



Introduction

This slide presentation reviews broad trends impacting healthcare and reviews several ideas that have been bouncing around the field since 2022.

Today's populist government in the U.S. has brought us the MFN conversation, threatened pharma tariffs, FDA uncertainties, and the MAHA Report.

Combined with ongoing budgetary pressures, it is a time of exceptional uncertainty in the overall healthcare environment in the United States.

This uncertainty has been coupled with fresh ideas and lots of debate about how to enhance healthcare in the U.S.

A number of venture capitalists have come forward and have suggested radical strategies for improving healthcare.

We take note of ideas for healthcare system and platform reform advocated by Andreesen Horowitz (A16z) and General Catalyst.

It is a vital moment and a time for conversations about healthcare reform both in the United States and other countries.

The hypergrowth of consumer-oriented e-Prescribing platforms like HIMS and Ro strike us as particularly important feature of today's dynamic healthcare environment.

It is easy to recoil and argue that these platforms are facilitating premature genericization of innovative drugs.

But, in the same sense that Napster spawned a gigantic transformation of the music industry, we believe that groups like HIMS are not going away, no matter what transpires with compounded GLP-1s.

The younger healthcare consumer wants to take more charge of their health and is perfectly comfortable doing so online.

A further factor is the ongoing struggle of the biotech sector and generalized underperformance of the pharma industry relative to tech peers.

One can't help but be struck that ongoing demonization of pharma industry pricing practices and internationalization of production is amazingly ill-timed.

Introduction (continued)

Politicians often wait for a long-time to get into power and launch ideological initiatives that they have been working on for years.

We recall Liz Truss's short-lived tenure as Prime Minister in the UK when she proposed unfunded tax cuts and a shift to supply-side economics at a moment of UK inflation. The ideas were wrong for the moment.

If you will, if anything, the Western biopharma industry would benefit from supportive policies – both in terms of pricing and encouragement of investment in innovation.

With a few exceptions like Eli Lilly and Vertex, the pharmaceutical sector has not been delivering great returns to shareholders in recent years.

Despite extraordinary scientific advance and product innovation, the pharma sector has been steadily outperformed by its tech peers since the end of the Pandemic.

Not so long ago, companies like Merck and Pfizer were similar in market cap to tech giants like Microsoft and Apple.

Today, that has all changed. Tech business models have led to dramatic outperformance versus the pharmaceutical industry.

There are some obvious issues bedeviling pharma.

The Hatch-Waxman Act of 1984 made it possible for one to easily create and launch a generic drug after an innovative drug loses its patent. At this point, 90% of scrip volume in the U.S. is generic. And now it looks increasingly likely that true substitutability is coming for biologics.

Further, aggregate returns on R&D that are below the cost of capital are a major issue for the pharmaceutical sector – particularly in this moment where China is disrupting the R&D cost curve.

But ease of genericization and subpar economic profits associated with R&D spend are not the only issues impacting pharmaceutical companies.

We discuss several deeper and more fundamental business model issues that are holding back value creation.



Introduction (continued)

To compound matters for the healthcare investor, the managed care sector is facing its own travails.

For example, UnitedHealth Group shares are down over 40% so far this year.

Many healthcare systems are also struggling, particularly those that are heavily dependent on federal research funding.

Historically, times of struggle have been times of opportunity.

An important background fact is that the global healthcare sector is likely to grow indefinitely at a rate that exceeds that of the overall economy.

And AI offers the promise of major transformation in the provision of healthcare.

Healthcare practice 25 years from now will be unrecognizable. It seems inconceivable to us that today's 35-year old consumer, well-versed in the use of Al programs for everything, will tolerate the nonsense facing today's consumer who encounters a waiting room at almost all major healthcare service providers.

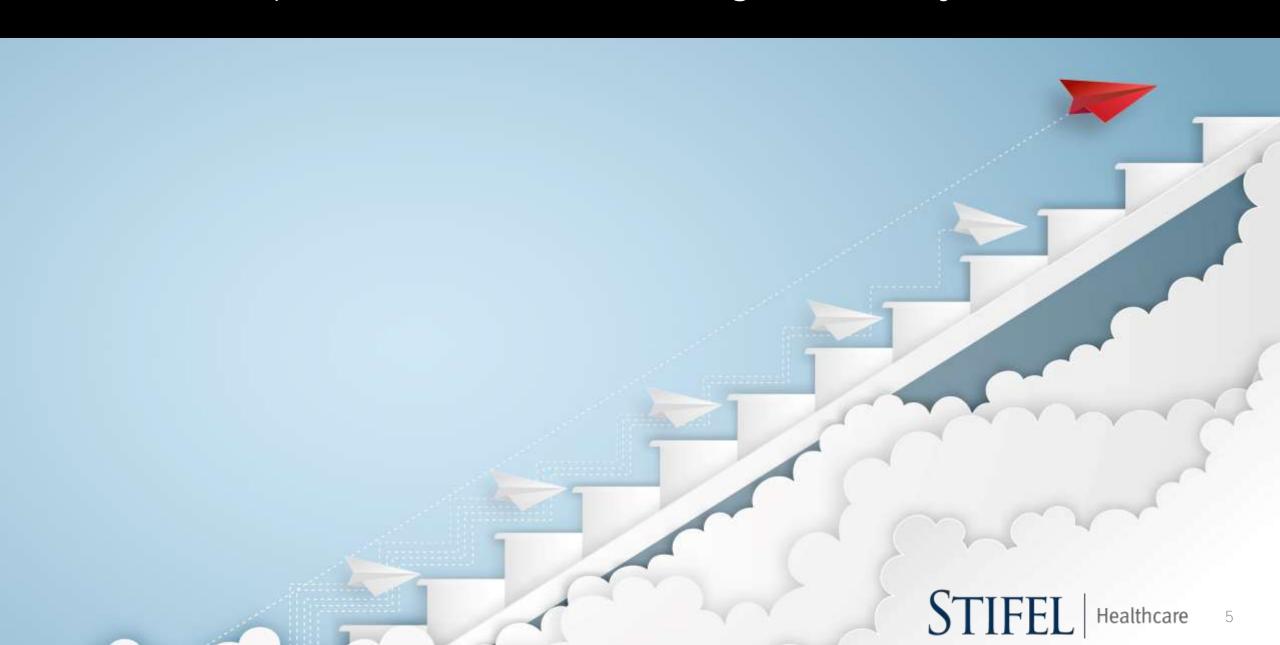
The confluence of innovation in biology, the power of AI, process innovation (e.g., hospital at home) and the online consumer is likely to lead to major transformation in healthcare. Upcoming breakthroughs involving the application of AI to the practice of real-world medicine, insights from proteomics and aging biology will be profound, promising and positive.

We believe that major disruption is likely in both the pharma and healthcare services sector and outline some thoughts on how this might play out.

We see a world of healthcare platform companies that cross today's lines between pharma, tech, payors and providers. These companies are likely to be much larger than today's healthcare players and may, themselves, come from tech founders rather than healthcare founders.

In no way are these thoughts intended to be prescriptive. Rather, our hope is to motivate you to imagine how things could be different. We very much hope that you participate in a positive way in the upcoming transformation of healthcare and pharma.

Healthcare Spend in to Continue Rising Indefinitely



Healthcare Spend to Grow with Wealth



At a societal level our ability to pay for healthcare is a function of the total budget. For example, how much money does the government collect a year? Or, what is the cost budget of an employer?



At the individual level, self-pay spending on healthcare is also driven by budget.

You can't spend money you don't have.

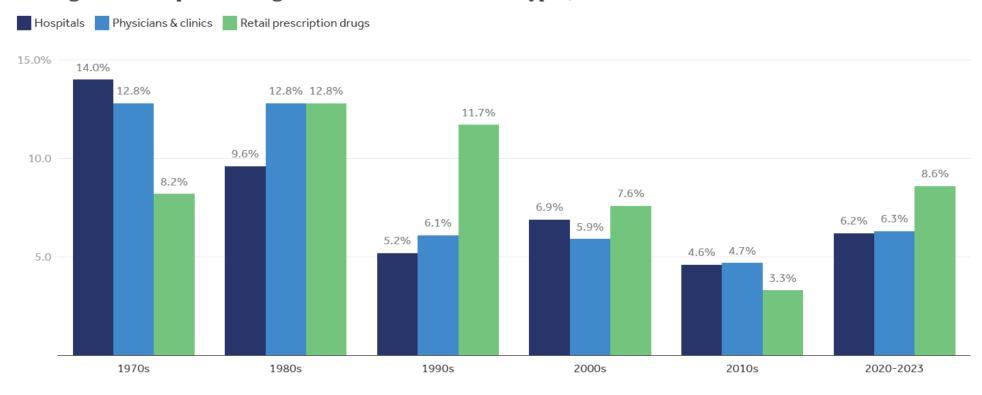


Growth in incomes and wealth is what causes budgets to expand. Healthcare spend increases disproportionally with wealth.



