[1] Vaccination update

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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 (vector vaccines)</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 Attenuated</td>
<td>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 Attenuated</td>
<td>A “killed” coronavirus that will get recognized as foreign matter by the immune system</td>
<td>Sinovac, SinoPharm, Covaxin</td>
<td>Polio (dev countries)</td>
</tr>
<tr>
<td>3 Recombinant</td>
<td>Recombinant coronavirus proteins, produced industrially in outside cell cultures, which are recognized as foreign matter by the immune system</td>
<td>GlaxoSmithKline/Sanofi, Novavax</td>
<td>Tetanus, pertussis, flu, shingles</td>
</tr>
<tr>
<td>4 Genetic</td>
<td>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, Oxford/AstraZeneca, J&amp;J, Gamaleya</td>
<td>Ebola</td>
</tr>
<tr>
<td>5 Genetic</td>
<td>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

“A pandemic (mostly) of the unvaccinated”: adverse outcomes in unvaccinated vs vaccinated people

While breakthrough infections are rising, the risk of infection, hospitalization and death for vaccinated people is still much lower than for unvaccinated people. In other words, while adverse COVID outcomes are not ONLY occurring among unvaccinated people, it is primarily unvaccinated people that are experiencing the most severe COVID outcomes and putting intense pressure on hospital systems. And for people who choose to receive booster shots, the outcomes are better still: a study at the Weizmann Institute in Israel found that people who received a third dose of the Pfizer vaccine were ~20 times less likely to get seriously ill from COVID, and 10 times less likely to be infected than were people only vaccinated twice as per the initial regimen.

There are two ways to illustrate these trends: through age- and population-adjusted data on infections (I), hospitalizations (H) and mortality (M); and through vaccine efficacy measures derived from such data.

Age and population adjusted data on vaccinated and unvaccinated people

The first two charts show COVID hospitalization and mortality outcomes from multiple states as reported by COVID-NET (a group of 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. If I were a cynical person, I would suspect that some states might be consciously making this data harder for the public to work with. In any case, their gaps are similar to the ones shown below.

Age adjusted hospitalizations: 250 acute-care hospitals

Daily hospital admissions, # per mm

![Graph showing age-adjusted hospitalizations for vaccinated and unvaccinated individuals.]

Source: CDC, JPMAM. November 27, 2021. Universe: CA, CO, CT, MD, MI, MN, NM, NY, OH, OR, TN, UT.

Age adjusted mortality: 20 US states

Daily deaths, # per mm

![Graph showing age-adjusted mortality for vaccinated and unvaccinated individuals.]


New York: infections

Daily infections, # per million

![Graph showing daily infections in New York for vaccinated and unvaccinated individuals.]


New York: hospitalizations

Daily hospital admissions, # per million

![Graph showing daily hospital admissions in New York for vaccinated and unvaccinated individuals.]

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


California: hospitalizations
Daily hospital admissions, # per mm


Virginia: hospitalizations
Weekly 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


Virginia: mortality
Weekly deaths, # per mm


Utah: age adjusted mortality
Weekly deaths, # per mm

A look at Europe/Canada

In late summer 2021, Belgium averaged ~200 infections per day per mm people. This figure began to spike in October, reaching ~1,200 infections by mid-November. Belgium released data on infections, hospitalizations and ICU admission by “immunity status” (they include vaccinated people and COVID survivors) for the period November 1 to November 14. For people over 65, there was practically no vaccine efficacy at all vs infection. Fortunately, efficacy remained high for all groups including 65+ when measured against hospitalization and ICU admission. We would like to see data for the vaccinated group on its own, but that has not been published.

Amongst older individuals the gap is narrower since a significant number of people over 70 are in the ICU despite being vaccinated (even when adjusted for population size), using data from the UK. The last chart shows vaccinated vs unvaccinated hospitalization trends in Ontario Canada for people over 60 years of age.

