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What Price Should We Pay for Specialty Drugs?

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We should be grateful to Gilead Sciences, Inc., really (well, sorta). Their business decision to charge $84,000 for Sovaldi, which cures Hepatitis C at $1000 per daily dose for 3 months, elevated the issue of specialty drug pricing to a level of health policy urgency that rivals the King v. Burwell Supreme Court case and SGR repeal (now done, Hallelujah Amen). The fact that Gilead earned a cool $12.1B in profit off its $24.9B in 2014 sales suggests the Sovaldi price is far from what would prevail in a competitive market[2], even for risky products like prescription drugs. The thesis of this paper is that this degree of profitability is higher than necessary to induce investors and researchers to develop the next Sovaldi, or specialty drugs in general, and therefore we should seek policy changes that would help re-balance our competing objectives of innovation and affordability.

Fellow citizens of the world, I write this issue brief neither to praise nor to bury Gilead, but to clarify the not so obvious and to offer a new policy solution crafted for expensive specialty drugs, especially biologics. I seek to establish two essential points. Point #1: we as a nation cannot afford the monopoly power we are now granting in the name of encouraging innovation, given the way that power is being used by Gilead and others. Point #2: policy makers are not helpless in the face of this reality, but it will take political courage, data collection, and some carefully re-balanced regulatory imagination to improve the situation. In short, we must reduce "launch" prices without unduly reducing the incentives to invest in innovation, and this is not a simple nut to crack.

We Cannot Afford the Monopoly Pricing Power We are Granting in Pursuit of Innovation

On the "we cannot afford this kind of pricing power" point, simply imagine if the people who had invented penicillin had priced it as high as Sovaldi. Penicillin has saved countless millions and was not patented because at the time it was invented in the UK (1928-1940) it was considered immoral to seek or grant a monopoly patent for life-saving medical advances. Eighteen percent of wounded US WWI soldiers died of pneumonia. Less than 1% did so in WWII, and penicillin is largely why.[3] By 1945 penicillin was widely available at nominal cost. If penicillin had been priced analogously to Sovaldi at the outset or even after the war, a small number of people would have gotten enormously wealthy and the suffering of millions could have continued for years if not decades.

To illustrate the growing size of the affordability problem, recent data and analysis from Altarum's Center for Sustainable Health Spending show that drug price growth (6% per annum) and spending growth (12% per annum per person) are a -- if not *the* -- major reason for the recent uptick in growth in per capita health care costs, after an unprecedented run of 5 straight years of low growth.[4] Specialty drug spending is a growing part of this problem. Specialty drugs represented only 1% of approved drugs but accounted for 25% of drug spending in 2013[5]. And spending on them is growing faster than for all others by far, headed to 50% of all drug spending by 2019[6].

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[2] *J. Lee, "Gilead's 2014 Profit Margin Nears 50%, Fueled by Hep C Drugs," Modern Healthcare February 3, 2015.*

[3] *http://www.botany.hawaii.edu/faculty/wong/BOT135/Lect21b.htm.*

[4] *Monthly Price and Expenditure Briefs can be accessed at http://altarum.org/our-work/cshs-health-sector-economic-indicators-briefs.*

[5] *J. Chambers et al, "Despite High Costs, Specialty Drugs May Offer Value for Money Comparable to That of Traditional Drugs," Health Affairs 33(10):1751-1760 (2014).*

[6] *http://lab.express-scripts.com/insights/industry-updates/~/media/b2d069aa4a2b4b188879a81ab0bab8aa.ashx*

The Policy Solution that Follows from this Fact is Not as Simple as We Would Like

Before you condemn Gilead and other specialty drug manufacturers (which includes by now all pharmaceutical manufacturers) outright, consider this fact: in the traditional "small molecule" market today (e.g., penicillin, Lipitor, valium, lisinopril (for hypertension)), 85% of prescriptions are generic.[7] In short, the market for traditional small molecule drugs for common problems has become intensely competitive, so new investment is increasingly focused on "specialty" areas affecting far fewer patients. There are different definitions of "specialty drugs" in use today, but for purposes of this paper, I prefer the one adopted by Spatz et al. as follows: complex to manufacture, can be difficult to administer, may require special patient monitoring, and sometimes have FDA mandated strategies to control and monitor their use.[8] Medicare and other payers use cost as a threshold defining line for the definition for cost sharing and formulary tier purposes, so any drug that costs more than $600 a month is in the class of concern. This is also a useful first order approximation definition.

Let me be clear, it is not a bad thing in the abstract for R&D investment to be flowing toward specialty drugs. Capitalism typically works best when capital flows to higher value uses, and patients with less common problems – e.g., particular cancers, Hepatitis C virus, rheumatoid arthritis and multiple sclerosis – may be far better served than in the past. Sovaldi does *cure* Hepatitis C, after all, and for anyone who has suffered from the advanced forms of this condition, that is a big deal even in the Joe Biden sense.

