Update on Omicron: antigenic drift, immunity escape, vaccine efficacy and Omicron booster testing

A few countries and US states are now experiencing a breakout in COVID hospitalizations linked to Omicron BA.4/5. So far, this increase is modest compared to prior waves since there is a large degree of seroprevalence in many places due to prior infection, vaccination or both.

Omicron hospitalization breakout

Summary

- BA.4/5 exhibits the highest observed degree of infectiousness of SARS Cov-2 variants to date (see chart)
- Some studies find that BA.4/5 exhibits higher potential immunity escape than prior variants (i.e., greater susceptibility to the virus despite vaccination or prior infection) but this is not a universal finding. In other words, recent infections may still be primarily first-time infections rather than reinfections
- For BA.1 and BA.2, 3-shot vaccine efficacy vs hospitalization is still high; there are conflicting observations as to the drop-off in efficacy with only 2 shots. The large population of previously infected/unvaccinated people with some immunity may be exaggerating some measures of the vaccine efficacy decline
- Omicron-specific boosters are under development, and show improvements vs the existing booster shots

US COVID variant prevalence

COVID replication number by variant

Source: CDC, JPMAM. November 19, 2022.

Source: Univ S Australia, Univ Tokyo, Umea Univ, Crotty (LJI), JPMAM. 2022.
Any immunity escape exhibited by BA.4/5 can be traced to its antigenic drift vs prior strains. BA.4/5 variants have evolved substantially from the original Omicron variant (B.1.1.529, shown in below in orange) and are even more genetically distant from prior variants and the original Wuhan strain (WA1). BA.5 in particular has substantial mutations outside the spike protein.

Evidence is mixed as to whether Omicron BA.4/5 has a materially higher tendency to escape natural or acquired immunity. A study from Beth Israel in Boson found the potential for higher immunity escape by BA.4/5. The two charts below show lower antibody responses for vaccinated or previously infected people when exposed to Omicron BA.4/5 variants than prior Omicron variants. However, a separate study from the University of Glasgow’s Center for Virus Research found no material difference between Omicron variant immunity escape. To be clear, these are in-vitro studies of the behavior of cells when exposed to the virus, and not field measurements of actual antibody responses.

Source: “Neutralization escape by SARS-CoV-2 Omicron sub-variants”, Hachmann (Beth Israel Deaconess Medical Center) et al, June 2022
Vaccine efficacy vs Omicron: despite Omicron mutations, mRNA vaccinations combined with multiple boosters still reduced Omicron risks substantially. The chart shows that the lowest COVID death rates observed in April 2022 were for people with a primary mRNA series and 2+ booster doses. Even with only one booster dose, efficacy vs mortality was still around 85%-90%. These measurements took place when BA.2 was the dominant variant circulating in the US. Vaccine efficacy vs hospitalization with Omicron is also still very high, although only with 3 shots; estimates differ markedly for efficacy vs hospitalization with only two shots.

**COVID-19 deaths by vaccination status in 50+ population**

The latest on vaccine efficacy vs hospitalization due to Omicron
- According to Kaiser Permanent, vaccine efficacy vs Omicron is still 99% vs hospitalization with 3 doses, and 85%-99% for 2 doses
- The UK health security agency cites lower figures of 80% for 3 shots, and 30%-50% for 2 shots
- Part of the difference may be explained by large populations of previously infected/unvaccinated people with some immunity that exaggerate the vaccine efficacy decline

**Omicron-specific vaccines.** The next chart below shows results from Moderna’s Omicron-specific booster tests. The booster that Moderna tested was derived based on BA.1/2 variants, and tested when these variants were dominant. As per the chart, Moderna’s Omicron booster increased antibody results relative to the existing booster formulation. The chart is shown in log scale, so small relative increases can translate into large antibody increases in absolute terms.

