HHP/HPH COVID-19 Community Webinar Series

Thursday, April 15, 2021

5:30pm – 6:30pm

HAWAIʻI PACIFIC HEALTH | HAWAIʻI HEALTH PARTNERS

Disclaimer:

- The following is intended as information resource only for HHP/HPH providers, clinicians, administrative and clinical leaders.

- Specific areas may not pertain directly to your clinical practice area and/or may not be applicable to your practice based on your existing workflows, infrastructure, software (e.g. EHR), and communications processes.

Webinar Information

- You have been automatically muted.
  You cannot unmute yourself.
- You will be able to submit questions via the Q&A section.
  - Due to time constraints, any unanswered questions will be addressed this week and posted on the HHP website
- A recording of the meeting will be available tomorrow on the HHP website and intranet.

How to Claim CME Credit

1. Step 1: Confirm your attendance
   - You should have completed a brief questionnaire before joining today's live webinar.

2. Step 2: HPH CME team will email you instructions
   - Complete and submit evaluation survey that will be emailed to you within one week of the offering.
   - Your CE certificate will be immediately available to you upon completion of your evaluation.
   - Questions? Email hphcontinuingeduc@hawaiipacifichealth.org

CME Accreditation Statement

- In support of improving patient care, Hawai‘i Pacific Health is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.
- Hawai‘i Pacific Health designates this webinar activity for a maximum of 1.0 AMA PRA Category 1 Credit (s) ™ for physicians. This activity is assigned 1.0 contact hour for attendance at the entire CE session.

JOINTLY ACCREDITED PROVIDER™

INTERPROFESSIONAL CONTINUING EDUCATION

Disclosures

- The planners and presenters of this activity report no relationships with companies whose products or services (may) pertain to the subject matter of this meeting

Community Update

Raymond P. Vara, Jr.

President and Chief Executive Officer,
Hawai‘i Pacific Health

HAWAI‘I PACIFIC HEALTH | HAWAI‘I HEALTH PARTNERS

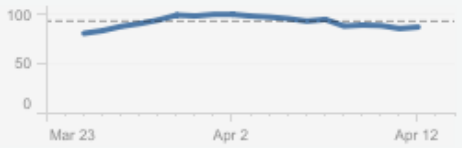
COVID Pau Dashboard

7-Day Avg of New Cases

Region: State

86.9

As of Apr 12



Clusters Under Investigation

(Top 3 In Last 14 Days)

Region: Honolulu County

Exposure Setting	Total Cases	Clusters
Food Suppliers	23	2
Restaurants	23	3
Social Gatherings	20	2

As of Apr 8

7-Day Avg of % Tests Yielding Positive Results

Region: State

1.6%

As of Apr 11

Total Vaccine Doses Administered

State Value

973,793

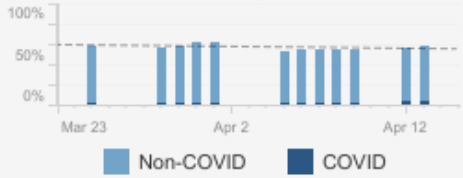
As of Apr 13

ICU Occupancy Rate

State Value

58%

As of Apr 13

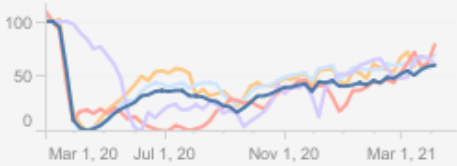


UHERO Economic Pulse Index

State Value

60 ↑

As of Apr 3



State Reopening Strategy for Businesses & Operations

(Strategy is being implemented by county, and is subject to change)

Stay at Home (Major Disruption)	Safer at Home (Moderate Disruption)	**Act with Care (Minor Disruption)**	Recovery (Minimal Disruption)	New Normal (No Disruption)

The "Act with Care" impact level anticipates some new COVID-19 cases, which are manageable, along with improved capacity utilization for testing, hospitals, and/or contact tracing.

Our Shared Responsibility under the Current Impact Level:

Safe Practices

Under all impact levels, follow the recommended Safe Practices: wash, mask and distance.

Stay at Home

Under the Act with Care impact level, at increased risk populations and kūpuna recommended to stay at home.

Gatherings

Under all impact levels, adjust gathering size in accordance with health guidance.