Our policy problem is rooted in the reality that striking the right regulatory balance between encouraging innovation -- by granting temporary monopoly pricing power -- and ensuring affordability by encouraging post-monopoly competition is, well, very, very hard. Of late, our policy effort has not been commensurate with the complexity of the problem. In effect, Gilead with Sovaldi and other new specialty drug manufacturers with more and more expensive drugs are using stratospheric launch prices to capture the maximum amount of value from their new drugs and leaving precious little net value for consumers and payers. These high drug prices also threaten other priorities in the health care system.

The complexity of these issues cannot be overstated. First, there is scientific uncertainty facing drug developers. The product is more likely than not to fail to earn final FDA marketing approval as safe and effective vs. a placebo. Even though the basic science is confirmed by NIH funded research, drug companies do not know that their product will effectively turn that knowledge into effective treatments until they've invested in pre-human testing and then Phase I-III clinical trials, and these don't pan out in most cases. Second there is competitive uncertainty -- someone else might develop a drug targeting the same conditions that yours does but uses a chemical structure sufficiently different that your patents or exclusivity rights cannot stop it from eroding your anticipated revenues. Third, the time lag between incurring the drug development costs and revenues can be quite long and unpredictable at the outset of investing. Fourth, different types of drug companies – established vs. the newer ones with no current drugs on the market and from whom much innovation actually originates – may have very different imperatives in terms of post-marketing cash flow to maintain desirable incentives to invest in new life-saving and -enhancing drugs. Finally, determining whether the monopoly protection that has been granted is too little, too much, or just sufficient to generate the innovation we want is as much art as science. This is a "Goldilocks" problem of the first degree.

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[7] *B. Hirsch, S. Balu, and K. Shulman, "The Impact of Specialty Pharmaceuticals as Drivers of Health Care Costs," Health Affairs 33(10):1714-20 (2014).*

[8] *I. Spatz et al, "Health Policy Brief: Specialty Pharmaceuticals," Health Affairs November 25, 2013.*

Nevertheless, this complexity need not be paralyzing. The issues are not impossible to understand and assess. And assess them we must, for the cost problem is sufficiently serious and escalating that it is impossible to believe that we are being well served by the current configuration of innovation encouraging policies and actual pricing choices that specialty drug manufacturers are making. We certainly should not accept the status quo just because it is "complex."

The truth is, there is insufficient data in the public domain to enable us to reach a fully informed judgment. The data we need are average price and sales trajectories over time, contemporaneous production and marketing costs, and (in some cases) the historical costs – including the opportunity cost of investment funds and the probability of failure – of the R&D development costs. These data are of course considered proprietary and partially or mostly hidden from public view, as competitors are wont to do, but their opaqueness leave us one of three tough choices: (1) making educated inferences based on incomplete data;[9] (2) reach judgments and develop and advocacy campaign based on truly scary list prices;[10] or (3) writing defenses of the status quo based on data that are shared only with industry supporters of the ideology of markets vs. regulation.[11]

The good part about judgments based solely on launch price information (e.g., Sovaldi costs $84k, can you believe it?) is that they enable the spread of enough moral outrage to explore policy solutions. The bad part of judgments based on launch prices alone is that they ignore statutory discounts (to Medicaid and to 340b providers) and price cuts in response to competition, once it starts. For example, at the end of 2014 some PBMs and some Medicaid programs and the government of India were reported to have bargained quite large discounts going forward by playing one Hepatitis C drug regimen off against another, as competitors to Sovaldi came on the market.[12]

But the problem with inferring that all is Panglossian, or the best of all possible worlds, based on incomplete data or ideology, is that it very well might not be and we would never know if we do not look deeper than we are now statutorily equipped to do in the United States. To really settle how satisfied we should be with drug market performance, on a drug by drug basis, we would need to know how much consumer surplus or extra value not captured by the manufacturer is created by each drug's introduction, both in terms of value to initial consumers and follow-on value to subsequent consumers. For example, the second (and third, etc.) drug may actually create most of the consumer surplus value, since without competitive entry drug prices would never come down from launch prices, which in the US, are very high and presumably absolutely short run profit maximizing. For a monopolist facing inelastic (price insensitive) demand, the profit maximizing price is high indeed. People who have no other hope for prolonged life – e.g., certain cancer patients, Hepatitis C patients near full liver failure with no hope of a transplant "in time" – are completely price insensitive, subject to their wealth or insurance coverage constraints.

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[9] *For some creative examples, see E. Berndt et al, "Decline in Economic Returns from New Drugs Raises Questions about Sustaining Innovations," 34(2):245-52 (2015), and R. Frank and J. Newhouse, "Should Drug Prices Be Negotiated Under Part D of Medicare? And if so, How?" Health Affairs 27(1):23-43 (2008).*

[10] *See the Campaign for Sustainable Drug Prices, http://www.csrxp.org/.*

[11] *For example, see H. Grabowski et al, "Evolving Brand Name and Generic Drug Competition May Warrant a Revision of the Hatch-Waxman Act," Health Affairs 30(11):2157-66 (2011), and J. Calfee, "When Patents are not Enough." American Enterprise Institute Health Policy Outlook #10 Dec 2008.*

[12] *A. Sifferlin, "Why Hepatitis C Drugs May Soon Get Far Less Expensive," Time Dec 22, 2014.*

So we need competition to drive prices down, but the profits earned by the company with the second drug in class are invariably less than that earned by the first drug to market. Thus, while society has a general interest in promoting innovation, the social value of competition may outweigh the social value that can be achieved from a monopoly drug product alone. That is, we have a compelling social interest in promoting *competition* as well as *innovation*.

