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EYE ON THE MARKET | SPECIAL EDITION

Sick as a Dog

The cheapness of US healthcare stocks, and the battle over publicly funded science research

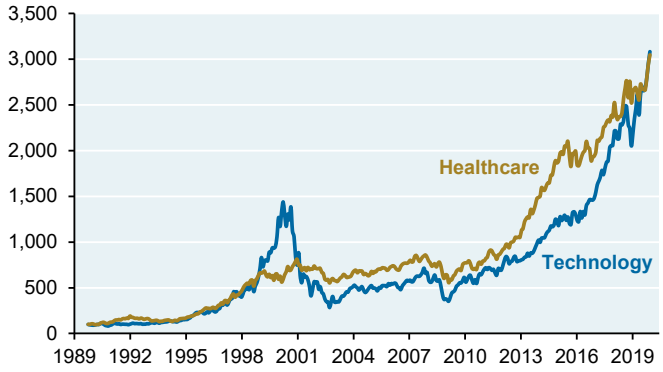
For three decades until 2020, US healthcare stocks generated roughly the same returns as the tech sector, and with much less volatility. Things have changed a lot since then as the tech sector has barreled ahead while healthcare has stagnated. In this special issue, we take a closer look at the many factors dragging down the healthcare sector to among the lowest relative valuations of the last 30+ years, and some possible catalysts for a rebound. To conclude, the latest in the battle over publicly funded US scientific research and a section on longevity drug studies in mice.

By **Michael Cembalest** | Chairman of Market and Investment Strategy for J.P. Morgan Asset & Wealth Management

Sick as a Dog: the cheapness of US healthcare stocks, and the battle over publicly funded science research

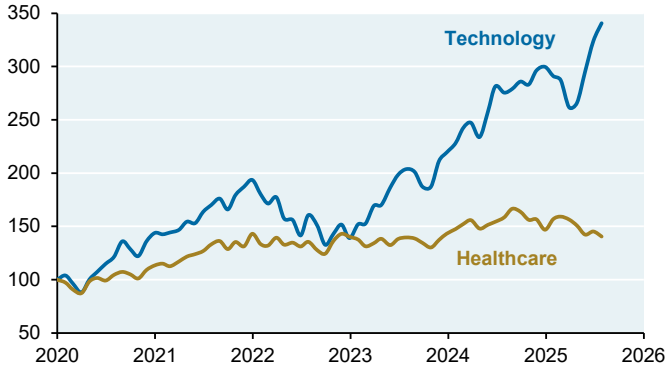
For the 30-year period from 1989 to 2019, the US healthcare sector closely tracked technology returns, and with considerably lower volatility (15% vs 24%). Things have changed markedly since then as tech barrels ahead while healthcare stagnates. The large cap pharma forward P/E of 14x doesn't sound that distressed, but Eli Lilly is 35% of the S&P 500 Pharma Index and trades at a forward multiple of 24x (down from 31x in July 2025 before LLY reported disappointing results from its oral GLP Phase 3 trials). Remaining pharma stalwarts like Merck, Pfizer and Bristol Myers trade at forward P/E ratios of just 8x-9x; biotech trades at one the largest valuation discounts in the market while 80% of biotech IPOs since 2018 have imploded; managed care returns have collapsed; and life sciences companies may be hurt by cuts to the NIH, NSF, CDC and other scientific research organizations, a trend which is already visible in the form of sharply reduced NIH grants through July of this year.

S&P 500 healthcare vs technology, 1989-2019
Total return index (100 = September 1989)



Source: Bloomberg, JPMAM, July 2025

S&P 500 healthcare vs technology, 2019-2025
Total return index (100 = December 2019)



Source: Bloomberg, JPMAM, July 2025

In this Eye on the Market, we review what's going on under the hood: healthcare valuations and earnings growth; bipartisan proposals to lower drug prices, including Most Favored Nation approaches; competition from China; pending Section 232 tariffs on the pharma sector; the pace of FDA drug approvals and the impact of RFK Jr at HHS; Trump proposals to cut NIH/CDC funding; the large cap pharma patent/revenue cliff; patent thickets and efforts to reduce them; the impact of the Big Beautiful Bill on the Managed Care sector; the rising rate of legal judgments favoring healthcare providers over insurers; and the challenges facing GLP manufacturers seeking to broaden adoption rates. At the end, an appendix on the battle over publicly funded US scientific research, and a section on recent longevity drug studies in mice and the future of organoids in clinical trials.

Michael Cembalest
JP Morgan Asset Management

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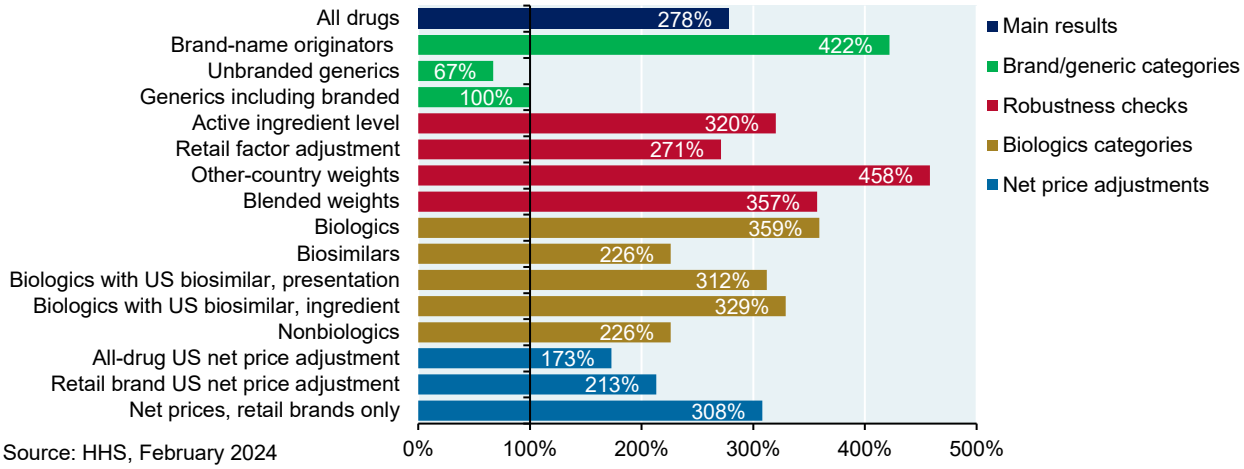
US drug prices as a % of select OECD country prices

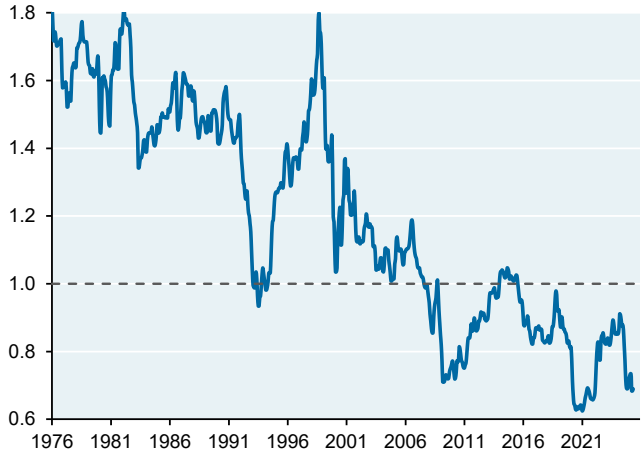


Source: HHS, February 2024

On valuations: how far healthcare has fallen

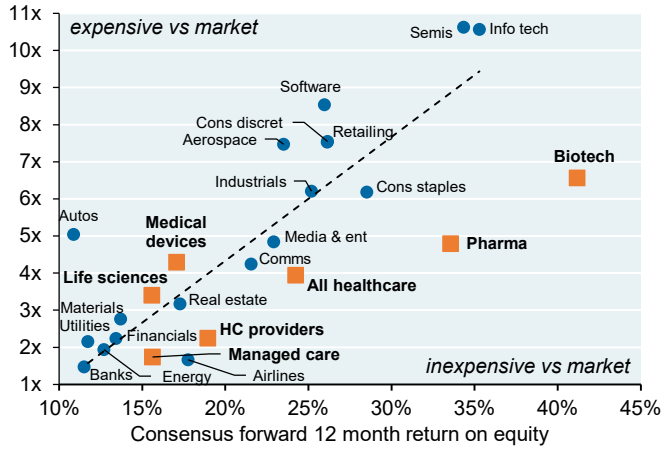
The first chart shows the collapse in healthcare P/Es vs the S&P 500. Healthcare has not traded at a premium to the S&P 500 since the early 2000's, but now trades at a substantial discount. The second chart shows the cheapness of healthcare industries when comparing price to book ratios with expected return on equity. In this framework, industries below the diagonal dotted line are less expensive. The third chart shows how healthcare industries are priced at the low end of their historical P/E ranges since the early 1990s. The last chart shows current healthcare market cap by industry.

Large cap pharma stock valuations
Forward P/E relative to the 750 largest stocks by market cap



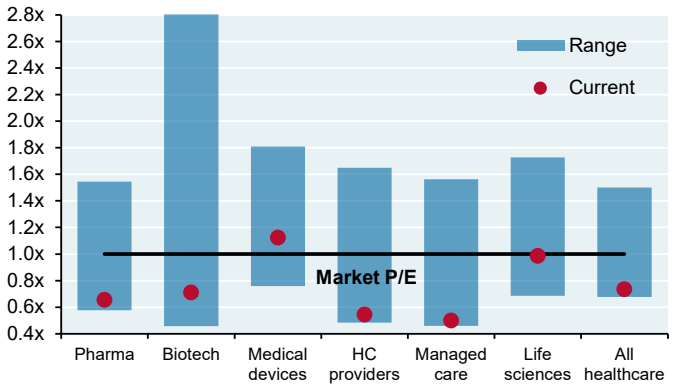
Source: Empirical Research, June 2025

S&P 500 valuations vs return on equity
Consensus forward 12 month price to book ratio



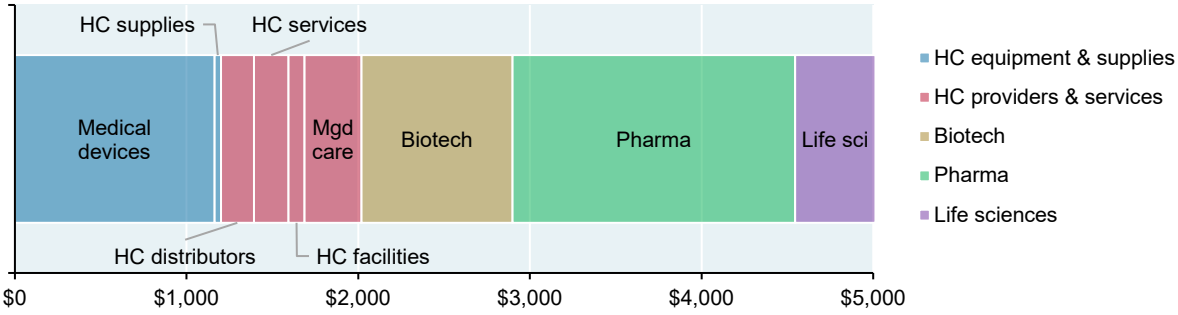
Source: Factset, JPMAM, August 7, 2025

Healthcare P/E ratios vs the market since 1992
Relative forward P/E ratio vs S&P 500



Source: Bloomberg, JPMAM, July 29, 2025. Life sciences since 2005

S&P 500 healthcare market cap by industry, US$, billions



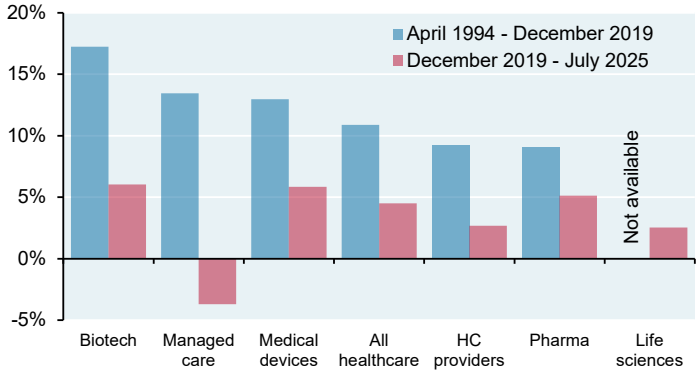
Source: Bloomberg, JPMAM, August 5, 2025

Healthcare market returns and earnings growth

In the first chart, you can see how much things have changed: the blue bars show annualized healthcare industry returns for 1994-2019, while the red bars show annualized returns for 2020-2025. The pre- and post-2020 gaps are even larger when looking at most healthcare industries in the mid-cap space (right chart), and when looking in the small cap space as well. HC Providers is a broad grouping that includes wholesale distributors, lab testing, pharmacy management, hospitals, nursing homes and managed care (insurance). Note how during the pre-2019 period, Biotech generated almost twice the annualized return as Pharma; since 2020, this performance premium has almost completely disappeared.

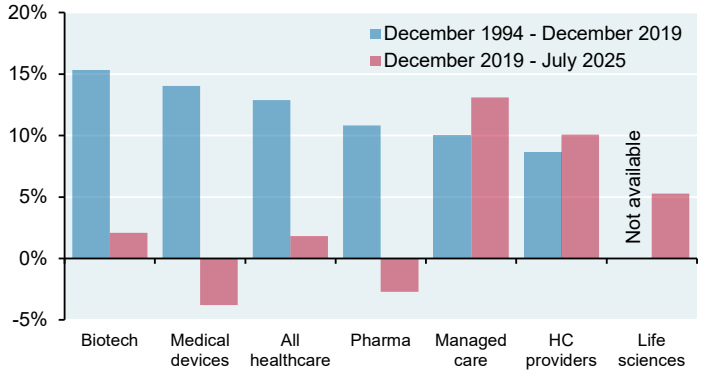
The fourth chart comparing earnings growth across healthcare and technology since 2017 is another way of understanding why pre-2020 patterns have broken down. Biotech earnings growth has been negative since 2017, and large cap pharma earnings have only exceeded telecom equipment within the tech sector.

