

WHY WAS THE MORTALITY RATE FOR THE SARS-COV-2
OMICRON WAVE **UNDERESTIMATED** FOR CANADA,
USA, UK & ISRAEL?

hervk102@substack.com March 4, 2022

Dr. Marian Laderoute

MORTALITY RATES PER MILLION BY

EARLY HIGHLY

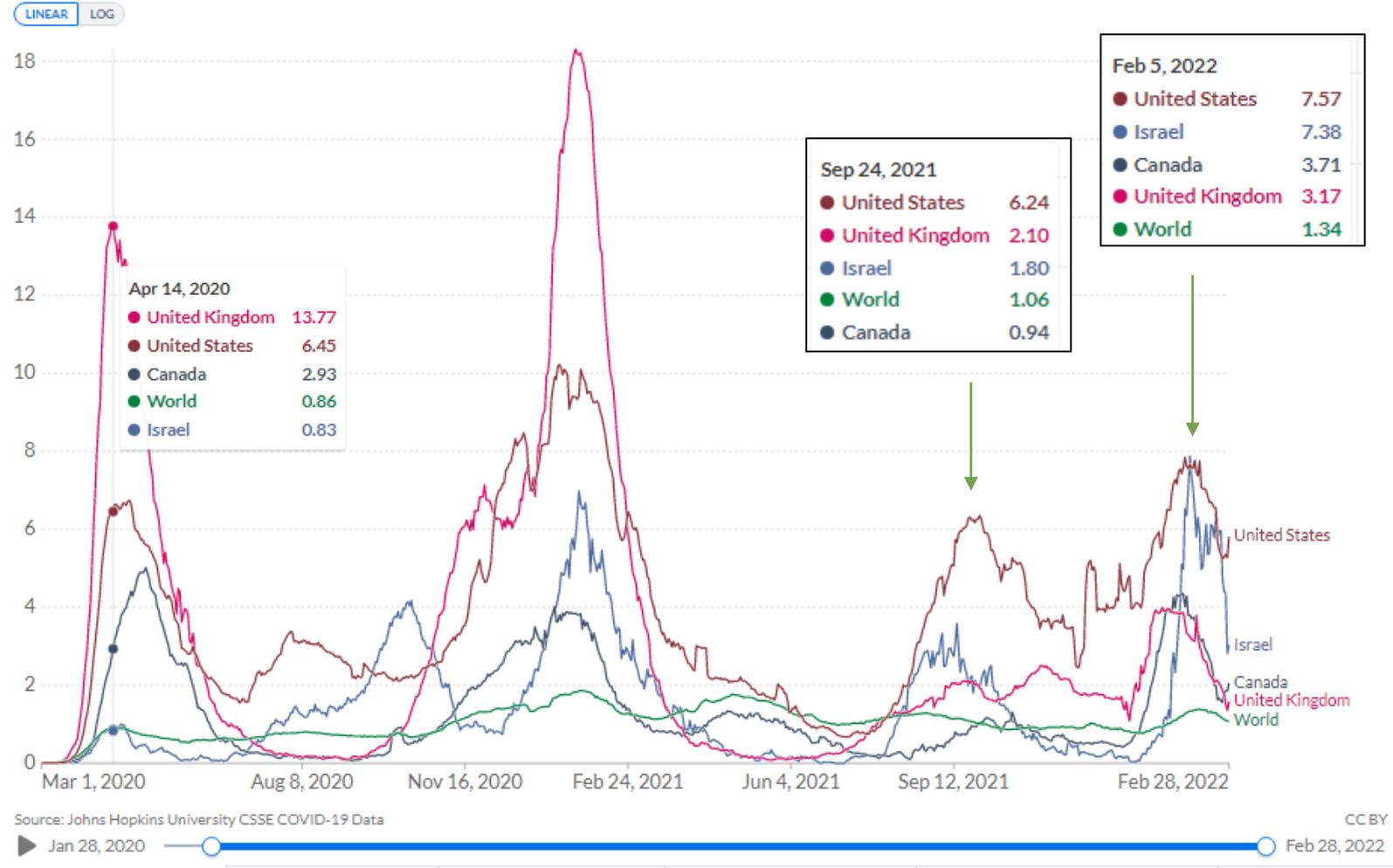
VACCINATING COUNTRIES

| Mortality | Sept 24, 2021 Delta Wave | Feb 5, 2022 Omicron Wave |
|-----------|-----------------------------|---|
| | Ratio with World | Ratio with World |
| USA | 5.9 X 55% vax | 5.6 X 60% vax, 28% boosted |
| Canada | 0.9 X 70% vax | 2.8 X 80% vax, 45% boosted |
| UK | 1.9 X 65% vax | 2.4 X 70% vax, 55% boosted |
| Israel | 1.7 X 60% vax | 5.5 X 62% vax, 55% boosted |
| World | 1.06/million 30% vax | 1.34/million 53% vax, 13% boosted |

Daily new confirmed COVID-19 deaths per million people

7-day rolling average. For some countries the number of confirmed deaths is much lower than the true number of deaths. This is because of limited testing and challenges in the attribution of the cause of death.