Hatch-Waxman[13] recognized this, and that is why it simultaneously increased exclusivity for truly new chemical entities (NCEs) and smoothed the pathway to market competition for generics. Without Hatch-Waxman we would have a much less robust generic sector than we have today. My point is that 30 years later, when innovation has shifted to specialty biologics and biosimilar competition has yet to really start, the time has come to re-examine the balance between incentives to innovate and ability to compete and drive price down to affordable levels.

The Affordable Care Act provision that was signed into law in March 2010[14], essentially incorporated the already written Biologics Price Competition and Innovation Act that was then being considered by the Senate. The intent was to smooth the pathway to market for biosimilars, analogous to the role of generics in Hatch-Waxman. But it took until April 28, 2015 for final regulations to lay out the specific steps biosimilars must take to achieve FDA approval. What did start immediately from this law was 12 years of additional exclusivity conveyed upon FDA approval for biologics. This provision of the ACA cannot be said to be working well yet, however, and it is hard to be optimistic given entrenched opposition to competition. We note the FDA approved the first biosimilar on March 6, 2015 (Zarxio, by Sandoz/Novartis), to compete with a biologic that was first approved in 1991 (Neupogen, by Amgen). Of course, Amgen immediately went to court to stop Zarxio's sale, and so far has succeeded at the appellate court level.[15]

Drug manufacturers naturally argue that ANY adjustment of their pricing power from the status quo – exploited only after they get their government-granted temporary monopoly protection – will stifle innovation and send us back into the dark ages. As much as they often overstate the case, they have a point: prices could be controlled and driven so low that private capital would flow away from new drug R&D spending. Many serious independent estimates are that in the aggregate, drug companies already spend far more on marketing as they do on R&D.[16] This ratio will not be improved with overly stringent price controls, which would lower the relative return to R&D with an uncertain payoff.

Still, I would argue that the Sovaldi case makes abundantly clear that specialty drug product revenues are not mostly paying for past R&D costs, they are at best being made available to pay for current and future R&D investments, and at worst flowing into excess returns that are being returned to stockholders for personal use. Berndt et al, a team led by one of the most respected scholars of technological change the US has to offer, after computing a declining ROI on new drug R&D for the cohort introduced between 2005-2009, concluded that "… the direction of causation runs from prices to research and development costs – as prices increase, manufacturers are willing to spend more to discover new drugs – rather than the other way around." They also note that "research and development costs are sunk at the time of product launch, and so they ought not to factor into the pricing decisions of a profit-maximizing firm once the product has been developed."[17]

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[13] *1984, PL 98-417.*

[14] *2010, PL 111-148.*

[15] *P. Loftus, "Court Blocks Novartis Copy of Amgen Cancer-Care Drug," Wall Street Journal May 7, 2015.*

[16] *Citing Global IMD data, in T. Staton, "New Numbers Back Old Meme: Pharma Does Spend More on Marketing than R&D," Fierce Pharma November 6, 2014.*

[17] *E. Berndt et al, op cit, cf. footnote 9.*

By "excess return" I mean a return beyond what is necessary to attract the capital into new drug development activities in the first place. Drug manufacturers will argue that interference with their pricing decisions will drastically reduce the funds flowing to new drug R&D investment. But if most payers and patients cannot afford to pay the "free market" price for Sovaldi or for a new cancer drug now, or for a new drug to treat the symptoms of MS or rheumatoid arthritis, I ask you, dear reader, what good exactly comes having more new drugs we cannot afford in the future, either?

It is true that sometimes appropriate medication use can reduce hospitalization and other health service costs. But excessively priced drugs can also force premiums up so much they reduce access to necessary services, forcing tradeoffs and clinically risky hard choices that would be avoidable if we had better drug pricing policies.

Toward a New Policy Framework: Fair Prices for Innovative Monopoly Products

A first step toward a policy solution may be to unpack the claim that $84,000 per episode, or over $100,000 for many new specialty cancer drugs, are free market prices. How can it be said that a market is free if there are absolute barriers to entry to that market? Government granted the monopoly and set the barriers, to encourage innovation. But whatever the reason for it, no monopoly market is "free."

Aristotle, in the first known analysis of a "just" price, eventually hit upon the notion that a price of one seller, a monopoly (he apparently invented the term), can never be fair. Indeed, only the result of multi-seller competition could and should be considered "just" and should be encouraged by public policy.[18] Today public policy grants temporary – though fairly long -- product monopolies to encourage innovation, but Aristotle's unassailable logic should compel us to evaluate if the revenue flowing to a company, post patent and exclusivity rights, is greater than that required to keep the right amount of innovation investment flowing in the right directions.

