COVID-19 and C3G

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Learning objectives

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- To review the emergence of the pandemic and the timeline of important events
- To understand how C3G patients with native kidneys or transplants fare with COVID
- To review COVID19 and vaccination and its safety for C3G patients
- To understand how you may/should be treated if you get COVID and have a transplant

What is COVID-19?

- The 2019 novel coronavirus infection is a respiratory infection caused by a virus
- SARS-CoV-2 is the name of the virus, COVID-19 is the disease it causes
  - Related to SARS and MERS
- Causes respiratory symptoms including fever, cough and shortness of breath, and can lead to pneumonia
- Identified in December 2019 in Wuhan, China and has spread globally
- Believed to have originated from an animal host and is now spreading via human-to-human transmission

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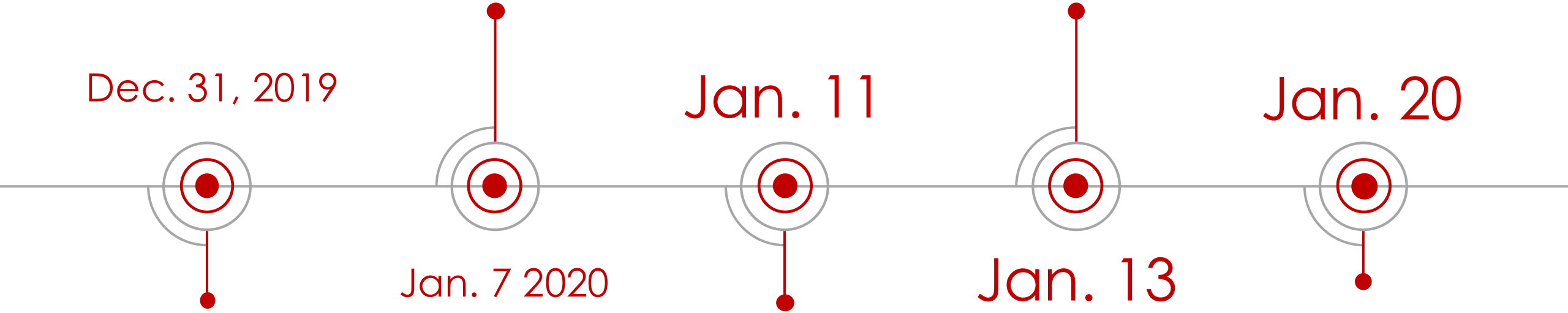
COVID-19: A Timeline



Dec. 31, 2019

China alerts WHO to several cases of unusual pneumonia in Wuhan.

Jan. 7 2020

WHO Officials announce they have identified a new virus, named 2019-nCoV and is identified as belonging to the coronavirus family, which includes SARS and the common cold.

Jan. 11

China announces its first death from the virus.

Jan. 13

The WHO reports the first case outside of China (Thailand) in a traveler who had visited Wuhan.

Jan. 20

A Chinese expert on infectious diseases confirmed human-to-human transmission to state broadcaster CCTV.

COVID-19: A Timeline

Jan. 30, 2020

WHO declares coronavirus a global emergency with cases being reported in the United States, Japan, Nepal, France, Australia, Malaysia, Singapore, South Korea, Vietnam and Taiwan.

Feb. 11

The WHO announces that the new coronavirus would be called "COVID-19".

Feb. 25

CDC warned that disruptions to the U.S. from COVID-19 could be severe. The agency expects the disease to begin spreading at the community level in the U.S

Feb. 5

NIH scientists began a randomized controlled trial of the antiviral drug remdesivir that had been developed for Ebola, on a patient infected with SARS-CoV-2. This is the first clinical trial in the U.S. for an experimental treatment for COVID-19

COVID-19: A Timeline

Feb. 29, 2020

The FDA took steps to expand novel coronavirus testing to hospital clinical microbiology laboratories.

Mar. 11

After more than 118,000 cases in 114 countries and 4,291 deaths, the World Health Organization declares the coronavirus outbreak a pandemic, acknowledging that the virus will likely spread to all countries on the globe.