COVID-19 Updates

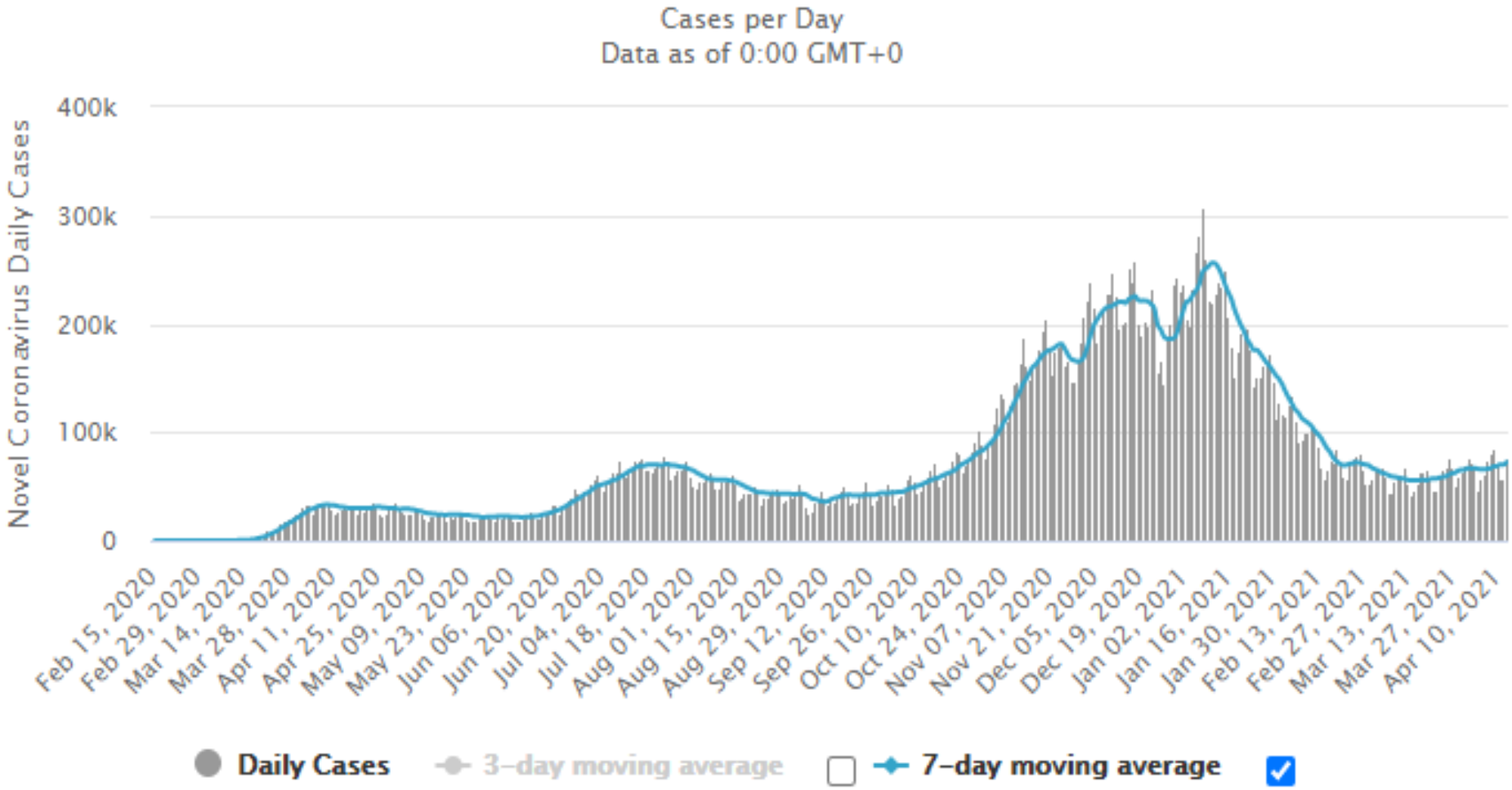
Gerard Livaudais, MD, MPH

Executive Vice President, Population Health and Provider Networks,

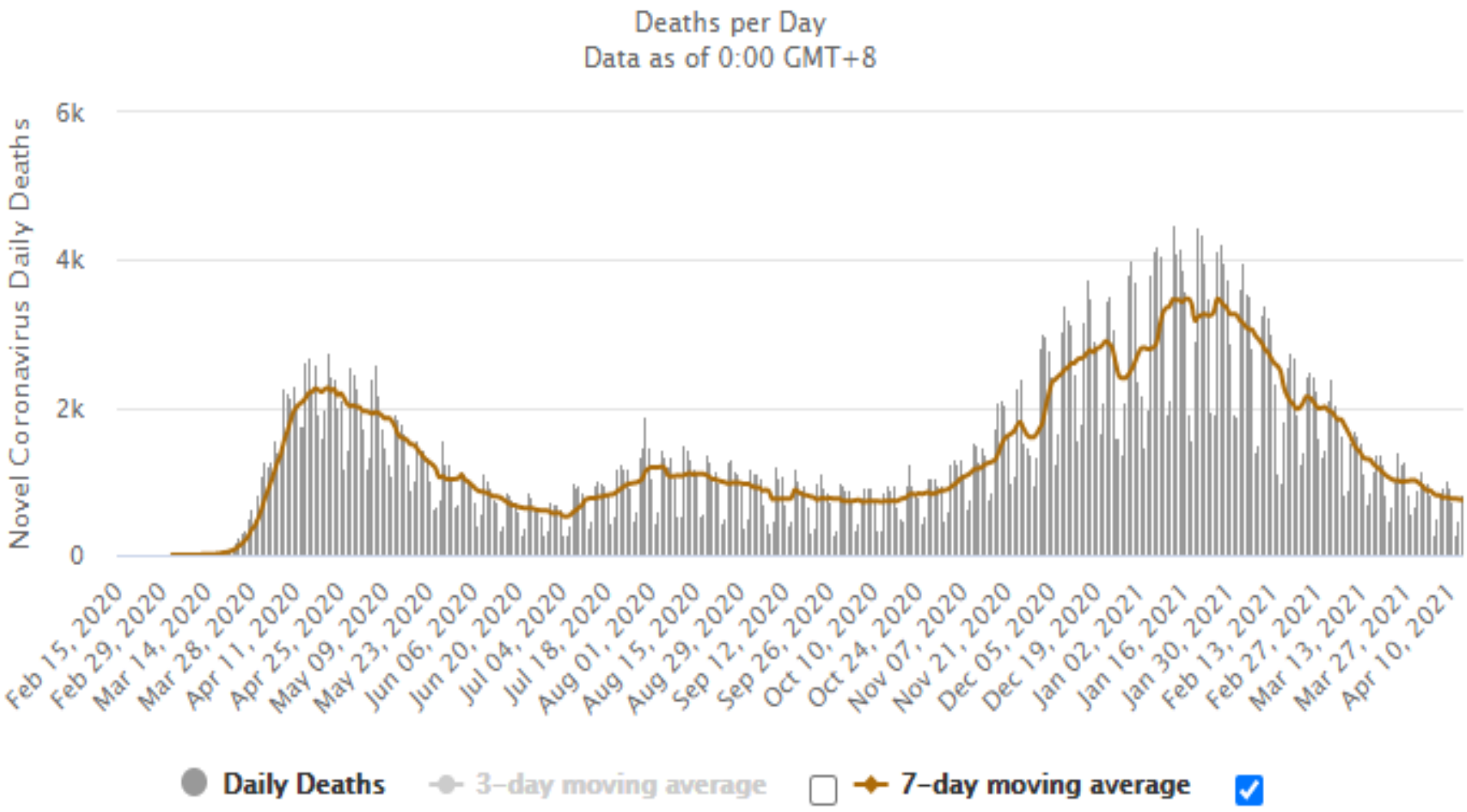
Hawai‘i Pacific Health

HAWAI‘I PACIFIC HEALTH | HAWAI‘I HEALTH PARTNERS

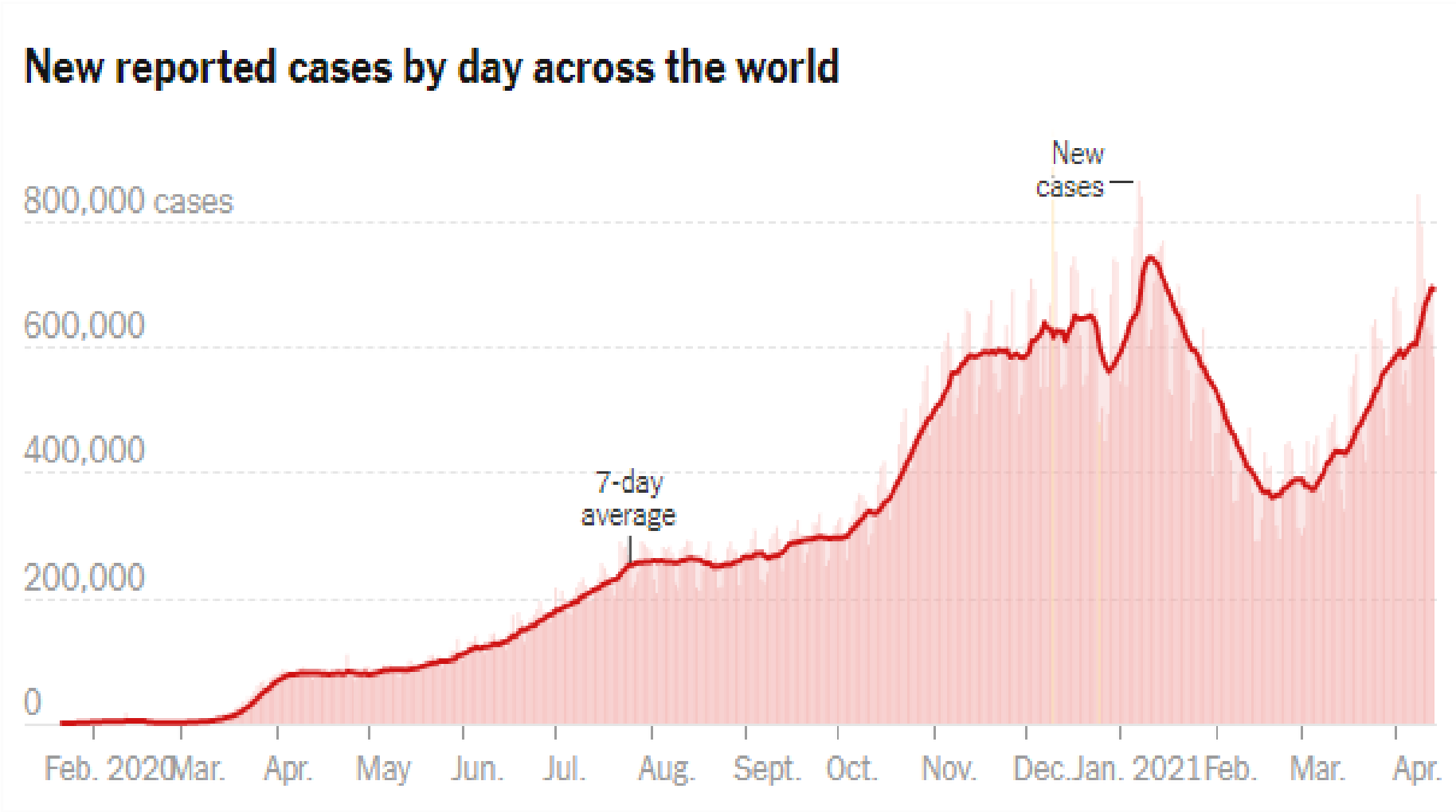
United States Daily New Cases



United States Daily Deaths



Source: Worldometer - www.worldometers.info

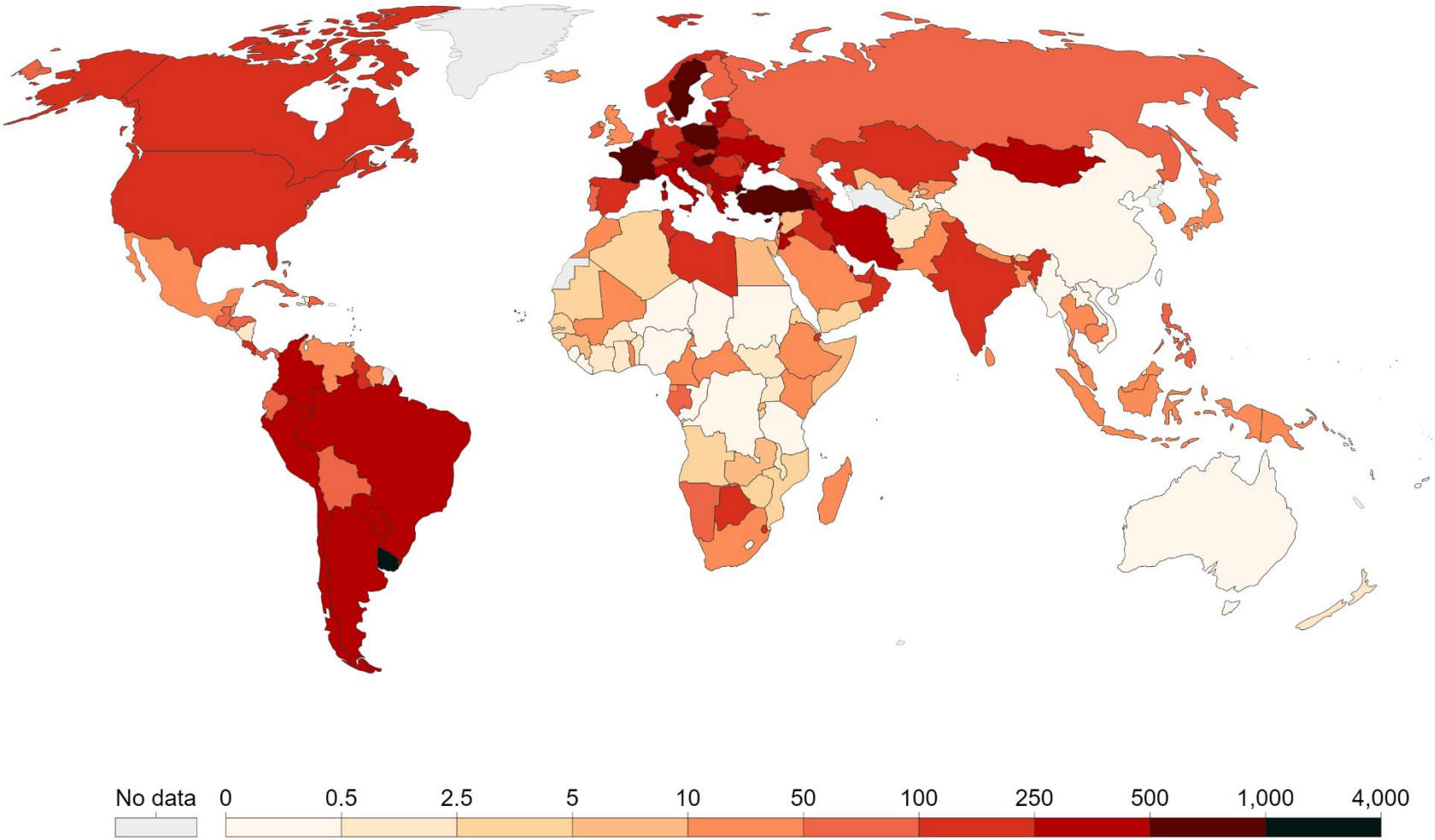

New reported cases by day across the world
800,000 cases
600,000
400,000
200,000
0
New cases
7-day average
Feb. 2020
Mar.
Apr.
May
Jun.
Jul.
Aug.
Sept.
Oct.
Nov.
Dec.
Jan. 2021
Feb.
Mar.
Apr.

Reported deaths by day across the world

Daily new confirmed COVID-19 cases per million people, Apr 13, 2021

Shown is the rolling 7-day average. The number of confirmed cases is lower than the number of actual cases; the main reason for that is limited testing.