Prices in competitive markets signal the value that consumers put on the product and that suppliers put on the resources required to bring the product to market. These values are distorted from market prices when markets are not competitive, i.e., when prices exceed costs. And this is the situation we have in drug prices now, by design.

Americans have always instinctively and rightly been reluctant to try to "interfere" with normal market allocation mechanisms. We prefer to allow capital to flow toward its highest value uses, and let sectors of the economy expand and contract as consumer tastes, purchasing power and technological advances have evolved. Most people today prefer their smartphones and year round fresh avocados to big box broadcast radio and the starchy, boring diets of the 1950s. We were right to allow the horse and buggy industry to fade away, painful though that was for some (especially horses) at the time.

But the reality is, we HAVE chosen to intervene in health care markets in general, mostly to help consumers and patients in markets with gross information imbalances between buyers and sellers. Think of rules requiring access to community rated or subsidized insurance for the sick and the low income, both before and after the ACA, or of the quality regulations that ensure health providers are properly trained and up to date.

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[18] *J. Schumpeter, History of Economic Analysis. Oxford: New York, Tenth Printing 1978, p. 61.*

These information asymmetries are present in drug markets as well. So we need to be more honest about what we have wrought in the prescription drug market: we have created very strong incentives for companies to try to be granted a temporary monopoly to charge outrageous prices to solve a relatively rare problem for the few rather than improve the health of as many as possible as cost effectively as possible.

To be fair, historically we probably stacked the deck too far the other way, against relatively rare conditions, and that is why we finally felt compelled to pass the Orphan Drug Act (ODA) in 1983.[19] Orphan drugs are defined to be those that are targeted for conditions that afflict fewer than 200,000 people in the US. The Act granted tax credits and extended periods of exclusivity for FDA approved drugs who met the criteria. The ODA worked: between 1983-2009, 399 drugs were approved as orphans, in the decade prior to 1983, exactly 10 new drugs met the same criteria.[20]

In some ways, the ODA may be working too well today, in that now more than 1/3 of all new drugs have the coveted orphan designation (ibid). And once they ride the designation to FDA approval, drugs are commonly prescribed for "off label" uses for a much larger population. Interestingly, the tax credits to offset clinical development costs for orphan drugs do not help new companies that have no current profits to offset, which is partly why established companies typically acquire the new ones on the way to market. It is also true that most orphan investment is for conditions with relatively more patients rather than fewer, so yet more targeted incentives may be needed for extremely rare conditions. [21]

But whether orphan or specialty (which have a larger target group than 200,000 but still a relatively small fraction of the population), we must face the reality that we cannot afford for all future drugs for "small" populations to be priced the way Sovaldi and many biologic drugs have been lately. There are 7000 rare diseases in the US, we add about 350 per year, and in total from 20-25 million Americans are affected.[22] At $100,000 per case in the current Sovaldi or anti-cancer drug pricing model, that would cost 2.5 *trillion* dollars, which would roughly double total national health spending in the United States. This cannot happen, regardless of drug company executives' indifference.

Some apologists of course argue that the market is working today, substitutes for Sovaldi are now available, and Medicaid programs have implemented prior authorization and other restrictions (e.g., no addicts allowed, one episode of treatment in a lifetime, only patients with liver failure will be allowed to receive the drug, etc.,) to minimize their financial liability. Prices are coming down, and so the argument goes we should all calm down and focus on ACO pricing or quality metrics or something else. They simply do not want us to focus on the imbalance between the value the firm is capturing through profit vs. the increase in value accruing to consumers, or what economists call "consumer surplus."