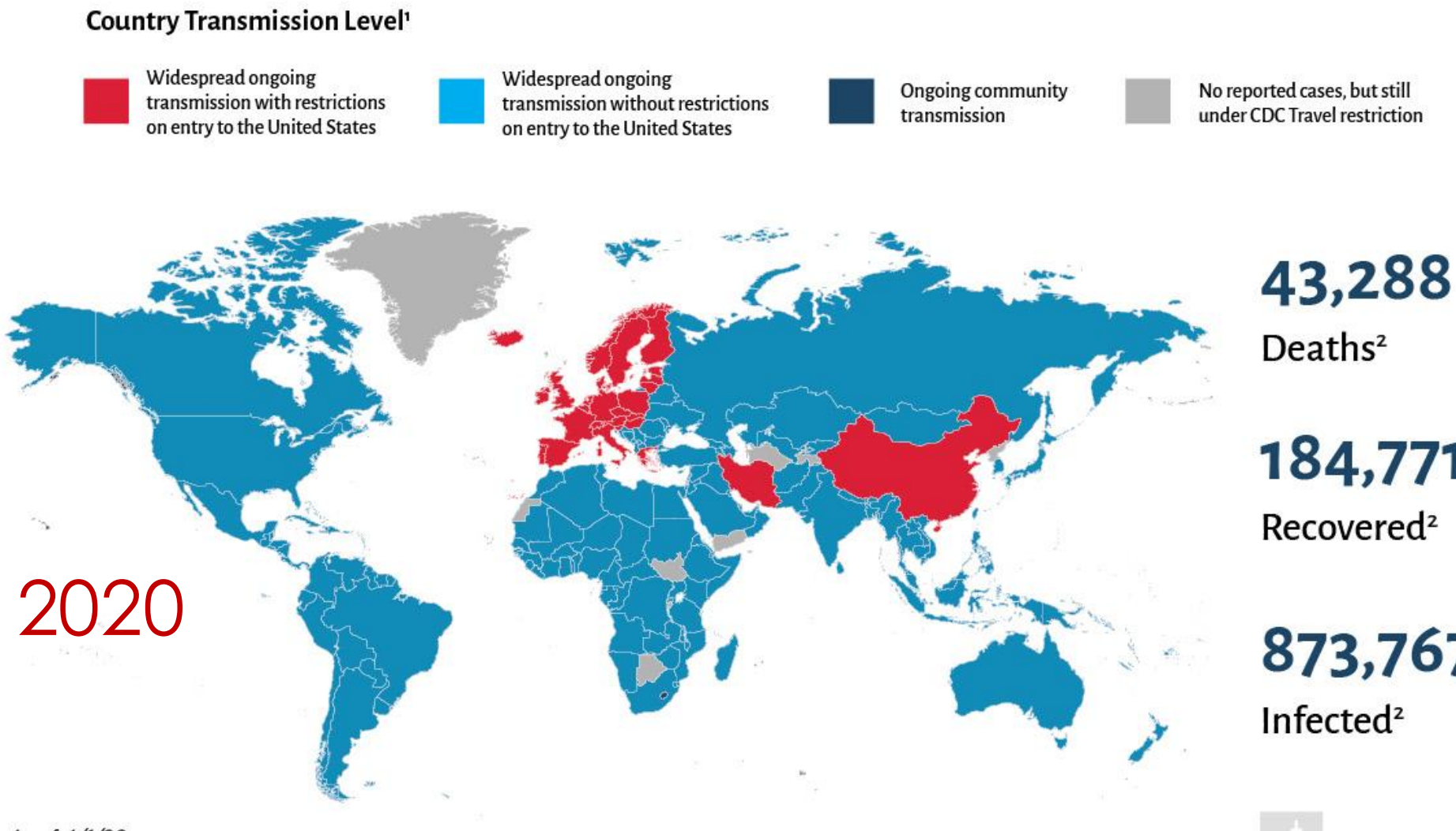
Mar. 16

The CDC recommends that for the next 8 weeks, organizers cancel or postpone in-person events that consist of 50 people or more throughout the United States.

Mar. 24

The FDA allows treatment of life-threatening COVID-19 cases with convalescent plasma.

