2017 and 2018, companies that should be competing with each other came together and offered "rebates" worth at least $6.5 billion to provincial governments purchasing medicines for social assistance recipients and, in exchange, provincial governments agreed not to implement open tendering processes. The Canadian Competition Bureau studied the generic pharmaceutical sector in 2007 and 2008 and found that competition was not lowering prices as expected in Canada, but these reports are largely ignored and Canadians continue to overpay for generic medicines. [20]

While some get rich, others die. Cost-related non-adherence to medicines—not taking pills as instructed due to the cost—is more common in Canada (8 percent) and the United States (17 percent) than in comparable high-income countries where it is typically below 5 percent. [21] The Centers for Disease Control and Prevention estimated that all-cause mortality was 15 percent to 22 percent higher among Americans with chronic diseases such as diabetes who cannot afford their medicines compared with those who could afford them. [22] Drug pricing is a life and death issue.

The distribution of the burden is inequitable. Medicine access is a highly racialized issue in both Canada and the United States. Taxi drivers, factory workers and food servers are among the Canadians who pay taxes that support the private drug plans—that enjoy public subsidies—and that exclude many "blue collar" workers with dark skin. Part of the legacy of enslaving Black people in North America is inequitable access to health care including to life-saving medicines, and opposition to ensuring access for everyone is rooted in racism. Downloading medications costs into people's pockets means that those who face discrimination in the workplace, including women, are harmed twice, first by the pay gap and then at the pharmacy.

We have studied the effects of the free distribution of essential medicines and found health improvements and substantial improvements in financial well-being: CLEANmeds.ca.

https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2752366

(3) Pursue and discipline the bloated pharmaceutical companies created by bloated drug prices.

The high prices Americans pay for patented medicines help make pharmaceutical companies so big and powerful that they openly engage in illegal marketing, as they can easily shrug off billion-dollar fines as the cost of doing business. Other companies watched Purdue Pharma almost literally get away with murder in creating the opioid crisis that has killed more than 500,000 Americans over more than twenty years. [23] Purdue invested hundreds of millions of dollars in spreading lies about long-acting opioid products and it was rewarded with billions in profits. Other companies saw how Purdue profited from its illegal conduct, despite tiny penalties, and decided to join in and share the spoils. This is just one example of high prices for patented medicines fuelling illegal marketing. Billion-dollar fines have been paid by GlaxoSmithKlein, Pfizer and Eli Lilly for illegal marketing practices. Tens of billions of dollars are spent on advertising and marketing of pharmaceutical products in the United States each year, and this marketing is fuelled by the high prices Americans pay for patented medicines.

Most inappropriate marketing practices violate existing laws in most countries including the United States where it is illegal to make false claims about pharmaceutical products. But authorities apparently often lack the will to pursue and prosecute offenders. This lack of willingness to hold pharmaceutical companies to account is rooted in concerns about harming an industry that plays an important societal role, undue influence of pharmaceutical companies and private insurers over authorities they lobby, and fear of investing resources in an investigation or prosecution that will fail to secure a conviction. Authorities often assume a meek pos-

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[20] *https://www.competitionbureau.gc.ca/eic/site/cb-bc.nsf/eng/03026.html*.
[21] *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5293866/*.
[22] *https://www.cdc.gov/pcd/issues/2020/20-0244.htm*.
[23] *https://www.cdc.gov/drugoverdose/epidemic/index.html*.

ture and seek voluntary undertakings and settlements with pharmaceutical companies that are "too big to jail".

In concert with efforts described above to limit the resources companies have to fuel illegal marketing campaigns, authorities must also promptly discipline companies that break the law. The opioid crisis shows that delays in holding companies to account can cost, not just $100 billion dollars per year, but also hundreds of thousands of lives.

Acknowledgements

I thank Danielle Martin, Marc-André Gagnon, Joel Lexchin and Matthew Herder for helpful comments. I thank the staff of the Patented Medicine Prices Review Board including Douglas Clark, Elena Lungu and Nevzeta Bosnic for a helpful meeting. I thank Lorenzo Moja of the Department of Essential Medicines and Health Products at the World Health Organization for a helpful discussion. The CLEAN Meds trial was funded by the Canadian Institutes of Health Research, the Ontario SPOR Support Unit, the St Michael's Hospital Foundation and the MAP Centre for Urban Health Solutions. I receive salary support through the Canada Research Chairs program, the University of Toronto Department of Family and Community Medicine and the Department of Family and Community Medicine at St Michael's Hospital in Unity Health Toronto. Of course, this testimony reflects my views and I am responsible for the content.

The CHAIRMAN. Thank you very much, Dr. Persaud.

Next we have Ms. Elia Spates, who lives in Derby, Vermont, who was diagnosed with Type 1 diabetes when she was 18. Her struggles to manage the disease and the associated costs have transformed her into an advocate for lower drug prices and better health care.

Ms. Spates, thanks so much for being with us.

STATEMENT OF ELIA SPATES, DERBY, VT

Ms. SPATES. Thank you. My name is Elia Spates. I was diagnosed with Type 1 diabetes 23 years ago, and quickly my parents and I got a crash course in the world of insurance and the serious expense of diabetes.

The insulin that I take now costs over $2,000 out of pocket per month. The rise that I have seen in this price in the last 23 years is astronomical. In fact, from 2002 to 2013 the cost of insulin tripled. When you pay over $800 per month for an individual in insurance premiums, and pay an additional $2,000 per month until your deductible is met, your family starts to feel a financial pinch. The only way you see to cut back on the spending is to cut back on the insulin. Before you know it, your diabetes is out of control, your blood sugars swing dramatically, seizures happen, and you are even found unresponsive. It's time to treat the disease seriously. The financial side of diabetes is as much or more a burden as the disease itself.

I am certainly not the only diabetic out there who has rationed insulin to help fend off a steadily accumulating debt. In fact, 45 percent of diabetics at one time or another will compromise their care to cut their costs. However, what is happening is that those who are not as fortunate as I land themselves in the hospital, in traumatic circumstances, and may even die. Seven-and-a-half million Americans rely on insulin; 1.5 million of those are Type 1 diabetics.

A few years ago my doctor suggested going to Canada. I live just four miles from the Canadian border, so this was logical, until you

give it just one ounce of thought. I pay over $10,000 a year in insurance premiums so that I can go buy my insulin in another country and it doesn't count toward my deductible? It is completely asinine to think that I would go to another country to buy inexpensive medication and yet pay for a health care plan in my own country that is only compounding my diabetic problems.

Twice I have arrived at the pharmacy to pick up medication that had been prescribed by my doctor, and both times I was told that my insurance company was no longer going to cover that brand without prior authorization. However, they were happy to cover another suggested brand that was biosimilar but not bioequivalent. With this medication it had taken me over a year to get it approved by the insurance company, and I was finally having success using it, and now it was being disallowed?

It is infuriating to know that in one fell swoop your perfect combination can be undone by the companies that produce the medication and the pharmacy benefits managers who market it to the insurance companies who now give it preferred status on their health care formularies.

Just six months later an insulin I had been on for over four years became no longer an option. Once again, it needed a prior authorization, but there was a similar medication that I could have. Now, had this been the difference in brand name to generic, I could have understood. However, this was from one name brand insulin to another. And, in fact, it was $5 more out of pocket for me. It doesn't take a genius to figure out that this was happening because of how the money passes between the hands of the producers of the insulin, the PBMs, and the insurance companies.

I appreciate being a part of a good business deal when I see one, and as a woman in business I fully understand supply and demand. I was raised in the humanitarian principles of achieving success. Doing things ethically and watching the bottom line to make a profit is essential. It is, however, unethical, unscrupulous, and completely wrong to gouge people, particularly so at the expense of their health.

To think that we are outpricing our own citizens and virtually holding out of reach scientific marvels to those who need it is an embarrassment.

We have seen a 300 percent rise in our cost of insulin in just a matter of years, yet in the same amount of time Canada has seen virtually no rise in cost at all. Three major producers of insulin have all had the same price hikes over that time. It is interesting that pharmaceutical companies provide amazing rebates on these products, yet the bulk of the rebates are cashed in by the PBMs and not the consumers. This practice provides preferred status on the insurance company formularies for the pharmaceutical companies, hardly an arms-length transaction. Rebates alone have risen from 2 percent in 2013 to 56 percent in 2018.

One hundred years after the invention of insulin there are, of course, generic insulins out there which have been formulated. My understanding is that they sit on a dark and dusty shelf in the back of the room titled "Pay for Delay." This is that devious little plan in which Big Pharma companies pay off the generic companies to delay the release of their product. Big pharma gets to keep the

largest part of their sales, the generic company makes even more than if they put it out on the market, and I continue to pay top dollar. Any middle school student working their vocabulary list can tell you that is a perfect description for collusion.

There are days that it is almost impossible to contemplate the unethical, immoral American healthcare and pharmaceutical system that has been created out of greed. I have to believe that those who perpetuate it probably haven't been burned by it. It is more than likely that they don't feel the initial pressure of the extreme insurance premiums because they don't have to pay them. Those participating probably don't drop thousands in deductibles either. And I am certain that they aren't showing up at the pharmacy counter to find out that the medication that had finally put them in good health is now not allowed because their insurance company has a different option for them, one not discussed with them or their doctor. Those perpetuating this travesty are probably also benefiting from some of Big Pharma's slice of the financial pie.

When we ask the question "Why does the U.S. pay the highest prices in the world for prescription drugs?", the answer should really be given by our elementary school children because it is that simple. It is simply because of greed. We are fooling ourselves and the citizens of this Country by behaving like we don't know why we pay more. We all know. The question just becomes who is going to fix it? Who is going to put themselves out there? Who is going to take the high road and not the handout? Who is going to say lives are at stake here and for once put yourself in those shoes and do what you would want done for you, your parents, your wife, your brother, your son, your daughter.

This is a bipartisan issue. Make it one. Do what's right, do it quickly, and then sleep well at night knowing you chose to help the people who, by voting, entrusted you with their well-being.

Thank you.

[The prepared statement of Ms. Spates follows:]

PREPARED STATEMENT OF ELIA SPATES

My name is Elia Spates. I was diagnosed with type 1 diabetes 23 years ago and quickly my parents and I got a crash course in the world of insurance and the serious expense of diabetes.

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I am certainly not the only diabetic out there who has rationed insulin to help fend off a steadily accumulating debt. In fact 45 percent of diabetics at one time or another will compromise their care to cut costs. However, what is happening is that those who are not as fortunate as I land themselves in the hospital, in traumatic circumstances, and maybe even die. 7.5 million Americans rely on insulin and 1.5 million of those are type 1 diabetics.

A few years ago my doctor suggested going to Canada. I live just 4 miles from the Canadian border so this was logical . . . until you give it just an ounce of thought. I pay over $10,000 a year in insurance premiums, so that I can go buy my insulin in another country and it doesn't count toward my deductible?! It is completely asinine to think I would go to another country to buy inexpensive medication

and yet pay for a health care plan in my own country that is only compounding my diabetic problems.

Twice I have arrived at the pharmacy to pick up medication that had been prescribed by my doctor and both times I was told that my insurance company was no longer going to cover 'that brand' without prior authorization, however they were happy to cover another suggested brand that was biosimilar NOT bioequivalent. With this first medication it had taken me over a year to get it approved by the insurance company and I was finally having success using it and now it was being disallowed?

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Just six months later an insulin I had been on for over 4 years became no longer an option. Once again it needed a prior authorization, BUT, there was a similar medication I could have. Now had this been the difference in brand name to generic I could perhaps have understood. HOWEVER, this was from one name brand insulin to another and in fact it was now $5 more out of pocket for me. It doesn't take a genius to figure out that this was happening because of how the money passes between the hands of the producers of the insulin, the PBM's and the insurance companies.

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When we ask the question "Why Does the U.S. Pay the Highest Prices in the World for Prescription Drugs?" the answer should really be given by our elementary school children because it is that simple. It is simply because of greed. We are fooling ourselves and the citizens of this country by behaving like we don't know why we pay more. We all know, the question just becomes who is going to fix it? Who is going to put themselves out there? Who is going to take the high road and not the handout? Who is going to say, "Lives are at stake here and for once put yourself in those shoes and do what you would want done for you, your parents, your wife, your brother, your son, your daughter.

This is a bipartisan issue. Make it one. Do what's right, do it quickly and then sleep well at night knowing you chose to help the people, who by voting, entrusted you with their well being.

The CHAIRMAN. Ms. Spates, thank you very much for your remarks.

Our last panelist is Mr. Alex Brill, who is a Resident Fellow with the American Enterprise Institute, the public policy think tank in Washington, DC. Previously he served as Chief Economist and Policy Director to the House Committee on Ways and Means and on the staff of the White House Council of Economic Advisors. Mr. Brill has an MA in Mathematical Finance from Boston University and a BA in Economics from Tufts University.

Mr. Brill, thank you very much for being with us.

STATEMENT OF ALEX BRILL, RESIDENT FELLOW, AEI, WASHINGTON, DC

Mr. BRILL. Thank you very much, Chairman Sanders. I must confess, the power just went out here in my office, and I hope this connection via my cell phone works.

I appreciate the opportunity to appear before the Committee to testify on this important topic. As you mentioned, I'm a Resident Fellow with the American Enterprise Institute. My written testimony has been submitted to the Committee for the record. It offers three broad observations and a series of policy recommendations which I'll briefly summarize.

First, perhaps predictably, is the importance of innovation in the pharmaceutical sector. Pharmaceutical innovation plays a critical role in improving health and well-being, and never has that been more important and more evident than today as multiple, highly effective coronavirus vaccines have been brought to the market in short order. These vaccines are the result not only of work that began after March 2020 but of decades of research funded by public and private investment and, of course, extraordinary support by the FDA.

Policies to curb U.S. drug costs must ensure adequate reward for future innovation. This is not an endorsement of the status quo but a recognition, rather, of the importance of new medicines.

Second, with respect to drug spending, U.S. prescription drug spending was $368 billion in 2019, nearly 10 percent of national health expenditures. It's important, however, to note the drivers of this cost. Biologics are driving much of the increase in national drug spending. In inflation-adjusted per capita terms, biologic drug spending increased from less than $300 to over $400 per capita from the period 2014 to 2018, while traditional small-molecule drugs, pills, fell on an inflation-adjusted per capita basis during that same time.

Notably, out-of-pocket spending, the patient's cost, as a share of total drug spending has declined significantly over the last few decades, from roughly 28 percent to roughly 14 percent in 2019. Out-of-pocket costs for those with the highest expenses who are low-and moderate-income actually fell, and out-of-pocket costs for those patients with the highest costs rose for higher-income individuals.

Of course, however, these broad trends are important to recognize, but they can also mask high financial burdens experienced by some patients, as we've heard already this morning.

Third, the importance of balance. The success of the U.S. pharmaceutical market is the result of a dual mandate embodied in landmark 1984 legislation commonly known as Hatch-Waxman. Hatch-Waxman legislation sought to both allow meaningful rewards for new innovative drugs and to encourage a robust generic drug industry. Today, we have the pharmaceutical innovation that I referenced a moment ago, and a generic industry that fills 90 percent of all retail prescriptions yet represents just 20 percent of overall drug spending. The average co-pay for generics is just $7.

Our peer nations are not as successful. Across the OECD, just over half of all prescriptions are filled with generic medicines. There are, however, important opportunities to further foster competition and realize additional drug savings in the U.S. pharmaceutical market. My written testimony notes six areas where I believe bipartisan cooperation can ensure more timely entry of generics or biosimilars without discouraging the risk-taking innovation of medicines. Let me briefly highlight just three.

First, biosimilars. Biosimilars have already yielded roughly $37 billion in savings to the U.S. health care system, but more can be done. One approach would be to align the incentives of prescribers with payers and patients. This could be achieved with a proposal considered by the Finance Committee for ASP+8 for biosimilars or the demonstration operated for Medicare Part B.

Second, the importance of complex generic medicines and their approval here in the United States. Congress should ensure that the FDA has the incentives and the resources to promptly review and approve complex generic applications. In some recent work, I have estimated that seven such products were not available here but are available in Canada or Europe, and bringing them to the United States could save $1.3 billion a year annually.

Finally, patent thickets, as noted earlier. Innovative drug companies are building patent thickets around lucrative products by obtaining myriad overlapping patents, many of those patents submitted after the launch of the initial product. To deter generic challenges or biosimilar challenges is the pure intent of these efforts. Without policy reform, these tactics will become the playbook for all innovator companies in the future.

Thank you for the opportunity to testify, and I look forward to your questions.

[The prepared statement of Mr. Brill follows:]

PREPARED STATEMENT OF ALEX BRILL

Chairman Sanders, Ranking Member Collins, and Members of the Subcommittee.

Thank you for the opportunity to testify on this important topic. My name is Alex Brill, and I am a resident fellow at the American Enterprise Institute, a public policy think tank here in Washington, DC. The views and opinions I offer today are mine alone and do not represent those of my employer or necessarily those of my colleagues at AEI.

In my testimony today, I will make three broad points:

1. The United States is a large market that offers substantial rewards to successful innovators. This structure encourages the development of valuable medicines.

2. Lowering the cost of medicines to the U.S. healthcare system can be achieved by promoting robust competition, but policymakers should be careful to ensure that adequate incentives remain in place to bring new products to market.

3. There are multiple existing barriers to robust pharmaceutical competition, and lower drug prices can be achieved by removing these barriers.

I would like to begin with a brief observation about the current pandemic, economic recession, and ongoing recovery.

The coronavirus pandemic, which hit the U.S. one year ago, has resulted in more than 540,000 confirmed deaths, more than 130 million probable and confirmed cases,[1] and tremendous economic upheaval and harm. The U.S. suffered a dramatic economic contraction in the second quarter of 2020. Though the economy has recovered significantly, total employment is down by more than 9 million compared to a year ago. Employment in the leisure and hospitality sector is 20 percent lower than it was a year ago; nearly 3.5 million jobs in that sector were lost.

The first coronavirus vaccine was deployed in December 2020, less than a year after the pandemic began. Today, three approved COVID–19 vaccines are being distributed in the U.S., and these products are quite literally saving not only our economy but our country. The vaccination rate is now near 2.5 million doses per day, and daily new cases are down nearly 80 percent from the peak.

The biopharmaceutical industry, including talent and capital from around the globe, has accomplished a stunning feat, and I look forward to receiving my vaccine as soon as possible. We should be thankful not only to those involved in the development and deployment of the vaccines but to all who have worked on vaccine development, including those whose projects did not yield successful products. Clearly, the ability to bring to market these highly effective vaccines is not only the result of work that began in 2020 but also the result of decades of research supported by both public and private investment.

1. U.S. Drug Spending Overview

To set the stage for policy recommendations to address drug costs in the United States, it is worthwhile to put in context the size and scale of drug spending at present. In 2019, the most recent year for which government statistics are available, U.S. prescription drug expenditures were $367.9 billion, 9.7 percent of national health expenditures, and $1,128 per capita. Growth in 2019 expenditures (5.7 percent) was driven by an increase in volume, not prices (CMS, 2020). An increasing share of this burden is borne by health insurers, though of course their higher costs are reflected in higher premiums. Notably, out-of-pocket spending on retail prescription drugs as a share of total prescription drug spending has declined significantly over the last two decades, from 28.5 percent in 2000 to 14.5 percent in 2019 (CMS, 2020).

There are, of course, important exceptions to these aggregate trends for individual patients who have experienced significant hardship. However, on average, out-of-pocket spending for households with the highest overall healthcare costs (those in the 95th percentile) declined for households below the Federal poverty line (FPL) and for households below 200 percent of the FPL from 2006 to 2017 (Glied and Zhu, 2020). For higher-income households with very high out-of-pocket costs, those costs have increased (Ibid.). Among those with the highest out-of-pocket medical costs across all income groups, average out-of-pocket drug costs have declined from near $2,300 in 2006 to $1,000 in 2017 (Ibid.). Among Medicare Part D beneficiaries, 90 percent had out-of-pocket pharmacy costs less than $500 (IQVIA, 2020a).

It is important to note that biologic drug spending is the driver behind overall rising drug spending in the United States in recent years. Biologics, which are highly complex drugs made from living cells, are among the most expensive pharmaceutical products. In inflation-adjusted terms, biologic drug spending increased from $291 to $435 per capita from 2014 to 2018 while small-molecule drug spending fell from $689 to $610 per capita during this period (IQVIA, 2019).

2. Balancing Innovation and Competition

The U.S. pharmaceutical market, with a relatively high level of prescription drug spending overall as well as a high generic utilization rate, reflects the outcome of

[1] This estimate is based on 28.9 million confirmed cases and a CDC estimate (CDC, 2021) that approximately 1 in 4.6 total COVID–19 infections were reported.

two complementary policy objectives: a system that both offers financial rewards to innovator drug companies who launch new drugs and encourages a robust competitive marketplace for generic drug manufacturers to sell at dramatic price discounts. This is the result of a dual mandate embodied in landmark legislation widely known as Hatch-Waxman, which was intended to foster both innovation and competition in the prescription drug industry. Broadly speaking, this system has worked well for traditional small-molecule drugs.

According to research by IQVIA published by the Association for Accessible Medicines, 90 percent of retail drug prescriptions are filled with a generic, and generics represent 20 percent of total prescription drug spending. The average generic prescription copay is approximately $7, and 92 percent of all generic prescriptions are filled for $20 or less (AAM, 2020). The utilization of generic drugs in the United States far exceeds most peer nations. According to the OECD, generic drugs are, on average, just 52 percent of the total pharmaceutical market in 2017 by volume. Generic utilization varies considerably across the OECD. In Canada, generics are reported to be 76 percent, by volume but in Italy only 25 percent (OECD, 2019).

Inherent in the broad policy framework in the United States that incentivizes both critical new pharmaceutical innovation and a robust generic market are several distinct forms of drug competition.

Brand-Brand Competition. Within a drug class, brand drugs can compete with other brand drugs that treat the same condition or disease, and this can result in lower prices for all competing products. In practice, the mechanism by which this form of competition yields price discounts is through rebates—that is, discounts paid to pharmacy benefit managers—not through reductions in list prices.

Generic-Brand Competition. As chemical copies of their brand counterparts, generics provide direct competition to brands. While research has shown that brand prices do not typically fall when facing generic competition, the first generic competitor is, on average, 30 percent lower than the brand price (Conrad and Lutter, 2019).

Generic-Generic Competition. The largest price effect arises when multiple generics for a product are on the market. Conrad and Lutter (2019) find that the generic price discount rises from 30 percent with one generic on the market to 55 percent with three generics and 85 percent with five generics.

Biosimilar Competition. A fourth type of pharmaceutical competition, a hybrid of the three above, is emerging in the U.S. biosimilars market. Since the passage and enactment of the Biologics Price Competition and Innovation Act (BPCIA), part of the Affordable Care Act, an additional regulatory pathway has existed to permit competition for biologics. This abbreviated pathway allows for the approval of what are known as biosimilars, more affordable versions of brand biologic drugs. While this market was somewhat slow to develop at first, today there are 29 biosimilars approved by the Food and Drug Administration (FDA) and 18 biosimilars available on the U.S. market. One favorable but unexpected pricing dynamic in this nascent market is that when a biosimilar competes with a reference biologic, we see a net price decline of the innovator product (Brill and Ippolito, 2019).

3. Promoting Drug Competition and Lowering Prices

In debates about U.S. drug spending, two competing policy frameworks exist. In the first, government controls are necessary to set drug prices because market failures are causing "wrong" prices to be paid by public programs, commercial insurance, and individuals. In the second, policymakers observe imperfections in the prescription drug market (some of which are policy-induced) and seek to adopt reforms to improve and strengthen the existing framework established by Hatch-Waxman and the BPCIA—that is, adequate incentives for innovation in a costly and risky industry combined with appropriate incentives and relatively little friction for generics and biosimilars to ensure robust competition.

Having spent the last decade studying competition in the U.S. pharmaceutical market, I can tell you that several incremental changes to our existing framework could make drug competition more robust. These changes could yield more small-molecule generics, more complex generics, more biosimilars, and more of the savings that competition induces.

Ways That Drug Competition is Stymied in the U.S.

There are a variety of reasons why there is room for improvement in the competitiveness of the U.S. pharmaceutical market, some systemic and some due to strategies of drug manufacturers to create excessive delays in the market entry of competitors.

Complex Generics. On delays arising in the system, consider the situation around complex generics. These are products with a complex molecular base, route of delivery, formulation, dosage form, or approval requirement. In Europe and Canada, some complex generics have already been approved and launched while applications for these same products are delayed at the FDA. By my estimation, generic competition for seven complex generics approved in Europe and/or Canada but not in the United States would yield annual U.S. savings of between $600 million and $1.7 billion, with a median savings estimate of $1.3 billion.

