What is the ability of natural immunity to protect against mild disease and severe disease?

*(based on epidemiological data)*

Eli Rosenberg, PhD
Deputy Director for Science, Office of Public Health, New York State Department of Health
Associate Professor, Department of Epidemiology and Biostatistics, University at Albany School of Public Health

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COVID-19 Cases and Hospitalizations by COVID-19 Vaccination Status and Previous COVID-19 Diagnosis — California and New York, May–November 2021

Tomás M. León, PhD¹; Vajeera Dorabawila, PhD²; Lauren Nelson, MPH¹; Emily Lutterloh, MD²,³; Ursula E. Bauer, PhD²; Bryon Backenson, MPH²,³; Mary T. Bassett, MD²; Hannah Henry, MPH¹; Brooke Bregman, MPH¹; Claire M. Midgley, PhD⁴; Jennifer F. Myers, MPH¹; Ian D. Plumb, MBB5⁴; Heather E. Reese, PhD⁵; Rui Zhao, MPH¹; Melissa Briggs-Hagen, MD⁴; Dina Hoefer, PhD²; James P. Watt, MD¹; Benjamin J. Silk, PhD⁴; Seema Jain, MD¹; Eli S. Rosenberg, PhD²,³
Analytic framework

- Matched laboratory, immunization, hospitalization databases building on prior methodology (Rosenberg et al MMWR, NEJM 2021)
- Analysis represents 32 million NYS and CA residents 18+
- Life-table hazard rates of incident laboratory-confirmed COVID-19 cases and hospitalizations
Results: New COVID-19 cases in NYS

- Rate highest for no previous diagnosis & not fully vaccinated
- Rate lowest for persons previously diagnosed & vaccinated (Small advantage to vaccine after diagnosis)
- Differences emerged in post-Delta era when vaccine effectiveness declined
- Additional analyses: Little evidence of waning protection from prior infection
Similar results for CA COVID-19 cases & hospitalizations

**Cases**

- Start of Delta variant predominance (≥50% of sequenced isolates)
- Unvaccinated, no previous COVID-19 diagnosis
- Vaccinated, no previous COVID-19 diagnosis
- Unvaccinated, previous COVID-19 diagnosis
- Vaccinated, previous COVID-19 diagnosis

- Booster for persons aged ≥65 yrs. Pfizer-BioNTech booster for certain persons aged ≥18 yrs in certain settings
- Moderna booster for certain persons aged ≥18 yrs in certain settings, booster for Jansen vaccine recipients

**Hospitalizations**

- Additional primary mRNA vaccine dose for certain immunocompromised persons
- Unvaccinated, no previous COVID-19 diagnosis
- Vaccinated, no previous COVID-19 diagnosis
- Unvaccinated, previous COVID-19 diagnosis
- Vaccinated, previous COVID-19 diagnosis

- Oct 3 - 16:
  - ↑ 56-fold risk persons aged ≥18 yrs in certain settings, booster for Jansen vaccine recipients
  - ↑ 59-fold risk
  - ↑ 21-fold risk

- Estimated hazard rate
Recent international results in alignment (all for cases)

- **France**: Nation-wide case-control study *(Grant et al, Lancet Reg. Health Nov 25)*
  - Relative to unvaccinated/no previous diagnosis, VE for symptomatic Delta variant cases
    - Lowest for those vaccinated/no previous diagnosis (67%).
    - Strong for those previously diagnosed within 2-6 months, whether vaccinated (VE = 96%) or unvaccinated (95%).
    - Decline in protection for “older” infections diagnosed >6 months ago (VE = 74%)

- **United Kingdom**: SIREN cohort of healthcare workers *(Hall et al, medrxiv Dec 1)*
  - Relative to unvaccinated/no previous diagnosis, estimated VE for cases:
    - Lowest for those vaccinated/no previous diagnosis (mid 60%).
    - Strong if previously diagnosed within 2-6 months, whether vaccinated (VE > 90%) or not (VE mid 80%).
    - Little decline in protection for “old” infections: Mid-80% VE up to 15 months prior, mid 70% for those ≥15 months.

- **Israel**: National database cohort *(Goldberg et al, medrxiv Dec 5)*
  - Rates: (no previous diagnosis & vaccinated) < (previous diagnosis & unvaccinated) < (previous diagnosis & vaccinated)
  - Rates declined with time since vaccine and since infection
  - Signal of high benefit from boosters
Conclusions from New York and California analysis

• Both vaccination and having survived COVID-19 provided protection
  ▫ Surviving previous infection more protective than vaccination alone, during Delta era
  ▫ Yet initial SARS-CoV-2 infection has significant risks for severe illness, death
  ▫ Only vaccination and staying up-to-date boosters is recommended

• Very high risks for unvaccinated
  ▫ Among unvaccinated, 20% previously diagnosed = only some may be relying on prior infection for protection
  ▫ Essential to reach the other 80%

• Key limitations
  ▫ Added value of boosters not demonstrated
  ▫ Analysis ends before Omicron variant, for which primary series and prior infection may be less protective

