



Pricing Drugs for Innovation and Affordability

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Overview

- The Aducanumab storm
- Prices need to be high; Prices need to be low
 - The price ceiling: Value for money
 - The price floor: Sustaining innovation
 - Pricing with evidence development

The Aducanumab Storm

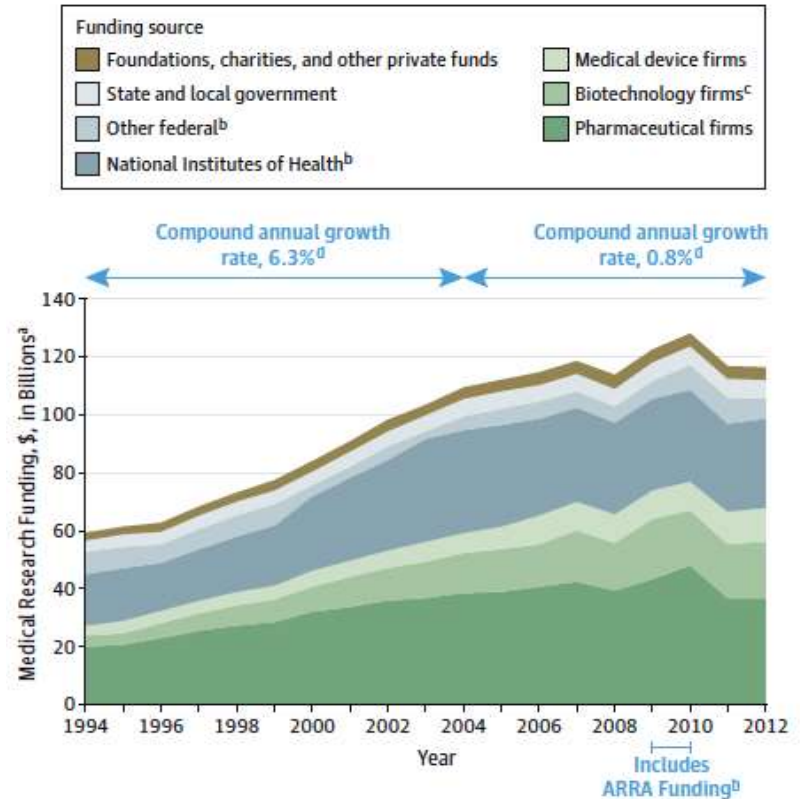
- Alzheimer's disease is a severe and very expensive condition afflicting 4 million Americans, with prevalence growing as the population ages
- Aducanumab effectively targets beta-amyloid plaque (biomarker), but the clinical evidence of efficacy in ALZ patients is weak (very weak)
- FDA approved the drug using highly unusual accelerated review
- The manufacturer Biogen set a very high price \$56,000/patient, not counting the cost of diagnostic scanning, for life
- Medicare established restricted 'coverage with evidence development'
- Most doctors have refused to prescribe the drug
- Sales have been negligible
- Biogen is threatened with insolvency, has begun layoffs
- Everyone is mad at everyone

The Drug Pricing Conundrum

- Prices need to be high to finance R&D
 - They must cover the costs of R&D, and not merely marginal costs of manufacturing. But prices vary across nations, and the burden of innovation is not shared. How should R&D be financed?
- Prices need to be low to ensure access and affordability
 - They should reflect value, but evidence of value is weak at time of initial market launch, when prices are set. Prices should evolve over time, along with the evidence, but don't

Drug Prices Need to be High

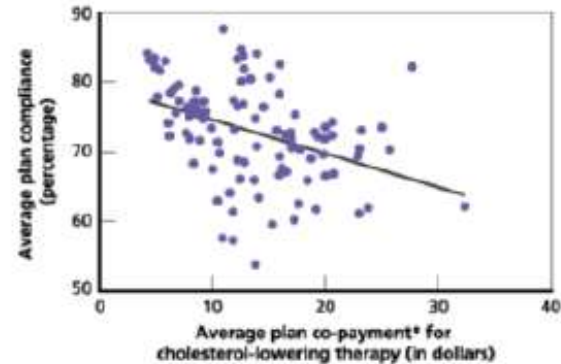
- Industry funds 60% of R&D in the US; this share has risen over time as governmental NIH funding has eroded and the government does not support product development
- Industry funds product development, and obtains its investment capital from profits based on prices that significantly exceed costs of production