Our World
in Data



MORTALITY RATES PER MILLION BY

LATE - LOW

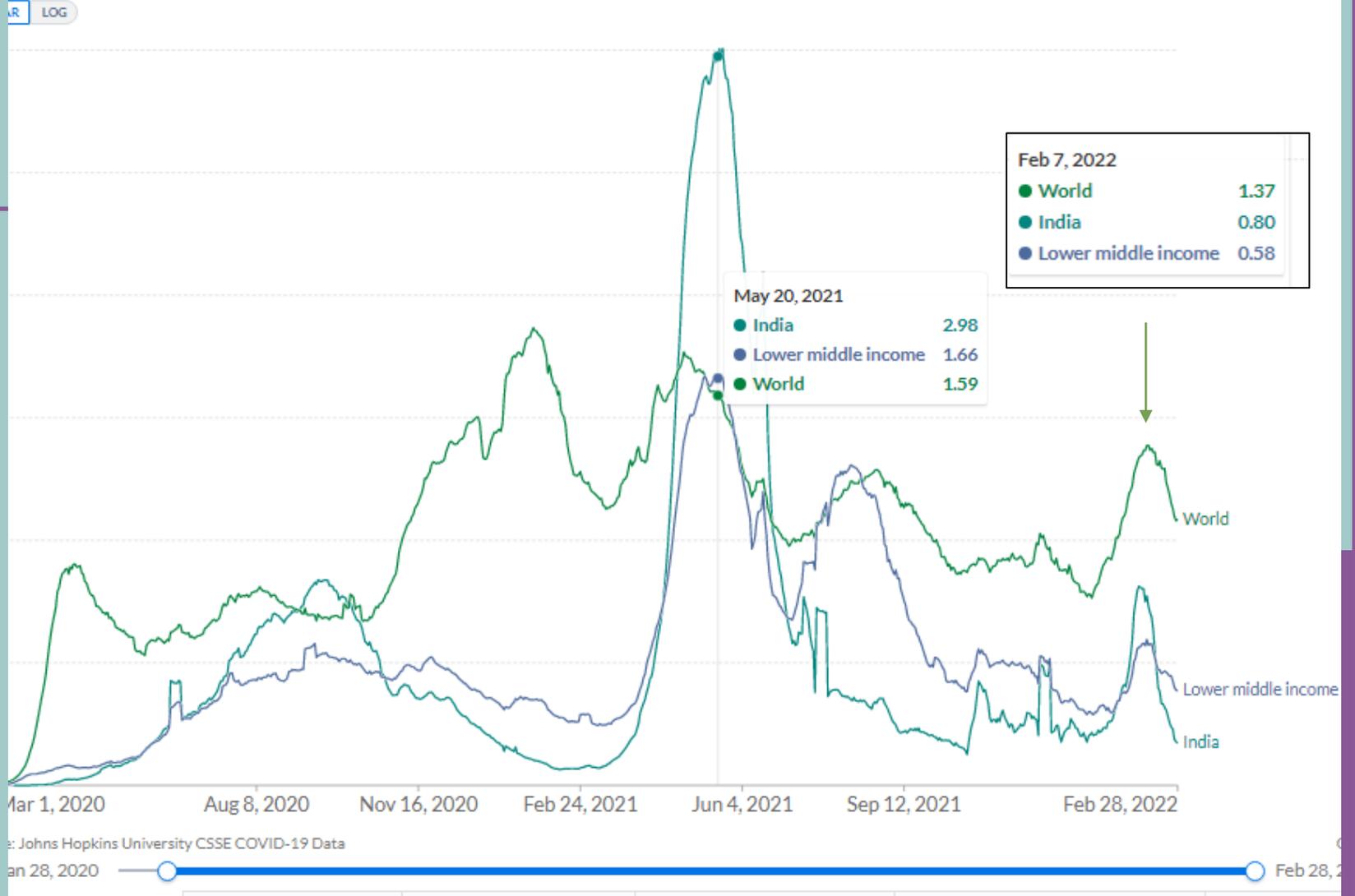
VACCINATING COUNTRIES

| Mortality | May 20, 2021 Delta Wave | Feb 7, 2022 Omicron Wave |
|----------------------------|-------------------------------|---|
| | Ratio with World | Ratio with World |
| INDIA | 1.9 X 5% vax | 0.6 X 50% vax, 1% boosted |
| Lower Middle Income | 1.0 X 2% vax | 0.4 X 40% vax, 3% boosted |
| World | 1.59/million 2% vax | 1.36/million 54% vax, 15% boosted |

