

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

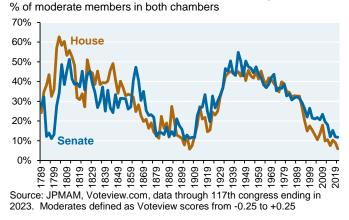
"The truth is rarely pure and never simple" – Oscar Wilde

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).

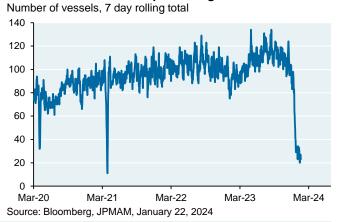
The rest of this note is about all the things that can be true at the same time. The collapse of the political middle in Congress should not be an excuse for everyone else to abandon the ability to believe things that may appear contradictory, but which are all part of a more complicated reality.

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.

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.

RECALL			BLACK BOX WARNING		
Drug	Manufacturer	Year Reason	Drug	Manufactu	

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
Posicor	Roche	1998	Mortality	Depakote	Abbott Labs	2006	Birth defects
Fen-Phen	Wyeth-Ayerst	1997	Heart disease	Prozac & Zoloft	Eli Lilly & Pfizer	2004	Mental health side effects
Seldane	Hoescht Marion	1997	Cardiac arrhythmia	Source: FDA, JPMAM, 2024. The table is not an exhaustive		e is not an exhaustive list and	
Diethylstilbestrol	~300 manuf.	1971	Rare cancers in offspring	shows indicative examples of recalls and black box warnings			

Drug company unlawful activity has eroded public perception of the industry

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	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 "Coverage with selected vaccines and exemption from school vaccine requirements", Seither et al, CDC, November 2023



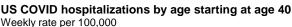
Original Covid vaccines and Omicron boosters were highly effective in preventing serious illness in 2021 and 2022, but protection waned over time as the virus mutated

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.

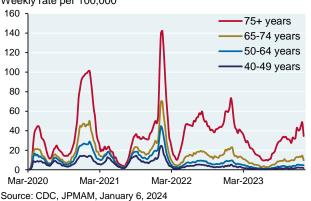
Study timeframe	Efficacy	Doses	Against	Ages	Source	Comments
May 2021 - Jan 2022	79%	1	Hospitalization	Pediatric	Fisman	
May 2021 - Jan 2022	85%	2	Hospitalization	Adolescents	Fisman	
June 2021 - Jan 2022	89%	2	Hospitalization	All	Stoliaroff-Pepin	
June 2021 - Jan 2022	77%	2	Hospitalization	60-75	Stoliaroff-Pepin	
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

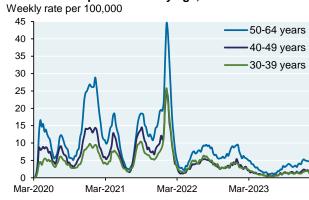
At the end of 2023, the protection against serious illness from the original vaccine and Omicron boosters had declined and was not much different from protection present in unvaccinated, previously infected people¹⁹. But this framing may overstate the risks to public health. At this point, 99% of people 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

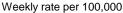
¹⁹ "BNT162b2 XBB1.5-adapted Vaccine and COVID-19 Hospital Admissions and Ambulatory Visits in US Adults", Tartof et al, Kaiser Permanente, December 28, 2023

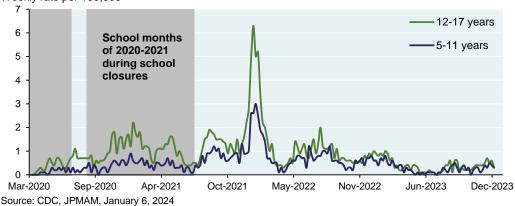
²⁰ Shane Crotty, Chief Scientific Officer at the La Jolla Institute of Immunology

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 &}quot;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 "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



IMPORTANT INFORMATION

KEY RISKS

This material is for information purposes only, and may inform you of certain products and services offered by private banking businesses, part of JPMorgan Chase & Co. ("JPM"). Products and services described, as well as associated fees, charges and interest rates, are subject to change in accordance with the applicable account agreements and may differ among geographic locations. Not all products and services are offered at all locations. If you are a person with a disability and need additional support accessing this material, please contact your J.P. Morgan team or email us at accessibility.support@jpmorgan.com for assistance. Please read all Important Information.