Global Spread is Expected to Continue



Apr 1, 2020

43,288
Deaths[2]

184,771
Recovered[2]

873,767
Infected[2]

As of 4/1/20

Source:
[1]hcdc.gov/coronavirus/2019-ncov/travelers/map-and-travel-notices.html
[2]Johns Hopkins University *gisanddata.maps.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6*

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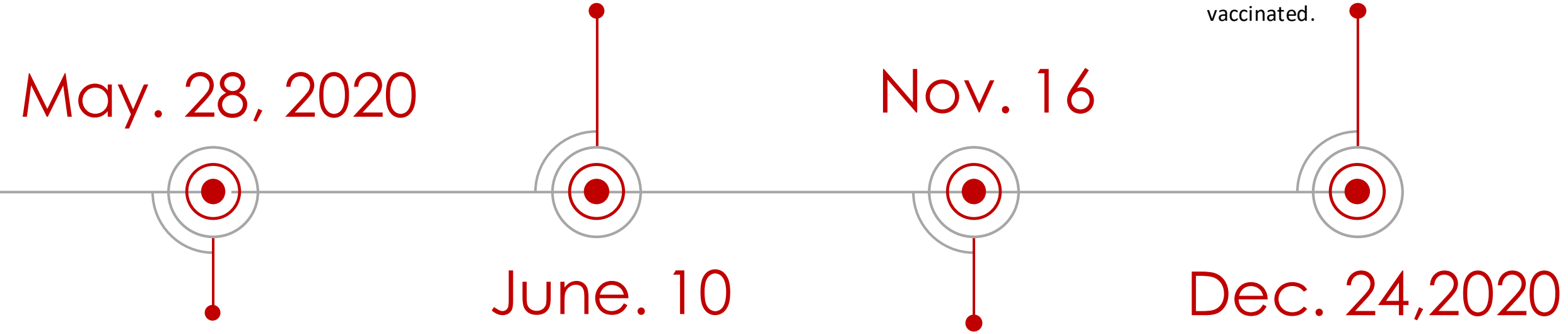
COVID-19: A Timeline



May. 28, 2020

The recorded death toll from COVID-19 in the U.S. surpasses 100,000.

June. 10

The number of confirmed COVID-19 cases in the U.S. surpasses 2 million.