When Congress reauthorizes the Generic Drug User Fee Amendments (GDUFA), it is my hope that the FDA commits to further prioritize the approval of complex generics, with objectives focused on outcomes rather than process metrics. The delay in the approval of some complex generics has already attracted bipartisan interest and concern among members of the House Energy and Commerce Committee in a letter to the FDA (Energy and Commerce Committee, 2020). Current acting FDA Administrator Janet Woodcock has also acknowledged complex generics' "outsized potential to increase patient access and lower drug spending" (Woodcock, 2019).

On strategies intended to delay generic entry, there are various tactics that brand drug manufacturers employ to limit or delay the availability of lower-cost drugs. These include product hopping, misuse of "orphan" drug exclusivity and citizen petitions, patent thickets, and other tactics that effectively suppress competition. (Below, I describe four of these tactics.) There is evidence that the average period a brand drug is on the market before generic entry increased by more than two years between 1995 and 2014 (Grabowski et al., 2016). From my own work, I estimate that if generic entry were to be accelerated to pre-1995 rates, the U.S. healthcare system would save nearly $32 billion.

Product Hopping. Product hopping describes the established brand strategy of making an inconsequential change to a drug and moving patients to this version before the original faces competition. The Alzheimer's drug Namenda IR represents a notorious example of product hopping. In 2013, before Namenda IR went generic, the manufacturer launched an extended-release version that could be taken once a day instead of twice a day. In 2014, the manufacturer removed Namenda IR from the market entirely. This is what is called a "hard switch." In a "soft switch," a manufacturer will leave the original product on the market but work to move patients to the slightly altered product, even at times intentionally undermining confidence in their original product. I have estimated that five instances of specific product hops cost the U.S. healthcare system $4.7 billion annually.

Misuse of Orphan Drug Exclusivity. Orphan drugs, defined as drugs treating conditions that fewer than 200,000 people in the United States suffer from, are eligible for six extra months of exclusivity from the FDA. This creates an incentive for drug manufacturers to develop products to treat rare diseases. But brand manufacturers have been obtaining orphan drug designations for products that treat much larger populations. Daniel et al. (2016) find that 7 of the 10 bestselling drugs in the world in 2015 were approved by the FDA as orphan drugs.

Misuse of Citizen Petitions. Citizen petitions are an important safety mechanism created to raise concerns with the FDA about a drug whose application is under review. But brand drug manufacturers have taken to using this mechanism, often right before facing generic competition, to delay generic entry while the FDA reviews the petition. A recent study showed that brand manufacturers filed more than 90 percent of petitions and less than 10 percent were eventually granted (Carrier and Shadowen, 2017).

Patent Thickets. Especially pernicious is a tactic known as a patent thicket. Brand manufacturers obtain as many overlapping patents as possible on a single product in order to create an impenetrable web for potential competitors. These patents are frequently broad and weak and often filed after the drug is on the market. Consider the blockbuster drug Humira©—89 percent of AbbVie's nearly 250 patent applications were filed after launch (I-MAK, 2020). While patenting strategies of this drug have attracted the most attention, the policy concern is much broader as these tactics may serve as a future playbook for other drug manufacturers to unduly delay generic entry.

A Word about Biosimilars

As I mentioned earlier, biosimilars represent a relatively new arena of drug competition in the United States, as the regulatory pathway for these products was established in 2010. According to IQVIA (2020b), biosimilar savings in the United States have reached $37 billion through 2019 and could exceed $100 billion through 2024. Despite their enormous cost savings opportunity, biosimilars face hurdles in

realizing their full potential. These hurdles range from lack of education among physicians and patients to contracting practices by originator companies to keep competitors from gaining an edge. Patent thickets, described above, are very problematic for biosimilars because biologics tend to be very lucrative, and originators have learned that they can build these thickets in the United States largely unchecked.

It is worth noting that Europe, which preceded the United States by nearly a decade in the launch of its first biosimilar, has done well in many regards. Many European countries have proactively engaged in education campaigns to familiarize patients and healthcare providers with biosimilars and have shared the savings from biosimilars with patients and providers. But not all European practices should be emulated. Some countries have established price controls or held winner-take-all tenders. These may have negative effects on the long-term sustainability of biosimilars.

Achieving greater uptake of biosimilars in the U.S. market would, in the near term, produce lower average spending on biologic medicines. In the medium and longer-term, policies that facilitate a larger biosimilars market in the U.S. will encourage more biosimilar manufacturers to pursue product launches in the United States. Broadly speaking, a robust biosimilars market would include both multiple competitors to a single reference biologic and more biosimilar entry to compete with smaller-market biologics. The approval of interchangeable biosimilars may also contribute to the realization of additional pharmaceutical cost savings, for biosimilars covered in the pharmacy benefit as opposed to the medical benefit.

To accelerate the adoption of biosimilars, policymakers should consider policies to align the incentives of prescribers with the cost savings objectives of payers, namely Medicare. Existing legislative proposals that could achieve this goal include ASP+8 reimbursement for Part B biosimilars or a demonstration run by the Center for Medicare and Medicaid Innovation that could establish an incentive to prescribers whose patients utilize lower-cost biosimilars. Either approach offers the opportunity to achieve cost savings by incentivizing the utilization of lower-cost biosimilars.

4. Conclusion

Any inquiry into the cost of medicines in the United States should be related closely to a careful review of the quality and quantity of pharmaceutical innovation also underway. As a large and prosperous market, the United States effectively entices significant investment in the private research and development of drugs and publicly funds significant amounts of related research. The United States is also a global leader with respect to its robust generic drug market, a testament to a successful commitment to a competitive marketplace. Nevertheless, opportunities to foster competition and realize additional cost savings do exist.

Congress should protect the intent of existing law but pursue improvements to facilitate more competition, curtail overly long monopolistic periods for brand drugs, and promote the approval of new innovative medicines to compete with existing brand drugs. Finally, biosimilars have shown initial success and cost savings in the U.S. market, and a larger and more robust biosimilars market should be encouraged.

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The CHAIRMAN. Thank you very much, Mr. Brill.

Let me start off the questioning, and let me ask a very simple question. That is that I recall about a year-and-a-half ago I took a trip from Detroit, Michigan into Ontario with a number of folks from the Midwest who were diabetic, and we purchased insulin, the same product made by the same company, for one-tenth of the price, 10 percent of the price.

Somebody jump in, Dr. Kesselheim, Dr. Persaud. Why is it that in Canada, tell us simply, that you can purchase the same exact widely used product for one-tenth the price that it costs in the United States?

Mr. BRILL. Thanks for the question, Senator.

Two reasons. First, patented medicines have their prices regulated in Canada because there's not going to be competition. If you want to pay a reasonable price for patented products, you have to regulate the prices. That's what's done in other high-income countries, not just in Canada.

The CHAIRMAN. Is there any other country—let me interrupt you. I apologize. Is there any other major country on earth that does not, in one way or another, regulate the price of drugs or allow the companies to charge any price they want? Is there any other country, other than the United States, that allows that?

Mr. BRILL. No.

The CHAIRMAN. Okay.

Dr. Kesselheim, did you want to jump in on that?

Dr. KESSELHEIM. Sure. No, there is no other country that does that. We are unique in the world in allowing the pharmaceutical companies to charge whatever price they want. As a result, the only type of—the only intervention in the U.S. market that actually lowers prices is the availability of interchangeable generics which, unfortunately for insulin, we don't have any, and as a result prices have not fallen because there is no pressure, no market pressure, no governmental pressure, no pressure at all on the pharmaceutical companies that sell insulin to lower their prices to the same extent that there is in Canada.

The CHAIRMAN. Let me ask the doctors another question. It is estimated that one out of four Americans cannot afford the prescription drugs their doctors prescribe. What does this mean for the health of the American people? If I'm sick and I go to a doctor, and the doctor writes a script for me, and I can't fill it, what impact does that have on health in the United States?

Dr. KESSELHEIM. I think it has a critically important impact. There are numerous studies showing that the high price of drugs can lead to non-adherence, which is when patients don't fill their prescription or they extend their prescription or use less of the medicine in ways that ultimately are harmful to them. Some studies led by people in our group here at the Division of Pharmacoepidemiology show that when people are prescribed higher-cost medicines instead of equally effective lower-cost medicines, that can lead to worse patient outcomes. So it is truly something that is problematic for patients and something that we can fix.

The CHAIRMAN. Let me ask you this. Dr. Persaud, you may have done a study on this. Tell me what I'm missing here. If I cannot afford my medicine and I get sicker than I should be, and maybe I end up in the emergency room, maybe I end up in the hospital, is it possible, in fact, that we end up spending more on health care because people simply cannot afford the medicine that they need?

Dr. PERSAUD. Yes, Senator. That's exactly what we found in our study. When we provided medicines to people who could not afford them, we realized savings of more than $1,000 per year per patient, and that was due to avoided hospitalizations, avoided emergency room visits. We're talking about life-saving medicines, medicines that we know work, treatments for high blood pressure and diabetes. So when people are able to take their medications, they are healthier.

We also found that people find it easier to make ends meet, to afford their rent and food, healthy housing, healthy foods that people need to be healthy, as well.

The CHAIRMAN. What you are saying is that the high cost of prescription drugs results in people getting sicker than they should and, in fact, ending up costing health care systems more money than we should be expending.

Dr. PERSAUD. Yes. You're paying at least twice, once the higher price for medicines, and second people who land in the hospital with a heart attack or stroke.

The CHAIRMAN. Which could have been prevented.

Dr. PERSAUD. Absolutely preventable.

The CHAIRMAN. Okay.

Senator Collins.

Senator COLLINS. Thank you, Mr. Chairman. Before I begin my questions, I would ask unanimous consent that a statement from Senator Burr be submitted for the record.

The CHAIRMAN. Without objection.

[The information referred to can be found on page 56]

Senator COLLINS. Thank you.

Mr. Brill, you mentioned the role of patent thickets in blocking access to more affordable biosimilars. You also talked about the fact that biologics are very expensive and are consuming an increasing amount of the cost of prescription drugs in this Country. Even though there are several biosimilars for the best-selling drug in the world, Humira, and they've been on the market in the European Union since 2018, American patients must wait another two years for them to be available here due to the manufacturer's aggressive patent thicket strategy of overlapping and late-filed patents.

Another method of fending off biosimilar competition is called a drip-feed strategy, where knowledge broadly disclosed in early patent applications is defined much more narrowly and specifically in subsequent patent applications, and AbbVie is using this strategy for a cancer drug that it has.

How should Congress ensure that we are recognizing innovative science versus rewarding an innovative legal strategy that is simply designed to block more affordable competitors by gaming the patent system?

Mr. BRILL. Thank you, Senator, for your question. The issue of patent thickets and related patenting strategies employed by some innovator companies is, I think—should be very concerning to policymakers. I think we're in the early innings of what will become an evolving set of tools that many innovator drug companies may engage with to protect their assets, and this runs completely counter to the objectives of competition for biosimilars or for other innovative products.

We have these pathways through the FDA to create and foster generic competition, biosimilar competition, and the patent system is getting in the way. I know that you have introduced in the past legislation with Senator Kaine. Senator Cornyn and Senator Blumenthal also have legislation focused on addressing these issues, finding ways to protect core patents and appropriate patents but to block or prevent the ability of innovators to stack patents on top of each other and create undue, unnecessary, excessive monopoly powers for their products.

Senator COLLINS. Thank you. I think this is an area that cries out for reform.

Dr. Kesselheim, the Veterans' Administration has some authority to negotiate favorable pricing and deeper discounts. But we also hear complaints that they have a national formulary, and we get complaints in my state offices from veterans who need drugs that are not available on that formulary. So how do we come up, if we move to broader use of negotiation by the Federal Government, while still ensuring that there is patient choice of medications, that their physicians can still prescribe and they can get reimbursed under the terms of their insurance for the medications that are best suited for them?

Dr. KESSELHEIM. Senator Collins, that's a great question and an important one. I think that the principle that I was outlining is really the principle of evaluating effectiveness of drugs and negotiating on that basis, not necessarily about restricting access to the products but providing coverage to products that are extremely effective and not providing the same level of coverage to products that don't offer additional benefits. That's the model that some states have used, like New York and Massachusetts are starting to employ, to try to negotiate prices better for their Medicaid programs. It just involves evaluating the utility of a drug as compared to standard of care, and then paying for the drug if it offers more but not providing the same level of coverage if it doesn't offer any additional benefits, and those organizations have found substantial success thus far in implementing that kind of a model.

Senator COLLINS. Thank you, Mr. Chairman.

The CHAIRMAN. Thank you, Senator Collins.

Senator Casey.

Senator CASEY. Mr. Chairman, thank you for having this hearing today. I want to commend you for having the hearing, you and the Ranking Member for doing this, because when so many of us go home and talk to our constituents, one of several big bags of rocks on the shoulders of American families is the cost of prescription drugs. We hear it all the time, everyone does, no matter where you're from. And the other bags of rocks on their backs or their shoulders are the cost of child care or higher education or health care generally.

We have an obligation to act, and I've heard it from folks all across Pennsylvania. By way of one quick example, a constituent of mine, Barbara Sissick, she's from Rural Ridge, Pennsylvania, she testified before our committee, an Aging Committee hearing that Senator Collins chaired in 2019. Barbara pays as much as $500 per month for multiple medications to manage bleeding ulcers, high blood pressure, and more.

People like Barbara, so many like her across the Country, expect us to take action. So I've supported, and I know this is true of a number of Senators, legislation to take steps in the right direction, whether it's the legislation to allow Medicare to use its purchasing power to negotiate prescription drug prices, or whether it's legislation like Senator Sanders has to allow for the importation of prescription drugs from countries like Canada that have similar regulations in place to ensure that drugs are safe and effective.

I also have legislation I've authored to expand low-income protection for seniors and people with disabilities to make sure they can afford Medicare premiums and out-of-pocket costs.

With regard to—and I'll direct my question to Dr. Persaud. With regard to Senator Sanders' legislation for drug importation, allowing Americans to purchase drugs from Canada, from countries like Canada that have comparable regulations in place, I'd ask you this simple question, doctor. Can you tell us, give us an answer to the following question: Do you believe that prescription drugs sold in Canada are safe and effective?

Dr. PERSAUD. Thank you, Senator. Yes, they're safe and effective, and they're the type of medicines that America, the superpower, should be able to negotiate reasonable prices for. Canada is a rel-

atively small country, with a population around 37 million, and the United States can implement measures to regulate the prices of medicines and negotiate prices for other medicines. Between Canada and the United States, there's only one superpower, and really it should be Canada hiding behind the United States when it takes on pharmaceutical companies.

Senator CASEY. Doctor, one follow-up to that just in terms of the types of controls in place, the policies in place the Canadian authorities have to make sure the prescription drugs are safe and effective for consumers, if you could just walk through that in summary fashion.

Dr. PERSAUD. Sure. So, first of all, Health Canada regulates every product here. Health Canada has the power to inspect facilities, including overseas facilities, where many medications consumed in Canada are produced. Standards would be similar to countries like the United States, similar to other countries like the United Kingdom and countries in Europe.

Senator CASEY. Doctor, thanks very much.

Thanks, Mr. Chairman.

The CHAIRMAN. Thank you, Senator Casey.

Senator Murkowski.

Senator MURKOWSKI. Thank you, Mr. Chairman. Thank you for this very important hearing.

This is going to be a question to Dr. Kesselheim, and this stems from a story that we had heard from a constituent in Wasilla, not too far north from Fairbanks. They have indicated that they've been paying $633 for a three-month supply of her inhaler. The price of the inhaler increased in January for the third year in a row. And like so many, they just don't get it. Why do we keep seeing these price increases?

Dr. Kesselheim, in your experience with these year-to-year price hikes on prescription drugs, in your view, what's prompting it? Do they usually result from changes or improvements to the drug's efficacy? Because I think if it was going to improve the drug, we can understand why that might be. Or is it because they are resulting from increased manufacturing costs or R&D? What do you tell somebody like this constituent from Wasilla?

Dr. KESSELHEIM. It's a very challenging issue. And, no, it doesn't arise from any of those things. It arises because manufacturers and pharmaceutical companies have investors that they need to maintain their profit margins for, and one of the ways they can do that, if they have an approved product, is by raising the price on that product year after year. Unfortunately, in the case of inhalers, we have a lot of the same issues that we have with insulin where manufacturers are able to get new patents, not on the underlying medicine itself but on the inhaler device, and those patents prevent the FDA from approving interchangeable versions of the product that might lower the prices. And, of course, we also just don't do any negotiation with manufacturers over the prices that they charge for their products.

As a result of all of those things, that gives manufacturers substantial freedom to raise their prices far beyond inflation on a year-over-year basis and leads to problems like you're describing for your constituent.

Senator MURKOWSKI. Do we have any way to determine whether these price hikes are justified? What you just outlined to me, I don't think that's going to be satisfactory to this individual from Wasilla. How can we know whether or not, when you have reformatted the device for the inhaler, that somehow or another increases the efficacy? Is there any way to determine whether these price hikes are justifiable?

Dr. KESSELHEIM. Sure. One of the ways you might do that is you might actually conduct a clinical trial in which you tested your new version against the old version and showed that one was superior. Most pharmaceutical companies don't fund that kind of comparative effectiveness research. Instead, they just rely on marketing to promote the new, improved product.

I would also say that if we did have a publicly funded, independent organization that evaluated the effectiveness of products and helped negotiate prices, if in fact a product was substantially improved by virtue of a change in manufacturing practice or something like that, then theoretically the pharmaceutical manufacturer could submit that information to the organization and it could be fairly reviewed, and the price could be increased if it was fair to do so.

Senator MURKOWSKI. Well, Mr. Chairman, we hear these stories all the time. This is the reason that we're having this hearing this morning. Senator Baldwin and I have reintroduced what we call the Fair Drug Pricing Act, which would require the manufacturers to actually provide some kind of a justification when we see this substantial increase to the list price for the medications. I think we recognize that people want to see some level of transparency here and accountability when you see these really sometimes incredible price hikes year over year over year.

I would hope that we'd be able to advance provisions like what Senator Baldwin and I are trying to do, along with leadership on this Committee. I thank you.

The CHAIRMAN. Thank you very much, Senator Murkowski.

Now we go to Senator Baldwin.

Senator BALDWIN. Thank you, Chairman Sanders.

I want to jump in just where Senator Murkowski dropped off with regard to the Fair Drug Pricing Act. But I also want to share a constituent experience first.

I hear all the time from Wisconsinites who cannot afford their prescription medication, people like Jackie Trapp, from Muskego, Wisconsin, who has terminal cancer. She wrote me that "The drug that keeps me alive is also driving my family toward bankruptcy. It has doubled in price in the very few years I've been on it, and it costs me $15,000 to $21,000 out of pocket per year. My husband is worried enough about being left alone, and I worry about him having to start over financially and his lifetime of savings is being wiped out for one drug, Revlimid." The price of this drug, Revlimid, has increased over 20 times.

Stories like this one are the inspiration for the bipartisan Fair Drug Pricing Act, which I'm reintroducing today with my colleagues Senator Murkowski, Senator Smith, Senator Braun. The bill requires manufacturers to submit a transparency and justifica-

tion report 30 days before they increase the price of a drug by more than 10 percent in one year or 25 percent over three years.

This is a first step, but it's a really important one. For the first time it gives taxpayers and patients advance notice of price increases, but it brings basic transparency to the market for prescription drugs.

Dr. Kesselheim, why is it important to require manufacturers to publicly justify their price increases, including by accounting for things like research and development costs, net profits attributed to the drug, and marketing and advertising spending? And what is the impact of transparency requirements when it comes to the list prices of medications?

Dr. KESSELHEIM. Thank you, Senator. I would say that one of the reasons it's important to require companies to disclose this information to a board or through some other means is, first of all, to give them the incentive to actually generate information that would justify the price increase. Right now, drug companies can raise prices without any justification and without doing any research, and if you required some kind of disclosure you could actually incentivize companies to generate high-quality research information that could then help guide physician and patient choices and provide more usefulness.

I think another thing to help guide prescribing practices, another thing that such a measure could do would be to actually dissuade companies from increasing prices when they don't have that information or when they don't have a justification, or if they don't want to provide insight into their marketing budgets, and so it could actually prevent these kinds of price hikes from happening in the first place unless they are really, truly justified by some kind of change in the supply chain or manufacturing practices.

Senator BALDWIN. Thank you. I want to continue in this vein. From 2010 to 2019, the FDA approved 356 drugs. Recent research from Bentley University finds that NIH funding contributed to every single new drug approved, at a cost to the taxpayer of roughly $230 billion. In spite of this contribution, the NIH is listed on only 27 of those patents. This suggests that while taxpayers provide funding for the bulk of the early stage research, they do not get patent protections supposedly secured by the Bayh-Dole Act. In essence, American taxpayers are paying the highest prices in the world for drugs that they already paid to help develop.

Dr. Kesselheim, are American taxpayers getting a fair deal for this research investment? And how should we be looking at and examining and accounting for the taxpayer contributions, and what could this mean ultimately for drug prices if we got it right?

Dr. KESSELHEIM. Well, I mean, I think Americans are getting advantages when the products that are developed by public funding end up leading to important new treatments, like, as we saw, the COVID–19 vaccines or other transformative drugs. Research from our group has shown that, by far, transformative drugs are much more likely to come out of public funding and NIH resources.

I think what this shows is that, first of all, the limitations of the patent system as a way of assigning credit for where products come from, because you can't get a patent until you are much closer to the final stages of costs of development. And even for those drugs,

though, we don't end up providing a lot of recognition of the public's support for those products in the prices that patients provide, and as a result some people argue that patients are paying twice for the drugs, first in the research leading up to their discovery, and then second in the super-high prices that we pay because we don't have any control over the prices in the U.S. market.

Senator BALDWIN. I yield back, Mr. Chairman.

The CHAIRMAN. Thank you, Senator Baldwin.

Senator Marshall.

Senator MARSHALL. Thank you so much, Chairman. I just want to emphasize that you and I, both sides of the aisle, agree on the same goal here, that we want to figure out affordable access to all prescriptions for all people. And just bringing some of my insight as a physician to this Committee, I think I want to talk about insulin just for a second, and I appreciate our testimony on this. This is a prescription I have written thousands of times, and it's part of this opaque game. I call it the opaque game.

There's a list price and a net price. The list price of insulin has gone up, up, up, thousands of times, percent, and that's what the out-of-pocket is based upon. So the person who testified today, the Medicare patient, they're paying out-of-pocket based on the list price. But the net price in many instances has gone down since 2007, and this is where the opaque process happens.

As far as I know, this is the only business in America that's allowed to have legal kickbacks. So there are legal kickbacks from the middlemen to Big Pharma, as well as insurance companies and we don't know who else, and that's the opaque process. There are claw-backs from community pharmacists, and subsequently we're losing more community pharmacies than ever before.

I think there are two simple solutions, and the first one is transparency. I think if my parents, 83 years of age, living in the home that I grew up in, who balance their checkbook every day, don't have a credit card, if they would see where those kickbacks are going, they would raise Cain, and I think that all of Congress could see that. And I think the second step is to eliminate kickbacks, that these kickbacks have to stop and all rebates should go to the patient. So those are the two solutions I hope we could agree to work upon.

I want to turn and talk about innovation, though, how innovation is important as well, that I think that of the top ten drugs that are in the world today over the last four or five years were all discovered and made here in America. And I think this goes to my point on process. Inhalers is another great example. One of our folks talked about that, inhalers, something I've written thousands of prescriptions for.

About five or six years ago I was writing a prescription, and it was an OB patient, so she came back in a week and said Dr. Marshall, I think you gave the wrong prescription, it went from $28 to $168. I said, oh, no, that's a generic, your pharmacist must have made a mistake, let me pick up the phone and call and talk to him. And sure enough, what we found out is the EPA had decided all the dispensers but one were not environmentally friendly. It gave one person control of that entire market. So I said, well, certainly someone will break into the world scene here and make a new dis-

pensing unit. But I found out it would take five to ten years and a billion dollars, perhaps, to get that certified.

There are multiple opportunities here to improve that process, and I know that some of my colleagues have legislation that would do that, as well.

I really think it's important that we protect innovation, and my question is going to go to Mr. Brill on this. As I think about the miracles of COVID, in January 2020 I reached out to the CDC to tell them my concern about the COVID virus, and they weren't quite as concerned as I was, so I immediately turned to the private sector. And as the CDC rolled out their testing, I asked the private sector to start working on testing, on therapeutics, and on vaccines, knowing that this was going to be a world problem very, very soon.

Thanks to those folks a miracle occurred, and we were able to develop a vaccine in months. What typically takes five or ten years they did in months. We implemented many processes that would improve the FDA process of approval that I think should be looked at long term, as well.