Growth in Pharma Spending Has Been Relatively Strong Over the Last 50 Years

Average annual expenditures growth rate for select service types, 1970-2023



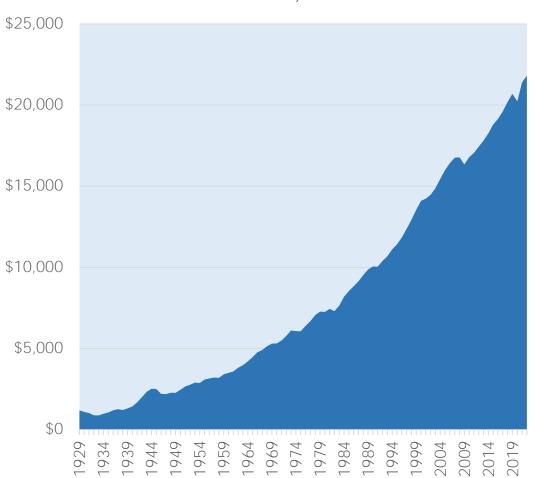
Note: 2020-2023 represents a 3-year change.

Source: KFF analysis of National Health Expenditure (NHE) data • Get the data • PNG

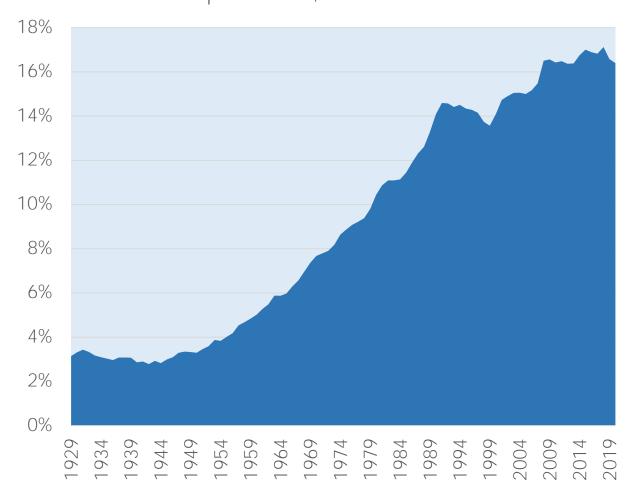
Peterson-KFF **Health System Tracker**

Real GDP is Up 20-Fold Since 1929. Health Spend Up Much More

U.S. Real GDP, 1929 to 2022 (Billions, 2017 Dollars)

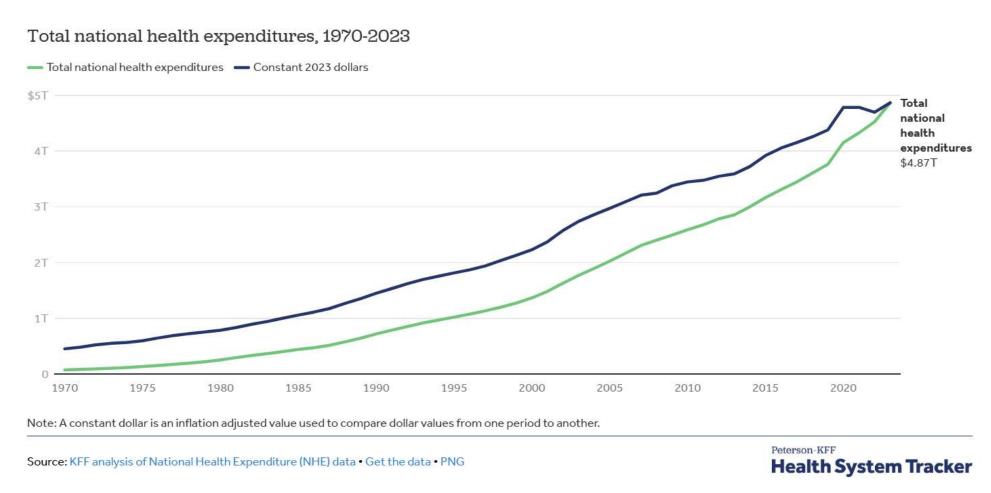


Healthcare Spend in the US / Total Economy Expenditures, 1929 to 2020



Healthcare Spending in U.S. is Accelerating in This Decade

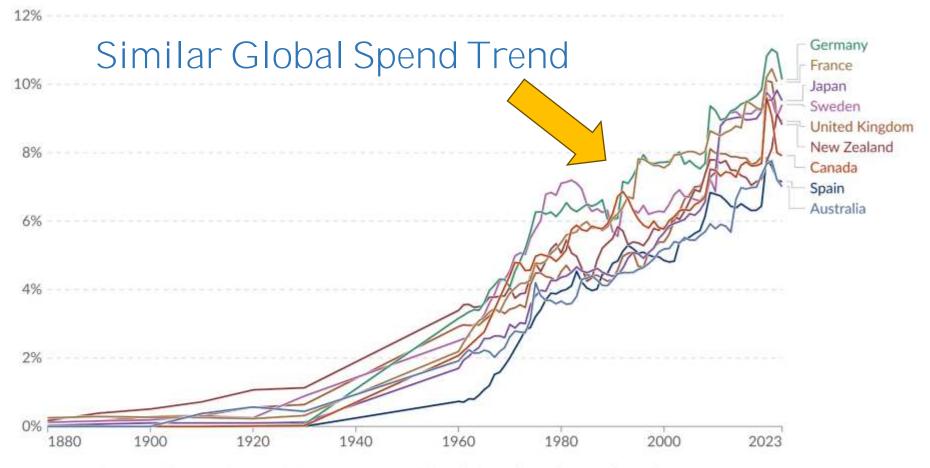
U.S. healthcare spending reached \$4.9 trillion in 2023, marking a 7.5% increase from the previous year. This growth outpaces the average annual growth rate of the 2010s (4.1%) and is significantly higher than the 4.6% increase observed from 2021 to 2022.



Government health spending as a share of GDP, 1880 to 2023



This metric captures spending on government funded health care systems and social health insurance, as well as compulsory health insurance.



Data source: OECD Health Expenditure and Financing Database (2024); OECD (1993); Lindert (1994)

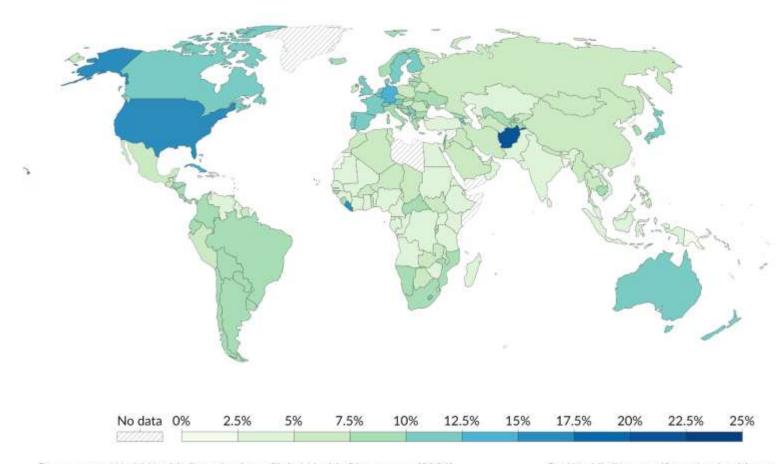
Note: Health spending includes final consumption of health care goods and services (i.e. current health expenditure). This excludes spending on capital investments.

OurWorldinData.org/financing-healthcare | CC BY

U.S. Spends More on Health as a Percent of GDP That Most

Total healthcare expenditure as a share of GDP, 2021

Total healthcare expenditure as the share of national gross domestic product (GDP).



There are two ways to interpret this data.

The most common is to argue that the U.S. is not efficient in healthcare. People point to lower life expectancy in the U.S. versus countries that spend less.

We don't doubt the inefficiency argument, but it ignores a different interpretation: the U.S. is a wealthy capitalist nation which means those that are better off can voluntarily choose to spend more on health because it is a luxury good. Lifespans for the well off in the U.S. are just as good, if not longer than those in Europe.* A U.S. 40-year old male in the top 1% of income can expect to live to age 87.

We think this interpretation is the predominant explanation and, ignoring the implied social justice implications of capitalism for a moment, we simply wish to observe that one can reasonably expect healthcare spend to rapidly rise in other countries as incomes rise over time.

Data source: World Health Organization - Global Health Observatory (2024)

OurWorldinData.org/financing-healthcare | CC BY

^{*} See https://nap.nationalacademies.org/catalog/19015/the-growing-gap-in-life-expectancy-by-income-implications-for

Forecast

We looked at the econometric relationship between incomes and healthcare spend share over time.

Assume (as does PWC) that real GDP in the U.S. rises at 2% per annum indefinitely.



Real healthcare spend in the U.S. will triple within the next forty years and double by 2050.*

^{*} In certain fast-growing countries like India healthcare spend to triple within twenty years or less.

Bottom Line



Healthcare spend is going to rise at an increasing rate for the foreseeable future.



Concerns about budget deficits and cost reform mask the effect of rising incomes and longer life spans on medical spend.



