



Partner in Academic Medicine

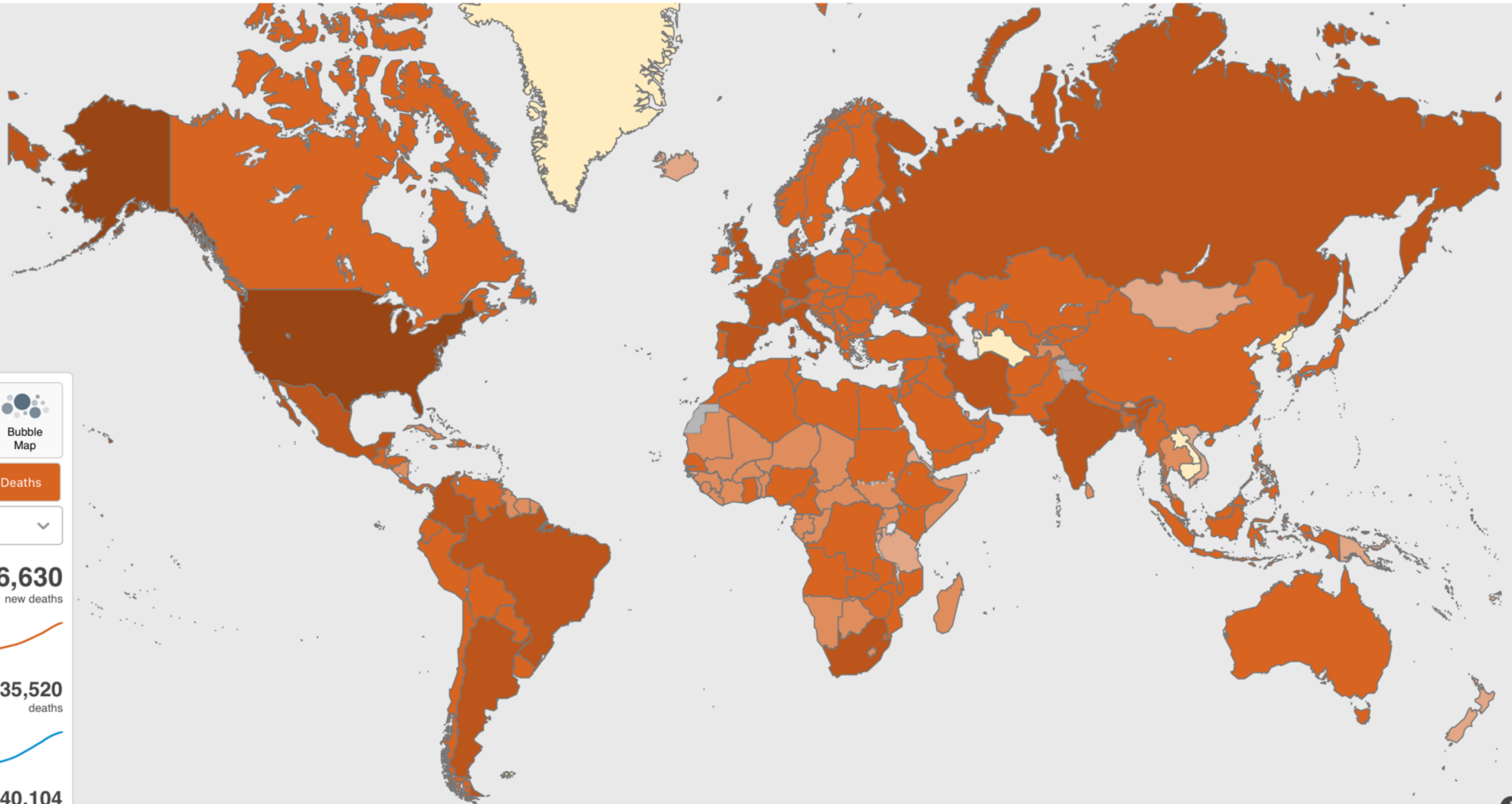


Covid-19 vaccination: the promised land?

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WHO Coronavirus Disease (COVID-19) Dashboard

Data last updated: 2021/3/2, 6:09pm CET

[Overview](#)[Data Table](#)[Explore](#)

Choropleth Map

Bubble Map

Cases

Deaths

Total

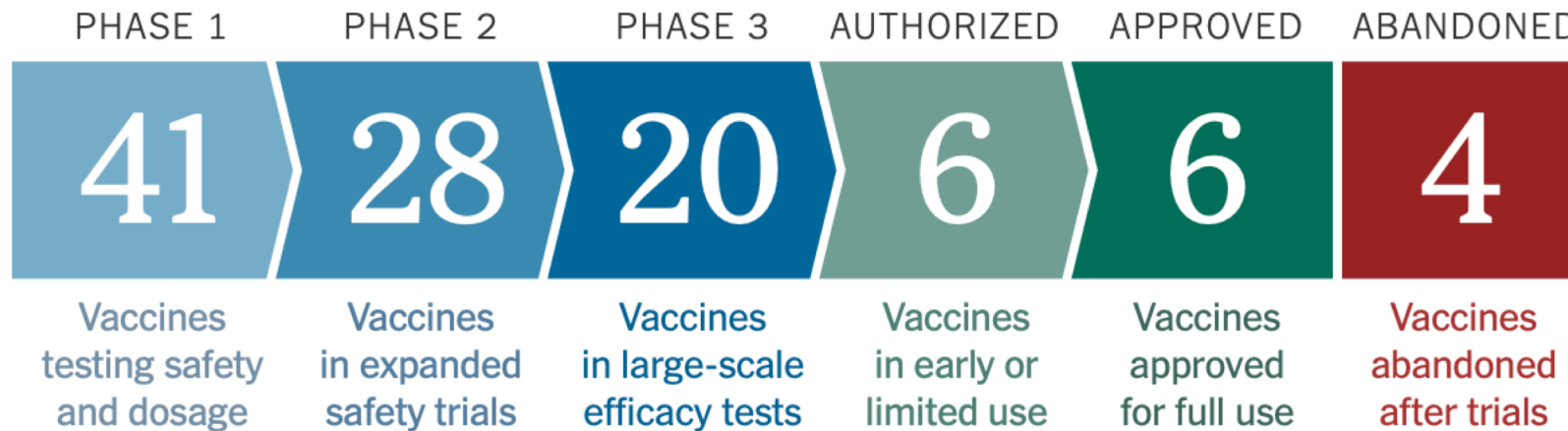
6,630
new deaths

2,535,520
deaths

114,140,104
confirmed cases

Coronavirus Vaccine Tracker

By [Carl Zimmer](#), [Jonathan Corum](#) and [Sui-Lee Wee](#) Updated March 2, 2021