S&P 500 healthcare returns
Annualized return, percent



Source: Bloomberg, JPMAM, July 2025

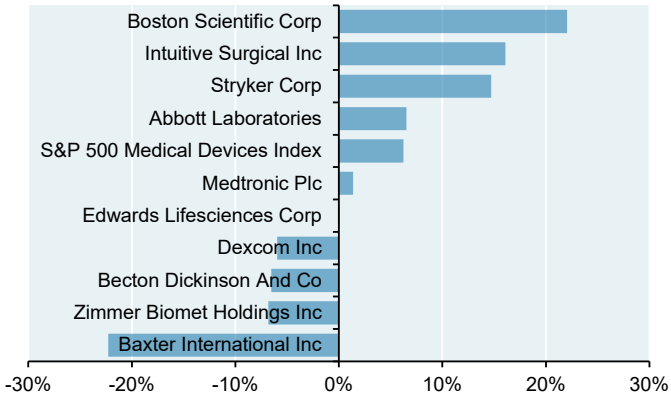
S&P 400 (mid-cap) healthcare returns
Annualized return, percent



Source: Bloomberg, JPMAM, July 2025

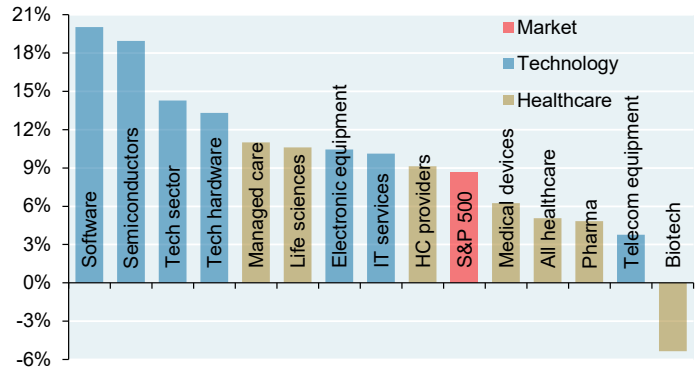
Like most sectors, there's plenty of performance dispersion across healthcare stocks, rendering the industry average a bit less relevant for stock pickers. Medical Devices is a great example of haves and have-nots, as shown below. The primary driver of outperformance among companies like Stryker, Boston Scientific and Intuitive Surgical has been double digit R&D as a % of sales or a consistent acquisition strategy of small companies as opposed to large M&A, which historically has led to decreases in return on invested capital and shareholder value, and the use of capital for debt paydown vs. investing in innovation[1].

Medical device annualized returns since July 2020



Source: Bloomberg, JPMAM, August 3, 2025

Technology and healthcare annualized earnings growth, 2017-2025, Percent



Source: Bloomberg, JPMAM, Q2 2025

[1] See "*Medical supplies and devices*", Robbie Marcus, JP Morgan North America Equity Research, June 3, 2024

Proposals to lower prescription drug prices in the US, closing the large gap vs other OECD countries

- As shown in the chart on the second page and in the table below, other than in the unbranded generics market, US drug prices are 2.5x-3.0x higher than drug prices in other OECD countries (CAN, FR, GER, IT, JPN, UK)[2]. These figures fall to ~1.75x when incorporating drug price rebates and other discounts, but are still much higher for retail dispensed brand name drugs even when including the impact of rebates/discounts
- Until 2025, most drug price proposals would only reduce drug prices by 0%-3%[3]. Such proposals included adding more drugs to CMS Medicare/Medicaid negotiations; making negotiated drug prices available to all commercial purchasers; requiring manufacturers to pay inflation rebates for sales in the commercial market; allowing commercial imports of prescription drugs from outside the US; facilitating earlier market entry for generics and biosimilars; and requiring public reporting of net prices for brand name drugs
- But now there's discussion of a **Most Favored Nation** policy to set drug prices covered by government programs like Medicare/Medicaid/VA based on drug prices outside the US. If this approach were adopted, drug prices could decline by 5%-10% and US large cap pharma earnings could decline by 9% by 2031[4].
- Some healthcare analysts are less concerned about MFN risks, citing lower US vs non-US price ratios for drugs covered by government channels vs commercial channels after rebates are taken into account. And to be clear, a gov't agency MFN edict (rather than a legislative one) would be challenged in court as tariffs have been, and would likely be limited in scope with respect to reimbursement channels, geography and impacted drugs
- **That said, pressure is building: there are at least six bipartisan bills designed to lower drug prices[5]**

US drug prices vs select OECD counterparts (US drug price divided by OECD country price, with 100% = parity)

						Retail dispensed brand name drugs, net					
	Prescription drugs	Brand name originator drugs	Unbranded generic drugs	Prescription drugs, active ingredient level	Prescription drugs, net of discounts and rebates	All drugs	Brand name drugs	Brand name retail drugs	Biosimilars	Reference biologics	Active ingredients with US biosimilars
All	278%	422%	67%	320%	173%	312%	308%	381%	216%	260%	312%
Canada	229%	324%	39%	215%	143%	173%	234%	276%	148%	155%	186%
France	326%	445%	53%	275%	203%	246%	325%	426%	221%	436%	347%
Germany	294%	387%	56%	255%	183%	223%	282%	320%	219%	371%	313%
Italy	268%	355%	46%	241%	167%	204%	259%	569%	161%	260%	253%
Japan	347%	464%	49%	328%	216%	260%	339%	391%	391%	836%	344%
Mexico	172%	402%	51%	186%	107%	126%	278%	311%	130%	#N/A	231%
UK	270%	385%	47%	274%	168%	205%	280%	434%	193%	252%	279%

Source: "International Prescription Drug Price Comparisons", Assistant Secretary for Planning and Evaluation, HHS, February 2024

Notes. The first three columns are presentation-level analyses in which active ingredients, dosage and strength match international counterparts. Active ingredient level results shown in the fourth column are higher since the US uses a more expensive mix of specific presentations and products within an active ingredient. Biosimilars refer to biological products similar to FDA-approved reference products, while biologics are medications derived from living sources

[2] "*International Prescription Drug Price Comparisons*", HHS, February 2024

[3] "*Alternative approaches to reducing prescription drug prices*", CBO, October 2024

[4] "*Health Care, Health Scare*", Empirical Research, June 17, 2025

[5] The following drug price bills have advanced to the full Senate by voice vote:

S. 527, Prescription Pricing for the People Act of 2025 (Grassley, Welch, Coons, Tillis, Blumenthal, Hirono)

S. 1040, Drug Competition Enhancement Act (Cornyn, Blumenthal, Grassley, Durbin)

S. 1041, Affordable Prescriptions for Patients Act (Cornyn, Blumenthal, Grassley, Durbin)

S. 1097, Interagency Patent Coordination and Improvement Act of 2025 (Durbin, Tillis, Grassley, Coons, Welch)

S. 1095, Stop STALLING Act (Klobuchar, Grassley, Durbin, Blumenthal, Cruz, Welch, Booker)

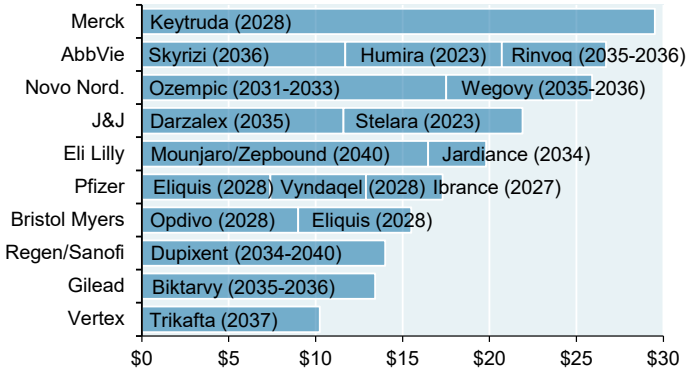
S. 1096, Preserve Access to Affordable Generics and Biosimilars Act (Klobuchar, Grassley, Durbin, Blumenthal, Welch)

The patent cliff, patent thickets and drug company war chests

Some pharma companies have billions in revenue linked to drugs going off patent over the next decade. For example, by 2036 AbbVie's patents for Skyrizi, Humira and Rinvoq will expire, products whose current revenues represent ~50% of AbbVie 2024 revenues. The cliff is even closer for Merck given Keytruda's patent expiry in 2028, and Pfizer's patent expirations on Eliquis, Vyndaqel and Ibrance in 2027-2028.

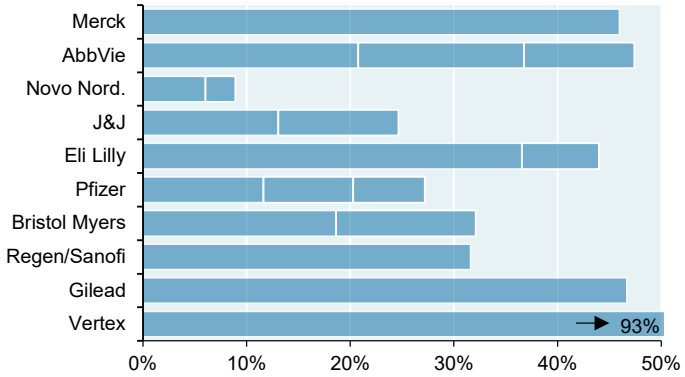
Some companies have also amassed large war chests for acquisitions, which could eventually be a catalyst for the biotech sector. Investing in possible targets sounds interesting although as we explain later, picking biotech IPO winners has been like finding a needle in a haystack. Another issue: there may not be a surplus of companies with seasoned drug product sales of $3 to $5 billion that would move the needle for the large cap pharma companies shown below.

Sales & patent expiry years for top selling drugs, 2024
US$, billions



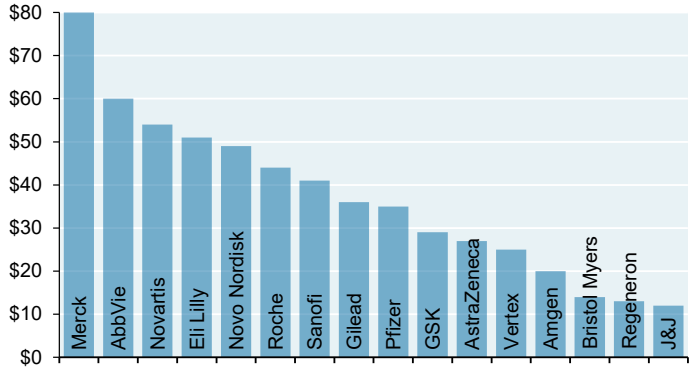
Source: JPMAM Equity Research, Evaluate Pharma, 2024

Patent expiry share of total 2024 company revenues
Percent



Source: JPMAM Equity Research, Evaluate Pharma, Bloomberg, 2024

2025 year end acquisition capacity by pharma company
US$, billions



Source: JPMAM 270 Life Sciences, May 12, 2025

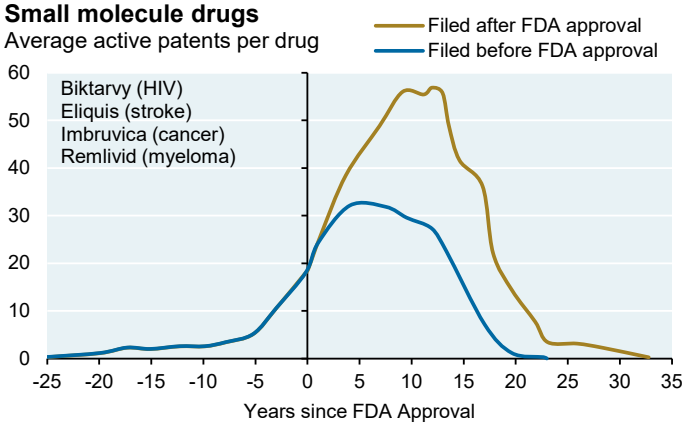
Acquisition capacity is measured differently by company according to breakpoints from rating agency reports (i.e., the amount of additional debt that can be taken on before a downgrade would occur) and is adjusted for any pro-forma new cash balances resulting from acquisitions, less minimum operating cash balances

It's worth spending a minute on how patents actually work[6]. In the US, drugs can have multiple patents that expire at different times (active ingredient, formulation, composition of matter, manufacturing process, method of use, etc). Patent expiration dates shown in the charts above reflect the longest periods of exclusivity for revenue purposes as determined by JP Morgan Asset Management's Healthcare Equity Research Team.

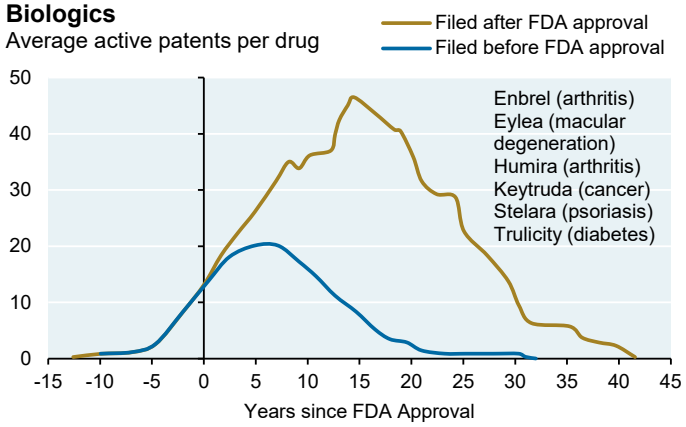
[6] Commerce Secretary Lutnick has floated the idea of an **intellectual property tax on biotech patents of 1%-5%** on patent value, instead of the current flat fee of roughly $10,000 over the entire life of a patent. Lutnick also sent a letter to **Harvard** last week indicating that the US government is investigating Harvard's compliance with certain disclosure rules related to patents obtained via federally funded research. Harvard held more than 58,000 patents as of July 2024 and maintains more than 900 active technology licenses with industry partners. These agreements often form the basis of high-value collaborations in biotechnology, medical devices, and pharmaceuticals. If the Commerce Department determines that Harvard failed to meet statutory obligations, it could seize titles to certain patents or grant licenses to third parties.