Anyway, I think there's this balance between innovation, encouraging innovation and not stifling it with government price controls, versus not allowing innovation to occur.

Mr. Brill, I'm just going to give you a second here to kind of speak about balancing this innovation and the cost of medicines and price controls. What would price controls do to innovation in America?

Mr. BRILL. Thank you, Senator, for your question. Obviously, policymakers are interested in both of these objectives, both ensuring new and innovative medicines, and the vaccines that are becoming more and more available every day are the clearest example of that. This science was developed over years through public and private investments together. We want to make sure to nurture and promote and facilitate this type of research and these investments over time.

Quite frankly, the credit goes not only to those manufacturers who have successfully brought products to market so far, but to all of the researchers who are working on vaccines, including those, quite frankly, whose efforts have failed. That's the innovative process that we want to foster.

How to balance that against our desire to keep prices low is a challenge, and in my view the answers to those challenges are best met by finding ways to create more competition rather than more price controls in the market, and that means more generics, not just a generic but multiple generics to compete, making sure that those generics are allowed onto market in a timely fashion.

The other type of competition that can be important is what's referred to as brand-to-brand competition. This often doesn't have the kind of effects we would like to see on list prices but does and can have that kind of positive effect that we're hoping for on net prices, which is an important price in the system as well.

Senator MARSHALL. Thank you so much, and I yield back.

The CHAIRMAN. Thank you, Senator Marshall.

Senator Kaine.

Senator KAINE. Thank you, Mr. Chairman. Thank you for holding this hearing, a very important one. And I just want to begin by thanking Ms. Spates. I hope I pronounced her name correctly.

I was not here for your verbal testimony because I was in two other hearings, but I read your written testimony and it's extremely powerful. Your conclusion, that we pay more than other nations because of greed, I think is partially accurate, but I think the other reason we pay more is because of us, Congress.

If we have a set of rules, people will operate under the rules as they exist, and then they'll maximize the money they can make. I think we might wish it were otherwise, but we can't pretend it is otherwise. So that puts the burden on our shoulders, Ms. Spates, to come up with the rules that will lead a person like you to not look five miles across the border and see people with similar health conditions to you who are not taxed to the very edge of their resources to deal with diabetes, as you are, living near the Canadian border. So thank you for basically encouraging us to do things to get this right.

I'm happy to have been working with Senator Collins on legislation dealing with biosimilars and trying to get biosimilars to the market quicker, because I think there are cost savings in there if we can do that right.

But let me do a couple of things. And forgive me, Mr. Chairman, if I may have missed questions like this when I was at the other hearings, but I want to ask Dr. Kesselheim, if I could, about international reference pricing.

I raised with the previous administration the notion that we pay so much more than other nations do, and many nations, in negotiating for pricing prescription drugs, use international benchmarks as a basis of negotiation. I actually thought that was one of the things that the Trump administration attempted to do that I thought was a really good idea. We don't have to pay the same price that a Third World nation does. I understand the notion of discounting pricing to nations with a lot of poor people so that they can have access to medicines. But when we pay dramatically more than other developed nations, I think the international reference pricing idea is a good one.

Dr. Kesselheim, could that be helpful as part of a broader pharmaceutical price reduction strategy?

Dr. KESSELHEIM. Certainly, Senator Kaine. I think that when you engage in international reference pricing, what you're doing is you're looking at other countries and asking what are the prices that they're paying for the exact same drug that you're paying for. In many cases what those countries are doing is they are assessing the clinical benefits of the drug and determining what a fair price should be.

Really, when you're doing international reference pricing, you're doing the exact same thing that I recommended we do up front, which is evaluate and negotiate, except we would just not be doing it; we would be relying on other countries doing it and then piggybacking on the conclusions that they made.

I think that international reference pricing might be a good fallback. It may be a good way of setting parameters. But I really

think that the U.S. could and should be able to make those same kinds of assessments and negotiations ourselves.

Senator KAINE. Dr. Kesselheim, it interests me as I see pharmaceutical companies oppose this, because to me the notion of international reference pricing is kind of like capitalism; why wouldn't we want to negotiate? I mean, why wouldn't we want to look at the prices that others are paying and try to negotiate? I was a lawyer for years, and you'd negotiate a provision in a contract, that if you offer a lower price to somebody else, I get it too. I mean, that just seems to be Basic Bargaining 101. Why wouldn't the U.S. engage in basic negotiating tactics in a way that other countries do?

Dr. KESSELHEIM. I think you're absolutely right, that they should do that, and the U.S. should, given the fact that it's such a large market, should be able to leverage the size of its market to be able to get lower prices.

I think that, actually, that raises an interesting point in another concern that I have about international reference pricing, which is that pharmaceutical companies often give other countries secret discounts on top of their list prices. So the list price that we see in another country might not actually be the real price that country pays. So we would be international reference pricing off of maybe not exactly the actual price for the product, which again suggests that while international reference pricing is a good model, what we really should be doing is doing those same kinds of evaluation and negotiation here in the U.S.

Senator KAINE. Then while we're on the negotiation topic, I'm sure this has already been raised, but I've just always been struck by the fact that the U.S. does not negotiate for prescription drug pricing under Medicare Part D, but we do allow the VA to negotiate prices of prescription drugs. How much might we save in Medicare Part D if the Medicare program was able to use the same negotiation strategy that the VA uses?

Dr. KESSELHEIM. Great question. We've done a number of studies, actually, led by Will Feldman in our group, to look at how—what that difference might be, and he found, in looking at insulin prices, for example, that Medicare could save billions of dollars each year if Medicare was able to negotiate and use its leverage in the same way that the VA is able to do that.

Senator KAINE. That would be billions of dollars in the Federal Treasury for deficit relief or whatever else we want to do. But it would also be substantial consumer savings, wouldn't it?

Dr. KESSELHEIM. That's just one drug for one year.

Senator KAINE. Yes.

Dr. KESSELHEIM. If you imagine how much that would be for all of the drugs that have been on the market for multiple years and have reached really high prices, then, yes, that would also translate to improved consumer savings and lower prices, lower health care premiums, which might translate to higher wages, and I think it would affect the entire economy.

Senator KAINE. Thank you.

Thank you, Mr. Chairman.

The CHAIRMAN. Thank you, Senator Kaine.

Senator Cassidy.

Senator CASSIDY. Hello, folks.

Mr. Brill, the Orphan Drug Act was supposed to incent and has incented the development of drugs for conditions which are below prevalence, but we know that some drugs start off for those with a low prevalence end up for other conditions with the same high price and exclusivity for the orphan drug and then translates over to the more common condition. What thoughts do you have about how we can address that? We want the orphan drug benefit, but we also don't want this kind of arbitrage where it then introduces a higher price than it should be for something else.

Mr. BRILL. Thank you, Senator Cassidy. As you may know, I think seven out of the top ten drugs being sold in the United States today were granted orphan drug exclusivities. And as you mentioned, the underlying principle here is desirable. There are rare diseases for which there may be underinvestment in R&D for products to treat those conditions, and some existing medicines may help in those smaller patient populations.

However, the current structure creates this very strong incentive to pursue orphan drug designation, thereby extending the monopoly power across the sales of all drugs. Policymakers need to think about this in careful balance and what is the appropriate amount of incentive to provide manufacturers and researchers to make sure that they know if their products are effective in small populations without extending the monopolies over a large——

Senator CASSIDY. I know that. I need some legislation. So what's my legislation going to read? How do we thread that needle?

Mr. BRILL. Well, I would say that we want to think about the standards for which those exclusivities are granted and that it shouldn't be just for investigations but for meaningful progress and meaningful treatment. We could think about engaging with the FDA in helping to make those determinations so they're not excessively awarded.

Senator CASSIDY. Dr. Kesselheim, you had mentioned the Federal Government negotiating with manufacturers, but this would be basically in some cases the U.S. Government would be a purchaser of 99 percent of the drug produced. Think of a prospective Alzheimer's drug, so-called monopsony power, a single purchaser, and certain oncolytics would be basically the Federal Government buying and no one else. It seems to me that could have a chilling effect upon a company's willingness to invest in a drug if they thought the Federal Government was going to be able to unilaterally set the price.

If a President Bernie Sanders decided that we're going to go to negotiating drugs, who would invest in developing an Alzheimer's drug knowing that the return on investment from Medicare would be so poor? Your thoughts on that?

Dr. KESSELHEIM. Sure. Thank you, Senator. I would say, first of all, there are certainly a lot of scientists out there trying to find treatments and effective cures for Alzheimer's disease, a disease that we do not have any effective treatments for, and I think that their work will continue.

But I would also say that if we do have a publicly funded, independent board that evaluates new products——

Senator CASSIDY. That's not my question. My question is the venture capital and the people that fund that translational research

from the bench to the dedicated scientists to the clinical trial, which so far has been very fruitless and very expensive, but they're expecting a return on investment, what return would they expect again if Bernie Sanders were president and you were his chief negotiator? Yes, you could have somebody do an independent evaluation, but oftentimes government puts its finger on the scale. So how do we avoid that trap of squelching innovation when the Federal Government would be expected to give a very poor return on investment?

Dr. KESSELHEIM. Well, I don't necessarily think the Federal Government would be expected to give a poor return on investment, because if there is a new drug, especially for a condition like Alzheimer's that doesn't have any good treatments, if a new drug was out there and it offered an extremely substantial benefit to patients with Alzheimer's disease, I would think that under this current system we would pay a lot of money for that drug because it would help reduce so much excess spending on care——

Senator CASSIDY. I'll dispute a little bit because there's a New York Times article basically saying we should march in on drug companies' technology to make the COVID–19 vaccine, which is to say they've invested so much to put out a vaccine so quickly, but now we're going to force you to share your technology with others. I think there's always going to be this populist impulse to give something away for free. Are you saying that would not operate, not be operative if there was a drug for Alzheimer's?

Dr. KESSELHEIM. Well, I think that's true, it does not have to operate. In fact, we see in places like Germany, they are able to negotiate and get prices out on the market and offer prices for which pharmaceutical manufacturers make a substantial profit in that market and be able to come to valid negotiations without having to go to that extreme circumstance of having to march in or do whatever else.

I think that there is a lot of opportunity to identify what an evidence-based, valid price for a product should be, and that price would provide substantial incentives for investment, because in cases of diseases like Alzheimer's disease where there is substantial unmet medical need, that price could be quite high. But the system will end up affording the high price for that important new drug because we're not paying for all of the eighth and ninth products for rheumatoid arthritis that don't offer any advantages over what products we already have. So we'll save money on that end, and as a result we'll be able to pay a lot more money for really meaningful, new innovation like the kind that you're describing.

Senator CASSIDY. I'll yield. I'm out of time. I'll just finish by saying I think you underestimate a politician's tendency to give things away for free, particularly when they belong to other people. And second, the German model has been criticized for having such a restrictive clinical benefit aspect that it's just not fair. With that said, we pay too much for drugs. I'm certainly in agreement with that.

With that, Mr. Chairman, I yield.

The CHAIRMAN. Senator Hassan.

Senator HASSAN. Well, thank you, Mr. Chairman and our Ranking Member. I want to thank the witnesses for being here today, as well. And to Ms. Spates in particular, thank you for true and

clear and therefore compelling testimony, and for being willing to talk about your own personal situation. It makes a real difference.

Mr. Chairman, I appreciate your work on this issue over the years, including on importation and allowing the Federal Government to negotiate Medicare drug prices. I believe there is bipartisan support in the Senate for legislation that meaningfully lowers the cost of prescription drugs, and we need to take action this year.

I want to ask questions to you, Dr. Kesselheim, following up on Senator Baldwin's line of questioning.

Drug companies often try to justify high prices by saying that they use this revenue to fund innovation for future breakthrough medications, and we all support innovations that effectively treat and cure diseases, but we also know that American taxpayers subsidize a significant portion of the research that leads to these innovations.

Dr. Kesselheim, let's just make clear who makes the majority of investments in the research that leads to breakthrough therapies and treatments for unmet health needs. Is it the drug companies or the American taxpayer?

Dr. KESSELHEIM. Well, I mean, I think there is usually a combination of factors that go into these kinds of discoveries. Our studies and other studies have shown that a substantial amount of basic and translational science, the vast majority of basic and translational science is funded by publicly funded systems, and then privately funded entities come in later in the development process to lead clinical trials and the regulatory approval process. So it is a little bit of a combination of both forces.

Senator HASSAN. I'm going to just stop you because I want to get to other questions, too.

Dr. KESSELHEIM. Sure.

Senator HASSAN. But it is a substantial amount of this innovation funding that comes from the American taxpayer.

Dr. KESSELHEIM. Yes. And the origins, as you mentioned, of transformative drugs often comes from publicly funded sources, even from concept through the clinical testing of them.

Senator HASSAN. Okay. So now let's move on to the broader topic here. Drug companies receive taxpayer support at just about every step of their business model, from the time a drug is developed to the time a pharmacy dispenses it to a patient. We are the only country that subsidizes these companies the way we do, yet according to a recent Rand study we are paying up to 250 percent more for prescription drugs than countries with similar GDP.

Dr. Kesselheim, I want to ask you about some of the tax breaks and subsidies the drug companies receive from American taxpayers, and I have several examples to get through in a limited amount of time, so if you can keep your answers brief, that would be helpful.

Drug companies receive billions of dollars in tax credits which subsidize the cost of ads that they run on television, online, and in print. Have these tax credits led to lower drug prices or more innovation for patients?

Dr. KESSELHEIM. No.

Senator HASSAN. Okay. Now, drug companies also establish charities that promote the drugs that they sell and receive tax deduc-

tions when they donate to those charities. A City Research report found that every $1 million a drug company donates to these charities can return up to $21 million in increased revenue.

Briefly, if you can, Dr. Kesselheim, why are drug companies choosing to put billions of dollars into these charities instead of simply lowering the price of their drugs?

Dr. KESSELHEIM. These charities can help people who have high out-of-pocket costs and have no other choices but to take that drug. But as a result of helping individual patients with their high out-of-pocket costs, drug companies are making a lot of money on the payments that insurance companies make that are behind the scenes and are able to sustain the high prices so that they can charge high prices for other payers.

Senator HASSAN. Right. So they could just lower their prices overall, and that would make a difference for the patients.

We do have some transparency, though, through the Medicare Open Payments Data base into payments drug companies make to prescribers. In 2019, companies gave away $2.3 billion in cash payments, free meals, and speaking fees, an average of over $3,700 to each prescriber who received a payment, and research shows that these payments influenced prescribing.

Dr. Kesselheim, why are companies choosing to spend billions of dollars each year on payments to prescribers instead of putting the money toward lowering the price of their drugs?

Dr. KESSELHEIM. Well, those prices actually increase drug prices because they go to encourage physicians to prescribe the high-priced products over lower-priced generic drugs because generic manufacturers don't advertise their products.

Senator HASSAN. Well, thank you, Dr. Kesselheim.

These are just a few examples of the uniquely American tools that the drug industry has at its disposal. So it should be no surprise that the cost of prescription drugs in America are uniquely high.

Thank you again, Mr. Chairman. I look forward to continuing this important work with you and our colleagues.

The CHAIRMAN. Thank you, Senator Hassan.

Senator Rosen.

Senator ROSEN. Thank you, Chairman Sanders, Ranking Member Collins, for holding this very important hearing today, and to the witnesses for sharing your perspectives on drug pricing. We have to do some work in this area, for sure.

But I'd like to continue the talk about innovation and competition and transparency that all of my colleagues have been discussing in some form or fashion, because Nevada is home to a number of smaller pharmaceutical firms who are developing new drugs and medical devices to improve lives, not only in our state but across the country. In Southern Nevada one company is working on an oral drug to treat lung cancer. In Northern Nevada another company is working on a drug to prevent Parkinson's and other neurologic diseases. And we know, again, research and development, clinical trials, they can take ten years or more, and startup costs do remain a significant barrier, but the new drugs on the market will ultimately increase competition and help reduce costs.

Dr. Kesselheim, what more can Congress do, or should do, to support our smaller, local startup pharmaceutical firms? They're taking on significant risk to develop these new, innovative drugs and devices that may eventually really help increase access and lower costs, not to mention saving lives or improving lives.

Dr. KESSELHEIM. Well, thank you for the question. I think that there are a number of things that government could do. I mean, I think that the example that we've seen in the last year relating to COVID innovation has shown the power that public-private partnerships can have when there is funding particularly for innovative, really new ideas to try to treat lung cancer, in this case, through some novel mechanism.

I think that a lot of small companies will suggest that they, unfortunately, can't get the support that they need to try to get these drugs through proof of concept, in part because the incentives are not necessarily there to support really important new products.

I think that one of the things that we could do is we could provide more up-front support for that. But in those cases I think we also need to make sure that when those products then do become available, that they're being made available at a fair price for consumers.

Senator ROSEN. Thank you. I want to say that I'm really interested in the lung cancer drug. My mother passed away from lung cancer, and I would not wish that on anyone else. So I hope we do see some movement forward on that.

But I'm also interested in our non-profit pharmaceutical company model. So can you talk about your understanding of this relatively newer model and some of the challenges of bringing a drug or a device to market as a non-profit? And how can the success we've seen so far in Congress from this, what can we do to support it and help that to grow in the non-profit sector?

Dr. KESSELHEIM. The most prominent non-profit drug development model is the Drugs for Neglected Diseases Initiative in Europe. What they've been able to accomplish getting new, effective treatments for neglected tropical diseases in countries around the world for relatively meager support just shows how effective pharmaceutical development can operate on a limited budget. These numbers that we're hearing about the cost of drug development are over-inflated in a number of different ways.

I think that based on the success of models like that, there have been some efforts in the United States to try to develop non-profit drug manufacturers. Mostly those kinds of organizations operate to address drug shortages or other older, off-patent products for which manufacturers have stopped manufacturing it, and we're starting to see some success. But I think that is an effective model, potentially an effective model for an important new drug that can't get the private funding that it needs in order to bring that product to market, as well.

Senator ROSEN. Thank you.

I'd like to move on in the quick time I have left. The 340B drug discount program is critical to Nevada. We have a diverse population, hundreds of thousands of people living in rural communities spread out across our state. Can you talk about the importance of

the 340B drug discount program, how it's helped increase access and affordability, please?

Dr. KESSELHEIM. Sure. So, the 340B program is a very complicated system that we have to try to provide certain drugs at a relatively low cost to safety-net hospitals, and it has provided a lot of useful drugs to low-income patients. It has expanded over the years, perhaps beyond what was originally intended by it, and as a result there have been some discussions about to what extent certain hospitals should qualify as 340B hospitals or not. But there's no doubt that 340B pricing is among the best prices that we offer for certain high-cost drugs.

Senator ROSEN. Thank you. I really appreciate you being here today.

I yield back.

The CHAIRMAN. Thank you, Senator Rosen.

Senator Braun.

Senator BRAUN. Thank you, Chairman Sanders.

I'm so glad we're having the discussion on health care costs in general, specifically on the high cost of drugs. Everybody in our country sooner or later comes across a prescription that they wrestle with, have no idea how to attain the price in the first place in terms of a fair price. The lack of transparency that is systemic throughout our health care system is, in my opinion, the main reason why we're here today.

In building a business over the years, if I had the ability to tell my customers what they were buying after the fact, it would be a lot different dynamic than what it would be with a free market where you've got an engaged consumer.

That's the other thing we don't talk about. Health care consumers have grown—don't blame it on them, it's evolved that way—to where they want no skin in the game. It's unaffordable in so many cases once you do confront the health care system. It's a mess across the board.

My question is going to be here in a moment for Dr. Kesselheim, but I've wrestled with it before I got to the Senate. There is no other sector of our economy that has less transparency, less competition, more barriers to entry, and a disengaged consumer.

One alternative is to bring government into play. And to be honest, I think many CEOs that don't run health care companies are going to be for that because the industry is dug in, resisting reform that I think needs to take place before you bring more government into play.

But it's clear we've got a broken health care system that costs way too much, and we need to figure out how to fix it. If the industry is not going to take on some of the reforms, you'll get what you deserve, and that's probably the heavy hand of government because you're like an unregulated utility when it comes to the way you operate.

Dr. Kesselheim, I'm hoping that I've got the right information here, but when it comes to transparency I think you've been quoted, "You might get more than what you've asked for," that transparency would actually maybe be a negative. I think that is so bizarre in the sense that any other aspect of our economy where you have everything I talked about—engaged consumers, robust

competition, full transparency, no barriers to entry—things work. Lasik surgery and things even within the medical field prove that.

Why would you have that point of view that it could stymie price competition if you put more transparency into the mix? That seems to me to be counter-intuitive. I'd love to hear your response to that.

Dr. KESSELHEIM. Sure, Senator. If all you do is include transparency but don't do anything else, then you actually risk raising prices because right now those secret back-room deals that PBMs arrange is really the only system that we have in our country for lowering prices. And if you take that away and you make everything fully transparent without doing anything else, then you take away one of the greatest tools, the only effective negotiators we currently have in the system, which are PBMs and insurance companies, for trying to lower prices.

I would be very much in favor of transparency if you marry it with evaluation and negotiation, because then you don't really need PBMs. You can just have what a fair price is, and you can offer that to private companies, and the value of the PBM and the value of the secrecy that they operate in plummets.

I would say that we could have transparency if we married it with some of the proposals that I suggested. But just transparency alone, I think that you are taking away the only strategy that we currently have in the market for lowering prices.

Senator BRAUN. I'm glad to hear you say that because I agree with you. I think that when you have transparency only, you don't have the other tools that go along with it, and that would be that employers across the country, as well as government, the two stakeholders in paying the bills, need to be able to negotiate with more bargaining power. And I think if we'd get that right—it happens everywhere else where government is able to negotiate. They hide behind the disguise that they're a free market. They are not a free market until they do the things I said earlier.

I think what you're talking about, including employers getting in the mix, that's how we bring drug prices down, and then maybe prices cascading down across the system of Pharma, hospitals, insurance, and even practitioners. Thank you.

The CHAIRMAN. Thank you, Senator Braun.

Senator Murphy.

Senator MURPHY. Thank you very much, Mr. Chairman.

Thanks, everyone, for this hearing.

This is a question to either Dr. Persaud or Dr. Kesselheim. A 2019 study in the Journal of American Medicine Association looked at 15 years of medical marketing in the U.S. and found that there was a 70 percent increase in health care marketing from 1997 to 2016, including a massive increase in direct-to-consumer advertising and promotion to physicians.

Clearly, this enormous surge in marketing and advertising provides a benefit to the companies. They wouldn't do it unless it led to the sale of more product. And clearly it has to be part of the story with respect to the increase in price if there's been this incredible surge in marketing and advertising spending.

But my question is, is it a benefit to the health care system as physicians, as folks through your conversations with colleagues? Does direct-to-consumer advertising provide the kind of benefit to

patients that the companies would have us believe, or is it just a benefit to their bottom line and a contributor to the increase in cost?

Dr. PERSAUD. Thank you, Senator. The answer is no, it does not benefit the public, it doesn't benefit patients. There have been studies of whether or not marketing is associated with better prescribing of medicines or more appropriate use of medicines, and there are no studies that indicate that this marketing improves the care that patients receive.

It is something that patients are paying for, and we are all paying for, and in the end it is driving in some cases prescribing toward more expensive medicines. So we pay for it multiple times, and there isn't a demonstrated benefit of a pharmaceutical company providing information either directly to consumers or to prescribers.

Senator MURPHY. Dr. Kesselheim.

Dr. KESSELHEIM. I agree with Dr. Persaud. I think that one of the things that direct-to-consumer advertising does, and I can tell you this as a primary care doctor, is it brings people to the office asking about medicines that they saw on TV, and usually the medicines that are being advertised are the most expensive, and they may not offer improvements over other therapies that aren't being advertised.

While direct-to-consumer advertising can alert people to the existence of drugs, it does drive prescribing practices in ways that aren't evidence driven.

Senator MURPHY. Just to give a sense of how much of the cost of the drugs may be determinative of the advertising spend for these companies, there's another study suggesting that for the big pharmaceutical companies as much as 19 cents of every dollar, nearly one-fifth of all of their spending, goes into advertising and marketing.

In my remaining time, Dr. Kesselheim, I was intrigued by the time that you spent in your written testimony on the question of comparative effectiveness. And I wondered if you might give us some suggestions as to how the United States can do a better job of making sure that we are getting a true bang for our buck. Other countries spend a lot more time making sure that they are only paying for drugs that are substantially better than other products that are on the market.

This issue is fraught with peril because for many folks, a 5 percent increase in effectiveness or the promise of a potential 20 percent increase in effectiveness, they're going to want that. They're not going to want the government deciding whether or not they get access to these drugs. But it's an enormous amount of money that we all pay for when some drugs are only getting tiny, incremental increases in quality or effectiveness. What's your recommendation for how we proceed on this topic?