**UK ICU admissions: vaccinated vs unvaccinated**

ICU admissions from August 20 - Sept 10, # per mm

**Ontario adults age 60+: hospitalizations by vaccination status**

Current hospitalizations, # per mm, smoothing = 7 days

Source: Belgium Public Health Institute. 11/19/2021.  
Source: Belgium Public Health Institute. 11/19/2021.  
Source: Belgium Public Health Institute. 11/19/2021.  
Latest data from the Robert Koch Institute

**Germany: 60 and older infections**
Current infections, # per mm


**Germany: 60 and older hospitalizations**
Current hospitalizations, # per mm


**Germany: Vaccine efficacy against symptomatic infection**


**Germany: Vaccine efficacy against hospitalization**


**Germany: Vaccine efficacy against ICU admission**


**Germany: Vaccine efficacy against mortality**

Vaccine efficacy data

Vaccine efficacy data is computed based on the decline in vaccinated COVID outcomes vs unvaccinated COVID outcomes (such as those illustrated on the prior pages), usually after creating matching cohorts by age and other factors. In September 2021, the CDC released data on vaccine efficacy for the period March to August 2021.

While the decline in efficacy vs infection is concerning given the rise in “long COVID” cases that may follow, vaccine efficacy vs hospitalization in the US remains high and is close to levels estimated during original vaccine trials, even for older individuals. The data on efficacy vs hospitalization below comes from the COVID Associated Hospitalization Surveillance Network. Similar results were published by NY State, the Vision Multistate Network of Electronic Health Records (187 hospitals) and the Ivy Network (21 medical centers in 18 states).

Vaccine efficacy in the UK has been estimated at levels close to the US: a study at the University of Edinburgh covering April to August 2021 found that the Pfizer and AstraZeneca vaccines were 90% and 91% effective in the UK at preventing death.

### Pfizer vaccine efficacy against symptomatic infections

![Graph showing Pfizer vaccine efficacy against symptomatic infections](source: CDC. September 22, 2021.)

### Moderna vaccine efficacy against symptomatic infections

![Graph showing Moderna vaccine efficacy against symptomatic infections](source: CDC. September 22, 2021.)

### J&J vaccine efficacy against symptomatic infections

![Graph showing J&J vaccine efficacy against symptomatic infections](source: CDC. September 22, 2021.)

### mRNA vaccine efficacy against hospitalization by age

![Graph showing mRNA vaccine efficacy against hospitalization by age](source: COVID-NET, CDC. September 22, 2021.)

### Vaccine efficacy against hospitalization by age over time

![Graph showing vaccine efficacy against hospitalization by age over time](source: VISION Network, CDC. September 22, 2021.)
The next set of data comes from a study in Science magazine which examined outcomes in 800,000 US veterans from Feb 2021 to Oct 2021. Similar trends, other than a very low J&J efficacy vs infection.

Vaccine efficacy vs infection and mortality
US veterans administration, Feb 2021-Oct 2021

<table>
<thead>
<tr>
<th>March data</th>
<th>September data</th>
</tr>
</thead>
<tbody>
<tr>
<td>March vs infection, Moderna</td>
<td>Sept vs infection, Moderna</td>
</tr>
<tr>
<td>March vs infection, Pfizer</td>
<td>Sept vs infection, Pfizer</td>
</tr>
<tr>
<td>March vs infection, J&amp;J</td>
<td>Sept vs infection, J&amp;J</td>
</tr>
<tr>
<td>89%</td>
<td>58%</td>
</tr>
<tr>
<td>87%</td>
<td>45%</td>
</tr>
<tr>
<td>86%</td>
<td>13%</td>
</tr>
<tr>
<td>Sept vs mortality, age &lt;65, Moderna</td>
<td>82%</td>
</tr>
<tr>
<td>Sept vs mortality, age &lt;65, Pfizer</td>
<td>84%</td>
</tr>
<tr>
<td>Sept vs mortality, age &lt;65, J&amp;J</td>
<td>73%</td>
</tr>
<tr>
<td>Sept vs mortality, age 65+, Moderna</td>
<td>76%</td>
</tr>
<tr>
<td>Sept vs mortality, age 65+, Pfizer</td>
<td>70%</td>
</tr>
<tr>
<td>Sept vs mortality, age 65+, J&amp;J</td>
<td>52%</td>
</tr>
</tbody>
</table>

Source: Science, November 4, 2021

The final table on this topic shows implied efficacy rates by state based on hospitalization and mortality rates for the period January through July 2021.