Multiple overlapping patents for a given drug are known as "patent thickets", and typically must all expire or be settled with manufacturers before generic and biosimilar drugs can be sold. Regardless of a patent's strength or validity, patent thickets can deter competition by raising the perceived litigation cost of entry. A 2024 JAMA article analyzed patent thickets for the 10 brand name drugs with the highest US sales[7]. The authors found that patents filed after FDA approval, **most of which were unrelated to each drug's active ingredient**, can substantially lengthen the effective period of patent protection and delay the impact of generic and biosimilar drugs. For the ten small molecule and biologic drugs in the JAMA analysis, almost 75% of all patents granted and all patent applications were filed after FDA approval.

Average patent thicket density for top selling small molecule and biologic drugs



Source: JAMA Internal Medicine, JPMAM, May 2024



Source: JAMA Internal Medicine, JPMAM, May 2024

There has been some discussion in policy circles on reforming the patent process to reduce the duration of these thickets. For example: the Biden administration issued an Executive Order in 2021 directing the FDA and US Patent and Trademark Office to cooperate "to help ensure that the patent system, while incentivizing innovation, does not also unjustifiably delay generic drug and biosimilar competition beyond that reasonably contemplated by applicable law". And in July 2025, Senators Welch (D-VT), Hawley (R-MO) and Klobuchar (D-MN) introduced legislation limiting the number of patents that pharma companies can assert in litigation, and prohibiting patent owners from asserting multiple patents in separate actions against the same alleged infringer.

Patent reform has the potential to substantially impact US drug prices. While the US has the highest generic drug utilization rate in the world at 90% by volume, generic drug consumption represents just 17.5% of total drug spending[8]. The remaining 10% of all drug prescriptions account for the other 82.5% of drug spending. These figures are remarkable; in other words, the issue is not that patients aren't using generic drugs; it's that the branded drug market remains heavily impacted by increasingly "creative" patent thickets that may exceed the original goal of protecting intellectual property investments in pharmaceuticals.

[7] "*Patent Portfolios Protecting 10 Top-Selling Prescription Drugs*", JAMA Internal Medicine, Aaron S Kesselheim (Brigham and Women's Hospital and Harvard Medical School) et al, May 2024

[8] Association for Accessible Medicines (trade association for generic and biosimilar drugs), September 6, 2023

Pending US tariffs on pharmaceutical imports and supply chain risks

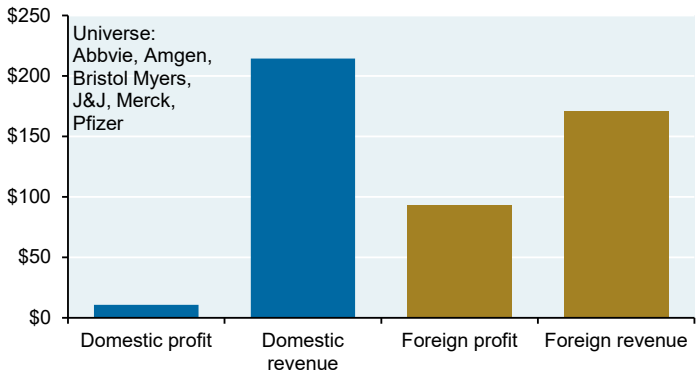
Section 232 tariffs (i.e., tariffs imposed for national security reasons) on pharmaceuticals are still pending. Why is there so much tariff/corporate tax attention on pharma?

According to Brad Setser at the Council on Foreign Relations[9] whose analysis is based on publicly available data, most large US drug companies report foreign profits in places like Ireland and Singapore, and simultaneously report losses on their US operations. As a result, they pay most of their corporate taxes offshore despite the US being their largest market in terms of actual sales to customers (first and second charts).

The US pharma trade deficit shown in the third chart appears to be of Trump's own making. This deficit averaged ~$30 bn from 2002-2015 but after the 2017 TCJA tax bill set a 10.5% minimum tax on global intangible income, US pharma companies appear to have moved production offshore, causing the deficit to balloon to $140 bn[10] by December 2024, and to $190 bn after tariff front-running this year. Profit-shifting is not unique to the pharma sector; as shown in the fourth chart, US companies have a decided preference for lower tax jurisdictions when siting operations overseas.

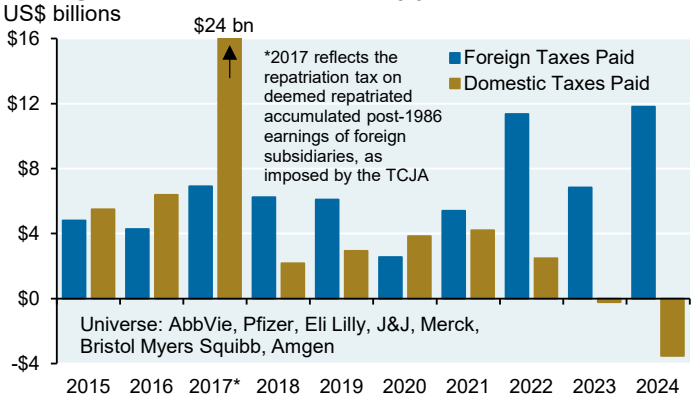
Section 232 tariffs would force large US drug companies to make the same tough choices as in other sectors: absorb the tariff and reduce operating margins, or pass price increases along to consumers.

Large cap pharma profits and revenues by region, 2022
US$, billions



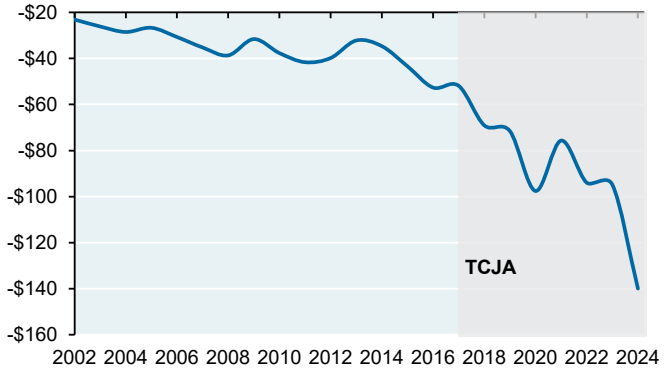
Source: Brad Setser, Council on Foreign Relations, 2022

US large cap pharma taxes paid by jurisdiction
US$ billions



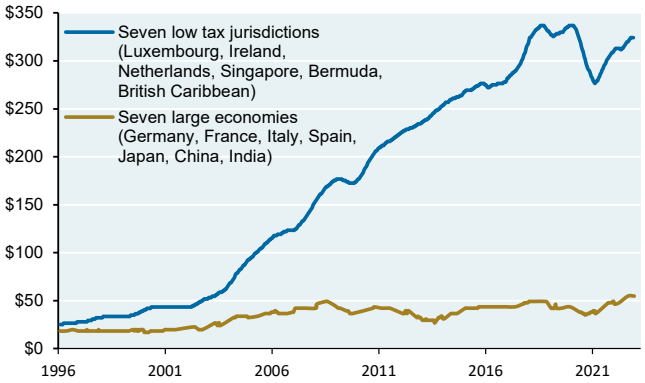
Source: Brad Setser, Council on Foreign Relations, March 14, 2025

US pharma trade deficit
US$ billions, trailing 12 months



Source: Brad Setser, Council on Foreign Relations, March 14, 2025

Offshore corporate profits in select jurisdictions
US$ billions



Source: Brad Setser, Council on Foreign Relations, May 11, 2024

[9] See "*American Pharmaceutical Companies Still Aren't Paying Tax in the US*, Brad Setser, Council on Foreign Relations, March 14, 2025; and Setser's May 2023 testimony at a Senate Finance Committee hearing "*Cross-border Rx: Pharmaceutical Manufacturers and US International Tax Policy*"

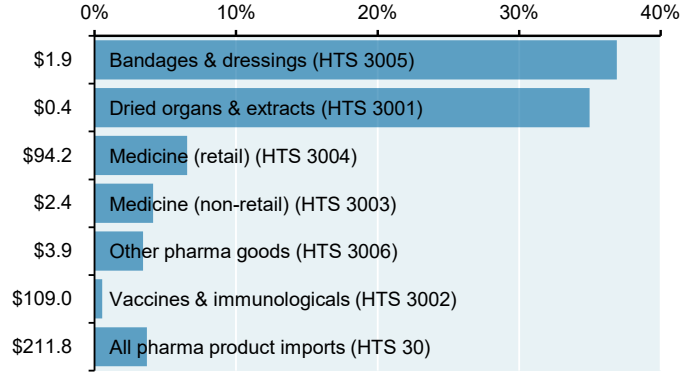
[10] The most straightforward way to address this, rather than higher tariffs: a higher US minimum tax on intangible income; limiting the ability of firms to claim tax breaks on R&D conducted in the US if the resulting intellectual property is moved offshore; or taxing profits on intrafirm transfers of IP

There's plenty of discussion of China's role in US pharma supply chains, particularly after China prioritized domestic supplies during COVID, a decision which led to shortages in other countries. The US has since established a Strategic Active Pharmaceutical Ingredients Reserve, but as of November 2024 it was only 1% filled according to the Council on Strategic Risks. As shown in the charts below, China's share of pharma product and active pharmaceutical ingredient (API) imports by the US varies substantially and are typically high for categories with lower import values. For example, while China's share is 30%+ in US imports of bandages and extracts, the dollar value of these imports is low compared to medicines and vaccines with much higher import values. Across all US pharma product imports, China only accounts for a 4% share in value terms.

The same is true for US API imports: high China shares for ibuprofen and acetaminophen, but lower for categories with higher import values. For all 10-digit API categories shown in the second chart, China also accounts for just 4%. When we zoom out and look at broader 4-digit API categories in the third chart, a similar story: China's share of US vitamin imports is 64%, but only 1% in the higher-value added hormone category and 7% across all four API categories shown. If there's one number that jumped out at me, it was China's 31% share of antibiotics imports.

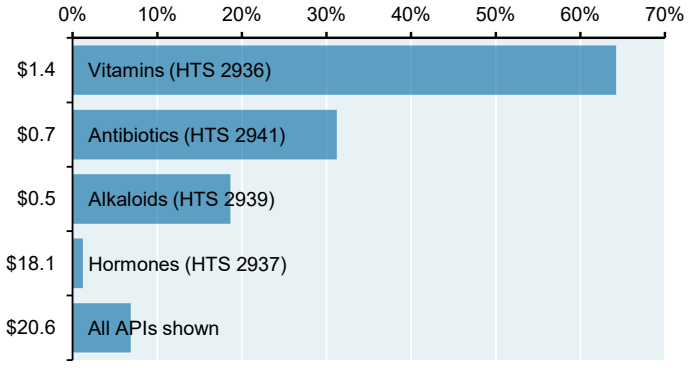
What about the India-China link? Around 70% of Indian imports of bulk and intermediate drug imports in 2024 were from China. But even when adding India to the charts below**, the combined China + India shares of US product, 10-digit API and 4-digit API imports only rise to 10%, 7% and 8% by value, respectively; and that assumes that all Indian exports are derived from Chinese imports**.

China share of US pharmaceutical product imports
Percent



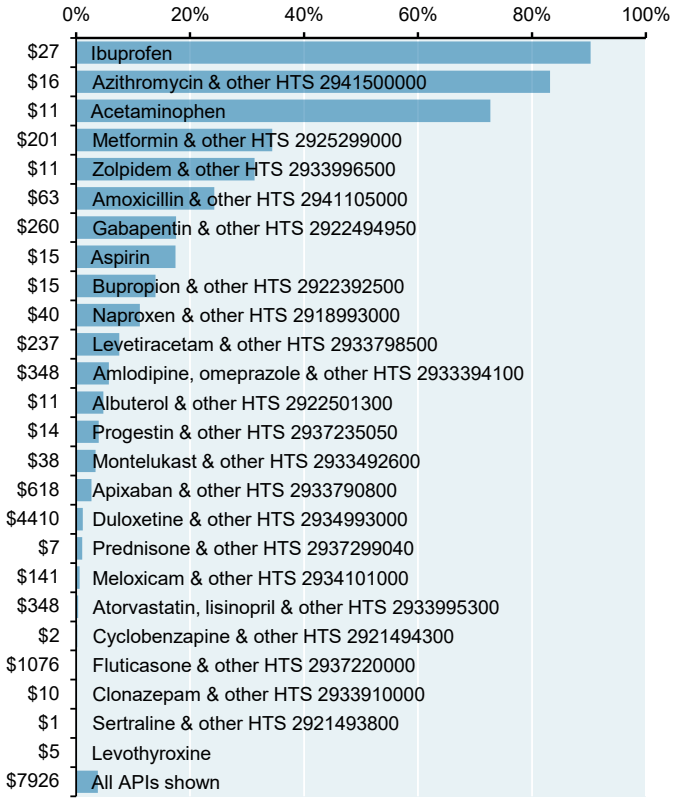
Source: USITC, JPMAM, 2024 *with US total 2024 imports in US$ bn*

China share of US bulk-form active pharmaceutical ingredient (API) imports, 4-digit HTS level, Percent



Source: USITC, JPMAM, 2024 *with US total 2024 imports in US$ bn*

China share of US bulk-form active pharmaceutical ingredient (API) imports, 10-digit HTS level, Percent



Source: USITC, JPMAM, 2024 *with US total 2024 imports in US$ mm*

While China import shares are in single digits, some argue that the US should attempt to reduce them further due to inadequate testing of Chinese production. See "*FDA Knows That China and India Drug Quality Is Poor, But Independently Collects and Tests Only about 0.001%*", Heritage Foundation, November 8, 2024

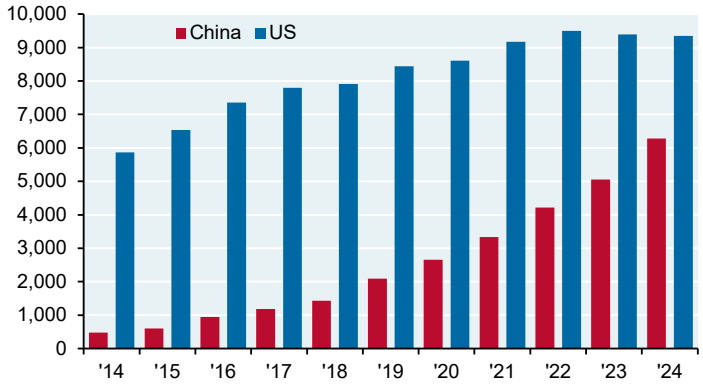
Drug development competition from China is growing, but how reliable are Chinese drug trial results?