Dr. KESSELHEIM. Well, Senator, I think this is an extremely important issue, and unfortunately, in the U.S. system, we do not invest nearly enough in doing the type of comparative effectiveness studies that we need in order to determine which drugs are better for which patients, and really this is the best way to empower patients to make decisions about their care, is to say, look, we've done

the studies and we know that this drug works X amount better, here are the side effects you have to weigh, and between you and your physician you can make a decision about the best way forward.

Unfortunately, we don't have enough of that, and what I would suggest that we do is invest more money up front in the same way that we invest money in basic science in generating this information, because it will actually save money on the back end because pharmaceutical companies leverage the lack of information in their promotional practices to encourage high-cost drugs when lower-cost products may be just as effective. And then what we do is we just pay many times more on the back end.

If we had more comparative effectiveness research and evidence up front, then we would be able to help guide prescribing practices and the best way forward for patients.

Senator MURPHY. It doesn't necessarily have to lead to drugs being on or off a formulary, just that information available to prescribers may end up in better care practices.

I appreciate the answers from both of you. Thank you.

The CHAIRMAN. Thank you, Senator Murphy.

I believe that ends our hearing. We have heard from many, many Senators, and I want to thank Dr. Kesselheim, Dr. Persaud, Elia Spates, and Alex Brill for their participation, as well.

I think what you have heard from virtually all Senators, regardless of their party or political persuasion, is they continue to hear from their constituents who are sick and tired of paying the highest prices in the world for prescription drugs, prices that in many cases they cannot afford. And what you have heard is that when people cannot afford the medicine they need, they will get sicker. Sometimes they will die. Sometimes they will end up in the hospital, at great cost to the health care system.

You have also heard, I think, today that we have been talking about the issue of the high cost of prescription drugs, not only for years but for decades, and that there is all kinds of legislation that has been offered. And yet, at the end of the day, the pharmaceutical industry continues to march along earning huge profits every year, paying their CEOs exorbitant compensation packages, and they continue to provide hundreds and hundreds of lobbyists and make all kinds of campaign contributions.

I think the conclusion that I have reached from this hearing is that the time is long overdue for the U.S. Congress to summon up the courage to take on perhaps the most powerful special interest in the United States, and that is the power of the pharmaceutical industry.

Our people are hurting, they want us to act, and now is the time to do that.

With that, let me conclude this hearing and thank again everybody for participating.

The hearing is ended, and people will have time to submit questions for the record, and testimony as well.

Thank you.

ADDITIONAL MATERIAL

STATEMENT FOR THE RECORD FROM SENATOR RICHARD BURR

ON WHY DOES THE U.S. PAY THE HIGHEST PRICES IN THE WORLD FOR PRESCRIPTION DRUGS?

The hearing today is focused on the cost of medications in the United States, comparing the price of these drugs to the prices available in other countries around the world. The drug pricing debate has been underway in the Senate for many years, with numerous bipartisan proposals put forward during the 116th Congress. But, I would like to remind my colleagues that the COVID–19 pandemic fundamentally altered these debates, showing us in Congress, Americans, and those around the globe the undertaking associated with biomedical research, and the importance of fostering an environment that rewards and stimulates innovation so we can bring treatments, therapies, and vaccines to market in as timely a manner as possible.

I agree with my colleagues that the cost of medications is an issue that deeply affects Americans, and our payment models in public and private health care programs must keep pace with the new products that come to market. The new ways in which we are able to address devastating diagnoses that, at one time, had no options for care are only as good as the ability for Americans to access them. Prior to the pandemic, Senator Crapo and I introduced legislation to improve this access, while maintaining the incentive to innovate, and encourage and foster American innovation.

The novel coronavirus pushed the American biomedical research enterprise to the brink of what few thought would be possible—three authorized vaccines in ten months. Not only were these vaccines brought through large-scale phase 3 trials, but they were made *available* to the American people immediately upon their authorization by the Food and Drug Administration (FDA). This availability was made possible through the foundational laws that streamlined the process for making these life-saving drugs available to the American people.

Many of these foundational laws were the result of the work in the HELP Committee. The 21st Century Cures Act recognized the critical importance of ensuring that the United States remained the global leader in biomedical research, and made the investments and policy changes necessary to maintain this leadership role. This hearing comes at a moment when every American stands to benefit from the efforts of the biomedical research community. We have three authorized vaccines to combat COVID–19, multiple medicines to reduce hospitalizations and deaths, and hundreds of tests to detect the virus.

As we examine our policies and programs that affect the costs of medications in the United States, we must balance the changes that we propose against the affects that they will have on the ability for our developers to innovate. America's ability to respond to the everyday health care challenges we face, as well as the next public health threat in the future will impacted by this balance. If we do not get it right, we will not have the countermeasures, medicines, and technologies we have today to save as many lives as possible, and that cost, would be too high.

National Council on Disability

An independent federal agency making recommendations to the President and Congress to enhance the quality of life for all Americans with disabilities and their families.

April 2, 2021

Statement for the Record
U.S. Senate
Committee on Health, Education, Labor, and Pensions
Subcommittee on Primary Health and Retirement Security

"*Why Does the US Pay the Highest Prices in the World for Prescription Drugs?*"
Hearing on March 23, 2021

Dear Chair Member Murray, Ranking Member Burr, Subcommittee Chair Member Sanders, Ranking Subcommittee Member Collins, and Members of the Subcommittee:

Thank you for the opportunity to submit this statement for the record. On behalf of the National Council on Disability (NCD), I write to raise concerns about adopting foreign drug prices that rely on the quality adjusted life year (QALY), a cost-effectiveness measure that devalues the lives of people with chronic illnesses and limits their access to highly effective drugs and treatments. As a voice within the Federal Government for over 61 million Americans with disabilities, NCD, an independent federal agency, provides advice to the President, his Administration, Congress, and federal agencies based on our comprehensive and objective analyses to inform policy development, improvement, and enforcement efforts.

In 2019, NCD investigated the design and impact of the use of QALYs and concluded that it discriminates against people with disabilities and chronic illnesses, both in design and its effect.[1] The methodology underlying the QALY assigns a lower value to the lives of people with disabilities resulting in a determination that they are too expensive to receive life-saving care. NCD's examination documents longstanding concerns raised by bioethicists, patient rights groups, and disability rights advocates about the limited access to lifesaving medications for chronic illnesses in countries where the QALY is frequently used. NCD is concerned about the growing interest in using QALYs in the United States either directly or indirectly through foreign drug prices that rely upon the QALY to contain healthcare costs despite its discriminatory effect on the availability of prescription drugs and medical care for people with disabilities and chronic illnesses. We encourage Committee members to consider the NCD report in its ongoing

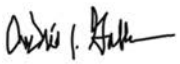
[1] NATIONAL COUNCIL ON DISABILITY, *Quality Adjusted Life Years (QALYs) and the Devaluation of Life with Disability* (2019), *available at*: https://ncd.gov/sites/default/files/NCD_Quality_Adjusted_Life_Report_508.pdf.

discussions regarding drug pricing and welcome the opportunity to brief your staff on these concerns.

Given the long-standing detrimental effects of the QALY methodology on the availability of medical care for people with disabilities and chronic illnesses, Congress prohibited its use by the Secretary of the Department of Health and Human Services (HHS) in coverage determinations in Medicare under the 2010 Patient Protection and Affordable Care Act.[2] It also prohibited its use by the Patient-Centered Outcomes Research Institute.[3] The use of QALY in foreign drug pricing should be equally unacceptable to Congress for the very reasons it found its use to be unacceptable domestically.

As NCD sets forth in its 2019 report, Congress should: (i) avoid enacting legislation that would require HHS to cover only the most cost-effective drugs and treatments or impose restrictions on less cost-effective treatments; (ii) enact legislation to prohibit the use of QALY under Medicaid and Medicare; (iii) provide funding to HHS for research on best practices on the use of cost-effectiveness to inform benefits and coverage decisions with respect to US national health insurance programs like Medicare and Medicaid;[4] and (iv) fund a Government Accountability Office study that examines how cost-effectiveness analyses influence agency decision-making. In addition, the prohibition on the use of QALY should extend to all federal agencies.

Most Respectfully,



Andrés J. Gallegos
Chairman

Encl. National Council on Disability, *Quality Adjusted Life Years (QALYs) and the Devaluation of Life with Disability* (2019).

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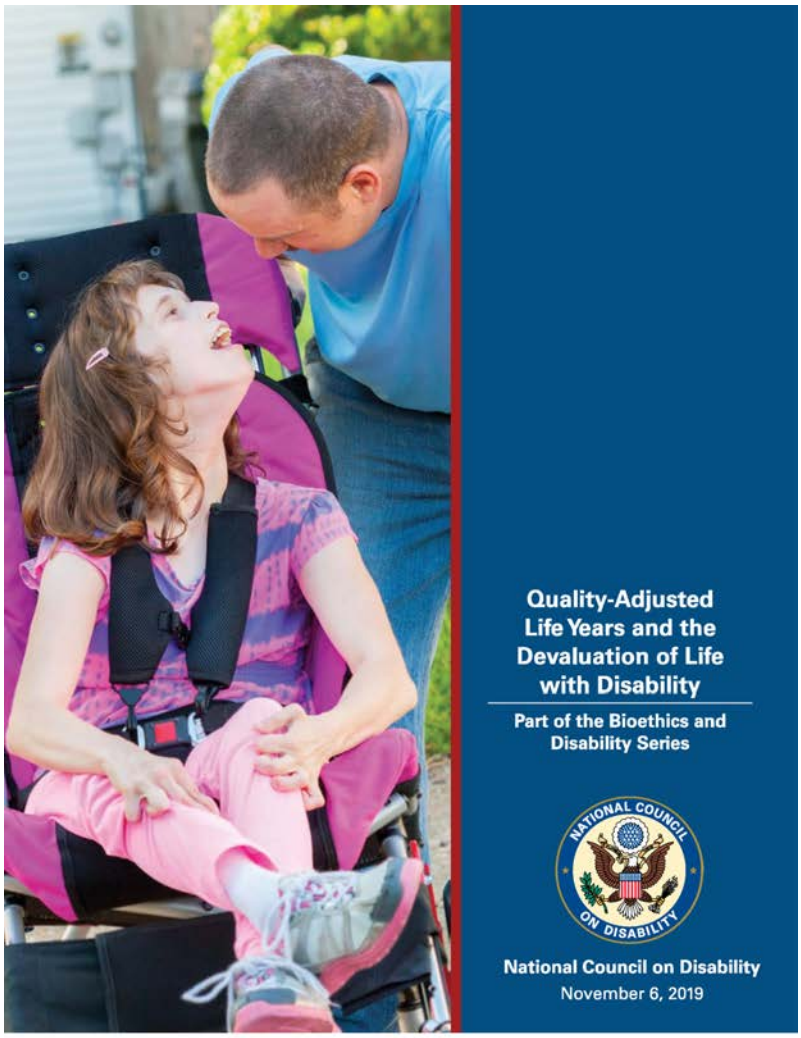
[2] Patient Protection and Affordable Care Act, Pub. L. 111–148, title VI, § 6301(c), Mar. 23, 2010 (codified as 42 U.S.C. 1320e-1(e))(The Patient-Centered Outcomes Research Institute…shall not develop or employ a dollars-per-quality adjusted life year (or similar measure that discounts the value of a life because of an individual's disability) as a threshold to establish what type of health care is cost effective or recommended…The Secretary shall not utilize such an adjusted life year (or such a similar measure) as a threshold to determine coverage, reimbursement, or incentive programs under subchapter XVIII).
[3] *Id.*
[4] "Best practices" in this case refers to a means of utilizing cost-effectiveness research that facilitates greater access to care and does not reduce access to care for people with chronic health conditions and disabilities.



Quality-Adjusted Life Years and the Devaluation of Life with Disability

Part of the Bioethics and Disability Series

National Council on Disability

November 6, 2019

National Council on Disability (NCD)
1331 F Street NW, Suite 850
Washington, DC 20004

Quality-Adjusted Life Years and the Devaluation of Life with Disability: Part of the Bioethics and Disability Series

National Council on Disability, November 6, 2019

National Council on Disability

An independent federal agency making recommendations to the President and Congress to enhance the quality of life for all Americans with disabilities and their families.

Letter of Transmittal

November 6, 2019

The President
The White House
Washington, DC 20500

Dear Mr. President:

On behalf of the National Council on Disability (NCD), I am pleased to submit *Quality-Adjusted Life Years and the Devaluation of Life with Disability*, part of a five-report series on the intersection of disability and bioethics. This report, and the others in the series, focuses on how the historical and continued devaluation of the lives of people with disabilities by the medical community, legislators, researchers, and even health economists, perpetuates unequal access to medical care, including life-saving care.

When health insurance will not cover medically necessary medications and treatments, individuals experience poorer health and a lower life expectancy. Nonetheless, in an effort to lower their healthcare costs, public and private health insurance providers have utilized the Quality Adjusted Life Year (QALY) to determine the cost-effectiveness of medications and treatment. QALYs place a lower value on treatments which extend the lives of people with chronic illnesses and disabilities. In this report, NCD found sufficient evidence of the discriminatory effects of QALYs to warrant concern, including concerns raised by bioethicists, patient rights groups, and disability rights advocates about the limited access to lifesaving medications for chronic illnesses in countries where QALYs are frequently used. In addition, QALY-based programs have been found to violate the Americans with Disabilities Act.

The US government does not have a single comprehensive policy on QALYs. Some federal agencies are banned from utilizing measurement tools like QALYs, while some state and federal partnership programs, such as state Medicaid programs, may. NCD is troubled that health insurance providers, government agencies, and health economists are showing increasing interest in using QALYs to contain healthcare costs despite QALYs' discriminatory effect.

The lives of people with disabilities are equally valuable to those without disabilities, and healthcare decisions based on devaluing the lives of people with disabilities are discriminatory. *Quality-Adjusted Life Years and the Devaluation of Life with Disability* explains QALYs and their effect on the availability of medical care for people with disabilities and chronic illnesses. It makes recommendations to Congress, federal agencies, and public and private insurers directed at rejecting QALYs as a method of measuring cost-effectiveness for medical care and offers alternatives.

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NCD stands ready to assist the Administration, Congress, and federal agencies to ensure that people with disabilities and chronic illnesses have access to the medical care they need.

Respectfully,

Neil Romano
Chairman

(The same letter of transmittal was sent to the President Pro Tempore of the U.S. Senate and the Speaker of the U.S. House of Representatives.)

National Council on Disability Members and Staff

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Acknowledgments

This report is part of a series of reports on bioethics and people with disabilities which was developed through a cooperative agreement with the Disability Rights Education & Defense Fund (DREDF). The National Council on Disability (NCD) appreciates the work of those who contributed their expertise in its development, including Kelly Israel, Policy Analyst, Autistic Self Advocacy Network (ASAN), and Samantha Crane, Director of Legal and Public Policy, ASAN. NCD also appreciates the work of Marilyn Golden, Senior Policy Analyst, DREDF, who shepherded the entire series in cooperation with NCD. We also thank those who participated on the Advisory Panel, in interviews, and in the stakeholder convening, whose knowledge and willingness to share information helped make this series possible.

Executive Summary

Purpose

Healthcare coverage decisions are of vital importance to people with disabilities and their families. If the medications and treatments that extend or improve the lives of people with disabilities are not covered by insurance, they will not have access to needed health care, and will have lower quality of life and lower life expectancy. Public and private insurance providers sometimes attempt to limit their healthcare spending in ways that reduce people with disabilities' access to health care. One of the means by which they do so is by refusing to cover (or by limiting access to) healthcare treatments based on their cost-effectiveness. One metric often used to help calculate cost-effectiveness—quality-adjusted life years (QALYs)—may have a negative impact on the health and welfare of people with disabilities.

QALYs are a number which (theoretically) represents the degree to which a drug or treatment extends life *and* improves quality of life—although quality of life is a difficult concept to define, quantify, and measure. However, QALYs aggregate quality and quantity of life simply by lowering the value of a year of treatment by the degree to which an illness, disability, or other health condition is perceived to harm the person's quality of life during that year.

There has been increasing interest among national health insurance programs (like Medicaid), private health insurance companies, and pharmacy benefit managers (PBMs; managers of drug benefits for health insurers) in using QALYs to inform their decisions about which drugs and treatments they will cover. Many individuals, however, have serious concerns with the use of QALYs.

[T]he QALY calculation reduces the value of treatments that do not bring a person back to "perfect health," in the sense of not having a disability and meeting society's definitions of "healthy" and "functioning". . .

The use of QALYs has been opposed by people with disabilities and disability rights advocates for more than 20 years. Their use is also opposed by some bioethicists and patient rights organizations. These stakeholders fear that use of QALYs undervalues vital treatments that extend or improve the lives of people with disabilities. This is because the QALY calculation reduces the value of treatments that do not bring a person back to "perfect health," in the sense of not having a disability and meeting society's definitions of "healthy" and "functioning"; uses

simplified assessments of value that do not account for the complexity of patient experience; and does not to take into account clinical expertise on rare disorders that may not have an extensive research literature available for use. Other stakeholders—often from the medical, health economics, and health insurance fields—argue that QALYs provide payers with valuable information on a treatment's potential benefits and costs and aid them in negotiating a reasonable price with the drug (or treatment)'s manufacturers.

Although QALYs have not historically been utilized for benefits and reimbursement decisions in the United States, prominent nonprofit corporations and professional associations are now using QALYs to evaluate the cost-effectiveness of new drugs and treatments. These evaluations now have a strong influence on many private and public health insurers' decisions about which drugs and treatments they will cover. Additionally, the use of QALYs to inform benefits and coverage decisions in other countries has limited access to lifesaving medications for people with disabilities and those with chronic illnesses.

[T]he use of QALYs to inform benefits and coverage decisions in other countries has limited access to lifesaving medications for people with disabilities and those with chronic illnesses.

NCD undertook this report to examine how use of QALYs may impact people with disabilities in the United States and will inform Congress and the executive branch on the ways in which QALYs impact people with chronic illnesses and disabilities' access to treatment and health care. The report includes recommendations aimed at ensuring that cost-effectiveness assessments of drugs and medical treatments, considered in benefits and coverage decisions, are fair and nondiscriminatory. NCD's research team used multiple methods to gather information, including a comprehensive literature review and interviews with experts and stakeholders who understand how QALYs may impact people with disabilities.

Background

Payers in the healthcare context—both private health insurance companies (for example, Anthem) and public health insurers (for example, Medicaid and the Veterans Administration)—typically have a limited amount of money to spend. Payers therefore want to fund treatments or drugs that are of high value and clinical effectiveness. For many payers, a high-value drug or treatment is equivalent to a cost-effective one, but patients may have different opinions on what constitutes value.

A cost-effective treatment is generally considered to be a treatment for which, from the perspective of the payer, the cost of the treatment does not outweigh the health improvements it provides. QALYs are used as one possible measure of the degree to which a treatment improves both quality and quantity of life. A drug or treatment that provides its beneficiaries with more QALYs is considered more effective. Therefore, a drug that provides its

beneficiaries with more QALYs for less money is considered more cost-effective.

QALYs are used in cost-effectiveness studies, in particular a type of cost-effectiveness study called a cost-utility analysis (CUA), as well as in decision-making tools known as value frameworks. Both are relied on by payers as a source of evidence of a drug or treatment's cost-effectiveness. The final decision made by payers is not dependent on cost-effectiveness as measured in QALYs, but instead is informed by it.

Key Findings

- QALYs have been the subject of considerable ethical debate since they were first invented. The primary ethical issues concern whether or not use of QALYs to calculate the cost-effectiveness of drugs and treatments discriminates against people with disabilities and chronic illnesses, how exactly they do so, and, if they do, whether or not that is ethical. There is not universal agreement on any of these issues. However, NCD has found sufficient evidence of QALYs being discriminatory (or potentially discriminatory) to warrant concern, including: (1) concerns raised by stakeholders in the interviews NCD undertook for this report (including bioethicists, patient rights groups, and disability rights advocates); (2) compelling arguments from prominent bioethicists condemning the use of QALYs; and (3) the inability of patients in countries where QALYs are used more heavily to obtain coverage of needed health care.

NCD has found sufficient evidence of QALYs being discriminatory (or potentially discriminatory) to warrant concern . . .

- The Federal Government does not have a single, comprehensive policy on the use of QALYs. The Federal Government has considered increasing its utilization of cost-effectiveness research and rejected the idea at different points in its history, leading to inconsistent policies across federal agencies. Some agencies are banned from using QALYs to make benefits and coverage decisions, while others use them frequently.
- There has been increasing interest by the Federal Government in reducing the cost of health care by modeling parts of its national health insurance programs after the healthcare systems of other countries, such as the United Kingdom. Several of these countries utilize QALYs to make benefits and coverage decisions. The coverage denials and loss of access to care faced by people with disabilities in these countries illustrate what might happen if the United States made a similar choice.
- QALYs and cost-effectiveness research are one of many different types of evidence insurers consider when making their decisions. There is limited publicly available evidence that shows to what extent private health insurance companies use QALYs and cost-effectiveness research to inform their medicine and medical treatment-related decision making.

QALYs and the analyses that rely on them are most likely utilized in insurers' internal decision-making processes, for which there is little transparency.

- There are alternatives to the use of QALYs. These alternatives range from well-established methods regularly used by United States federal agencies already, such as cost-benefit analysis, to unexplored but promising alternatives such as value frameworks that use patient preferences to determine the value of healthcare treatments. Many alternatives may themselves be discriminatory if used in certain contexts, or if they are used without paying sufficient attention to the possibility that discrimination may occur. However, several (such as multi-criteria decision analysis [MCDA], which allows its user to consider multiple unrelated benefits of a treatment and weight each benefit individually before arriving at a decision) can be used in a nondiscriminatory manner. It is much more difficult, if not impossible, to use QALYs in a nondiscriminatory manner. No single alternative serves all of the functions of QALYs.

QALYs and the analyses that rely on them are most likely utilized in insurers' internal decision-making processes, for which there is little transparency.

Key Recommendations

Congress

When enacting health reform bills, Congress should:

- Avoid creating provisions of any bill that would require the agency with management and oversight responsibilities (such as, for example, HHS) to cover only the most cost-effective drugs and treatments, or to require the agency to impose restrictions on less cost-effective treatments.

Congress should pass legislation:

- Prohibiting the use of QALYs by Medicaid and Medicare.
- Provide funding to Health and Human Services (HHS) for research on best practices on the use of cost-effectiveness to inform benefits and coverage decisions with respect to US national health insurance programs, such as Medicare and Medicaid. "Best practices" in this case refers to a means of utilizing cost-effectiveness research that facilitates greater access to care, and does not reduce access to care for people with chronic health conditions and disabilities.

US Department of Health and Human Services (HHS), Office for Civil Rights (OCR); US Department of Justice (DOJ) Civil Rights Division

DOJ and OCR should jointly issue guidance clarifying that the ADA applies to coverage programs that states operate such as Medicaid.

OCR, in consultation with DOJ as appropriate, should issue guidance to HHS sub-agencies, such as the Centers for Medicare and Medicaid Services (CMS) as well as to state Medicaid agencies, clarifying that:

Section 504 and Section 1557 also apply to Medicaid programs because they receive federal financial assistance. The guidance should specifically discuss how these authorities apply to benefits and reimbursement decisions, and that payment decisions should not rely on cost-effectiveness research or reports that are developed using QALYs.

Section 504 and Section 1557 apply to health insurance programs operated by recipients of federal financial assistance from HHS. The guidance should discuss that covered health insurance programs should not rely on cost-effectiveness research or reports that gather input from the public on health preferences that do not include the input of people with disabilities and chronic illnesses.

HHS

- HHS should consider including explicitly recruited people with disabilities and chronic illnesses as members of committees and working groups formed to develop effective healthcare reform and strategies for lowering the cost of prescription drugs.
- HHS should support healthcare providers by issuing guidance on what steps to take if their patient's health insurance agency refuses to cover recommended treatment on the basis of that treatment's cost-effectiveness.

HHS, OCR

- OCR should issue guidance to HHS sub-agencies, such as Centers for Medicare and Medicaid Services, State Medicaid Agencies, clarifying that:
  - Title II of the Americans with Disabilities Act (ADA) applies to national health insurance programs jointly run by the Federal Government and the States, such as Medicaid. The guidance should specifically discuss how the ADA applies to benefits and reimbursement decisions, and that payment decisions should not rely on cost-effectiveness research or reports that are developed using QALYs; and
  - Insurance programs jointly run by the Federal Government and the States, such as Medicaid, should not rely on cost-effectiveness research or reports that gather input from the public on health preferences that do not include the input of people with disabilities and chronic illnesses.