Hospitalizations and death rates: vaccinated vs unvaccinated people

<table>
<thead>
<tr>
<th>State</th>
<th>Hospitalizations</th>
<th>Vaccine efficacy</th>
<th>Deaths</th>
<th>Vaccine efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>AL</td>
<td>90</td>
<td>6960</td>
<td>30</td>
<td>1240</td>
</tr>
<tr>
<td>AK</td>
<td>90</td>
<td>1540</td>
<td>10</td>
<td>110</td>
</tr>
<tr>
<td>AZ</td>
<td>270</td>
<td>13060</td>
<td>20</td>
<td>1820</td>
</tr>
<tr>
<td>CA</td>
<td>90</td>
<td>6470</td>
<td>10</td>
<td>580</td>
</tr>
<tr>
<td>CO</td>
<td>240</td>
<td>5670</td>
<td>40</td>
<td>370</td>
</tr>
<tr>
<td>DC</td>
<td>70</td>
<td>33260</td>
<td>20</td>
<td>550</td>
</tr>
<tr>
<td>DE</td>
<td>70</td>
<td>9780</td>
<td>20</td>
<td>260</td>
</tr>
<tr>
<td>GA</td>
<td>50</td>
<td>7350</td>
<td>10</td>
<td>990</td>
</tr>
<tr>
<td>ID</td>
<td>110</td>
<td>2880</td>
<td>20</td>
<td>300</td>
</tr>
<tr>
<td>IL</td>
<td>200</td>
<td>10010</td>
<td>50</td>
<td>680</td>
</tr>
<tr>
<td>IN</td>
<td>90</td>
<td>5470</td>
<td>40</td>
<td>290</td>
</tr>
<tr>
<td>KY</td>
<td>210</td>
<td>8930</td>
<td>40</td>
<td>850</td>
</tr>
<tr>
<td>LA</td>
<td>120</td>
<td>3470</td>
<td>30</td>
<td>540</td>
</tr>
<tr>
<td>ME</td>
<td>60</td>
<td>5710</td>
<td>30</td>
<td>240</td>
</tr>
<tr>
<td>MA</td>
<td>150</td>
<td>6150</td>
<td>40</td>
<td>870</td>
</tr>
<tr>
<td>MI</td>
<td>240</td>
<td>6930</td>
<td>90</td>
<td>870</td>
</tr>
<tr>
<td>MN</td>
<td>400</td>
<td>4650</td>
<td>60</td>
<td>710</td>
</tr>
<tr>
<td>MS</td>
<td>170</td>
<td>7020</td>
<td>40</td>
<td>1270</td>
</tr>
<tr>
<td>MT</td>
<td>110</td>
<td>4720</td>
<td>20</td>
<td>420</td>
</tr>
<tr>
<td>NE</td>
<td>130</td>
<td>4580</td>
<td>30</td>
<td>480</td>
</tr>
</tbody>
</table>

US vaccination overview

US vaccination progress
% of US population

0% 10% 20% 30% 40% 50% 60% 70% 80%

1/1 2/1 3/4 4/4 5/5 6/5 7/6 8/6 9/6 10/7 11/7 12/8 1/8

Unique people vaccinated
Fully vaccinated

Source: OWID, JPMAM. December 26, 2021. Dotted lines indicate estimated vaccination rate based on trailing 7-day average vaccination rate.

US daily vaccinations
Millions of people, 7-day average

Source: OWID, CDC, JPMAM. December 26, 2021.

