COVID-19 LITERATURE BRIEFING
January 6th, 2021

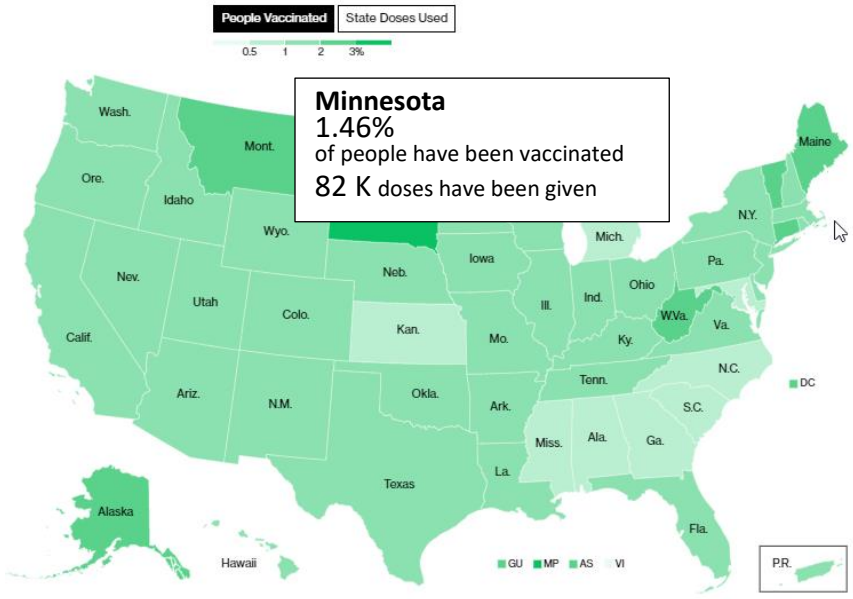
Children's MINNESOTA

Reference of the Week

- Vaccine tracker sites:

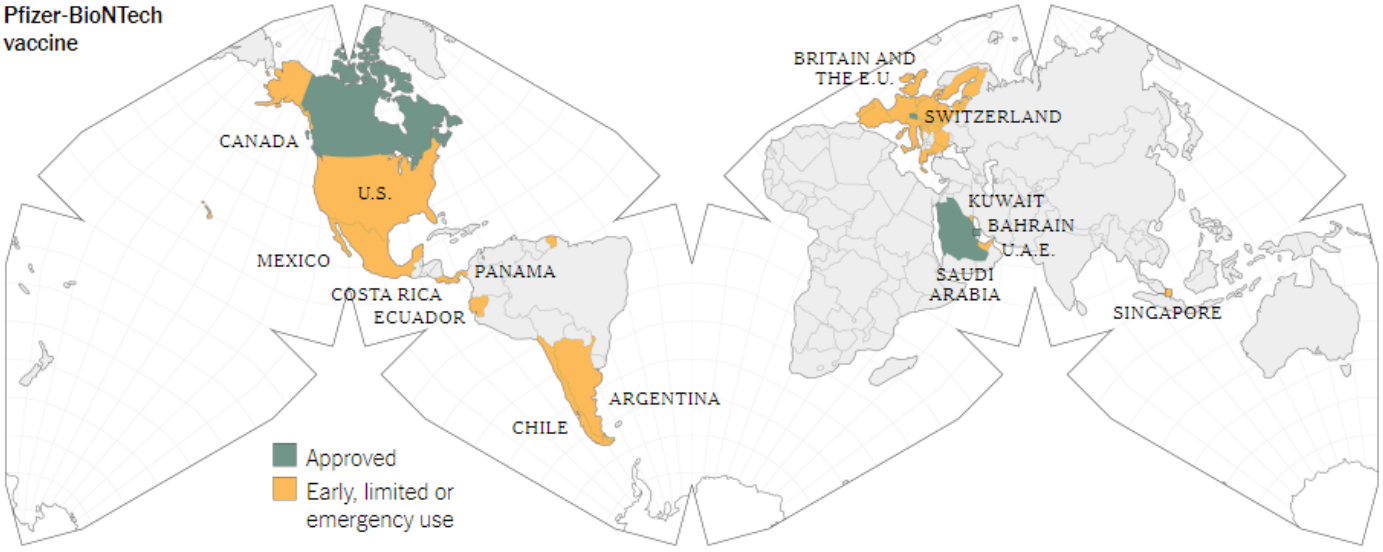
1. Bloomberg vaccine tracker. https://www.bloomberg.com/graphics/covid-vaccine-tracker-global-distribution/