Vax= full vaccination
Usually 2 doses

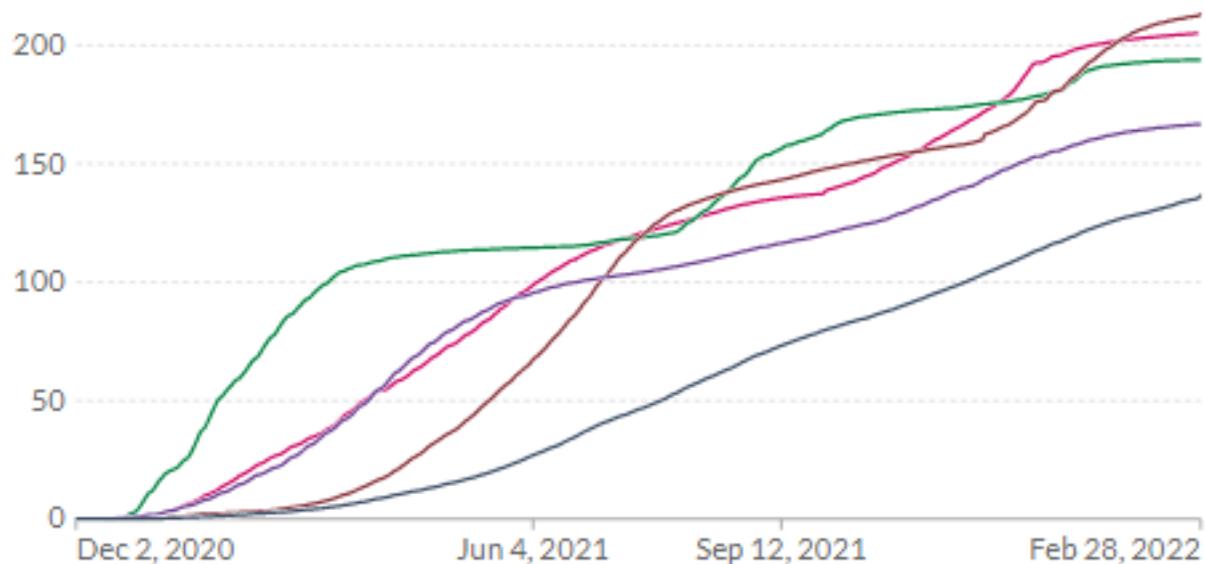
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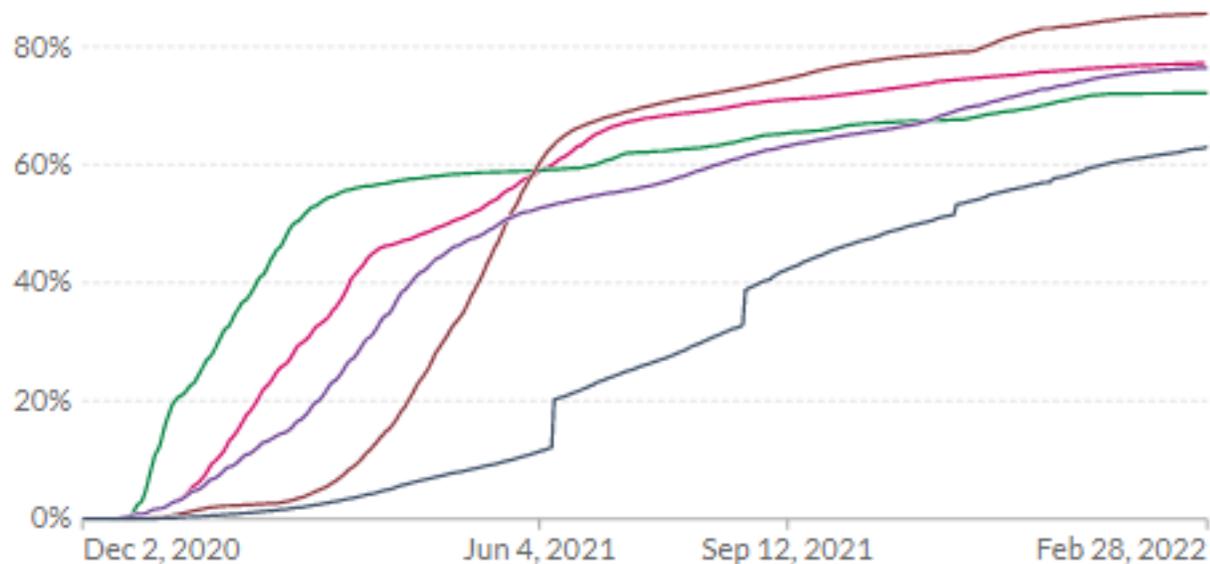


World United States Canada Israel United Kingdom

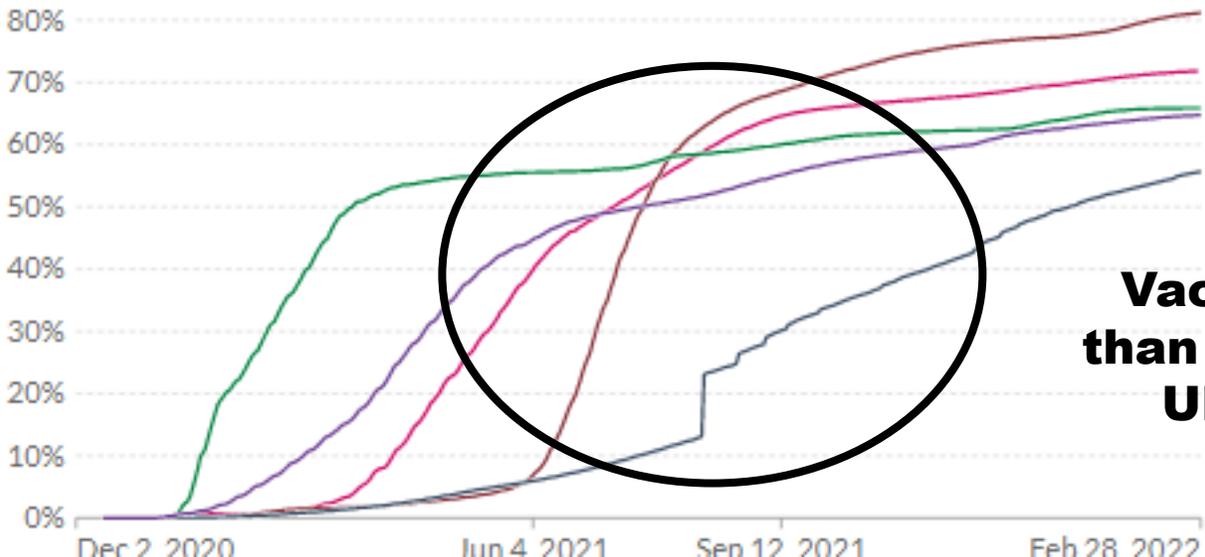
Vaccine doses (per 100)