Further, the more we spend on medicine, the longer we live. The longer we live, the more we spend on medicine.

Implications for Investors

Healthcare is the ultimate growth area for investment. It is hard to imagine any other part of the economy that will experience greater dollar growth in spend over the next century.

Staying healthy and living longer requires innovation and innovation costs money.

Despite today's gloom, many healthcare entrepreneurs and investors will generate large fortunes in the years ahead.

The key sector issues involve the ongoing collision between capitalist motives, government exigencies, hypergrowth in innovation and the growing power of computation.

Simultaneously, the power of medicine to deliver longer lifespans and more fulfilling lives for humans is exploding.

Overall, we believe that the healthcare sector is going to deliver excellent returns over decades, but investors need to be patient and prepared to face major sector transformation and turbulence.



Medicine is Evolving Fast



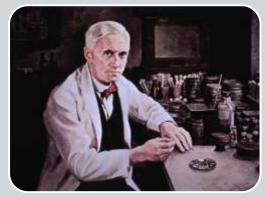
A Brief Tour Through History, Science and Medicine



Hippocrates and Galen



James Lind: First Clinical Trial



Fleming Finds Penicillin



Biology Everywhere

1000BC to 1500 AD

Galenic thought – four humors drove body – no use of data.

Life spans were very short. Infectious disease was the big killer.

Medicine added very little value and was often harmful

1501 to 1850

The main growth area of medicine was surgery. Big progress in understanding anatomy, the role of the heart and other organ systems.

Introduction of rational thought and clinical trials.

Medicine still not very good for patients

1851 to 1953

Growth in understanding of the cell and genetics.

Major growth in understanding cancer and neuroscience.

Medicine gets a lot better, especially in dealing with infectious disease.

Anatomy is the foundation.

1954 to Today

Explosion of knowledge of biology.

Medicine gets radically better at transforming the care of cancer, heart disease, kidney disease and genetic disease.

Still very focused on organ systems.

A Core Truth:

Progress in Medicine is About What We Can See and Measure

Power of medicine set to explode because of new tools

Aristotle and
Galen Era

16th to 17th Centuries

18th and 19th Centuries

1900 to 2000

2000 to 2025

We could see the patient We built the idea of but nothing beyond that. science from the works

No framework of science either.

We "made up" a theory about disease and applied it - wholly lacking an empirical theory of the organism. of Bacon and Descartes.

We conducted dissections and built out the anatomy.

We began to learn how the body worked (e.g., the heart circulation), abandoning Galen.

The advent of the microscope rapidly led to the understanding of infectious disease (germ theory) and cells as the basis of life.

New evolution framework improved understanding of disease.

Nucleic acid sequencing, X-Rays, CT, MRI have allowed much better views of the body.

Immunoassays facilitated the explosion in immunology and other core areas of molecular biology.

Bioelectronics CRISPR Cryo-EM EEG analysis Electron microscopy Flow Cytometry 11 Ms Live cell microscopy Mass Proteomics Mass Metabolomics RNA types Single cell

Where Medicine is Going From Here: Our View



Improved Understanding of Biology

What matters is how biologic systems work together (or not) to lead to death and aging. Much less about organ systems and more about cells, genes and proteins.

Today's view of "disease" and "health" will change to "where's your biology"?



Improved Ability to Measure Biology with a Blood Sample

With a much deeper understanding of core organismal molecular biology, it will also be possible to learn what is going with a patient leveraging new techniques

We can now use proteomics to measure a person's biological status



Improved Ability to Customize Interventions

Statistical analysis of measures of underlying biology with patient outcomes and the role of customized interventions will improve massively over time.

The role of AI is going to be critical. Machine learning can be quite helpful here.



Ability to Deliver Solutions to Improve Health

We are already seeing Al engines clobber doctors in clinical decision-making. Google's engine and DeepSeek both look surprisingly good.

We think of a physician of the future as a "pilot flying with instruments" – we are not getting rid of the airpline pilot. We Can Measure Biology Comprehensively with Modern Tools

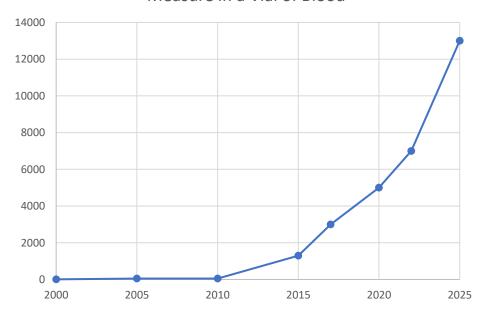
Proteins

express health

Modern proteomic analysis allows us to gain a far deeper understanding of a person's health than was previously possible. While genetics are fixed at birth, proteins can be far more informative over our lifespan because they reflect environmental and physical conditions.*

New technologies allow scientists to measure thousands of proteins from a vial of blood.

Number of Proteins that Researchers Can Easily Measure in a Vial of Blood



Key Technologies:







^{*} See PLoS One. 2016 Apr 22;11(4):e0154387; Aging Cell. 2010 Dec;9(6):1057-64. Commun Biol. 2021 Jun 18;4(1):758.

Modern Proteomics: A simple blood draw can give a very good read of mortality risk

- In a June 2021 research paper scientists from deCODE, a subsidiary of Amgen, describe a predictor of human mortality.
- Using a dataset of ~5000 protein measurements in 22,913 Icelanders, the scientists developed a predictor of life expectancy that substantially outperformed predictors based on traditional risk factors.
- "The predictor gives a good estimate of general health from a single blood draw," says Thjodbjorg Eiriksdottir scientist at deCODE genetics.





Kari Stefansson and Thjodbjorg Eiriksdottir, deCODE

Key Idea: 'Omics Facilitate Massively Better Disease Diagnosis

It's possible to build much better disease diagnosis algorithms than those which are available today. Most of the factors that associate with diseases in the Decode studies involve subclinical pathologies, including ECM and cellular stress. None of the factors are in current FDA-approved tests. If one could diagnose disease more accurately and more quickly, there are major benefits for patients and payors. In the same sense that GRAIL built a pan-cancer detection algorithm, it may be possible to build an inexpensive pan-disease detection algorithm using modern proteomics and metabolomics.

Al is Made for Medicine



VC Perspective

John Doerr, Chairman Kleiner Perkins, 2023

"Generative AI means that an individual with far less medical training than a doctor can collect observations on a patient and deliver basic advice. In many cases, individuals themselves can obtain surprisingly good medical advice from the computer.

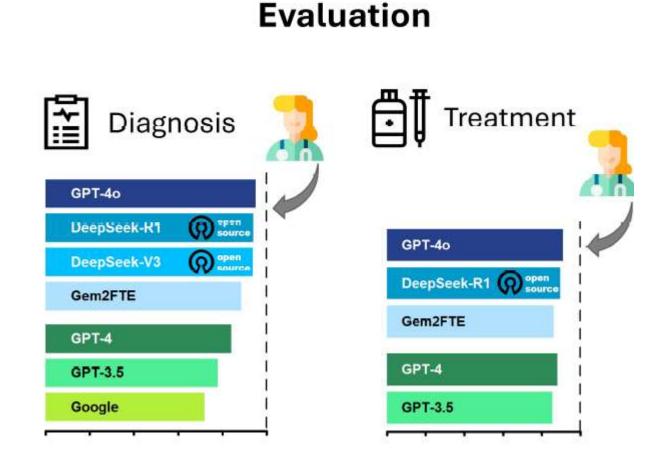
The reality is that managed care is going to exploit the spectacular power of this technology with the result that within a decade's time the number of doctors and nurses used on the frontlines of medicine will fall by half."



DeepSeek Compares Well to Proprietary LLM in Clinic

Sandmann, S., Hegselmann, S., Fujarski, M. et al. Benchmark evaluation of DeepSeek large language models in clinical decision-making. *Nature Medicine*, April 23, 2025

Large Language Models (LLMs) are increasingly transforming medical applications. However, proprietary models such as GPT-40 face significant barriers to clinical adoption because they cannot be deployed on site within healthcare institutions, making them non-compliant with stringent privacy regulations. Recent advancements in open-source LLMs such as DeepSeek models offer a promising alternative since they allow efficient fine-tuning on local data in hospitals with advanced IT infrastructure. To demonstrate the clinical utility of DeepSeek-V3 and DeepSeek-R1, we benchmarked their performance on clinical decision support tasks against proprietary LLMs, including GPT-40 and Gemini-2.0 Flash Thinking Experimental. Using 125 patient cases with sufficient statistical power, covering a broad range of frequent and rare diseases, we found that DeepSeek models perform equally well and in some cases better than proprietary LLMs. Our study demonstrates that open-source LLMs can provide a scalable pathway for secure model training enabling real-world medical applications in accordance with data privacy and healthcare regulations.