HHS, CMS

- CMS should utilize well-established alternatives to QALYs, such as MCDA, which is a method that better acknowledges the complexity of healthcare coverage decisions, or cost-benefit analysis, when the exact benefits and costs of a drug or treatment are known. CMS could utilize these methods in combination, such as using cost-benefit analysis as one component of an MCDA. If CMS does utilize cost-effectiveness analysis, it should consider utilizing it as one component of a condition-specific MCDA.

Acronym Glossary

ADA	Americans with Disabilities Act
ASAN	Autistic Self-Advocacy Network
CBO	Congressional Budget Office
CDC	Centers for Disease Control and Prevention
CEA	cost-effectiveness analysis
CMS	Centers for Medicare and Medicaid Services
CUA	cost-utility analysis
DOJ	US Department of Justice
DREDF	Disability Rights Education & Defense Fund
evLYG	equal value of life years gained
FDA	US Food and Drug Administration
GDP	gross domestic product
HHS	Health and Human Services
HTA	health technology assessment
ICER	Institute for Clinical and Economic Review
IPI	International Pricing Index
ISPOR	International Society for Pharmacoeconomics and Outcomes Research
MCDA	multi-criteria decision analysis
NCD	National Council on Disability
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
OCR	Office for Civil Rights
PBM	pharmacy benefit managers
PCORI	Patient Centered Outcomes Research Institute
PIPC	Partnership to Improve Patient Care
PPVF	Patient Perspective Value Framework
QALY	quality-adjusted life years
VA	Department of Veterans Affairs


Some stakeholders, but especially bioethicists and people with disabilities, have argued that QALYs are built on a faulty premise: that life with a disability is inherently worse than life without a disability.
National Council on Disability

Introduction

Healthcare spending has become a major concern in policy discussions across the United States. Concern is growing in large part due to the rapidly rising cost of health care. In 1973, healthcare spending amounted to 7.5 percent of US gross domestic product (GDP), while in 2017, healthcare spending more than doubled to approximately 18 percent of US GDP.[1] In 1973, the United States spent just $102.8 billion dollars[2] on health care, while in 2017 total US healthcare spending had risen to nearly 3.5 trillion dollars.[3] In this context, policymakers have rightly sought various means of lowering total healthcare costs.

In 1973, healthcare spending amounted to 7.5 percent of US gross domestic product (GDP), while in 2017, healthcare spending more than doubled to approximately 18 percent of US GDP.

One of the major means that has been considered by healthcare policymakers (such as US federal agencies, health economists, etc.) is the idea of health insurers and other payers funding "high-value" treatments over "low-value" treatments.[4] Patients and payers may significantly differ in how they interpret which treatments are of "high value" to them. For many payers, however, a high-value drug or treatment is merely a cost-effective one. A cost-effective treatment is a treatment that significantly extends life or improves patient quality of life (or both), at a cost which, to the payer, does not outweigh the improvements to health it provides. Payers may rely on a variety of evidence to determine cost-effectiveness, particularly cost-effectiveness analysis (CEA) studies, which examine the cost-effectiveness of drugs and treatments.

Patients and payers may significantly differ in how they interpret which treatments are of "high value" to them.

Several nonprofit organizations and professional associations in the United States have also attempted to help payers determine which treatments are of the highest value. To this end, they have created decision-making tools known as value frameworks, many of which primarily focus on cost-effectiveness.[5] Value frameworks can be used to produce reports that evaluate new drugs and treatments (sometimes known as health technology assessment reports, or HTAs).[6] The most influential of these HTAs are produced by

the Institute for Clinical and Economic Review (ICER), whose reports are relied on by payers as varied as the pharmacy benefit manager CVS Caremark and the Veterans Administration.

In prioritizing cost-effective treatments and treating cost-effectiveness as identical to value, however, payers may risk using means of quantifying which treatments are cost-effective that are simplistic and potentially discriminatory, such as QALYs.

QALYs are a measure that attempts to show the extent to which a particular treatment extends life and improves quality of life at the same time. QALYs are an important outcome measure in several influential value frameworks, such as ICER's value framework. QALYs are also used extensively to make healthcare coverage and reimbursement decisions in other countries. For example, the National Institute for Health and Care Excellence (NICE) in the United Kingdom uses QALYs when determining what Britain and Wales' single-payer healthcare system, the National Health Service (NHS), will cover. Health outcomes for some patients with chronic illnesses and disabilities (such as patients with lung cancer) are notably worse in the United Kingdom than in the United States.[7]

Many stakeholders are therefore concerned that the way QALYs are calculated devalues treatments that extend the lives of people with disabilities, or treatments that mitigate—without eliminating—the impact of disability on their health. They argue that if value frameworks that use QALYs become more influential, people with disabilities will lose access to needed care. Other stakeholders view QALYs as a way to provide necessary information on the benefits and costs of healthcare in a healthcare system that has been put under strain by rising costs. This report examines how QALYs are calculated, the bioethical implications of using QALYs, and the history of the use of QALYs in the United States.

Summary of Methodology

In order to get a clear and comprehensive picture of the use of QALYs in the United States, the NCD research team consulted bioethicists, patient rights advocates, researchers and health economists, people with disabilities and their families, and relevant scholarly articles from bioethical, economic, insurance agency, and healthcare system perspectives.

Qualitative Data

To understand how the quality-adjusted life year was used by payers and to better inform the conclusions reached, NCD conducted seven in-depth interviews with disability rights advocates, representatives of advocacy organizations who serve patients, two bioethicists with a significant understanding of the ethical issues presented by QALYs, a representative of an organization that reviews value frameworks to determine their degree of patient-centeredness, and a representative of the nonprofit Institute for Clinical and Economic Review, which uses QALYs. Additionally, the research team conducted a stakeholder convening on September 24, 2018 to inform and aid NCD in the initial development of this report.

Literature Review

To obtain information on how QALYs are used, as well as the perspectives and opinions of ethical experts and experts in the field of health

economics on its use, NCD reviewed articles from research journals, bioethics journals, and news articles pertaining to the use of the quality-adjusted life year. NCD also conducted an in-depth review of several value frameworks, including FasterCures' Patient Perspective Value Framework, ICER's Value Assessment Framework, and the condition-specific decision-making tools created by the Innovation and Value Initiative.

Chapter 1: How QALYs Are Calculated and the Impact on People with Disabilities and Patients with Chronic and/or Degenerative Illnesses

The Purpose of QALYs

In order to understand how to calculate QALYs, it is important to explain both what QALYs are supposed to represent, and why they are used.

What QALYs Represent

Normally, when a researcher or scientist tries to determine whether or not a healthcare treatment (like chemotherapy) improves health, they are looking at one of two different things:

- whether the treatment extends the patient's life, or
- whether the treatment improves the quality of the patient's life.[9]

While measuring whether or not a treatment extends life is fairly straightforward, measuring the degree to which a treatment improves someone's quality of life is more complicated. The portion of a person's quality of life that relates to their health is called their health-related quality of life.[9]

Health-related quality of life is a broad concept. According to the Centers for Disease Control and Prevention (CDC), at the individual level, it may include a person's mood and energy levels, their physical and mental health, and the elements of the person's life that contribute to these factors—such as some aspects of the person's disabilities, health risks, and their social and socioeconomic status. If measured at the population level, it includes any "conditions, policies, and practices that influence a population's health perceptions and functional status."[10] Health researchers and government agencies (including the CDC itself, by conducting population-level surveys using a set of 14 questions called "Healthy Days Measures")[11] have created different means of measuring health-related quality of life.

When healthcare payers decide how to spend their money, they are often looking for some way to represent all the benefits a particular treatment provides at once, as this saves them time. However, studies of treatments tend to measure benefits of treatment that are qualitatively different from one another, such as life extension and quality of life, separately from one another. For example, a study could measure the length of time a patient survives after treatment, or the number of days the person is free from pain, but perhaps not both in the same study.[12] It may be difficult, therefore, to directly compare the value of a treatment that primarily extends life to the value of a treatment that primarily improves quality of life.[13]

QALYs are one attempt to get around this problem. QALYs are the product of an equation designed to "combin[e] the effects of health interventions [treatments] on morbidity [quality

of life] and mortality [quantity of life] into a single index."[14] The QALY equation does this in a rather simplistic fashion. It simply lowers the value of a year of treatment by the degree to which an illness or disability is perceived to harm the person's quality of life during that year.[15] QALYs typically are calculated before and after treatment to determine the degree to which a treatment improves the number of QALYs gained by the patients being studied.[16]

QALYs are calculated by multiplying a decimal number between 0 and 1, which represents a person's health-related quality of life, by a number representing quantity of life. The "quantity" can be the number of years by which the treatment extends life, the number of years a person expects to have to take the treatment, the amount of time a person has left to live, or any other time period relevant to the researcher. A typical QALY calculation is shown in the "QALY Calculation" box.

"The QALY works by weighting the lives of people with disabilities: If we were to assign autism a disability weight of 0.2, that [number] would mean that a year in the life of an autistic person would be worth 80 percent of a nondisabled person's life. Different disabilities would get a different number . . ."

Ari Ne'eman, a disability rights advocate and expert on QALYs, described what QALYs are and what they do in this way:

> The QALY works by weighting the lives of people with disabilities: If we were to assign autism a disability weight of 0.2, that [number] would mean that a year in the life of an autistic person would be worth 80 percent of a nondisabled person's life. Different disabilities would get a different number, if you assigned 0.5 to a mobility impairment, then a year in that person's life would equal 50 percent of a nondisabled life year.

A flowchart showing how QALYs would be calculated if the researcher or scientist used a commonly utilized questionnaire—the EQ-5D—is included as Appendix A of this report.

Why QALYs Are Used

Why would it be *necessary* to measure both quantity of life and health-related quality of life at the same time? The most frequently provided explanations in research literature for the use of QALYs are: (1) to compare the impact of multiple treatments for unrelated conditions to one another; or (2) to assess whether a new treatment or drug would be more cost-effective than the drug or treatment that is currently being used.[17]

This report focuses on the most common use of QALYs: their use by health economists, researchers, and nonprofits to perform cost-effectiveness analyses (CEAs) and health technology assessments (HTAs); the

QALY Calculation

Number between 0 and 1 representing quality of life of x number of years = number of QALYs

subsequent use of CEAs and HTAs by private and public health insurers to determine what drugs or treatments they will fund; and the real and potential negative impact CEAs and HTAs have on people with chronic illnesses and disabilities' access to physician-recommended drugs and treatments.

Cost-Effectiveness Studies

Cost-effectiveness studies are designed to compare various healthcare treatments to each other and determine whether the benefits of a healthcare treatment are worth the treatment's cost. The type of cost-effectiveness study that uses QALYs is called a cost-utility analysis (CUA).[18] In a CUA, the number of QALYs gained from treatment is a measure of the "health outcome," or the overall benefit of the treatment.

The difference between the cost-effectiveness of the treatment being examined and another treatment being examined by the researcher (typically, the treatment currently in use) is referred to as the treatment's incremental cost-effectiveness ratio, or "ICER."[19] The ICER is often used when comparing the cost-effectiveness of multiple treatments.[20] When using QALYs, the ICER is often referred to as the treatment's "cost per QALY," although it is possible to get the "cost per QALY" of a single treatment.[21] At its most simple, it is important to know that the lower the cost per QALY, the more cost-effective the treatment is considered to be.

QALYs are also used in some of the decision-making tools known as "value frameworks." When QALYs are used in a value framework, it is typically because CUA studies are used as evidence of the benefits and costs of the treatment being evaluated by the report. Use of the report can mean that, instead of having to weigh any number of complex considerations relating to whether or not a treatment should be covered, payers can simply fund the treatment that has a better "cost per QALY," according to its corresponding report. CUAs and other QALY-based reports and research studies are *not* healthcare policies in and of themselves, but rather are used to inform the development of healthcare policies (for example, insurers' drug formularies).

The EQ-5D, a questionnaire frequently used to calculate QALYs, is used in countries as diverse as the United Kingdom, Iran, and China.

Calculation of Quality-Adjusted Life Years

While the equation used to calculate QALYs is always the same, there is no one single way to calculate the numbers that go into that equation. For instance, there are many different ways to calculate the number between 0 and 1—often called the "health utility"—that represents health-related quality of life. However, there are common methods typically used by many health economists and researchers employing QALYs in CUA studies. Many components often used to calculate QALYs are used internationally. The EQ-5D,[22] a questionnaire frequently used to calculate QALYs, is used in countries as diverse as the United Kingdom,[23] Iran,[24] and China.[25]

Health Utilities

To calculate a QALY, it is necessary to determine *by how much* not being in perfect health impacts a person's quality of life. QALYS do this by assigning a number between 0 and 1, called a health utility, to the various conditions a person's health could be in (often called "health states").[26] A 0 would represent the lowest possible quality of life, while a 1 would represent the highest possible quality of life. Health states are represented by points on the scale of 0 to 1—for example, 0.2, 0.5, 0.8.

Health utilities are typically derived from surveys, which attempt to determine how much survey participants would prefer to be in one health state as compared to another. Health states do not correspond directly to specific disabilities—they instead represent the degree of impairment a person has in specific, limited categories of functioning (such as mobility, ability to perform tasks, etc.). However, most disabilities share some or all characteristics of a health state. Therefore, the goal of a "health utility" is, in effect, to measure the degree to which having a particular form of a disease or disability, such as "having late-stage cancer" or "having a specific type or degree of type 2 diabetes," is viewed as negatively impacting quality of life as compared to a state of perfect health.[27]

Use of the EQ-5D requires patients to rate the degree to which they have "problems" with only a few extremely broad categories of "physical, cognitive, or social functioning," rather than the myriad of effects someone's health could have on their quality of life.

Questionnaires Used to "Describe" the Health State, and Their Flaws

As noted above, the first thing the researcher has to do is determine how having a disability or illness impacts a person. Typically, in order to obtain this information, the researcher has a sample of patients with the illness, condition, or disability fill out a survey or questionnaire.[28] There is no one, single definitive questionnaire or survey that is used.[29] The most common questionnaire is the EQ-5D.[30] The EQ-5D is extremely popular internationally.[31]

The EQ-5D takes an extremely limited approach to measuring "quality of life." Use of the EQ-5D requires patients to rate the degree to which they have "problems" with only a few extremely broad categories of "physical, cognitive, or social functioning," rather than the myriad of effects someone's health could have on their quality of life.

The EQ-5D surveys patients' health as it relates to five "dimensions" of quality of life: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression.[32] These five categories do not measure the wide variety of impacts a disability or illness could have on quality of life. NCD interviewed the bioethicist Joseph Stramondo, who said "I think that, while there is a relationship between disability and quality of life, it is extremely variable, and impossible to generalize. There are all kinds of things [about disability and illness] that impact quality of life on a case-by-case basis: relationships, income, accessibility considerations." Moreover, neither "self-care" nor "usual activities" are defined in detail anywhere in the sample questionnaires available

on the EQ-5D website, meaning that many patients may not know what these terms mean for them. Furthermore, there is no way to account for external factors, like the availability of reasonable accommodations or the accessibility of the built environment, as a factor in the assessment of quality of life with a disability, despite the fact that these factors play a significant role in determining the life experience of many people with disabilities.

Impacts on these dimensions are then rated by "severity." Different forms of the EQ-5D exist. The oldest and most commonly used form, the EQ-5D-3L,[33] assigns three "levels of severity" to each of the five dimensions. For each dimension, it is possible for the person taking the survey to respond "I have no problems," "I have some problems," or "I have extreme problems."[34] For example, the EQ-5D-3L User Guide includes the following sample question on mobility:

Questions Asked on the EQ-5D-3L Questionnaire

Mobility

- I have no problems in walking about
- I have some problems in walking about
- I am confined to bed

Note that this question is focused on whether a person has problems "walking about," and the most severe problems are described as the person "being confined to bed." The questions do not appear to consider the possibility that a person who cannot "walk about" can still move, such as a person who cannot walk but who can use a wheelchair.

Nor does the EQ-5D consider the possibility that a person who can walk may nevertheless have significant trouble leaving the home due to other concerns, such as the need to stay near medical equipment, concerns about exposure to infections, or agoraphobia.

"I think that, while there is a relationship between disability and quality of life, it is extremely variable, and impossible to generalize. There are all kinds of things [about disability and illness] that impact quality of life on a case-by-case basis: relationships, income, accessibility considerations."

As noted by Stramondo and a colleague in an article on disability and its relationship to quality of life, impairment in performing a specific task may have no relationship to quality of life.[35] The questionnaire assumes that a person will experience difficulty with walking as a significant barrier to subjective quality of life when, in fact, this is not true of many people with mobility impairments. Although there are several versions of the EQ-5D, and other versions do not phrase the question and/or questions in this manner, the other versions also assume that being unable to walk has a severely negative impact on quality of life.[36]

In the EQ-5D-3L, each dimension receives a score from 1 to 3, where one is the best possible score and 3 is the worst possible score. Thus, a person who checked the first box, "I have no

problems," would be assigned a score of 1 for mobility.[37] Filling out the entire questionnaire generates a series of five numbers, each of which is between 1 and 3. For example, a score of 11111 means the person is in perfect health, whereas a score of 11223 means the person has no problems with the first two dimensions, some problems with the next two, and extreme problems with the final dimension.[38]

When using the EQ-5D-3L to calculate QALYs, it is this series of five numbers which was actually evaluated, as opposed to the actual disability and the actual effect of the disability on physical or psychological functioning as reported by people with that disability. The people who decided the value of life with a particular condition only saw those five numbers and/or a description of what those numbers meant.[39]

Aside from the dehumanizing implications of disability's impact on quality of life being reduced to a series of five numbers, if two different disabilities had exactly the same impact on physical or psychological functioning, they would have exactly the same health utility value for the purpose of calculating QALYs—even if they had other differences that some people may consider relevant to "quality of life." The numbers are based only on the disability or illness' impact on "physical, psychological, cognitive, social or other kinds of functioning,"[40] as defined by the survey.

Patients with two conditions with the same utility value may have very different opinions about which aspects of their conditions are most important to address, and what kinds of treatments would most improve their lives. Nonetheless, treatments that improved their health utility scores to the same degree would be treated as having the exact same value to the patients. For example, patients with Disability A could place a higher value on reducing pain and a lower value on reducing anxiety and depression. Patients with Disability B could place a lower value on reducing pain and a higher value on reducing anxiety and depression. If patients with these disabilities received the same average EQ-5D score, a treatment that reduced pain would be treated as if patients with Disability B valued it to the same degree as patients with Disability A.

Patients with two conditions with the same utility value may have very different opinions about which aspects of their conditions are most important to address, and what kinds of treatments would most improve their lives. Nonetheless, treatments that improved their health utility scores to the same degree would be treated as having the exact same value to the patients.

Most other questionnaires share similar issues. For example, the SF-6D looks at the impact of an illness or disability on "physical functioning," the degree to which one's emotional problems limit their ability to perform daily tasks, and so on, and uses specific, narrow questions to determine the impact.[41] Additionally, using different questionnaires results in different numbers of QALYs, which raises validity and reliability concerns, when different methods produce results that are not comparable.[42]

The validity of these generic questionnaires can be called even further into question by the

fact that the utility values are often not calculated separately for each individual cost-effectiveness study. Instead, the utility values are often based on the outcome of specific past studies in which members of the general public valued a sample of the possible health states (with values for the health states not valued determined mathematically from the values of the health states that were valued).[43] The EuroQoL group, maker of the EQ-5D, refers to these studies as "value sets."[44]

Valuation of Disability

Regardless of how the impact is assessed, once the researcher assesses the impact of a health condition on health, the researcher needs to determine how much "worse" it is to be in that condition as compared to perfect health. This is done by determining the degree to which a group of people would prefer to be in that health state as compared to perfect health.

[U]sing different questionnaires results in different numbers of QALYs, which raises validity and reliability concerns, when different methods produce results that are not comparable.

The researcher can either measure the preferences of patients with the disability or measure the preferences of the general population.[45] While there are those in the field that advocate for using "patient preferences"[46] and those who advocate for using "population preferences,"[47] the overwhelming majority of studies use the preferences of members of the general population (76 percent, according to one study).[48]

The preferences of the general population are typically calculated by surveying a sample of the general public and asking them a series of questions. Researchers performing a CUA ask a person to imagine a hypothetical situation and respond to questions about that hypothetical situation. There are two types of questions researchers typically ask the public: Time Trade-Off questions and Standard Gamble (SG) questions.[49]

In a Time Trade-Off, survey participants are asked to determine how many years of living with a particular disability (for example, 70 years of blindness) they would trade for a shorter number of years spent in perfect health (for example, 50 years of perfect health).[50] In a Standard Gamble, the participants are asked to imagine having a disability and then are asked whether they would undergo a procedure that had, for example, a 50 percent chance of returning them to perfect health and a 20 percent chance of instantly killing them.[51]

If members of the public respond in a way that suggests that they see 20 years in a health state corresponding to a specific type of blindness and 17 years of perfect health as having the same value, the researcher will divide 17 by 20 to get a health utility value of 0.85 for the health state corresponding to that specific type of blindness.[52]

Many would contend that members of the general public do not accurately understand the experience of life with a disability and will systematically underestimate the value of disabled quality of life. However, surveying people with disabilities poses other problems. Since people with disabilities tend to rate their quality of life as higher than the perception of it from the

general public, leading to lower health utilities, the use of survey responses from people with disabilities will increase the value of life-extension while reducing the value of quality of life improvements. Because the QALY compresses these two factors into a single number, it forces a choice between prioritizing life extension and quality of life improvement. In one article, bioethicists referred to QALYs' inability to simultaneously value treatments that extend and improve the lives of people with disabilities as "the QALY trap."[53] According to Ne'eman, this problem can be substantially mitigated or eliminated by using diagnosis- or domain-specific measures, such as lung function, pain scales, or functional skills, since these do not conflate morbidity and mortality into a single number. As Ne'eman stated in his interview with NCD:

> If you go with a system [for calculating QALYs] that surveys the general public, you are likely to end up with more resources willing to be spent on disability or disease mitigation. If you survey [people with disabilities], you're likely going to end up with more going to life extension. But it forces you to choose. Then you should ask—is this a good system?

This speaks to one of the fundamental flaws of the QALY: that the conflation of life extension and quality of life improvement benefits into a single number forces people with disabilities into a cruel trap: picking whether they would rather live longer or have improved quality of life, when both are entirely feasible in a society willing to invest sufficient resources.

Dr. Steve Pearson, bioethicist at the National Institutes of Health and the President of ICER, agrees that surveying only people with the condition is problematic, but surveying the healthy community is also problematic unless they are informed about the conditions they are judging. According to Dr. Pearson,

> In order to get the best information, they [the healthy community] need to know what it is like to live with that condition. You want to know if their opinion on how bad something is, is higher or lower or the same as the person who actually does have the condition. . . . Maybe the healthy person, with no knowledge of the condition, would think the opposite of the person with the condition. Maybe they think it is not so bad having psoriasis, maybe it's a skin rash that's not so bad. But then you talk to a person with psoriasis and they say, "It's awful—you never want to have this! It's painful—you have no idea." . . . Though there are hypothetical and ethical reasons people tend to still use the healthy community, it still should be informed by the patients.[54]

In one article, bioethicists referred to QALYs' inability to simultaneously value treatments that extend and improve the lives of people with disabilities as "the QALY trap."

David Wasserman, a bioethicist at the National Institutes of Health, also agrees with the limitation of surveying only people with the conditions, but believes that surveying the healthy community, even when they are provided

with information about the condition, is not effective. According to Wasserman,

> Public opinion is extremely labile. It's influenced by a lot of factors like media presentation, exaggerated optimism, occasionally by excessive skepticism, by poignant anecdotes . . . so, I don't think that you can generally trust popular judgments. Even carefully elicited popular judgments have serious problems. One approach is that we should rely on the preferences of the general public about health states, but the general public doesn't have the health states in question, so let's give them information on how people in those health states regard them. But even if you give them that information, they will almost surely disregard it. . . .[55]

Calculating QALYs

The method for calculating QALYs is best expressed using an example. This example additionally demonstrates one of the primary ethical objections to the use of QALYs.

Example 1: Connie and Bill

Connie has a disability. People with Connie's disability have difficulty performing daily living tasks and lose the ability to walk. Connie now uses a wheelchair for mobility, as do most people with Connie's disability. Without treatment, people with Connie's disability have 4 years left to live after they are diagnosed. Based on the responses of patients with Connie's disability to the EQ-5D, researchers have calculated the health utility, or value of a life with Connie's problems with daily living and need for a wheelchair, as 0.5. To get the number of quality-adjusted life years she would get from living for 4 years with her disability, one must use the following equation:

> 0.5 (health utility) × 4 (the number of years Connie has left to live) = 2 QALYs

Thus, the 4 years people with Connie's disability are expected to live without treatment would be valued at only 2 QALYs.