Drug Prices Need to be Low

- High drug prices place budgetary burdens on insurers, who then must raise premiums (private plans) and taxes (public programs), as well as increase coinsurance and deductibles
- High cost-sharing requirements induce even very sick patients to abandon their prescriptions and suffer adverse effects

Figure 3. As Co-Payments Rise, Compliance with Drug Therapy Falls

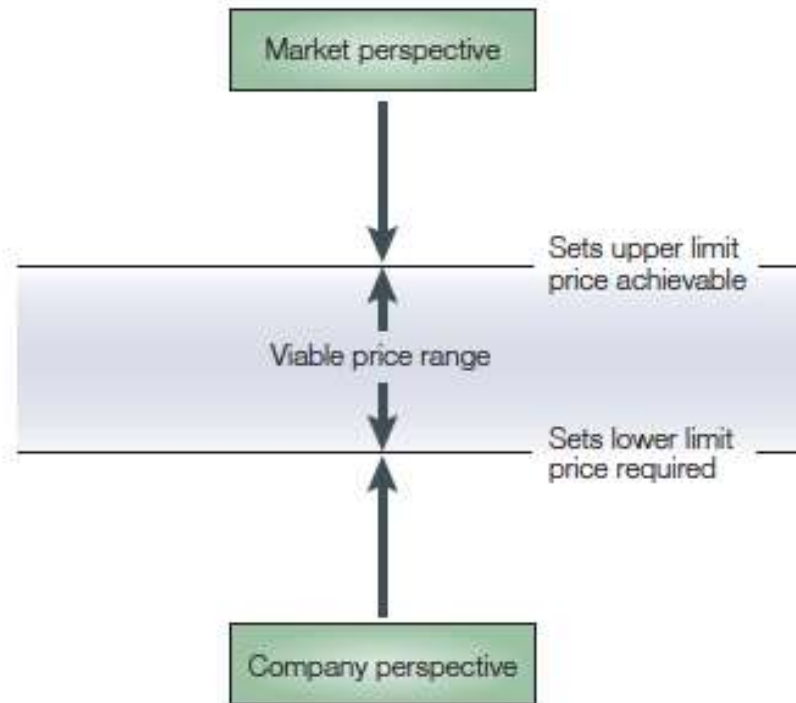


SOURCE: Goldman et al., 2006. Used with permission.

*Average co-payment for each plan year is for a 30-day supply of cholesterol-lowering therapy.

Prices Must Fall below the Purchaser's Maximum (Value) and above the Producer's Minimum (Cost)

- What is the social value of a drug (the maximum price a purchaser will pay instead of going without)? How do we measure comparative clinical and cost effectiveness?
- What is the efficient cost of developing a drug, including R&D, manufacturing, and distribution (the minimum the innovator can accept and sustain itself)?





The Ceiling on Drug Prices: Obtaining Value for Money

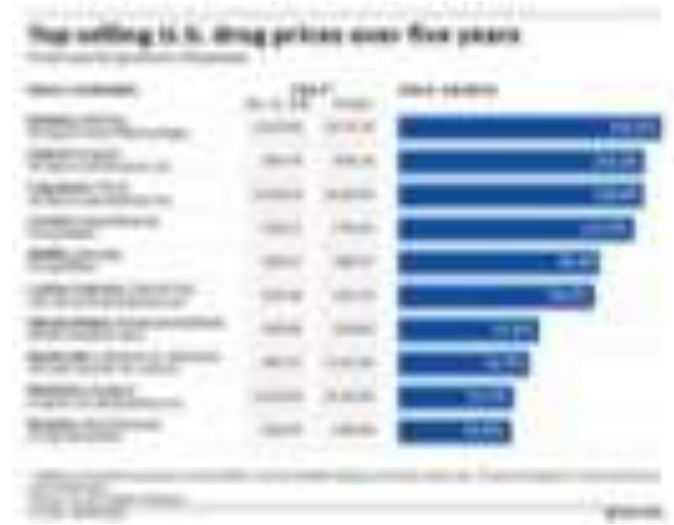
The more that purchasers spend on drugs, through high prices, the less they can afford to pay for other needed products and services. It is imperative that they obtain value for their (our) money.