• However, a number of new studies in recent two weeks …
### New UK SIREN results: post-Omicron, with boosters (Jan 14, for cases)

SARS-CoV-2 variants of concern and variants under investigation in England: Technical briefing 34

#### Table 3. Incidence of Omicron infections in the SIREN cohort between 1 December 2021 and 4 January 2022 by vaccination and prior infection status on 30 November 2021 (n=18,464)

<table>
<thead>
<tr>
<th>Status</th>
<th>Number of participants</th>
<th>Number of days of follow up</th>
<th>Number of infections</th>
<th>Crude incidence rate (per 10,000 person days)</th>
<th>Vaccine effectiveness (%) (100 x IRR)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No previous infection and vaccine status on 30 November 2021</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unvaccinated</td>
<td>87</td>
<td>1,935</td>
<td>21</td>
<td>108.5</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>Vaccinated 2 dose</td>
<td>1,156</td>
<td>24,801</td>
<td>182</td>
<td>73.4</td>
<td>32%</td>
<td>-6% - 57%</td>
</tr>
<tr>
<td>Vaccinated 3 dose</td>
<td>9,841</td>
<td>225,126</td>
<td>937</td>
<td>41.6</td>
<td>62%</td>
<td>41% - 75%</td>
</tr>
<tr>
<td><strong>Prior infection and vaccine status on 30 November 2021</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unvaccinated</td>
<td>255</td>
<td>5,750</td>
<td>35</td>
<td>60.9</td>
<td>44%</td>
<td>4% - 67%</td>
</tr>
<tr>
<td>Vaccinated 2 dose</td>
<td>1,333</td>
<td>28,255</td>
<td>123</td>
<td>43.5</td>
<td>60%</td>
<td>36% - 75%</td>
</tr>
<tr>
<td>Vaccinated 3 dose</td>
<td>5,386</td>
<td>121,762</td>
<td>377</td>
<td>31.0</td>
<td>71%</td>
<td>56% - 82%</td>
</tr>
</tbody>
</table>

Notes: IRR Incidence Rate Ratios. IRR are not adjusted.

Reinfections in NYS suggest changing protection from prior infection, post-Omicron

• Extends past new MMWR into Omicron period

• 3.7% of 4.9 million positive results are reinfection
  ▫ 83% occurred > Dec. 13
  ▫ But still only a small portion of total cases

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**New York State: Reinfections**

<table>
<thead>
<tr>
<th>Region</th>
<th>Cumulative First Infections</th>
<th>Cumulative Reinfections</th>
<th>First Infections (Prior Week)</th>
<th>Reinfections (Prior Week)</th>
<th>First Infection rate per 100k (Prior Week)</th>
<th>Reinfection rate per 100k (Prior Week)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statewide</td>
<td>4,711,368</td>
<td>182,195</td>
<td>132,294</td>
<td>10,506</td>
<td>97</td>
<td>8</td>
</tr>
<tr>
<td>Capital Region</td>
<td>155,999</td>
<td>5,021</td>
<td>8,343</td>
<td>574</td>
<td>110</td>
<td>8</td>
</tr>
<tr>
<td>Central New York</td>
<td>158,075</td>
<td>4,875</td>
<td>7,680</td>
<td>546</td>
<td>141</td>
<td>10</td>
</tr>
<tr>
<td>Finger Lakes</td>
<td>224,371</td>
<td>6,388</td>
<td>8,060</td>
<td>648</td>
<td>96</td>
<td>8</td>
</tr>
<tr>
<td>Long Island</td>
<td>796,410</td>
<td>35,420</td>
<td>17,182</td>
<td>1,817</td>
<td>86</td>
<td>9</td>
</tr>
<tr>
<td>Mid-Hudson</td>
<td>556,188</td>
<td>22,962</td>
<td>14,987</td>
<td>1,207</td>
<td>87</td>
<td>7</td>
</tr>
<tr>
<td>Mohawk Valley</td>
<td>97,987</td>
<td>2,894</td>
<td>4,259</td>
<td>411</td>
<td>125</td>
<td>12</td>
</tr>
<tr>
<td>New York City</td>
<td>2,204,540</td>
<td>90,956</td>
<td>53,727</td>
<td>3,819</td>
<td>91</td>
<td>6</td>
</tr>
<tr>
<td>North Country</td>
<td>70,525</td>
<td>1,373</td>
<td>3,736</td>
<td>238</td>
<td>127</td>
<td>8</td>
</tr>
<tr>
<td>Southern Tier</td>
<td>123,850</td>
<td>3,826</td>
<td>5,102</td>
<td>438</td>
<td>115</td>
<td>10</td>
</tr>
<tr>
<td>Western New York</td>
<td>285,513</td>
<td>8,459</td>
<td>10,139</td>
<td>808</td>
<td>105</td>
<td>8</td>
</tr>
</tbody>
</table>

*Grey shaded regions of figures and tables reflect recent weeks for which data are still accruing and estimates are subject to most change.*

Thank you!

Eli Rosenberg, PhD
New York State Department of Health
eli.rosenberg@health.ny.gov

With much thanks to the full collaborative NYS DOH, CA DPH, CDC team