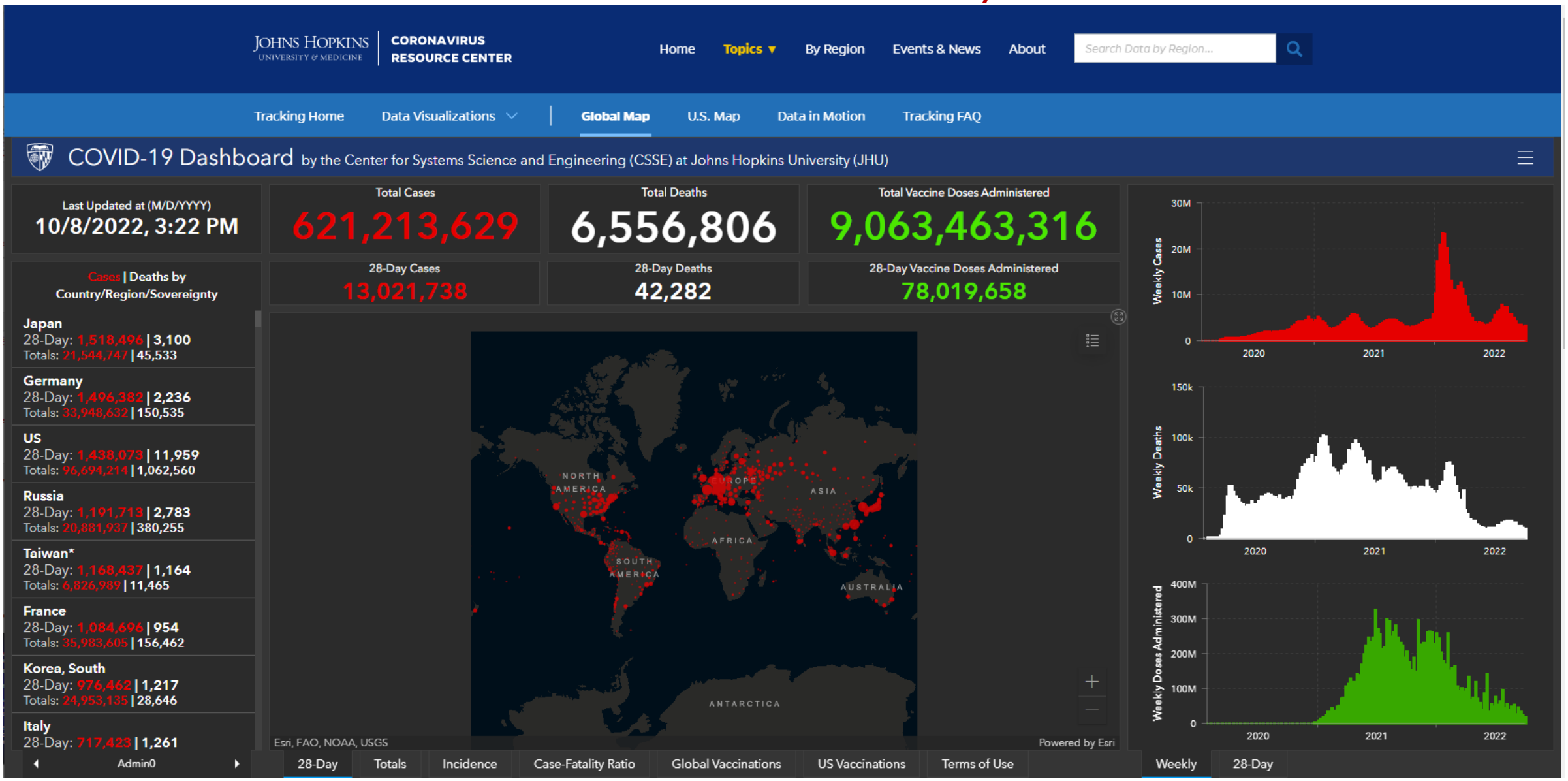
Nov. 16

Moderna’s COVID-19 vaccine is found to be 95.4% effective in its clinical trial.

Dec. 24,2020

More than 1 million COVID-19 vaccine doses were administered in the U.S. in just 10 days: healthcare workers and older adults living in long-term care facilities are the first to be vaccinated.

COVID19 today



~600 million cases, 6.5 million death, 9 billion vaccine doses

https://coronavirus.jhu.edu/map.html

Treatment

In the beginning:

Early 2020: Dexamethasone

March 30, 2020: FDA issues EUA for hydroxychloroquine (already in use for lupus and other conditions)

May 1, 2020: FDA issues EUA for remdesivir (antiviral developed for Ebola)