Value is Demonstrated Value

- The value of a new drug is its performance (safety, efficacy) relative to products already on the market. Price should align with evidence: 'value-based pricing' (VBP)
- The development of evidence is central to determining value
- The US needs, but lacks, a reputable public entity to conduct health technology assessments (comparative clinical and cost effectiveness).
- We are lucky to have a reputable private nonprofit HTA entity: The Institute for Clinical and Economic Review

Value Evolves over the Product Lifecycle

- The evidence on drug performance is weakest at time of initial market launch and then gradually improves over time, with experience and follow-on studies.
- Value-based pricing should be dynamic pricing
- In the US, however, manufacturers can (and do) raise prices each year absent positive new evidence of patient benefit
- In the EU, in contrast, many nations impose price reductions each year, when sales targets are reached, absent negative new evidence



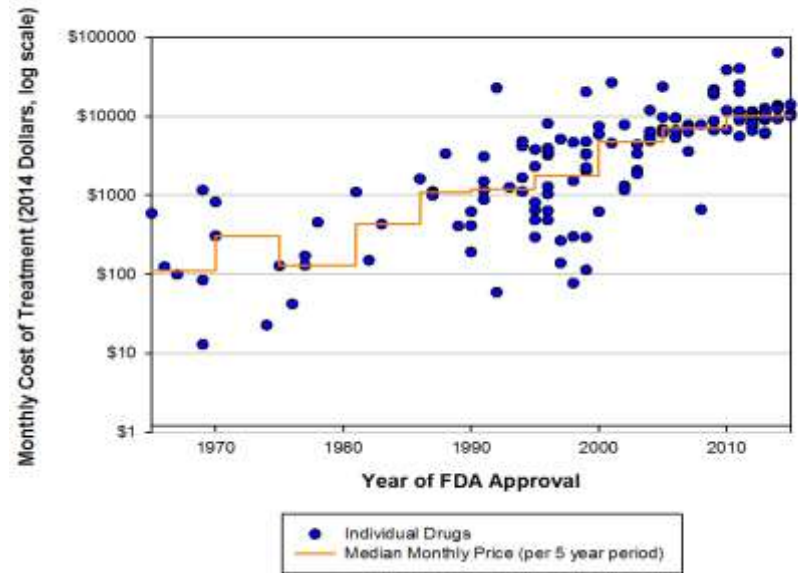
FDA Is Reducing Evidentiary Requirements

- In the laudable effort to reduce costs of innovation and delays in patient access, FDA has been steadily reducing the evidentiary burden on new drugs
- The accelerated authorization pathways were developed for HIV, extended to cancer, and are being applied to other conditions
- Typically these drugs are approved based on biomarker evidence, to be followed by required clinical trials
- But there is no enforcement mechanism and, meanwhile, firms can market and sell their drugs at whichever price they choose
- 74% of drugs approved by FDA in 2021 went through one of the expedited pathways: fast track, breakthrough, priority, or accelerated approval

FDA Accelerated Authorization Creates Dilemmas for Medicare and Private Insurers

More and more drugs are coming onto the market with less and less evidence. This puts the payers in the difficult position of deciding whether to cover a new drug that lacks convincing evidence of value, and of negotiating a price aligned with value. Not surprisingly, prices have been rising rapidly

Monthly and Median Costs of Cancer Drugs at the Time of FDA Approval
1965-2015



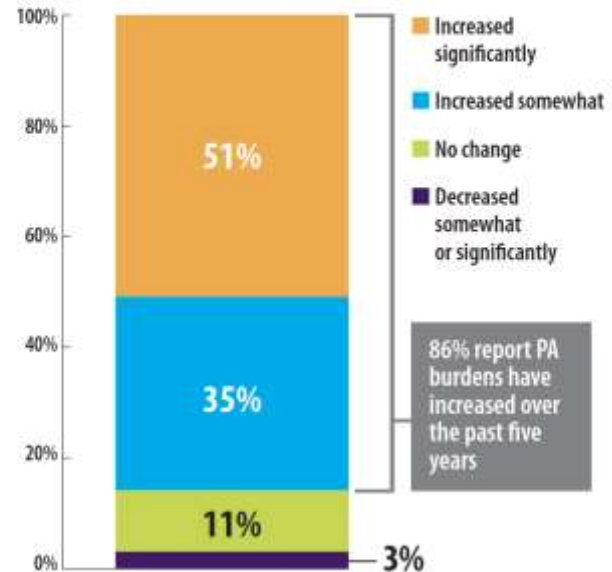
Source: Peter B. Bach, MD, Memorial Sloan-Kettering Cancer Center

The War of All Against All

Insurers have little leverage on price and are responding to weak-evidence on new drugs by restricting patient access: formulary exclusions, prior authorization requirements for physicians, cost sharing requirements for patients. These have gotten much more prevalent and onerous in recent years.