Our World in Data

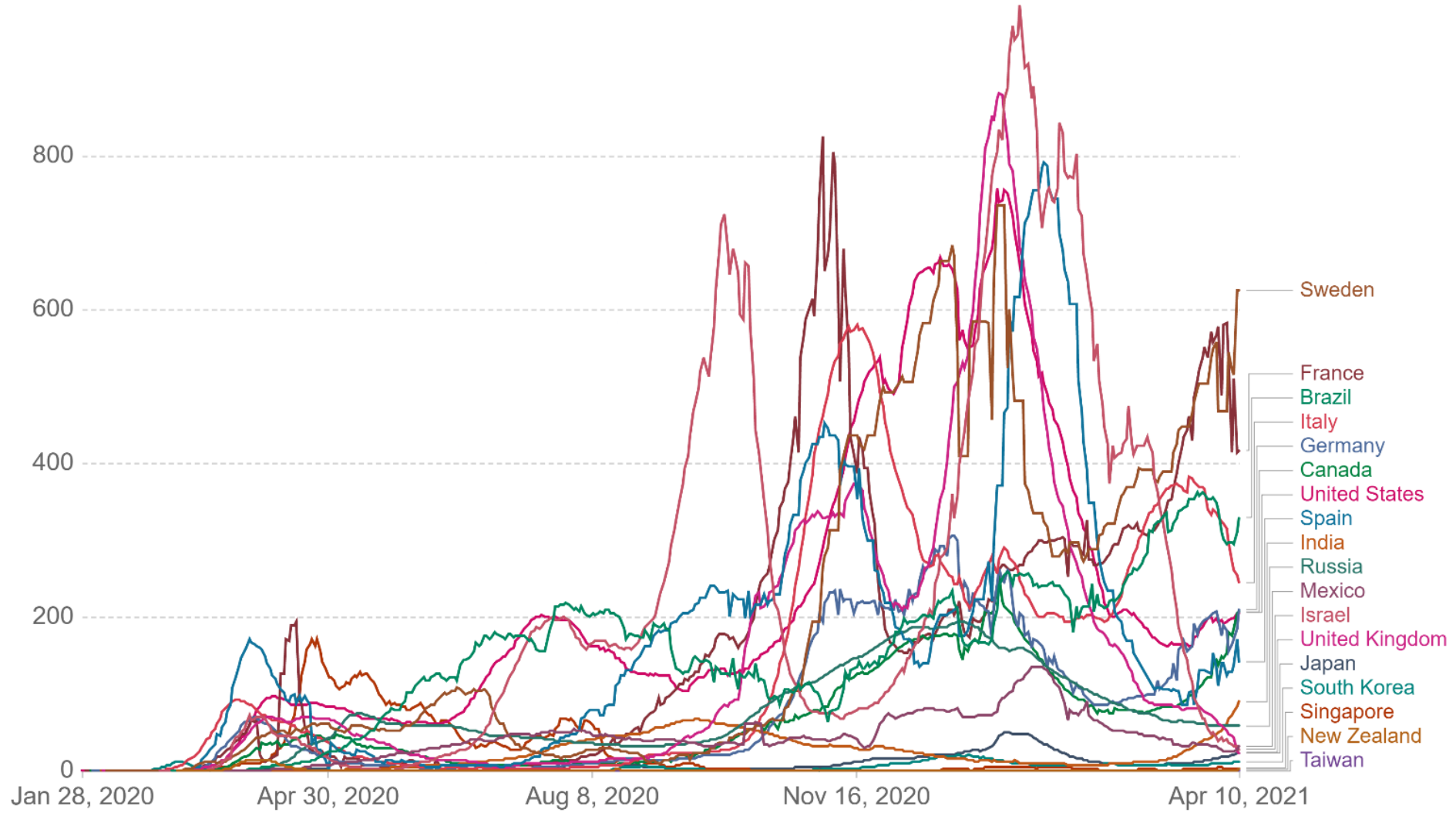


Source: Johns Hopkins University CSSE COVID-19 Data

Daily new confirmed COVID-19 cases per million people

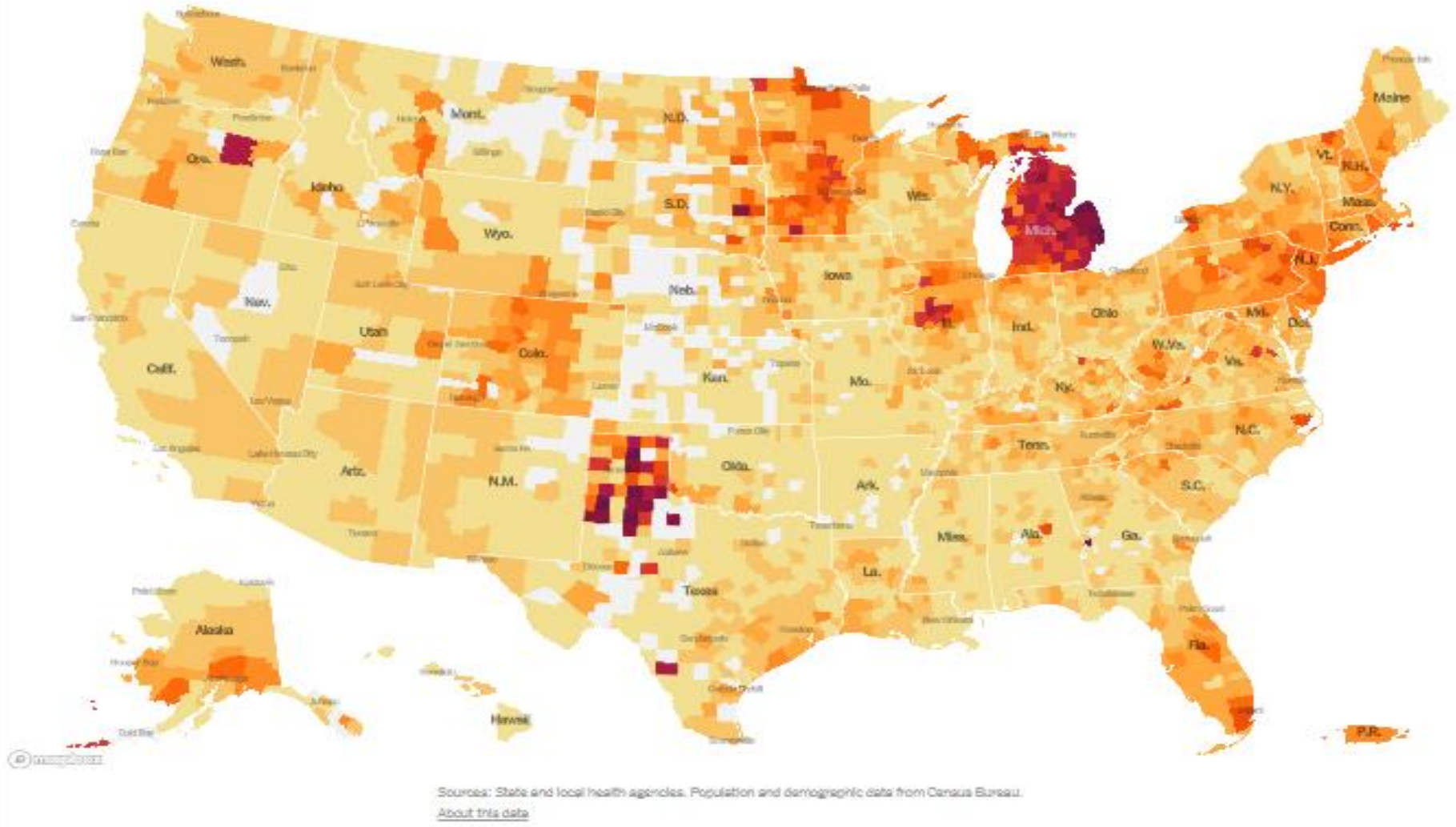
Shown is the rolling 7-day average. The number of confirmed cases is lower than the number of actual cases; the main reason for that is limited testing.

Our World in Data



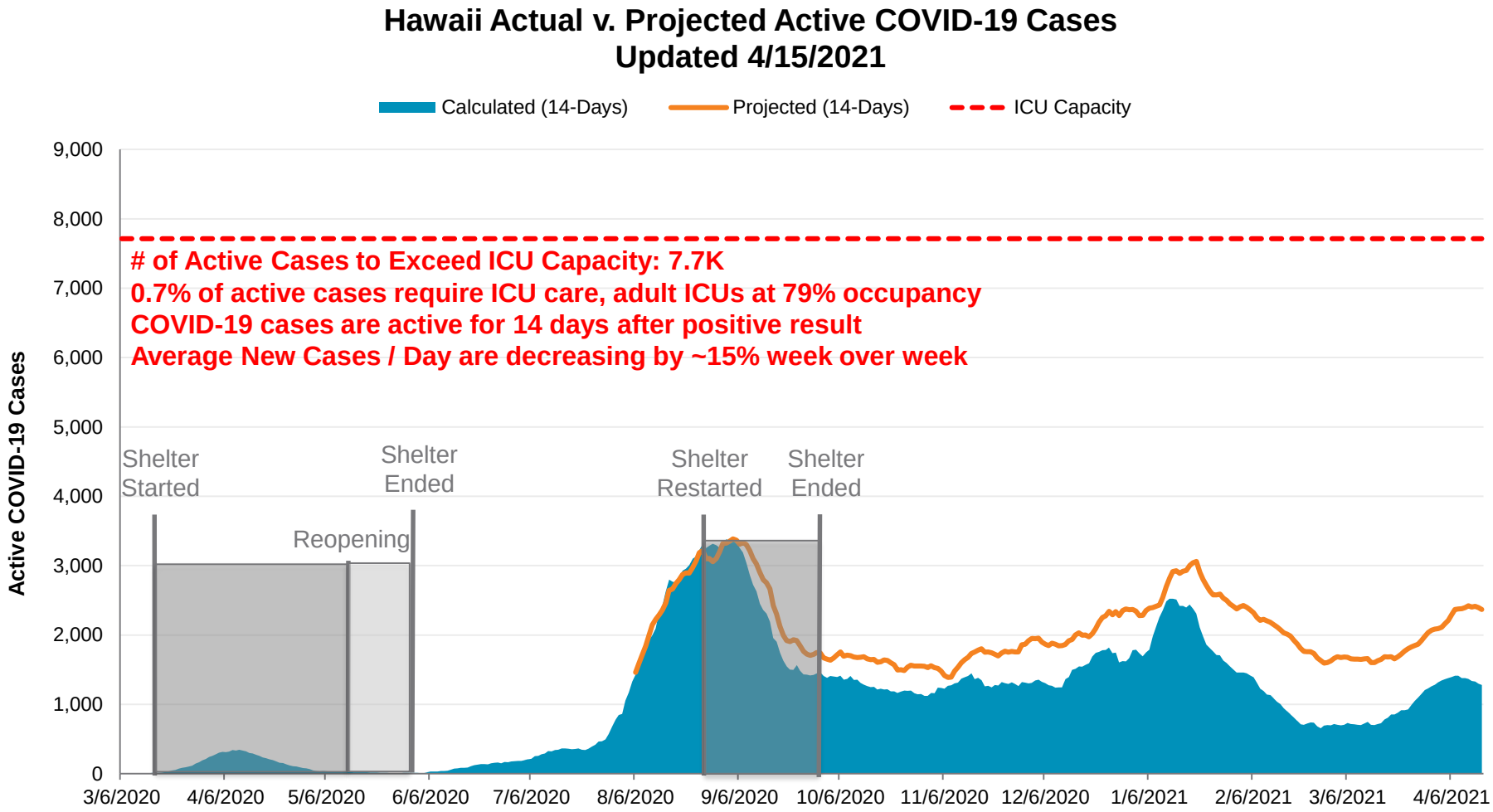
Source: Johns Hopkins University CSSE COVID-19 Data

Hotspots are changing…

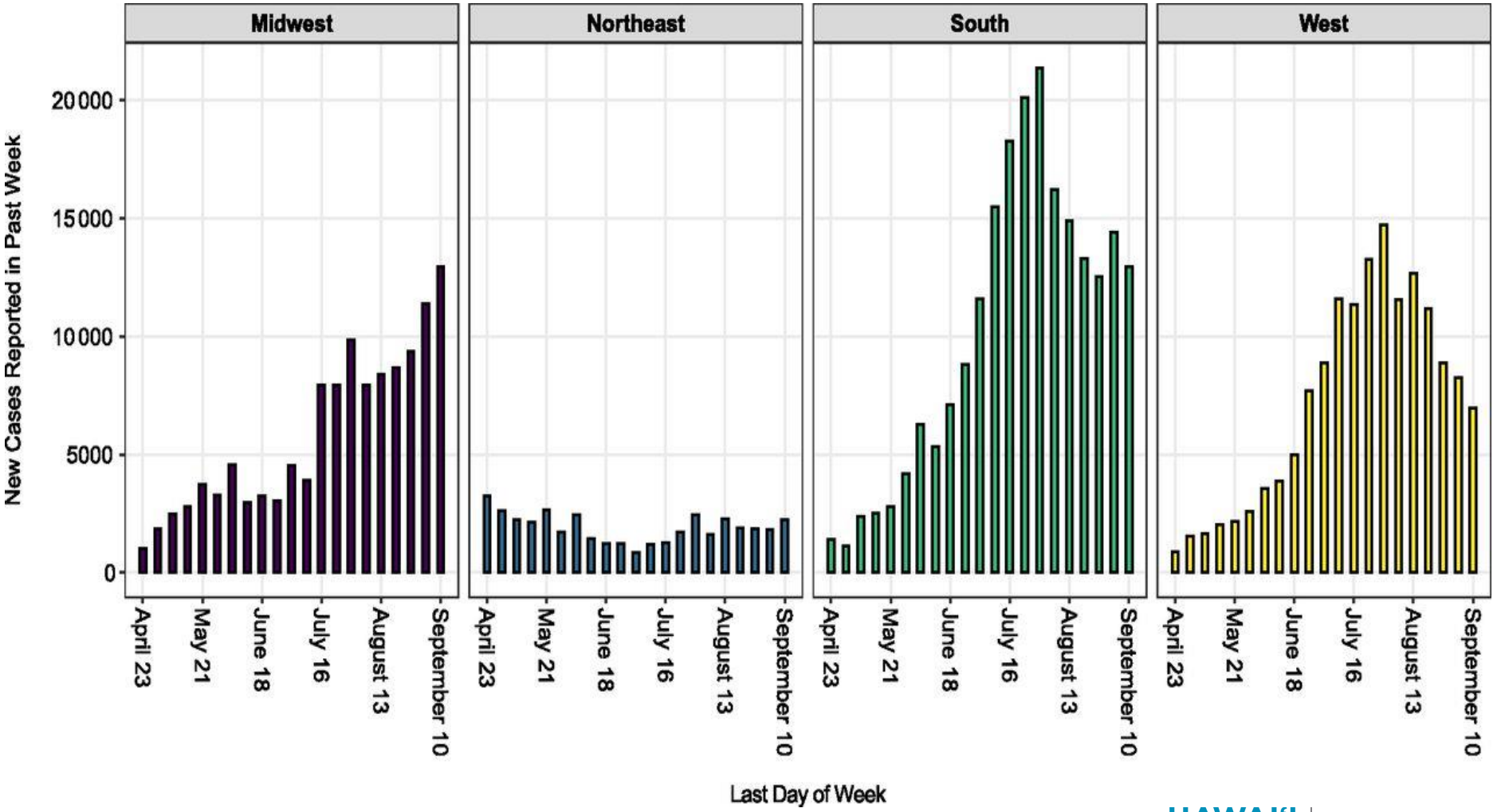


Sources: State and local health agencies. Population and demographic data from Census Bureau.
About this data