GENERAL RISKS & CONSIDERATIONS

Any views, strategies or products discussed in this material may not be appropriate for all individuals and are subject to risks. Investors may get back less than they invested, and past performance is not a reliable indicator of future results. Asset allocation/diversification does not guarantee a profit or protect against loss. Nothing in this material should be relied upon in isolation for the purpose of making an investment decision. You are urged to consider carefully whether the services, products, asset classes (e.g. equities, fixed income, alternative investments, commodities, etc.) or strategies discussed are suitable to your needs. You must also consider the objectives, risks, charges, and expenses associated with an investment service, product or strategy prior to making an investment decision. For this and more complete information, including discussion of your goals/situation, contact your J.P. Morgan team.

NON-RELIANCE

Certain information contained in this material is believed to be reliable; however, JPM does not represent or warrant its accuracy, reliability or completeness, or accept any liability for any loss or damage (whether direct or indirect) arising out of the use of all or any part of this material. No representation or warranty should be made with regard to any computations, graphs, tables, diagrams or commentary in this material, which are provided for illustration/ reference purposes only. The views, opinions, estimates and strategies expressed in this material constitute our judgment based on current market conditions and are subject to change without notice. JPM assumes no duty to update any information in this material in the event that such information changes. Views, opinions, estimates and strategies expressed herein may differ from those expressed by other areas of JPM, views expressed for other purposes or in other contexts, and this material should not be regarded as a research report. Any projected results and risks are based solely on hypothetical examples cited, and actual results and risks will vary depending on specific circumstances. Forward-looking statements should not be considered as guarantees or predictions of future events.

Nothing in this document shall be construed as giving rise to any duty of care owed to, or advisory relationship with, you or any third party. Nothing in this document shall be regarded as an offer, solicitation, recommendation or advice (whether financial, accounting, legal, tax or other) given by J.P. Morgan and/or its officers or employees, irrespective of whether or not such communication was given at your request. J.P. Morgan and its affiliates and employees do not provide tax, legal or accounting advice. You should consult your own tax, legal and accounting advisors before engaging in any financial transactions. YOUR INVESTMENTS AND POTENTIAL CONFLICTS OF INTEREST

Conflicts of interest will arise whenever JPMorgan Chase Bank, N.A. or any of its affiliates (together, "J.P. Morgan") have an actual or perceived economic or other incentive in its management of our clients' portfolios to act in a way that benefits J.P. Morgan. Conflicts will result, for example (to the extent the following activities are permitted in your account): (1) when J.P. Morgan invests in an investment product, such as a mutual fund, structured product, separately managed account or hedge fund issued or managed by JPMorgan Chase Bank, N.A. or an affiliate, such as J.P. Morgan Investment Management Inc.; (2) when a J.P. Morgan entity obtains services, including trade execution and trade clearing, from an affiliate; (3) when J.P. Morgan receives payment as a result of purchasing an investment product for a client's account; or (4) when J.P. Morgan receives payment for providing services (including shareholder servicing, recordkeeping or custody) with respect to investment products purchased for a client's portfolio. Other conflicts will result because

of relationships that J.P. Morgan has with other clients or when J.P. Morgan acts for its own account.

Investment strategies are selected from both J.P. Morgan and third-party asset managers and are subject to a review process by our manager research teams. From this pool of strategies, our portfolio construction teams select those strategies we believe fit our asset allocation goals and forward-looking views in order to meet the portfolio's investment objective.

As a general matter, we prefer J.P. Morgan managed strategies. We expect the proportion of J.P. Morgan managed strategies will be high (in fact, up to 100 percent) in strategies such as, for example, cash and high-quality fixed income, subject to applicable law and any account-specific considerations.