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[19] *PL 97-414.*

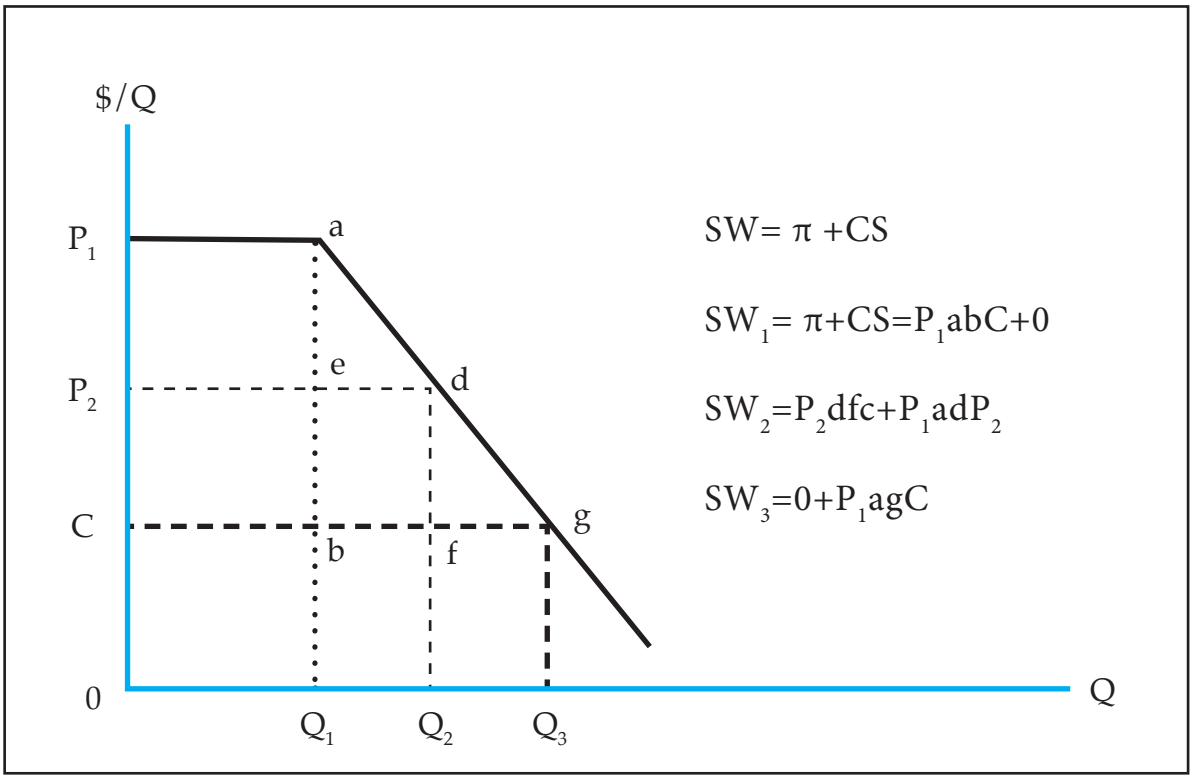
[20] *A. Valverde, S. Reed, and K. Shulman, "Proposed 'Grant and Access' Program with Price Caps Could Stimulate Development of Drugs for Very Rare Diseases," Health Affairs 31(11):2528-35 (2012).*

[21] *See Valverde, ibid, and G. Gimm and L. Nichols, "Ebola Crisis of 2014: Are Current Strategies Enough to Meet the Long-Run Challenges Ahead?" American Journal of Public Health Public Health Policy Brief, published online ahead of print, March 19, 2015.*

[22] *See Valverde, ibid.*

High cost specialty drugs seem to me to function today something like the story one can tell from Figure 1.

Figure 1. Market for Specialized Drugs



Let the vertical axis measure prices under different scenarios and C = unit cost of production and sales for all scenarios for simplicity. Cost in this case includes a "normal" profit, a return equal to the cost of capital for the firm. Q represents quantity sold or numbers of patients. The contribution to social welfare (SW), or value, is always excess profit plus consumer surplus. Excess profit is profit over and above the cost of capital of attracting investment. This is the lure for investors to invest in risky ventures like new drug development in the first place.

Consumer surplus is the difference between what consumers are willing to pay – displayed in the kinked demand curve in bold (the line P_1adg), and what they have to pay, or price. This demand curve is meant to reflect the simplifying assumption that exactly Q_1 patients are willing to pay P_1 for the drug. Consumers get the value they pay for if price is what they are willing to pay, but they as a group get a "bargain" or a surplus if at least some of them are willing to pay more than they have to in the (more competitive) marketplace. There is today a LOT of consumer surplus in the market for antibiotics, which also save lives, but are so ubiquitous we sometimes forget they have been cheap for a very long time. This is simply to say that market prices reflect scarcity value, not necessarily clinical value. Patents and exclusivity rights give the inventors of new drugs the power to control scarcity value.

In the proverbial case of a very high specialty drug launch price, $P = P_1$, and there is no consumer surplus, but profits, price minus cost multiplied by quantity (the area P_1 abC) are quite large. In this case, the drug company captures all the SW value of the drug, and the people with the highest willingness to pay, the rich or those with great insurance coverage with no restrictions on access, are the only ones who get it. After patents or exclusivity have expired, competition from follow-on generics or biosimilars -- if biosimilars are approved for use -- enters the market and price falls to P_2. Now more consumers can afford to access the drug, SW in total rises, consumer surplus rises to the area P_1adP_2 and profit falls to P_2 dfC. In the long run, at least theoretically, more entry by generics or biosimilars or different delivery mechanisms drives the market for this drug to a perfectly competitive state, price falls to C, no excess profit is earned, and consumer surplus now captures all the maximum value of SW represented by the area P_1agc. Do note that SW = CS = P_1agc in perpetuity is an outcome of the original investment in the drug by the first company. We sometimes forget this when focused on the high profit of P_1 abc at the launch of a new drug. Drug companies know they will *never* capture all of the SW that their innovation will generate over time. That is why they need to be encouraged by public policy to invest in the first place.

To simplify and recap, consumer advocates want prices to be as low as they can be, as soon as they can be, to tilt the balance in SW toward consumer surplus and away from profit, *given* that we keep the right kinds of innovation flowing. Manufacturers, on the other hand, want more of SW to be captured in profits as long as possible, as that does keep the incentive to invest high. Public policy is about setting rules and regulations to balance these two competing forces – competition and innovation – to maximize social welfare while being mindful of the distribution of SW as well.