June 4, 2020: Lancet and NEJM retract studies on hydroxychloroquine

August 23, 2020: FDA issues EUA for convalescent plasma

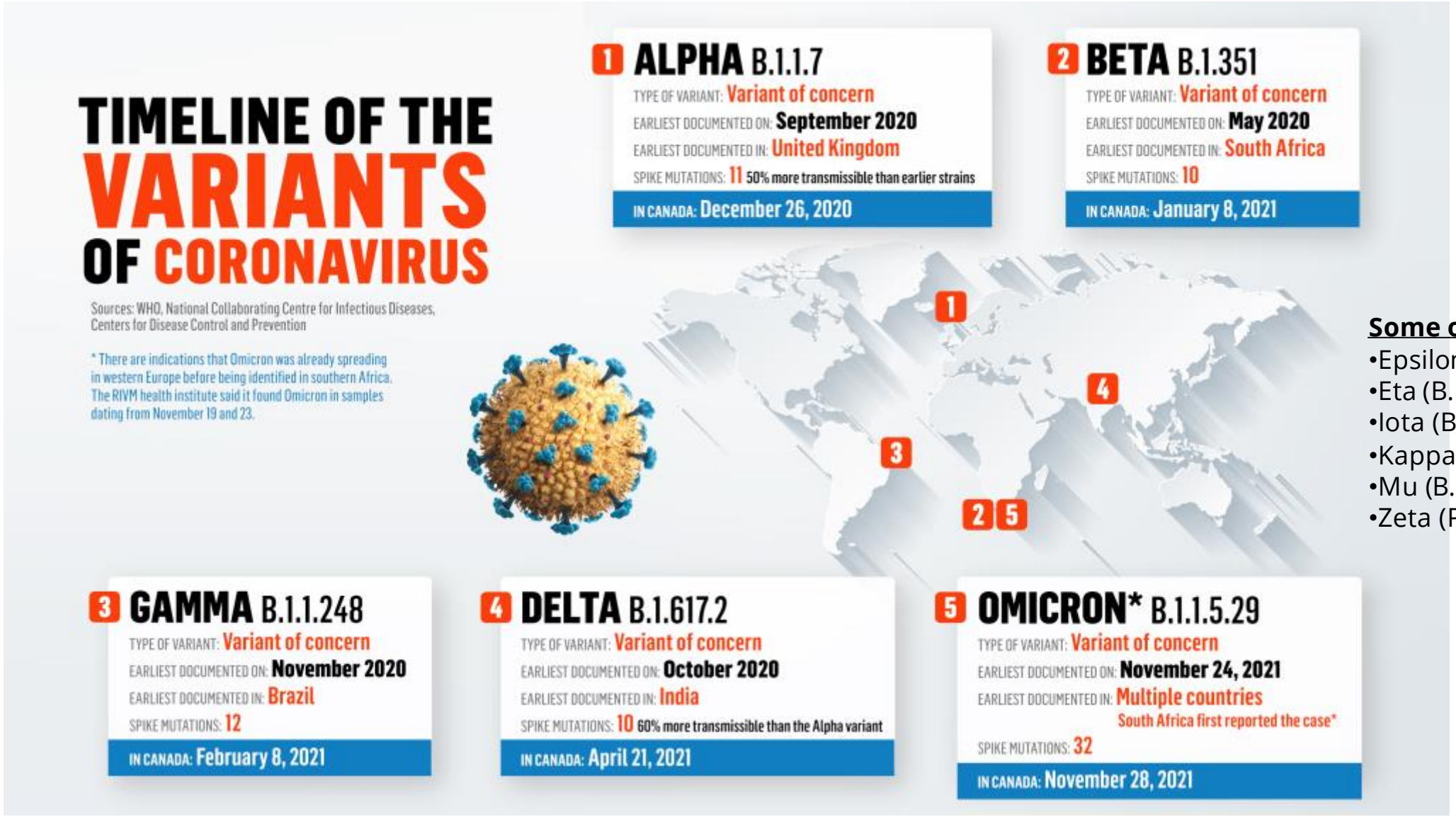
November 9, 2020: FDA issues EUA for monoclonal antibody, banlanivumab

November 21, 2020: FDA issues EUA for monoclonal antibody combination, casirivimab and imdevimab (REGN-COV2)

March 27,2021: FDA issues EUA for monoclonal antibody, sotrovimab

Today, none of these drugs (except dexamethasone and remdesivir) are in use

Sars-CoV2 variants



Some others

- Epsilon (B.1.427 and B.1.429)
- Eta (B.1.525)
- Iota (B.1.526)
- Kappa (B.1.617.1)
- Mu (B.1.621, B.1.621.1)
- Zeta (P.2)

Omicron lineage subvariant BA.5 makes up 80% of today's isolates in the US

Treatment today - Antivirals

Outpatient

Oral:

Nirmatrelvir + ritonavir (Paxlovid): > 12 yr and onset no more than 5 days ago

or

Molnupravir (Lagevrio): > 18 yr and onset no more than 5 days ago: 800 mg po x 5 days

IV:

Bebtelovimab: onset no more than 7 days ago

or

Remdesivir (Veklury): onset no more than 7 days ago. IV daily for 3 days

Eligibility

COVID-19 positive and symptomatic but not hospitalized

High risk for progression

Treatment today - Antivirals

Hospitalized

Baricitinib

Remdesivir

Other

Tocilizumab

Dexamethasone

Prevention (PrEP)

Tixagevimab co-packaged with cilgavimab (Evusheld)

Eligibility

- Not currently infected with COVID19
- Not recently exposed to someone with COVID19