Change in PA burden over last five years

Q: How has the burden associated with PA changed over the last five years for the physicians and staff in your practice?





The Floor on Drug Prices: Supporting Innovation

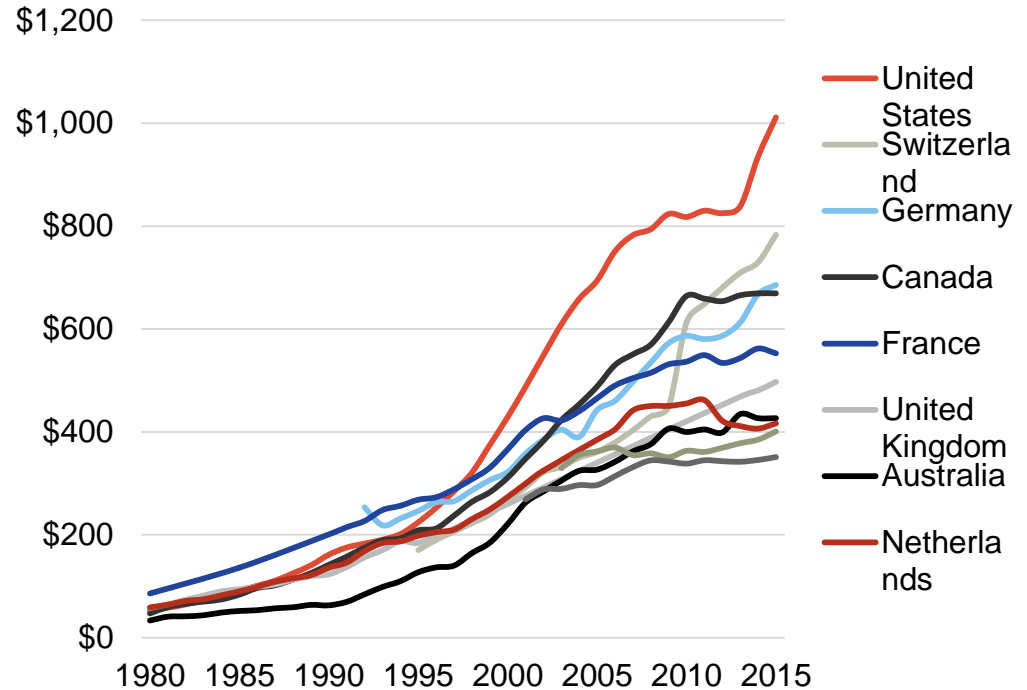
- Prices and profits from today's drugs supply the investment capital for tomorrow's drugs
- But the US bears, through much higher prices, most of the R&D financing burden for the world
 - Is there another way?

Prices Must Cover Costs. What are Costs?

- Drug firms must cover their costs via product revenues
- In the short term, prices for each pill and vial must cover the marginal costs of manufacturing and development
 - Prices for generic drugs need not cover R&D, and hence average 20% of the prices of branded drugs
- Over the long term, prices must also cover the fixed costs of R&D
 - Patent and FDA regulatory exclusivity protect the prices of newly launched drugs from competition. Monopoly profit by design

The US Spends the Most on Drugs in the World

- Drug firms charge different prices to different national payers depending on their GDP/capita and purchasing sophistication
- The US pays by far the highest prices, due to high GDP and low sophistication



The United States has the Most Innovative Life Sciences Industry in the World

The FREOPP World Index of Health Innovation gives the US low marks for affordability but high marks for science and tech innovation

Overall Rank	Country	Overall Tier	Overall Score	Quality	Choice	Science & Technology	Fiscal Sustainability
1	Switzerland	Excellent	59.56	73.35	46.53	47.28	71.06
2	Germany	Excellent	59.28	60.99	47.95	46.90	81.28
3	Netherlands	Excellent	59.14	65.70	50.42	49.97	70.46
4	United States	Excellent	54.96	59.71	57.65	75.14	27.33
5	Ireland	Excellent	54.48	67.07	41.77	40.71	68.39
6	Israel	Good	51.14	63.89	43.20	38.79	58.69
7	Singapore	Good	50.37	55.77	46.84	47.98	50.89
8	Czech Republic	Good	49.80	52.22	40.80	27.39	78.78
9	Belgium	Good	49.65	56.55	39.23	44.89	57.95
10	Taiwan	Good	49.19	57.15	46.42	25.28	67.90
11	Australia	Good	48.38	69.51	45.38	26.67	51.97
12	Norway	Good	48.26	64.16	32.06	43.74	53.11
13	United Kingdom	Good	47.78	58.76	42.01	49.39	40.97

What if US Drug Prices are Squeezed?