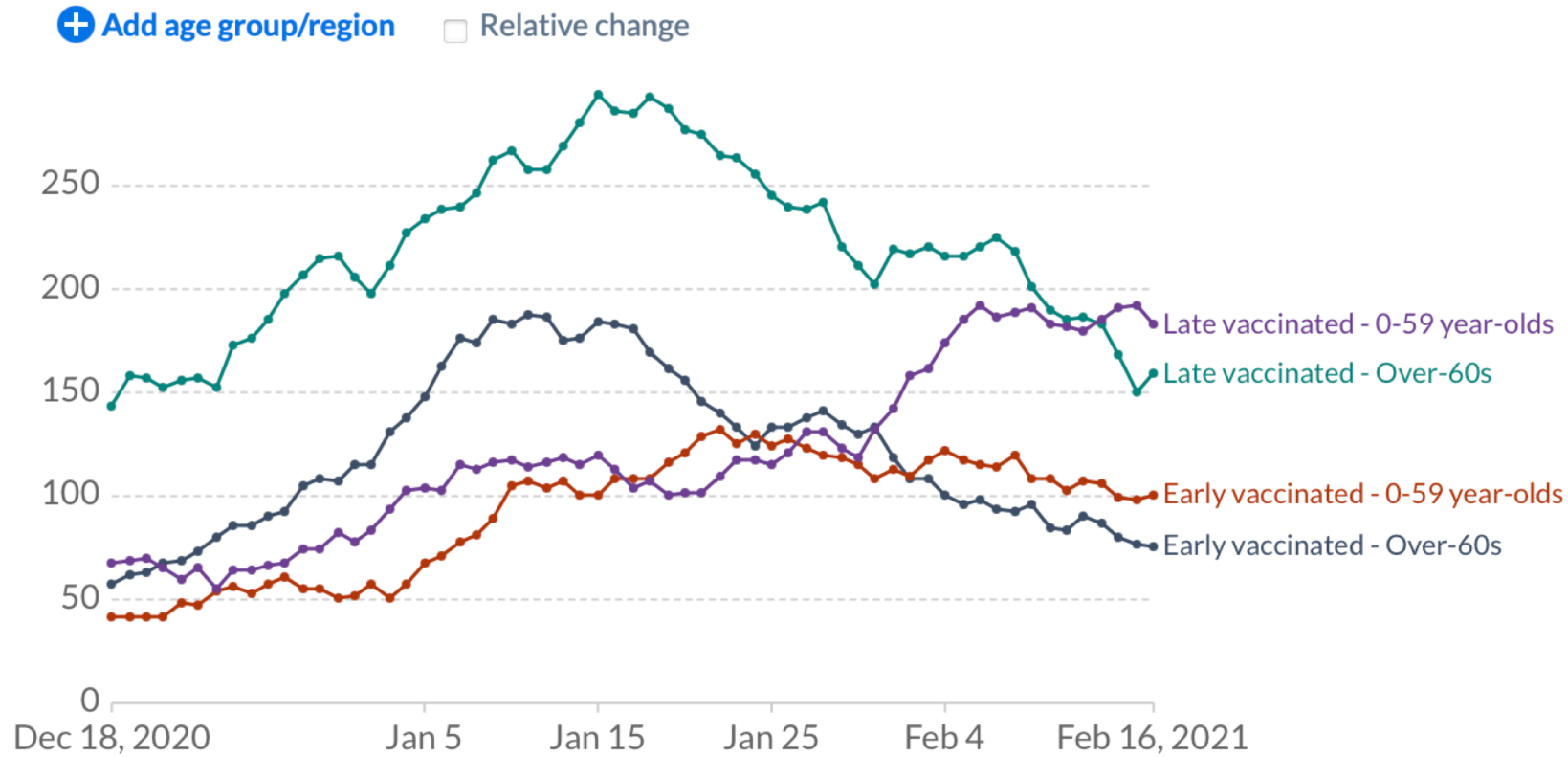


Israel: New hospitalizations for COVID-19 by age



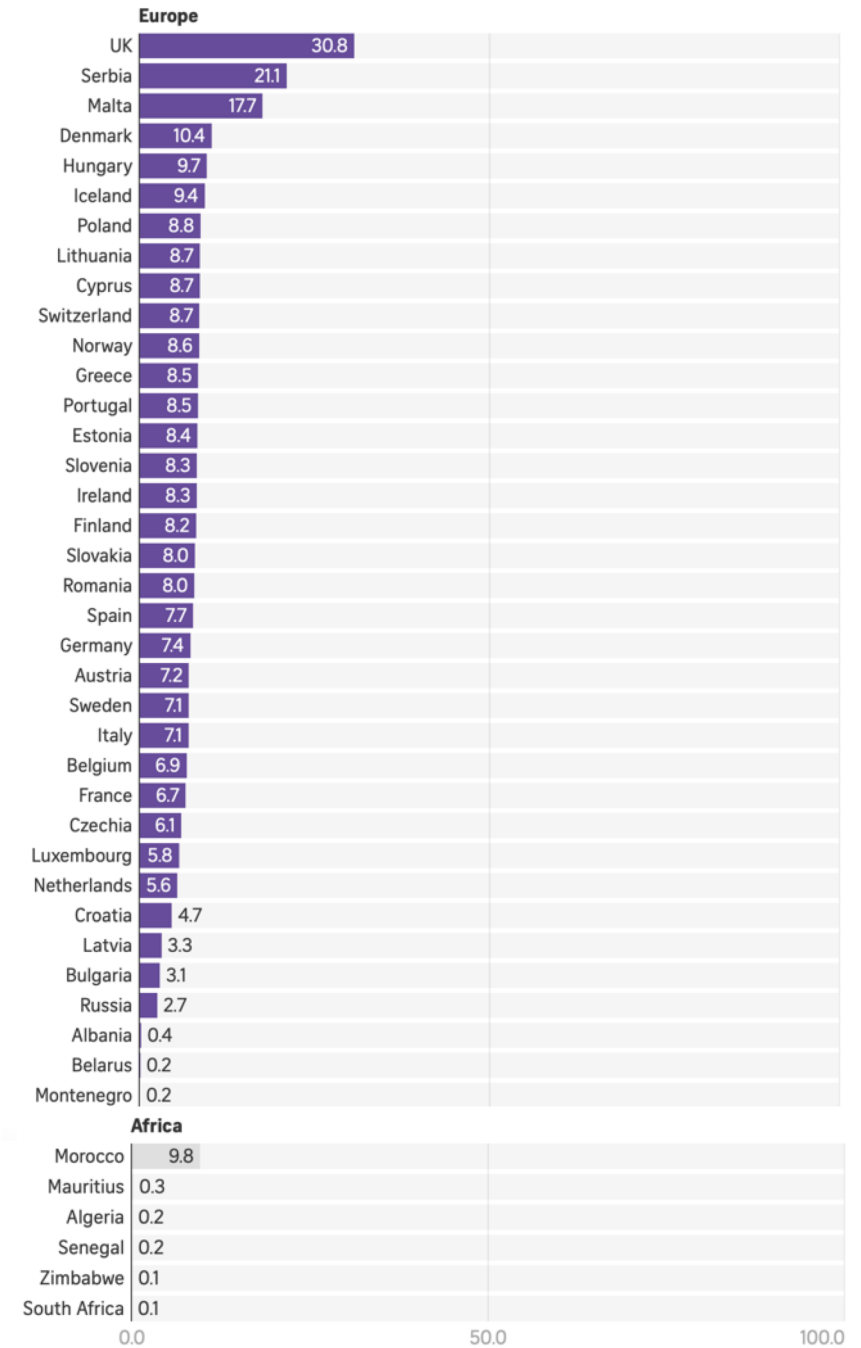
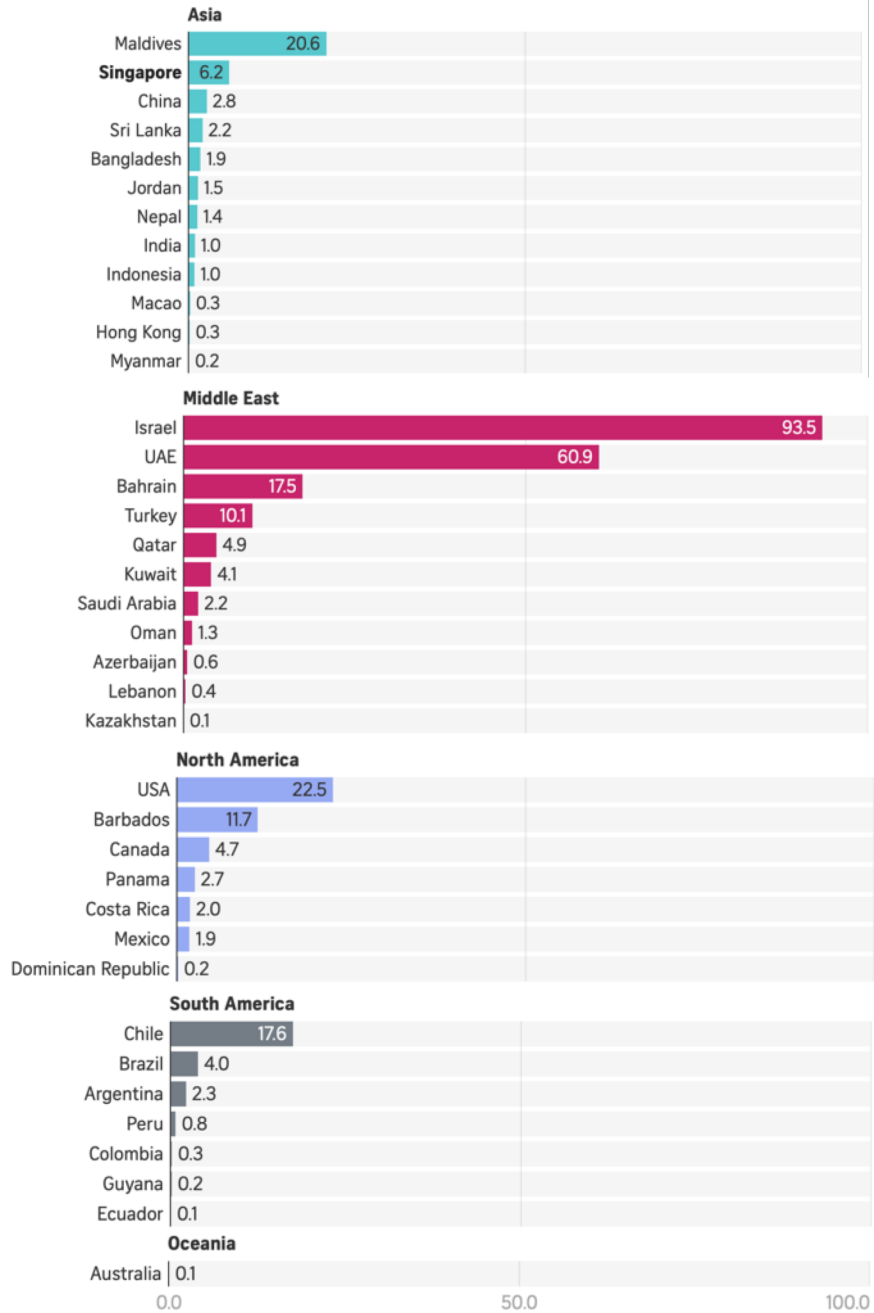
Shown is the rolling weekly sum of COVID-19 hospitalizations. Data is available at the national level, plus breakdown by regions where vaccination began early or late.

Vaccination in Israel began on December 19 2020. Israel imposed a third national lockdown on January 8 2021.