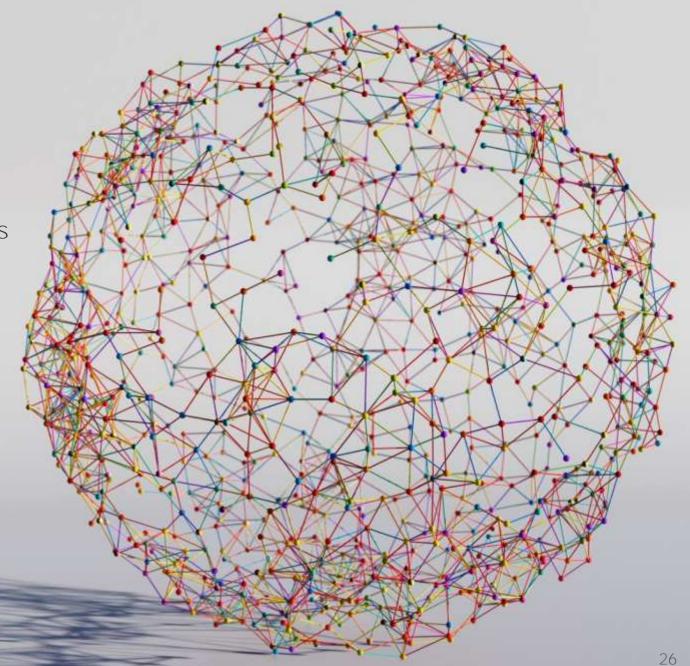
Source: https://www.nature.com/articles/s41591-025-03727-2

Foundation Models

A Foundation Model (FM) is a form of generative artificial intelligence. It generates output from one or more inputs (prompts) in the form of human language instructions. Models are based on complex neural networks inclu (Fding transformers, and variational encoders.

In general, a FM uses learned patterns and relationships to predict the next item in a sequence.

Foundation models use self-supervised learning to create labels from input data. This means no one has instructed or trained the model with labeled training data sets.



An Obvious Idea: FM's for Specific Areas of Biomedicine

A foundational model can be large enough to span the knowledge and meaning in a dataset.

The excitement about foundational models in biology arises from the notion that they can learn basic rules of biology and easily translate onto new patients or other diseases related to the data learnt about.

This, for instance, could allow a neural foundational model to understand and detect the many facets of brain and neural activity, from disease to wellbeing and then easily diagnose a wide range of conditions or provide biomarkers in clinical trials.

There is an obvious opportunity to build up foundation models for dealing with situations that arise in a specific department (e.g., emergency department or cardiology).

Context-specific AI engines are being developed rapidly and create enormous potential for disruption to existing care models and healthcare systems.

Changing Physician Roles

Algorithmic care will not put physicians out of work at all but will increase the premium on knowledge of medicine and diagnostic technologies. LLM's won't take over the doctor. Rather, the doctor needs to take over the Al engine.

Master Physicians

- People with both deep clinical experience and/or strong understanding of bioinformatics, 'Omics and biological research.
 Substantial diversity here.
- 2. These persons help to review data and appropriateness of algorithmic approaches to disease.
- 3. These persons are available for complex cases that get escalated.

Clinicians

- 1. A clinician can be either a nurse or a physician.
- 2. The key is experience in positively interacting with patients and understanding disease state etiology and their treatment.
- 3. These persons will have realtime access to algorithmic /Al type advice based on patient interactions – typically using something like an iPad.
- 4. A good clinician will be trained to escalate tougher cases rapidly.

Medical Technicians

- 1. Medical technicians are already becoming the first line of encounter with patients in many ambulatory settings like urgent care clinics. This will continue.
- 2. A well-trained medtech armed with an LLM-linked iPad in the future should be able to make much more progress than can be done today with Epic, for example.
- 3. A good medtech will rapidly escalate complex cases to a clinician.

Al is Made for Medicine: Three Giant Opportunities in Health and Al

1

Building foundational models in biology and medicine for specific problems like kidney function.

Using AI driven differential diagnosis models and care/outcome prediction models to deliver better care to those that lack access to good care.

3

Artificial agents in the back office for dealing with paperwork, insurance companies and the like.

How AI Can Transform Medicine

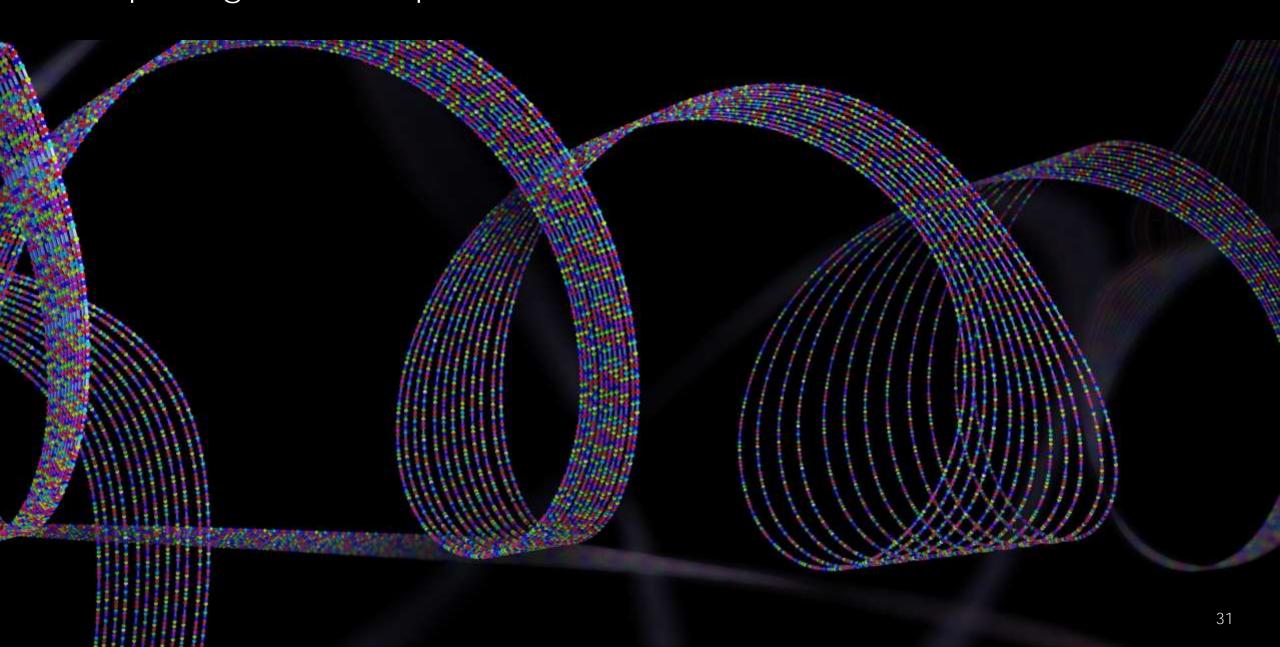
Self Care: Patients go from "Dr. Google" to a much better curated AI solution that escalates for them when they need it. I have personally been using DeepSeek in recent months and have been quite impressed.

Patients with Poor Access: Sicker patients who aren't going to be able to manage interaction with an app can consult with nurses by phone or technicians who pay home visits to sort out what to do, collecting key diagnostic data before making choices.

Auto Care: Patients with routine needs respond to questions. The computer analyzes the situation, recommends prescriptions while the doctor reviews and approves them (or asks to see the patient). This is working quite well now in some settings.

High End / Specialty Care: Today, physicians hit online sources, colleagues and the library to sort out what to do in difficult cases. An Al engine can be incredibly helpful in this case if properly prepared. A similar approach can be used in specialty situations.

Comparing Value Capture in Healthcare vs. the Tech Sector



Tech Companies Dwarf Healthcare Peers

World's Top Five Tech Companies are Worth \$13.9 Trillion.

World's Top Five Healthcare Companies are Worth \$2.1 Trillion.

Apple's EV is larger than the top five healthcare companies combined.

Actually, any of the top four **techco's** are worth more than the top five **healthco's** combined.

But the GDP contribution of healthcare is far larger than the GDP contribution of technology

Healthcare is 20%+ of U.S. GDP whereas tech is around 7%.

Enterprise Value (\$ billions, May 28, 2025)



Enterprise Value (\$ billions, May 28, 2025)



Source: CapitalIQ

The Obvious Question

Why are the top five tech companies worth well over six times as much the top five healthcare companies?



Explanation #1: Pharma IP is Not Effective in Excluding Competition

- 1. Pharma products get 20-year patent lives and then are genericized.
- 2. **It's hard to sustain high value if one is going through a sequence of 20**-year patent monopolies, each which requires enormous amounts of time, money and risk to achieve.
- 3. A new drug usually doesn't get close to 20 years of exclusivity. The average time for arrival of branded competition is seven years and dropping. On average, sales start to decline twelve years after launch.¹
- 4. Less than three percent of preclinical drugs are ever approved. And, after approval, less than five percent of drugs ever achieve \$1 billion in sales. Average returns on pharma R&D investment have been zero.²
- 5. Other large healthcare companies such as those in health insurance and medtech face even tougher competition.
- 6. In contrast, the top five technology companies exploit a variety of mechanisms to build powerful protective moats for their businesses.