However, we have no data from Moderna on how its BA.1/2 booster would perform vs BA.4/5 variants. We do have clues from Pfizer, which tested two different boosters in mice (one was Omicron specific, and the other was a combination of the original booster with the Omicron booster). Results:
- both of Pfizer’s new boosters delivered higher antibody responses in mice than the original booster
- however, Pfizer’s Omicron boosters generated substantially lower antibody responses vs BA.4/5 than vs BA.1
- bottom line: BA.1/2 booster effectiveness vs BA.4/5 may be lower, but is still expected to be higher than using the existing booster which was designed based on the original variant’s spike protein

**Moderna booster vs Moderna Omicron booster efficacy**

**Pfizer booster response in mice by variant and vaccine type, Neutralization titer (log scale)**
**Vaccine types and locations**

The table outlines the approaches that vaccine companies are taking to provoke an antibody response. Vaccines train the immune system to recognize the disease-causing part of a virus so that when people are infected, their bodies are prepared to fight the virus with a combination of antibody and T-cell responses. Historically, most vaccines contained either weakened viruses or the signature proteins of the virus (Types 1, 2 and 3), but the first approved vaccines for COVID were genetic (Types 4 and 5).

<table>
<thead>
<tr>
<th>Type</th>
<th>Method of provoking antibody response to SARS-CoV-2</th>
<th>Drug companies (bold = approved)</th>
<th>Existing licensed vaccines</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Attenuated A live but weakened coronavirus that will infect cells and cause them to make viral proteins</td>
<td>Codagenix</td>
<td>Measles, yellow fever, mumps, smallpox, polio</td>
</tr>
<tr>
<td>2</td>
<td>Attenuated A “killed” coronavirus that will get recognized as foreign matter by the immune system</td>
<td>Sinovac(^1), SinoPharm(^2), Covaxin(^3)</td>
<td>Polio (dev countries)</td>
</tr>
<tr>
<td>3</td>
<td>Recombinant Recombinant coronavirus proteins, produced industrially in outside cell cultures, which are recognized as foreign matter by the immune system</td>
<td>GlaxoSmithKline/Sanofi, Novavax(^4)</td>
<td>Tetanus, pertussis, flu, shingles</td>
</tr>
<tr>
<td>4</td>
<td>Genetic (vector vaccines) A different virus (human or ape adenovirus, measles, etc) that is engineered to include genetic components coding for the SARS-CoV-2 spike proteins, which causes the body to produce them</td>
<td>CanSino(^5), Oxford/AstraZeneca(^6), J&amp;J(^7), Gamaleya(^8)</td>
<td>Ebola</td>
</tr>
<tr>
<td>5</td>
<td>Genetic DNA or RNA that will be taken up by cells and will cause them to make coronavirus proteins</td>
<td>Moderna, Inovio, BioNTech/Pfizer</td>
<td></td>
</tr>
</tbody>
</table>

1: Sinovac has been approved for use in China, Hong Kong, Indonesia, Philippines, Brazil, Chile, Mexico, Turkey and several other countries
2: Sinopharm has been approved in China, UAE, Bahrain, Egypt, Hungary and Jordan and several other countries
3: Covaxin has been approved for emergency use in India, Iran, Philippines, Paraguay, Guatemala and several other countries
4: Protein vaccines are not new, but the Novavax vaccine is combined with a proprietary adjuvant which has not been approved for use before
5: CanSino has been approved for use in China, Mexico, Pakistan, Argentina, Chile, Indonesia, and several other countries
6: Oxford/AstraZeneca's vaccine has been approved for use in the UK, Europe, South Africa, Brazil, Chile, and several other countries
7: J&J's vaccine has been approved for use in the US, UK and more than 60 other countries.
8: Gamaleya's vaccine has been approved in Russia, Argentina, Venezuela, Mexico, Hungary, Iran, UAE, and several other countries


**Vaccine type usage by country**

![Pie chart showing vaccine type usage by country](image)

Source: OWID, JPMAM. December 7, 2022.
“A pandemic (mostly) of the unvaccinated”: adverse outcomes in unvaccinated vs vaccinated people

The first two charts show COVID hospitalization and mortality outcomes from multiple states as reported by COVID-NET (250 acute care hospitals) and by select state health departments reporting directly to the CDC. The subsequent charts show the same gaps for states that publish high-frequency downloadable information to the public. Other states like Michigan, Georgia, Pennsylvania, Texas, Alaska and Arizona also publish this data, but in PDF form that also tends to be more dated; the trends are similar.

**Age adjusted hospitalizations: 250 acute-care hospitals**

Daily hospital admissions, # per mm

Source: CDC, JPMAM. September 1, 2022. Universe: CA, CO, CT, MD, MI, MN, NM, NY, OH, OR, TN, UT.