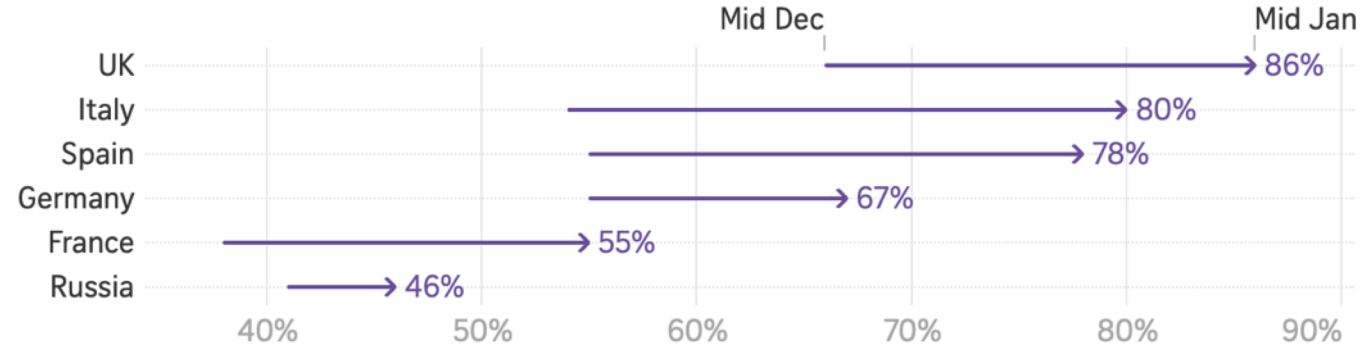
Source: Rossman, Shilo, Meir, Gorfine, Shalit & Segal (2021). Patterns of COVID-19 pandemic dynamics following deployment of a broad national immunization program.
CC BY

Vaccine doses administered per hundred

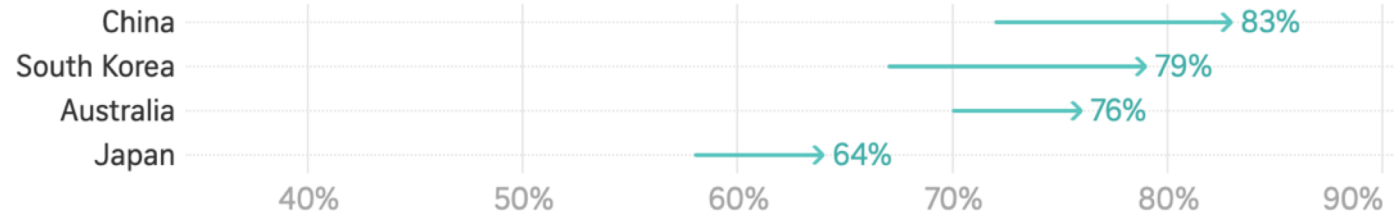


Percentage of strongly agree on getting vaccines if offered

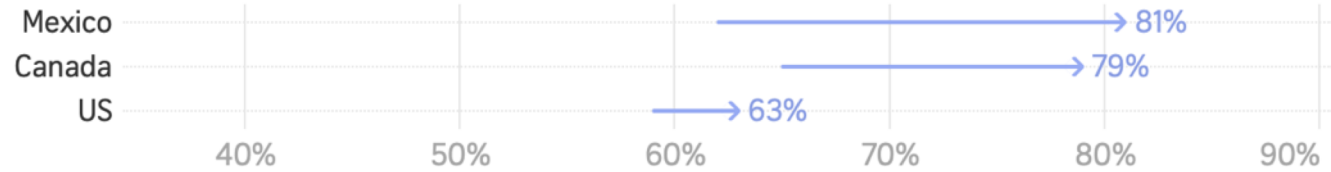
Europe



Asia & Oceania



North America



Africa & South America



Online samples in Brazil, China, Mexico, Russia, and South Africa tend to be more urban, educated, and/or affluent than the general population.

Source: Ipsos

Smallpox

Three Egyptian
Mummies
1570-1085 BC

Ramses the Vth
Died 1157 BC



18th century rhyme

Where are you going, my pretty maid

I'm going a milking, sir, she said

May I go with you, my pretty maid

You're kindly welcome, sir, she said

What is your father, my pretty maid

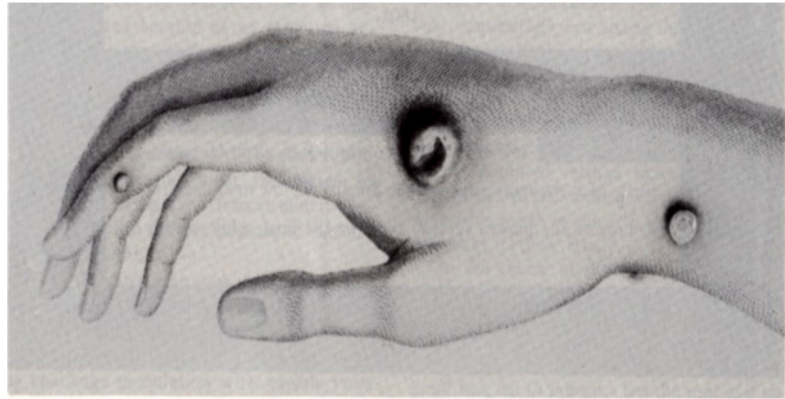
My father's a farmer, sir, she said

What is your fortune, my pretty maid

My face is my fortune, sir, she said

Smallpox vaccines

Jenner 1796



Cowpox lesions on the hand of Sarah Nelmes (case XVI in Jenner's *Inquiry*), from which material was taken for the vaccination of James Phipps below in 1796



Jenner's experiment

- 1st example of vaccination
- The word “vaccination” was coined in honour of Jenner's work
 - Louis Pasteur chose this word after developing a fowl cholera vaccine
 - *Vacca* is Latin for cow

Smallpox vaccine met with opposition from peers

- The Royal Society rejected his manuscript.
 - “in variance with established knowledge”
 - “he had better not promulgate such a wild idea if he valued his reputation.”
- Jenner published his findings in a pamphlet at his own expense.
 - *An Inquiry in the Causes and Effects of the Variolae Vaccinae, a Disease Discovered in Some of the Western Counties of England, Particularly Gloucestershir and Known by the Name of Cowpox*

Anti-vaccination sentiments

*“Now look around, and turn each trifling page,
Survey the previous works that please the age;
What varied wonders tempt us as they pass!
The cowpox, tractors, galvanism and gas in turn appears”*

Lord Byron



The Cow Pock — or — the Wonderful Effects of the New Inoculation! — See the Publications of J. Ashurst & Co. No. 1, St. Paul's Churchyard.

Recognition of Jenner's work

Yours is the comfortable reflection that mankind can never forget that you have lived. Future nations will now by history only that the loathsome smallpox had existed and by you has been extirpated.

Letter from President Thomas Jefferson to Jenner, 1806

Napolean released English prisoners of war upon Jenner's request and remarked that he could not "*refuse anything to such a great benefactor of mankind.*"

Types of vaccines

Live attenuated

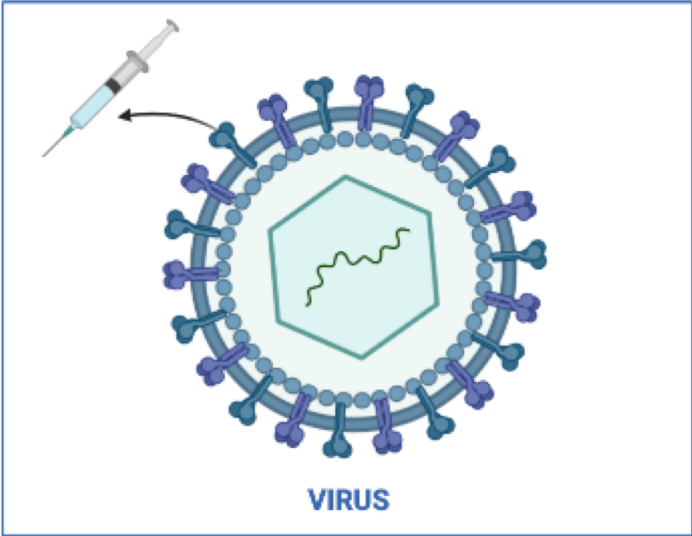
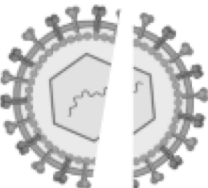