"A good business is like a strong castle with a deep moat around it. I want sharks in the moat. I want it untouchable."

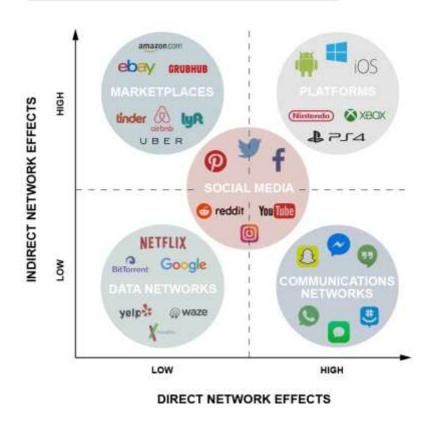
Warren Buffett, Chairman, Berkshire Hathaway

Tech Companies Build Moats Without Relying on IP:

Tool A: Network Effects

- 1. Network effects happen when a product or service increases in value with the total number of customers. The classic example is the telephone: The more people who have one, the more useful each phone is.
- 2. Tech services like WhatsApp and Airbnb benefit from massive network effects.
- 3. Platforms that serve multiple customer groups can also have *indirect* network effects, meaning that when one user group grows, the platform becomes more valuable to a complementary user group.
- 4. Operating systems are a case in point: Developers' demand for adopting a particular operating system depends on the number of users, and users' demand depends on the number of developers creating applications.
- 5. Another example would be Uber. There are more customers when there are more drivers and vice-versa.
- 6. Once a platform has achieved **critical mass** in a network it is very hard for others to compete in the market. Network effects facilitate high market power.

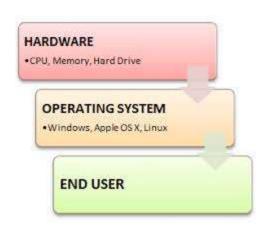
DIGITAL NETWORK EFFECTS MARKET MAP



Source: European Commission, NFX, a16z.

Tech Companies Build Moats:

Tool B: Operating System and Algorithm Control



An operating system ("OS") intermediates the interaction between the user of a computer and the base hardware of the computer.

The two most valuable companies in the world control computer operating systems and have used their OS's to (1) charge tolls on all parties that create applications on the OS and (2) preferentially create applications. The world's most valuable player has sequentially expanded into new forms of hard (e.g., iPhone, Apple Watch) that employ proprietary operating systems. See photo at right.





A further critical aspect of tech company OS control involves *ecosystem competition*. The three companies above go to great lengths to attract developers to their ecosystem – making it as easy as possible to program applications on their system.

Algorithm Competition

If frequent interaction with customers creates valuable data, then the software that translates that data into content is algorithmic. Who gets what content and why? Who sees what commerce opportunity and why? This is all controlled by algorithms. The ability to code and build algorithms is one of the most valuable skills in Silicon Valley.



A critical aspect of algorithm competition is secrecy. Amazon, Facebook and Google would *never* publish their algorithms. In contrast, in healthcare, treatment guidelines and algorithms are almost always published.

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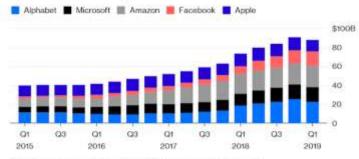
Tech Companies Build Moats:

Tool C: Data Moats Fed by Artificial Intelligence

facebook.

Quite a Moat

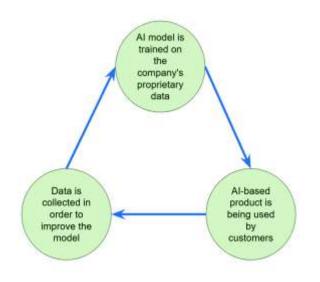
The five biggest U.S. technology companies spend a collective \$90 billion yearly on big-ticket projects such as package warehouses and data centers. Capital expenditures for the trailing 12 months:



Notes: Figures shown here include capital spending under leases, and reflect calendar quarters rather than fiscal quarters. Alphabet spending for 2018 includes a \$2.4 billion real estate purchase. Source: Bloomberg and Bloomberg Opinion calculations BloombergOpinion Yahoo News (July 5, 2019): "As U.S. anti-monopoly authorities weigh possible investigations into America's technology superpowers, there is one advantage the government can't touch: the size, scale and might of the tech giants' computer networks, logistics machines and other infrastructure. The word "moat" is overused jargon for companies' unique advantages that let them stay ahead of competitors. ...the five biggest U.S. technology companies have a heck of a moat in the form of their physical infrastructure — everything from Amazon's package centers and delivery airplanes to Google's sophisticated computer data centers and privately built undersea internet cables."

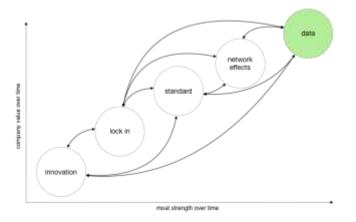
Facebook has made a significant investment in AI research and development. While Facebook CEO Mark Zuckerberg has "tripled its investments in processing power for AI and machine learning research" in recent years, and the social media company employs hundreds of employees working on AI. So, what's the outcome? Facebook now employs artificial intelligence to provide users with relevant material in the form of text, photographs, and videos, as well as to affect how its ad product functions.

Artificial intelligence is a classic tool to create a data moat. As customers generate data for the company, the data can be used to create better insights. These insights in turn can be used to improve the business and deliver value to customers. This creates a virtuous cycle where more customers use the product, in turn generating yet more data, etc.



Data Moats Feed Lock-in and Network Effects

It starts with innovation that attracts customers. A well-designed product can lock in customers and even become a standard for an industry. This can be fed by powerful network effects. All of these virtuous effects are fed by data.



Explanation #2:

Differences in Scale

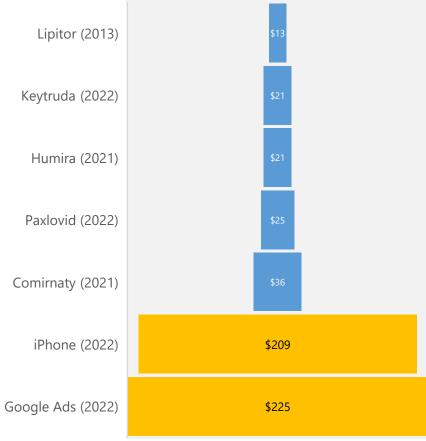
The top 5 tech companies generated \$1.5 trillion in annual revenue in 2022. The top 5 healthcare companies generate \$563 billion in annual revenue (39% as much) in 2022.

Operating margins in healthcare are slightly better than those in tech.

Scale is a key difference between tech and healthcare.

- 1. Many tech products scale well with relatively high gross margins.
- 2. That is, once you have made the initial investment in developing the iPhone or Microsoft Windows you can then sell these to billions of customers.
- 3. The marginal cost per unit of a sale drops with quantity sold. Obviously, the marginal cost of selling software or something online approaches zero.
- 4. While there are large economies of scale in pharma, these do not match the scale of the operations of companies like Amazon, Apple and Google. See chart at right. The iPhone outsells the all-time top five drugs combined.
- 5. The high valuations of top tech companies very much reflect the scale of their products.

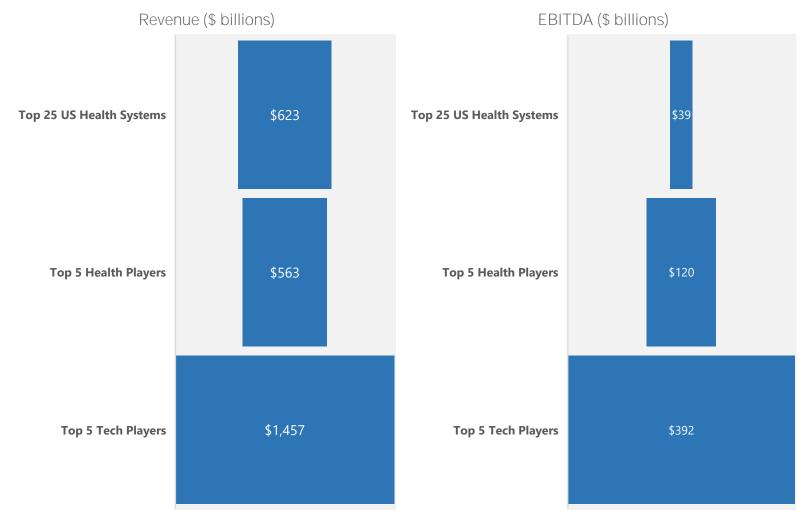
Top Tech Product Revenue v. All-Time Top Drug Revenue in Orange (\$ Billions)



On the Scale Point

Profitability is Also Highly Relevant

If you left out Optum and HCA, the top 25 U.S. healthcare systems make around 5% of the profits of the top 5 tech companies. If you left them in it would be 10%.