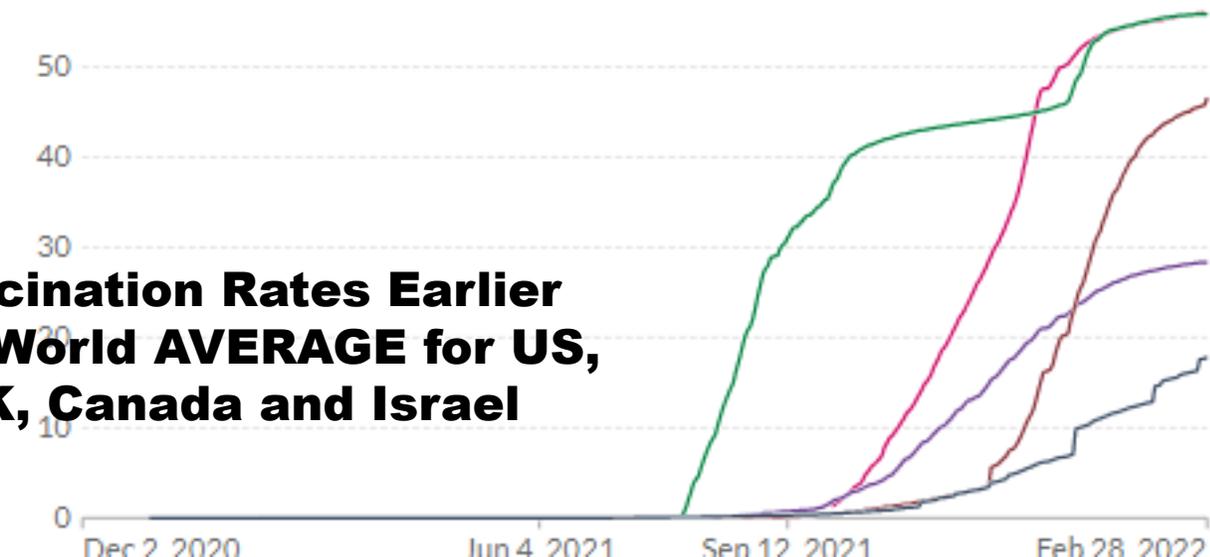
People with at least one dose (per 100)



People fully vaccinated (per 100)



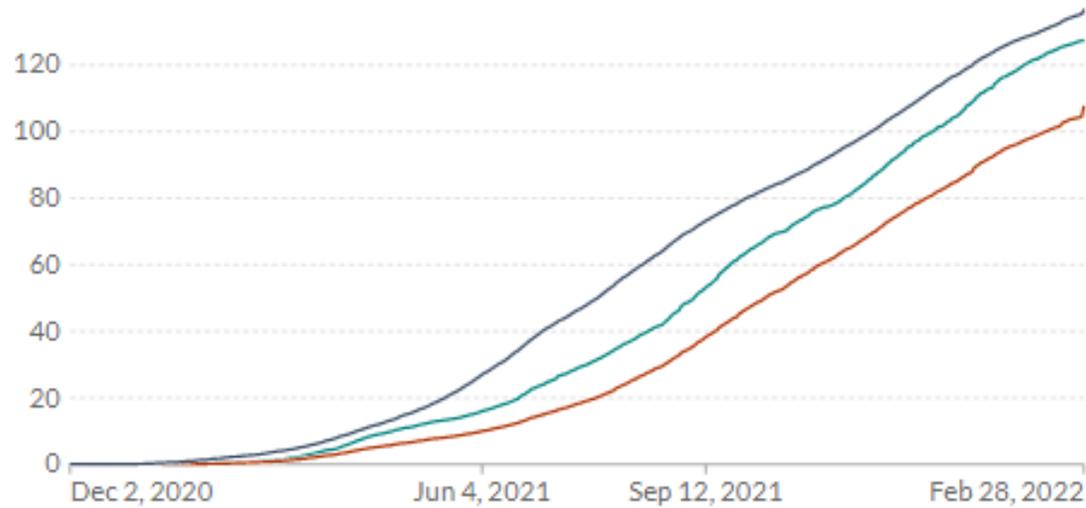
Booster doses (per 100)



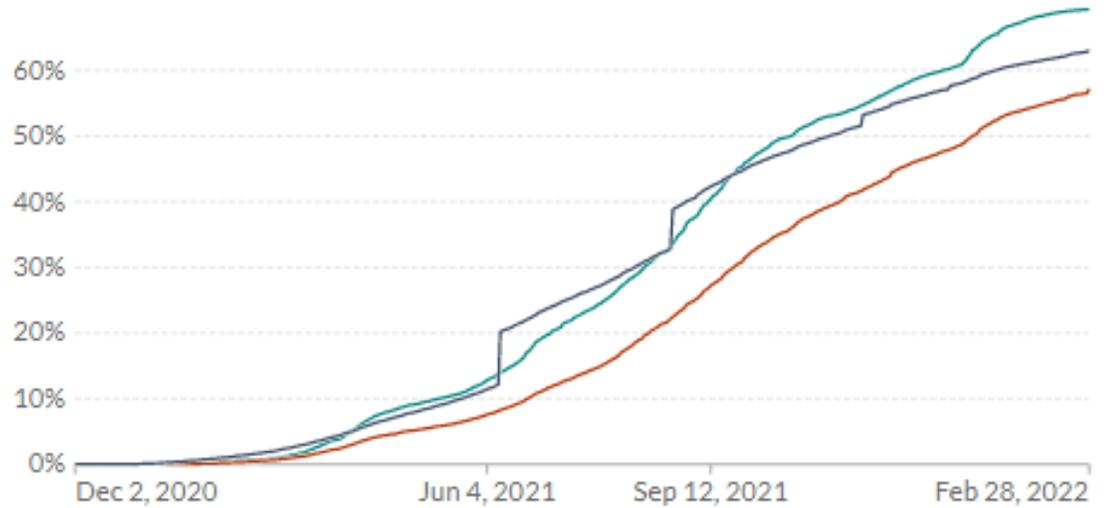
Vaccination Rates Earlier than World AVERAGE for US, UK, Canada and Israel