Inactivated

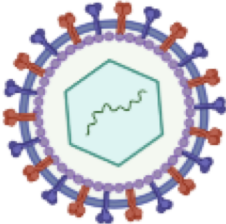


Sinovac
Bharat Biotech

Split inactivated



Recombinant viral vector



Astra Zeneca
J&J
Sputnik V

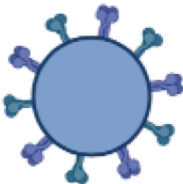
Recombinant bacterial vector



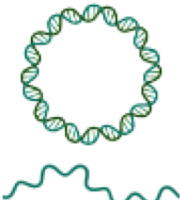
Synthetic peptides



Virus-like particles



DNA or RNA



Recombinant subunits



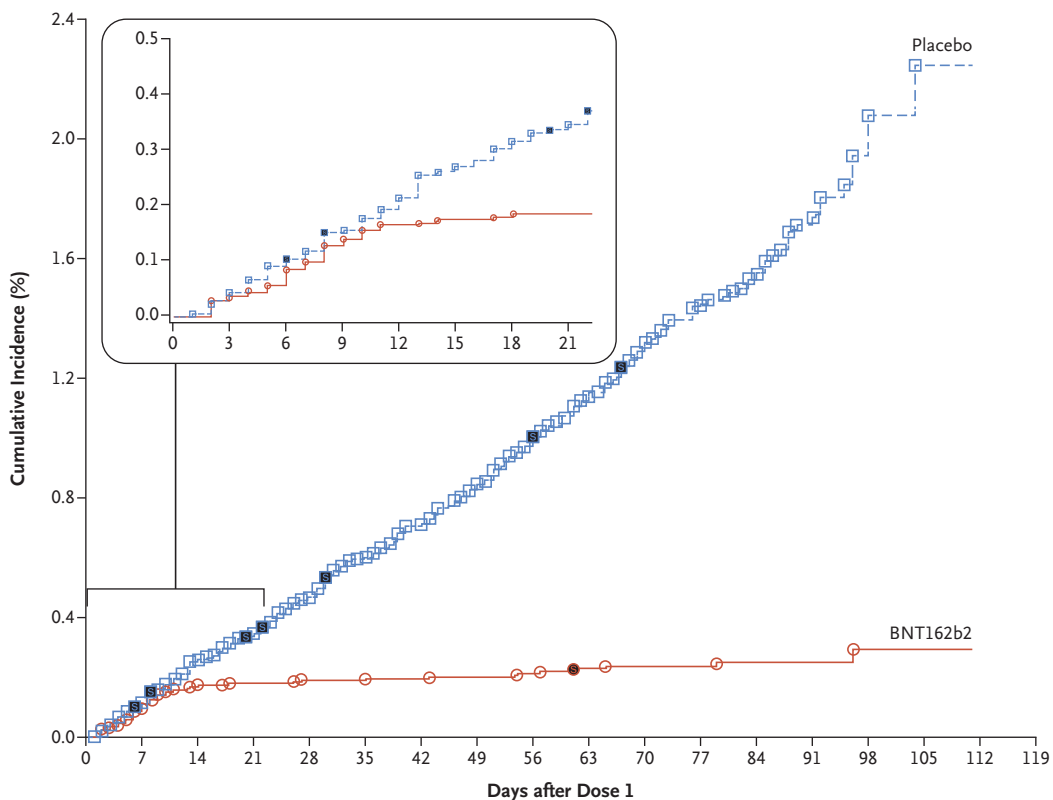
Novavax

Created in BioRender.com 

Pfizer, Moderna
Arcturus/Duke-NUS

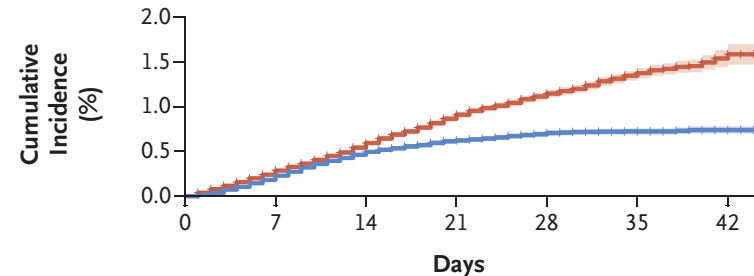
BNT162b2 show efficacy ~12 days after 1st dose

Pfizer/BNT



Polack et al, NEJM 2020

B Symptomatic Covid-19



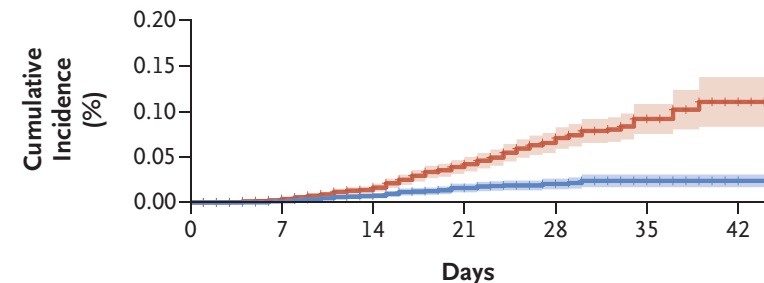
No. at Risk

Unvaccinated	596,618	413,768	262,662	187,784	108,242	37,564	4204
Vaccinated	596,618	414,140	263,179	188,740	109,261	38,299	4288

Cumulative No. of Events

Unvaccinated	0	1419	2393	3079	3433	3582	3607
Vaccinated	0	1103	1967	2250	2373	2387	2389

D Severe Covid-19



No. at Risk

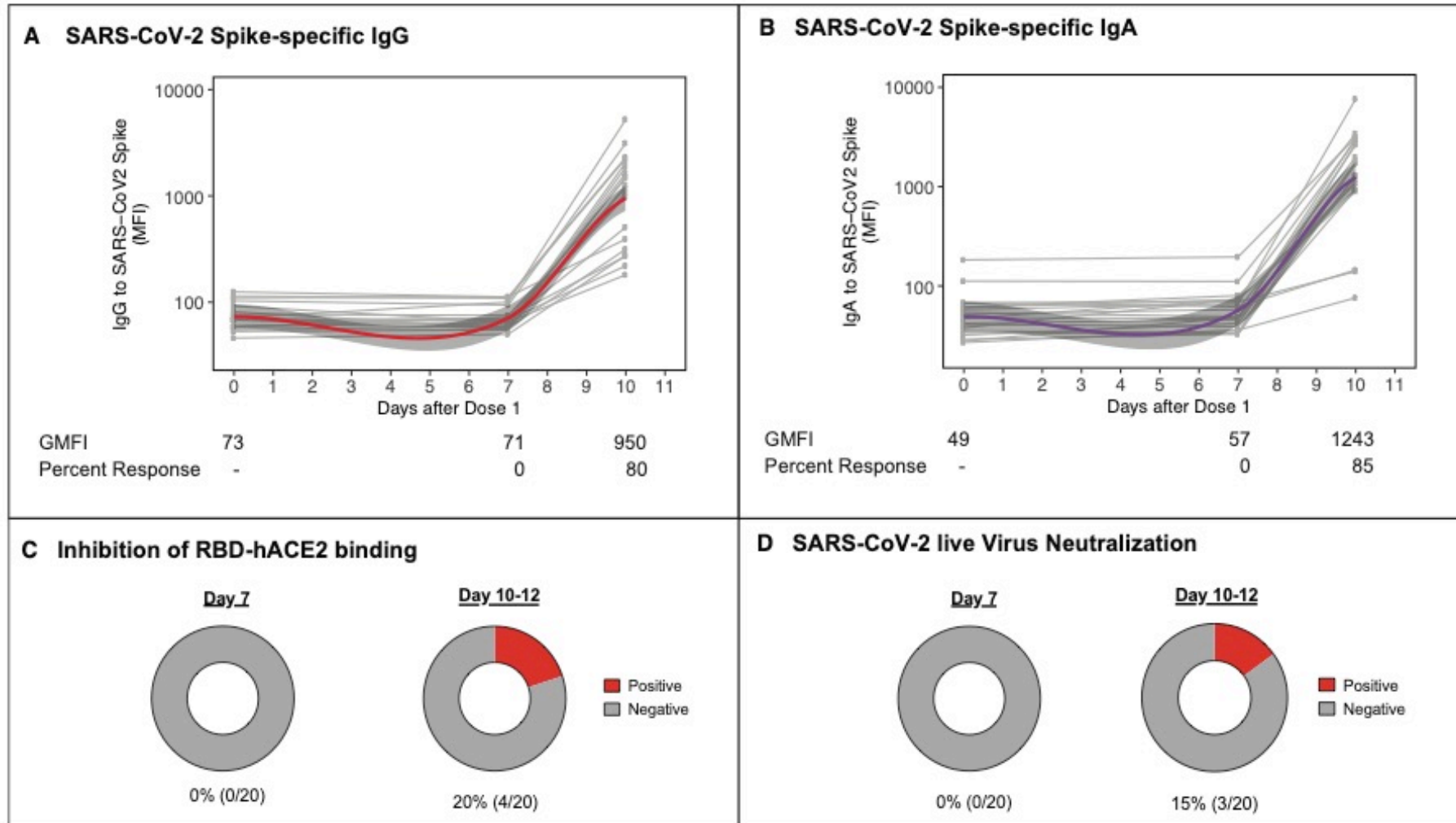
Unvaccinated	596,618	414,898	264,437	189,874	109,929	38,467	4310
Vaccinated	596,618	414,933	264,516	190,000	110,076	38,571	4322