**Age adjusted mortality: 20 US states**

Daily deaths, # per mm

Source: CDC. October 1, 2022. Universe: AL, AZ, AR, CO, CT, FL, GA, ID, IN, LA, MD, MA, MI, NE, NM, NY, PA, RI, TN, UT.

**250 acute-care hospitals: 50-64 year old hospitalizations**

Daily hospital admissions, # per mm

Source: CDC, JPMAM. September 1, 2022. Universe: CA, CO, CT, MD, MI, MN, NM, NY, OH, OR, TN, UT.

**New York: infections**

Daily infections, # per million


**250 acute-care hospitals: 65 and older hospitalizations**

Daily hospital admissions, # per mm

Source: CDC, JPMAM. September 1, 2022. Universe: CA, CO, CT, MD, MI, MN, NM, NY, OH, OR, TN, UT.

**New York: hospitalizations**

Daily hospital admissions, # per million

Seattle: age adjusted infections
Daily infections, # per mm, smoothing = 7 days

California: hospitalizations
Daily hospital admissions, # per mm

Utah: age adjusted hospitalizations
Weekly hospital admissions, # per mm

Seattle: age adjusted hospitalizations
Current hospitalizations, # per mm, smoothing = 7 days

California: mortality
Daily deaths, # per mm

Utah: age adjusted mortality
Weekly deaths, # per mm


**Switzerland: mortality**
Weekly deaths, # per mm

- Unvaccinated
- Fully vaccinated, no booster
- Fully vaccinated + booster

Source: OWID, JPMAM. November 6, 2022.

**Chile: mortality**
Weekly deaths, # per mm

- 0 or 1 dose
- 2 doses
- 3 doses
- 4 doses


**OECD countries by highest share of unvaccinated people**
Not fully vaccinated people as % of population

Source: OWID, JPMAM. Dec 6, 2022. Largest 25 OECD countries by GDP

**Current hospitalizations vs boosted population**
Current hospitalizations per mm, 7 day avg

Source: OWID, JPMAM. Dec 6, 2022. Largest 25 OECD countries by GDP
IMPORTANT INFORMATION

The views, opinions and estimates expressed herein constitute Michael Cembalet’s judgment based on current market conditions and are subject to change without notice. Information herein may differ from those expressed by other areas of J.P. Morgan. This information in no way constitutes J.P. Morgan Research and should not be treated as such.

The views contained herein are not to be taken as advice or a recommendation to buy or sell any investment in any jurisdiction, nor is it a commitment from J.P. Morgan or any of its subsidiaries to participate in any of the transactions mentioned herein. Any forecasts, figures, opinions or investment techniques and strategies set out are for information purposes only, based on certain assumptions and current market conditions and are subject to change without prior notice. All information presented herein is considered to be accurate at the time of production. This material does not contain sufficient information to support an investment decision and it should not be relied upon by you in evaluating the merits of investing in any securities or products. In addition, users should make an independent assessment of the legal, regulatory, tax, credit and accounting implications and determine, together with their own professional advisers, if any investment mentioned herein is believed to be suitable to their personal goals. Investors should ensure that they obtain all available relevant information before making any investment. It should be noted that investment involves risks, the value of investments and the income from them may fluctuate in accordance with market conditions and taxation agreements and investors may not get back the full amount invested. Both past performance and yields are not reliable indicators of current and future results.

Non-affiliated entities mentioned are for informational purposes only and should not be construed as an endorsement or sponsorship of J.P. Morgan Chase & Co. or its affiliates.

For J.P. Morgan Asset Management Clients:

J.P. Morgan Asset Management is the brand for the asset management business of JPMorgan Chase & Co. and its affiliates worldwide.

To the extent permitted by applicable law, we may record telephone calls and monitor electronic communications to comply with our legal and regulatory obligations and internal policies. Personal data will be collected, stored and processed by J.P. Morgan Asset Management in accordance with our privacy policies at https://am.jpmorgan.com/global/privacy.

ACCESSIBILITY

For U.S. only: If you are a person with a disability and need additional support in viewing the material, please call us at 1-800-343-1113 for assistance.