Projected Active COVID-19 Cases



Current Drivers: Pediatric COVID-19

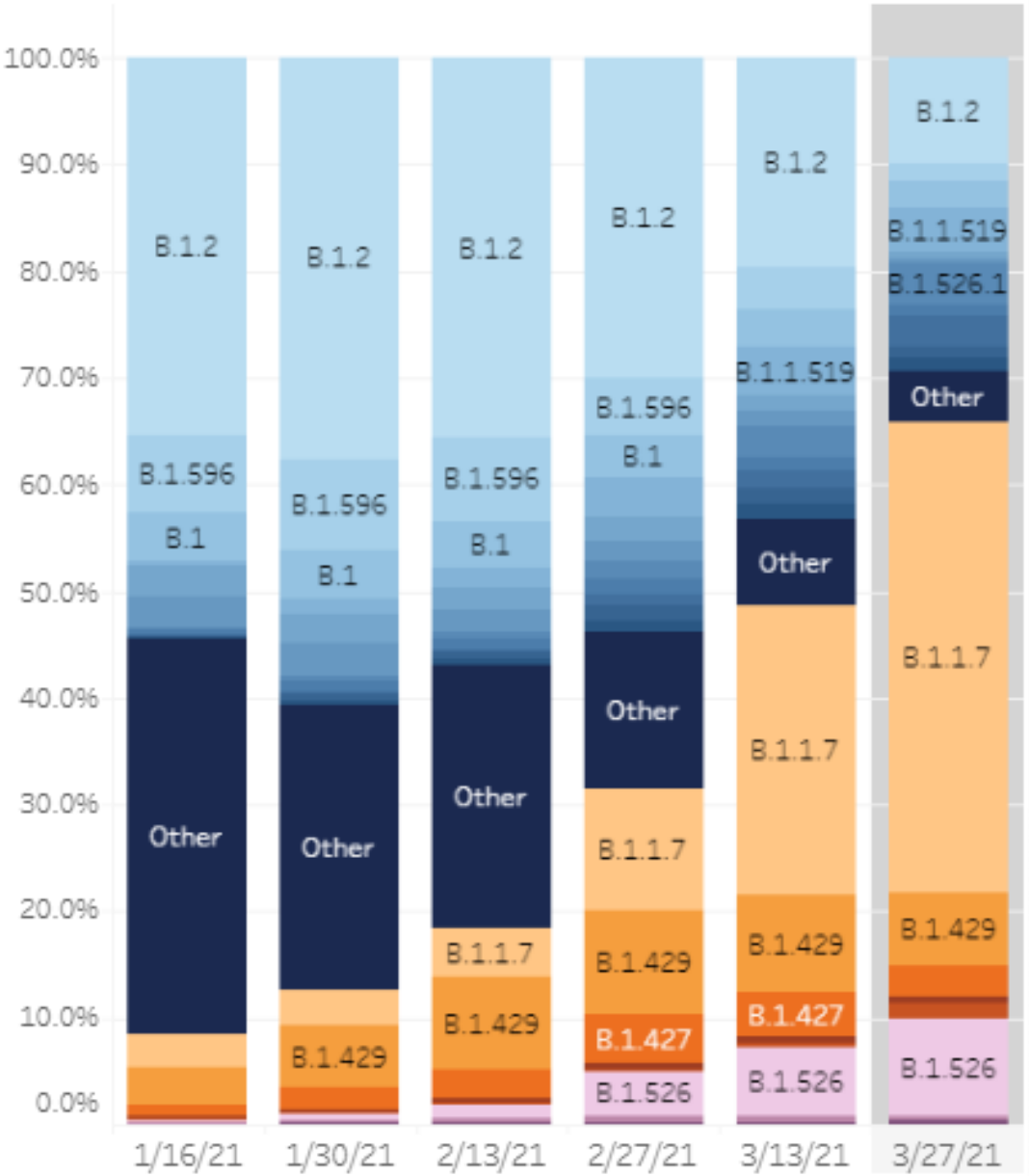


Current Drivers: Variants

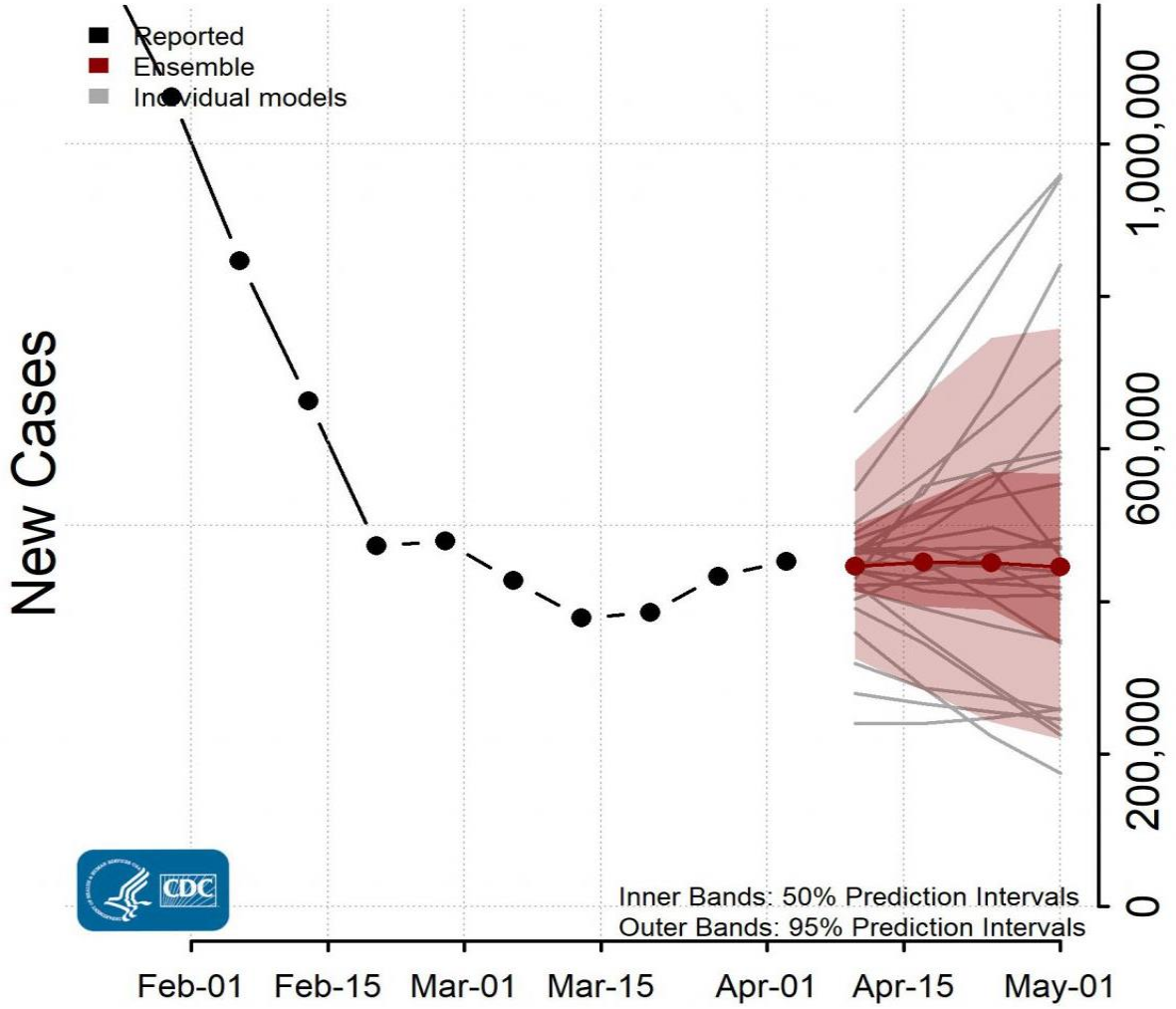
Known genetic variants of

Variant	First identified in
B.1.1.7	United Kingdom
B.1.351	South Africa
P.1	Brazil
B.1.526	New York
B.1.525	New York
P.2	Brazil
B.1.427	California
B.1.429	California
P.3	Philippines
A.23.1 with E484K	England
B.1.1.7 with E484K	England
B.1.525	England
B1.1.318	Unknown
B1.324.1 with E383K	Unknown
B.1.111 with E383K and 429S	Columbia

