

Medical Complications: a lot of things can be true at the same time

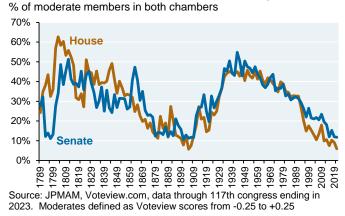
"The truth is rarely pure and never simple" – Oscar Wilde

Our 2024 Outlook was released on January 1st and can be accessed at the link above. Markets are pricing in very soft landing outcomes as the Fed pivot was largely reflected in Q4 rallies in stocks and bonds. Meanwhile, the economic spillover in the Middle East has broadened: 12%-15% of world trade passes through the Red Sea, including 30% of global container traffic. More than 100 ships have already been diverted around South Africa, causing shipping rates from Asia to North America to rise by 75% over the last month; Flexport expects them to increase by an additional 50%-100% by the end of January. Most large shipping groups have suspended Red Sea operations, leading to a 1.3% decline in world trade in December. But the overall inflation impact is likely to be modest given very high inventory to sales ratios, deflation in e-commerce, cooling global demand for goods and plenty of capacity in the logistics industry (record containership deliveries expected in 2024).

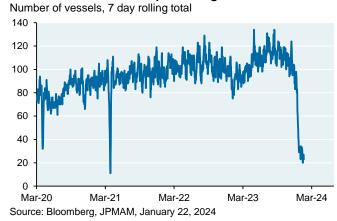
The rest of this note is about all the things that can be true at the same time. The collapse of the political middle in Congress should not be an excuse for everyone else to abandon the ability to believe things that may appear contradictory, but which are all part of a more complicated reality.

Michael Cembalest, JP Morgan Asset Management

The extinction of political moderates in Congress



Suez Canal container ship crossings



Venture capital, office-to-residential conversions and Chick-Fil-A

Last week I presented to venture capital clients in San Francisco and to real estate clients in Utah. Commonly stated themes from VCs: 2020-2021 vintages are still highly challenged and will be subject to further writedowns; the next five years of VC investing will be a golden era for GPs/LPs due to AI/LLM applications; and the decline in Wall Street research coverage of small cap companies is a main reason why small cap IPOs are harder to execute. There are other factors at work in the latter (2003 Wall St research settlement, a move away from soft dollar commissions, Sarbanes Oxley and the SPAC debacle), but I agree in principle.

Real estate developers agreed that office-to-residential conversions are hard to do without massive discounts. But more may be coming: Blackstone defaulted on a building at 55th and Broadway after L Brands vacated 70% of the space, and its appraisal is now down 70% from 2014 levels. In Salt Lake City I also had a Chick-Fil-A chicken sandwich for the first time. It was quite good.



All of these things can be true at the same time.

Posicor

Fen-Phen

Diethylstilbestrol

Seldane

Roche

Wyeth-Ayerst

~300 manuf.

Hoescht Marion

The costs of Covid lockdowns in the US will linger for years and perhaps decades

In the 1976 movie *Logan's Run*, the world is turned upside down to preserve the younger generation at the expense of the older one. In 2020-2021, one could argue that the opposite approach was taken in real life. School closures took 50 million children out of class and may prove to be the most damaging disruption in the history of American education, setting student progress in math and reading back by two decades and widening the achievement gap separating the rich and poor¹. This cohort of children is projected to experience diminished lifetime earnings and be a drag on growth. Lockdowns also resulted in increased domestic violence, loneliness, depression and anxiety². Hazardous alcohol use and dependence increased for those under lockdowns compared to those not under restrictions³. Stanford estimates that chronic absenteeism rose from 15% before the pandemic to 25+% at a national level in 2021-2022 and doubled in states like California in 2022-2023.

The FDA has recalled major drugs and has issued black box warnings on others

Substantial risks are sometimes not discovered until well after completion of trials and FDA approval.