China is closing the gap with the US regarding industry-sponsored clinical trials and the number of drugs in development. That said, acquiring Chinese drug companies has not always been highly accretive to US large cap pharma. One example cited by healthcare analysts: Merck's P/E is still close to historical lows at 8x-9x after partnering with Chinese pharma companies in 2023-2024 (Curon, LaNova, Hengrui, Kelun, Hansoh), although the Keytruda loss of exclusivity is program the main driver of Merck's low P/E. To be clear, China's share of global pharma and biotech market cap is still pretty small at ~3.5%.

Industry-sponsored clinical trials for innovator drugs
Number

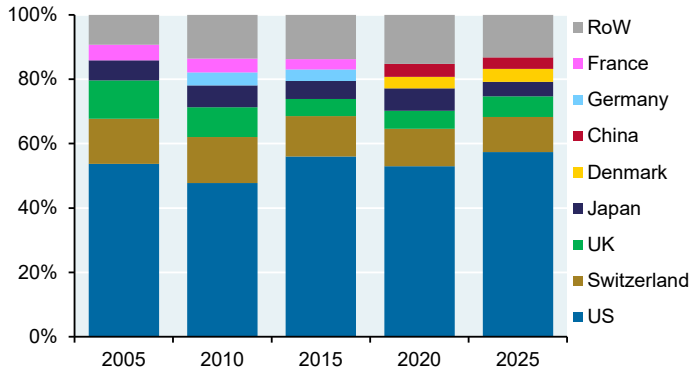
Source: GlobalData, 2025

Drugs in development by company headquarters
Number



Source: Pharmaprojects, Citeline, 2025

Country shares of global all-cap pharma & biotech index
Market cap weight, percent



Source: Bloomberg, JPMAM, August 7, 2025

Some of the same questions facing investors regarding reliability of Chinese economic data also revolve around Chinese drug trial results. Chinese clinical trial results are increasingly published in Western medical journals, including publications such as the New England Journal of Medicine, JAMA and The Lancet. Can such trial results be trusted?[11]

- Until 2020, China paid some researchers up to $100,000 for articles appearing in Western journals. The practice only ended in 2020
- As of August 2025, almost half of the 60,000+ retracted articles in Crossref's Retraction Watch's database of retracted journal articles originated in China
- 75% of the ~14,000 papers retracted from English language journals in 2023 involved a Chinese co-author
- Surveyed Chinese scientists and engineers said they believed that 40% of Chinese biomedical papers are tainted by research misconduct

[11] MIT Technology Review; "*China bans cash rewards for publishing papers*", Nature, February 28, 2020; Crossref Retraction Watch Data, August 12, 2025; "*China conducts first nationwide review of retractions*", Nature, February 22, 2024; "*Perceptions of Chinese biomedical researchers towards academic misconduct: a comparison between 2015 and 2010*", Science and Engineering Ethics, April 10, 2017

The pace of drug approvals, the FDA, RFK Jr at HHS and a personal note on the MMR vaccine

The biotech sector's R&D to market cap ratio has risen much faster than for the S&P 500 over the last few years, so the pace of drug approvals is quite important for pharma and biotech investors. The pace of drug approvals has slowed under Trump so far, as shown on the right. The Trump Administration claims it will speed things up by reducing animal testing requirements, integrating AI into drug approvals and reducing red tape.

Biotech accumulated R&D as a share of market cap relative to the market, Percent, trailing 8 year horizon

Source: Bloomberg, JPMAM, June 2025

Quarterly FDA novel drug approvals
Number of novel drugs approved

Source: FDA, JPMAM, June 17, 2025

I will believe it when I see it. Instead, pharma and biotech investors have had to deal with:

- reports of unorthodox and unexplained **interventions** by the new head of the FDA and by his deputies in the drug approval process (examples: KalVista's Ekterly, Sarepta's Elevidys, Novavax's Nuvaxovid)[12]
- **departures** of senior FDA officials with decades of experience: the Directors and Deputy Director of the FDA's Center for Drug Evaluation and Research and Center for Biologics Evaluation and Research (CBER), and the directors of the Office of New Drugs and cell/gene therapy office; and 19% DOGE cuts to the overall FDA workforce. Vinay Prasad, the head of CBER who was pushed out just two weeks ago, is now reportedly being brought back to his prior role[13]. Prasad was reportedly sacked after attempting to halt shipments of Elevidys, a muscular dystrophy treatment, after deaths had occurred
- RFK Jr **firing** all 17 members of the CDC's Advisory Committee on Immunization Practices, and announcing last week that the Biomedical Advanced Research and Development Authority (BARDA) will **terminate** 22 contracts with university researchers and private companies to develop new uses for mRNA technology
- On mRNA contract termination, Michael Osterholm who runs the Center for Infectious Disease Research and Policy at the University of Minnesota had this to say: "This may be the most dangerous public health judgment that I've seen in my 50 years in this business. It is baseless, and we will pay a tremendous price in terms of illnesses and deaths. I'm extremely worried about it".[14] From Rick Bright who ran BARDA during the Trump's first term: "It's irresponsible to strip funding from future technologies with great potential and shift it towards outdated old-fashioned technologies. We're taking our country from 2025 back to 1940, and we all know that's a recipe for disaster and failure".
- **To be clear, there are differing views on mRNA**. Some healthcare professionals believe that mRNA approaches warrant caution due to the risks of off-target integration (unintended insertion of mRNA-encoded genetic material into a cell's genome) or immune dysregulation, and should only be used to treat rare single-gene disorders; and that innovation can be sustained by relying on peptide-based vectors instead

[12] "*FDA's Makary sought rejection of KalVista's drug in an unusual move by commissioner, sources say*", Endpoints News, June 24, 2025; "*FDA head Makary's short-lived CRL ask on KalVista's drug raises more concerns of political Intervention*", Endpoints News, June 27, 2025

[13] "*Vinay Prasad is back at the FDA after last month's surprise ouster*", Fierce Pharma, August 9, 2025

[14] "*Public health experts dismayed by RFK Jr's defunding of mRNA vaccine research*", NPR, August 6, 2025

A personal note on the MMR vaccine and the US measles outbreak, now at its highest level in 33 years

US measles cases have hit a three-decade high, reaching the highest yearly total since 1992 in less than seven months. More than 90% of those infected were unvaccinated or had an unknown MMR vaccine status.

US adults immunized between 1963 and 1967 (when the first live MMR vaccine was approved) received an inactivated version of the MMR vaccine. The inactivated version of the MMR vaccine offers lower long-term immunity than the live vaccine; one study found that just one year after getting the inactivated MMR vaccine, only 25% of people still had detectable antibodies. The CDC recommends that individuals vaccinated during this period get a new live vaccine, but for certain conditions (like one I have), vaccines containing live attenuated viruses are not given due to immune deficiency. Since I was immunized during the 1963-1967 window and cannot be revaccinated, I should avoid areas with large measles outbreaks and places with plummeting MMR vaccination rates.

Some MMR not-so-fun facts:

- The MMR vaccine's two dose-regimen is 97% effective against measles infection. Since the disease is highly contagious, 95% of a population needs to be vaccinated to achieve herd immunity (protection that stops spread). The infectiousness measure (Ro) for COVID and the flu is 1-2; for polio and smallpox 5-7; and for measles 12-18
- From 2013 to 2023, the median US MMR vaccination rate fell from 95% to 92%. States below 90% include Georgia, Colorado, Wisconsin, Alaska and Idaho; Idaho MMR vaccination rates fell from 90% in 2013 to 80%
- The median percentage of kindergarten age children who have received non-medical exemptions to vaccines has risen from 1% in 2011 to 3.7% in 2023
- JB Cantey, a University of Texas associate professor of pediatrics, warned that measles is "the canary in the coal mine for other vaccine-preventable diseases that are going to start to rear their ugly heads in the next few months, next few years, if our vaccine rates continue to drop"
- A recent study from Stanford estimated that measles could become endemic again within two decades given the decline in vaccination. Since measles is more common outside the US, travelers to the US would be like "matches" given declining US vaccinates rates
- Sign of the times: Saravir Biopharma is working on monoclonal antibodies to treat measles, and is banking on a continued decline in people receiving the MMR vaccine
- Instead of consistently messaging the importance of the MMR vaccine, RFK Jr has at times cited its effectiveness but has also directed health agencies to explore potential new treatments for measles, including Vitamin A and cod liver oil. While Vitamin A can be used to treat measles patients that suffer from Vitamin A deficiency, the NIH estimates that only 1% of Americans fall into this category

Sources: Scientific American, Ripley Cleghorn, March 20, 2025; "*Modeling reemergence of vaccine-eliminated infectious diseases under declining vaccination in the US*", Kiang et al (Stanford Department of Epidemiology), JAMA, April 24 2025; WSJ, July 9, 2025; WSJ August 8, 2025

Additional reading:

"How RFK Jr distorted vaccine science" [Scientific American]

"How RFK Jr Falsely Denied His Connection to a Deadly Measles Outbreak in Samoa [Mother Jones]"

"RFK Jr spent years stoking fear and mistrust of vaccines. These people were hurt by his work [AP News]"

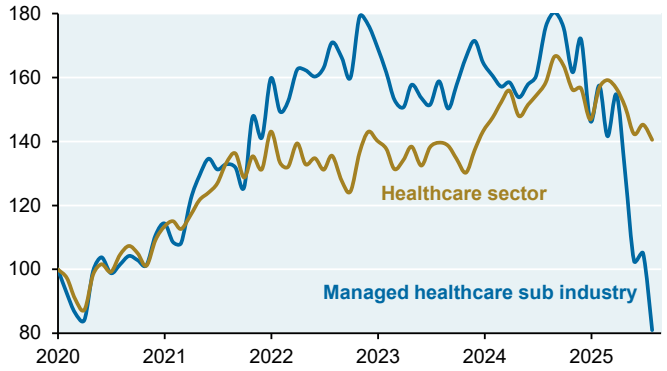
"The Anti-Vaccine Propaganda of RFK Jr [McGill University]"

"RFK's error-ridden piece on vaccine-autism links [Nation]"

Managed care "Big Beautiful Bill" headwinds, AI algorithms and the pace of denied claims

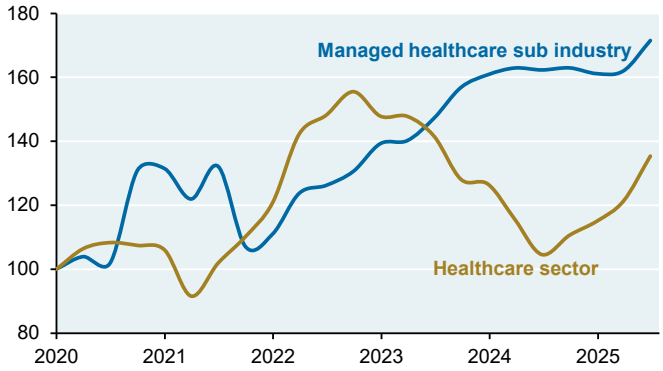
Large cap managed care companies are mostly health insurance providers such as Centene, Elevance, Humana, Molina and United Healthcare. The sharp decline in managed care returns this year is not the byproduct of declining earnings, at least not yet. However, as shown in the third chart, industry guidance has been cut due to (a) provisions in the Big Beautiful Bill which cut Medicaid and ACA funding, (b) lower CMS reimbursement rates for Medicare Advantage programs, and (c) in the case of United Healthcare, scrutiny of Medicare Advantage billing/risk coding practices and an influx of higher risk patients associated with higher costs. One example of the bill's impact on managed care: in July, Centene withdrew its full-year 2025 earnings guidance and slashed its adjusted EPS forecast from $7.25 to $1.75 per share, driven by lower market growth in 22 of the 29 states where Centene operates, particularly affecting its ACA exchange business.