Cumulative No. of Events

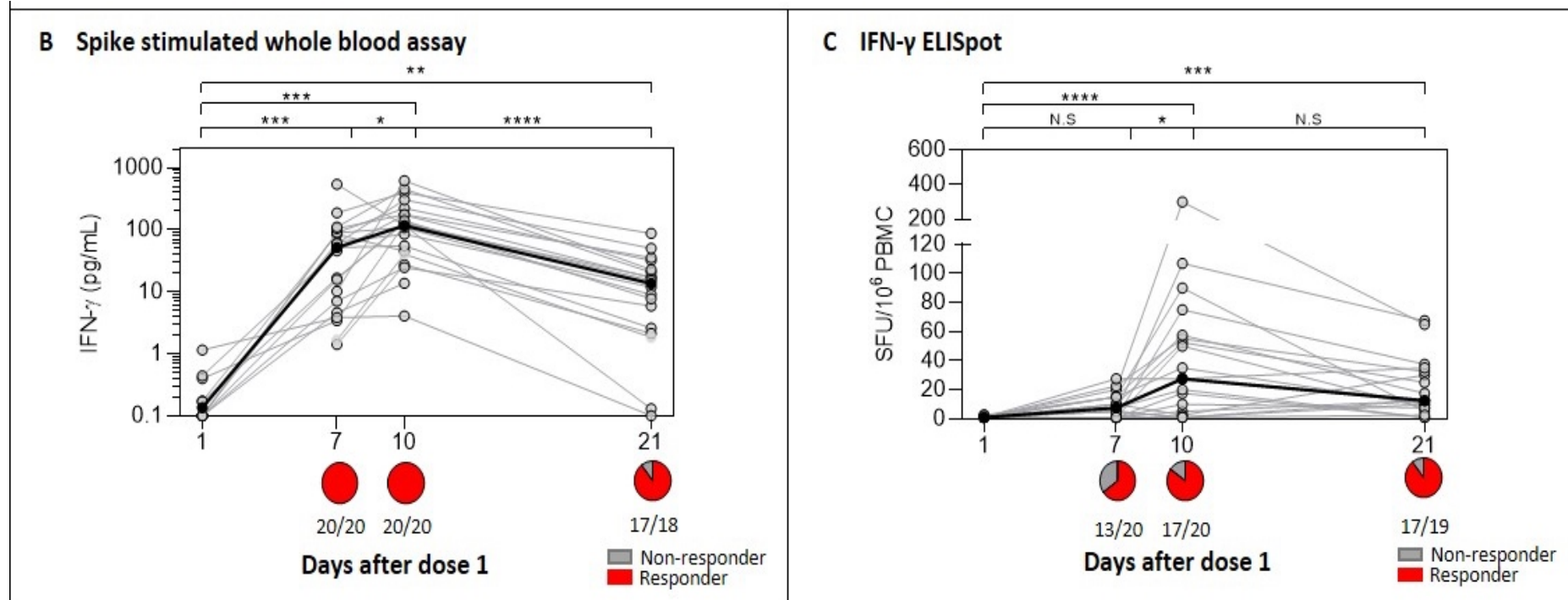
Unvaccinated	0	17	57	114	157	171	174
Vaccinated	0	6	26	45	52	55	55

Dagan et al, NEJM 2021

Serological response at days 7 and 10 after dose 1 of BNT162b2



T cell responses at days 7 and 10 after dose 1 of BNT162b2

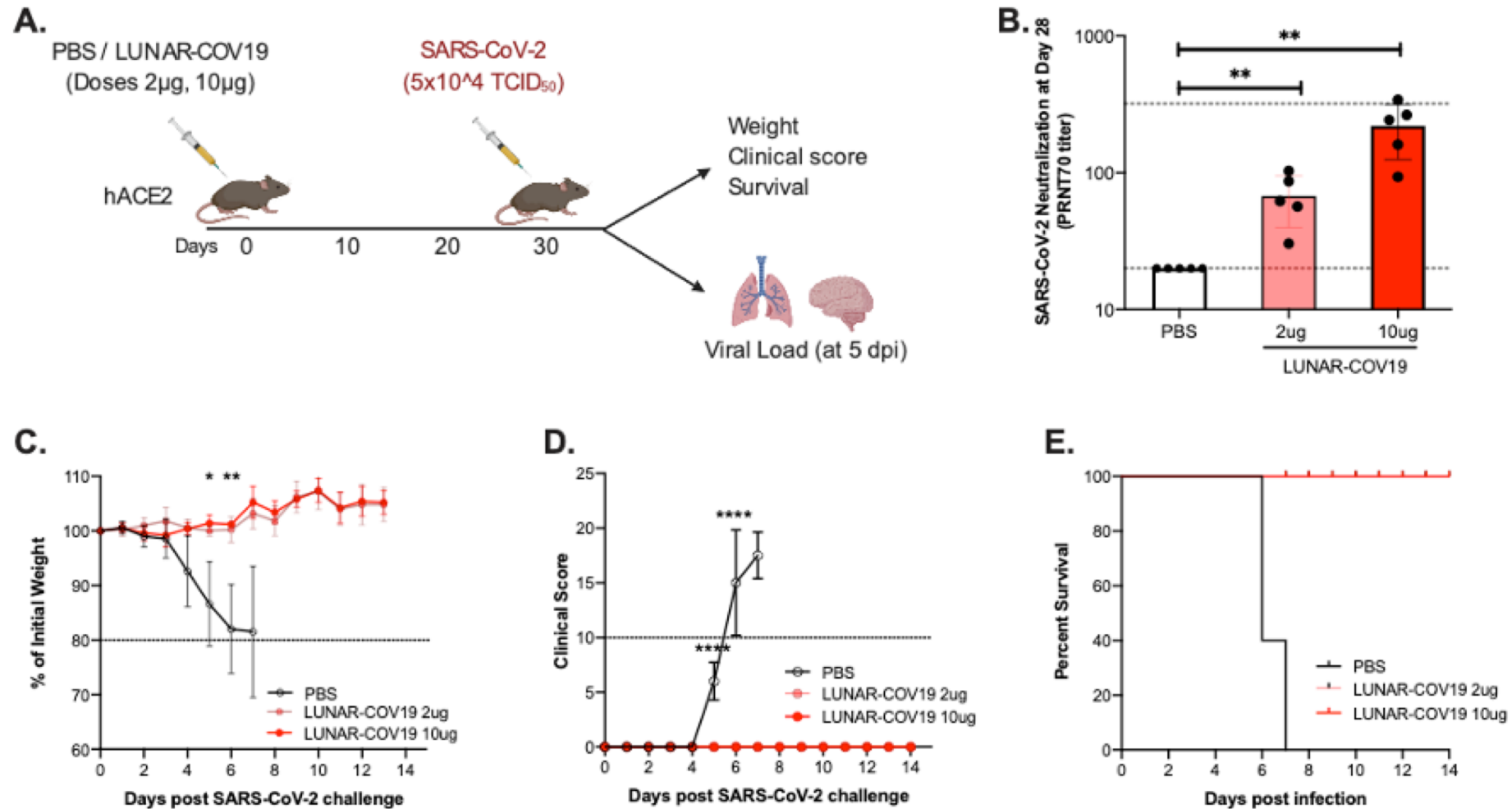


Bertoletti Lab

Kalimuddin et al, manuscript submitted

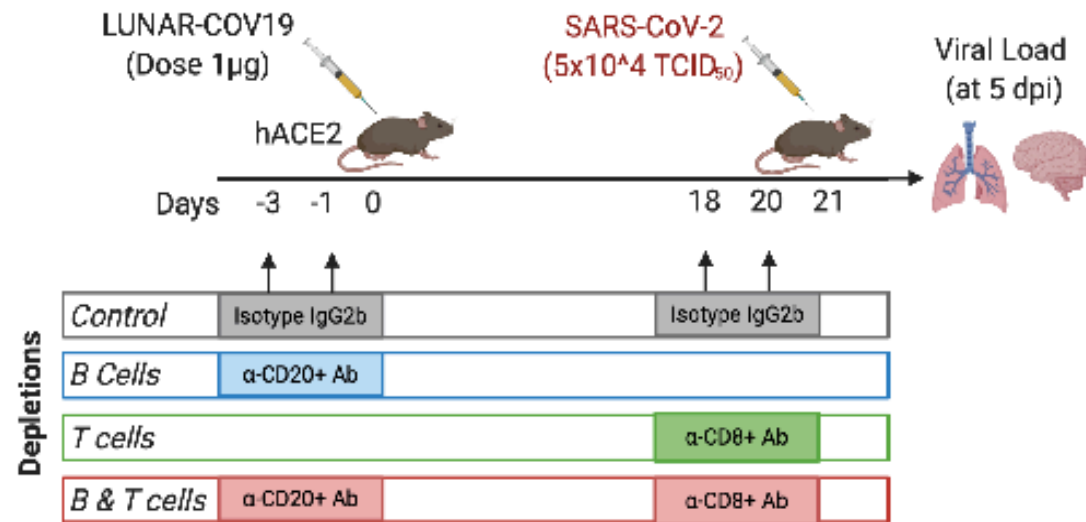
T cell responses as a critical determinant of human immunity?