BLACK BOX WARNING

RECALL				BLACK BOX WARNING			
Drug	Manufacturer	Year	Reason	Drug	Manufacturer	Year	Reason
Bextra	Pfizer	2005	Heart attack and stroke	Singulair	Merck	2020	Mental health side effects
Vioxx	Merck	2004	Coronary heart disease	Tygacil	Pfizer	2013	Increase in all-cause mortality
Baycol	Bayer	2001	Rhabdomyolysis (muscle disorder)	Lamictal	Glaxo	2010	Skin and organ disorders
Phenylpropanolamine	Multiple manuf.	2000	Cardiac events and stroke	Remicade	Janssen Biotech	2009	Infection risk
Rezulin	Warner-Lambert	2000	Sudden liver failure	Actos	Takeda Pharma	2007	Heart failure

Depakote

Source: FDA, JPMAM, 2024. The table is not an exhaustive list and shows indicative examples of recalls and black box warnings

Prozac & Zoloft Eli Lilly & Pfizer 2004 Mental health side effects

2006 Birth defects

Abbott Labs

Drug company unlawful activity has eroded public perception of the industry

1971 Rare cancers in offspring

1998 Mortality

1997 Heart disease

1997 Cardiac arrhythmia

Purdue pled guilty multiple times to criminal charges related to Oxycontin; its \$6 billion settlement is now being reviewed by the Supreme Court⁴. Other examples⁵: in 2012, GlaxoSmithKline paid \$3 billion to resolve civil and criminal liability related to unlawful promotion of Paxil and Wellbutrin, failure to report safety data on Avandia and civil liability for alleged false price reporting. In 2013, J&J paid \$2.2 billion to resolve criminal and civil liability related to Risperdal, Invega and Natrecor. In 2009, Pfizer was fined \$2.3 billion for illegal off-label marketing of Bextra and paid to resolve claims related to Geodon, Zyvox and Lyrica. A 2020 JAMA research letter details instances of adulterated drugs, bribery, off-label marketing and kickbacks by drug company⁶.

By 2019, the pharmaceutical industry had sunk to the bottom of the Gallup industry poll with a -31 net negative rating, lower than the Federal gov't, oil & gas and law firms. Since then, the industry's net ranking has fallen further to a -42 net negative rating. Its legal issues are affecting these rankings and may explain a decline in medication adherence, difficulty in recruiting clinical trials participants and rejection of effective health interventions, including vaccines⁷.

¹ New York Times, November 18, 2023 in its overdue epiphany on the issue of lockdown costs

² "The Causal Role of Lockdowns in COVID-19: Conclusions from Daily Epidemiological, Psychological, and Sociological Data", Psychiatric Quarterly, Vardi and Lazebnik, June 2023

³ "Alcohol dependence during COVID-19 lockdowns", Killgore et al, Psychiatry Research, 2021

⁴ Purdue remains in Chapter 11 bankruptcy. In May 2023, the Court of Appeals for the Second Circuit approved Purdue's bankruptcy plan, overturning the district court's rejection. The plan calls for the Sacklers to contribute \$6 bn to satisfy Oxycontin claims in exchange for a release of third-party claims without having to declare bankruptcy, and after the Sacklers withdrew \$11 bn from Purdue. The Department of Justice appealed the Second Circuit's ruling to the Supreme Court. The Court agreed to hear the case and stayed the Second Circuit's ruling, preventing the bankruptcy plan from being put into effect until the Court rules. Oral arguments occurred a month ago and a ruling is expected this spring

⁵ US Department of Justice Press Releases: July 2, 2012 (Glaxo), September 2, 2009 (Pfizer), November 4, 2013 (J&J)

⁶ "Financial Penalties Imposed on Large Pharmaceutical Firms for Illegal Activities", Arnold et al, JAMA, November 17, 2020

⁷ "Factors associated with public trust in pharmaceutical manufacturers", Singh et al, JAMA, March 2023



Vaccines have had remarkable success in reducing the frequency of preventable diseases around the world

You wouldn't know it by reading Twitter or listening to sports talk shows, but vaccines are among the greatest achievements in biomedical science and public health. When unchecked, vaccine preventable diseases (VPDs) have enormous social and economic costs in addition to premature deaths they cause. The table shows prevaccine incidence of VPDs in the US and 90%-100% post-vaccine declines⁸. In the US, for a single birth cohort, vaccines prevent 20 mm cases of disease and more than 40,000 deaths⁹. Similar results are found in China.