The collapse in Managed Care returns
Total return index, 100 = December 2019



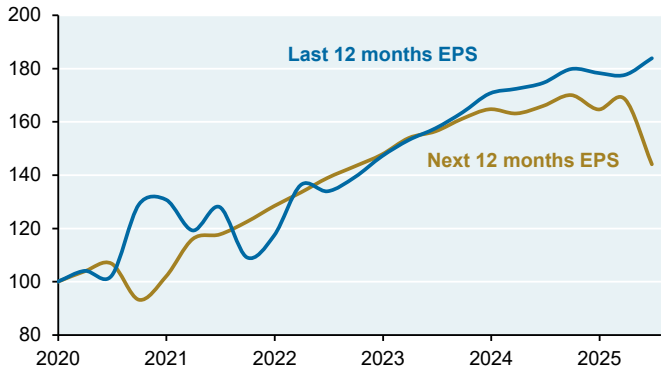
Source: Bloomberg, JPMAM, July 2025

Managed Care vs Healthcare sector operating income
Index, 100 = December 2019



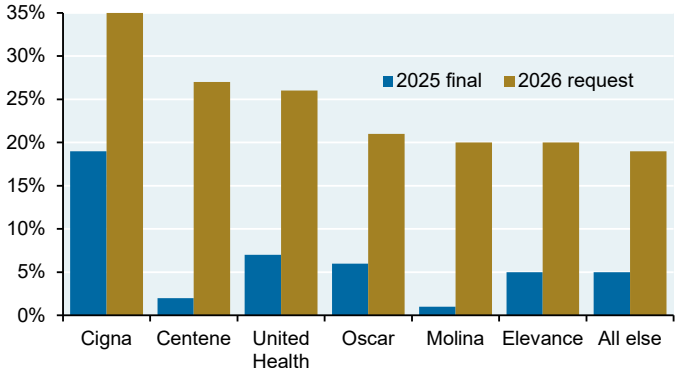
Source: Bloomberg, JPMAM, Q2 2025

Managed Care earnings per share
Index, 100 = December 2019



Source: Bloomberg, JPMAM, Q2 2025

Member-weighted average ACA rate requests by company
Percent increase vs prior year



Source: Barclays Equity Research, August 5, 2025

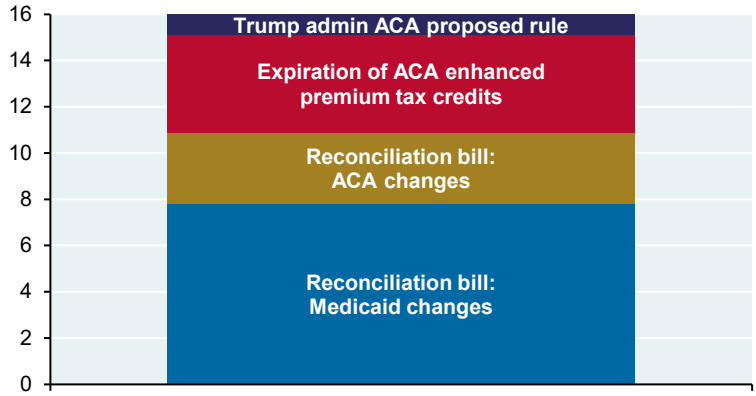
Centene's CEO announced plans to restore profitability in 2026 by repricing plans to reflect increased costs and morbidity shifts. The same is true across the managed care industry, as shown in the fourth chart. CMS recently released 2026 Individual ACA preliminary rate requests by plan and state which provides an early look at 2026 pricing, an important variable in potential margin recovery[15]. **On average, the plans shown are requesting 20%-30% increases, with some requests as high as 40%-60% in certain states**. The CMS data likely shows a mix of initial and refiled rate requests with submission dates ranging from early June to late July. These requests are subject to state approval, so final rates may differ.

[15] "*CI, CNC, UNH Request Highest ACA Rate Increases for 2026*", Barclays Equity Research, August 5, 2025

For a closer look at the regulatory issues driving some of the projected earnings declines, here are the main features of the Big Beautiful Bill, changes to Medicaid and changes to the ACA

- **Spending reductions:** The CBO estimates a reduction of $911 billion in federal Medicaid spending over the next decade, a 14% cut to projected Medicaid expenditures for the period
- **Coverage:** KFF projects that OBBBA and ACA changes will result in 16 million people losing insurance coverage by 2034. The OBBBA creates Medicaid work requirements for adults 19 to 64 who don't have disabilities or dependents, mandating at least 80 hours a month of work or other qualifying activities. These requirements are the largest source of Medicaid savings, reducing spending by $326 billion over ten years
- **Expiration of Enhanced Tax Credits**: The OBBBA did not extend enhanced ACA premium tax credits which are set to expire at the end of 2025. The expiration of these subsidies and new administrative restrictions could lead to a one-third decline in ACA marketplace enrollment

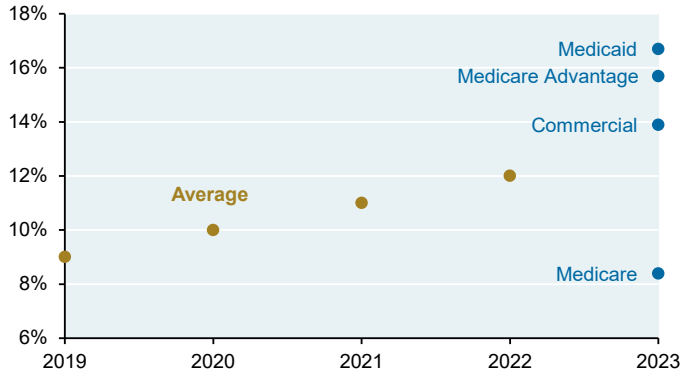
Projected increase in number of uninsured by 2034
milions of people



Source: KFF, CBO, June 2025

In recent years, another part of the narrative on the health insurance industry has focused on the issue of denied claims. The next chart illustrates some observations on denied claims rates[16], while the text box cites difficulties mentioned by the AHA regarding member experiences with commercial healthcare insurers.

Healthcare claim denial rates
Percent



Source: Change Healthcare Revenue Cycle Denials Index, Premier (2023)

From the American Hospital Association, 2022:

- 78% of hospitals reported that their experience with commercial payers was getting worse
- 84% of respondents said the cost of complying with insurer policies was increasing
- 95% of hospitals and health systems reported that staffs were spending more time on prior approvals
- Denied claims tended to be more prevalent for higher-cost treatments, with the average denial pegged to charges of $14,000+

[16] There are multiple sources for denied claims rates, and each is a function of the universe examined. The chart above shows denial rates for 2019-2022 from Change Healthcare, which canvassed a group of small, medium and large facilities regarding primary institutional inpatient and outpatient claims. The data for 2023 comes from Premier Healthcare, which conducted a national survey of member hospitals and health systems.

A 2024 paper from Indiana University Law School addressed the big picture on denied claims. Its major findings:

- *Clinical care vs insurance coverage algorithms*. Unlike *clinical care* algorithms used by providers to diagnose and treat patients, healthcare insurance *coverage* algorithms are generally unregulated and not evaluated for safety and effectiveness by the FDA. Algorithm creators (many of whom are health insurance companies using them to make coverage decisions) take the view that their products are proprietary and not subject to public disclosure regarding weighting schemes and bias mitigation protocols
- *Examples*. In one study, only 1 in 500 patients appealed insurance claims that were denied. Similarly, a 2023 Kaiser study found that less than two-tenths of 1% of all claims denials were appealed in the Affordable Care Act Marketplace. Given low appeal rates, the author concludes that refusing payment for medical care has become a staple of insurer business models since they are insulated from defending or revisiting the vast majority of denied claims
- *What physicians think*. The AMA released a 2023 survey in which 94% of physicians reported that prior authorization requirements delayed access to necessary patient care; 78% argued that the practice can lead to patients abandoning recommended courses of treatment; and roughly one in four reported that prior authorization caused one of their patients to experience a serious adverse life event
- *AI programs*. Over a period of two months, doctors at one insurer denied over 300,000 requests for payments using its PXDX AI program, spending an average of 1.2 seconds on each case despite regulatory requirements for some human oversight and for patient medical needs to drive coverage decisions. While some healthcare analysts believe that AI can contribute to a faster pace of insurer responses, that doesn't necessarily translate into a higher rate of approved claims
- *Poor AI performance on appeal*. Some AI programs have poor track records upon further review. A study of the prior authorization program nHPredict found that ~90% of its denials were then reversed on appeal by Federal administrative law judges. Similarly, the American Hospital Association found that 62% of prior authorization denials and 50% of initial claims denials that were appealed were ultimately overturned
- *Survival and vindication*. On appeals, patients only succeeded after numerous rounds of lengthy and costly appeals and some do not survive long enough to be vindicated. In some cases, insurers seek dismissal of lawsuits on the grounds that plaintiffs failed to exhaust the five-year, five-level Medicare appeals process
- *Source*: "*Regulating Healthcare Coverage Algorithms*", Jennifer D. Oliva, Indiana School of Law, Dec 2024. Professor Oliva is a US Army veteran who serves as a Research Scholar at Georgetown Law's O'Neill Institute for National & Global Health Law and a Senior Scholar with the UCSF/UC Law Consortium on Law, Science & Health

In June 2025, over 50 insurers pledged to standardize and reform prior authorization processes to reduce the burden on providers and provide better access to care for patients. Efforts will reportedly include a reduction in the number of medical services requiring prior authorization, honoring existing authorizations when patients change health plans during treatment, increasing transparency around authorization decisions/appeals and ensuring that medical professionals review non-approved requests.

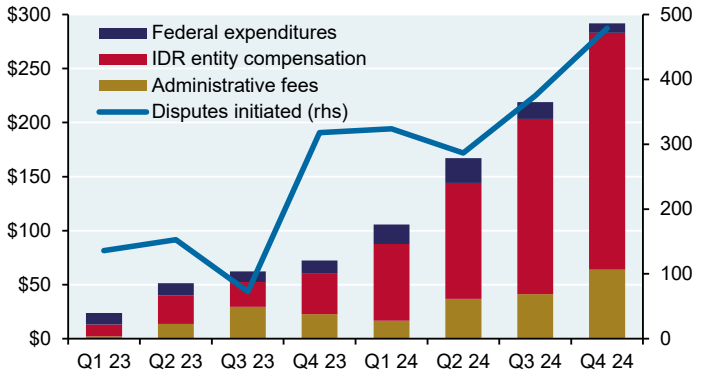
While providers expressed approval of the initiative, many are skeptical the promised changes will come to fruition since health insurers have made similar commitments in the past. From the SVP of government affairs at Premier: while a voluntary pledge could go a long way, it will still be important for the government to intervene in certain areas. "There is no level of accountability here. A lot of it is self-governed. What we would love to see is some guardrails continue to be put into place by CMS and Congress to ensure this does get put into place and it's truly in the best interest of patients and providers".[17]

[17] "*50+ insurers pledged to reform prior authorization. What's next?*", Advisory Board Daily Briefing, June 6, 2025

The balance of power may now be changing, at least temporarily. As shown below, there has been a surge in provider disputes, driven in part by the No Surprises Act of 2020 which in many cases requires third party arbitration in place of patients simply appealing disputed claims directly with the insurer. According to the Niskanen Center[18], well-funded private equity backed healthcare providers have been winning a rising share of these disputes at insurers' expense (the top 10 parties initiated 71% of all disputes, and the top 3 initiated 43% of disputes). According to CMS, providers filed 1.5 mm billing disputes in 2024, more than 70x the annual predicted caseload (!!). Providers also appear to be boosting arbitration offers relative to median in-network costs in hopes of higher eventual settlements. It may take time for the insurance industry to adapt to this new reality by passing along higher settlement costs in the form of higher premiums.

Independent Dispute Resolution (IDR) costs and disputes

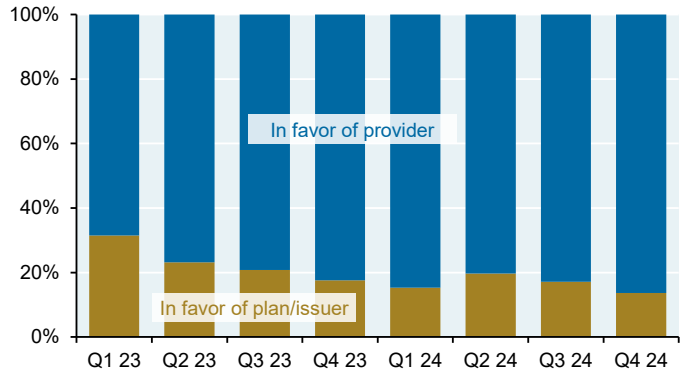
US$, millions | Disputes, thousands



Source: Niskanen Center, June 18, 2025

Providers are winning an increasing share of disputes

Share of Independent Dispute Resolution cases



Source: Niskanen Center, June 18, 2025

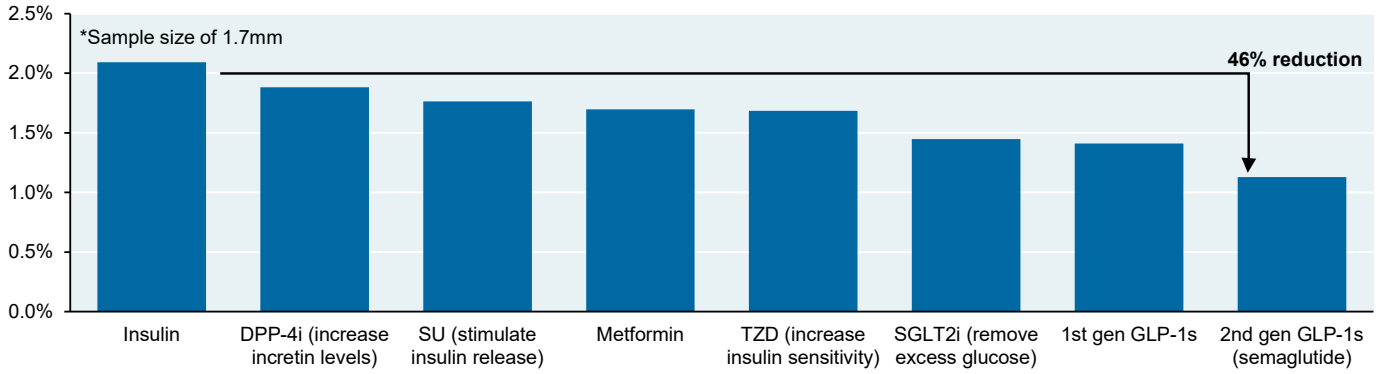
[18] "*New data shows No Surprises Act arbitration is growing healthcare waste*", Niskanen Center, June 18, 2025

GLPs: cardiovascular benefits, possible dementia benefits and the path to greater adoption

To be clear, this study[19] was not a double-blind trial with control groups and placebos; it was an after-the-fact analysis of recently diagnosed diabetes patients that were treated with insulin, metformin, first generation GLP-1s, second generation GLP-1s (containing semaglutide) or other drugs. But the size of the study was very large (1.7 million people), allowing for robust assessments of subsequent dementia risk.