Sources: Rappler.com, CDC.gov, Health.com, WHO



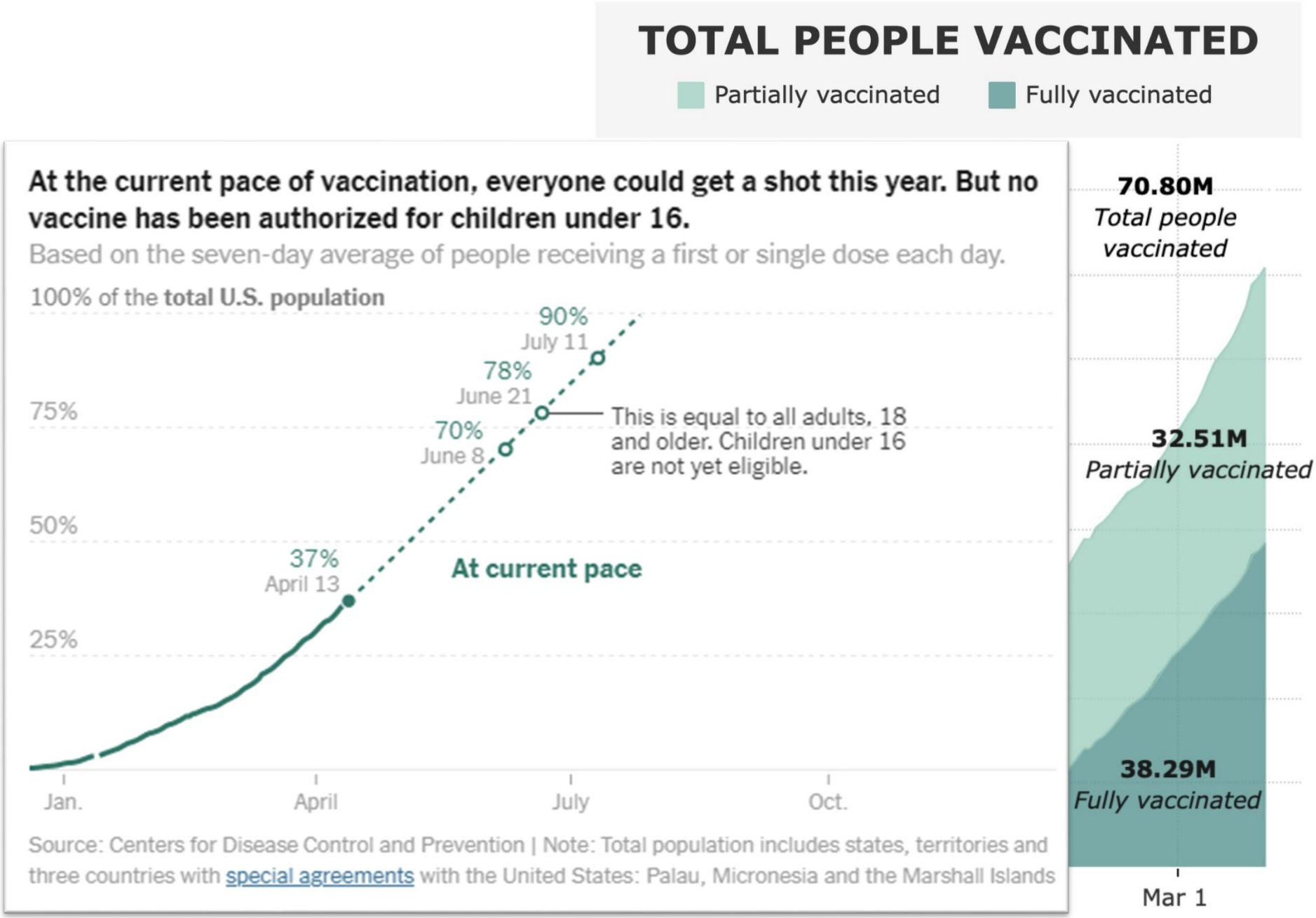
National Forecast



Variant Wins

Vaccine Wins

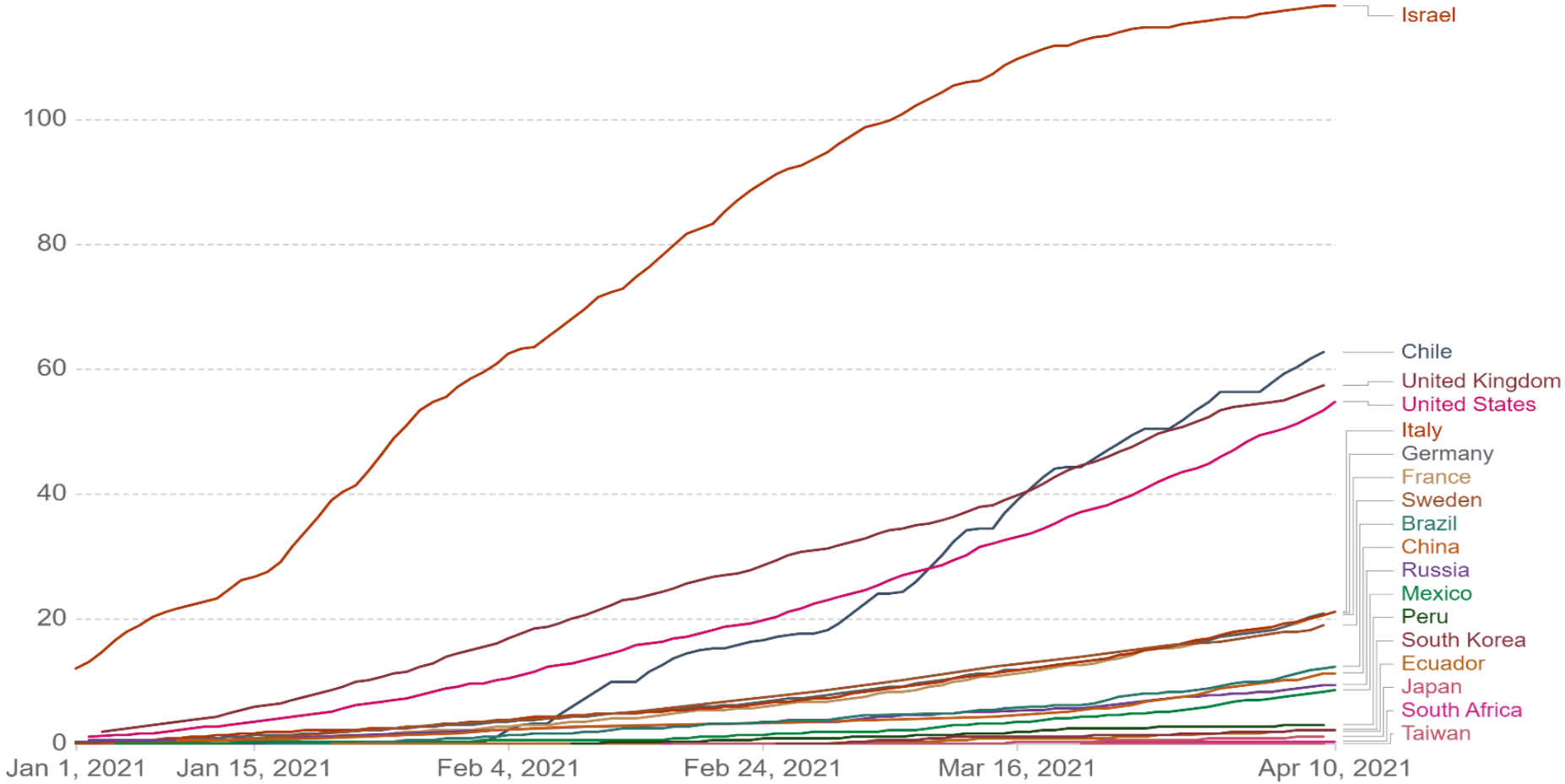
Ensemble forecase. https://www.cdc.gov/coronavirus/2019-ncov/images/case-updates/National-Forecast-Incident-Cases-2021-04-05.jpg


TOTAL PEOPLE VACCINATED
Partially vaccinated
Fully vaccinated
At the current pace of vaccination, everyone could get a shot this year. But no vaccine has been authorized for children under 16.
Based on the seven-day average of people receiving a first or single dose each day.
100% of the total U.S. population
75%
50%
25%
90%
July 11
78%
June 21
70%
June 8
37%
April 13
At current pace
This is equal to all adults, 18 and older. Children under 16 are not yet eligible.
Jan.
April
July
Oct.
Source: Centers for Disease Control and Prevention | Note: Total population includes states, territories and three countries with special agreements with the United States: Palau, Micronesia and the Marshall Islands
70.80M
Total people vaccinated
32.51M
Partially vaccinated
38.29M
Fully vaccinated
Mar 1

COVID-19 vaccine doses administered per 100 people

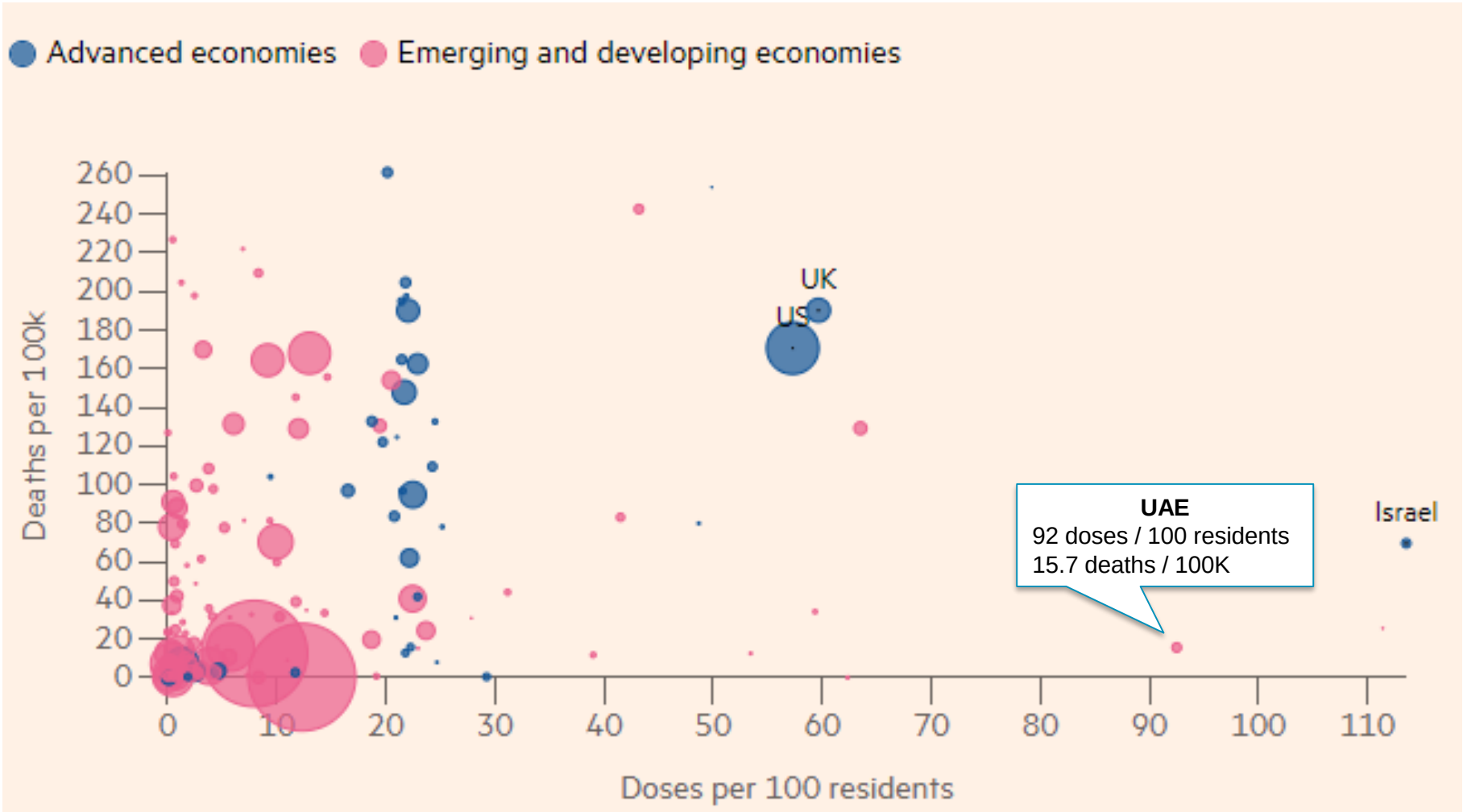
Total number of vaccination doses administered per 100 people in the total population. This is counted as a single dose, and may not equal the total number of people vaccinated, depending on the specific dose regime (e.g. people receive multiple doses).

Our World in Data



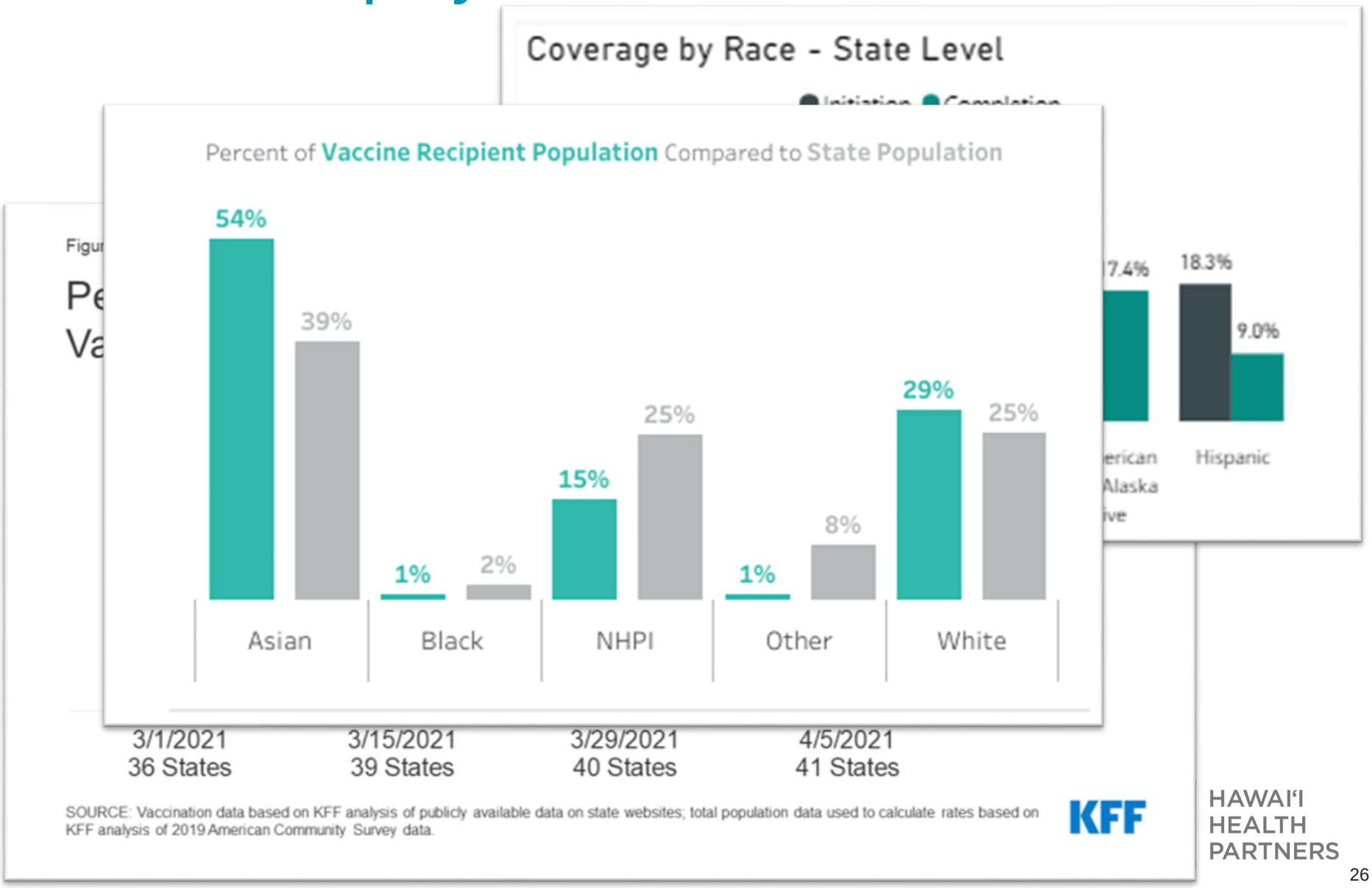
Source: Official data collated by Our World in Data

Vaccine Equity



https://ig.ft.com/coronavirus-vaccine-tracker/?areas=gbr&areas=isr&areas=usa&areas=eue&cumulative=1&populationAdjusted=1

Vaccine Equity



HAWAIʻI HEALTH PARTNERS

- Belize
- Ecuador
- Estonia
- Georgia
- Guatemala
- Iceland
- Madeira
- Seychelles

Entry for Knicks & Rangers games just got easier! Show proof of a negative antigen COVID-19 test or full vaccination. Onsite antigen COVID-19 testing available on game days – with results delivered within 30 minutes for $30. **Learn more**

MADISON SQUARE GARDEN ENTERTAINMENT

Events & Tickets | Our Venues | Our Brands

MADISON SQUARE GARDEN
THE WORLD'S MOST FAMOUS ARENA

Buy Tickets | Premium Hospita

← Back

Welcome Back Fans

Israelis get a "green pass" after vaccination which is being used to gr

JACK GUEZ/AFP via Getty Image

English

Excelsior Pass

EXCELSIOR PASS

What is Excelsior Pass?

Excelsior Pass provides secure, digital proof of COVID-19 vaccination or negative test results.

Access Your Pass On the Go.

Print your Pass or use the Excelsior Pass Wallet app to store Passes on a mobile device for easy access at any time.