Vaccine preventable diseases in the US

	PRE-VAC	CINE	POST-VACCINE			
VPD	Annual cases	Annual deaths	Vaccine decade	Cases (2006)	Deaths (2004)	Case decline
Diptheria	21,053	1,822	1940's	0	0	100%
Measles	530,217	440	1960's	55	0	100%
Mumps	162,344	39	1940's	6,584	0	96%
Pertussis	200,752	4,034	1940's	15,632	27	92%
Polio (acute)	19,794	1,393	1950's	0	0	100%
Rubella	47,745	17	1960's	11	0	100%
Smallpox	29,005	337	1790's	0	0	100%
Hepatitis A	117,333	137	1990's	15,298	18	87%
Tetanus	580	472	1940's	41	4	93%

Source: Roush and Murphy, JAMA, 2007

Vaccine preventable diseases: China

	Case	
VPD	decline	by
Measles	80%	1980's
Pertusis	83%	1980's
Diptheria	81%	1980's
Polio	75%	1980's
Rubella	83%	2010's
Hepatitis A	66%	2010's
Meningitis	78%	2010's
Encephalitis	65%	2010's

Source: Fudan University, 2020

Incidents of vaccine safety problems are extremely rare but have occurred

There have been three safety-related vaccine recalls/withdrawals since the 1950's: polio vaccine safety incident (1955), swine flu vaccine leading to Guillain-Barre syndrome (1976) and the rotavirus vaccine leading to infant bowel obstruction (1998-1999). Other recalls occurred due to testing irregularities in specific vaccine batches.

The CDC has funded research on aluminum content in vaccines and possible connections to childhood asthma¹⁰. By age 2, the US recommends that children be vaccinated against 15 diseases; aluminum adjuvants appear in seven of them (aluminum is not used in Covid or flu vaccines). While the authors found an empirical association between the degree of vaccine aluminum exposure and persistent asthma, they don't believe their findings constitute strong evidence for questioning safety of aluminum in vaccines. Experts have highlighted other aluminum pathways that were not explored in the study and some data inconsistencies; research is ongoing.

Vaccination trends in the US have been declining, leading to measles outbreaks

Vaccination rates in children fell from 95% before Covid to 93% for the 2021-2022 school year¹¹. While a 2% decline doesn't sound like much, the CDC estimates that ~250,000 children are unprotected against measles. In the fall of 2022, Columbus Public Health in Ohio reported 85 cases of measles with 36 children hospitalized; 80 of the 85 infected children had never received a measles-mumps-rubella vaccine¹². A measles outbreak in Clark County Washington occurred in 2018-2019 affecting 71 people; 86% of the mostly young children infected were unvaccinated¹³. A Kaiser Survey found that 28% of US adults are against mandatory vaccination for children entering kindergarten, up from 16% in 2019¹⁴. Fifteen states now allow non-medical vaccination exemptions. A 95% vaccination rate is needed to achieve herd immunity against measles; **36 states are below this level**¹⁵.

⁸ "Historical Comparisons of Morbidity and Mortality for Vaccine-Preventable Diseases in the United States", JAMA American Medical Association, Roush and Murphy, November 14, 2007

⁹ "Simply put: vaccination saves lives", Proceedings of the National Academy of Science, Orenstein and Ahmed, 2017

¹⁰ "Association between aluminum exposure from vaccines before age 24 months and persistent asthma at age 24-59 months", Daley et al, Academic Pediatric Association, August 2022

¹¹ "Vaccination Coverage with Selected Vaccines and Exemption Rates Among Children in Kindergarten, 2021–22 School Year", Seither et al, CDC report, January 13, 2023

¹² Measles Case Summary, Central Ohio Outbreak, February 2023

¹³ "Community Outbreak of Measles - Clark County, Washington, 2018–2019", CDC, May 2019

¹⁴ Kaiser Family Foundation KFF COVID-19 Vaccine Monitor, Lopes et al, December 2022

^{15 &}quot;Coverage with selected vaccines and exemption from school vaccine requirements", Seither et al, CDC, November 2023



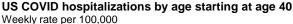
Original Covid vaccines and Omicron boosters were highly effective in preventing serious illness in 2021 and 2022, but protection waned over time as the virus mutated