A drug that is found that would extend the life of people with Connie's disability by 20 years, but it would not remove or reduce the impact of the disability on daily living; they would still use wheelchairs. The health utility of their condition is still 0.5. Thus, Connie's life expectancy with treatment is valued at 10 QALYs. This can be expressed via the following equation:

> 0.5 (utility value) × 20 (the number of years Connie would have to live if the treatment for patients with her disability was covered) = 10 QALYs

If people with Connie's disability were the only patient demographic that needed health care, the treatment that people with Connie's disability needed would probably be considered cost-effective for the insurer because these individuals would gain 8 QALYs from being treated.

However, there is another patient, Bill. Bill has a medical condition that also has a health utility of 0.5 and that causes patients with that disability to need a wheelchair. Patients with Bill's disability will only live for another 4 years without treatment, and would also gain only 2 QALYs during those 4 years without treatment.

There is a drug that would extend the lives of these patients to 20 years, but would also raise their quality of life back up to 1—the utility value for "perfect health." This would mean that Bill and other patients with his disability would no longer have difficulty with daily living tasks and no longer need a wheelchair. This can be shown using the following equation:

1 (health utility) × 20 (the number of years Bill could live if the treatment for patients with his disability was covered) = 20 QALYs

Given that patients with Bill's condition will gain 18 QALYS from being treated as compared to patients with Connie's condition, who would only gain 8 QALYs, the drug for patients with Bill's condition will be considered more cost-effective than the drug for patients with Connie's condition. For the purposes of this example, the two treatments cost exactly the same amount of money, and the payer only has enough money to pay for one of these two treatments at this time. If the payer relies on QALYs to determine how cost-effective the two drugs are, the payer will favor covering the treatment patients with Bill's disability need over the treatment patients with Connie's disability need.

In an environment with scarce resources, Bill's condition will be more likely to have treatments for it funded than Connie's. While these decisions are typically made at the population level, rather than in relation to specific patients, they create an environment of systemic inequality, where people with disabilities and chronic conditions that will be managed, rather than cured, are less likely to receive access to treatment under health systems that ration care utilizing the QALY.

Calculating Cost per QALY

When trying to decide whether to cover a treatment, most payers are interested in the "incremental cost-effectiveness ratio," which is typically the difference between the cost-effectiveness of the treatment that is being studied as compared to another treatment (which is often either another possible treatment for the same illness or problem, a placebo, or the standard therapy that is currently in use).[56] In the box "Cost per QALY," "ICER" stands for incremental cost-effectiveness ratio. As explained above, the ICER is often referred to as the "cost per QALY," although the cost per QALY of a single treatment can theoretically be calculated. One can calculate the ICER by using this formula.[57]

Cost per QALY/ICER

$$ICER = \frac{(C1 - C0)}{(E1 - E0)}$$

In this formula, C means "Cost," C1 represents the treatment being studied, and C0 represents either the current treatment or another treatment being considered for coverage. E means "Effect," E1 represents the number of QALYs gained from the treatment being studied, and E0 represents the number of QALYs gained from either the current treatment or another treatment being considered for coverage. To obtain the "cost per QALY" of a single treatment rather than an ICER (although this is less common), divide the treatment's cost by the number of QALYs gained from treatment.

Some payers have a specific threshold cost-per-QALY. For example, a payer could decide that they will not cover any treatment that costs more than $50,000 per QALY.

Methodological Flaws of Quality-Adjusted Life Years

QALY calculations are subject to several methodological flaws that seriously undermine their use as a fair method of comparing the relative value of treatments.

QALYs Do Not Fully Measure Health-Related Quality of Life

One significant flaw of QALYs is simply that they do not measure what their proponents claim they measure: the combined impact a treatment has on life expectancy and quality of life. As discussed in the section "Questionnaires Used to 'Describe' the Disability and Their Flaws," the generic, population preference-based questionnaires often used to calculate QALYs only measure a few specific impacts of health on quality of life, such as pain or anxiety/depression, and may not measure these accurately and in a way that fully considers the possible accommodations available to a person with a disability. This means that QALYs undervalue treatments that affect aspects of quality of life other than what they specifically measure. For example, many people with psychiatric disabilities report significant side effects associated with certain medications, like tardive dyskinesia or weight gain. QALY calculations might not value medications that allow people with disabilities to avoid these side effects, since they focus only on measures surrounding the mitigation of the primary condition rather than the complex context surrounding that individual's life.

This means that QALYs undervalue treatments that affect aspects of quality of life other than what they specifically measure.

Similarly, the level of quality of life experienced by a person with a disability or patient may shift dramatically based on nonhealth factors, such as the availability of reasonable accommodations or the accessibility of the built environment. For example, the impact of a mobility impairment on quality of life is significantly altered based on the availability of a wheelchair and a built environment that encompasses ramps. Similarly, the impact of a cognitive disability is significantly altered based on the availability and quality of special education services. Typically, the use of QALY assessments in healthcare contexts do not consider these factors, which may play an equal or greater role in quality of life than a purely medical assessment. Additionally, the utility values used to describe the extent to which a disability impacts quality of life are derived from people without disabilities, who often have prejudices and biases that lead them to drastically undervalue life with a disability.

Palliative Care

Failure to consider all aspects of quality of life, combined with the weighting of quantity and quality of life simultaneously, may lead QALYs to undervalue treatments that are purely palliative in nature. The main purpose of palliative care is to alleviate the pain and suffering of a person who has a serious and/or life-threatening illness. Often, these illnesses are expected to lead to death, as in the case of late-stage cancer or kidney

disease.[58] Palliative care may include treating pain, fatigue, reducing the difficulty the person has sleeping, or reducing the amount of anxiety and depression experienced by the person.[59]

The first problem is simply that palliative care patients often are not expected to live for many more years. Since QALYs measure both quality *and* quantity of life in the aggregate, and palliative care rarely improves a patient's life expectancy, a patient cannot expect to gain many QALYs from a palliative care treatment.[60]

The second problem is that there are things that are very important to palliative care patients' evaluation of their own quality of life—such as spiritual contentment and personal dignity—that are rarely if ever measured by the generic questionnaires (such as the EQ-5D) used to calculate QALYs.[61] This may mean that palliative care is undervalued as compared to other treatments.

Failure to consider all aspects of quality of life, combined with the weighting of quantity and quality of life simultaneously, may lead QALYs to undervalue treatments that are purely palliative in nature.

Finally, QALYs assume that the value of a year of life to the patient is the same regardless of when that year is lived, which most studies have found is simply not true, from the patient's perspective. Patients with a limited number of years left to live typically value a year much more highly than people who have many more years left to live.

Dr. Steve Pearson disagrees with the concern that, due to their design, QALYs may undervalue palliative care treatments and treatments that mitigate the impact of a disabling condition, but do not cure it or extend the patient's life. Pearson told NCD that the QALY would do exactly the opposite, and that,

> We [the Institute for Clinical and Economic Review] did a cost-effectiveness analysis of outpatient palliative care that showed it was cost-saving. When something is cost-saving you don't do cost-effectiveness analysis per se, but the thing about palliative care is that it improves quality of life without extending life—although some palliative care does, and the sicker you are the better that will look, in some sense, because if you are already quite well there's not much to palliate . . . the QALY was built to capture improvement in quality of life of that type.

Pearson thinks that "the question is which is the more cost-effective way to provide pain control for [people who are] dying, not whether we [as a society] should or shouldn't."[62] This may be the case if the cost-effectiveness of palliative care treatments were being compared to hospitalization (or another high-cost, low-value treatment for the patients who typically utilize palliative care) or only to other palliative care treatments. It is, however, difficult to know if this would be true if palliative care treatments were competing with other uses of the same funds, at the budgeting level.[63] Even researchers who support the use of QALYs in palliative care note that "the brevity of lifespan affected results in palliative care yielding a fraction of a QALY unit," and that the use of QALYs to help allocate healthcare funding means that new palliative care treatments are always competing with alternative uses of the same money.[64] While payers are not attempting to

determine whether pain care for the dying is "worth it," they may be attempting to determine whether *improving* pain care is, as compared to some other use of their limited funds.

Additionally, researchers who are interested in utilizing QALYs for palliative care typically propose modifying the standard QALY, either by using palliative care-specific questionnaires that do evaluate the quality of life aspects most important to palliative care patients or by incorporating their higher valuation of time spent at the end of life into the calculation.[65] Other researchers propose only comparing end-of-life treatments to other end-of-life treatments.[66]

The need to modify the standard QALY to work for palliative care indicates that QALYs are unsuitable without modifications. There are likely many other specific diseases and circumstances for which the use of QALYs is unsuitable without modifications, which undermines the claims of those who state that QALYs are a metric that can be used to compare the value of treatments for unrelated conditions.

When Health Utilities Are "Zero"

QALYs could produce problematic results if a treatment extends the life but does not significantly improve the "quality of life" (as measured by QALYs), of a patient whose life's worth has been measured as 0, close to 0, or less than 0. In these cases, even the cheapest treatments to extend life would not be considered "cost-effective" according to a cost-per-QALY standard.

There are likely many other specific diseases and circumstances for which the use of QALYs is unsuitable without modifications, which undermines the claims of those who state that QALYs are a metric that can be used to compare the value of treatments for unrelated conditions.

When Health Utilities Are Less Than 0

Patients with Life-Threatening Condition Y fill out the EQ-5D questionnaire and get a score of 33333. Solely in this example, members of the general population who performed a Time Trade Off decided that the utility value of this health state (and by extension, therefore, Life-Threatening Condition Y) was 0. Treatment 1 would extend the lives of patients with Life-Threatening Condition Y by a year. However, the following simple equation illustrates that these patients would nonetheless obtain 0 QALYs:

0 (health utility) X 1 (number of years by which Treatment 1 extends their life) = 0 QALYs

This is due to the way that QALYs aggregate quality of life and quantity of life. "When Health Utilities Are Less Than 0" explains how this can happen in more detail.

For example, if the health utility of having a particular disease or disability is measured as 0 or negative, it may inevitably lead to the conclusion that the person is "better off dead" and that treatments that prolong such a life are not cost-effective.[67] Such an outcome would only be acceptable if a person were in a health state in which everyone

would agree that continued life has no value. However, as the bioethicist Stephen Barrie noted, the meaning of the "zero" on the health utility scale is ambiguous and patients do *not* always agree that continued life in a health state that earns very low or even 0 QALYs has no value. A score of 0 QALYs has meant "being dead," "dying," and "worst possible health state," depending on the study and who was doing the calculating—and these are three very different things.[68] Some individuals may believe "dying" is worse than "being dead." Some people with a health state that has been judged to be the "worst possible" may wish to discontinue treatment, while others may still highly value an additional year of life. QALYs do not make these distinctions—researchers using them would need to treat all three health states as equally valueless.

A score of 0 QALYs has meant "being dead," "dying," and "worst possible health state," depending on the study and who was doing the calculating—and these are three very different things.

Distinguishing Between Subgroups of Patients with the Same Condition

Some individuals argue that QALYs do not distinguish between subgroups of patients with the same condition. Subgroups of patients include but are not limited to patients of different races/ethnicities, patients with different genders or ages, and patients with other co-occurring illnesses.[69]

Differences between patient subgroups may have a significant impact on the outcome of a CUA study. One study, which reviewed 200 of the 642 English-language CUAs in the Tufts Medical Registry, found that only 19 percent of these studies reported on any differences between subgroups.[70] Additionally, most studies only reported differences based on age.[71] The authors hypothesized that failure to account for subgroup differences may lead to payers funding treatments that are of relatively low value or even harmful to some subgroups.[72] Additionally, if payers only study subgroups for whom the treatment is of low value, they may not fund treatments that are of high value to some subgroups but of low value to others.

Different groups of patients, people with disabilities, or people with chronic illness may have dramatically different medication responses. QALYs often rely on research that does not adequately account for the ways in which many people—especially, though not exclusively, those with rare conditions—may have medication responses that vary dramatically from the average, either in terms of medication efficacy or side effects. This can create serious challenges under QALY-based systems, since a QALY calculation may result in a particular medication

QALYs often rely on research that does not adequately account for the ways in which many people—especially, though not exclusively, those with rare conditions—may have medication responses that vary dramatically from the average . . .

being deemed cost-ineffective based on the average patient response, whereas for patients within a particular subgroup or who have atypical medication responses, it is the only medication that works or the only one that provides outcomes without terrible side effects.

Accounting for Clinical Knowledge Not Reflected in the Research Literature

For individuals with rare conditions or who come from groups underrepresented in research, like people with disabilities and people of color, the inability of QALYs to account for information that primarily exists within clinical knowledge but has not yet made it into the research literature constitutes a serious problem. Many rare conditions do not have an adequate research literature to account for different subgroups or variation between patients in medication response. Since it can be difficult to study small populations, such knowledge may only exist on the part of the relatively small number of clinicians who specialize in treating such patients.

There have been ethical objections to use of QALYs nearly since they were first invented. There are three primary ethical objections: (1) that disability may not actually reduce quality of life; (2) that QALYs discriminate against people with disabilities; (3) that QALYs fail to account for differences between what patients with the same condition value.

Does Disability Reduce Quality of Life?

Some stakeholders, but especially bioethicists and people with disabilities, have argued that QALYs are built on a faulty premise: that life with a disability is inherently worse than life without a disability. As established in the section "Calculation of Quality- Adjusted Life Years," QALYs work by lowering the value of the life-extending properties of treatment (or the number of years the individuals being treated would normally have left to live) by the degree to which an illness or disability negatively impacts quality of life.[73] While QALYs are theoretically determining the "worth" of living in specific health *states* and not with specific disabilities (and from this, the value of treatments that extend life or affect these health states), the reality is that people with specific disabilities have characteristics that match up with these health states. Being unable to walk, for example, is a core characteristic of paraplegia.

As described earlier in this report, QALYs typically evaluate the worth of a life with a disability based on the preferences of people from the general healthy population, most of whom do not have disabilities.[74] Disability rights advocates are rightly concerned that these preferences are not based on an accurate understanding of what it is like to have a disability, but on stereotypes and a lack of understanding about disabilities. While some bioethicists believe that this can be mitigated by providing the general healthy population with information about the conditions to help inform their responses, others see this as flawed, such as Dr. David Wasserman, bioethicist at NIH, who told NCD that there is a great deal of evidence that most of the general public and the medical profession in particular, overestimate the badness of being in various health conditions that are classified as disability.[75]

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Legal scholars Wendy Hensel and Leslie Wolf state that

> quality of life considerations are not neutral, even when couched in mathematical terms, and are very likely to be driven by prejudices and stereotypes concerning the desirability of life with disabilities. . . . By favoring those with no functional impairments, the protocols implicitly endorse the belief that the lives of individuals without disabilities are more valuable than that of their unfortunate counterparts.[76]

"By favoring those with no functional impairments, the protocols implicitly endorse the belief that the lives of individuals without disabilities are more valuable than that of their unfortunate counterparts."

Although surveyors continue to rely on the healthy community's preferences for various health states, it is well known that this will skew the results of QALY analysis. The general population consistently rates life with a disability much more negatively than people with disabilities themselves do. In a study with more than 2,044 participants from the general US population, 47 percent of all participants rated blindness as "the worst health condition that might befall them."[77] They ranked blindness as worse than AIDS, heart disease, the loss of a limb, and arthritis.[78] Bioethicist Sean Sinclair, citing a UK study of more than 1,000 people, said that in this study 24 percent of those studied said needing to use a wheelchair for the rest of their life would be *worse than death*.[79]

People with disabilities, however, consistently report that they get approximately the same degree of satisfaction from their lives as people without disabilities. One study reported that patients with "locked-in syndrome"—a disability in which individuals are unable to move part or all of their bodies—self-report having a similar quality of life to people without disabilities.[80] An older 1979 study found that blind people, contrary to the beliefs of the general population, were about as happy or slightly happier than people who could see.[81] Gallaudet professors Dirksen Bauman and Joseph Murray have written that Deafness should be reframed from "hearing loss" to "Deaf Gain," in recognition of the ways in which Deaf people contribute to human diversity.[82]

People with disabilities, however, consistently report that they get approximately the same degree of satisfaction from their lives as people without disabilities.

Does the Use of QALYs Discriminate Against People with Disabilities?

The use of QALYs may lead to the devaluing of treatments that extend the lives of people with disabilities. One of the earliest and most well-known explanations of this problem was by Harris, who articulated his concerns in a 1987 journal article.[83] Harris argued that the use of QALYs would lead to a situation in which funding treatments that extended the lives of people who could be restored to perfect health would be valued over treatments that extended the lives of people who could not be restored to

perfect health, such as people with disabilities and chronic illnesses.[84] Harris argued that it was morally unjust for QALYs to lead to the prioritization of the former over the latter.[85] Harris said we should adopt policies that "do not violate the individual's entitlement to be treated as the equal of any other individual in the society."[86]

Disability rights advocates and people with disabilities oppose the use of QALYs for similar reasons.[87] Disability rights advocates are concerned that the widespread use of QALYs by health insurance companies and healthcare agencies will deny people with disabilities access to the care that they need.[88] Disability rights advocate Ari Ne'eman explained that such denials of care have in fact already happened to people with disabilities in countries that use QALYs more regularly. For example, as described in more detail in Chapter 3, the United Kingdom's NICE determines which drugs Britain's national health insurance program will cover by using QALYs. NICE recently denied coverage of three "groundbreaking" drugs for extremely rare and debilitating conditions.[89]

Ne'eman's article states:

> All three drugs work by slowing irreversible organ damage and cell death. While they can and do improve current symptoms, their greatest promise is in halting or delaying disease progression. . . . Specialty drugs may still be able to add years to these patients' lives, but NICE and other QALY-based systems discount the value of each of these years [because they are years lived with a disability.][90]

Proponents of QALYs argue that such a discount is irrelevant. They argue that QALYs are not used to decide whether to treat individual patients,[91] but, instead, to decide which treatments payers will fund.[92] Bioethicist Greg Bognar states that if a treatment or drug is cost-effective, it will likely be covered. If it is covered, it will be offered to "all patients who need it, regardless of their other characteristics," such as disability or race.[93] Some ethicists argue that in fact, if people with disabilities *are* assessed as having a low quality of life, a treatment that dramatically improved the types of quality of life measured by QALYS would probably be considered very cost-effective.[94]

Additionally, they argue that the number of QALYs a person starts with before treatment does not matter. While people with disabilities seeking treatment for a disability will have lower "baseline" QALYs than a person without a disability, QALYs are primarily designed to determine the degree to which the treatment improves their health. Dr. Pearson provided an example during his interview which illustrates this point:

> So, let's say that you're very sick and your quality of life is 0.3, and we have two treatments. We have a standard treatment, [which] improves the quality of life to 0.4 and we have one that raised quality of life . . . to 0.5. We're trying to figure out which is most cost-effective. Now [next], I've got two other treatments for people that are going to start off at 0.8, which is pretty good. I've got the same two drug treatments—one makes you better by 0.1 and one makes you better by 0.2. The cost-effectiveness calculation is going to be exactly the same for those two comparisons among people that are very

> sick, and the other among people that are pretty healthy. It's a comparison of how much better one is versus the other. . . . It doesn't matter where you start.

However, these arguments do not actually resolve the main concerns of QALY opponents such as Ne'eman—which is that use of QALYs may have the effect of devaluing treatments primarily designed for a population of people with a chronic illness or disability, in practice. If the primary purpose of QALYs is to allow decision makers to determine how best to spend money on health care, which proponents of QALYs do not dispute, then almost necessarily these decision makers are comparing unlike treatments and deciding which of these to fund. As established in Example 1 about Connie and Bill, patients with chronic illnesses and disabilities who retain their disability after treatment do not just start with fewer QALYs than people who can be restored to perfect health—they also *gain* fewer QALYs from treatment than people who can be restored to perfect health. As noted in the section "Methodological Flaws of Quality- Adjusted Life Years" and earlier in this section, there are likely many classes of both treatments, drugs, and the patients they serve where this is the case. Use of QALYs will therefore prioritize treatments like the one for Bill rather than treatments like the one for Connie, even if what is measured is how many QALYs both would gain from treatment.

> *"That's like saying that drugs for cystic fibrosis are also unavailable to patients without cystic fibrosis."*

Health insurers are also not merely choosing between treatments within conditions, although some proponents of QALYs claim as much. Researchers and health economists have repeatedly stated that the primary purpose of QALYs is to allow decision makers to compare the cost-effectiveness of treatments for unrelated conditions.[95]

Further, use of QALYs would not be necessary if health insurers were comparing the cost-per-QALY or QALYs gained from only related treatments. Chapter 5, "Alternatives to the Use of QALYs," describes other ways that payers may compare the cost-effectiveness of different treatments for the same condition without the use of QALYs. It is unlikely, after the passage of the Affordable Care Act, that payers in the United States would refuse to cover an entire class of patients, and QALYs would not act as justification for doing so. However, even if a payer treats all classes of patients, the quality of some classes of patients' care may be worse, or their options more limited, because some of the potential treatments available to them were not deemed cost-effective and therefore not covered by their insurance due to the impact of their disability on QALY calculations.

Harris had an additional objection that is also of significance. In the real world, payers rarely face a choice between treating two disabilities of equal severity. Instead, payers more often face a choice akin to providing a little bit of quality of life to many people versus saving one person's life. For example, a health insurance provider with a limited amount of money may have to choose between funding hip replacement surgery for many people, and funding a high-cost treatment that saves the lives of only a few people with a rare disease. QALYs do not distinguish between the two types of treatment.[96] If funding hip replacement surgery

for a hundred people obtains more QALYs than funding the high-cost treatment, then funding the hip replacement surgery will more than likely be given higher priority, even if the high-cost treatment saves lives. As Harris points out, this is quite inconsistent with the moral intuitions of many people.[97]

More significant ethical problems exist when the only class of drugs known to be effective for a certain group of patients with disabilities is not covered because the drugs are not considered cost-effective.[98] In that situation, it does not matter that QALYs are theoretically meant to be used to evaluate treatments rather than patients. As Ne'eman wryly stated: "That's like saying that drugs for cystic fibrosis are also unavailable to patients without cystic fibrosis." Chapter 3 provides specific examples of situations in which just such a problem has happened in other countries.

Chapter 3: Utilization of QALYs in the United States

Introduction

QALYs have a complicated history of use in the United States. Although QALYs are frequently used in research, their use to determine benefits and coverage has historically been more limited compared to their use for this purpose in other countries. There are likely multiple reasons for this; some health economists attribute it to the United States' cultural aversion to metrics that may discriminate, or the United States' multi-tier, complex healthcare system.[99] To understand this complex usage history, NCD undertook a comprehensive review of how QALYs are used in the United States.

One of the most prominent attempts to utilize QALYs in a state-run health insurance program was found to violate the Americans with Disabilities Act (ADA).

Use of QALYs by the US Federal and State Governments

There is no one, singular policy on the use of QALYs across the entirety of the US government. Each federal agency has a distinct and separate policy, although the overall use of QALYs has followed a pattern over time. QALYs grew in popularity as a measure of cost-effectiveness during the 1990s to 2000s, declined in popularity due to failed implementations of the metric during that time and the passage of the Affordable Care Act, and have recently increased in prominence and popularity due to concerns about rising healthcare costs in the United States.

One of the most prominent attempts to utilize QALYs in a state-run health insurance program was found to violate the Americans with Disabilities Act (ADA). Starting in 1989 and continuing into the early 1990s, the state of Oregon attempted to reform its Medicaid program by ranking treatments in terms of their cost-effectiveness.[100] Oregon created a list of more than 700 paired treatments and diagnoses (an example of a paired treatment and diagnosis on the first list was "Diagnosis: mental disorders with no effective treatment; Treatment: evaluation") and decided it would cover the 587 most cost-effective items on the list.[101] Oregon ranked these pairs according to 13 criteria.[102] Oregon used QALYs in order to measure some of these criteria, particularly quality of life and life expectancy.[103]

The use of QALYs produced counterintuitive results: capping teeth was ranked above

appendectomy as it produced more QALYs for more people in the aggregate, even though an appendectomy saves a life.[104] The Bush administration ultimately rejected Oregon's Medicaid plan, as it was found to violate the Americans with Disabilities Act.[105] A Bush administration official stated in a letter to the editor sent to the *New York Times* that the plan was rejected because it "in substantial part values the life of a person with a disability less than the life of a person without a disability."[106] Oregon's Medicaid program has continued to ration care according to cost-effectiveness, however.[107]

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From the 1990s to the late 2000s, different Federal Government agencies considered how (and where) the Federal Government should utilize cost-effectiveness research. Each of these agencies came to different conclusions about use of QALYs. For instance, in 2007 the Congressional Budget Office (CBO) expressed concerns about QALYs in a paper titled *Research on the Comparative Effectiveness of Medical Treatments: Issues and Options for an Expanded Federal Role*.[108] In the paper, the CBO argues that the United States should take more of a role with respect to promoting the use of comparative effectiveness research.[109] One of the ways the CBO proposes doing this is by creating a new federal entity that commissions, performs, and evaluates comparative effectiveness research and how it relates to policy.[110] The paper evaluates cost-effectiveness in this context. It notes that the use of "common metrics like QALYs" may "raise concerns among patients" and other stakeholders.[111]

In 2006 the Department of Health and Human Services evaluated the cost-effectiveness of one of its population-wide vaccination programs using "years of healthy life saved," a direct reference to the use of QALYs.[112] The US Public Health Service's "Healthy People Initiative," which measured progress toward US public health goals, in 2006 used QALYs "as one of its key metrics."[113] Throughout the late 1990s and the early and mid-2000s the US Food and Drug Administration (FDA) utilized QALYs as part of its agency rulemakings.[114]

The trend toward QALY usage changed with the passage of the Affordable Care Act in 2010. Certain federal agencies, particularly health-related agencies, were prohibited or severely limited in how they could utilize QALYs by the Affordable Care Act.