Generally given to people at high risk for serious COVID19

High risk for covid progression

- > 65 yr
- Obesity (BMI ≥30 kg/m^2)*
- Cancer
- Cerebrovascular disease, Chronic kidney disease, lung disease or liver disease*
- Diabetes mellitus, type 1 and type 2*
- Disabilities*
- Heart disease (such as heart failure, coronary artery disease, or cardiomyopathies)
- HIV (human immunodeficiency virus)
- Immunocompromised or use of immunosuppressive medications
- Mental health disorders*
- Dementia
- Pregnancy and recent pregnancy
- Phvsical inactivity

COVID19 in Dialysis Patients

Prior to vaccination (original strain of virus)

- 20-fold higher prevalence of disease compared to overall population
- 50% of recipients needed hospitalization and 20-30% mortality
- Lower risk for disease with at home dialysis

Post vaccination (and against variant strains – delta and omicron)

- 90% of vaccine recipients develop antibodies

COVID19 in Kidney Transplant Recipients

Prior to vaccination (original strain of virus)

90% of transplant recipients needed hospitalization

30% mortality

Post vaccination (and against variant strains – delta and omicron)

In one study – 50% of recipients needed hospitalization and 5-10% mortality

Overall:

Excess mortality rate in US population (26 per 10,000)

Excess mortality rate in kidney transplant recipients (188 per 10,000)

Clark et al., Transplantation 2022 Aug 31. doi: 10.1097/TP.0000000000004341

COVID19 vaccines

Vaccine types

- mRNA: Moderna, Pfizer (2-3 doses) – Full FDA approval
- Viral vector: J&J – FDA EUA; Other countries: AstraZeneca (Oxford), Sinopharm, Sinovac, Covaxin
- Protein subunit vaccine: Novavax – FDA EUA

Vaccine response

- Antibodies against the virus (Spike protein)
- Development of T cell immunity (harder to measure)

Vaccine effectiveness

- Prevention of infection/transmission
- Prevention of hospitalization
- Prevention of death

COVID19 mRNA vaccines

Effectiveness and vaccine response in general population

~95% effective against preventing hospitalizations and death

~100% of vaccinated people have robust antibodies

Effectiveness in dialysis patients

Not enough data to know about effectiveness

~90% of vaccinated people have robust antibodies

mRNA vaccine in transplant patients

After 1st dose

- 5% had antibody response

After 2nd dose

- 40% of a patients had antibody response

After 3rd dose

- 45% of negative patients developed an antibody response
- A total of 70% had antibody after 3rd dose

CDC recommends a 4th dose (2nd booster) for immunosuppressed patient

- In one study 19% had no antibody after 4th dose

CDC recommends an additional bivalent booster on top of prior monovalent vaccines

Pfizer-BioNTech and Moderna

COVID19 vaccination and GN

Case series of 13 patients with data on disease after vaccination:

- 8 with newly diagnosed GN and 5 with relapses
- 5 had IgA and 3 had membranous and 2 had minimal change disease

Additional 20 articles reporting on 27 cases

- 13 with newly diagnosed GN and 14 with relapses
- 11 had IgA and 10 had minimal change disease

Recent study from Switzerland using a nationwide cohort showed no increase with vaccination

Note:

Other vaccines are also reported to be associated with new or relapsed GN

COVID19, the disease, also reported to be associated with new or relapsed GN

My take:

Possibly a true association, but given the rarity, more likely a fortuitous occurrence

Klomjit et al., Kidney Int Reports 2021, 6:2969-2979
Diebold et al., Kidney Int 2022, doi: 10.1016/j.kint.2022.08.021

Options in transplant and other immunosuppressed recipients

Obtain primary vaccination series against COVID19: mRNA vaccines preferred

Continue to mask around unvaccinated people

Maintain social distancing

Consider Evusheld for preexposure prophylaxis especially if high risk occupation

Seek medical attention early if symptoms develop

Outpatient Rx if symptomatic: Bebtelovimab (monoclonal antibody) or Paxlovid

Avoid Paxlovid if on tacrolimus

Paxlovid not recommended if eGFR is <30 mL/min

Take additional booster shots when recommended

Must have finished the primary series

Wait at least 2 months since primary or last booster

Current booster: bivalent (effective against original strain and against Omicron variants)