As shown below, the risk of developing Alzheimer's related dementia within three years of diabetes diagnosis was 2% for insulin-treated patients, and half that level for patients taking second generation GLP-1s. The strongest effect cited by the study was for *vascular dementia,* which may be explained by semaglutide's association with reduced vascular inflammation, a known dementia precursor. These are impressive results since almost half of all Americans are either diabetic or pre-diabetic, according to the CDC.

Risk of Alzheimer's related dementia in type 2 diabetics by T2D drug, % of patients developing Alz related dementia in 3 years

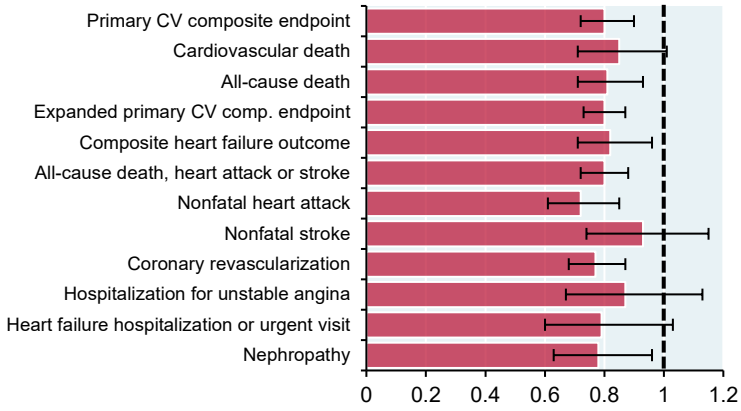


Source: Journal of Alzheimer's Disease, JPMAM, May 13, 2025

Novo's SELECT trial assessed cardiovascular outcomes for patients taking Wegovy. As per the chart below, the trial showed a reduction in major adverse cardiac events (MACE) of ~20% relative to the placebo group. However, the absolute reduction in MACE incidence was just 1.5% (placebo group 8.0%, Wegovy 6.5%) and it took three years of GLP treatments to derive that absolute benefit[20]. What's the more meaningful figure here, a 20% reduction in relative risk or a 1.5% reduction in absolute risk? That's up to you.

Major adverse cardiovascular event: semaglutide vs placebo

Hazard ratio (1 = placebo), error bars show 95% confidence interval



Source: Eric Topol, Scripps Research, November 2023

Low dose GLP regimens might one day be used to replace a combination of statins and antihypertensives, and to prevent/ treat osteoporosis

[19] "*Associations of semaglutide with Alzheimer's disease-related dementias in patients with type 2 diabetes*", Journal of Alzheimer's Disease, Wang et al, May 13, 2025

[20] "*The Big Trial of a GLP-1 drug to reduce major cardiovascular events*", Eric Topol, Scripps Research, Nov 2023

The challenges for GLP manufacturers:

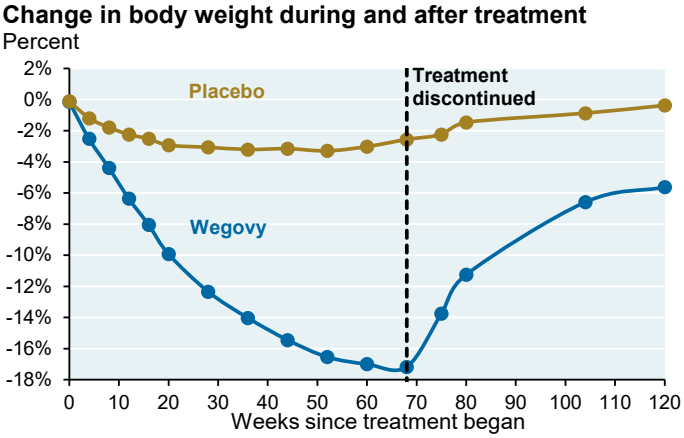
- A January 2025 JAMA paper shows very high GLP discontinuation rates for non-diabetic patients, although a meaningful subset eventually reinitiated treatment since they regained so much weight, or since they had discontinued involuntarily due to temporary shortages of the drugs[21]. As explained in our 2024 Outlook, patients discontinuing GLPs typically regain most of their lost weight in weeks when terminating Wegovy and Zepbound. Similarly, other cardiometabolic improvements also regress to baseline levels after treatments end (blood pressure, LDL and hemoglobin readings)

GLP discontinuation rates for non-diabetic patients

	Discontinuation rate within two years of initiation date	Reinitiation rate within two years of discontinuation date
Patients with type 2 diabetes	64.1%	57.2%
Patients without type 2 diabetes	84.4%	46.3%

Source: JAMA, January 2025. Discontinuation: 60 days without prescription refill

Change in body weight during and after treatment



Source: DOM Journal of Pharmacology and Therapeutics, April 2022

- There has been a plateau in the number of companies covering GLP use. To increase GLP penetration, insurance companies have had to cut pricing after negotiating price cuts with drug makers. GLP prices have been declining at 10%-15% per year; it is not clear that such price declines will be offset by rising volumes
- As a reminder, Medicare does not cover GLP use for obesity, while Medicaid covers GLP for obesity in 13 states. **CMS is now reportedly exploring GLP-1 demonstration programs for both Medicare and Medicaid**. If approved, the experiment is expected to start in April 2026 for Medicaid and January 2027 for Medicare plans, conducted by the Center for Medicare and Medicaid Innovation. The CBO estimates that Medicare coverage of GLPs would cost $35 billion from 2026-2034. Medicaid coverage would cost the Federal government another $11 billion. High discontinuation rates for GLPs shown above and in the table below suggest the need for some kind of cost-sharing to balance affordability and patient accountability
- Greater penetration of oral GLPs might be needed to boost adoption rates and restore the GLP investment thesis which was a major driver of pharma stocks in 2023-2024. **However**: Phase 3 trial results released by Eli Lilly last week on oral Orforglipron showed lower than expected weight loss (8%-12% over 18 months) and higher than expected dropout rates (22%-24%). LLY stock fell 14% on the news

Comparison of oral and injected GLPs

	LLY: Orforglipron				NVO: Semaglutide	
Duration	72 weeks				68 weeks	
Treatment	Placebo	6 mg	12 mg	36 mg	Placebo	2.4 mg
Weight change	-1%	-8%	-9%	-12%	-2%	-17%
Incidence rates						
Nausea	10%	29%	36%	34%	17%	44%
Vomiting	4%	13%	21%	24%	7%	25%
Diarrhea	10%	21%	23%	23%	16%	32%
Constipation	9%	22%	30%	25%	10%	23%
Discontinuation						
From Adverse Events	3%	5%	8%	10%	3%	7%
All discontinuation	30%	22%	23%	24%	NA	NA

Source: Wells Fargo, JPMAM, August 2025

[21] "*Discontinuation and Reinitiation of Dual-Labeled GLP-1 Receptor Agonists Among US Adults With Overweight or Obesity*", E. Emanuel et al, JAMA, January 2025

Healthcare services: drug prices and the negligible impact on Pharmacy Benefit Managers

The prospect of drug price cuts may negatively affect investor sentiment on CVS and Cigna[22], the two large Pharmacy Benefit Manager companies within Healthcare Services[23]. Lower drug prices could in principle be negative for PBMs which earn a share of whatever rebates are paid from drug manufacturers to plan sponsors. However, both CVS and Cigna now pass through 95%+ of the rebates they receive to plan sponsors and rely on other forms of fee-based revenue[24]. Furthermore, PBMs do not receive any rebates on Medicare-related drugs, so annual CMS negotiations would not impact PBMs even when negotiated discounts are large.

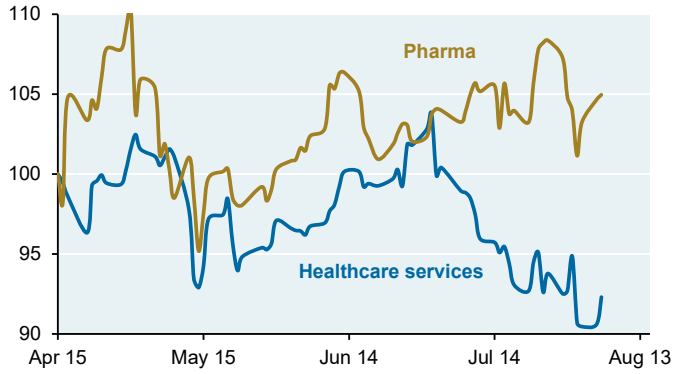
Even so, since the White House executive order on April 15 to reduce the role of PBMs as middlemen, CVS and Cigna have underperformed lab diagnostics companies and drug distributors. The executive order calls for new recommendations to promote a more competitive and transparent pharma value chain that lowers drug prices, and for new DoL regulations requiring more transparency on PBM compensation.

A sign of the times: a bill debated in the Senate would reduce the role and revenue prospects of PBMs, although our analysts believe that impacts would be manageable even if the bill passed given its scope and ample implementation time[25]. Since 2010, most proposed Federal and state PBM bills have not passed; even so, the issue remains a bipartisan focus. At least Section 232 tariffs would not be a headwind: most PBMs have clauses in their contracts that if pharmaceutical pricing changes materially, they can maintain their economics by passing higher costs on to plan sponsors.

The legislative focus on PBMs is coming after an intense period of consolidation over the past 25 years; CVS, Cigna and UHG's Optum RX PBM represent the roll-up of 39 individual PBM entities. In 2024, the FTC sued the three largest PBMs, accusing them of steering diabetes patients towards higher priced insulin.

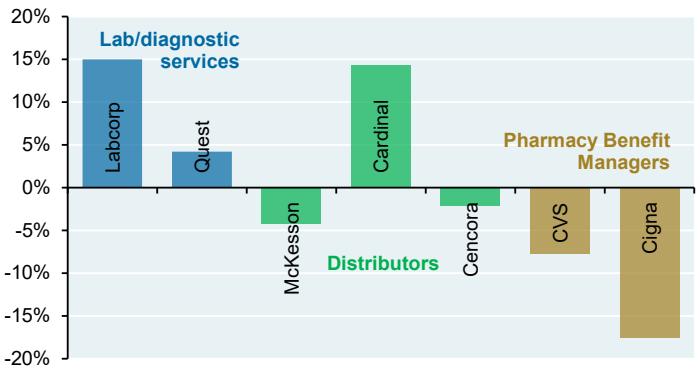
Bottom line: CVS and Cigna are interesting stocks to consider after their declines since legislative proposals on drug prices may overstate the real risks to PBM revenues.

Healthcare services returns
Total return index, 100 = April 15, 2025



Source: Bloomberg, JPMAM, August 5, 2025

Healthcare PBM companies vs Diagnostics/Distributors
Returns since April 15, 2025 drug price executive order



Source: Bloomberg, JPMAM, August 7, 2025

[22] For CVS and Cigna, we estimate that PBMs represent 40% - 45% of their total revenues

[23] Healthcare Services also includes hospitals, a topic we do not cover in this report other than to note allegations of **abuse of the 340B program**. This program is intended to help hospitals and clinics that serve low-income patients purchase outpatient drugs at discounted prices. Some reports suggest that 340B-eligible hospitals generate significant revenue from buying discounted drugs and then charging patients much higher prices, including those with commercial insurance

[24] "*Pharmacy Benefit Managers: Here we go again – new administration, same misunderstandings*", Lisa Gill, JP Morgan North America Equity Research, April 16, 2025

[25] The Patients Before Middlemen Act sponsored by Blackburn (R-TN) bill has three main aims: 1) moving to a "bona fide service fee" for Part D PBM compensation (de-linking from drug prices); 2) amending the rules around "any willing pharmacy" in Part D (creating standards for contract terms, defining essential retail pharmacies and adding incremental reporting requirements); and 3) increasing transparency via reporting requirements

Biotech IPOs: since 2018, harder than finding a needle in a haystack

Biotech investors have had a rough ride even *before* the impact of recent changes at HHS and the FDA. Other than Managed Care, Biotech has seen the largest gap between annualized returns before and after 2020. Before 2020, S&P 500 biotech returns compounded at 17% annually over an incredibly successful 25-year run. Since then: just 6% annualized returns.

The generally dismal performance of biotech IPOs since 2018 is another example of biotech distress. The exhibits below speak for themselves (the first table should be used in high school stats classes to explain the importance of mean vs median). Holding period returns are computed on a cumulative basis since IPO date. The histogram shows the big picture: finding biotech IPO winners has been like finding needles in a very unpleasant haystack. Since 2018, half of all biotech IPOs have lost 80%+ of their value, and only 20% had positive holding period returns. Poor performance was seen across all therapeutic categories: immune diseases, rare diseases, cancer, central nervous system disorders and infectious diseases.