Lowest vaccination counties with more than 100,000 people

1 Shelby AL 28.4% 11 Houston AL 34.1% 21 Richland OH 35.8% 31 Ouachita LA 36.8%
2 Matanuska-Susitna AK 31.6% 12 Tuscaloosa AL 34.1% 22 Spartanburg SC 36.0% 32 Wayne OH 36.8%
3 Harnett NC 31.9% 13 Calcasieu LA 34.1% 23 Randolph NC 36.0% 33 Jefferson MO 36.9%
4 Lee AL 32.0% 14 Mohave AZ 34.6% 24 Rowan NC 36.1% 34 Tangipahoa LA 37.2%
5 Etowah AL 32.0% 15 Allen OH 34.7% 25 Jackson MS 36.4% 35 Mobile AL 38.0%
6 Livingston LA 32.1% 16 Morgan AL 35.1% 26 Warren KY 36.4% 36 Miami OH 38.3%
7 Robeson NC 32.2% 17 Craighead AR 35.3% 27 Mesa CO 36.5% 37 Bossier LA 38.5%
8 Anderson SC 33.9% 18 Kings CA 35.4% 28 Kootenai ID 36.5% 38 Aiken SC 38.5%
9 Bradley TN 33.9% 19 Calhoun AL 35.6% 29 Terrebonne LA 36.6% 39 Berkeley SC 38.6%
10 Canyon ID 34.1% 20 Flathead MT 35.6% 30 Elkhart IN 36.8% 40 York SC 38.8%


5 lowest vaccination states compared to the US average

<table>
<thead>
<tr>
<th>State</th>
<th>IN</th>
<th>LA</th>
<th>WY</th>
<th>MS</th>
<th>ID</th>
<th>USA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total population</td>
<td>58%</td>
<td>57%</td>
<td>56%</td>
<td>55%</td>
<td>52%</td>
<td>73%</td>
</tr>
<tr>
<td>18-64 population</td>
<td>63%</td>
<td>64%</td>
<td>60%</td>
<td>61%</td>
<td>63%</td>
<td>79%</td>
</tr>
<tr>
<td>18+ population</td>
<td>69%</td>
<td>69%</td>
<td>67%</td>
<td>67%</td>
<td>69%</td>
<td>83%</td>
</tr>
<tr>
<td>65+ population</td>
<td>91%</td>
<td>90%</td>
<td>91%</td>
<td>89%</td>
<td>93%</td>
<td>97%</td>
</tr>
</tbody>
</table>

Source: OWID, CDC, JPMAM. December 26, 2021.
Vaccination vs infection, mortality, hospitalization and 2020 Trump voting share

US county infections vs vaccinations
Cumulative infections per mm since July 2021

US county deaths vs vaccinations
Cumulative deaths per mm since July 2021

US state hospitalizations vs vaccinations
Average hospitalization rate per mm since July 2021

Trump share of 2020 vote and vaccination by county
Fully vaccinated people as a % of county population


Source: Harvard Dataverse, CDC, State Health Depts, JPMAM. December 26, 2021.

R² = 0.40
Vaccine update by country and US state

**Country/Region vaccination rates**
Unique people vaccinated as % of population

- Continental W. Europe
- United Kingdom
- United States
- South/Central America
- EM Asia ex-China
- India
- Eastern Europe/Russia
- Africa

**Country vaccination rates: Europe/CAN/AUS/NZ**
Unique people vaccinated as % of population

- Canada
- New Zealand
- France
- Denmark
- Australia
- Italy
- Netherlands
- Sweden
- Germany

**Country vaccination rates: Large EM**
Unique people vaccinated as % of population

- China
- Brazil
- Turkey
- India
- Russia

**Country vaccination rates: Other EM**
Unique people vaccinated as % of population

- Chile
- South Korea
- Saudi Arabia
- Hong Kong
- Czechia
- Mexico
- Indonesia

**OECD countries by highest share of unvaccinated people**
Unvaccinated people as % of population

1 Vaccination data can indicate the number of people that vaccinated (either with one or two doses), or the total number of vaccinations given. The latter will always be higher because it includes people who received multiple doses. Unless stated otherwise, we show people that have been vaccinated rather than doses.
Percent of population that received at least one vaccination
Sorted in descending order by highest vaccination rate