The site has tabs for Vaccine Tracker, Vaccine Contracts, Global Cases, US Cases, US Hospitalization , and US Regions. An interactive US map follows vaccine administration on a state-by-state basis.:



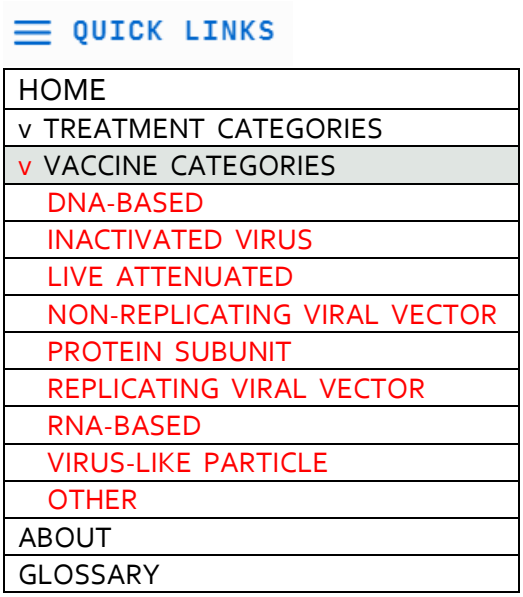
2. The New York Times Coronavirus Vaccine Tracker: https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html

The site has a wealth of information about vaccines, products, trial status, and global approval status. The graphics are in some cases stunning particularly secondary sites within the tracker.



SEE THE ARTICLE CABINET ON THE S: DRIVE, "COVID-19 ARTICLE RESOURCE CABINET" FOR CHILDREN'S FULL COLLECTION

3. Milken Institute: COVID-19 Treatment and Vaccine Tracker https://covid-19tracker.milkeninstitute.org/
This site tracks not only vaccines (236) but also COVID-19 treatments (319). There is a section on *vaccines in use* worldwide and a SPREADSHEET (Airtable) with multiple well sorted columns to find information relatively quickly.



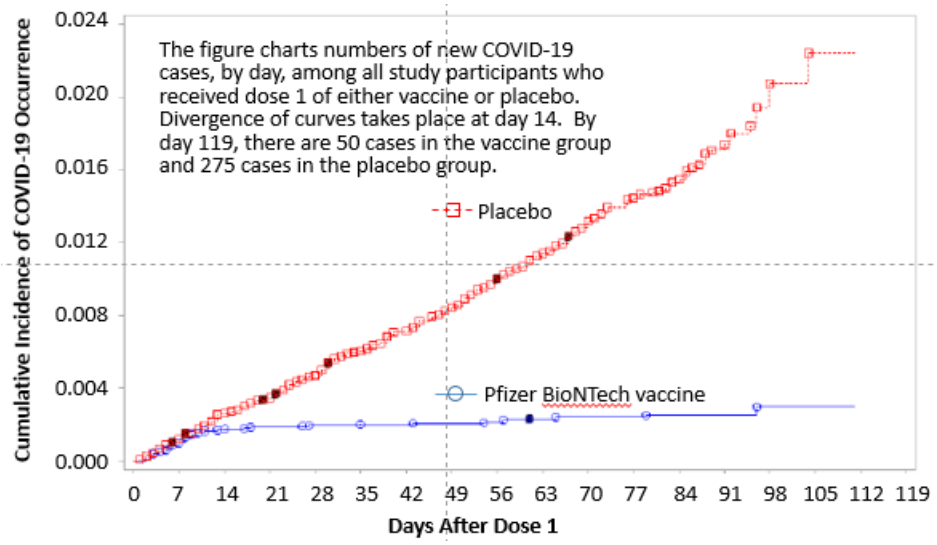
Other References:

- Volz E. Transmission of SARS-CoV-2 Lineage B.1.1.7 in England: Insights from linking epidemiological and genetic data. Report 42. Imperial College of London. MRC Centre for Global Infectious Disease Analysis. 12.31.2020. https://www.imperial.ac.uk/mrc-global-infectious-disease-analysis/covid-19/report-42-sars-cov-2-variant/ pdf
Findings: 1. The transmission advantage of the B.1.1.7 variant increase the reproductive number (R) between 0.4 and 0.7 or a 50% - 75% increase in transmission consistent with exponential growth. **2.** The change in transmission detected took place when social distancing, masking, and public health alerts were in place. **3.** There is concern that a small but statistically significant shift towards the under 20 year old age group is more affected by the B.1.1.7 variant. **4.** The B.1.1.7 variant includes at least 6 substitutions in the spike protein including the N501Y replacement that has been shown to increase ACE2 binding and cell infectivity in animal models.