Biotech performance since IPO by vintage year

Vintage	IPO Count	Average return	Median return	% with positive returns	Returns greater than 100%	Returns less than -80%	Preclinical + Phase 1 share
2025	7	87%	-2%	43%	2	0	14%
2024	24	-53%	-70%	8%	0	6	42%
2023	19	-13%	-70%	21%	3	9	42%
2022	22	11%	-70%	23%	2	10	64%
2021	104	-54%	-88%	11%	5	67	62%
2020	78	-48%	-77%	19%	6	40	67%
2019	47	41%	-88%	26%	10	26	53%
2018	54	-14%	-77%	26%	8	30	43%

Source: BioPharma Dive, Bloomberg, JPMAM, August 11, 2025

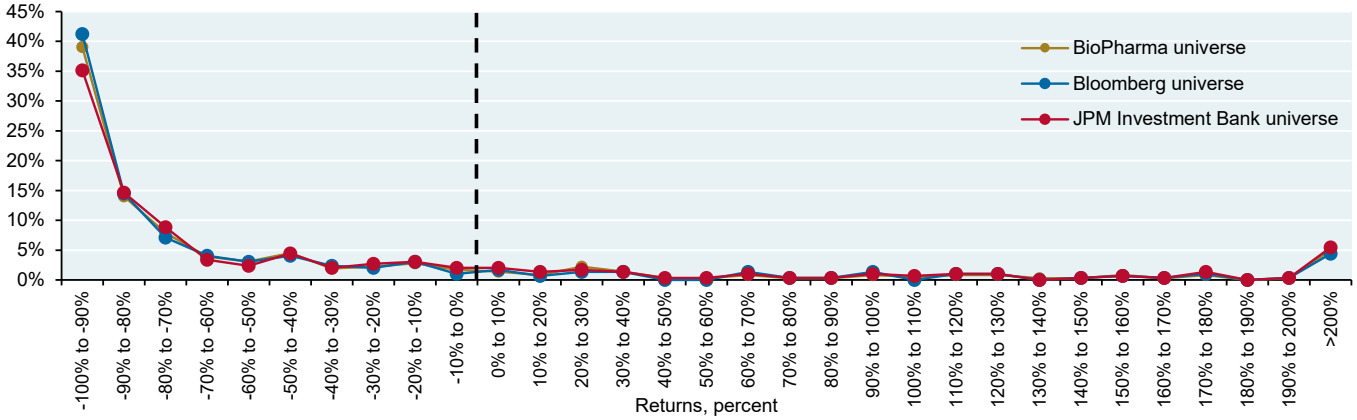
Biotech performance since IPO by clinical stage

Stage	Average return	IPO Count
Preclinical	-46%	88
Phase 1	-46%	109
Phase 2	-11%	97
Phase 3	28%	44
Marketed	-34%	14

Source: BioPharma Dive, Bloomberg, JPMAM, August 11, 2025

Needles in a haystack: biotech IPO holding period returns since January 2018

Percent of companies



Source: BioPharma Dive, Bloomberg, JPM Healthcare Equity Capital Markets, JPMAM, August 4, 2025

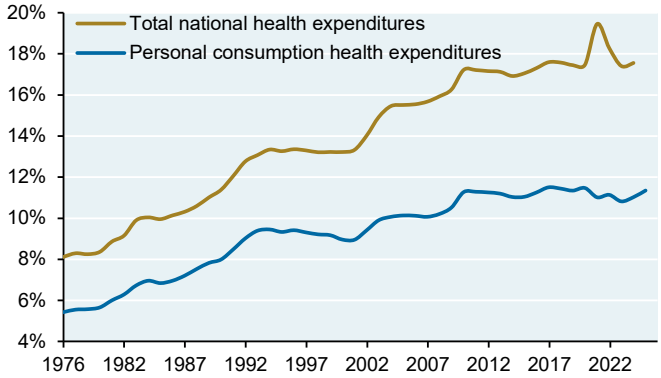
On biotech IPO universes. The tables above show results based on a universe of 356 biotech IPOs since January 2018 as defined by BioPharma Dive, an industry portal which tracks IPO data. BioPharma includes companies that issued on a US exchange and which develop new prescription medicines. They exclude makers of generic or OTC drugs, makers of diagnostic and medical devices, and all SPACs. For comparison, we also show two other biotech universes in the histogram: 296 IPOs from a Bloomberg dataset, and 293 biotech IPOs from JP Morgan's Equity Capital Markets Group. The IPO performance results across all three datasets are almost identical.

New drug discoveries on the horizon, US healthcare spending and conclusions for investors

There may be significant drug discoveries on the horizon, including bispecific antibodies to revolutionize cancer care, new products for treatment of neuropsychic conditions, antibody products recently approved that slow progression of Alzheimer's, non-CRISPR/Cas9 gene editing formats that may cure disease and longevity drugs that may extend health spans and promote healthier aging (see Appendix II). In addition, there's still work to be done on cancers (most of which are still not curable), debilitating autoimmune diseases, cardiovascular disease and dozens of genetic diseases with high mortality rates.

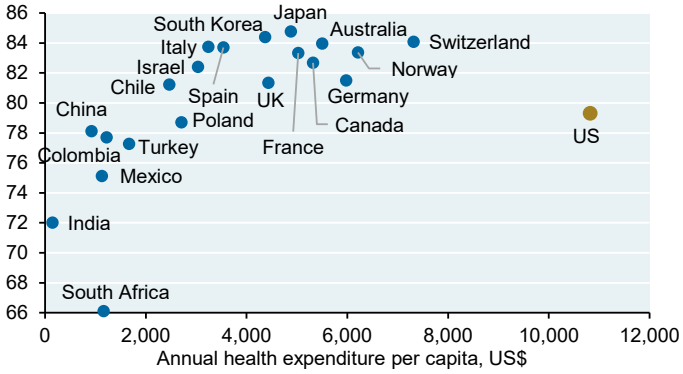
That said, there may not be much room for the US public or private sector to add to healthcare spending. As shown below, personal consumption spending on healthcare as a share of GDP rose from 5% in 1976 to 11% by 2008 but has flatlined since 2008; the same trend is true for national health expenditures. In other words, **US healthcare spending was consistently rising as a share of GDP during the period when healthcare was tracking the returns of the technology sector, from the 1980s to 2019**. But for a country like the US that already spends the most on healthcare per capita (with apparently limited life expectancy benefits), there may be a threshold beyond which the US cannot afford to spend more. The cost of Medicare and Medicaid entitlements relative to non-defense discretionary spending shown in the last chart is continuing to rise. I believe we're getting closer to an informal national referendum to narrow this gap, rather than taking steps to keep increasing it.

US healthcare spending as a share of GDP
Percent



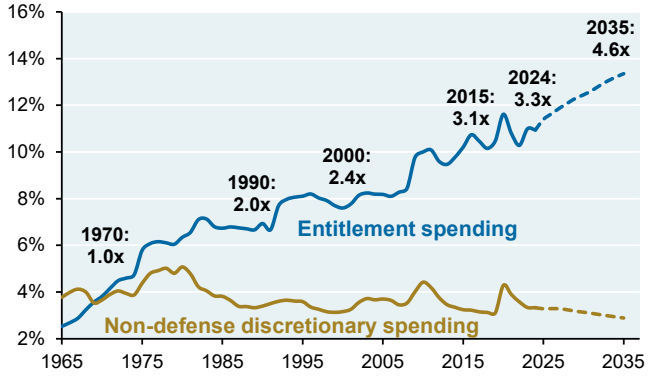
Source: Bloomberg, JPMAM, December 2024

Life expectancy vs annual health expenditure, 2023
Life expectancy



Source: UN, OECD, Our World in Data, 2023

What does the Federal government spend money on?
% of GDP, with ratio of entitlement to non-defense discretionary



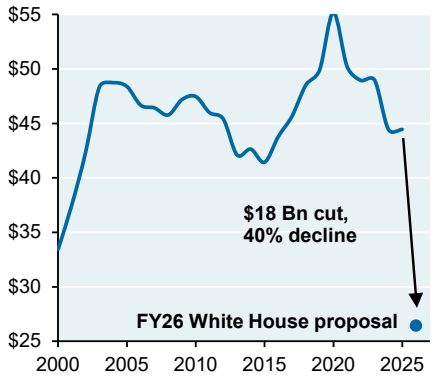
Source: CBO, JPMAM, 2025. Dots are CBO projections

Bottom line: the US healthcare sector is pricing in a lot of bad news and is worth a look as a long-term value play; low valuations cure a lot of ills. Possible biotech targets of drug companies also look interesting, and CMS coverage of GLPs could be a big deal for some pharma companies if it happened. But if bipartisan efforts to reduce US drug prices or enact patent reform are successful, it may take time for the sector to demonstrate that it deserves higher multiples than today's. On page 21 we cover the battle over of publicly funded US scientific research, and on page 24 we conclude with recent peer reviewed studies of longevity drugs in mice.

Appendix I: the political battles over publicly funded US scientific research

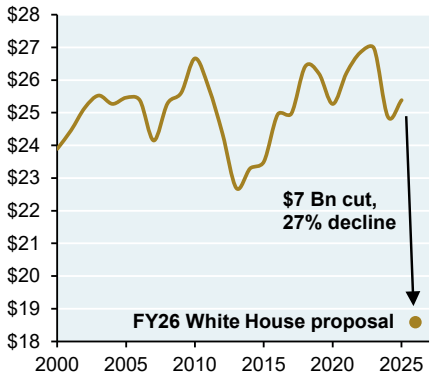
The American Association for the Advancement of Science has highlighted Trump Administration proposals to cut the budgets of major US scientific organizations by 27%-62% in FY2026. Around 80% of the White House's $44 billion in proposed cuts would target early-stage research, with the largest cuts at the National Institute of Health. The NIH is a combination of 27 individual institutes and centers which focus on specific diseases and medical conditions. The largest NIH centers by number of active projects focus on cancer, infectious diseases, biological processes, heart/lung disorders and aging.

NIH research budget
2024 US$, billions



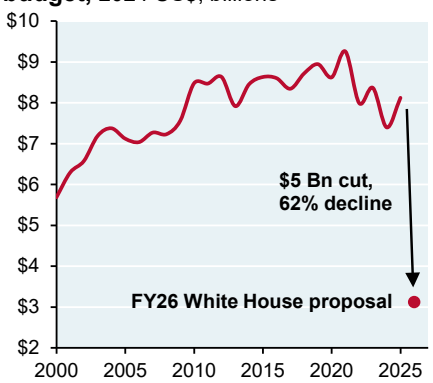
Source: AAAS, JPMAM, 2025

NASA total budget
2024 US$, billions



Source: AAAS, JPMAM, 2025

National Science Foundation research budget, 2024 US$, billions



Source: AAAS, JPMAM, 2025

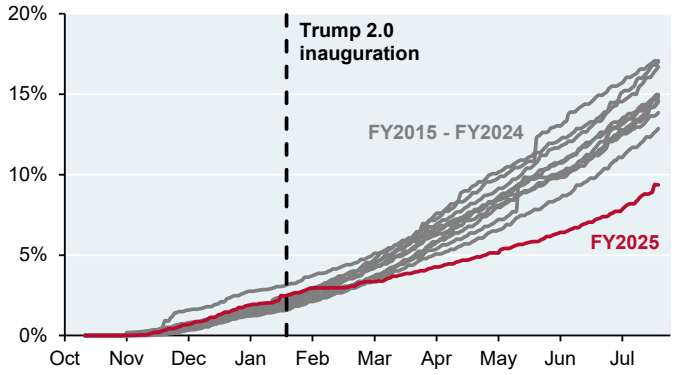
However…the political process is complicated and does not allow the White House to decide these things unilaterally. Here are some general principles which govern the process:

- As a general principle, Congress decides funding amounts for entities like the NIH. While the White House might submit a recissions package on the NIH, we consider it unlikely to pass both chambers
- In the short term, Congress is likely to pass a Continuing Resolution which maintains all funding at levels similar to prior years (a government shutdown might happen first), and which does not restructure the NIH
- Since Appropriations bills cannot be passed via reconciliation, they require 60 votes in the Senate and therefore must be passed on a bipartisan basis. As a result, the likelihood of the sharp NIH cuts shown above occurring via an Appropriations bill appears low, at least right now
- As a sign that the Senate view on NIH funding differs from the President, the GOP-led Appropriations Committee approved the Senate FY 2026 Labor, Health and Human Services bill by a vote of 26 to 3. The bill authorized roughly flat year on year funding for the NIH
- While the White House has floated the idea of pocket rescissions of certain NIH funds (i.e., allowing funds previously appropriated for designated NIH programs to expire), that has not yet occurred. Senate Appropriation Chair Collins (R-ME) has declared that any such attempts would be unconstitutional and violate the 1974 Impoundment Control Act

That said, the White House goal of reducing publicly funded science research is having an impact. See the first chart below on the decline in new and competitive NIH renewal grants through July of each year. NIH funding contributed to early-stage research supporting many of the drugs approved from 2010 to 2019 and totaled $187 billion, around the same amount spent by the pharmaceutical industry[26]. Cutting NIH funding could hinder early-stage drug research which has been the bedrock of 21st century medical breakthroughs[27], and raises questions regarding US leadership in healthcare innovation.

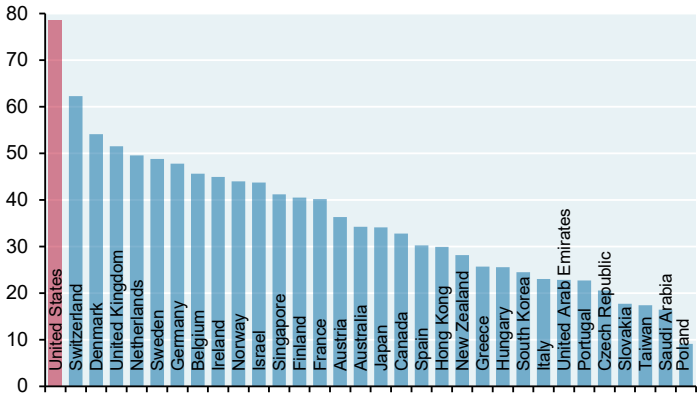
For balance, some feedback I got on the NIH process indicates some degree of waste. Examples: grants that are highly RFP-tuned non-novel proposals which slide through as non-competitive renewals; too many grants which create a tenure protection pipeline with minimal full-stack translation to patients; and non-merit based grants which divert resources from high-impact science.