Source: OWID, JPMAM. December 26, 2021.
<table>
<thead>
<tr>
<th>Country</th>
<th>Unique ppl vax (mm)</th>
<th>% of pop.</th>
<th>Full vax (mm)</th>
<th>% of pop.</th>
<th>Boosters (mm)</th>
<th>% of pop.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Algeria</td>
<td>7.02</td>
<td>16%</td>
<td>5.55</td>
<td>13%</td>
<td>0.03</td>
<td>0%</td>
</tr>
<tr>
<td>Argentina</td>
<td>37.86</td>
<td>84%</td>
<td>32.13</td>
<td>71%</td>
<td>4.56</td>
<td>10%</td>
</tr>
<tr>
<td>Aruba</td>
<td>0.08</td>
<td>77%</td>
<td>0.08</td>
<td>72%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Australia</td>
<td>20.41</td>
<td>80%</td>
<td>19.70</td>
<td>77%</td>
<td>2.09</td>
<td>8%</td>
</tr>
<tr>
<td>Austria</td>
<td>6.59</td>
<td>73%</td>
<td>6.40</td>
<td>71%</td>
<td>3.55</td>
<td>39%</td>
</tr>
<tr>
<td>Bahamas</td>
<td>0.16</td>
<td>40%</td>
<td>0.15</td>
<td>38%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Bahrain</td>
<td>1.20</td>
<td>71%</td>
<td>1.17</td>
<td>69%</td>
<td>0.81</td>
<td>48%</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>87.55</td>
<td>53%</td>
<td>44.74</td>
<td>27%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Belgium</td>
<td>8.90</td>
<td>77%</td>
<td>8.79</td>
<td>76%</td>
<td>3.96</td>
<td>34%</td>
</tr>
<tr>
<td>Belize</td>
<td>0.23</td>
<td>57%</td>
<td>0.20</td>
<td>50%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Bermuda</td>
<td>0.05</td>
<td>77%</td>
<td>0.05</td>
<td>75%</td>
<td>0.02</td>
<td>32%</td>
</tr>
<tr>
<td>Bhutan</td>
<td>0.59</td>
<td>77%</td>
<td>0.57</td>
<td>73%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Bolivia</td>
<td>5.45</td>
<td>47%</td>
<td>4.51</td>
<td>39%</td>
<td>0.50</td>
<td>4%</td>
</tr>
<tr>
<td>Botswana</td>
<td>1.13</td>
<td>48%</td>
<td>1.01</td>
<td>43%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Brazil</td>
<td>165.89</td>
<td>78%</td>
<td>142.81</td>
<td>67%</td>
<td>24.69</td>
<td>12%</td>
</tr>
<tr>
<td>Brunei</td>
<td>0.41</td>
<td>92%</td>
<td>0.39</td>
<td>88%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Bulgaria</td>
<td>1.90</td>
<td>27%</td>
<td>1.90</td>
<td>27%</td>
<td>0.25</td>
<td>4%</td>
</tr>
<tr>
<td>Cambodia</td>
<td>14.24</td>
<td>85%</td>
<td>13.62</td>
<td>81%</td>
<td>3.28</td>
<td>20%</td>
</tr>
<tr>
<td>Canada</td>
<td>31.64</td>
<td>84%</td>
<td>29.36</td>
<td>78%</td>
<td>5.97</td>
<td>16%</td>
</tr>
<tr>
<td>Chile</td>
<td>17.20</td>
<td>90%</td>
<td>16.45</td>
<td>86%</td>
<td>10.20</td>
<td>53%</td>
</tr>
<tr>
<td>China</td>
<td>1,225.00</td>
<td>85%</td>
<td>1,193.47</td>
<td>83%</td>
<td>120.58</td>
<td>8%</td>
</tr>
<tr>
<td>Colombia</td>
<td>38.13</td>
<td>75%</td>
<td>27.85</td>
<td>55%</td>
<td>2.99</td>
<td>6%</td>
</tr>
<tr>
<td>Costa Rica</td>
<td>3.93</td>
<td>77%</td>
<td>3.44</td>
<td>68%</td>
<td>0.20</td>
<td>4%</td>
</tr>
<tr>
<td>Croatia</td>
<td>2.25</td>
<td>55%</td>
<td>2.12</td>
<td>52%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cuba</td>
<td>10.39</td>
<td>82%</td>
<td>9.60</td>
<td>85%</td>
<td>1.16</td>
<td>10%</td>
</tr>
<tr>
<td>Czechia</td>
<td>6.80</td>
<td>63%</td>
<td>6.62</td>
<td>62%</td>
<td>2.19</td>
<td>20%</td>
</tr>
<tr>
<td>Denmark</td>
<td>4.78</td>
<td>83%</td>
<td>4.54</td>
<td>78%</td>
<td>2.45</td>
<td>42%</td>
</tr>
<tr>
<td>Dominican Rep.</td>
<td>6.93</td>
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<tr>
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<td>56%</td>
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</table>