- The US market accounts for 4% of global sales by volume, 40% of global revenues (due to high prices) and 75% of global profits (costs are similar across nations, while revenues are higher in the US)
- If net prices, after discounts and rebates, are squeezed in the US, it will have major impacts on the global industry and its ability to fund R&D
- The alternatives include:
 - Higher prices in other nations (unlikely)
 - Reductions in R&D investments (unfortunate)
 - Increased reliance on government grants for R&D
- Are there new models for financing product development?

Public Grants for Product Development: The OWS Experience with Covid Vaccines

Firm	Total Public Investment (millions)	Product Development	Clinical Trials	Manufacturing Capacity	Procurement (AMC)
Moderna	\$4,146	Yes	Yes	Yes	Yes
Pfizer/BioNtech	\$3,961	No	No	No	Yes
Sanofi/GSK	\$2,073	Yes	Yes	Yes	Yes
Novavax	\$1,600	No	No	Yes	Yes
Janssen (J&J)	\$1,458	Yes	Yes	Yes	Yes
AstraZeneca	\$1,600	Yes	Yes	Yes	Yes
Merck/IAVI	\$38	Yes	No	No	No

From OWS to ARPA-H

The Biden administration has proposed the creation of an Advanced Research Projects Agency for Health, on the model of DARPA and BARDA, to promote domestic product development in the life sciences. There is broad support in principle but serious political opposition in practice.

Created correctly, the Advanced Research Projects Agency for Health will accelerate medical innovation

By George Vradenburg and Ellen V. Sigal May 27, 2021





A Tonic for the Aducanumab Storm?

- Coverage with Evidence Development (CED)
- What is Pricing with Evidence Development (PED)?
 - Would PED have helped with Aducanumab?

Coverage with Evidence Development

- Medicare can decide to pay for a drug through the pathway of 'Coverage with Evidence Development' (CED)
- A manufacturer obtains reimbursement despite having weak evidence of patient benefit but is required to finance follow-on clinical trials and/or observational studies.
- In principle, coverage could be withdrawn if the follow-on studies are not conducted or if they generate negative evidence of benefit. In practice, it is politically almost impossible for Medicare to withdraw coverage, and many follow-on studies are late or never done at all
- Meanwhile, the manufacturer can set whatever price it chooses and market its product aggressively

Pricing with Evidence Development

- The principle of Pricing with Evidence Development (PED) is that price should align with evidence across the life cycle of the drug
- At time of launch, the product's price should be low, as the evidence of effectiveness typically is limited (FDA accelerated review)
 - Launch price can be based on health technology assessment
- In the years after launch, price should increase if the manufacturer presents new evidence of patient benefit. The extent of the new evidence needed to generate a defined increase in price can be negotiated at time of launch (to reassure the manufacturer)
 - Absent new evidence on benefit, the low launch price would not be increased

Comparing PED with CED

- Pricing with Evidence Development is less restrictive on patient access than CED, since coverage is extended to all patients, not only for those in clinical trials
 - It could be combined with requirements that new evidence be collected in patient registries, to facilitate analysis
- PED forestalls the ability of the manufacturer to charge high prices and earn high profits on a drug of unproven effectiveness
- It create an incentive for manufacturer to conduct and complete the follow-on clinical trials, since this is the only way to increase price
- This would have been very useful for aducanumab

Aducanumab

- The manufacturer (Biogen) won their battle but lost the war
 - Accelerated FDA review, albeit with very weak evidence
 - Very high price per patient
 - Narrow CED, physician non-prescription
 - Future of firm is in doubt, layoffs have begun
- Purchasers won their battle but lost the war
 - Spending is low but patient access is very restricted
 - There will be very little new evidence being generated
 - Other drug firms will hesitate to launch their ALZ drugs
- There must be a better way