Top 25 Health Systems by Revenue, US 2022 (\$ millions)

Approach	System	Doctors	Revenue	EBITDA
Non-Profit	Kaiser Permanente	25,000	\$95,408	\$1,948
For Profit	Optum Health	70,000	\$71,174	\$6,032
For Profit	HCA Healthcare	47,000	\$61,920	\$12,308
Non-Profit	CommonSpirit Health	25,000	\$33,907	-\$316
For Profit	CVS Clinics	50,000	\$28,000	\$2,000
Non-Profit	Ascension	36,000	\$27,975	-\$799
Non-Profit	Providence St. Joseph	34,000	\$27,747	\$1,241
Non-Profit	UPMC	5,400	\$25,744	\$321
Non-Profit	Trinity Health	5,300	\$20,878	\$709
For Profit	Tenet Health	6,000	\$17,640	\$3,693
Non-Profit	Univ of California	7,000	\$17,520	\$331
Non-Profit	Mass General Brigham	3,300	\$16,710	\$1,669
Non-Profit	Mayo Clinic	5,500	\$16,300	\$595
Non-Profit	AdventHealth	2,000	\$14,900	\$300
Non-Profit	Sutter Healthcare	5,000	\$14,800	\$1,221
For Profit	Fresenius Medical Care	4,000	\$14,293	\$1,400
Non-Profit	Corewell Health	5,000	\$14,136	\$489
Non-Profit	Intermountain Health	3,900	\$14,000	\$121
Non-Profit	Cleveland Clinic	3,351	\$13,943	\$781
For Profit	Universal Health Services	10,000	\$13,799	1733
For Profit	LifePoint Health	3,000	\$13,600	800
Non-Profit	Advocate Health	10,000	\$13,132	\$565
For Profit	Community Health Systems	20,000	\$12,390	1244
Non-Profit	NYU Langone	5,100	\$11,800	750
Non-Profit	Mount Sinai	7,400	\$11,500	205

Source: CapitalIQ and Stifel Research

Tech Company Business Model Variants

Subscription Models

Customers will spend more if the cost is spread out over time. The tech sector has been rapidly migrating to a subscription model.



Services Include: Apple Music, Apple TV+, iCloud, Apple Arcade, Apple News+, Apple Fitness+, App Store, and licensing deals.

Revenue (2024): \$96 billion / 1 billion subscribers

Film and TV shows by subscription.



Revenue (2024): \$38 billion

270mm subscribers



CRM software by subscription.

Revenue (2024): \$34 billion

Uber Model

Uber finds customers for drivers and takes a cut for doing it. This model attracts service providers who couldn't get customers on their own.

Sector	Company / Platform	Description
Transportation	Uber	Disrupted taxi industry by enabling ride-hailing via apps.
Food Delivery	DOORDASH	Connects restaurants with customers and drivers for real-time delivery.
Short-Term Rentals	airbnb	Disrupted hotels by letting individuals rent out homes/apartments.
Freelance Labor	fiverr	Enabled on-demand hiring for digital freelancers and gig workers globally.

Is there an opportunity to redefine healthcare product scale and profitability?

Specifically...

Can one build a highly profitable healthcare company that has \$170 billion or more in sustainable revenue?

Profitable healthcare companies trade today at 6X revenue. This is what it would take to get to a \$1 trillion pharma / healthcare co.

Healthcare Platform Visions



Platform Visions

We will review four different approaches to healthcare platform innovation today. They are not necessarily mutually exclusive.

Aspect	Pande & Wolf (a16z)	Hemant Taneja (General Catalyst)	Bob Nelson (Arch Venture)	Tim Opler (Stifel)
Core Model	Payvidor & Horizontal Marketplace	Health Assurance	Fully vertically integrated healthcare innovator	Packaged Process Innovation Based on Science Innovation
Focus	Consumer-centric tech, AI, automation	Proactive care, long- term transformation	Delivering value for all payors including government	Delivery of low-cost superior care
Strategy	Platform building, interoperability	Systemic change through collaboration	Efficiency through innovation and integration	Efficiency through Al and care innovation
Investment Approach	Venture capital with tech emphasis	Patient capital with decades-long horizon	Not specified	Not specified
Key Initiatives	Infrastructure layers, scalable platforms	Bought Summa Health for transformation	Disintermediate pharma and hospitals	Partnership with providers / ConsumerCo possible

Vision 1: Customer Oriented Tech Company

From Andreesen Horowitz



Andreesen Horowitz (A16Z): Future Health Giant Will be Tech and Consumer Obsessed

andreessen. horowitz It's time to build

By Daisy Wolf and Vijay Pande, Nov 12, 2022

We think the biggest company in the world will be a consumer health tech company.

This may sound crazy to some, but why shouldn't this be true? Four of the top five biggest companies in the world are consumer companies, and healthcare is one of the nation's biggest industries.

In fact, those massive consumer companies— Google, Apple, Facebook, Amazon (GAFA, for short)—are all working to move into healthcare because they realize the size of the opportunity: a \$4 trillion American industry that makes up 20% of US GDP (and growing).

On the other hand, the world's biggest healthcare company (the 8th biggest company in the world), UnitedHealth Group (UHG), is not a tech company and is also seriously lacking in the consumer engagement department. While they're technically a consumer company, selling half of their products direct to consumer (DTC), their poor consumer engagement—reflected in their net promoter score of 4—will always cap their potential and keep them trapped as the 8th biggest company in the world.

Our bet is the future's biggest company, the consumer health giant, won't be one of today's big tech or incumbent healthcare companies. It will be a consumer-obsessed, healthcare-native tech company that reimagines what care can look like.

When many people think "consumer health company," they think Hims or Ro, but a consumer health company doesn't need to be DTC for distribution nor does the consumer have to be the one paying. Instead, what matters is that consumers know they're interacting with the company and have the opportunity to feel loyalty toward it.

Andreessen Horowitz Article (continued)

To be the biggest company in the world, a company would need to be valued at over \$2 trillion. Many things would have to be true for one of these companies (or more likely, a company we haven't even heard of today) to climb to #1.

How to break out

First, the initial business must be a wedge into a bigger product surface area. These companies eventually need to cover most specialties and likely launch an insurance product as well, becoming a payvidor like UHG. Apple's mastery in cross selling and maximizing lifetime value should also be an inspiration for any ambitious consumer health company: Apple sells a large percentage of consumers four expensive devices with very similar functionality (MacBook, iPhone, iPad, Apple Watch). Consumers buy in because of the devices' sleek UX and interoperability, and Apple further monetizes through music, television, storage, and the app store.

Second, this future consumer health giant will likely eventually need both cash pay and reimbursed revenue streams, though it could start with one, just as the iPhone launched with Cingular (now AT&T), but eventually expanded to be compatible with all carriers. The payors in healthcare are diverse—consumers, insurance companies, employers, and government agencies—so to maximize revenue, ambitious companies will want to be compatible with all payors.





The idea here is that you go straight to the consumer with a great brand and become a payvider.

Source: https://a16z.com/2022/11/11/the-biggest-company-in-the-world/



Bio + Health CHANGING HEALTHCARE



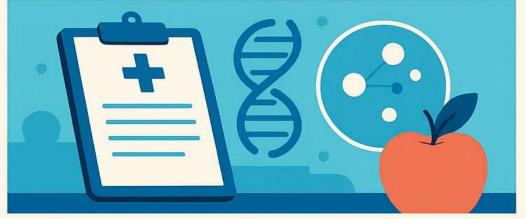
AI AS A CATALYST FOR **TRANSFORMATION**



ENHANCING THE CONSUMER EXPERIENCE



MODERNIZING HEALTHTECH **INFRASTRUCTURE**



INVESTING IN PREVENTIVE AND PERSONALIZED CARE

Related Area: Weight Loss Drugs and Consumerized Health

We estimate that more than eight million Americans went online to buy prescription drugs in 2024 through services like HIMS and Ro.

Most of this has been for the purchase of weight loss drugs.

The online consumer is younger, wealthier and healthier.

There is a huge opportunity to engage with the online consumer on their health through the many proliferating telehealth platforms in use today.



Vision 2: Health Assurance Model

From Hemant Taneja / General Catalyst



HEALTH ASSURANCE Hemant Taneja, General Catalyst



- Health Assurance Transformation Corporation (HATCo)
 Collaboration with over 20 health systems to drive transformation toward health assurance
- Long-Term Investment Horizon Emphasis on patient capital with decades-long timeframes to enact change
- **Platform Innovations** Building scalable platforms and fostering interoperability and innovation
- Radical Collaboration Encouragement of open innovation and sharing of best practices among partners
- Value-Based Care Advocacy for aligning stakeholder incentives to improve access, outcomes, and costs



Health Assurance Idea is to use Tech Standards to Deliver Great Care and Lower Costs

Health assurance is an emerging category of consumer-centric, data-driven healthcare services that are designed to bend the cost curve of care and help us stay well. Built on the principles of open technology standards, these services employ empathetic user design and responsible AI. This is the future of your health experience.