Source: OWID, JPMAM. December 26, 2021.
Vaccination vs previous COVID infection (acquired vs natural immunity)

To illustrate infection risk across immunity types, let's use this framework of 4 groups. There is universal agreement that Group A has much lower infection risk than Group D, since vaccination and prior infection provide antibodies which reduce risk of disease relative to people without antibodies. There is also emerging consensus that infection risk in Group A is lower than in Group B, since vaccines add to natural immunity; and that infection risk is lower in Group A than in Group C (and lower in Group B than Group D), since some natural immunity is always better than none. The big question is the comparison of Group B vs Group C.

Settled science: Group A (previously infected, vaccinated) vs Group B (previously infected, unvaccinated). The state of Kentucky analyzed people who had been infected in 2020 and were reinfected in May-June 2021 (during the initial Delta variant wave) and compared their vaccination status. Residents who were not vaccinated had 2.3x higher reinfection rates when compared with fully vaccinated people (95% confidence interval of 1.6x–3.5x). The authors concluded that for people with previous SARS-CoV-2 infection, full vaccination provides additional protection against reinfection. The latest study from Israel came to similar conclusions on this issue: people who had SARS-CoV-2 previously and received one dose of the Pfizer vaccine were more highly protected against reinfection than unvaccinated COVID survivors. The risk ratio of 2x was almost the same as in the Kentucky study. These results confirm prior in-vitro laboratory studies showing that immune system responses are exceptionally strong when natural immunity resulting from infection is combined with mRNA or vector vaccination.

Settled science: Group A (previously infected, vaccinated) vs Group C (previously uninfected, vaccinated). On why Group A infection risks are lower than Group C infection risks: “We continue to underestimate the importance of natural infection immunity ... especially when infection is recent. And when you bolster that with one dose of vaccine, you take it to levels you can’t possibly match with any vaccine in the world right now.” [Eric Topol at Scripps Research]

The more complicated question: what about infection risks in Group B (previously infected, unvaccinated) vs Group C (previously uninfected and vaccinated)? There have been some studies concluding that while both immunities were high, natural immunity was “better/stronger” than acquired immunity through vaccination. Some scientists believe that natural immunity is more protective since vaccines only contain the spike protein of the virus, rather than the whole virus; and that in a natural infection, antibodies will be made to other antigens in the virus which might give more comprehensive immunity.

However, in recent months, two things happened: first, questions have been raised about the methodology used in the Israeli paper last February that ignited this whole debate. And second, a new CDC paper concludes that the risks are actually higher for unvaccinated survivors.

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2 https://www.cdc.gov/mmwr/volumes/70/wr/mm7032e1.htm#contribAff
4 See research from Nussenzweig and Bieniasz at Rockefeller University in Nature and Immunity, June 2021
5 https://news.emory.edu/stories/2021/07/covid_survivors_resistance/index.html
James Lawler, an infectious disease expert at the University of Nebraska Medical Center took a look at the Israeli study and identified two concerning sources of error that were not corrected for: survivorship bias and selection bias. The title of his presentation: “Myth: Natural Immunity from COVID-19 is Superior to Vaccine Imparted Immunity Against the Delta Variant”. Another reminder that peer-reviewed papers are preferable to pre-print studies. Lawler’s main points focused on the lack of pre-planned control groups, survivorship bias, mismatched dates between vaccination and observation periods, selection bias in group characteristics, etc.

An Oxford study concluded that acquired immunity modestly outperformed natural immunity, a result which has now been seconded by a larger CDC study. **Main findings:** after adjusting for age and other factors, the CDC found that unvaccinated survivors that checked themselves into a hospital were determined to have COVID at 5x the rate of vaccinated non-survivors who also checked themselves into hospitals, fearing COVID. To be clear, the actual rates of both re-infection and breakthrough infection were low, but there was a clear relative gap between the two.