The original vaccine and the bivalent booster which targeted Omicron subvariants were highly effective in 2021 and 2022 in preventing serious illness¹⁶. Commonwealth Fund estimates that vaccines prevented more than 18 mm hospitalizations by December 2022¹⁷; as a reminder, many emergency room and ICU departments were filled to or above capacity with sick Covid patients before vaccination began. By the end of 2022, vaccine and booster efficacy began to decline after several months. The primary reason: the SARS-Cov-2 virus accumulates mutations 2.5x faster than the influenza A flu virus and 7x faster than other coronaviruses¹⁸.

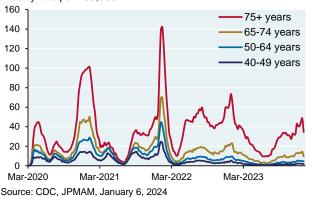
Study timeframe	Efficacy	Doses	Against	Ages	Source	Comments
May 2021 - Jan 2022	79%	1	Hospitalization	Pediatric	Fisman	
May 2021 - Jan 2022	85%	2	Hospitalization	Adolescents	Fisman	
June 2021 - Jan 2022	89%	2	Hospitalization	All	Stoliaroff-Pepin	
June 2021 - Jan 2022	77%	2	Hospitalization	60-75	Stoliaroff-Pepin	
June 2021 - Jan 2022	93%	3	Hospitalization	All	Stoliaroff-Pepin	
Mar 2021 - Mar 2022	78%	3	Hospitalization	All	Bermingham	Declined to 68% after 3 months
Mar 2021 - Mar 2022	88%	3	Hospitalization	65-79	Bermingham	
Mar 2021 - Mar 2022	93%	3	Mortality	All	Bermingham	
Dec 2021 - Aug 2022	68%	3	Hospitalization	All	Link-Gelles (JAMA)	Declined to 36% after 6 months
Jan 2020 - Dec 2022	92%	2	Hospitalization	All	Bacon	Declined to 79% after 7 months
Jan 2020 - Dec 2022	91%	2	Mortality	All	Bacon	Declined to 86% after 5 months
Jan 2020 - Dec 2022	89%	Booster	Hospitalization	All	Bacon	Declined to 71% after 4 months
April 2022 - Mar 2023	76-79%	2 nd booster	Hospitalization	All	ECDC	Vs primary vaccination; declined to 43% after 6 months
April 2022 - Mar 2023	76-85%	2 nd booster	Mortality	All	ECDC	Vs primary vaccination, declined to 50% after 6 months
Sept 2022 - April 2023	62%	Booster	Hospitalization	18+	Link-Gelles (CDC)	Vs primary vaccination, declined to 24% after 4 months

Further mutations have rendered protection from original vaccines and Omicron boosters not that different from being unvaccinated; fortunately, both cohorts benefit from some degree of immunity

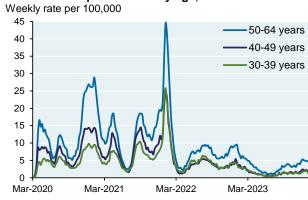
At the end of 2023, the protection against serious illness from the original vaccine and Omicron boosters had declined and was not much different from protection present in unvaccinated, previously infected people¹⁹. But this framing may overstate the risks to public health. At this point, 99% of people have had at least one vaccine dose, have been infected or have had both an infection and a vaccine²⁰; and so far, **both vaccine-induced and acquired immunity from prior infection are holding up well.** As shown below, Covid hospitalizations are much lower than in prior infection waves, particularly for those below the age of 65.