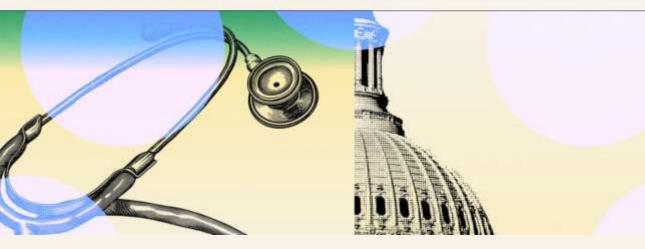


General Catalyst Whitepaper in March 2025 Argues for an Al-Oriented, Patient-Centric Approach to Care



U.S. HEALTHCARE AT THE AI INFLECTION POINT

Market-Driven Healthcare Resilience



Source: https://www.generalcatalyst.com/stories/u-s-healthcare-at-the-ai-inflection-point

CATALYZING CARE: A FRAMEWORK FOR A HEALTHIER AMERICA



Advance U.S. Healthcare Provider Mobility

Transform U.S. healthcare delivery through market-driven health assurance approaches to include healthier outcomes for all, technological innovation, patient-first care, data, and accessibility, prudent fiscal practices that reduce fraud and waste, as well as U.S. talent to deliver healthcare that works.

Healthcare Workers

SHORT-TERM ACTIONS	LONGER-TERM ACTIONS
Launch Regional Healthcare Innovation Sandboxes	Upgrade Rural Health Clinics for Greater Access and AI-Augmented Care
2. Refine Needed Innovations Without Red Tape	
SHORT-TERM ACTIONS	LONGER-TERM ACTIONS
Establish a Fast-Track AI Approval Process	Implement AI-Driven Measurements To Eliminate Red Tape and Waste
3. Advance Patient-First Care, Data, and Accessit	pility
SHORT-TERM ACTIONS	LONGER-TERM ACTIONS
Create Patient-Controlled Health Data Infrastructure	Upgrade Rural Health Clinics for Greater Access and AI-Augmented Care LONGER-TERM ACTIONS Implement AI-Driven Measurements To Eliminate Red Tape and Waste essibility LONGER-TERM ACTIONS Launch an Interoperable, State-Based Health Data Infrastructure althcare LONGER-TERM ACTIONS Advance Comprehensive Cost-Saving Preventive Care Programs
4. Maximize Fiscal Responsibility for U.S. Healtho	are
SHORT-TERM ACTIONS	LONGER-TERM ACTIONS
Implement Next-Gen AI-Powered Fraud Detection Systems	
5. Enhance U.S. Medical Talent for Today and Tor	norrow
SHORT-TERM ACTIONS	LONGER-TERM ACTIONS
10 10 10 10 10 120 400 AVAILA	Accelerate Training for AI-Empowered

Vision 3: R&D Based Vertically Integrated HC Provider

From Bob Nelsen / Arch Venture





"I think the biggest company in the world will be one that can invent technology to prevent or reverse disease (or both) and vertically integrates (like tech has done, and like you mention) to own the entire care system. Disintermediating hospitals and Pharma. Better for people."

Bob Nelsen

Partner ARCH Venture Partners

(reacting to A16z article on twitter)

Vision 4: Algorithmic Control of Care

From Tim Opler / Stifel in 2023

(with a few 2025 additions)



Prognostic 'Omics-Driven Algorithms Have Enormous Utility in Healthcare

Modern proteomics allows one to associate prognosis, care and outcomes using AI. This allows the build out of care algorithms that should be far superior to what is done today.

An important idea is that algorithms can be far more complex **than today's care** guidelines that are administered by physicians from memory.

Physicians still need to be involved but can use algorithms that drive care in the same sense that a pilot can oversee a plane run by instruments.

Example: Octave Bio Uses Serum Proteomics to Describe Pathways in MS and Then Impute Treatment Response

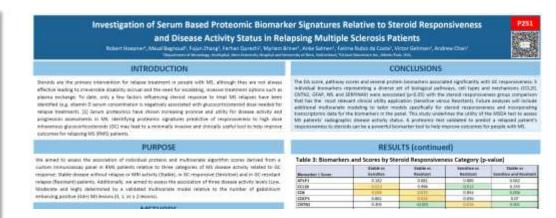
Octave MS Disease Activity Test Report

Figure MS Disease Activity Test Report

Octave MS Disease Activity Test Report

Octave

Figure 4: Octave MSDA Patient Report



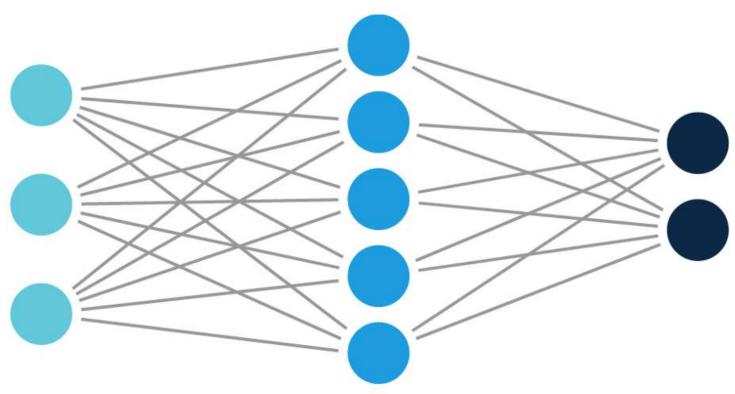


Steroids are, by far, the least expensive option to treat MS. Octave is able to use biomarkers to provide physicians with information on which patients will respond to steroids.

Source: https://www.octavebio.com/our-science/

A Future Potential Model: Similar to Neural Net in Structure

Multiple interventions for multiple diseases (and subclinical states) recommended by computer but managed by a physician.



Analytes and Subclinical Disease Observations Algorithmic Conclusion on Multiple Patient Outcomes Recommended Pharmaceutical Interventions (dynamic)

Comment Elements in Every Health Algorithm: Detect, Treat, Track

Detect

- Use biomarkers to identify the specific form of disease that is present
- Potentially, use a computerized, Al approach to map biomarker and observational data into a specific diagnosis and treatment plan.

Treat

- Follow the treatment plan for the patient
- Potentially use multiple modalities to interact with the patient including traditional physician visits, telehealth interactions, email interactions and at-home interactions

Track

- Some diseases of interest to us are very difficult to directly observe except through symptomatic patient reported outcomes
- The best trackers for a disease are prognostic algorithms, for example, the predicted risk of a cardiac event

Healthcare Algorithms Particularly Well Suited to What Economists Call the "Club Good" Model

Excludable

ا ما

Not Excludable

Rival in consumption Nonrival in consumption

Private goods

- Fruits & vegetables
- Furniture
- Candy bars

Common Resources

- Clean water
- Nature
- Fishing ponds

Artificially Scarce Goods

On-demand movies

"Club Goods'

- Computer software
- Private parks

Public Goods

- Public sanitation
- National defense (military)
- Court systems

Health systems can form a club in which proprietary healthcare algorithms are shared in exchange for some type of toll charge.

The most common setting for this today is called an MSO (managed service organization).

Note: tech firms have perfected club good business models with subscription models for content and software.

Disease Management in the Future

Diagnostics

- 1. Diagnostic services provided that are linked to populations with a specific disease
- 2. The diagnostics are designed to subtype diseases into treatable forms identified via reaction algorithms
- 3. Diagnostics can be delivered via existing lab infrastructure or using point-of-care technology

Interventions

- One can develop a reaction space to diagnostic outcomes using machine learning based on treatment evidence
- The reaction space would include existing drugs, other therapies (e.g., diet, digitalTX, devices and new drugs)
- 3. The goal of an algorithm is to meet or beat the standard of care for a disease at a lower cost

Payment in a Value-Based Environment

- Newco takes on risk-based contracts for care outcomes for pre-specified patient populations
- 2. For example, a club of healthcare systems pool knowledge on how to optimize care outcomes using an MSO
- 3. Or could be done by a single provider
- 4. Newco partners with current service-providers to deliver care using an MSO model

Illustrative Algorithm for T2DM Pharmacology

		Core Conditions					Overlay Conditions			
	Cost	SAID (Autoimmune Diabetes)	SIDD (Low ß-cell Function)	NOIS/MARD (Not obese, insulin sensitive)	NOII - Not obese, Insulin insensitive	OII/MOD (Obese, insulin insensitive)	SIRD (Severe insulin resistance)	High Kidney Risk	High CV Risk	Severe Inflammation Status
Risks		CKD, neuro, rt	Neuro, ret	CV, CKD	Low risk	Low risk	CKD, CV, liver	CKD (GFR <90)	CV	CKD, Heart
Population %		6%	18%	39%	Unknown	22%	15%	40%	Approx 40%	Approx 10%
Total Drug Cost		Moderate	Moderate	Low cost	Low	Low	High	High		Moderate
Insulin	\$\$	1 st line	1 st line							
GLP-1	\$\$\$\$						1 st line			
SGLT2	\$\$\$				2 nd line	1 st line	1 st line			
DPP4	\$\$			1 st line				Drug specific		
PPARy	\$				1 st line	1 st line	2 nd line			
RAS Inhibitors	\$			1 st line			1 st line			
Sulfonylurea	\$	1 st line	1 st line	1 st line						
Metformin	\$		1 st line	1 st line	1 st line	1 st line	1 st line			
Diet	\$					1 st line				
DHODH Inhibitor	\$	1 st line								
Inflammation In	\$									
Carbonic Al's	\$\$									

Some Feedback We Have Received

We have presented the idea of leveraging AI, proteomics and improvements in medicine to deliver proprietary care algorithms to senior leaders at two major healthcare systems. We used the type 2 diabetes example to illustrate how current healthcare models could be vastly improved. The illustrative conditional pharmacology on the previous page is quite simplified versus what could be possible with a foundation model approach driven by historical clinical observation, proteomic and metabolomic input.