So what should we do? Given the stakes involved there is no shortage of suggestions, most of which are either variants on substituting public capital – through tax credits, grants, or prizes – for private capital, and thus allowing "comparable" rates of return to today to be earned on lower private investment with lower new drug launch prices,[23] OR they require the more precise use of existing expedited access and post-launch diagnostic programs to get the right drugs to the patients most likely to benefit from them.[24] Other variants include freeing government and commercial payers to refuse to cover some drugs and indication specific pricing, especially those that either do not extend the quality or length of life very much compared to existing treatments,[25] and binding arbitration for truly unique drugs.[26]

All of these policy ideas have merit and should surely be tested, for problems of this scale require all the arrows in our quiver. I propose to add a more structural suggestion that might in the long run enable us to avoid federal bureaucracies and expert consultants – however talented – being forced to make complex judgments about which company's products are more promising in early phases of research in order to invest *public* capital at a time of federal budget stress, or which tests clinicians should be required to perform before access to rare drugs for life threatening conditions at reasonable prices will be granted.

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[23] *Valverde et al, op cit; Hirsch et al, op cit; J. Stiglitz and A. Jayadev, "Medicine for Tomorrow: Some Alternative Proposals to Promote Socially Beneficial Research and Development in Pharmaceuticals," Journal of Generic Medicines 7(3):217-26 (2010).*

[24] *A. Kessleheim et al, "Existing FDA Pathways Have Potential to Ensure Early Access to and Appropriate Use of Specialty Drugs," Health Affairs 33(10):1770-78 (2014).*

[25] *P. Bach, "Indication Specific Pricing for Cancer Drugs," Journal of the American Medical Association 312(16):1629-30 (2014); P. Bach, "Why Drugs Cost So Much," New York Times Jan 14, 2015.*

[26] *Frank and Newhouse, op cit. footnote 9.*

Although penicillin does present a quaint counter example, innovation in scientific knowledge that can improve millions of lives today does require substantial investment and a reasonable expectation of return to at least cover the cost of capital and risk inherent to such investments. The prospect of outsize (or "excess") returns may direct short run capital flows and excite a kind of frenzy of effort, but outsize returns are not necessary for the sustaining investment, they are merely icing on the cake, icing that would be licked away soon enough if markets are allowed to become truly competitive, i.e., as efficient as they can be over time.

A Modest Proposal

What if we changed existing law enough to say this to developers of newly approved specialty drugs: you can price them as you will, this is America, but if you price them high enough, you will forfeit the marketing and/or data exclusivity grants that the FDA is empowered to make – but not your patents from the US Patent Office -- and encourage competitors to enter the market with all our regulatory powers and fast track authorities.

We cannot revoke patents without running afoul of international trade agreements, not to mention the legitimate ire of other technologically dependent industries, but we can darn well refuse to protect abusive monopolists from competition from similar drugs one day longer than absolutely necessary. Long-time observers and supporters of the drug industry have recently written: "Data exclusivity is arguably more important for modern biologics than for any other industry."[27] This is because patents are applied for early in the development process, development time for biologics is longer, so effective, post-marketing patent life is shorter for them than for traditional small molecule drugs. Most of the recently approved and coming specialty drugs that clinicians and payers are worried about paying for are biologics. Thus, threatening to revoke exclusivity for bad pricing behavior by specialty biologics is a powerful deterrent in the hands of policy makers. And giving this tool away by relinquishing Congress' right to revisit exclusivity from time to time, as is rumored to be in the still secret Trans-Pacific-Partnership trade agreement, is a *very* bad idea. Call your senators *now*.

So we could decide (today) to make "exclusivity" conditional on launch prices, and deny it if prices are "too high." How high is "too high?" Where is Aristotle when we need him? I would suggest there are two kinds of drug companies, those that are established and have a robust ongoing research program, and those who are new and have no products earning substantial funds at the present time and who put all their hopes on the new drug coming down the pike.

For the established firm, "too high" is a price that net of production, marketing *and current R&D costs* will yield a rate of return on sales more than 20% above the cost of market capital for the manufacturer, the rate at which the firm can raise new funds from shareholders, investors and bankers. This implicitly assumes the amount of R&D they are doing at any given time is an "equilibrium" amount and thus this approach will fund today's R&D activities even given the expectation that some will not pay off. Thus, the "regulated" price preserves cash flow for a robust amount of R&D, the major purpose of new cash flow for an established firm.

[27] *Calfee, op cit footnote 11.*

The market cost of capital is observable from publicly traded company documents and is relatively objective, for the sophisticated investors who collectively determine such interest rate costs are privy to risk and return realities and alternative productive uses inside the drug industry and across the world economy. For example, if a company can borrow in competitive capital markets, either debt or equity, at 10%, the price of a new specialty drug is too high if it would enable them to earn (properly discounted for time and interest costs) 12% or more going forward. Since Gilead earned almost 50% in 2014, they clearly were charging "too much" initially by this standard.