Pfizer-BioNTech – one dose in age > 12

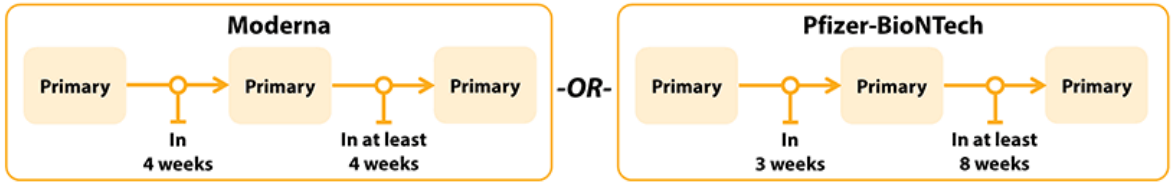
Moderna – one dose in age > 18

https://www.cdc.gov/coronavirus/2019-ncov/index.html

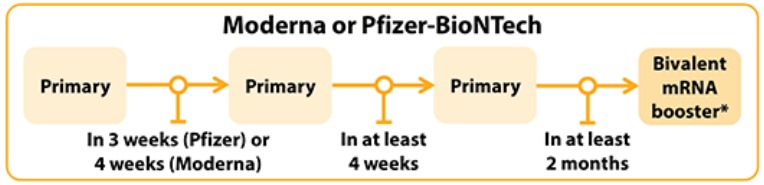
Questions?

COVID-19 Vaccination Schedule Infographic for People who are Moderately or Severely Immunocompromised

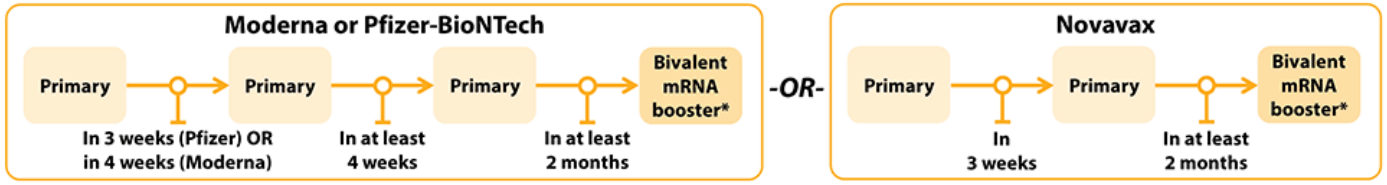
People ages 6 months through 4 years



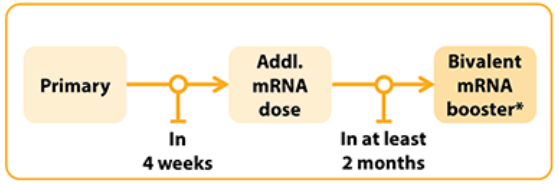
People ages 5 through 11 years



People ages 12 years and older

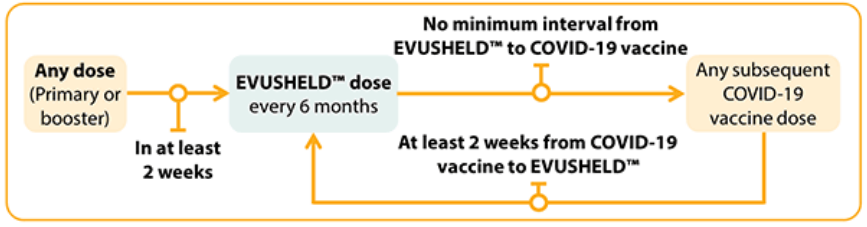


People ages 18 years and older who previously received Janssen primary series dose†



Monoclonal antibodies (EVUSHELD™) for COVID-19 pre-exposure prophylaxis

People ages 12 years and older (must weigh at least 40kg)



*Administer an age-appropriate mRNA bivalent booster (i.e., Pfizer-BioNTech for people age 5 years and either Pfizer-BioNTech or Moderna for people ages 6 years and older). For people who previously received a monovalent booster dose(s), the bivalent booster dose is administered at least 2 months after the last monovalent booster dose.

†Janssen COVID-19 Vaccine should only be used in certain limited situations. See: https://www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerations-us-appendix.html#appendix-a

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