Leaders at both healthcare systems indicated to us that the reality of everyday primary care in the U.S. is not pretty. All agree that having a great tool to sort out diabetics and treat them well is an idea with obvious merit.

However, we also heard that the non-compliant diabetic isn't showing up for care, that the quality of the doctors that diabetic is seeing may be poor and that the follow-on on care driven by novel guidelines may be less than ideal. A constant refrain was that doctors are not ready for type of changes implied by novel Aldriven care guidelines.

Our view coming out of these discussions is that algorithmic care cannot be delivered in a vacuum. Algorithmic care needs to be part of an organization that deals with broader issues in healthcare. One way to do this would be through the type of system transformation discussed by General Catalyst. Another less ambitious way to do this would be through MSO's.

Vision 4A: One Implementation Approach - Physician MSO Partnership Model



ACO's and MSO's

Accountable Care Organizations (ACO's) are physician or healthcare groups that contract to participate in the savings offered by the US government via HHS

ACO's can take on partial or full risk with Medicare insurers and other federal payors.

Managed services organizations, or MSOs, also offer assistance to independent providers.

Independent physicians can band together to launch an MSO that serves all its members.

MSO's often take on risk by contracting with ACO partners.

An Example:



Nashville, TN, Conshohocken, PA, San Francisco And Fort Worth, Texas – April 20, 2023 — TPG (NASDAQ: TPG), a global alternative asset management firm, and AmerisourceBergen Corporation (NYSE: ABC) today announced that they have agreed to acquire OneOncology, a network of leading oncology practices, from General Atlantic, a leading global growth equity firm. TPG has agreed to acquire a majority interest in OneOncology, and AmerisourceBergen will acquire a minority interest in the company. **OneOncology's** affiliated practices, physicians, and management team will also retain a minority interest in the company. The transaction values OneOncology at \$2.1 billion.

"OneOncology's physician leadership and partnership model provide access to the latest clinical pathways, research, and technology to deliver personalized care with market-leading patient outcomes and experiences.," said Kendall Garrison, Partner at TPG.

Pathway Standardization



Nashville, TN – August 28, 2023 – OneOncology, the fastest-growing national platform for independent practices, announced today it has finalized 25 unique oncology and hematology pathways and published each pathway inside the platform's clinical decision support tool.

Vision 4B: Illustrative Thoughts on Implementation

Very Important to Follow the Money Trail

One needs to be very careful of visions of healthcare ecosystems developed by parties who have not themselves lived in the system. While laudable, some of the ideas espoused by financial investors and tech observers may overlook key practicalities and sources of profitability in healthcare.

We have seen CVS and Walgreens both struggle after acquiring expensive primary care platforms designed to implement efficient care models that delight customers. Amazon has also struggled with its OneMedical platform.

Healthcare system profitability comes from expensive acute procedures like cardiac catheterization, cancer care and prostate surgeries. Lab services are also highly profitable.

Most healthcare systems lose money on everything else, particularly primary care which may partly explain why they are so bad at it.

David Wainer, WSJ, Oct 2, 2024

Walmart and Walgreens have both been pulling back from primary care recently after finding out how challenging it is to make money in clinics.

In recent years, CVS tried to grow beyond its roots by attempting to chart a course similar to that of UnitedHealth Group, the large healthcare organization with thousands of doctors, a pharmacy benefit manager business and an insurance arm. CVS acquired Aetna for nearly \$70 billion in 2018. More recently it acquired Oak Street Health, a primary-care doctor chain, for \$10.6 billion, and Signify Health, a home-care provider, for \$8 billion.

The strategy of bringing together insurance and medical care requires careful execution and expertise. "If you put a V-8 engine in your car, it doesn't automatically make it a Ferrari," says Justin Simon, a portfolio manager at the healthcare hedge fund Jasper Capital Management. "You need to fine-tune ways to drive synergies between owning doctors and an insurer."

It's All a Matter of Perspective

The healthy consumer

- Wants preventive care
- 2. Wants the good life
- 3. Wants rapid answers to routine questions
- 4. Wants convenience

The sick consumer

- Wants the best care they can get
- 2. Wants care coordination
- 3. Wants to avoid waiting

The employer (or government)

- Wants good outcomes at the lowest possible cost
- 2. Wants to avoid risk
- 3. Wants happy constituents

The healthcare system

- 1. Wants to get profitable customers
- 2. Would rather not try to attract unprofitable customers

Various constituents have vastly different perspectives on what they want from healthcare. The key to making all parties happy is to achieve efficiencies in care and this starts with designing biologically sound algorithms and/or biologic foundation models that exploit the latest technologies. The perspective offered in this section is closest to the Arch Venture approach – which is also biology heavy. Ideas of buying up healthcare systems and payors as pursued by CVS are brave but highly risky given the challenges from reshaping behavior of incumbent stakeholders. The licensure of intellectual property can be used as an overlay approach to the status quo through an asset light approach via an MSO type model. But one could obviously go far beyond this and employ some of the ideas outlined by A16Z and General Catalyst.

One Possibility: A Distributed System (DSCo)

Key ideas are to delight consumers while keeping patients out of hospitals/care systems that don't need to be there. This should be good for care systems, payors and providers.

ConsumerCo (CCo)

Provides a HIPAA-compliant app that allows consumers to access (1) ondemand advice from an LLM, (2) tracking of their HC info and (3) instant access to a HC provider when needed. The consumer would need to consent to the risks of Al-driven care and physician supervision would be essential. This would not cost much more than Netflix monthly and would come with some HC credits. We like the A16Z ideas here. The app knows your insurance and who to refer you to. The app also allows you to get prescriptions at a discount. Could be employer / government backed or consumer driven.



MSO's

The ConsumerCo partners with MSO's who provide the medical backing for its services and directs valuable customers to the MSO. The MSO compensates ConsumerCo for this flow.

But just as importantly, the members of the MSO have access to proprietary algorithms that allow them to provide better care at lower costs than competing providers. The MSO goes out and competes for insurance business, Medicaid business or Medicare Advantage business in the same way that MSO's operate today.



Care Systems (ACOs)

Receives patients via referral from the CCo and MSO's. There is a compliant economic relationship that allows this to happen.
Importantly, the CCo and MSO's understand the incentives of the care company and act accordingly, obviously not sacrificing what is right for patients.

The care systems are highly focused on delivering quality care in an efficient way using the type of proprietary care algorithms described here, obviously giving physicians latitude to exercise discretion as they see fit.

How Does DSCo Stack Up Versus Tech Models?

Network Effects: Strong network effects just like Uber. The more players in the ecosystem the more valuable it becomes.

Operating System Control: The app would probably be open to others and the LLM would need to be compliant with HIPAA requirements of all players in the ecosystem so the "operating system" of the core software would not be proprietary. However, the algorithms used to make recommendations and guide care could be proprietary. Eventually, they could be unbeatable.

Algorithm Control: This would be a key feature of the system.

Data Moats fed by AI: The system would collect copious amounts of data and should be able to build up substantial data moats and will use AI heavily.

Lock-in: If this system is really good, consumers would not want to migrate elsewhere.

Subscription Models: Core aspect of the system. Lowers costs throughout and raises long-term profitability potential.

Uberization: While attractive, there may be compliance barriers to direct pay for patients hence we anticipate payments to be made at the parent co levels rather than provider levels.

Appendix: Details on Stifel and Healthcare Publications



Stifel Investment Banking Contacts in Biopharma



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Links to Stifel Biopharma Special Topic Publications

To get on the mailing list for these publications feel free to contact Jenna Hill (hillje@stifel.com). Past special issues from Stifel on biopharma are available at:

Aging Biology, Part I



Mar 26, 2025

2025 Biotech Outlook



Jan 8, 2025

2024 Biotech Mid-Year Outlook



July 15, 2024

Obesity Drug Update



July 8, 2024

Al in medicine



Jan 22, 2024

2024 Biotech Outlook



Jan 8, 2024

Why Invest in Biotech?



November 22, 2023

Obesity Drug Review



July 1, 2023

Feel Free to Join Us at Biotech Hangout



Please join us this Friday at noon EST for the latest episode.

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