What if the drug was a true breakthrough, for example, a Hepatitis C or even an Alzheimer's cure? Shouldn't it be allowed to earn a rate of return commensurate with the value this would convey to our society? Remember the point of regulation is to keep launch prices below the profit maximizing one with which the firm would capture *all* of the social welfare value of the drug until competition – however long it takes -- begins to erode profit. One could preserve incentives for "breakthrough" investments by allowing them to earn 40% more than the cost of capital, compared to 20% more for a more modest clinical and social value drug. This calibration could evolve into a form of "pay for performance" for new drugs.

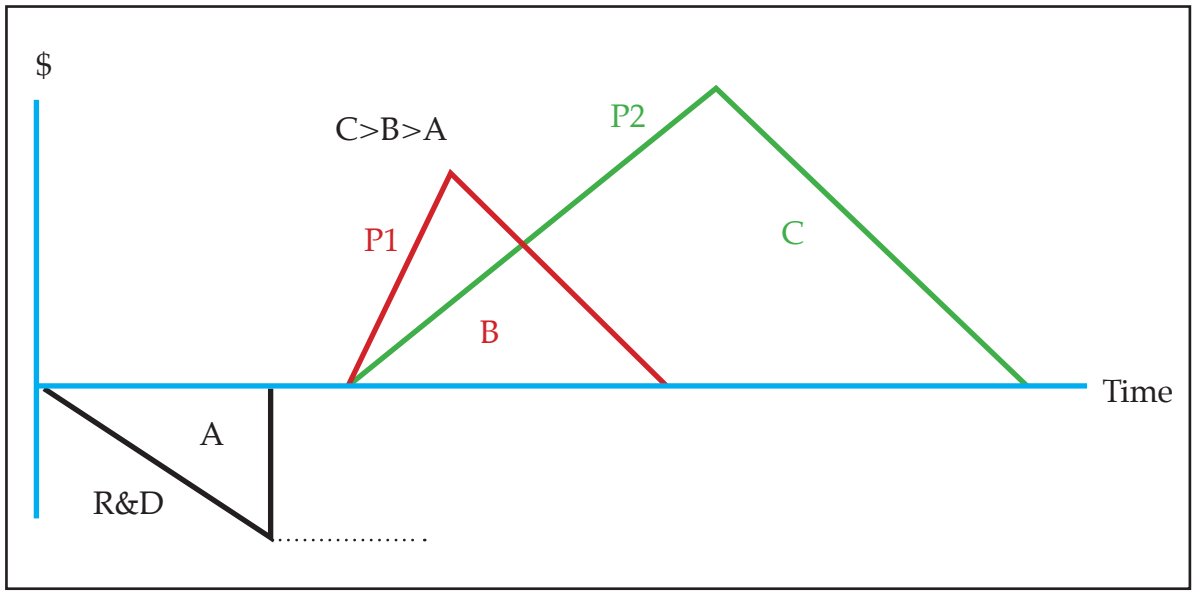
If you really want to use policy to improve the social value of investment, you could discount the amount of marketing costs allowed in this rate of return calculation, in the limit at 100% but in the beginning perhaps at 50%. Not counting marketing costs as much in the allowed price/rate of return would discourage marketing expenses, which many consider to be excessive, since they outweigh R&D by almost 2:1. Only television stations will complain if direct to consumer advertising begins to decline, finally.

New firms with new products who are without a portfolio of products to sell at the moment and a pipeline that is being developed in a kind of equilibrium will need a higher rate of return than this. They do have to pay off the past R&D, or at least pay off the venture capitalists that funded them to this point, presumably near completion of stage III clinical trials. They could sell their firm or product to an established firm, who would then be entitled to earn 20% more than their cost of capital on a base that includes the newly acquired debt. But in the long run more drug companies implies more competition both post-marketing and in the development stages. I propose allowing the new firm to earn 50% more than their cost of capital upon launch of a new, first in class specialty drug, where the cost of capital includes the cost of servicing and eventually retiring their new product-specific debt. We should also recognize that new firms need marketing spending to take market share from established treatments, however inferior, so they should have a smaller or zero marketing discount in their rate of return calculation. This will preserve the incentive for the new firm to develop and market new drugs and to remain independent. Their higher rate of return will still very likely be well below what Gilead earned due to Sovaldi in 2014.

A Graphical Example

Let Figure 2 represent cost, revenue and net present value of profit flows to a drug company under different launch pricing choices. The oversimplified graph illustrates that R&D costs must be incurred before revenues and that higher launch prices (P1 > P2) will yield more revenue during the monopoly period, of course. But if we imposed the conditional exclusivity policy that I am proposing, so that we end the company's monopoly with patent life if they priced "too high" but not if they priced below that, then the subtleties of Figure 2 would be relevant.

Figure 2. Net Operating Profit from Alternative Launch Pricing Strategies and Policies



The area A is the total (past) R&D cost. Area B is the area under the red triangle, the profit that would ensue if the company chose the launch price P1 which is "too high," so high that exclusivity will not be granted and therefore the monopoly will end with patent life, typically a few years at most from FDA approval and market launch of biologics. Area C could be earned if the lower launch price P2 was chosen, for then the period of exclusivity would last much longer. Thus, with a credible threat of removing exclusivity, the drug company can be "nudged" to P2 and still make a healthy ROI while charging lower prices for the life of its monopoly period.