While our internally managed strategies generally align well with our forward-looking views, and we are familiar with the investment processes as well as the risk and compliance philosophy of the firm, it is important to note that J.P. Morgan receives more overall fees when internally managed strategies are included. We offer the option of choosing to exclude J.P. Morgan managed strategies (other than cash and liquidity products) in certain portfolios.

The Six Circles Funds are U.S.-registered mutual funds managed by J.P. Morgan and sub-advised by third parties. Although considered internally managed strategies, JPMC does not retain a fee for fund management or other fund services.

LEGAL ENTITY, BRAND & REGULATORY INFORMATION

In the United States, bank deposit accounts and related services, such as checking, savings and bank lending, are offered by JPMorgan Chase Bank, N.A. Member FDIC.

JPMorgan Chase Bank, N.A. and its affiliates (collectively "JPMCB") offer investment products, which may include bank managed investment accounts and custody, as part of its trust and fiduciary services. Other investment products and services, such as brokerage and advisory accounts, are offered through J.P. Morgan Securities LLC ("JPMS"), a member of FINRA and SIPC. Insurance products are made available through Chase Insurance Agency, Inc. (CIA), a licensed insurance agency, doing business as Chase Insurance Agency Services, Inc. in Florida. JPMCB, JPMS and CIA are affiliated companies under the common control of JPM. Products not available in all states.

In Germany, this material is issued by J.P. Morgan SE, with its registered office at Taunustor 1 (TaunusTurm), 60310 Frankfurt am Main, Germany, authorized by the Bundesanstalt für Finanzdienstleistungsaufsicht (BaFin) and jointly supervised by the BaFin, the German Central Bank (Deutsche Bundesbank) and the European Central Bank (ECB). In Luxembourg, this material is issued by J.P. Morgan SE - Luxembourg Branch, with registered office at European Bank and Business Centre, 6 route de Treves, L-2633, Senningerberg, Luxembourg, authorized by the Bundesanstalt für Finanzdienstleistungsaufsicht (BaFin) and jointly supervised by the BaFin, the German Central Bank (Deutsche Bundesbank) and the European Central Bank (ECB): J.P. Morgan SE – Luxembourg Branch is also supervised by the Commission de Surveillance du Secteur Financier (CSSF): registered under R.C.S Luxembourg B255938. In the United Kingdom, this material is issued by J.P. Morgan SE – London Branch, registered office at 25 Bank Street, Canary Wharf, London E14 5JP, authorized by the Bundesanstalt für Finanzdienstleistungsaufsicht (BaFin) and jointly supervised by the BaFin, the German Central Bank (Deutsche Bundesbank) and the European Central Bank (ECB); J.P. Morgan SE - London Branch is also supervised by the Financial Conduct Authority and Prudential Regulation Authority. In Spain, this material is distributed by J.P. Morgan SE, Sucursal en España, with registered office at Paseo de la Castellana, 31, 28046 Madrid, Spain, authorized by the Bundesanstalt für Finanzdienstleistungsaufsicht (BaFin) and jointly supervised by the BaFin, the German Central Bank (Deutsche Bundesbank) and the European Central Bank (ECB); J.P. Morgan SE, Sucursal en España is also supervised by the Spanish Securities Market Commission (CNMV); registered with Bank of Spain as a branch of J.P. Morgan SE under code 1567. In Italy, this material is distributed by J.P. Morgan SE - Milan Branch, with its registered office at Via Cordusio, n.3, Milan 20123, Italy, authorized by the Bundesanstalt für Finanzdienstleistungsaufsicht (BaFin) and jointly supervised by the BaFin, the German Central Bank (Deutsche Bundesbank) and the European Central Bank (ECB); J.P. Morgan SE - Milan Branch is also supervised by Bank of Italy and the Commissione Nazionale per le Società e la Borsa (CONSOB); registered with