NIH new & competitive renewal grant funding, FY15 - FY25
Percent of annual grant funding



Source: Jeremy Berg (University of Pittsburgh), July 25, 2025

Healthcare innovation: science & technology score



Source: FREOPP World Index of Healthcare Innovation, 2024

The NIH, NASA and NSF are not the only science-related government entities targeted for budget cuts by the White House. Additional proposed cuts to federally funded scientific research include a 14% decrease of $1.15 billion from the Department of Energy's Office of Science, a 22% decrease of $325 million from the National Institute of Standards and Technology and a 25% decrease of $193 million in basic (earliest stage) research from defense agencies such as DARPA. In addition to cuts to these agencies, the CDC budget is also slated for a 54% decline in FY2026. The largest single component of the CDC budget is the Vaccines for Children program that provides vaccines at no cost to uninsured or underinsured children. The potential cost: the loss of direct and indirect savings resulting from this program. The CDC estimated in August 2024 that $500 billion spent on this program from 1994-2023 resulted in lifetime health related savings of almost $4 trillion[28].

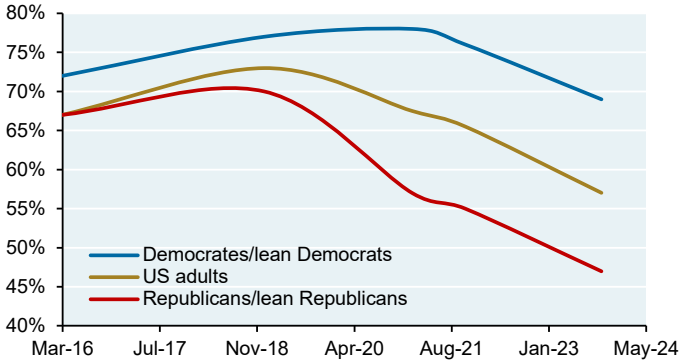
[26] *"Comparison of research spending on new drug approvals by the national institutes of health vs the pharmaceutical industry, 2010-2019"*, Ekaterina Cleary (Bentley University) et al, April 2023

[27] NIH funded projects include treatments for rheumatoid arthritis, lupus, Crohn's disease, psoriasis and multiple sclerosis; research on immune checkpoint inhibitors which led to rising survival rates for melanomas and other cancers; proglucagon, the protein precursor of GLP-1s; mRNA vaccines; Piezo channels to deal with chronic pain; HPV vaccines; human genome sequences; and AZT cancer/HIV therapies.

[28] "*Health and economic benefits of routine childhood immunizations in the era of the Vaccines for Children program*", CDC, August 2024

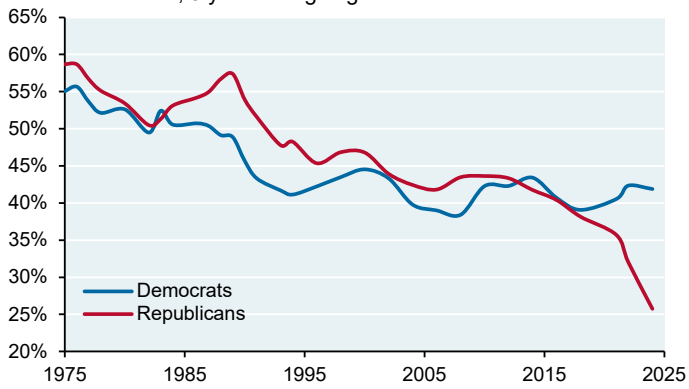
"I'm doing my own research". The precursor to today's science funding battles: a gradual decline in public confidence in both science and in the people in charge of the medical establishment. I can't explain why this is happening, other than to say that this is not the first era in history in which belief and trust in science gradually eroded, and which was replaced by something else. In the 1930's, Soviet scientists rejected traditional genetics and science-based agriculture, describing the concept of a gene as a "bourgeois invention". They opted instead for a Marxist version of genetics; 3,000 Soviet scientists were dismissed, imprisoned or executed, with negative impacts lasting through to the 1990's when some scientists were finally rehabilitated.

Has science had a mostly positive effect on society?
Percent of US adults who respond yes



Source: Pew Research Center, JPMAM, 2023

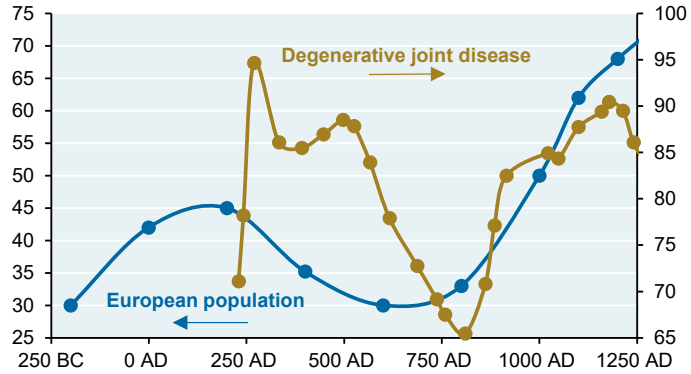
US public confidence in the people running healthcare
Percent confident, 3 year rolling avg



Source: NORC at UChicago, JPMAM, 2024

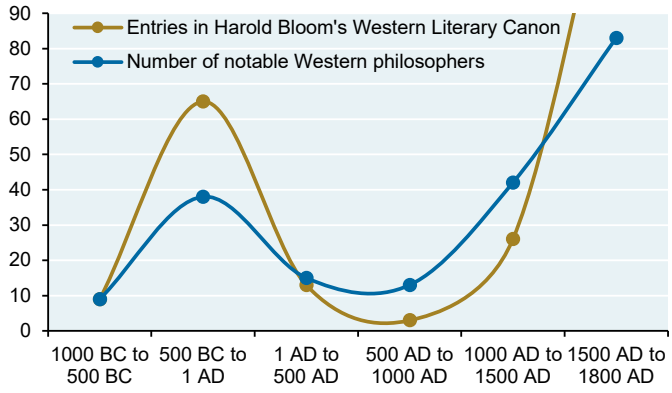
As I was wrapping up this piece, my mind began to wander and I started thinking about what it must have been like to live in Europe during the transition from the Roman Empire to the Dark Ages. It took a really long time for Europe to recover.

The Dark Ages: population and degenerative joint disease
Population, millions Health index (lower = more DJD cases)



Source: Dudin et al (JAES), Galofré-Vilà et al (Oxford), JPMAM, 2025

The Dark Ages: literature and philosophy



Source: Harold Bloom (Yale), JPMAM, July 27, 2025

Appendix II: peer-reviewed evidence on longevity drugs in mice, and the future of organoids in clinical trials

There's some excitement about longevity drugs right now. Given the rise of the GLP market from $5 bn in 2018 to $53 bn by 2024, many healthcare investors are watching to see how the longevity market evolves. While longevity is not widely recognized as a formal disease area, that could change. But there's also a lot of room for hype and hyperbole; the FTC actively pursues companies making false anti-aging claims.

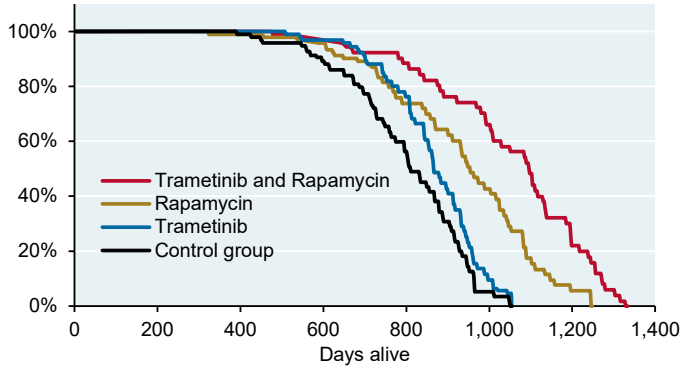
The main premise: there's a gap between lifespan (how long you live) and health span (how long you lead an actively independent and fully functioning life, which is of course a subjective definition). Some estimates for the US show a gap of around 12 years. If the biological processes which affect aging could be managed at the cellular level, health spans could increase relative to lifespans.

Areas of longevity research include metabolic restoration which aims to correct metabolic dysfunction that accumulates with age and which contributes to type 2 diabetes, cardiovascular diseases and fatty liver disease; senotherapy which focuses on targeting senescent cells that contribute to aging and tissue dysfunction; and immunoregulation, which focuses on reducing inflammation.

Is there evidence that pharmaceutical approaches can extend lifespans? As a matter of principle, I ignore self-promoting longevity gurus and people selling longevity products on the internet. I'm more interested in peer reviewed studies, and there are two worth mentioning. Mice are **very** different from people (see next page), but it's a start.

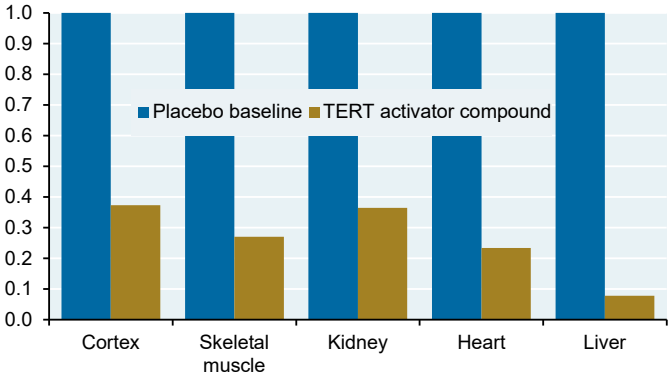
- In April 2025, a study in Nature Aging[29] reported that the FDA-approved drug Trametinib combined with the mTOR inhibitor Rapamycin increased lifespans in mice, attenuated their decline in heart function with age, delayed tumor growth/load and reduced brain and peripheral inflammation, suggesting improved health at old age. Combined treatment with Rapamycin and Trametinib increased lifespans by 29% and 27% in female and male mice. Ongoing clinical trials now assess the potential of mTOR inhibitors as "geroprotective" drugs in humans, which refers to compounds that slow biological aging
- In July 2024, a study in CellPress[30] reported the ability of activator compounds to restore TERT levels in very old mice, resulting in reduced aging activity. TERT is a gene that protects chromosome endcaps, hence preventing their deterioration; but may also be a master regulator of many genes involved in aging, including those controlling inflammation, cellular repair, brain health and more. In the study, mice receiving the activator compounds showed improved memory, new neuron growth, increased strength-balance-coordination, reduced chronic inflammation and other signs of reversed molecular aging. The chart on the right shows the resulting 60%-70% declines in a measure of cellular aging across multiple organ systems

Life expectancy of mice taking select longevity drugs vs control group, Percent of female mice living



Source: Nature Aging, April 2025

Impact of TERT activator compound on cellular aging activity in mice, Cellular aging measure (lower = less aging)



Source: CellPress, JPMAM, July 2024

[29] "*The geroprotectors Trametinib and Rapamycin combine additively to extend mouse health span and lifespan*", Nature Aging, Linda Partridge et al, Department Biological Mechanisms of Ageing, Max Planck Institute for Biology of Ageing, Cologne, Germany, April 2025

[30] "*TERT activation targets DNA methylation and multiple aging hallmarks"*, CellPress, Ron DePinho et al, Department of Cancer Biology, University of Texas MD Anderson Cancer Center, July 2024

Man vs Mouse: why animal models can have high failure rates, and the future of organoids

Much of the last century's progress in understanding the molecular and biological bases of human disease has come from models: yeast, C. elegans, Drosophila and the mouse. The mouse has had the greatest impact due to its genetic tractability, and with the advent of sophisticated genetically engineered mouse models, their utility and accuracy have increased. **That said, the inability of some preclinical animal models to predict clinical efficacy and safety in humans has led to failure in related drug trials**. This section is not meant to discredit animal models as a basis for drug testing, but to make investors aware of their potential limitations:

- False negative errors: potentially good drugs are abandoned due to lack of efficacy or side effects in animals that would not occur in human trials
- False positives: drugs that "work" in animals may still fail in human trials
- Adverse events and safety issues in human volunteers and patients that were missed by prior animal testing
- Mice lack many human disease phenotypes and viral susceptibilities, and their use often requires heavy genetic manipulation that introduces artifacts and undermines relevance
- Other factors limit the accuracy of animal models: inbred strains vs. genetic diversity in humans; often young, healthy animals, unlike aged, sick humans; molecular differences altering drug effects; artificial experimental conditions; housing, diet and environments that differ from human lifestyles
- Disease that is induced artificially may differ from naturally occurring illness
- Study design: small, short studies vs. lifelong human exposures; high doses triggering irrelevant effects; each test uses limited animal groups unlike large, diverse human trials

Imperfect animal models may be supplemented with more reliable human-based techniques such as miniature bioengineered "**organs-on-chips**" (microfluidic devices that recreate the microenvironment of an organ, including tissue interfaces and mechanical forces). The future lies in an integrated approach: using each model for what it does best, strategically combining insights from cells, chips, computers, animals and humans to minimize failures and surprises before entering large clinical trials.

As of 2023, the FDA no longer requires animal testing to proceed to first-in-human studies. **Organoids** (3D cell cultures that self-organize from stem cells, resembling the structure and function of organs) may be an even better approach. Organoids are faster and more representative of human biology than organ-on-chip platforms, which are constrained by artificial variables and structural density. They offer better predictive validity for toxicology and efficacy, cost savings and a clearer ethical profile.

Sources: "*The (misleading) role of animal models in drug development*", Frontiers in Drug Discovery, Thomas Hartung (Bloomberg School of Public Health, Whiting School of Engineering, Johns Hopkins), April 2024; "*From mice to medicine: six questions with Nadia Rosenthal*", Jackson Laboratory for Genomic Medicine, August 2024; "*Why animal studies are often poor predictors of human reactions to exposure*", Journal of the Royal Society of Medicine, Michael Bracken (Yale School of Public Health, Yale School of Medicine), March 2009; Melanie Walker, Rockefeller Fellow and Clinical Associate Professor, University of Washington School of Medicine; Ron DePinho, MD Anderson Cancer Center

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