This lower launch price is key, for all follow-on biosimilars or other competitors, when they enter, will discount off of the first in class and first to market's chosen launch price. Thus, lower launch prices reduce average prices in all time periods. The point of the policy is to reduce launch prices, which in essence makes the market behave more like a competitive one from the outset.

Important as follow-ons are to competition and to ultimately moving the larger SW toward more consumer surplus, we must take care not to overly encourage them. The profit for the first-to-market should be and is highly likely to always be greater than for those who enter second or third. To ensure that, we should make clear these policy changes are not meant to become guaranteed rate of return regulation for all drug companies. That is, only the first in class will go through the rate of return calculation process, and that is to constrain launch prices if necessary. For later arrivals, they will simply not be allowed to charge more than the initial entrant charged at launch; they are guaranteed nothing. This price regulation will not likely be binding on their choices, for new entrants are normally forced to undercut the first in class product from the outset anyway, to gain market share. Again, the point of the upper bound regulation is to lower average prices throughout the product life-cycle.

Allowed rate of return regulation for the innovative first movers – the markups over the cost of capital I have discussed, of 20% for established firms and 50% for start-ups -- could be adjusted over time as perceptions of the importance of more innovation might change. The policy would create for the US the first explicit tradeoff and choice about how much we are willing to pay – in terms of higher launch prices – for more or less innovation in the future. This explicit tradeoff function might be very valuable as we balance competing health policy priorities throughout the 21st century.

Concluding Thoughts

Lest you think the sort of accounting reporting that would be required to regulate these upper bound prices is unprecedented and intrusive, please remember that through Medicare cost reports, which hospitals are required to file, CMS policy makers (including the Medicare Pricing Advisory Commission, or MEDPAC) actually know the margins that specific hospitals make today. Through practice expense surveys essential for Medicare fee schedule updates CMS policy makers also have pretty good ideas of the margins earned by physician practices, by specialty. The ACA requires not only medical loss ratio reporting but also regulation of it by the federal government for all insurers, by market segment (small group, individual) for the first time ever. Why should drug manufacturers - - and device companies for that matter – be exempt from having their margins evaluated by policy makers? We would not be in this situation if health care did not cost too much and if the temporary monopolies granted for a public purpose – to encourage innovation – were not being so obviously abused. But here we are.

The general policy of limiting launch prices through profit rate regulation could be tied to coverage decisions for new drugs, instead of to the grant of marketing or data exclusivity. For example, Medicare could say no drug priced "too high" as defined above will be covered. The UK does something similar in the NHS today.[28] Medicare is most vulnerable for Part B drugs which tend to be the anti-cancer biologics that are administered by physicians and have been so outrageously priced lately. In the sad event the contingent exclusivity option is foreclosed by an international trade agreement, this might be a useful place to start, though doing so will not be easy, since Medicare has historically been prevented by Congress from using cost as a criteria for coverage of anything.

[28] *https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/282523/Pharmaceutical_Price_Regulation.pdf*

But the recent commitment to alternative payment models,[29] and the coming debate over "entitlement reform," i.e., restructuring Medicare for long run sustainability, present opportunities to finally modify this policy constraint. Once in place, private insurers and PBMs could follow Medicare's lead with this "too high" pricing policy, and if they all stick together, collective bargaining power could reduce launch prices to something closer to P2 than they are today. It is also true that bundled and reference pricing arrangements between payers and service providers could incentivize providers to use only those drugs with the most clinical and economic value, but in a world with few competitors – i.e., before biosimilars are common – this tool alone will be of limited value.

There is some risk that this "excess price" determination process could devolve into a kind of public utility rate of return regulation for the first-to-market firms. Economists have long pointed out that rate of return regulation can lead to too much capital investment since total profits typically rise with greater capital investment in such arrangements. The analogy under my proposal is that drug companies would be incentivized to invest in low value drug prospects because the more R&D spending the company could count either toward past or current expenses, the higher the price they could earn on the few that make it to become exploitable market opportunities. The first line of defense against this risk is that the proposed rate of return regulation would only apply to first in class, not follow on products. Still, any regulation might ultimately require clinical judgment about actual R&D spending promise, rather than just counting whatever the drug company wanted to claim. However, this is a lever that can be dialed up or down, and at the outset, precisely because the world seems more worried about too little investment in drug R&D in general and in both the specific blockbuster and in the smaller specialty categories, maybe encouraging "too much" drug R&D for a change might be smart public policy. At a minimum it could be monitored and modified over time.

So what price should we pay for specialty drugs? Enough to keep productive R&D investment flowing into a risky and vital industry, but not whatever the successful companies want to charge just because they can, due to the monopoly we granted them. In short, we need to make clear that monopolies come with responsibility and accountability, and that competition is more important to public policy than a blank check for innovation.

[29] *http://www.hhs.gov/blog/2015/01/26/progress-towards-better-care-smarter-spending-healthier-people.html*