Sources: see footnotes below



US COVID hospitalizations by age, 30 to 64



Source: CDC, JPMAM, January 6, 2024

¹⁶ For the table: Fisman, *PLOS One*, March 31, 2023; Stoliaroff-Pepin, *Vaccine*, December 2, 2022; Bermingham, UK Office for National Statistics, June 7, 2023; Link-Gelles, *JAMA*, March 15, 2023; Bacon, *The Lancet*, February 10 2023; European Center for Disease Prevention and Control, November 2023; Link-Gelles, CDC, May 26, 2023

¹⁷ Fitzpatrick (University of Maryland) et al, Commonwealth Fund, December 2022

¹⁸ "An atlas of continuous adaptive evolution in endemic human viruses", Kistler and Bedford, November 2023

¹⁹ "BNT162b2 XBB1.5-adapted Vaccine and COVID-19 Hospital Admissions and Ambulatory Visits in US Adults", Tartof et al, Kaiser Permanente, December 28, 2023

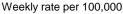
²⁰ Shane Crotty, Chief Scientific Officer at the La Jolla Institute of Immunology

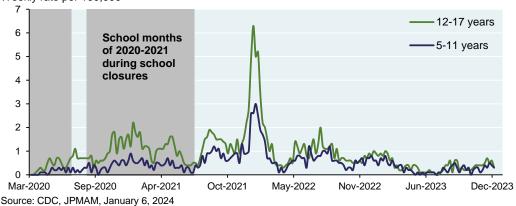
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Hospitalization rates are currently extremely low for school aged children, and were not much higher when schools were closed in 2020 and 2021...

Covid hospitalization rates for school aged children are now less than 1 per 100,000. Note that during the school months from March 2020 to September 2021 when many schools were closed, hospitalization rates were not much higher. When considering lifelong costs that the Covid generation of students incurred (see page 2), I can't imagine how the school closures that took place could be justified.

US COVID hospitalizations by age, school aged children





While the latest XBB booster is not protective against infection...

The XBB booster was released in Sept 2023, targeting XBB 1.5, EG.5 and BA.2.86 strains. The XBB booster doesn't do much to prevent Covid transmission; it might suppress infection risk by 30%-40% in the first month and then its efficacy vs infection declines²¹.

...it is still highly effective at preventing serious disease, and more protective than being unboosted...

Individuals who took the XBB booster vaccine in the fall of 2023 had a 68% lower chance of hospitalization than unboosted people²². Similarly, the Netherlands reports ~70% XBB booster efficacy rates with respect to risk of hospitalization and ICU admission even for older people²³. In other words, XBB boosters provide more protection than acquired or induced immunity from prior vaccines/boosters.

...and Covid vaccines/boosters also reduce risks of long Covid, which you do not want to get

Long Covid cognitive deficits in patients requiring hospitalization are equivalent to 20 years of aging and are associated with evidence of brain injury and reduced grey matter volume²⁴. One vaccine dose reduced long Covid risk by 21%, 2 doses reduced risk by 59% and 3+ doses reduced risk by 73%²⁵. Unlike Covid mortality risk, long Covid is not just an issue for older people. In the US and UK, long Covid prevalence is highest among those aged 35-44²⁶. Researchers at Cornell believe there may be increased risk of Parkinson's-like symptoms due to Long Covid²⁷; after the 1918 influenza pandemic, the frequency of Parkinson's disease increased threefold.

²¹ Eric Topol, Ground Truths, December 16, 2023

²² "BNT162b2 XBB1.5-adapted Vaccine and COVID-19 Hospital Admissions and Ambulatory Visits in US Adults", Tartof et al, Kaiser Permanente, December 28, 2023

²³ "Early COVID-19 vaccine effectiveness of XBB.1.5 vaccine against hospitalization and ICU admission in the Netherlands, October - December 2023", de Gier (Netherlands Center for Infectious Disease Control), BMJ, December 13, 2023

²⁴ "Post-COVID cognitive deficits at one year are global and associated with elevated brain injury markers and grey matter volume reduction", Michael (University of Liverpool) et al, Nature Portfolio, January 2024

²⁵ "COVID-19 vaccine effectiveness against post-covid-19 condition among 589,722 individuals in Sweden: population-based cohort study", Bygdell (University of Gothenburg) et al, British Medical Association Journal, October 2023

²⁶ "Long COVID and Significant Activity Limitation Among Adults", Ford et al, CDC, August 2023

²⁷ "SARS-Cov-2 infection causes dopaminergic neuron senescence", Yang et al, Cell Stem Cell Journal, January 2024



Covid mRNA vaccines are not riskless...