The trend toward QALY usage changed with the passage of the Affordable Care Act in 2010. Certain federal agencies, particularly health-related agencies, were prohibited or severely limited in how they could utilize QALYs by the Affordable Care Act. 42 U.S. Code § 1320e-1(e), which came from the Affordable Care Act, prohibits the Patient Centered Outcomes Research Institute (PCORI)

from using QALYs or any other similar measure that "discounts the value of a life because of an individual's disability," as a "threshold" for determining what type of health care is cost-effective.[115] It also prohibits PCORI from using QALYs when developing healthcare coverage, incentives, or reimbursement programs.[116]

Medicare is similarly prohibited from utilizing "cost-effectiveness research" (a much more general term that applies to more than just QALYs) in a manner that treats "extending the life" of an elderly, ill, or disabled person as of less value than "extending the life" of someone who is none of the above.[117]

Medicare *can* use cost-effectiveness research if it is instead used for "determining coverage, reimbursement, or incentive programs under subchapter XVIII based upon a comparison of the difference in the effectiveness of alternative treatments in extending an individual's life due to the individual's age, disability, or terminal illness."[118] This may mean that Medicare can use cost-effectiveness research to compare related treatments to one another, such as two different treatments that extend the life of someone with cystic fibrosis, and consider how disability impacts the degree to which these treatments extend life. However, the exact meaning of the phrase is ambiguous.[119]

The use of QALYs among federal agencies has increased in recent years. Dr. David Wasserman, at the National Institute of Health's Department of Bioethics, said that "use of QALYS has modestly increased in the face of opposition. It is used by at least one US agency . . . Some sort of cost-effectiveness analysis is commended to various agencies. I could say that there is a general trend toward quantifying outcomes. There's a related overlapping trend to use patient reported outcome measures for quality of care assessments, which may appeal to a broader constituency and patient advocacy groups."[120]

QALYs are rarely explicitly used by health insurers in the United States.

The Department of Veterans Affairs (VA)'s PBM Services office utilizes the HTA reports produced by ICER (described in the Introduction and Chapter 1) to aid the development of its drug formularies, which generally means the lists of drugs that a health insurer will cover, although sometimes a health insurer will cover a drug not listed on its formulary.[121] ICER's reports, as stated, utilize QALYs. The VA's formulary development process is well-developed, extensive, and utilizes many forms of data other than ICER's reports.[122] The VA does not utilize a cost-effectiveness threshold.[123]

Use of QALYs by Private Health Insurers

Limited information is publicly available on the degree to which private insurance companies utilize QALYs to make benefits and coverage decisions. According to most scholarly sources, QALYs are rarely explicitly used by health insurers in the United States. Louis P. Garrison reported in his 2016 article that US private payers, with a few limited exceptions, rarely explicitly used cost-utility analyses (CUAs), the cost-effectiveness studies that rely on QALYs, in their benefits and reimbursement decisions.[124] He stated that it was a "puzzle" that the United States had so many competent health economists who made so many CUAs, but that US private and public payers

rarely made direct use of their material.[125] Health economist Peter Neumann has said in multiple[126] articles[127] that QALYs are rarely used explicitly for benefits and coverage decisions in the United States.

For many health insurers, use of QALYs or QALY-based valuations may instead be implicit, and part of an internal decision-making process over which there is little transparency or oversight. Eleanor Perfetto, Executive Vice President of Strategic Initiatives for the National Health Council, an organization which developed a Patient-Centered Value Model Rubric that is used to evaluate the patient-centeredness of value frameworks,[128] said at the September 2018 NCD stakeholder convening:

> There's not much documentation . . . They may or may not have used QALYs. We don't know. But if they did . . . [use] them in their decision making, it probably isn't well documented . . . And even if it is, it's not public information. . . . or [they've] been used in terms of publications that might come out that people might put in journal articles, [such cost-effectiveness studies by researchers], for others [such as health insurers] to use or to consider in their decision making.

One important interview supported a similar conclusion. In Spring 2016, the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) produced a Special Task Force Report on US value frameworks. As part of its research, ISPOR interviewed members of key stakeholder groups, including Brian Solow and Edmund J. Pezalla, who are PBM representatives.[129] Solow and Pezalla were asked questions on the extent to which insurance agencies utilized cost-effectiveness research and value frameworks in decision making. Solow reported that "maybe they do," but that with the exception of a few small plans, "nobody has a clinical policy that says we're constructing this on cost-effectiveness grounds."[130] This appears to mean that, while cost-effectiveness is used, there is no explicit written policy that would require insurers to make decisions based on cost-effectiveness.

For many health insurers, use of QALYs or QALY-based valuations may instead be implicit, and part of an internal decision-making process over which there is little transparency or oversight.

Solow and Pezalla were also asked to what extent payers used the value frameworks ISPOR investigated in its report. Solow and Pezalla reported that "everybody" read ICER's reports, which rely on QALYs.[131] However, Solow and Pezalla also reported that payers rarely followed the recommendations made in ICER's reports "to the letter."[132] According to the two managers, many plans do not rely on QALY-related aspects of these value frameworks, and instead attempt to do "the economic calculation without the QALY," while taking the clinical and economic evidence ICER used to generate QALYs or the cost-per-QALY into account.[133]

Several of the individuals that NCD researchers interviewed did not agree with these statements. These individuals felt that private health insurers' interest in QALYs had been steadily increasing over the last few years.

Sara van Geertruyden of the Partnership to Improve Patient Care said that use of QALYs was "increasing" and that CVS Caremark's announcement in 2018 of their intent to base their benefits and coverage decisions on ICER's QALY-based reports[134] indicates that "private plans and pharmacy benefit managers are referencing QALY-based reports [such as ICER's] and using them to inform coverage and formularies." Ne'eman similarly stated[135] that, while QALYs have been used in academic contexts for some time, that they have had "increased utilization" in recent years in the benefits and reimbursement context by PBMs, citing the recent proposal from CVS Caremark to adopt a QALY threshold.

Van Geertruyden referenced a specific situation in which consideration of QALYs by health insurers had a specific impact on a population of patients in the United States. The incident involved two anti-cholesterol drugs, Praulent and Repatha, which target a protein known as PCSK9.[136] As van Geertruyden explained, "Certain patients with genetic, familial high cholesterol (FH) and some other patients don't respond well to statins [commonplace drugs that reduce high cholesterol]. PCSK9s are designed for this population."[137]

Unfortunately, the first clinical study available on a PCSK9 (Repatha) was of a general population who were at relatively low risk for heart attack and stroke, rather than the patients with high cholesterol that the drug was actually intended to treat.[138] Consequently, some of the benefits of the drug (such as prevention of deaths) appeared lower than they actually were.[139] An initially high cost-per-QALY for these two medications was reported by ICER and, partially as a result of that report, according to van Geertruyden, as well as the higher initial cost of the drug, countless patients who did need the drug were denied it.[140]

The evidence presented neither indicates that QALYs are a controlling variable for all health insurance decisions in the US nor that QALYs are not used by health insurers at all. While few health insurance agencies explicitly mention cost-effectiveness as the basis for their decisions, QALYs and the cost-effectiveness research they support are most likely important evidence that supports and guides, rather than mandates, various courses of action that private health insurers could take.

Ethical Concerns with Respect to the Use of QALYs in the United Kingdom and Their Relationship to Concerns in the United States

The concerns of disability rights advocates, bioethicists, and patient rights groups in the United States who oppose widespread use of QALYs are informed by their use in countries where QALYs play a much more significant role in healthcare decision making. QALYs are a key metric used by the United Kingdom's NICE.[141] The primary purpose of NICE is to decide which drugs and treatments will be funded by Britain and Wales' national healthcare system, the NHS.[142] To do this, NICE analyzes how cost-effective each new drug or treatment is by calculating the treatment's cost per quality-adjusted life year.[143] NICE publicly publishes its analyses of each new drug or treatment, which it refers to as "health technology appraisals" or "guidance."[144]

NICE's reports are known to reduce patients' access to care. This is particularly likely to happen to patients who have a complex condition which

may require intensive, expensive treatment in order to manage it—which describes many people with disabilities.[145] For example, NHS patients lack unrestricted access to most cancer drugs. According to a 2018 Avalere Health study of over 329 HTAs of cancer drugs created by governmental agencies between 2013 and 2017, NICE recommended access restrictions for nearly 70 percent of the cancer drugs it assessed, and it rejected 22 percent of the cancer drugs.[146] By contrast, in the United States, cancer patients gain access to cutting-edge medications earlier and are diagnosed earlier[147] than in the United Kingdom. For some cancers (such as lung cancer) US patients have a higher survival rate than UK patients, which is related to their quicker access to diagnosis and medication.[148]

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Alzheimer's Disease

One prominent example of how NICE's QALY-reliant reports can have a negative impact on patients was its 2005 rejection of the drugs donepezil, galantamine, rivastigmine and memantine for use by patients with mild to moderate Alzheimer's Disease.[149] Alzheimer's Disease is a progressive neurological disease that, over time, reduces and eventually eliminates the affected person's ability to learn and remember new information.[150] The four drugs are standard treatments for Alzheimer's Disease, and mainly maintain rather than improve the affected person's functioning.[151] According to patients with the disease and their families, they significantly benefit from maintaining their functioning at earlier stages of the disease.[152]

NICE's draft recommendations nonetheless found that the drugs were not cost-effective despite evidence of this benefit to patients.[153] Notably, the drug donepezil (Aricept) only cost 2.50 pounds per day per patient in 2007, only 2 years after the draft guidance was released, which at the time was around the price of a cup of coffee.[154]

NICE's recommendations were widely criticized by patients and other prominent stakeholders in the United Kingdom.[155] Several criticisms focused on the validity of QALY calculations used by NICE. The Royal College of Psychiatrists, for example, argued that it made no clinical sense to deny patients with mild and moderate forms of the disease access to the medications, as these would be the very patients who would obtain a greater benefit from retaining a higher level of functioning for longer.[156]

Some researchers and doctors argued that using a quality-of-life focused measure was improper given that it is difficult to estimate health-related quality of life in patients with a progressive neurological disorder.[157] It is difficult to translate the small but important cognitive or behavioral gains from these drugs into evidence of clinical efficacy in controlled conditions.[158] Most evaluations of the quality of life of patients with Alzheimer's Disease were based on the responses of doctors or caregivers, and it was

known that the use of different proxies produced different results, bringing the validity of the utility values into question. Additionally, some individuals have argued that NICE's recommendations were based on limited empirical data that, where it did exist, was entirely invalid when applied to some categories of patients. NICE's 2005 recommendations were based primarily on a US study of Alzheimer's Disease patients who took a specific cognitive functioning test known as the Mini Mental State Exam (MMSE), which the Royal College of Psychiatrists in the United Kingdom argued was highly influenced by age, sex, and English proficiency and was invalid for patients with intellectual and developmental disabilities.[159]

These heavy criticisms prompted NICE to revise its guidelines in 2006, which still restricted access,[160] and led to significant legal challenges by trade associations and the pharmaceutical industry.[161] These efforts failed,[162] and patients with mild Alzheimer's Disease in the United Kingdom were unable to obtain the drugs until 2010, when NICE again changed its guidelines, likely due to a committed campaign by patients and patient rights organizations.[163] Currently, NICE recommends the use of the first three drugs for all patients and the last drug for patients with severe Alzheimer's Disease.[164]

To a certain extent, the limitations NICE imposes on patient access to care in England and Wales are mainly due to the United Kingdom's national healthcare system. The NHS has a limited budget and yet must provide care to all citizens. The issue of how to allocate scarce funds is therefore particularly pressing. A UK reporter argued that the United Kingdom has no choice but to limit patient access to high-cost treatments, even if it means utilizing metrics such as QALYs, because paying for high-cost drugs depletes the NHS's funds and therefore its capacity to serve many more people than the few who benefit from a high-cost treatment.[165] However, similar problems exist in the US's national healthcare programs, which must provide a basic level of care to everyone who is eligible. While this type of rationing may be inevitable in healthcare, it nonetheless poses an existential threat to many people with disabilities. Crucially, there may be alternatives to the use of the quality-adjusted life year. For more information on the alternatives that have been proposed, see Chapter 5, "Alternatives to the Use of QALYs."

A UK reporter argued that the United Kingdom has no choice but to limit patient access to high-cost treatments, even if it means utilizing metrics such as QALYs, because paying for high-cost drugs depletes the NHS's funds and therefore its capacity to serve many more people than the few who benefit from a high-cost treatment.

Cystic Fibrosis

NICE's treatment of the cystic fibrosis drug Orkambi (lumacaftor/ivacaftor) illustrates the risks QALYs pose to people with rare and complex conditions even when the cost-effectiveness assessment does not assign patients a markedly reduced health utility value. Cystic fibrosis is a genetic disease which causes thickened mucus

secretions to progressively block the lungs and digestive system.[166] Eventually, most people with CF will die from respiratory failure.[167] In 2017, the median age of death for patients with CF in the UK was 31 years.[168]

Until recently, only treatments for the symptoms of CF existed. Nebulized medications such as Pulmozyme and hypertonic saline thin mucus so it is easier to clear, but do not correct the defect leading to the production of thickened mucus.[169] Orkambi, manufactured by Vertex Pharmaceuticals, is a member of a new class of drugs known as CFTR modulators.[170] These drugs partially restore correct production and function of the protein that is defective in cystic fibrosis.[171] Each CFTR modulator is only clinically appropriate for a subset of CF patients with specific mutations.[172]

In July 2015, the FDA approved Orkambi for patients 12 years and older with homozygous F508del mutations.[173] About half of CF patients in both the United States and the United Kingdom have this genotype. NICE issued an initial rejection in mid-2016, estimating the drug's incremental cost-effectiveness ratio to be between £218,248 to £349,337 per QALY (approximately $280,000 to $460,000 per year; the lower value relies on the assumption that after 10 years, prices would be reduced by the introduction of a generic).[174] NICE's officially recommended cost-effectiveness threshold window is far below this, ranging from £20,000 to £30,000 per QALY.[175]

The detailed justification of NICE's cost-effectiveness assessment illustrates the problems with attempting to capture treatment benefits perceived by people with disabilities using general population measures. Though many adults with CF have significant functional limitations and may spend weeks per year in the hospital or on home IV treatments, patients often give high ratings on general quality of life (QoL) scales.[176] Patients in Vertex's study gave baseline health-related QoL ratings on NICE's preferred instrument that corresponded to a median health utility value of 1, equivalent to the healthy, nondisabled population.[177] This left no room for subjective improvement in quality of life. The NICE appraisal states that "both the clinical and patient expert explained [to the committee] that people with cystic fibrosis may perceive their health-related quality of life to be equivalent to that of people without cystic fibrosis because they have never known any other health state."[178] However, the committee "understood from the clinical experts that they considered that the 5 dimensions of the EQ-5D questionnaire generally captured most of the important effects of cystic fibrosis" and deemed there to be insufficient evidence that the general population measure was inappropriate.[179] As a result, the estimated cost-per-QALY for Orkambi could only incorporate its predicted longevity benefit.

In the United States, ICER has also used the QALY to evaluate Orkambi's cost-effectiveness.[180] ICER chose to assign health utility values based on a measure of patients' lung function.[181] A CF patient's health utility value could be at minimum 0.625 and at maximum 0.92.[182] This meant that the expected reduction in rate of disease progression could be reflected in increased amounts of time at higher utility values. However, this degree of discounting meant that ICER's assessment resulted in an incremental cost-effectiveness ratio of $890,700 per QALY,[183] much higher than NICE's estimate (and providing justification for potential denial of coverage by payers).

In both evaluations, patients are disadvantaged by the forced tradeoff between increased length and quality of life. Additionally, the discrepancy in methods and assessed treatment value make the metric's claimed objectivity seriously questionable.

Three years after NICE's initial rejection, CF patients still do not have access to Orkambi on the English NHS. In the summer of 2018, NHS England offered to cover all of Vertex's existing and future therapies at a 90 percent reduction from the list price.[184] This would amount to less than £10,000 per patient per year.[185] This cost is less than that of Pulmozyme, a symptomatic treatment first approved by the US FDA in 1993.[186] Vertex has refused this offer, stating that it would set a precedent for price negotiations in other countries that would make funding further research and development impossible.[187]

[S]trict prioritization that is overly reliant on QALYs, similar to the kind utilized in the United Kingdom, is contrary to US civil rights law and disability policy.

Use of Similar Models in United States National Health Insurance Programs

Disability and patient rights advocates have expressed concerns that, as the United States increasingly attempts to find ways to save money in healthcare contexts, it will look towards modeling its own national health insurance programs after those in the United Kingdom and other countries that use QALYs. Some US government agencies are already investigating the prospect of doing so. The Centers for Medicare and Medicaid recently published an Advance Notice of Proposed Rulemaking (ANPRM) which proposes an International Pricing Index (IPI).[188] The IPI would base the prices of certain drugs covered under Medicare Part B on reference prices from 16 other countries. Many of these countries—for instance, the United Kingdom, Ireland,[189] and Canada[190]—use QALYs to make benefits and coverage decisions and limit their healthcare costs. At the state level, the Drug Utilization Review board in New York voted unanimously in April 2018 to recommend that state Medicaid payments for Orkambi be reduced by 70 percent in order to meet ICER's recommended maximum threshold of $150,000 per QALY. Drug manufacturers are unlikely to accept such extreme price reduction demands, posing a threat to treatment access for patients in states choosing to enforce cost-effectiveness thresholds.

The failure of Oregon's initial waiver is instructive. While some consideration of cost-effectiveness is reasonable in national health insurance programs, strict prioritization that is overly reliant on QALYs, similar to the kind utilized in the United Kingdom, is contrary to US civil rights law and disability policy.

Chapter 4: Case Study: CVS Caremark

Introduction

NCD's case study for this report investigates one particular upcoming use of the quality-adjusted life year in the United States: the PBM CVS Caremark's recent decision, in August 2018, to allow self-insured employers to exclude drugs from their formularies that were found to not be cost-effective, based on the cost exceeding a threshold of $100,000 per QALY.[191] CVS Caremark's decision is controversial. A wide variety of stakeholders have spoken on how CVS Caremark relates to the viability of QALYs as a means to cut healthcare costs and aid healthcare coverage decisions in the United States. While some stakeholders lauded the decision as a victory that would drive down costs for consumers, others were concerned that CVS Caremark's use of QALYs would lead to blanket, one-size-fits-all coverage decisions that would prevent people with disabilities from accessing the medications and treatments that they need.

Background

CVS Caremark is a type of company known as a pharmacy benefit manager, or PBM. PBMs contract with health insurers and employer sponsors of health insurance plans and act as administrators of their prescription drug benefits.[192] Their clients are diverse, and can be private health insurance companies, employer sponsors of employee health insurance plans, and state Medicare and Medicaid agencies, among others.[193] While PBMs began largely as "middlemen" who processed health insurance claims, they now have many other important roles in the health insurance industry.[194] Modern-day PBMs can: (1) help determine which drugs will be covered by aiding in the development of drug formularies; (2) make reimbursement decisions, deciding how much pharmacies in their client's network will be reimbursed for their services; and (3) operate pharmacies themselves.[195]

PBMs, given that they manage the prescription drug benefits of more than 266 million Americans according to the Pharmaceutical Care Management Association,[196] have significant influence over what drugs are and are not covered by health insurance. According to Ne'eman, PBMs are, from the insured person's perspective, "payers themselves."[197] CVS Caremark is a particularly large PBM. CVS Caremark, along with two other PBMs, Express Scripts and OptumRx, administer 70 percent of

all PBM-managed prescription drug claims in the United States.[198] Any action CVS Caremark takes, therefore, has an impact on the lives of millions of Americans.

CVS Caremark's Decision

In August 2018, CVS Caremark released a white paper titled, *Current and New Approaches to Making Drugs More Affordable*. The white paper described the steps that CVS Caremark intends to take to reduce the cost of prescription drugs in the United States.[199] One of the steps CVS Caremark described in its white paper is "Reducing Launch Price Using Comparative Effectiveness." In the white paper, CVS Caremark stated that parts of Europe have a loose cost-effectiveness threshold of $50,000 per QALY, which in CVS Caremark's view encouraged drug manufacturers in Europe to launch new prescription drugs at lower prices in order to meet this threshold.[200] CVS Caremark stated that the US "does not have any such programs," and that therefore the launch prices of new prescription drugs in the United States continues to rise.[201]

CVS Caremark then explained that it was launching a new program, which would allow some of the PBM's clients to exclude from their drug formularies any drug with a launch price greater than $100,000 per QALY.[202] CVS Caremark would use the HTAs produced by ICER to determine whether a drug's launch cost-per-QALY fell below or at the threshold.[203] CVS Caremark's policy is only available to self-funded insurance plan sponsors, who are mostly employers.[204] CVS Caremark's policy does not affect "breakthrough therapies," which are medications that the Food and Drug Administration deems more effective at treating a "serious or life-threatening" condition than existing therapies.[205] CVS Caremark's theory was that if enough PBM clients agree to exclude drugs from their formularies in this manner, drug manufacturers will be forced to lower the launch prices of their drugs.[206]

PBMs, given that they manage the prescription drug benefits of more than 266 million Americans according to the Pharmaceutical Care Management Association, have significant influence over what drugs are and are not covered by health insurance.

Responses to the CVS Caremark Decision

CVS Caremark's decision attracted controversy as soon as it was published, with both positive and negative responses written in response to CVS Caremark's announcement.

Positive responses emphasized the significant role that drug manufacturers play in driving up the price of prescription drugs, and saw CVS Caremark's policy as a "bold move" to curtail expanding launch prices.[207] Max Nisen, a *Bloomberg Opinion* columnist, stated that CVS Caremark's policy was a positive change but that it "did not go far enough," suggesting that CVS Caremark should also exclude "breakthrough therapies" as they were becoming more commonplace and were often highly expensive.[208] The online magazine *Vox*, summarizing the statements of Dr. Wallid Gellad, stated that "Stricter formulary designs are one of the few direct tools that might be

able to influence drug manufacturers' behavior," and Gellad said that "something like this is the inevitable future."[209] However, Gellad criticized CVS Caremark's exclusive use of ICER's cost-effectiveness analyses, stating that "the idea that we base something solely on a cut point determined by one cost effectiveness analysis from ICER is a big step to take."[210] Gellad, like Nisen, also wondered if the new program would actually impact that many drugs, given that it would exclude high-cost "breakthrough" drugs.[211]

Negative responses emphasized the arbitrary nature of the $100,000 cost-per-QALY threshold, the inability of QALYs and other kinds of cost-effectiveness to fully gauge a medication's worth to patients, and the danger that the use of QALYs will greatly reduce access to care. Robert W. Dubois, of the National Pharmaceutical Council, stated that evaluating all medications for all conditions using a single $100,000-per-QALY cutoff threshold was "inappropriately blunt" and arbitrary. Dubois noted that most other entities that use cost-effectiveness, including ICER itself, either use variable thresholds (such as between $100,000 to $150,000 per QALY) or do not use their threshold as an absolute cut-off point.[212] He stated that a singular threshold did not account for significant differences between how different patients with the same condition can respond to a medication.[213] Two subgroups of patients with the same condition could receive a different number of QALYs, and thereby a different cost per QALY[214] would be calculated for the drug. Dubois also said that CVS Caremark's plan failed to account for societal benefits of a drug, such as reduced caregiver burden or increased productivity.[215]

Patient rights organizations shared Dubois' concerns and additionally criticized CVS Caremark's proposed use of the quality-adjusted life year itself. Tony Coelho of the Partnership to Improve Patient Care (PIPC) argued that CVS Caremark's new policy, by relying on QALYs, would discriminate against people with disabilities and elderly people in the ways described in Chapter 2, "Bioethics and the Quality-Adjusted Life Year,"[216] in that QALYs will undervalue treatments for people with chronic conditions and disabilities who can never be returned to "perfect health," as defined by researchers using QALYs. Ninety patient and disability rights organizations signed onto a September 2018 letter to CVS's CEO, Larry Merlo, which opposed the policy.[217] Disability rights advocates raised similar concerns, and highlighted the particularly negative impact of such a policy on people with rare diseases and conditions.[218]

Ninety patient and disability rights organizations signed onto a September 2018 letter to CVS's CEO, Larry Merlo, which opposed the policy.