This communication is issued by the following entities:

In the United States, by J.P. Morgan Investment Management Inc. or J.P. Morgan Alternative Asset Management, Inc., both regulated by the Securities and Exchange Commission; in Latin America, for intended recipients’ use only, by local J.P. Morgan entities, as the case may be; in Canada, for institutional clients’ use only, by JPMorgan Asset Management (Canada) Inc., which is a registered Portfolio Manager and Exempt Market Dealer in all Canadian provinces and territories except the Yukon and is also registered as an Investment Fund Manager in British Columbia, Ontario, Quebec and Newfoundland and Labrador. In the United Kingdom, by JPMorgan Asset Management (UK) Limited, which is authorized and regulated by the Financial Conduct Authority; in other European jurisdictions, by JPMorgan Asset Management (Europe) S.à r.l. in Asia Pacific (“APAC”), by the following issuing entities and in the respective jurisdictions in which they are primarily regulated: JPMorgan Asset Management (Asia Pacific) Limited, or JPMorgan Funds (Asia) Limited, or JPMorgan Asset Management Real Assets (Asia) Limited, each of which is regulated by the Securities and Futures Commission of Hong Kong; JPMorgan Asset Management (Singapore) Limited (Co. Reg. No. 197601586K), which this advertisement or publication has not been reviewed by the Monetary Authority of Singapore; JPMorgan Asset Management (Taiwan) Limited; JPMorgan Asset Management (Japan) Limited, which is a member of the Investment Trusts Association, Japan, the Japan Investment Advisers Association, Type II Financial Instruments Firms Association and the Japan Securities Dealers Association and is regulated by the Financial Services Agency (registration number “Kanto Local Finance Bureau (Financial Instruments Firm) No. 330”); in Australia, to wholesale clients only as defined in section 761A and 761G of the Corporations Act 2001 (Commonwealth), by JPMorgan Asset Management (Australia) Limited (ABN 55143832080) (AFSL 376919). For all other markets in APAC, to intended recipients only.

For J.P. Morgan Private Bank Clients:

ACCESSIBILITY

J.P. Morgan is committed to making our products and services accessible to meet the financial services needs of all our clients. Please direct any accessibility issues to the Private Bank Client Service Center at 1-866-265-1727.

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. J.P. Morgan 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 (“JPM”), a member of FINRA and SIPC. Annuities are made available through Chase Insurance Agency, Inc. (CIA), a licensed insurance agency, doing business as Chase Insurance Agency Services, Inc. in Florida. JPMCB, JPM and CIA are affiliated companies under the common control of JPMorgan Chase & Co. Products not available in all states.

In Luxembourg, this material is issued by J.P. Morgan Bank Luxembourg S.A. (JPMBL), with registered office at European Bank and Business Centre, 6 route de Treves, L-2633, Senningerberg, Luxembourg. R.C.S Luxembourg B10.958. Authorised and regulated by Commission de Surveillance du Secteur Financier (CSSF) and jointly supervised by the European Central Bank (ECB) and the CSSF. J.P. Morgan Bank Luxembourg S.A. is authorized as a credit institution in accordance with the Law of 5th April 1993. In the United Kingdom, this material is issued by J.P. Morgan Bank Luxembourg S.A.– London Branch. Prior to Brexit,(Brexit meaning that the UK leaves the European Union under Article 50 of the Treaty on European Union, or, if later, loses its ability to passport financial services between the UK and the remainder of the EEA), J.P. Morgan Bank Luxembourg S.A.– London Branch is subject to limited regulation by the Financial Conduct Authority and the Prudential Regulation Authority. Details about the extent of our regulation by the Financial Conduct Authority and the Prudential Regulation Authority are available from us on request. In the event of Brexit, in the UK, J.P. Morgan Bank Luxembourg S.A.– London Branch is authorised by the Prudential Regulation Authority for the purposes of regulation of its carriage of investment business and subject to regulation by the Financial Conduct Authority and limited regulation by the Prudential Regulation Authority. Details about the extent of our regulation by the Prudential Regulation Authority are available from us on request. In Spain, this material is distributed by J.P. Morgan Bank Luxembourg S.A.– Milan Branch, registered office at Via Catena Adalberto 4, Milan 20121, Italy, and registered by Bank of Italy and the Commissione Nazionale per le Società e la Borsa (CONSOB). In the Netherlands, this material is distributed by J.P. Morgan Bank Luxembourg S.A., Amsterdam Branch, with registered office at World Trade