World Lower middle income India

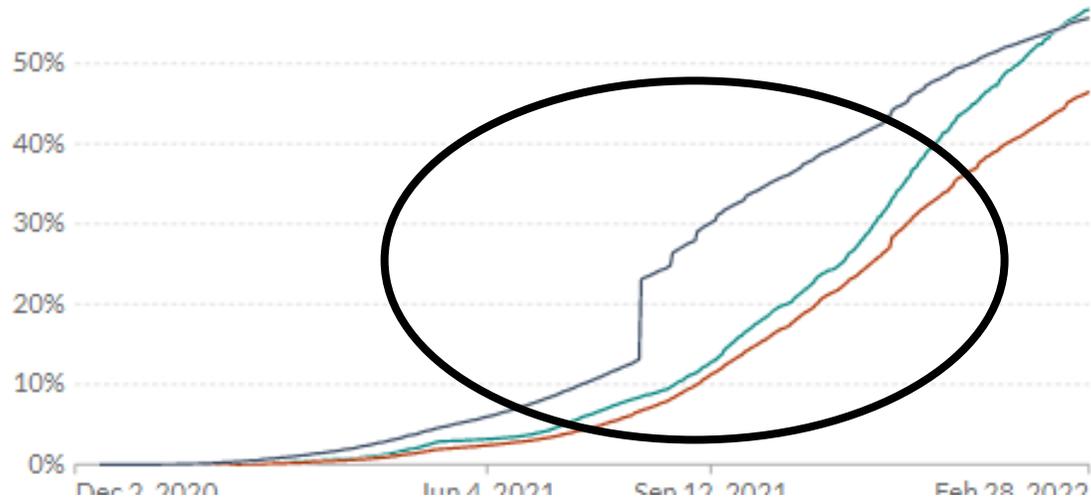
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People with at least one dose (per 100)

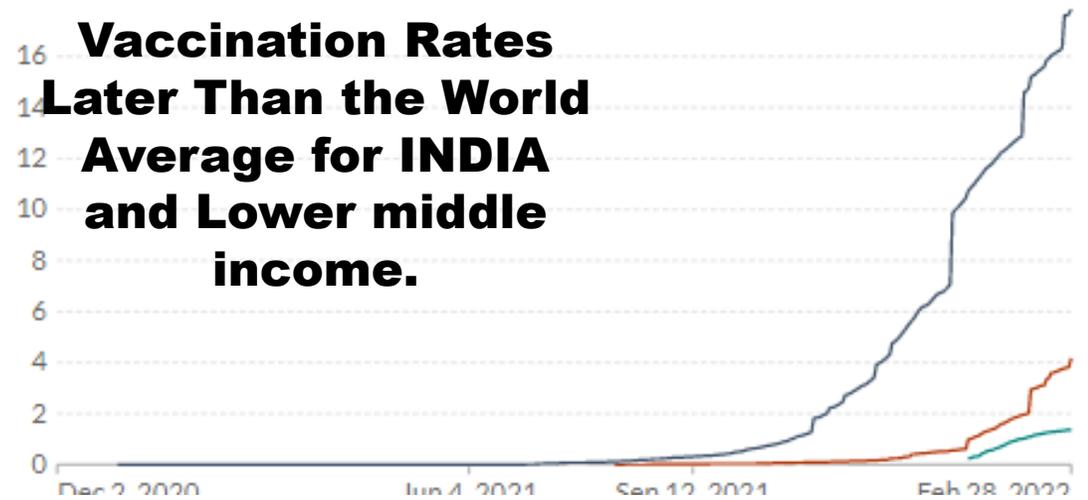


People fully vaccinated (per 100)



Booster doses (per 100)

**Vaccination Rates
Later Than the World
Average for INDIA
and Lower middle
income.**



DOMINANCE of the Delta Variant was Swift in Israel While Canada Was Intermediate and the UK and India the Lowest

| Country | 50% Delta | >90% Delta | Lag time from around 50% to >90% |
|---------------|--|----------------|----------------------------------|
| India | April 19, 2021 | May 17, 2021 | 4 weeks |
| UK | May 24, 2021 | June 21, 2021 | 4 weeks |
| Israel | June 7, 2021 | June 28, 2021 | 2 weeks |
| USA | June 28, 2021 | July 21, 2021 | 4 weeks |
| Canada | July 12, 2021 * | August 9, 2021 | 3 weeks |
| | * 50% of the Canadian population had received 2 nd dose by July 4, 2021; 10% by May 30, 2021. | | |

RELATIVE MORTALITY RATES (STANDARIZED TO WORLD AVERAGE) WERE LOWER FOR OMICRON IN THE LATE VACCINATING COUNTRIES Possibly DUE TO NATURAL IMMUNITY BY DELTA VARIANT EXPOSURES

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Canada was spared DELTA variant relative mortality due to lingering effects of trained innate immunity perhaps due to delay of 2nd dose by NACI.

National Advisory Committee on Immunization (NACI) Decided to Delay 2nd Dose Due to Limited Supply of Vaccine to Provide Innate Immunity to **More** Susceptible Canadians **RATHER THAN** Provide Adaptive Immunity to **Far Fewer** Susceptible Canadians

| Two to One Dose Ratios | | | | | | |
|--|---------------------|-------------|------------|-----------------|------------------------------|-----------------|
| for COVID-19 Vaccine Use In Canada | | | | | | |
| By Date in 2021 (from Our World in Data) | | | | | | |
| DATE | % At Least One Dose | % Two Doses | % One Dose | Two / One RATIO | EVENTS | NOTES |
| 22-Dec | 0.071 | None | 0.071 | N/A | | |
| 29-Dec | 0.19 | None | 0.19 | N/A | | |
| 3-Jan | 0.3 | None | 0.30 | N/A | | EACM Decreases |
| 10-Jan | 0.84 | 0.1 | 0.74 | 0.135 | | |
| 17-Jan | 1.5 | 0.6 | 0.9 | 0.667 | | EACM flattened |
| 24-Jan | 2.03 | 0.15 | 1.88 | 0.080 | | |
| 31-Jan | 2.3 | 0.3 | 2 | 0.150 | | |
| 7-Feb | 2.4 | 0.47 | 1.93 | 0.244 | | |
| 8-Feb | 2.4 | 0.5 | 1.9 | 0.263 | | |
| 10-Feb | 2.5 | 0.6 | 1.9 | 0.316 | | Enters Neg EACM |
| 14-Feb | 2.59 | 0.81 | 1.78 | 0.455 | 14 days prior | Feb 14-28 |
| 21-Feb | 2.9 | 1.1 | 1.8 | 0.611 | 7 days prior | |
| 22-Feb | 3 | 1.2 | 1.8 | 0.667 | Alpha emerges | |
| 25-Feb | 3.2 | 1.3 | 1.9 | 0.684 | | |
| 26-Feb | 3.4 | 1.4 | 2 | 0.700 | | |
| 27-Feb | 3.5 | 1.4 | 2.1 | 0.667 | NACI Intervention on Feb 27? | |
| 28-Feb | 3.63 | 1.41 | 2.22 | 0.635 | | |
| 7-Mar | 4.85 | 1.52 | 3.33 | 0.456 | | Peak in -EACM |
| 8-Mar | 5.1 | 1.6 | 3.5 | 0.457 | | |
| 11-Mar | 5.67 | 1.59 | 4.08 | 0.390 | | |
| 14-Mar | 6.5 | 1.6 | 4.9 | 0.327 | | |
| 15-Mar | 6.8 | 1.6 | 5.2 | 0.308 | 14 days prior | |
| 21-Mar | 8.83 | 1.7 | 7.13 | 0.238 | 7 days prior | Lowest EACM |