Safely Visit Businesses

Easily present your Pass at participating businesses and become part of New York's safe reopening. Businesses will scan your Pass with a mobile device or tablet.

Get Started

To receive your Pass, you'll need to complete some brief information to verify your identity.

Any personal information provided is processed in compliance with data protection laws. It's not used for marketing purposes.

GET STARTED

COVID-19 Vaccination Updates

Melinda Ashton, MD
Executive Vice President and
Chief Quality Officer
Hawai‘i Pacific Health

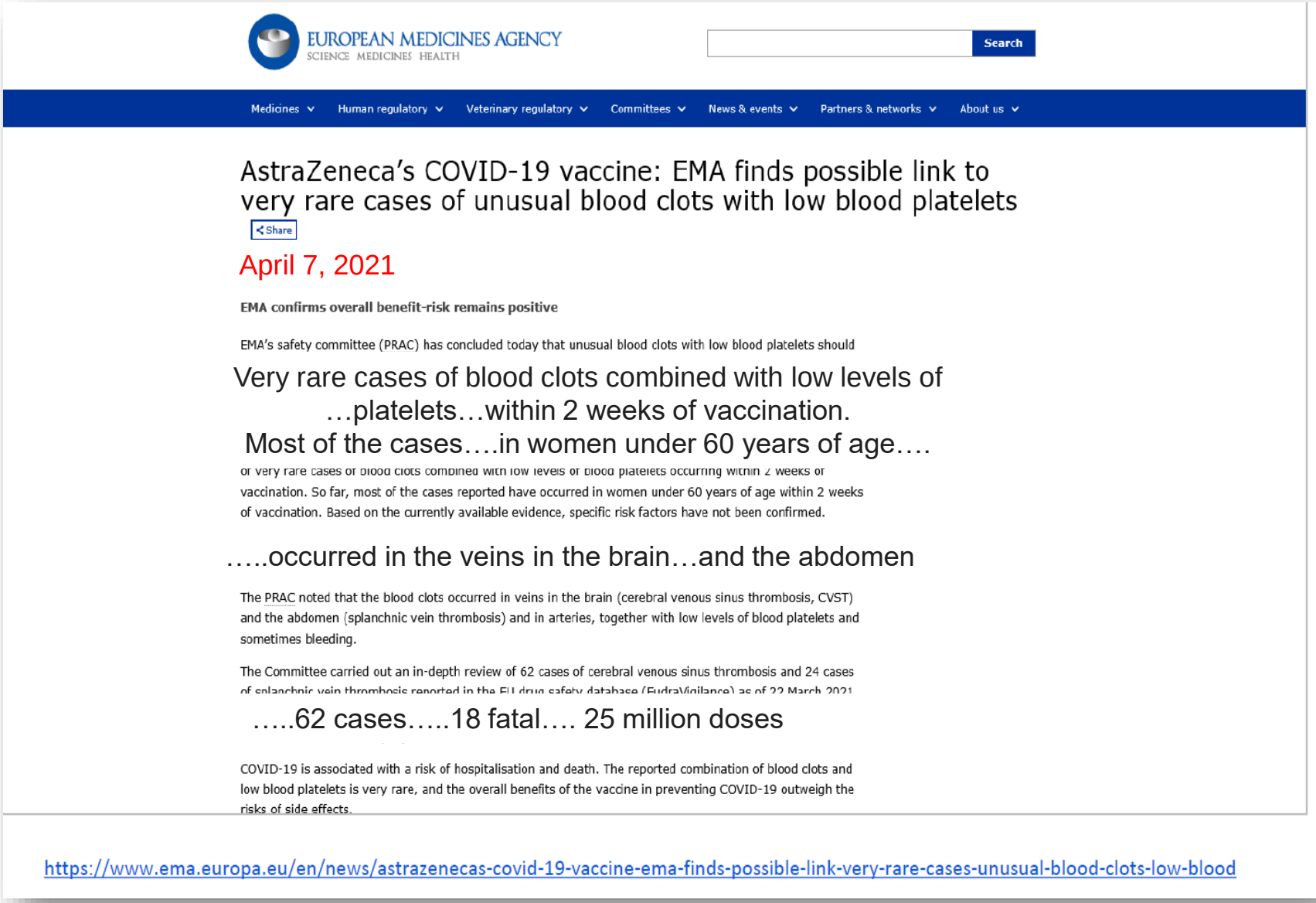
HAWAI‘I PACIFIC HEALTH | HAWAI‘I HEALTH PARTNERS

Centers for Disease Control and Prevention
Center for Preparedness and Response

Johnson & Johnson/Janssen COVID-19 Vaccine and Cerebral Venous Sinus Thrombosis with Thrombocytopenia – Update for Clinicians on Early Detection and Treatment

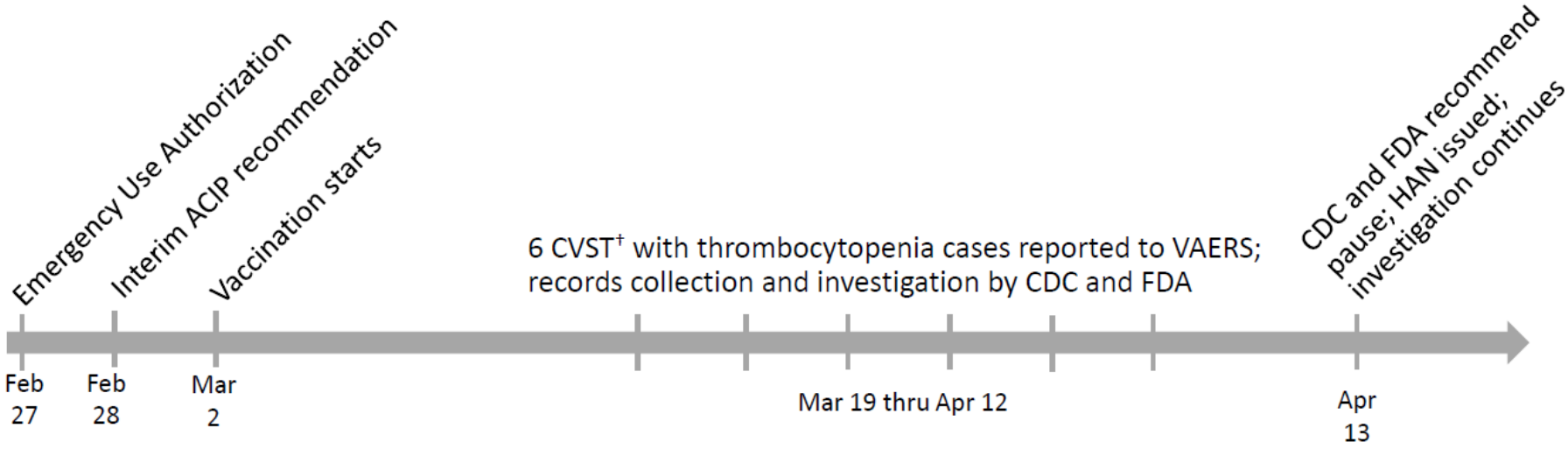
Clinician Outreach and Communication Activity (COCA) Webinar

Thursday, April 15, 2021



https://www.ema.europa.eu/en/news/astrazenecas-covid-19-vaccine-ema-finds-possible-link-very-rare-cases-unusual-blood-clots-low-blood

Janssen COVID-19 vaccine timeline* (2021)



* For illustrative purposes, not drawn to scale, † cerebral venous sinus thrombosis

Cerebral venous sinus anatomy

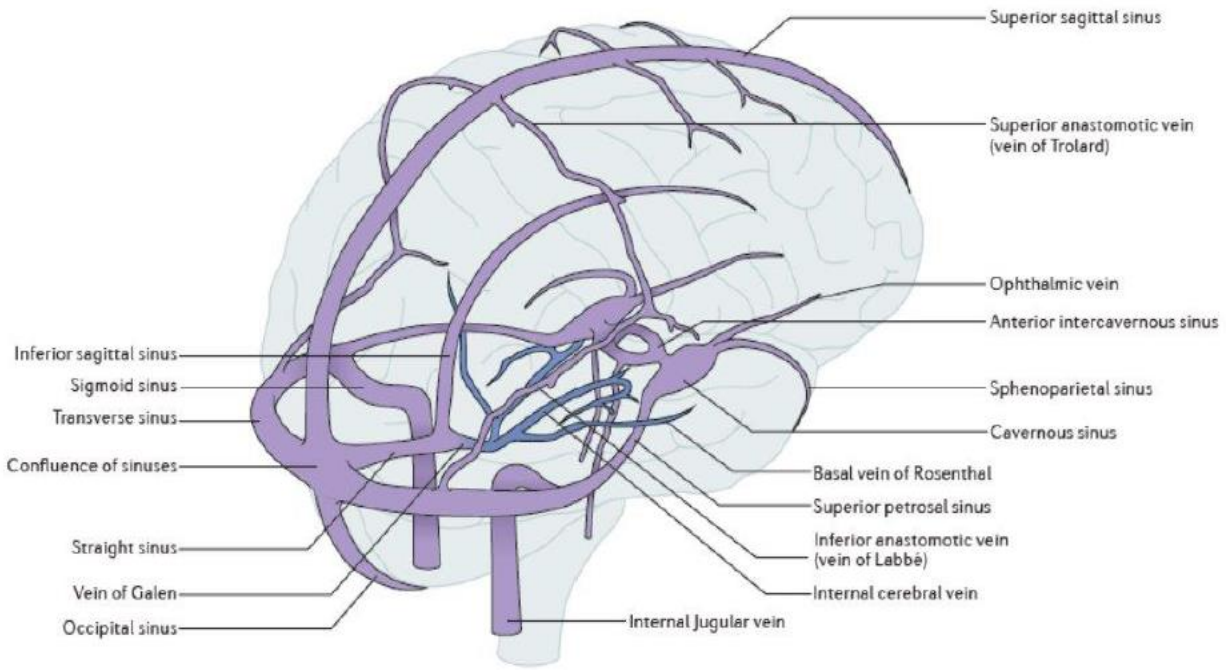


Figure 1 | **Anatomy of the cerebral venous system.** Diagram showing the main components of the cerebral venous system. Blue vessels represent the deep venous system.

Silvis SM et al, Nature Reviews Neurology 13, 555-565(2017)

Cerebral venous sinus thrombosis (CVST)

Background epidemiology[1-3]

- Rare, 0.22–1.57 per 100,000, ~0.5-1% of all strokes
- Median age 37 years
- 8% of patients >65 years
- Female:male ratio of 3:1

Risk factors[4]

- Prothrombotic conditions (genetic or acquired)
- Oral contraceptives
- Pregnancy and the post-partum period
- Malignancy
- Infection
- Mechanical precipitants (lumbar puncture)

[1] Cerebral vein and dural sinus thrombosis in Portugal: 1980-1998. Ferro JM, Correia M, Pontes C, Baptista MV, Pita F, Cerebral Venous Thrombosis Portuguese Collaborative Study Group (Venoport) Cerebrovasc Dis. 2001;11(3):177.
[2] The incidence of cerebral venous thrombosis: a cross-sectional study. Coutinho JM, Zuurbier SM, Aramideh M, Stam J. Stroke. 2012 Dec;43(12):3375-7..
[3] Cerebral Venous Sinus Thrombosis Incidence Is Higher Than Previously Thought: A Retrospective Population-Based Study. Devasagayam S, Wyatt B, Leyden J, Kleinig T. Stroke. 2016 Sep;47(9):2180-2.
[4] Diagnosis and management of cerebral venous thrombosis: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Saposnik G, et al. 2011;42(4):1158.