The CDC study findings are augmented by other ones. For example, some people who get COVID receive no protection from reinfection since their natural immunity is nonexistent. One study found that a third of COVID-19 cases didn't result in SARS-CoV-2 antibodies. A prior CDC study found that 28% of COVID cases experienced complete “seroreversion” within 60 days, which refers to a decline in antibodies to levels below the threshold for positivity. In this study, 65% of people with a lower baseline antibody from infection to begin with completely lost their COVID antibodies within 60 days.

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6 [https://echo360.org/media/df6327b6-1e39-401e-affb-5220eaeef8e/public](https://echo360.org/media/df6327b6-1e39-401e-affb-5220eaeef8e/public)
7 [https://www.medrxiv.org/content/10.1101/2021.08.18.21262237v1](https://www.medrxiv.org/content/10.1101/2021.08.18.21262237v1)
8 [https://www.cdc.gov/mmwr/volumes/70/wr/mm7044e1.htm?s_cid=mm7044e1](https://www.cdc.gov/mmwr/volumes/70/wr/mm7044e1.htm?s_cid=mm7044e1)
10 [https://www.cdc.gov/mmwr/volumes/69/wr/mm6947a2.htm](https://www.cdc.gov/mmwr/volumes/69/wr/mm6947a2.htm)
Public policy implications: what to do about COVID survivors who don’t get vaccinated?

I spoke about all of this to some of my science advisory contacts. The bottom line: the “horse race” debate of whether natural immunity is better or worse than vaccine immunity might be missing the broader point. As cited above, natural immunity can be an effective barrier against further infection and transmission. Even if we ignore the Israeli study for its computational inadequacies, there’s plenty of evidence supporting the benefit of natural immunity in absolute terms (i.e., not relative to vaccine immunity) for many (but not all) individuals who have had a symptomatic case of COVID.

The larger challenge for governments and private sector companies is this: vaccine mandates are hard enough to administer on their own. The incremental challenge of having a carve-out policy for prior infection is both scientifically and administratively complicated:

- First, each organization would have to determine WHICH polymerase chain reaction (PCR), antigen and/or antibody tests to accept as proof of infection, since they vary in terms of their propensity to deliver false negatives and false positives. On PCR tests, there are two kinds: nasopharyngeal (the deeper swab test) and mid-turbinate (the more shallow swab test); the former is more accurate than the latter, and PCR tests are generally much more reliable than antigen tests\(^\text{11}\)

- Second, the magnitude of viral or antibody presence might need to be determined to qualify for a carve-out; a sound carve-out policy would ideally not be based on a “yes/no” litmus test, since asymptomatic COVID infections tend to yield less robust antibody and T-cell responses.

- Third, natural immunity has only been demonstrated to last reliably for some number of months, in which case each organization would have to maintain a “roll-off” calendar for people with prior infection so that they would rejoin the list of people subject to mobility restrictions and/or mandatory testing.

As a result, the most straightforward and executable policy most entities choose will likely be based on vaccination alone, even if that restricts the mobility and interactions of COVID survivors unnecessarily.

\(^{11}\) See [https://www.yalemedicine.org/news/which-covid-test-is-accurate](https://www.yalemedicine.org/news/which-covid-test-is-accurate) and [https://www.cochrane.org/CD013705/INFECTN_how-accurate-are-rapid-tests-diagnosing-covid-19](https://www.cochrane.org/CD013705/INFECTN_how-accurate-are-rapid-tests-diagnosing-covid-19)
Coronavirus

Vaccine risk-benefit data

For CDC reports on foregone COVID cases, hospitalizations, ICU admissions and deaths vs adverse vaccine outcomes, for mRNA vaccines see here: [https://www.cdc.gov/mmwr/volumes/70/wr/mm7027e2.htm#T2](https://www.cdc.gov/mmwr/volumes/70/wr/mm7027e2.htm#T2), and J&J vaccine see here: [https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-07/05-COVID-Rosenblum-508.pdf](https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-07/05-COVID-Rosenblum-508.pdf)

Vaccine safety history: 3 examples of withdrawals

Below are 3 instances of vaccine safety concerns cited by the CDC that resulted in suspension and withdrawal: 1955 Cutter Incident (withdrawn after 2 weeks), 1976 Swine Flu/GBS issue (withdrawn after 10 weeks), and the 1999 Rotavirus issue (withdrawn after 10 months).