| DATE | % At Least One Dose | % Two Doses | % One Dose | Two / One RATIO | EVENTS | NOTES |
|--------|---------------------|-------------|------------|-----------------|------------------|----------------------|
| 21-Mar | 8.83 | 1.7 | 7.13 | 0.238 | 7 days prior | Lowest EACM |
| 22-Mar | 9.2 | 1.7 | 7.5 | 0.227 | Alpha dominates | |
| 28-Mar | 11.81 | 1.81 | 10 | 0.181 | | Peak in -EACM |
| 4-Apr | 15.07 | 1.92 | 13.15 | 0.146 | | |
| 11-Apr | 19.04 | 2.19 | 16.85 | 0.130 | | Peak in -EACM |
| 18-Apr | 24 | 2.5 | 21.5 | 0.116 | 14 days prior | |
| 19-Apr | 25 | 2.5 | 22.5 | 0.111 | | |
| 25-Apr | 29.18 | 2.75 | 26.43 | 0.104 | 7 days prior | |
| 26-Apr | 30 | 2.8 | 27.2 | 0.103 | | |
| 28-Apr | 31 | 2.9 | 28.1 | 0.103 | | Exit Neg EACM |
| 2-May | 33.58 | 3.05 | 30.53 | 0.100 | Delta emerges | |
| 3-May | 34 | 3.1 | 30.9 | 0.100 | | |
| 9-May | 39 | 3.4 | 35.6 | 0.096 | | |
| 16-May | 45 | 3.8 | 41.2 | 0.092 | | |
| 17-May | 46 | 3.9 | 42.1 | 0.093 | Max alpha at 59% | |
| 23-May | 51 | 4.05 | 46.95 | 0.086 | | |
| 30-May | 56.69 | 5.45 | 51.24 | 0.106 | | |
| 2-Jun | 58.8 | 6.11 | 52.69 | 0.116 | | |
| 11-Jun | 63.87 | 10.82 | 53.05 | 0.204 | | |
| 14-Jun | 64.86 | 13.11 | 51.75 | 0.253 | | |
| 20-Jun | 66.29 | 18.85 | 47.44 | 0.397 | | |
| 26-Jun | 67.38 | 26.47 | 40.91 | 0.647 | 14 days prior | |
| 4-Jul | 68.31 | 35.02 | 33.29 | 1.052 | 7 days prior | 50% Receive 2nd Dose |
| 12-Jul | 69.27 | 44.33 | 24.94 | 1.777 | Delta Dominant | |
| 19-Jul | 69.99 | 50.61 | 19.38 | 2.611 | | 50% Fully Vaxxed |
| 25-Jul | 71 | 55 | 16 | 3.438 | | |
| 1-Aug | 71 | 59 | 12 | 4.917 | | |

Measurable Negative Effects of Vaccination on Subsequent Variant (relative**) Mortality Rates**

In a report on deaths per 100,000 in the USA in 25 US jurisdictions, the average weekly incidence of deaths in the *fully vaccinated* increased **7 fold** during the delta dominant wave and **5 fold** in the omicron emergent wave when compared with pre-delta rates, whereas for the *unvaccinated* these were **4.2 fold and 3.6 fold respectively** (Johnson AG et al., MMWR, January 28, 2022).

This showed natural immunity (and/or the lack of vaccine induced high levels of sub-neutralizing antibodies to spike protein) placed the unvaccinated *at lower increased relative risk of death* when confronted with the alpha and delta waves compared to the pre-delta period than that experienced for the double vaccinated.

This is similar to what was seen globally in that the countries with more opportunity to get natural infection (especially with the delta variant) ***before vaccination***.

Interpretation: DATA Argues That Relative Protection Against Mortality with Sequential Variants Better With Natural Immunity

There may have been more people in India and in the lower middle income countries who might have been naturally infected with SARS-CoV-2 with the delta variant before becoming vaccinated.