Bank of Italy as a branch of J.P. Morgan SE under code 8076; Milan Chamber of Commerce Registered Number: REA MI 2536325. In the Netherlands, this material is distributed by J.P. Morgan SE – Amsterdam Branch, with registered office at World Trade Centre, Tower B, Strawinskylaan 1135, 1077 XX, Amsterdam, The Netherlands, authorized by the Bundesanstalt für Finanzdienstleistungsaufsicht (BaFin) and jointly supervised by the BaFin, the German Central Bank (Deutsche Bundesbank) and the European Central Bank (ECB); J.P. Morgan SE - Amsterdam Branch is also supervised by De Nederlandsche Bank (DNB) and the Autoriteit Financiële Markten (AFM) in the Netherlands. Registered with the Kamer van Koophandel as a branch of J.P. Morgan SE under registration number 72610220. In Denmark, this material is distributed by J.P. Morgan SE - Copenhagen Branch, filial af J.P. Morgan SE, Tyskland, with registered office at Kalvebod Brygge 39-41, 1560 København V, Denmark, authorized by the Bundesanstalt für Finanzdienstleistungsaufsicht (BaFin) and jointly supervised by the BaFin, the German Central Bank (Deutsche Bundesbank) and the European Central Bank (ECB); J.P. Morgan SE - Copenhagen Branch, filial af J.P. Morgan SE, Tyskland is also supervised by Finanstilsynet (Danish FSA) and is registered with Finanstilsynet as a branch of J.P. Morgan SE under code 29010. In Sweden, this material is distributed by J.P. Morgan SE - Stockholm Bankfilial, with registered office at Hamngatan 15, Stockholm, 11147, Sweden, authorized by the Bundesanstalt für Finanzdienstleistungsaufsicht (BaFin) and jointly supervised by the BaFin, the German Central Bank (Deutsche Bundesbank) and the European Central Bank (ECB); J.P. Morgan SE - Stockholm Bankfilial is also supervised by Finansinspektionen (Swedish FSA); registered with Finansinspektionen as a branch of J.P. Morgan SE. In Belgium, this material is distributed by J.P. Morgan SE – Brussels Branch with registered office at 35 Boulevard du Régent, 1000, Brussels, Belgium, authorized by the Bundesanstalt für Finanzdienstleistungsaufsicht (BaFin) and jointly supervised by the BaFin, the German Central Bank (Deutsche Bundesbank) and the European Central Bank (ECB); J.P. Morgan SE Brussels Branch is also supervised by the National Bank of Belgium (NBB) and the Financial Services and Markets Authority (FSMA) in Belgium; registered with the NBB under registration number 0715.622.844. In Greece, this material is distributed by J.P. Morgan SE - Athens Branch, with its registered office at 3 Haritos Street, Athens, 10675, Greece, authorized by the Bundesanstalt für Finanzdienstleistungsaufsicht (BaFin) and jointly supervised by the BaFin, the German Central Bank (Deutsche Bundesbank) and the European Central Bank (ECB); J.P. Morgan SE - Athens Branch is also supervised by Bank of Greece; registered with Bank of Greece as a branch of J.P. Morgan SE under code 124; Athens Chamber of Commerce Registered Number 158683760001; VAT Number 99676577. In France, this material is distributed by J.P. Morgan SE - Paris Branch, with its registered office at 14, Place Vendôme 75001 Paris, France, authorized by the Bundesanstaltfür Finanzdienstleistungsaufsicht(BaFin) and jointly supervised by the BaFin, the German Central Bank (Deutsche Bundesbank) and the European Central Bank (ECB) under code 842 422 972; J.P. Morgan SE - Paris Branch is also supervised by the French banking authorities the Autorité de Contrôle Prudentiel et de Résolution (ACPR) and the Autorité des Marchés Financiers (AMF). In Switzerland, this material is distributed by J.P. Morgan (Suisse) SA, with registered address at rue du Rhône, 35, 1204, Geneva, Switzerland, which is authorised and supervised by the Swiss Financial Market Supervisory Authority (FINMA) as a bank and a securities dealer in Switzerland.

This communication is an advertisement for the purposes of the Markets in Financial Instruments Directive (MIFID II) and the Swiss Financial Services Act (FINSA). Investors should not subscribe for or purchase any financial instruments referred to in this advertisement except on the basis of information contained in any applicable legal documentation, which is or shall be made available in the relevant jurisdictions (as required).