While instances are rare (2 to 34 cases per million), mRNA vaccinated individuals are twice as likely as uninfected and unvaccinated individuals to experience short-term myocarditis/pericarditis²⁸. Prognosis of carditis following mRNA vaccines is generally good with most recovering within a month. Hong Kong implemented a single-dose mRNA policy for adolescents aged 12-17 after which no further carditis cases occurred²⁹. Also: myocarditis from getting Covid is more likely than getting myocarditis from the vaccine for all age cohorts except males under 40, and mRNA vaccine-induced myocarditis risk is roughly the same as for people taking flu vaccines³⁰.

...and Covid "Trojan Horse" vector vaccines (J&J and AstraZeneca) are not riskless either...

In rare instances, the J&J vaccine led to "thrombosis with thrombocytopenia syndrome" (TTS) which involves blood clots and low blood platelets. TTS from the J&J vaccine resulted in 60 cases and 9 deaths out of 60 million vaccines administered, with greatest risks for women aged 30-49³¹. The J&J vaccine is no longer available in the US; blood clot risks also led to restrictions on AstraZeneca's vector vaccine in Europe.

...but blood clot risk from getting Covid is greater than blood clot risk from receiving a vaccine

Increased risk of blood clots from receiving a vaccine is ~1.4 per 1,000,000. But blood clot risk from *getting* Covid is much greater: blood clots were a major factor for hospitalized (8%) and ICU (22%) Covid patients, occurring at a rate of over 12,000 per 1,000,000 people who got Covid³². In the first week of getting Covid, blood clot risk is 33x normal levels and in some patients was still 2x higher a year later³³.

Most reported instances of cardiac arrest and sudden death are not attributed to Covid vaccines...

An analysis in the American Heart Association Journal *Circulation* did not find increased rates of sudden cardiac death in young people due to Covid vaccines. Causes of sudden cardiac death, including those who experienced it within 30 days of their vaccine, were consistent with prepandemic causes as established by autopsy³⁴.

...despite all the references to such events on Twitter...

Twitter's decision to no longer analyze Covid tweet content "opened the floodgates for conspiracy theorizing and misinformation" according to Tim Graham at Queensland University, who also believes that "the sudden deaths trope is perhaps the most salient of the false Covid narratives circulating now, and the most dangerous from a public health perspective"³⁵. Wired and Fast Company cited a December 2022 CCDH analysis of Twitter Blue posts with the most interactions; of those containing the word "vaccine", 30% featured misinformation³⁶.

...and in books published by vaccination opponents...

"Cause Unknown" was co-published by Children's Health Defense in November 2022 and argues that Covid vaccines caused a spike in sudden deaths. The book's cover shows a 12 year-old boy that collapsed and died at football practice as an example. But: the boy was never vaccinated against Covid and died due to a malformed blood vessel in his brain; no one contacted the family to ask about their son's death or for permission to use the photo; and no one asked to confirm the date of his death, which the book misdated by a year³⁷. If there is a connection between vaccines and sudden death or autism, are these the people you would trust to find it?

²⁸ "Risk of myocarditis and pericarditis in mRNA COVID-19-vaccinated and unvaccinated populations: a systematic review and meta-analysis", Alami et al, British Medical Association Journal, June 2023

²⁹ "Benefits v. risks of COVID vaccination: myocarditis and pericarditis", Carleton et al, Univ. of British Columbia, May 2023

³⁰ Katelyn Jetelina, University of Texas Health Science Center

³¹ "The Link Between J&J's COVID Vaccine and Blood Clots", Kathy Katella, Yale Medicine, May 2023

^{32 &}quot;COVID vaccination and venous thromboembolism risk in older veterans", Journal of Clinical Science, Elkin et al, Feb 2023

^{33 &}quot;Blood clot risk remains elevated nearly a year after COVID-19", Merschel, American Heart Association News, Sep 2022

³⁴ "Rate and Cause of Sudden Cardiac Death in the Young During the Pandemic/Vaccination", Basso et al, Circulation, 2023

^{35 &}quot;Twitter is a megaphone for Sudden Death vaccine conspiracies", Lydia Morrish, Wired, January 2023

³⁶ "Twitter Blue profiles are already a hotbed of misinformation", Chris Stokel-Walker, Fast Company, December 2022