Some news outlets primarily commented on the relationship between CVS Caremark's new policy, the Institute for Clinical and Economic Review, and QALYs. Economics magazine *Forbes*, for instance, commented that ICER's methodology was very similar to the methodology used by the United Kingdom's NICE agency, and titled its article, "Will CVS Caremark Make ICER the American NICE?"[219] ICER has defended its use of QALYs in response to the widespread criticisms of the metric by patients

and disability rights groups. An ICER representative stated the following:

> QALY is recognized as the gold standard for measuring how much a treatment improves patient lives, and it effectively rewards innovative medicines that significantly improve the lives of patients most in need. Patient populations that start off with a lower quality of life—whether because of a serious chronic illness or disability—actually represent the greatest opportunity for treatments to achieve a significant improvement in QALYs.[220]

CVS Caremark's Response to Criticisms and Stakeholder Concerns

CVS Caremark's initial response to the criticisms has been limited. In a *HealthAffairs* blog article responding to Dubois, CVS representatives Troyen Brennan and Surya Singh explained that the cost per QALY is determined by both the medication's impact on "quality of life" (as measured by QALYs) *and* the price the manufacturers set for the drug.[221] Given this, a manufacturer could lower the drug's cost-per-QALY by setting a lower launch price for the drug.[222] The article did not address concerns that QALYs inherently undervalue certain categories of patients, and describes QALYs as a "quantitative method" that "help[s] stakeholders compare the costs and effectiveness of medications."[223] They also do not address Dubois' concern that a singular cost-per-QALY threshold does not account well for situations in which different groups of patients respond differently to a medication and thereby generate different cost-per-QALY estimates for the same drug.[224]

"Will CVS Caremark Make ICER the American NICE?"

An article by *STAT News* in September 2018 reports that CVS Caremark is engaged in discussions with representatives of some of the 90 groups that signed PtPC's September 12th letter.[225] Troyen Brennan, CVS's Executive Vice President said, "It behooves us to spend some time to understand the concerns of the disability community and, if necessary, modify the measures so the process treats every life as being of equal value. We'll go with the program we have now, but we're looking for ways that we might modify it down the line."[226] As of the time the article was written, CVS Caremark's policy was still set to begin in 2019.[227]

Conclusion

As of February 2019, there was no news available that indicates the impact of CVS Health's implementation of its new policy. Its ultimate effect on patient access to prescription medications is therefore unknown. The discussion surrounding CVS Caremark's new policy, however, brought the QALY into the public eye. CVS Caremark's status as one of the largest pharmacy benefit managers in the United States meant that its change in policy could have an impact on millions of Americans, particularly Americans with disabilities. Central to the debates about CVS Caremark's policy was its use of QALYs, and whether or not it can be used as a tool to control rising prescription drug costs without harming patients with chronic illnesses and people with disabilities. Some individuals

lauded CVS Caremark's attempt to bring down prescription drug costs, while others raised reasonable concerns about CVS Caremark's use of both a bright-line cost-effectiveness threshold and the flawed but ubiquitous QALY. NCD presents this case study as an overview of the arguments for and against use of QALYs in benefits and coverage decisions, and recommends that the Department of Health and Human Services carefully consider all of the issues and avoid the use of QALYs or any similar metric in its own health programs.

Chapter 5: Alternatives to the Use of QALYs

Various alternatives to the use of quality-adjusted life years have been proposed. These alternatives differ from one another in a variety of ways, including: (1) whether or not the alternative attempts to serve all of the same functions as QALYs; (2) whether the alternative uses the same means of assessing which treatments are most "valuable" as conventional QALYs, or whether it uses a different means of assessing the "value" of a treatment; and (3) whether the alternative has actually been used in practice, or whether it is only theoretical.

In response to criticism from disability rights activists regarding the QALY, in December 2018, ICER announced their intent to use a supplementary measure in addition to the QALY, entitled the equal value of life years gained (evLYG).

Equal Value of Life Years Gained (evLYG) Supplementary Measure

In response to criticism from disability rights activists regarding the QALY, in December 2018, ICER announced their intent to use a supplementary measure in addition to the QALY, entitled the equal value of life years gained (evLYG). The evLYG is intended to act as a supplement, rather than a replacement, for the QALY. It offers an additional unweighted measure of years of life extended utilizing particular treatments (without the reduction in value of a year of life extended created by the use of a health utility or disability weight), intended to allow an observer or payer to see if there is a significant discrepancy between the QALY and evLYG outcome. Early use of the evLYG indicates that there are such discrepancies. For example, in ICER's analysis of Spinraza, a new breakthrough therapy for Spinal Muscular Atrophy with significant life-extension potential, ICER concluded that utilizing a $100,000 to $150,000 per Quality-Adjusted Life Year (QALY) threshold, Spinraza's maximum permissible reimbursement level for people with presymptomatic SMA would be $72,000 to $130,000 for the first year of treatment and between $36,000 to $65,000 for each successive year. Utilizing the evLYG at the same monetary threshold, the maximum permissible reimbursable price would be between $83,000 to $145,000 during the initial year and $41,00 to $72,000 for each successive year. Both are significantly below Spinraza's cost of $750,000 for the initial year and $375,000 per year thereafter, suggesting that Spinraza would not be covered

under QALY systems or systems that utilized the QALY and the evLYG together. (In the United Kingdom, Spinraza is not covered due to the QALY analysis conducted of the drug by NICE.)

There are other challenges to the evLYG that indicate that it is not a suitable alternative to the QALY. First, as evidenced by the assessment of Spinraza, denial of coverage is possible under the QALY/evLYG system, even where a drug would provide significant clinical benefit, including life extension. Second, the QALY/evLYG system still relies on health utility weights to measure quality of life improvements, despite the fact that such measures are typically derived from survey data and do not account for the complexity of the preferences and experiences of people with disabilities. Third, the QALY/evLYG system affords no opportunity to account for clinical knowledge not reflected in the research literature, a significant concern articulated in Chapter 1. Finally, even within the narrow emphasis on life extension, ICER provides no guidance to payers as to which reimbursement level to prioritize—the one derived from the QALY or the one derived from the evLYG.

Not Using QALYs When Determining Cost-Effectiveness

Payers could simply not use QALYs when determining the cost-effectiveness of treatments or drugs at all. QALYs are only *one* possible outcome measure that researchers could use to determine the impact of a treatment on extension of life and quality of life.[228] Cost-effectiveness studies could instead use other measures that present fewer ethical problems, or simply are better at expressing the true benefit patients gain from treatment, than QALYs.

For example, the researcher could determine the number of individual cases of disease prevented, the number of deaths that were prevented, the number of years of life that were saved or would be saved, or any other possible benefit of the treatment. Payers could then evaluate whether this health outcome was worth the cost of the treatment.[229] Ariel Beresniak provides an example where, for rheumatoid arthritis, if the benefit of the treatment is remission, the researcher could determine the "cost per clinical remission."[230] The use of cost-effectiveness generally may still devalue clinically effective but high-cost treatments (such as, especially, cancer treatments),[231] which may harm individuals with disabilities and other chronic illnesses.

[T]hey could use a cost-benefit analysis, which converts the health outcomes resulting from treatment into an amount of money and then subtracts that amount of money from the cost of the treatment.

Instead of using a cost-effectiveness analysis, policymakers and researchers could also determine whether a treatment's value outweighs its costs in some other way. For instance, they could use a cost-benefit analysis, which converts the health outcomes resulting from treatment into an amount of money and then subtracts that amount of money from the cost of the treatment.[232] For example, in a cost-benefit analysis, an insurer could determine how much money the insurer would save if a specific type of cancer were treated (as compared to the costs of hospitalization) and then subtract that amount of money from the cost of the cancer treatment.

There are still ethical concerns about the use of cost-benefit analysis in a healthcare context. One concern is that converting healthcare outcomes into money is a controversial idea that is often described as "putting a dollar value on life." This is also similar to the idea of "cost per QALY," which is also a way of putting a cost on a healthcare outcome and determining whether the cost is reasonable.[233] Nonetheless, cost-benefit analysis is one of the more frequently used alternatives to cost-effectiveness analysis. Cost-benefit analysis is commonly used in non-healthcare sector contexts that still concern public health and wellness. For instance, the Environmental Protection Agency uses cost-benefit analyses when analyzing the impact of its environmental regulations. These regulations are analyzed primarily in terms of the degree to which they improve the health of the American public at large.[234] The Environmental Protection Agency has experimented with the idea of using QALYs,[235] but primarily uses cost-benefit analysis.[236]

MCDA allows decision-makers to simultaneously consider many different factors relevant to a healthcare decision (such as cost, clinical outcomes, and administrative burdens) and determine how important each of these factors is to them.

Multi-Criteria Decision Analysis

Multi-criteria decision analysis (MCDA) is another alternative to QALYs that better acknowledges the complexity of healthcare decision-making. As explained by the Innovation and Value Initiative, MCDA allows decision-makers to simultaneously consider many different factors relevant to a healthcare decision (such as cost, clinical outcomes, and administrative burdens) and determine how important each of these factors is to them.[237]

A payer using MCDA would first rank each factor that is relevant to the decision against one another.[238] For instance, the decision-maker would determine whether clinical outcomes or cost matters more to them in a healthcare decision. Each of the criteria would then be given a weighted "score" representing that criteria's importance to the decision-maker. Normally, when MCDA is used, there are a great many criteria that are being ranked in order of importance—sometimes as many as 15.[239]

Next, researchers would compare how each of the *treatments* being considered relate to one another. For example, Treatment A might have better clinical outcomes, but Treatment B costs less. Researchers would then create a score representing how each of the treatments fare with respect to each of the criteria being considered. For example, Treatment A would receive a higher score for clinical outcomes than Treatment B, but a lower score for cost.

The next step is dependent on the decision that's being made and the criteria that are being assessed, but when making a health care decision, it often involves generating a single average weighted score for each treatment that is the aggregate of both how the treatment scores on each of the criteria and how important those criteria are to the decision-maker, which then shows the relative value of the treatments to one another.[240]

MCDA has a variety of possible applications. For example, the Innovation and Value Initiative uses MCDA in its condition-specific model for rheumatoid arthritis. The model is intended to help a variety of different healthcare decision-makers determine the value of different anti-rheumatic (that is, anti-arthritis) drugs to them.[241] Importantly, the model can be altered to allow the decision-maker to consider how the drug will impact different subgroups of patients, such as subgroups of patients of a specific age, gender, severity of arthritis, etc.[242] As established in the section "QALYs Fail to Distinguish Between Subgroups of Patients with the Same Condition," QALYs' limited use for these purposes is a flaw of QALYs. Some stakeholders, such as some health economists, feel that use of MCDA is the most promising alternative to QALYs.[243]

MCDA does possess a number of flaws, the largest of these being ease of use. Researchers must accurately weigh what can be a large number of possible criteria accurately to make decisions. Additionally, according to Beresniak, many MCDA models are more complex than QALYs and may require a greater degree of expertise in order to be used.[244] However, given that MCDA can be used to compare a wide variety of health-related criteria simultaneously—including both life extension, specific clinical benefits of treatment, and quality of life—a form of MCDA may represent the most likely effective alternative to the use of QALYs. NCD recommends that a condition-specific form of MCDA, with values based upon the perspectives of patients with the condition as seen in the Patient Perspective Value Framework, be utilized by payers to gauge the cost-effectiveness of treatments for the same condition.

Alternatives to QALYs That Use Primarily Patient Preferences

Patient rights groups believe that the best alternatives to QALYs allow patients with the condition being treated to define which treatments for the condition are of the highest "value," and also what a "high-value" treatment is. While public and private insurers consider low-cost, clinically effective treatments to be of the highest value, patients may consider a wider variety of factors as important, such as the treatment's impact on the ability to maintain relationships with one's family and friends.[245] Patient rights groups also argue that a good alternative to QALYs allows patients to evaluate the costs and benefits of a treatment across multiple areas of patients' lives.

Patient Perspective Value Framework

FasterCures' "Patient Perspective Value Framework" (PPVF) is a value framework that may satisfy PIPC's criteria.[246] While the PPVF has not yet been used extensively, FasterCures provides general examples of how the PPVF could be used in a number of situations, including by individuals as a decision-making aid and by public healthcare programs.[247]

The PPVF is divided into five broad "domains," which are the five types of information patients usually consider when making healthcare decisions.[248] These five domains are:

- **Domain 1: Patient Goals and Preferences,**
- **Domain 2: Patient-Centered Outcomes,**
- **Domain 3: Patient and Family Costs,**
- **Domain 4: Quality and Applicability of Evidence, and**
- **Domain 5: Usability and Transparency.**[249]

Information from Domains 1 through 4 is used by the decision maker to determine how valuable a drug or treatment is as compared to another drug or treatment, or multiple drugs or treatments, for the same condition. Researchers first attempt to determine what patients with the condition being treated value most in a healthcare treatment—that is, evidence for Domain 1. They then gather evidence related to: (1) Domain 2, which represents the health benefits and drawbacks of each intervention or drug for the patient; (2) Domain 3, the financial costs to the patient; and (3) Domain 4, how high-quality and comprehensive the evidence of a drug or treatment's clinical effectiveness is. Domain 5 acts as a "foundation" for the other four Domains. A metric must be usable to be useful.

Researchers then weight the evidence from Domains 2, 3, and 4 based on the evidence they gathered for Domain 1, which is evidence of the goals and preferences of patients with the condition.[250] PPVF then assigns a score to each treatment based on these calculations. PPVF's assessment method appears similar to a form of multicriteria decision analysis, described further in the "Multicriteria Decision Analysis" section, which specifically considers matters of import to patients.

The PPVF uses "patient goals and preferences" to evaluate a far broader array of information about a treatment's impact on patient quality of life than whether the treatment extends life or has an impact on the specific, limited aspects of health-related quality of life typically measured by QALYs. For example, Domain 2, "Patient-Centered Outcomes," uses patient preferences to evaluate the complexity of the treatment regimen and the treatment's risks, side effects, and complications for patients.[251] This is a more realistic assessment of the myriad possible impacts a healthcare treatment can have on the lives of patients. The broader array of quality of life considerations would also prevent two treatments from receiving the exact same score, as no two treatments would have exactly the same impact on every single domain.

The PPVF uses "patient goals and preferences" to evaluate a far broader array of information about a treatment's impact on patient quality of life than whether the treatment extends life or has an impact on the specific, limited aspects of health-related quality of life . . .

PPVF and similar methods can only be used to compare two different drugs or treatments for the same condition.[252] Payers could not use the PPVF to determine whether a drug for cystic fibrosis would be of higher value than a drug for hypertension. Some stakeholders feel that this would not be a flaw at all, as it protects against many of the ethical issues that occur when QALYs are used to compare unlike treatments. The PPVF has never been used, however.[253] It is therefore unclear how it would operate in practice.

The Efficiency Frontier

The German Institute for Quality and Efficiency in Health Care has adopted a method of assessing cost-effectiveness known as the efficiency frontier.[254] Generally, an "efficiency frontier" in

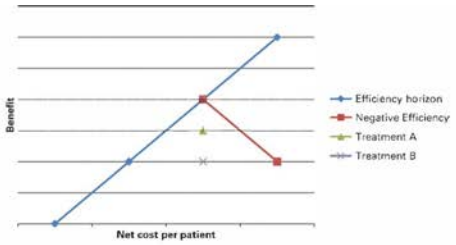

Figure 1. Example of an efficiency frontier.
Source: German Institute for Quality and Efficiency in Health Care.[257]

economics is the set of possible actions that offer either the greatest possible benefit for the cost involved or the lowest possible cost for the amount of benefit involved.[255] A set of possible actions can be expressed as points on a scatter plot, and the "efficiency frontier" can be expressed as any of these points that line up with a line going through the center of the graph.[256] Figure 1 is an example of an efficiency frontier.

The line going through the center of the graph is the efficiency frontier. The points on the graph represent, in the healthcare-specific example in Figure 1, treatments. The points along the line represent the most cost-effective options. While in an investment context, no points above the line could exist, in a healthcare context, they would represent healthcare treatments that are highly cost-effective, or much more cost-effective than current approaches.[258]

The approach Germany proposed for evaluating healthcare treatments is to place the cost per patient on the x-axis (horizontal axis) of the graph, and the possible benefit on the y-axis (vertical axis) of the graph.[259] The researcher would then add points to the graph representing different possible treatments for the same condition, and could use the resulting scatterplot to see which of these treatments is most cost-effective—such as how cost-effective a new treatment would be as compared to current treatments.[260]

Generally, an "efficiency frontier" in economics is the set of possible actions that offer either the greatest possible benefit for the cost involved or the lowest possible cost for the amount of benefit involved.

The graph format allows health economists to easily compare the costs and benefits of various interventions to one another. For example, in Figure 1, the "negative efficiency" line shows that

the hypothetical treatment represented by the red point closest to the blue line is clearly more cost-effective than the red point farther away. However, Treatment A provides slightly more benefits but costs more than the treatment on the blue line beneath it, though it is less cost-effective than the treatment on the line above it.

A researcher using an efficiency frontier could determine that the benefit of a lung cancer treatment was "restoring/maintaining lung function," and determine a way to measure lung function in terms of percentages or numbers.[261] The researcher could also determine how much each lung cancer treatment would cost per patient per year. The researcher would then graph each lung cancer treatment along a scatter plot where "restoring/maintaining lung function" was the benefit on the y-axis, and cost per patient per year was along the x-axis. The researcher could then see visually which lung cancer treatments were the most efficient use of resources.

The main benefit of this approach is that it is clear, easy to use, and transparent. Additionally, it does not require the health economist to use QALYs as the measure of a treatment's benefit.[262] The benefit on the graph could instead be the specific benefit that comes from the treatments, rather than an arbitrary number representing only some limited aspects of "quality of life" combined with the extent to which a treatment extends life. However, if QALYs are not used, it would only be possible to look at either one benefit of a healthcare treatment at a time, or different benefits that have been aggregated into a single number.[263]

Are There Alternatives to QALYs That Perform the Same Functions as QALYs?

QALYs continue to enjoy widespread use by health economists, researchers, and policymakers internationally and in the United States, despite the existence of alternatives. This is likely because, as multiple researchers have noted, QALYs are: (1) easy for policymakers to use (as they combine quality and quantity of life together and so payers would not need to determine how effective the drug is at improving quality and quantity of life separately); (2) well-established; and (3) allow policymakers to compare unrelated treatments to one another. As explained in the sections pertaining to each alternative, no one alternative serves all of the functions of QALYs.

Many health economists have remarked that one of the reasons QALYs persist despite their flaws is that there is no perfect replacement.

Many health economists have remarked that one of the reasons QALYs persist despite their flaws is that there is no perfect replacement. These individuals have stated that while QALYs are imperfect at best, there are no sufficiently developed alternatives to QALYs and therefore QALYs remain "the best option available."[264] Other stakeholders disagree with this premise. Beresniak has argued that it is not sufficient, if QALYs lack scientific validity and do not measure what they claim to measure, to simply state that QALYs are the "best" option available, although he, too, says that no single alternative can act as a replacement.[265]

Some of the individuals NCD interviewed argued that *no* metric should serve all of the

functions of QALYs, such as comparing unrelated treatments to one another.

Stramondo remarked,

> I think it would be impossible to make judgments about how different technologies impact something as complex as quality of life. You could make a good judgment on Assistive Devices A and B assisting with the same function. Wheelchair A and B could be better or worse at assisting the same function. You could make comparisons among treatments with similar goals. The problem is when you want to compare an anti-nausea medication against a new stair-climbing wheelchair. How do you decide which one to fund based on which improves quality of life more? A concept like quality of life is so multidimensional, that's really tricky and probably impossible.[266]

Ne'eman stated something similar:

> There's no reason why you must conflate life extension and disability mitigation into a single number. The only reason to do that is because they want a measure that can be used across categories, [a measure] that can compare a cancer and a cystic fibrosis drug. If you don't require comparisons across categories, you can use diagnosis-specific measures. . . . I advocate saying, "Let's compare cancer drugs to other cancer drugs."[267]

Dr. Steve Pearson of ICER stated, "In my view, the current system is not working for patients, and [they're] being harmed every single day by the fact that the prices for drugs and treatments are so poorly aligned for their benefits." He believes it is "healthy for us to help force these questions into the forefront and have them in public as uncomfortable as they may be . . . [it is] important enough given the cost and the access problems . . . to try to do it in the open and [to] try to use evidence of cost-effectiveness as one important anchor [for] that discussion."[268] Pearson's concerns are shared by many in the United States.

While these conversations are clearly necessary, it is not clear that QALYs are the best means of facilitating such conversations. There may be alternative means of incorporating "value" into healthcare coverage decisions.

Chapter 6: Recommendations

Congress

When enacting health reform bills, Congress should:

- Avoid creating provisions of any bill that would require the agency with management and oversight responsibilities (such as, for example, HHS) to cover only the most cost-effective drugs and treatments, or to require the agency to impose restrictions on less cost-effective treatments.

Congress should pass legislation:

- Prohibiting the use of QALYs by Medicaid and Medicare.
- Congress should provide funding to HHS for research on best practices on the use of cost-effectiveness to inform benefits and coverage decisions with respect to United States national health insurance programs, such as Medicare and Medicaid. "Best practices" in this case refers to a means of utilizing cost-effectiveness research that facilitates greater access to care and does not reduce access to care for people with chronic health conditions and disabilities.
- Congress should fund a report by the Government Accountability Office that examines how cost-effectiveness studies influence agency decision making, particularly cost-utility analysis (CUA) studies.

Department of Health and Human Services (HHS)

- HHS should consider including explicitly recruiting people with disabilities and chronic illnesses as members of committees and working groups formed to develop effective healthcare reform and strategies for lowering the cost of prescription drugs.
- HHS should support healthcare providers by issuing guidance on what steps to take if their patient's health insurance agency refuses to cover recommended treatment on the basis of that treatment's cost-effectiveness.

US Department of Health and Human Services (HHS) Office for Civil Rights (OCR); US Department of Justice (DOJ) Civil Rights Division

- DOJ and OCR should jointly issue guidance clarifying that the ADA applies to coverage programs that states operate, such as Medicaid.
- OCR, in consultation with DOJ as appropriate, should issue guidance to HHS sub-agencies, such as the Centers for Medicare & Medicaid Services as well as to State Medicaid Agencies, clarifying that:
  - Section 504 and Section 1557 also apply to Medicaid programs because they receive federal financial assistance. The guidance should specifically discuss how these authorities apply to benefits and reimbursement decisions, and that payment decisions should not rely on cost-effectiveness research or reports that are developed using QALYs; and
  - Section 504 and Section 1557 apply to health insurance programs operated by recipients of federal financial assistance from HHS. The guidance should discuss that covered health insurance programs should not rely on cost-effectiveness research or reports that gather input from the public on health preferences that do not include the input of people with disabilities and chronic illnesses.

HHS Centers for Medicare and Medicaid Services (CMS)

- CMS should utilize well-established alternatives to QALYs, such as Multicriteria Decision Analysis, which is a method that better acknowledges the complexity of healthcare coverage decisions, or cost-benefit analysis, when the exact benefits and costs of a drug or treatment are known. CMS could utilize these methods in combination, such as using cost-benefit analysis as one component of a Multicriteria Decision Analysis. If CMS does utilize cost-effectiveness analysis, it should consider utilizing it as one component of a condition-specific Multicriteria Decision Analysis.
- CMS should refrain from pursuing means of reducing Medicare and Medicaid prescription drug costs that attempt to model US pricing after the pricing in other countries, which may heavily rely on QALYs and often deny people with disabilities access to needed care.
- CMS should rescind the Advanced Notice of Proposed Rulemaking, which proposed an IPI for Medicare Part B.
- CMS should contribute to the development and use of value frameworks that utilize patient preferences to define which drugs and treatments are valuable, such as FasterCures' PPVF.

Appendix A: Calculation of QALYs Flowchart

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[Whereupon, at 11:58 a.m., the hearing was adjourned.]

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