In Hong Kong, this material is distributed by JPMCB, Hong Kong branch. JPMCB, Hong Kong branch is regulated by the Hong Kong Monetary Authority and the Securities and Futures Commission of Hong Kong. In Hong Kong, we will cease to use your personal data for our marketing purposes without charge if you so request. In Singapore, this material is distributed by JPMCB, Singapore branch. JPMCB, Singapore branch is regulated by the Monetary Authority of Singapore. Dealing and advisory services and discretionary investment management services are provided to you by JPMCB, Hong Kong/Singapore branch (as notified to you). Banking and custody services are provided to you by JPMCB Singapore Branch. The contents of this document have not been reviewed by any regulatory authority in Hong Kong, Singapore or any other jurisdictions. You are advised to exercise caution in relation to this document. If you are in any doubt about any of the contents of this document, you should obtain independent professional advice. For materials which constitute product advertisement under the Securities and Futures Act and the Financial Advisers Act, this advertisement has not been reviewed by the Monetary Authority of Singapore. JPMorgan Chase Bank, N.A., a national banking association chartered under the laws of the United States, and as a body corporate, its shareholder's liability is limited.

With respect to countries in Latin America, the distribution of this material may be restricted in certain jurisdictions. We may offer and/or sell to you securities or other financial instruments which may not be registered under, and are not the subject of a public offering under, the securities or other financial regulatory laws of your home country. Such securities or instruments are offered and/or sold to you on a private basis only. Any communication by us to you regarding such securities or instruments, including without limitation the delivery of a prospectus, term sheet or other offering document, is not intended by us as an offer to sell or a solicitation of an offer to buy any securities or instruments in any jurisdiction in which such an offer or a solicitation is unlawful. Furthermore, such securities or instruments may be subject to certain regulatory and/or contractual restrictions on subsequent transfer by you, and you are solely responsible for ascertaining and complying with such restrictions. To the extent this content makes reference to a fund, the Fund may not be publicly offered in any Latin American country, without previous registration of such fund's securities in compliance with the laws of the corresponding jurisdiction.

JPMorgan Chase Bank, N.A. (JPMCBNA) (ABN 43 074 112 011/AFS Licence No: 238367) is regulated by the Australian Securities and Investment Commission and the Australian Prudential Regulation Authority. Material provided by JPMCBNA in Australia is to "wholesale clients" only. For the purposes of this paragraph the term "wholesale client" has the meaning given in section 761G of the Corporations Act 2001 (Cth). Please inform us if you are not a Wholesale Client now or if you cease to be a Wholesale Client at any time in the future.

JPMS is a registered foreign company (overseas) (ARBN 109293610) incorporated in Delaware, U.S.A. Under Australian financial services licensing requirements, carrying on a financial services business in Australia requires a financial service provider, such as J.P. Morgan Securities LLC (JPMS), to hold an Australian Financial Services Licence (AFSL), unless an exemption applies. JPMS is exempt from the requirement to hold an AFSL under the Corporations Act 2001 (Cth) (Act) in respect of financial services it provides to you, and is regulated by the SEC, FINRA and CFTC under US laws, which differ from Australian laws. Material provided by JPMS in Australia is to "wholesale clients" only. The information provided in this material is not intended to be, and must not be, distributed or passed on, directly or indirectly, to any other class of persons in Australia. For the purposes of this paragraph the term "wholesale client" has the meaning given in section 761G of the Act. Please inform us immediately if you are not a Wholesale Client now or if you cease to be a Wholesale Client at any time in the future.

This material has not been prepared specifically for Australian investors. It:

- may contain references to dollar amounts which are not Australian dollars;
- may contain financial information which is not prepared in accordance with Australian law or practices;
- may not address risks associated with investment in foreign currency denominated investments; and
- does not address Australian tax issues.

References to "J.P. Morgan" are to JPM, its subsidiaries and affiliates worldwide. "J.P. Morgan Private Bank" is the brand name for the private banking business conducted by JPM. This material is intended for your personal use and should not be circulated to or used by any other person, or duplicated for non-personal use, without our permission. If you have any questions or no longer wish to receive these communications, please contact your J.P. Morgan team.

© 2024 JPMorgan Chase & Co. All rights reserved.