CVST signs and symptoms

- More common presentations
  - Isolated intracranial hypertension syndrome (headache with or without vomiting, papilledema, and visual problems)
  - Focal syndrome (focal deficits, seizures, or both)
  - Encephalopathy (multifocal signs, mental status changes, stupor, or coma)

- Rare presentations
  - Cavernous sinus syndrome
  - Subarachnoid hemorrhage
  - Cranial nerve palsies

Reports of CVST to VAERS after COVID-19 vaccines as of April 12, 2021

- Janssen COVID-19 vaccine
  - 6 reports of CVST with thrombocytopenia (platelet counts <150K/mm^3) following 6.86 million doses administered
    - Reporting rate of 0.87 cases per million doses administered
- Pfizer-BioNTech COVID-19 vaccine
  - 0 reports following 97.9 million doses administered
- Moderna COVID-19 vaccine
  - 3 reports following 84.7 million doses administered
  - All 3 with normal platelet counts; onset 2, 6, and 12 days after vaccination

Source of doses administered: https://covid.cdc.gov/covid-data-tracker/#vaccinations

Characteristics of patients with CVST and thrombocytopenia* after Janssen COVID-19 vaccine, N=6

- Median age 33 years (range 18–48)
- Median time to symptom onset 8 days (range 6–13 days)
- All cases occurred in white females
- Current estrogen/progesterone use (n=1)
- Pregnant or post-partum (n=0)
- Pre-existing conditions
  - Obesity (n=3)
  - Hypothyroidism (n=1)
  - Hypertension (n=1)
  - Asthma (n=1)
  - Coagulation disorders (none known)

* Note: Thrombosis usually does not occur in the presence of low platelets; these case presentations are atypical and consistent with cases observed after AstraZeneca COVID-19 vaccine

Initial and late signs and symptoms among CVST patients*, N=6 (patients listed in no particular order)

	Initial features	Late features
Patient 1	Headaches, lethargy	Severe headache, left-sided weakness, vomiting
Patient 2	Headaches	Severe headache, aphasia
Patient 3	Headaches, vomiting, fever	Left arm weakness, right gaze deviation, left neglect
Patient 4	Headaches, chills, myalgias	Severe abdominal pain and fever
Patient 5	Headache, chills, dyspnea, fever	Bruising, unilateral leg swelling, loss of consciousness
Patient 6	Back pain, bruising	Headache, abdominal pain

*All were hospitalized and admitted to the intensive care unit

Locations of CVST, intracerebral hemorrhage, and other thromboses, N=6

Characteristic	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Location of CVST	Right transverse sinus and right sigmoid sinus	Left transverse sinus, left sigmoid sinus, confluence of sinuses, and straight sinus	Superior sagittal sinus, inferior sagittal sinus, and straight sinus	Right transverse sinus and right sigmoid sinus	Right transverse sinus and right sigmoid sinus	Right transverse sinus
Location of intracerebral hemorrhage	Right temporo-parietal lobe	Left temporal lobe	Bilateral frontal lobes, intraventricular	None	None	Occipital lobe
Locations of other thromboses	None	None	None	Portal vein and right pulmonary artery	Bilateral lower extremity VTE, right internal jugular vein	Portal vein

Observed vs. expected CVST cases following Janssen COVID-19 vaccine

- Estimated annual incidence of CVST ~0.5–2 cases per 100,000 population*
- Assumed risk period of 5.6% of a calendar year: (41 days/2) ÷ 365 days
- Doses administered among women aged 20–50 years = 1,402,712 doses (as of Apr 12)

Est. annual background incidence	Obs. cases in women aged 20–50 yrs	Exp. cases in women aged 20–50 yrs	Reporting ratio, women aged 20–50 yrs
0.5 per 100K	6	0.39	**15.4**
1.0 per 100K	6	0.79	**7.6**
1.5 per 100k	6	1.18	**5.1**
2.0 per 100k	6	1.58	**3.8**

* https://www.hopkinsmedicine.org/health/conditions-and-diseases/cerebral-venous-sinus-thrombosis, http://www.med.umich.edu/1libr/Stroke/SinusVeinThrombosis.pdf, https://www.nejm.org/doi/10.1056/NEJMra042354?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub, https://www.ahajournals.org/doi/pdf/10.1161/STROKEAHA.116.013617, https://www.nature.com/articles/nrneurol.2017.104

Summary

- CVST is rare, but clinically serious, and can result in substantial morbidity and mortality; not usually associated with thrombocytopenia
- Observed cases following Janssen COVID-19 vaccines appear to exceed expected based on background rates of CVST among women aged 20–50 years (3-fold or greater)
  - All 6 reports were in women age range 18–48 years, all with thrombocytopenia
  - No obvious patterns of risk factors detected
- CVST with thrombocytopenia has not been observed after the two authorized mRNA vaccines
  - 182 million mRNA COVID-19 doses administered with no reported cases to date
- Clinical features of Janssen cases are similar to those observed following the AstraZeneca COVID-19 vaccine in Europe
- Both Janssen and AstraZeneca vaccines contain replication-incompetent adenoviral vectors (human [Ad26.COV2.S] for Janssen and chimpanzee [ChAdOx1] for AstraZeneca)

Summary (cont.)

- **For clinicians**
  - Maintain a high index of suspicion for symptoms that might represent serious thrombotic events or thrombocytopenia in patients who have recently received the Jansen COVID-19 vaccine, including severe headache, backache, new neurologic symptoms, severe abdominal pain, shortness of breath, leg swelling, petechiae (tiny red spots on the skin), or new or easy bruising. Obtain platelet counts and screen for evidence of immune thrombotic thrombocytopenia.
  - In patients with a thrombotic event and thrombocytopenia after the Jansen COVID-19 vaccine, evaluate initially with a screening PF4 enzyme-linked immunosorbent (ELISA) assay as would be performed for autoimmune HIT. Consultation with a hematologist is strongly recommended.
  - Do not treat patients with thrombotic events and thrombocytopenia following receipt of Janssen COVID-19 vaccine with heparin, unless HIT testing is negative.
  - If HIT testing is positive or unable to be performed in patient with thrombotic events and thrombocytopenia following receipt of Jansen COVID-19 vaccine, non-heparin anticoagulants and high-dose intravenous immune globulin should be strongly considered.
  - Report adverse events to VAERS, including serious and life-threatening adverse events and deaths in patients following receipt of COVID-19 vaccines as required under the Emergency Use Authorizations for COVID-19 vaccines.

Vaccinations All HPH Sites - HAWAII PACIFIC HEALTH SA

	4/14	FYTD
Administrations of COVID-19 Vaccine	2,582	162,065

Wilcox Medical Center Vaccination Center (Kaua'i) - Vaccination Clinic - Kauai Medical Clinic/Wilcox Memorial Health + 1 more

	4/14	FYTD
Administrations of COVID-19 Vaccine	297	13,972
Administrations of COVID-19 Vaccine (Age 50+)	216	12,083
Administrations of COVID-19 Vaccine (Age under 50)	81	1,889

Pier 2 Vaccination Center (O'ahu) - Vaccination Clinic - Pier 2 Cruise Terminal

	4/14	FYTD
Administrations of COVID-19 Vaccine	2,282	132,712
Administrations of COVID-19 Vaccine (Age 50+)	1,271	96,262
Administrations of COVID-19 Vaccine (Age under 50)	1,011	34,926

Pfizer vaccine	124,089
Moderna vaccine	7,099
Janssen vaccine	1,524

COVID-19 Variant & Treatment Updates

Douglas Kwock, MD
Vice President of Medical Staff Affairs
Hawai‘i Pacific Health

HAWAI‘I PACIFIC HEALTH | HAWAI‘I HEALTH PARTNERS

COVID-19 Variants

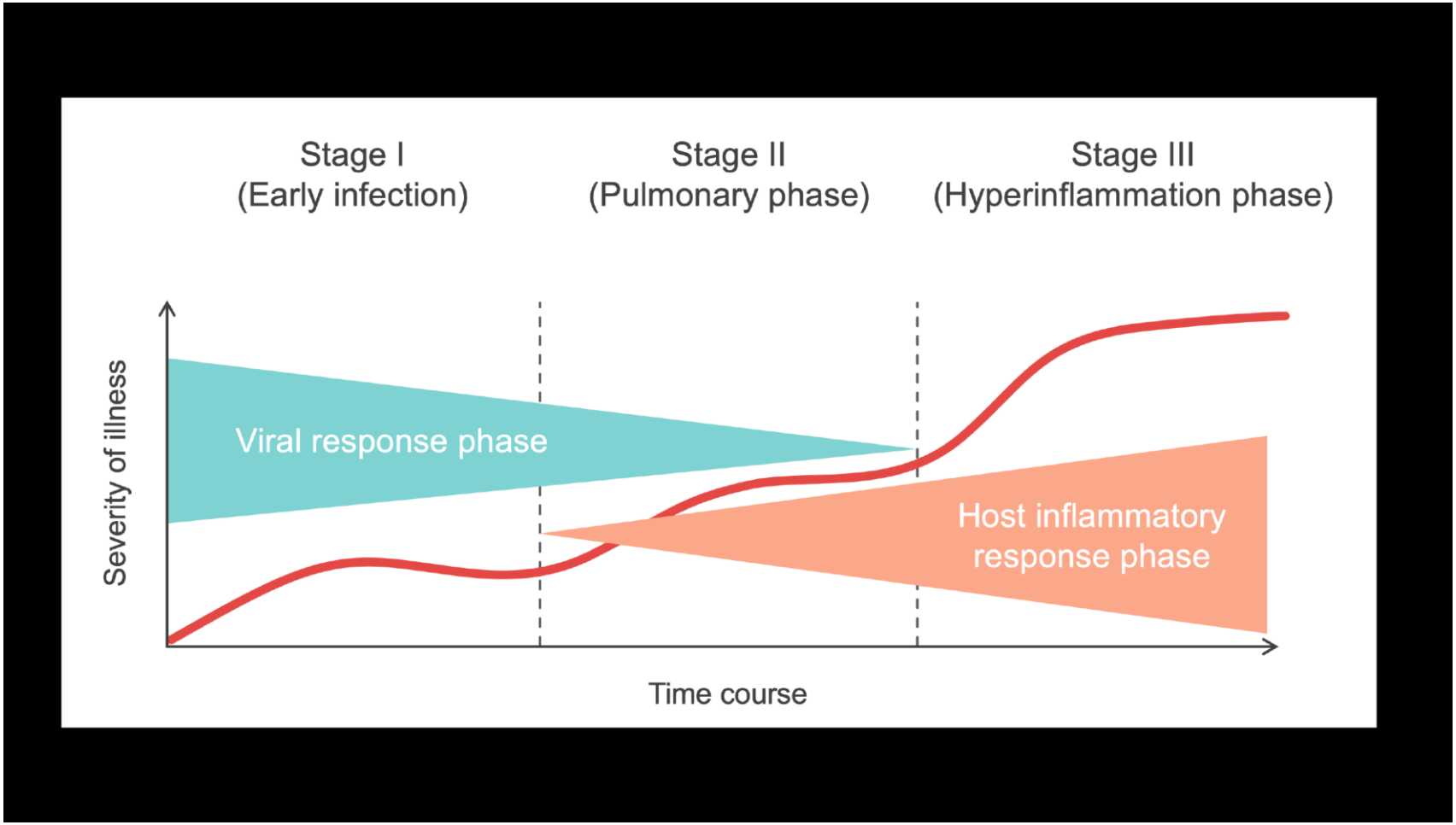
Variant	Common Name	Effect of mutations
B.1.1.7	UK	- Increased transmission - Might increase severity
B.1.351	South African	- Increased transmission - Antibodies less effective
P.1	Brazil	- Antibodies less effective
B.1.429	California	- Increased transmission - Antibodies less effective

COVID-19 Variants: Hawai‘i

	B.1.429 (CA)	B.1.1.7 (UK)	B.1.351 (SA)
State	59%	8%	2%
Honolulu County	59%	8%	3%
Maui County	82%	3%	0%
Hawai‘i County	19%	16%	0%