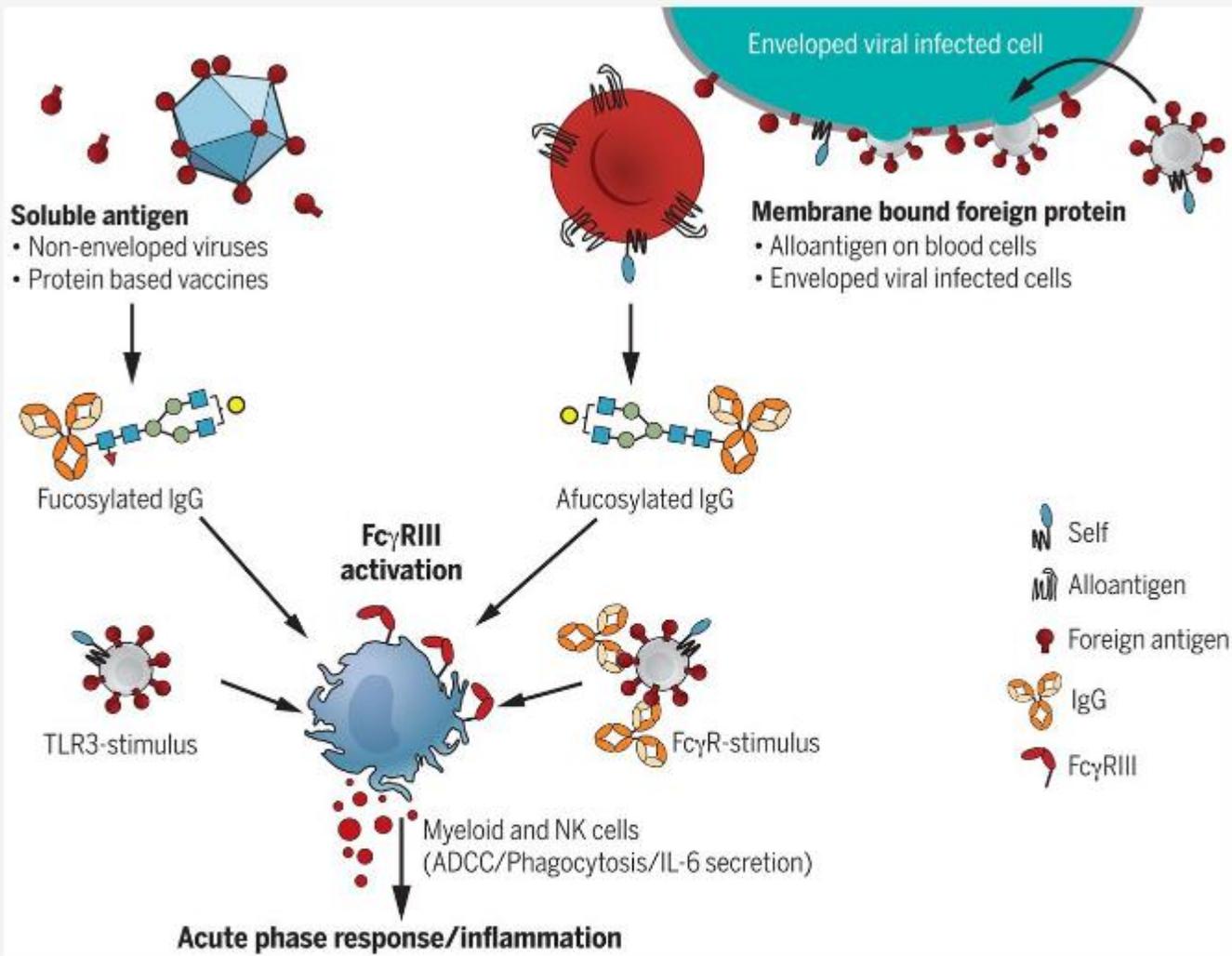
These countries had vaccination curves under the world average.

Conversely, in the nations where vaccination rates were higher than the world's average, more people would be vaccinated before becoming naturally infected. The latter group was associated with higher omicron and delta wave mortality ratios except Canada during the delta wave.

The latter may have been because of the protection associated with the delay of the administration of the second dose by the National Advisory Committee on Immunization due to limited supply.

Recent evidence suggests that the naturally infected have as good as or often better protection against SARS-CoV-2 *infection* than those with 2 doses (Hall V *et al.*, NEJM, Feb 16, 2022).

On the other hand, the naturally infected who then received two doses of vaccine showed the best enduring protection *against SARS-CoV-2 infection* (Hall V *et al.*, NEJM, Feb 16, 2022).



Afucosylated IgG response requires membrane context and results in strong Fc γ RIII-mediated activity. Only membrane association on host cells endows foreign antigens to trigger the B cell receptor in the context of other self receptors, leading to an afucosylated IgG response. The elevated Fc γ RIII binding and activity of afucosylated IgG can in some cases be protective, but for SARS-CoV-2, this triggers excessive inflammation during a natural infection.