Single dose Lunar-CoV19 protects human ACE2 transgenic mice against lethal SARS-CoV-2 infection

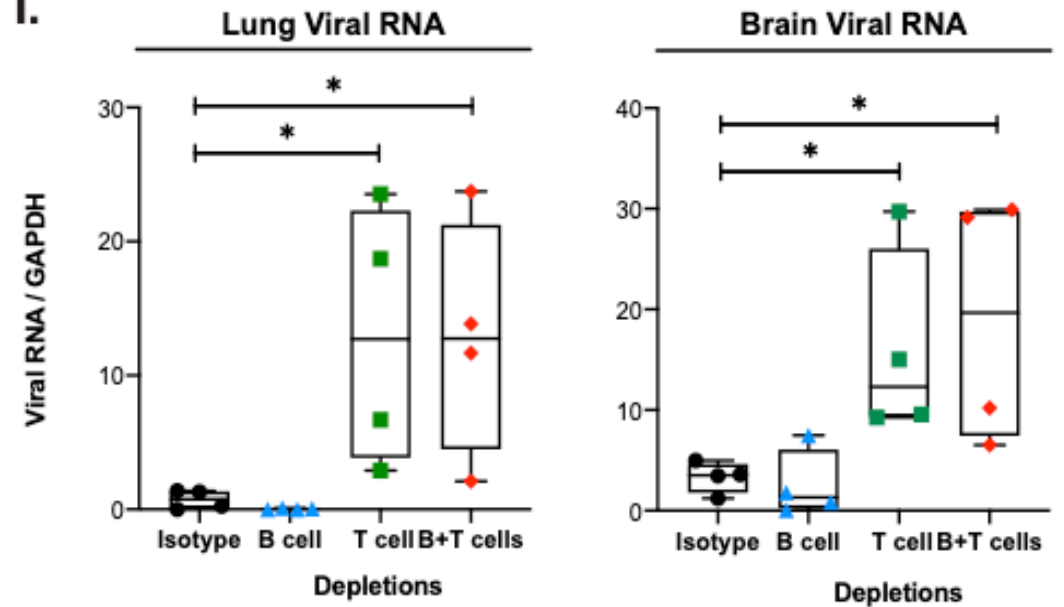


CD8+ T cells play a critical role in preventing SARS-CoV-2 infection

H.



I.

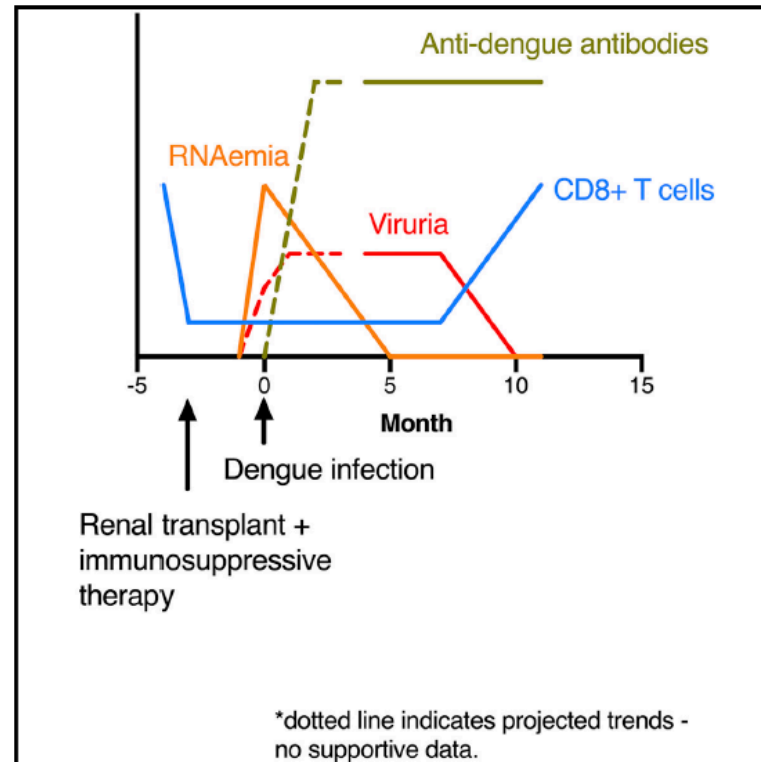


Clinical evidence for protective role of T cells

Cell Host & Microbe

Persistent Dengue Infection in an Immunosuppressed Patient Reveals the Roles of Humoral and Cellular Immune Responses in Virus Clearance

Graphical Abstract



Authors

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Hwee Cheng Tan, ...,
Paul Ananth Tambyah, Eng Eong Ooi,
Hui-Kim Yap

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In Brief

Examining a lymphopenic kidney transplant patient presented with dengue virus (DENV) infection, Ng et al. observed that the virus persisted in blood and urine despite detectable antibodies. Full resolution of DENV infection coincided with recovery of CD8+ counts, suggesting a role of cellular immunity in sterilizing dengue virus infection.

SARS-CoV-2-specific T cell immunity in cases of COVID-19 and SARS, and uninfected controls

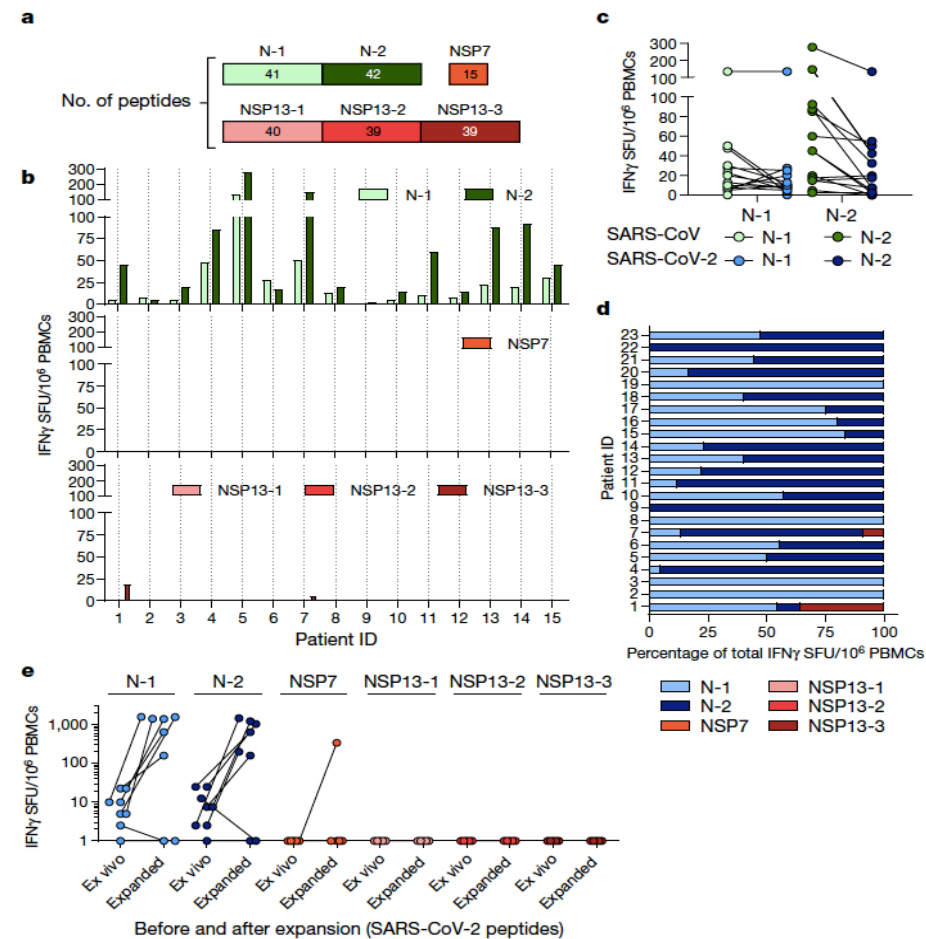
<https://doi.org/10.1038/s41586-020-2550-z>