[1] Cutter Incident (1955)

In 1955, batches of polio vaccine produced by Cutter Laboratories were contaminated with live polio virus. 260 cases of polio, 11 deaths and many cases of paralysis were attributed to the contamination. Clinical trials from April 1954 to April 1955 showed the vaccine had been 80-90% effective against paralytic polio with no harm to children in the studies. The vaccine was licensed in spring 1955 and Eisenhower began a national immunization program. Two weeks into the program, the surgeon general reported that 7 children became paralyzed as a result of Cutter’s deviation from standard procedures and all vaccinations were suspended. Commercial vaccine production differed from field trials: while trials required 3 tests for live virus, commercial vaccine production only involved 1 test by the company itself, as the gov’t did not have resources to test all manufactured vaccines. The polio vaccine program resumed after stricter manufacturing guidelines were imposed.


Due to fears of a potential swine flu epidemic after an outbreak at a military base in February 1976, emergency legislation to fund a mass swine flu immunization program was signed in April, and vaccinations began in October. Within a few days, reports emerged that the vaccine was linked to increased risk of Guillain-Barre syndrome. The swine flu program was halted 10 weeks into the program in December 1976, after 45 million people (~25% of US population) had received the vaccine. According to the CDC, the increased risk was 1 additional case of GBS for every 100,000 people vaccinated.


In August 1998, RotaShield, a vaccine to prevent severe gastrointestinal disease in children, was licensed by the FDA. In trials, intussusception (a rare type of bowel obstruction) was noted in 0.05% vaccine recipients vs 0.02% of placebo recipients (differences the FDA described as not statistically significant). By June 1999, 12 cases of intussusception were reported and in July the CDC recommended that vaccinations be suspended pending investigations. The Advisory Committee on Immunization Practices announced in October 1999 that there was a strong causal relationship – about 1 in 5,000 vaccinations – between rotavirus vaccine and intussusception. The manufacturer withdrew the vaccine from the market a week before the ACIP announcement.
Variant prevalence by country

The table shows variant prevalence for select countries from GISAID, an open-source global science information sharing initiative. Only a handful of countries are sequencing more than 250 people per month, which is the threshold we use for inclusion. GISAID data may reflect data aggregated two weeks prior. In a world of rapidly changing variant shares, the numbers can change a lot when they’re updated.

<table>
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<th>Country</th>
<th>B.1.1.7 - Alpha (UK)</th>
<th>B.1.1.529 - Omicron (S Afr/Botswana)</th>
<th>B.1.640 - Delta (Congo/France)</th>
<th>B.1.617 - Delta (India)</th>
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<td>South Korea</td>
<td>0.0%</td>
<td>0.6%</td>
<td>0.0%</td>
<td>99.4%</td>
</tr>
<tr>
<td>Spain</td>
<td>0.0%</td>
<td>18.9%</td>
<td>0.0%</td>
<td>79.1%</td>
</tr>
<tr>
<td>Sweden</td>
<td>0.0%</td>
<td>10.5%</td>
<td>0.0%</td>
<td>89.2%</td>
</tr>
<tr>
<td>Switzerland</td>
<td>0.0%</td>
<td>8.4%</td>
<td>0.0%</td>
<td>91.6%</td>
</tr>
<tr>
<td>Thailand</td>
<td>0.0%</td>
<td>4.2%</td>
<td>0.0%</td>
<td>95.8%</td>
</tr>
<tr>
<td>Turkey</td>
<td>0.0%</td>
<td>1.2%</td>
<td>0.0%</td>
<td>98.8%</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>0.0%</td>
<td>23.2%</td>
<td>0.0%</td>
<td>76.8%</td>
</tr>
<tr>
<td>United States</td>
<td>0.0%</td>
<td>73.2%</td>
<td>0.0%</td>
<td>26.8%</td>
</tr>
</tbody>
</table>

Source: GISAID, CDC. December 27, 2021. Includes countries with 250 or more total genomic sequences analyzed over trailing 4 weeks. Table does not show prevalence of specific mutations e.g. the D614G mutation, which was found in many circulating variants in 2020.
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