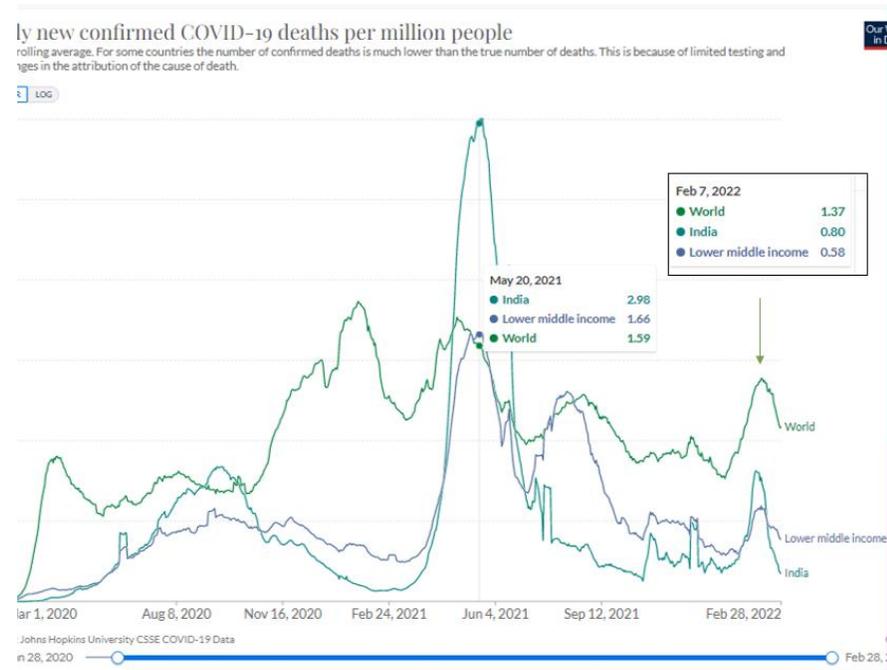
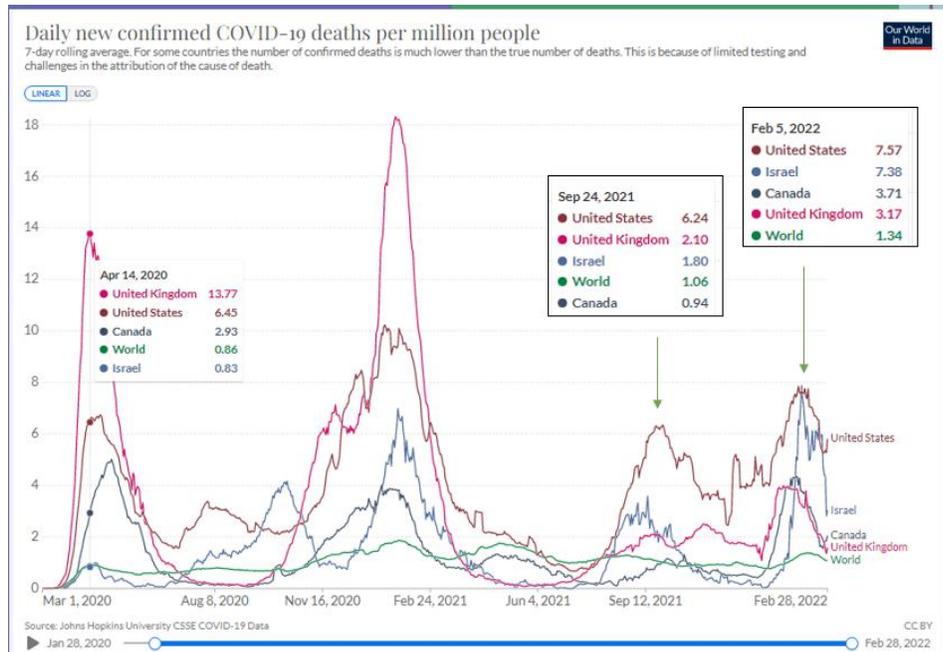
Larsen MD, de Graaf EL, Sonneveld ME, et al. Afucosylated IgG characterizes enveloped viral responses and correlates with COVID-19 severity. *Science*. 2021 Feb 26;371(6532):eabc8378. doi: 10.1126/science.abc8378.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)–specific afucosylated IgG were also found in critically ill COVID-19 patients but not in individuals with mild symptoms.

Over the 2 weeks after seroconversion, the amount of fucosylated anti-SARS-CoV-2 IgG increased markedly, in most reaching relative levels similar to those found in total IgG. Afucosylated IgG promoted interleukin-6 (IL-6) release in macrophages cultured in vitro, which is in line with an observed association of SARS-CoV-2–specific IgG afucosylation with IL-6 and C-reactive protein (CRP) in these patients.

However, for SARS-CoV-2, this **heightened afucosylated IgG response (that promotes ADE with FCGR3A) enhanced by mRNA or attenuated virus vaccines promotes the exacerbation of COVID-19 under conditions with high viral loads.**

Recall That the Omicron Mortality Peaks were HIGHER than Delta in the Early Vaccinating Countries, but LOWER in the Late Vaccinating Countries



This is consistent with the notion that of the total IgG against SARS-CoV-2 in the naturally immunized there may have been overall **relatively** less afucosylated antibodies to spike protein as it was diluted by natural immunity to a wide assortment of SARS-CoV-2 proteins, many not expressed on the cell surface and thus not resulting in afucosylated IgG. Natural immunity may have also favored trained innate immunity with zero risk of ADE.

Summary

Omicron was less lethal (relative to world mortality rates) in countries with more natural immunity exposures to the delta variant before vaccination.

CANADA benefitted by the delay in the second dose, a NACI decision announced on April 7, 2021, but implemented by February 27, 2021, which may have significantly decreased the relative to world mortality rates for the "highly pathogenic" delta variant for Canadians by prolonging the benefits of trained innate immunity against emerging RNA viruses.

Omicron '*relative to world mortality rates*' were higher in the early vaccinating countries potentially due to *usurping* the protection offered by natural immunity.

As well enhanced afucosylated IgG spike specific antibodies promoted by the vaccines (non-peptide type) may have caused increased pathogenesis during the omicron wave via ADE due to FCGR3A.

This is why the pathogenesis of omicron (death rates per million) were underestimated in Canada, UK, USA and Israel. It looked like the intrinsic pathogenesis of the omicron variant was less, but in fact pathogenesis was less due to more natural immunity exposures to the delta variant. Indeed, omicron pathogenesis was higher than delta in the early vaccinating countries possibly due in part to enhanced ADE via FCGR3A (and/or FCGR2A).

Conclusions

1. **More is not better!** More IgG to the receptor binding domain (RBD) and more neutralizing IgG to spike protein which favors afucosylated IgG does NOT provide more protection against COVID-19 mortality at a population basis (by country).
2. **Natural Immunity Protection is Far Better than Spike IgGs from mRNA or attenuated virus vaccines due to:**
 - relatively less afucosylated IgGs to spike protein
 - longer lasting trained innate immunity with zero risk of promoting ADE
3. **Evaluation of potential for COVID-19 severity of emerging SARS-CoV-2 variants needs assessment of the virus intrinsic properties AND host immunological history (quantity, quality, innate vs adaptive).**
4. **Interference of natural immunity by early vaccination caused enhanced mortality with the omicron variant.**
5. **Vaccines induced many COVID-19 associated deaths during the omicron wave.**
6. **Adaptive immunity vaccination is not as safe as one was led to believe.**
7. **The public health authorities & governments should be held accountable for pushing adaptive immunity (spike-specific) vaccine mandates. DANGERS known as early as **December 23, 2020** (the Larsen MD et al. Science paper on afucosylated IgG).**