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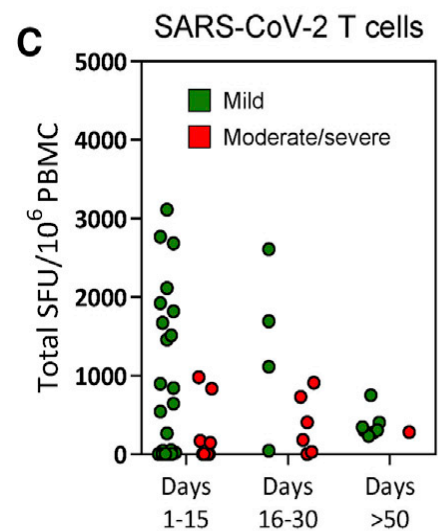
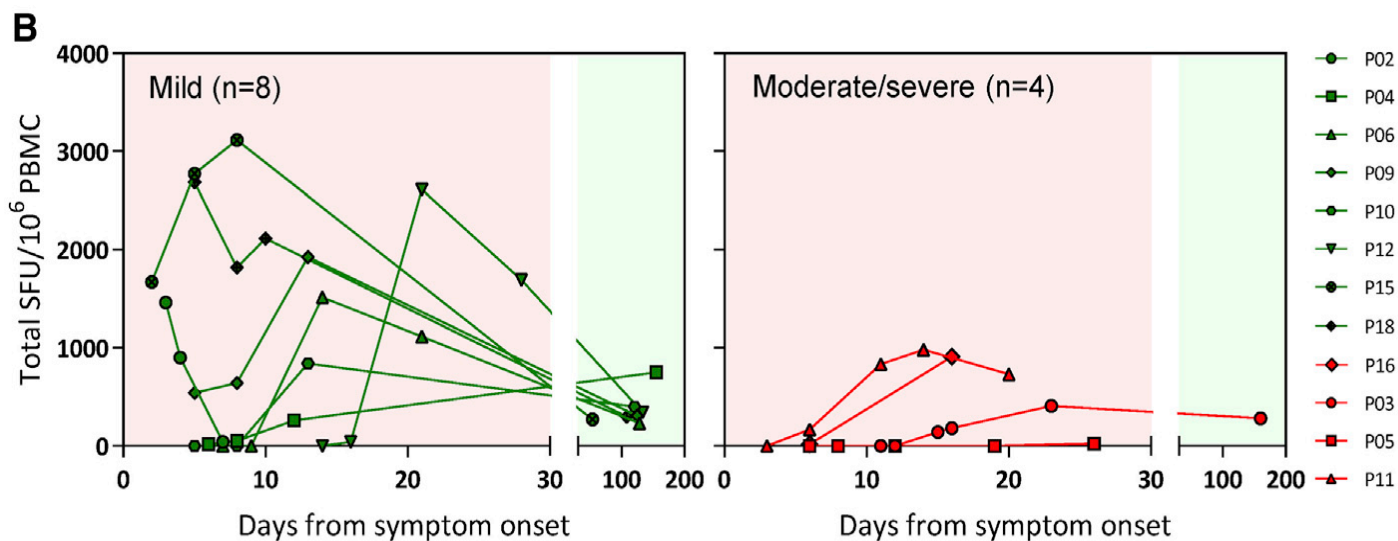
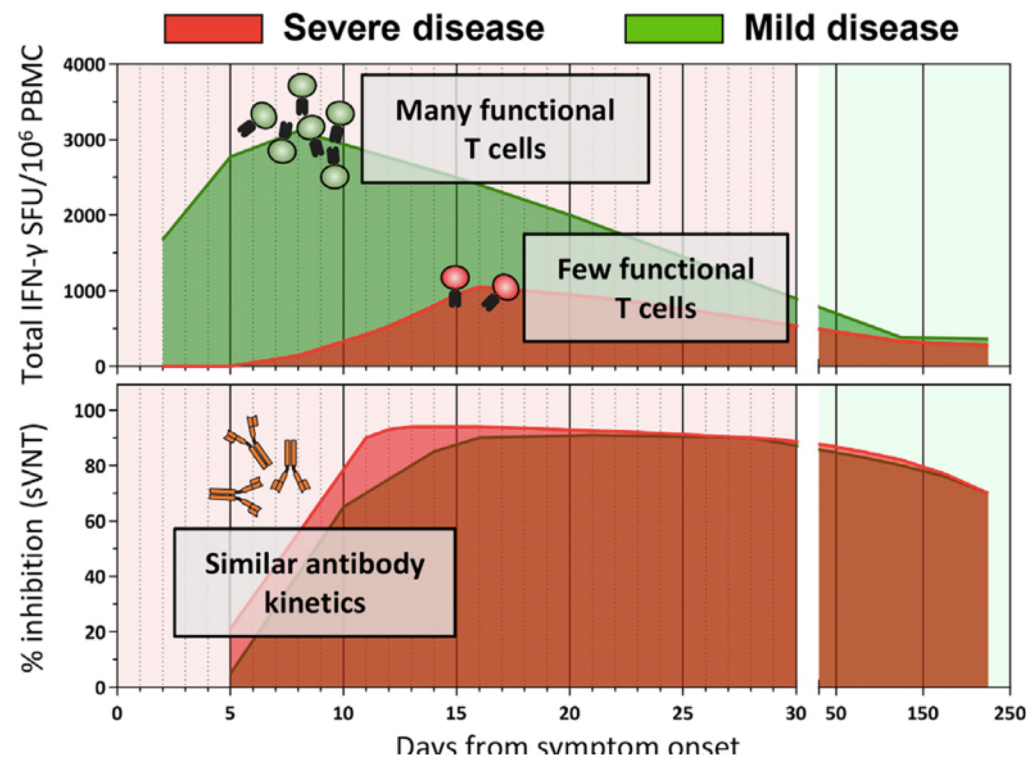
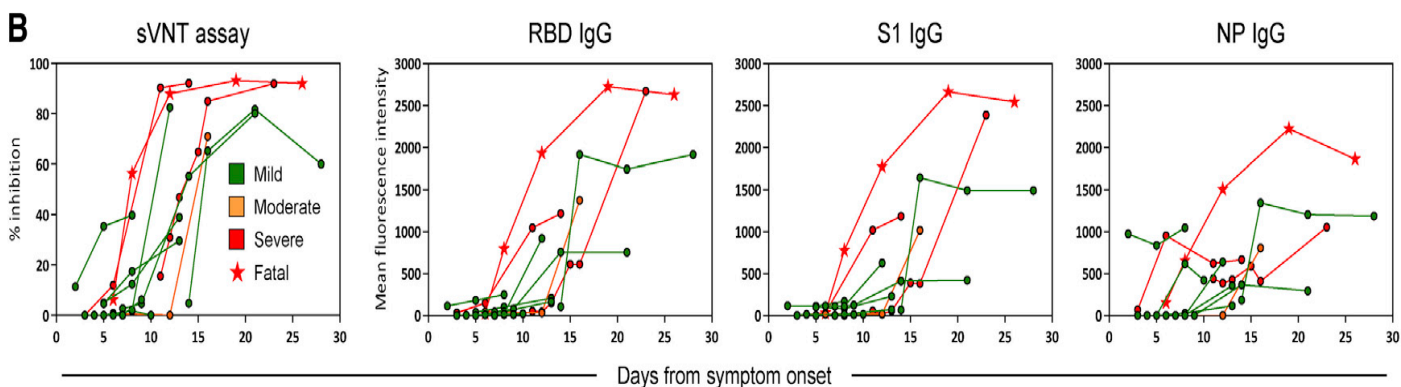
Nina Le Bert^{1,9}, Anthony T. Tan^{1,9}, Kamini Kunasegaran¹, Christine Y. L. Tham¹, Morteza Hafezi¹, Adeline Chia¹, Melissa Hui Yen Chng¹, Melyin Lin^{1,2}, Nicole Tan¹, Martin Linster¹, Wan NI Chia¹, Mark I-Cheng Chen³, Lin-Fa Wang¹, Eng Eong Ooi¹, Shirin Kalimuddin⁴, Paul Anantharajah Tambyah^{5,6}, Jenny Guek-Hong Low^{1,4}, Yee-Joo Tan^{2,7} & Antonio Bertoletti^{1,8}✉



Report

Early induction of functional SARS-CoV-2-specific T cells associates with rapid viral clearance and mild disease in COVID-19 patients

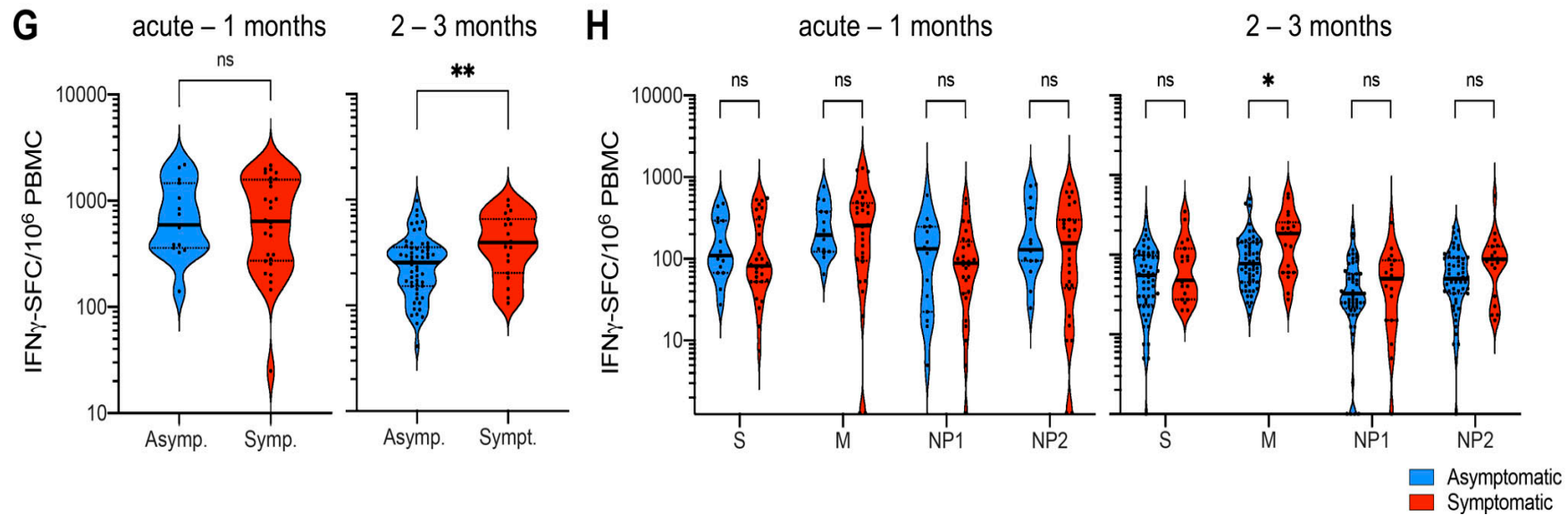
Anthony T. Tan,^{1,8} Martin Linster,^{1,8} Chee Wah Tan,¹ Nina Le Bert,¹ Wan Ni Chia,¹ Kamini Kunasegaran,¹ Yan Zhuang,¹ Christine Y.L. Tham,¹ Adeline Chia,¹ Gavin J.D. Smith,¹ Barnaby Young,^{2,3,4} Shirin Kalimuddin,^{1,5} Jenny G.H. Low,^{1,5} David Lye,^{2,3,4,6} Lin-Fa Wang,¹ and Antonio Bertoletti^{1,7,9,*}