- Baden LR. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine [Moderna]. NEJM. 12.30.2020. https://www.nejm.org/doi/full/10.1056/NEJMoa2035389 pdf
Premise/Methods: 1. mRNA technology has evolved over the last decade but no mRNA vaccine has been approved for human use other than the recently EUA of the Pfizer-BioNTech vaccine (BNT162b2). **2.** The global SARS-CoV-2 vaccine requirement exceeds the capacity of any single company necessitating development of multiple vaccines. **3.** Phase 3 placebo randomized control trial of 2 IM injections of mRNA-1273 with the primary endpoint being prevention of COVID-19. **4.** Vaccine mRNA-1273 was stored at 2° to 8°C (35.6° to 46.4°F) at clinical sites. Doses could be held in syringes for up to 8 hours at room temperature before administration.
Findings: 1. 30,351 subjects were randomized: demographics balanced between the two groups; mean age, 51.4 years; 24.8% were 65 years or older; 16.7% were 65 years or older and at risk for severe COVID-19; participants 79.2% White, 10.2% Black, 20.5% Hispanic or Latino; both groups had participants with serologic evidence of SARS-CoV-2 (2.3% mRNA, 2.2% placebo). **2.** Injection site adverse event were common in the mRNA group after both the first (84.2% vs 19.8%) and second (88.6% vs 18.8%) doses. Solicited systemic adverse events occurred more often in the mRNA group than in the placebo group after both the first dose (54.9%, vs. 42.2%) and the second dose (79.4%, vs. 36.5%). Severe events in both groups were uncommon and no evidence of vaccine-associated enhanced respiratory disease was noted. **3.** 196 cases of COVID-19 were diagnosed: 11 cases in

the mRNA group and 185 cases in the placebo group indicating 94.1% in the study population and there were 30 cases of severe disease, all in the placebo group.
This favorable vaccine safety and efficacy study does not answer key questions: 1) what is the durability of protection; 2) does asymptomatic infection occur; 3) are vaccinated individuals with asymptomatic disease infectious; and 4) what is the rate of anaphylaxis (3 cases thus far with Pfizer) and long term safety profile of vaccinated individuals.

- EMERGING CONTROVERSY: Immunizing as many individuals as possible by delaying the administration of the second dose. Although the phase 3 trials of Pfizer-BioNTech and Moderna did not seek efficacy in a single dose regimen there is some evidence in the materials submitted to the VRBPAC (Vaccines and Related Biological Products Advisory Committee) by Pfizer that such a strategy may have merit (see pdf) as efficacy after day 10 and before the second dose was over 85% (see Figure below). Similar findings are revealed in the NEJM Moderna article reviewed in this newsletter. On **12/30/2020** England announced that the second dose would be delayed from 3 weeks to 12 weeks in order vaccinate more individuals (Campbell D. *The Guardian*). On **01/01/2021** Dr. Fauci announced that the US would not be following the UK in delaying the second vaccine dose in order to vaccinate more individuals. To embark on such a strategy would not be in keeping with Dr. Fauci's insistence on data driven formulas to meet the challenge of the pandemic.



On **01/03/2121** Drs. Wachter and Jha supported a delay in administering a second dose due to supply constraints, distribution bottlenecks, pandemic surging, and a more infectious variant on the horizon (*The Washington Post).* On **01/04/2021** the FDA press release commented on delaying the second dose, reducing the dosage, and mix and matching vaccine administration. Succinctly, "Until vaccine manufacturers have data and science supporting a change, we continue to strongly recommend that health care providers follow the FDA-authorized dosing schedule for each COVID-19 vaccine" https://www.fda.gov/news-events/press-announcements/fda-statement-following-authorized-dosing-schedules-covid-19-vaccines#:~:text=The%20available%20data%20continue%20to,the%20first%20and%20second%20dose.

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