³⁷ AP News, Michelle Smith and Ali Swenson, October 18, 2023 on RFK Jr and Children's Health Defense



...including RFK Jr

When I was 6, I sent a condolence letter to Ethel Kennedy after RFK Sr's assassination. I received a handwritten reply (which I choose to believe came from Ethel) which hung on my wall until I went to college. I like to read RFK Jr's opinions on Ukraine and the military-industrial complex even when I disagree. But as it relates to RFK's statements on vaccines, an October 2023 article in the *Philadelphia Citizen* by Dr. Paul Offit is very revealing. You can decide for yourself: https://thephiladelphiacitizen.org/guest-commentary-a-conversation-with-rfk-jr/

Despite its efficacy vs hospitalization, the XBB booster is not very popular...

As of early January 2024, the CDC reported that only 20% of adults have received the XBB vaccine, and that only 38% of those over 65 received it³⁸.

...perhaps since politics plays a role in XBB vaccine uptake...

80% of Democrats trust the XBB booster compared to 33% of Republicans; and ~68% of Democrats will either definitely or probably get the XBB booster compared to 25% of Republicans as per a September 2023 survey³⁹.

...which may explain relative Covid mortality trends as well

Once Covid vaccines became available, mortality trends differed by party affiliation. One example: Yale researchers found that in Florida and Ohio, the all-cause excess death rate among Republican voters (26%) was much higher than among Democratic voters (18%); the two rates were virtually identical before the pandemic began⁴⁰. Another example: as each Congressional District's exposure to conservatism across several political metrics increases (including the VoteView data we've cited elsewhere), that District's Covid mortality rate and its stress on hospital ICU capacity increases as well⁴¹.

And before I forget...

The 2020 Proximal Origin paper that dismissed possible Covid lab origins should be officially withdrawn

The infamous March 2020 "*Proximal Origin*" article⁴² dismissed the possibility of Covid laboratory origins barely one month into the pandemic. I agree with those who believe it should be officially retracted by its authors due to a highly compromised editorial process⁴³. In a 2023 piece in the Intercept, David Relman at Stanford highlights the many problems with *Proximal Origin*: flawed assumptions, unspoken bias, scant data and unjustified reliance on statements by Chinese researchers⁴⁴. *Proximal Origin* became one of the most widely read papers in the history of science; it might also be one of the **worst**.

Michael Cembalest

JP Morgan Asset Management

SARS-Cov-2 research was one of the first real-world applications of Alphafold (biological AI)

When developing a vaccine to neutralize SARS-Cov-2, biologists sought a 3D rendering of the virus proteins. In one of its first real-world applications, Google/Deep Mind's Alphafold program was used for this purpose. Several SARS-Cov-2 proteins were unknown to researchers, so they used AlphaFold to predict their designs. A few months later, scientists used electron microscopes to determine the exact structure of two of the proteins and confirmed that Alphafold predictions were accurate

³⁸ https://www.cdc.gov/respiratory-viruses/data-research/dashboard/vaccination-trends-adults.html

³⁹ "KFF COVID-19 Vaccine Monitor: Partisanship Remains Key Predictor", Kirzinger et al, September 2023

⁴⁰ "Excess Death Rates for Republican and Democratic Registered Voters in Florida and Ohio During the COVID-19 Pandemic", Wallace et al (Yale School of Public Health), July 24, 2023

⁴¹ "Relationship of political ideology of US federal and state elected officials and key COVID pandemic outcomes following vaccine rollout to adults: April 2021-March 2022", Krieger et al, Harvard School of Public Health, October 2022

⁴² "The proximal origin of SARS-CoV-2", Kristian Andersen (Scripps), Andrew Rambaut (University of Edinburgh), Ian Lipkin (Columbia), Edward Holmes (University of Sydney) and Robert Garry (Tulane), Nature Medicine, March 17, 2020

^{43 &}quot;Why Proximal Origins Must Be Retracted", Roger Pielke, July 2023

⁴⁴ "Evolution of a theory: Unredacted NIH Emails Show Efforts to Rule Out Lab Origin of COVID", James Tobias, The Intercept, January 19, 2023



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