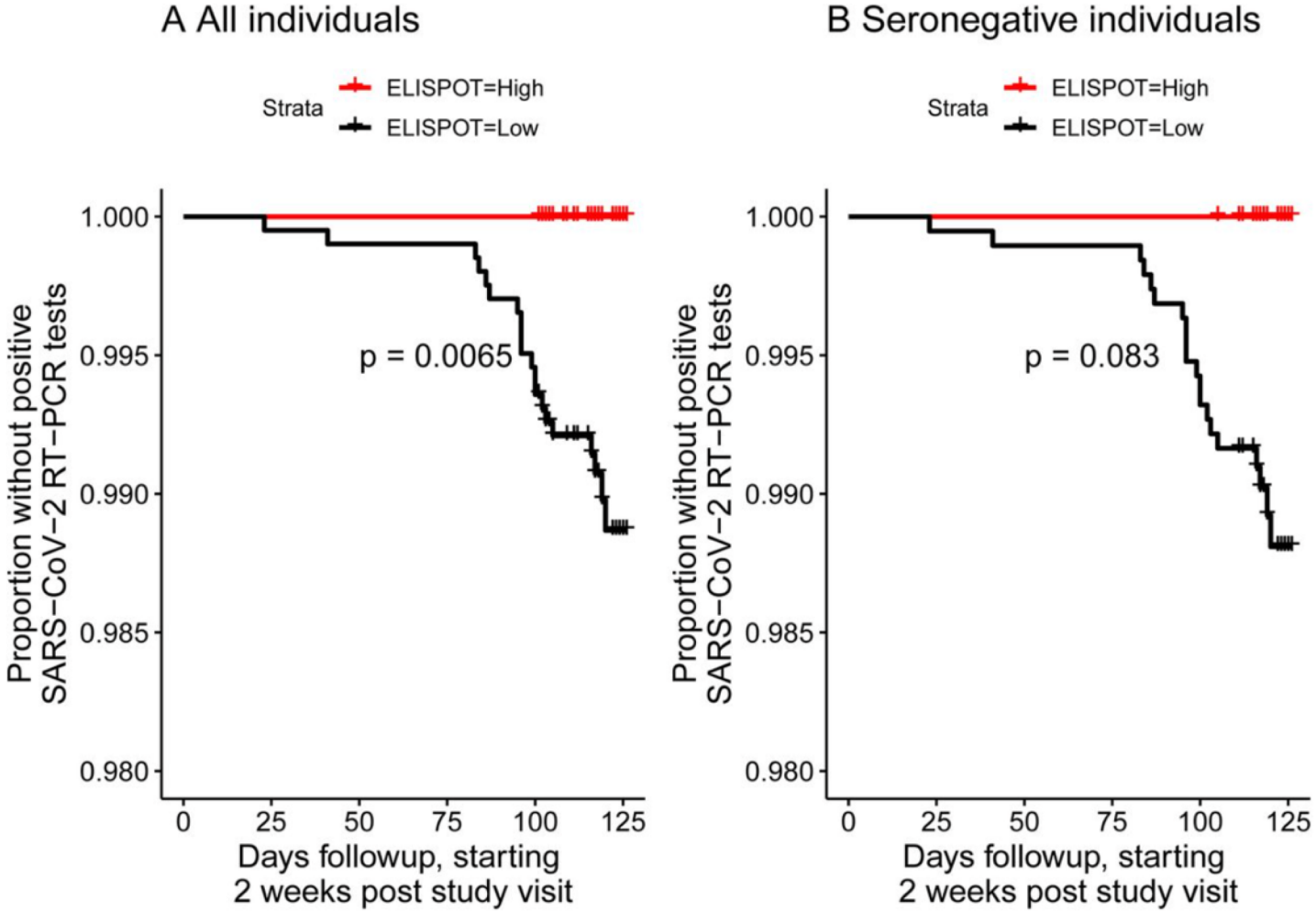
ARTICLE

Highly functional virus-specific cellular immune response in asymptomatic SARS-CoV-2 infection

Nina Le Bert¹, Hannah E. Clapham², Anthony T. Tan¹, Wan Ni Chia¹, Christine Y.L. Tham¹, Jane M. Lim², Kamini Kunasegaran¹, Linda W.L. Tan², Charles-Antoine Dutertre³, Nivedita Shankar², Joey M.E. Lim¹, Louisa Jin Sun⁴, Marina Zahari², Zaw Myo Tun², Vishakha Kumar², Beng Lee Lim¹, Siew Hoon Lim⁵, Adeline Chia¹, Yee-Joo Tan^{6,7}, Paul Anantharajah Tambyah⁸, Shirin Kalimuddin^{1,9}, David Lye^{6,10,11,12}, Jenny G.H. Low^{1,9}, Lin-Fa Wang¹, Wei Yee Wan⁵, Li Yang Hsu², Antonio Bertoletti^{1,13*}, and Clarence C. Tam^{2,14*}

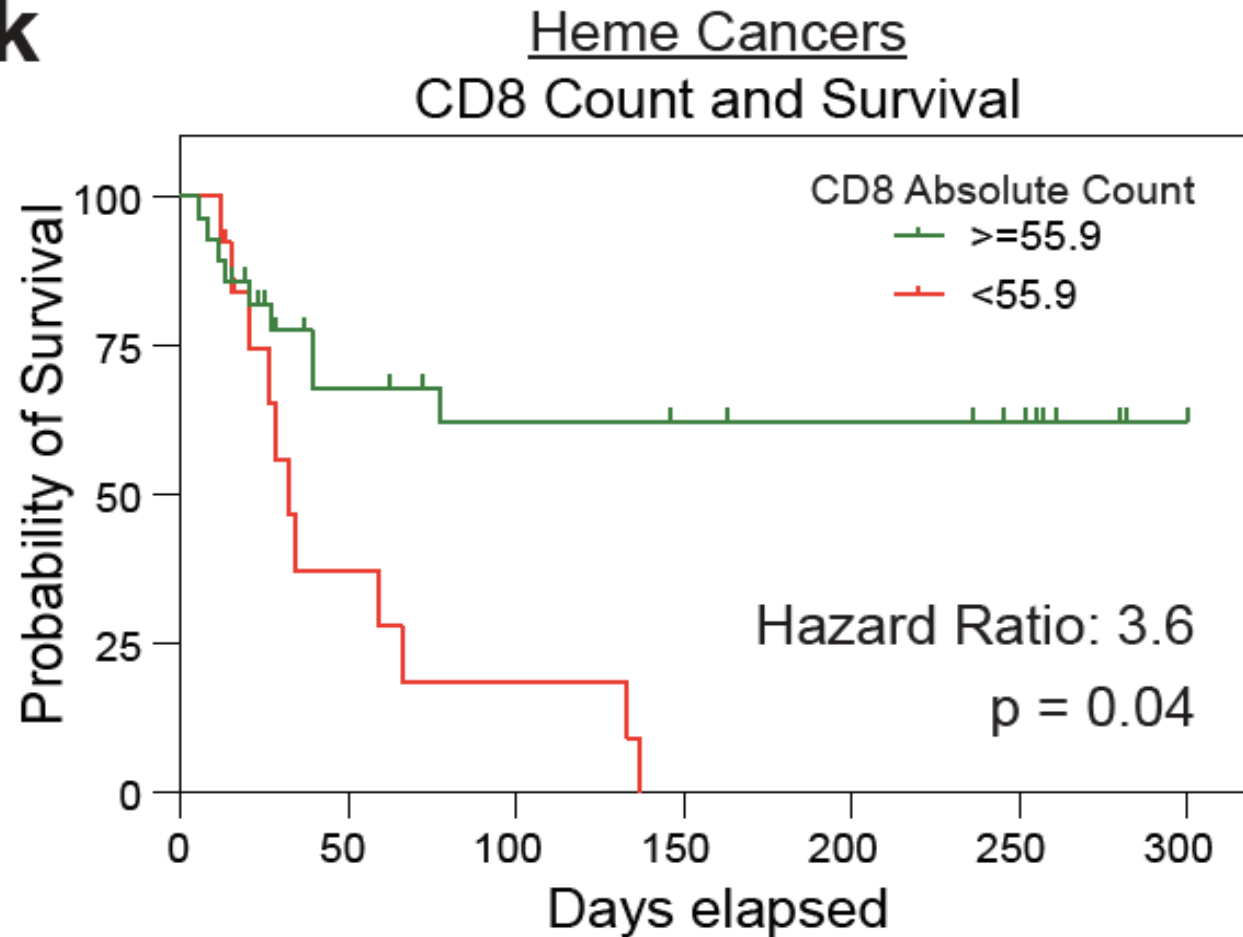


SARS-CoV-2 responsive T cells protect against COVID-19



CD8 T cells compensate for impaired humoral immunity in COVID-19 patients with hematologic cancer

k



Conclusion

- Total binding antibodies and T cells appear sufficient for protection against Covid-19
- Depletion of T cells but not B cells associated with severe Covid-19 in animal model and in hematological malignancy patients
- Early T cell response associated with better clinical outcome in Covid-19 patients
- Vaccine that produces good T cell immunity would be less impacted by SARS-CoV-2 variants

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Abigail Wong

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Jun Tanaka