PRELIMINARY DOH DATA, March 2021

COVID-19 Infection



COVID-19 Treatment

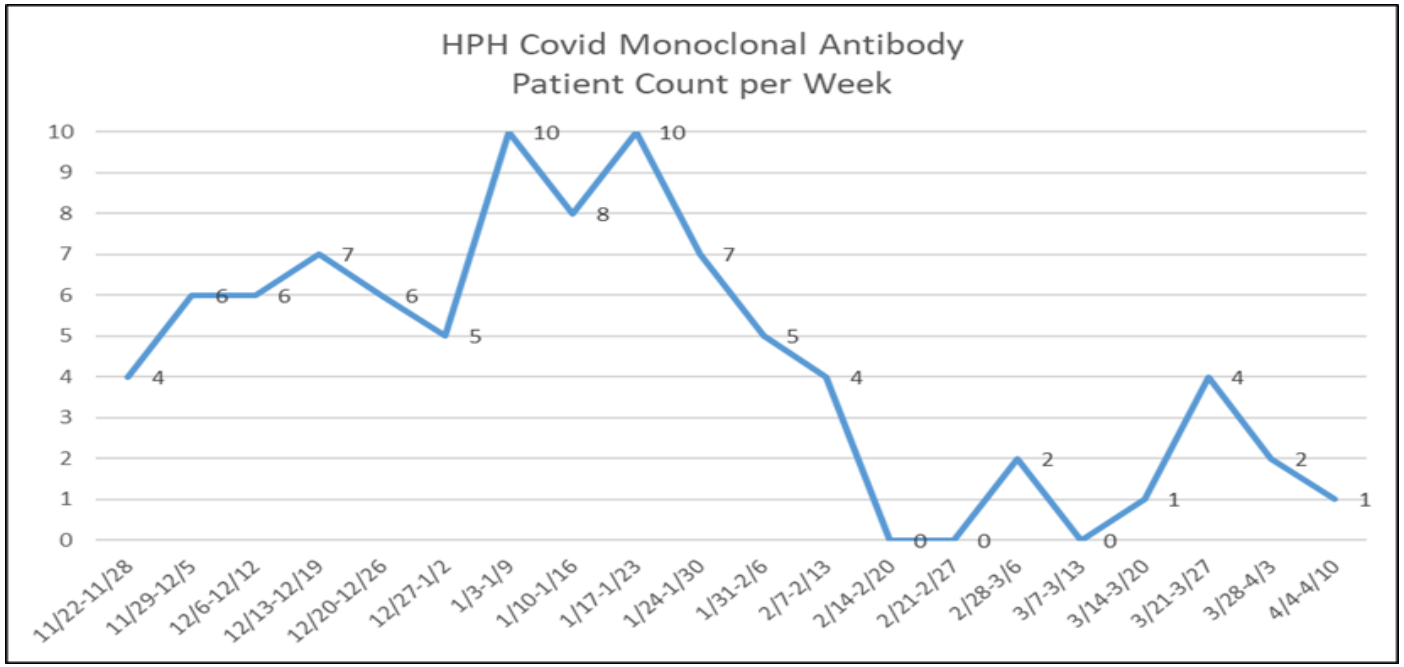
Stage	Therapy
Pre-Exposure Protection	• Vaccination
Post-Exposure Prophylaxis	• None
Not Hospitalized • Mild to Moderate illness	• Supportive care • Consider monoclonal antibody therapy if at high risk for disease progression

COVID-19 Treatment

Stage	Therapy
Hospitalized • No supplemental oxygen requirement	• Supportive care • Consider Remdesivir • Consider high titer CCP
Hospitalized • Requires supplemental oxygen • No mechanical ventilation or ECMO	• Supportive care • Remdesivir • Consider high titer CCP • Dexamethasone
Hospitalized • Mechanical ventilation or ECMO	• Supportive care • Dexamethasone

Treatment Updates: Moab Therapy

- Bamlanivimab monotherapy
  - Fair data to support use
  - Started Straub REC & Wilcox infusions on 11/24/2020
  - Five COVID-19 hospitalizations after Bamlanivimab infusion



Treatment Updates: Moab Therapy

- Bamlanivimab monotherapy
  - No longer recommended

Table 3: Pseudovirus Neutralization Data for SARS-CoV-2 Variant Substitutions with Bamlanivimab Alone

Lineage with Spike Protein Substitution	Key Substitutions Tested[a]	Fold Reduction in Susceptibility
B.1.1.7 (UK origin)	N501Y	no change[b]
B.1.351 (South Africa origin)	E484K	>2,360[c]
P.1 (Brazil origin)	E484K	>2,360[c]
B.1.427/B.1.429 (California origin)	L452R	>1,020[c]
B.1.526 (New York origin)[d]	E484K	>2,360[c]

[a] For variants with more than one substitution of concern, only the one with the greatest impact on activity is listed.
[b] No change: <5-fold reduction in susceptibility.
[c] No activity was observed at the highest concentration tested. Bamlanivimab alone is unlikely to be active against variants from this lineage.
[d] Not all isolates of the New York lineage harbor the E484K substitution (as of February 2021).

Treatment Updates: Moab Therapy

- Bamlanivimab/Etesevimab combination therapy
  - Better data than Bamlanivimab
    - Decreased viral load by day 11 vs placebo
    - Decreased hospitalizations vs placebo

Table 3: Pseudovirus Neutralization Data for SARS-CoV-2 Variant Substitutions with Bamlanivimab and Etesevimab Together (1:2 Molar Ratio)

Lineage with Spike Protein Substitution	Key Substitutions Tested[a]	Fold Reduction in Susceptibility
B.1.1.7 (UK origin)	N501Y	no change[b]
B.1.351 (South Africa origin)	K417N + E484K + N501Y	>45[c]
P.1 (Brazil origin)	K417T + E484K + N501Y	>511[c]
B.1.427/B.1.429 (California origin)	L452R	7.4
B.1.526 (New York origin)[d]	E484K	17

[a] For variants with more than one substitution of concern, only the one(s) with the greatest impact on activity is(are) listed.
[b] No change: <5-fold reduction in susceptibility.
[c] No activity observed at the highest concentration tested. Bamlanivimab and etesevimab together are unlikely to be active against variants from this lineage.
[d] Not all isolates of the New York lineage harbor the E484K substitution (as of February 2021).

Treatment Updates: Moab Therapy

- Bamlanivimab/Etesevimab combination therapy
  - Started Straub REC & Wilcox 4/12/2021
  - Same safety profile as Bamlanivimab monotherapy
  - Same workflows
  - Same criteria for use as Bamlanivimab monotherapy
    - Treatment of mild to moderate COVID-19 in patients 12 years and older (at least 40kg weight)
    - Non-hospitalized
    - Positive COVID-19 test result
    - Infuse within 10 days of symptoms onset
    - At high risk for progressing to severe COVID-19 and/or hospitalization

Treatment Updates: Moab Therapy

High risk is defined as patients who meet at least one of the following criteria:

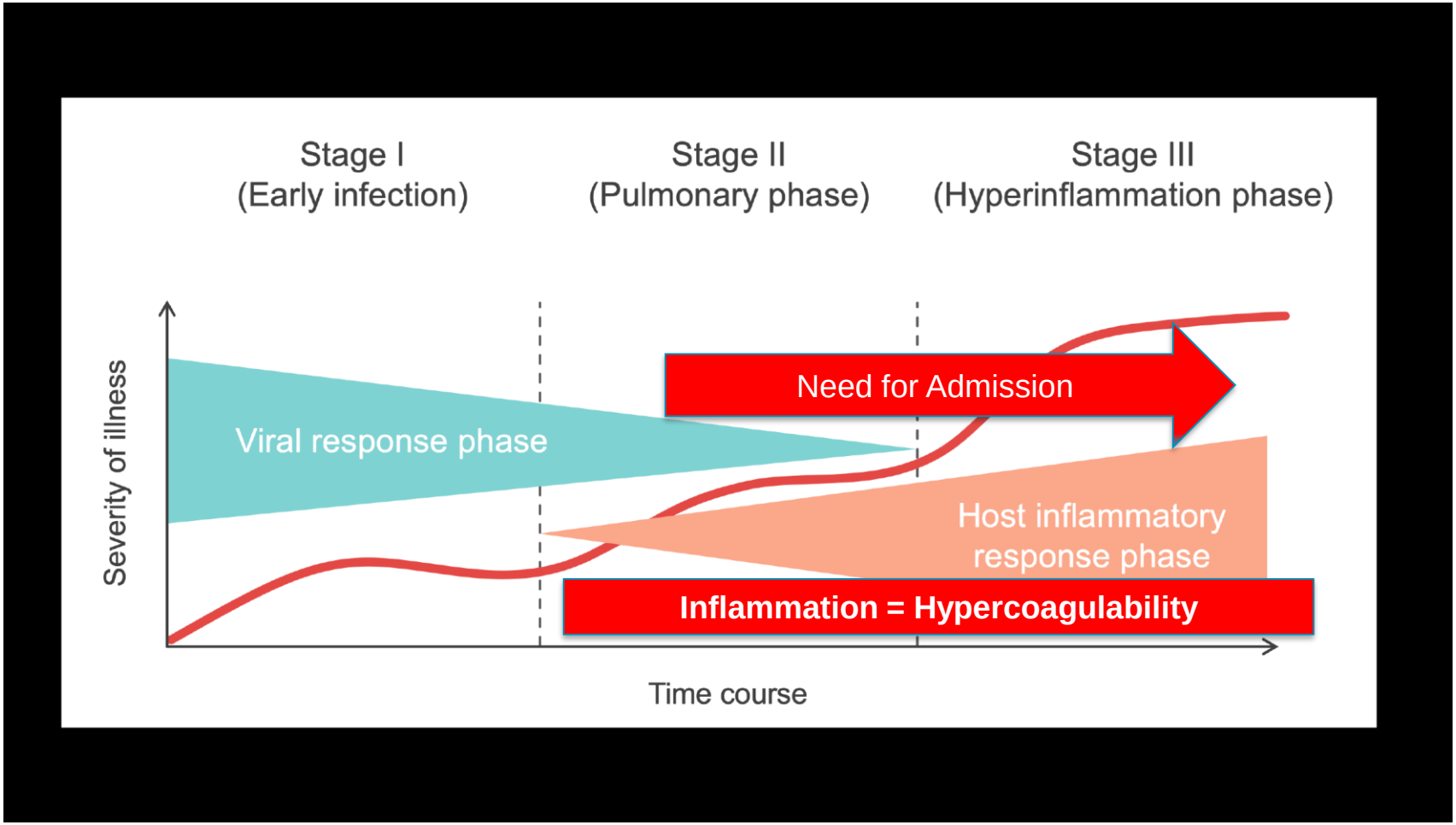
- Have a body mass index (BMI) ≥35
- Have chronic kidney disease
- Have diabetes
- Have immunosuppressive disease
- Are currently receiving immunosuppressive treatment
- Are ≥65 years of age
- Are ≥55 years of age AND have
  - cardiovascular disease, OR
  - hypertension, OR
  - chronic obstructive pulmonary disease/other chronic respiratory disease.
- Are 12 – 17 years of age AND have
  - BMI ≥85th percentile for their age and gender based on CDC growth charts, https://www.cdc.gov/growthcharts/clinical_charts.htm, OR
  - sickle cell disease, OR
  - congenital or acquired heart disease, OR
  - neurodevelopmental disorders, for example, cerebral palsy, OR
  - a medical-related technological dependence, for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19), OR
  - asthma, reactive airway or other chronic respiratory disease that requires daily medication for control.

Treatment Updates: Anticoagulation and IL-6

Wade Kyono, MD
Medical Director, Hawai‘i Pacific Health Research Institute
Principal Investigator, Children’s Oncology Group,
Kapi‘olani Medical Center for Women and Children
Pediatric Hematology/Oncology, Hawai‘i Pacific Health
Assistant Professor of Pediatrics, University of Hawai‘i,
John A. Burns School of Medicine

HAWAI‘I PACIFIC HEALTH | HAWAI‘I HEALTH PARTNERS

COVID-19 Infection



Hawaii Pacific Health Research Institute (HPHRI)

NIH/NHLBI: Accelerating COVID-19 Therapeutic Interventions and Vaccines-4 (ACTIV-4)

HAWAIʻI PACIFIC HEALTH | HAWAIʻI HEALTH PARTNERS

The link between blood clots and COVID-19

- Increased **inflammation** is associated with **hypercoagulability**
  - Lungs – Virchow‘s triad: hypercoagulable state, endothelial injury, and stasis of blood flow
  - Cytokine storm triggers the coagulation system and a hypercoagulable state
  - ARDS leads to increased microthrombi
- Autopsies of COVID-19 patients who die at home reveal pulmonary emboli/microthrombi
- Severe COVID-19 is complicated by coagulopathy and DIC which leads to a pro-thrombotic state with a high risk of venous thromboembolism (VTE)
- DIC a strong predictor of mortality (71% of nonsurvivors and 0.6% of survivors have evidence of overt DIC)

Treating Hypercoagulability – NIH/NHLBI

- **ACTIV-4a – Hospitalized (Completed)**

  - Full-dose therapeutic anticoagulation (AC) is superior to prophylactic dosing in **hospitalized but noncritically ill**. . . In critically ill/ICU level patients therapeutic anticoagulation was NOT beneficial and was associated with increased bleeding/mortality vs prophylactic dosing (INTERIM Conclusions!)

- **ACTIV-4b – Pre-Hospitalization (Recruiting)**
  - **Now OPEN at HPH Facilities!!**
  - Apixaban (Eliquis) vs low dose aspirin vs placebo orally x 45 days **as an outpatient**
  - Eligibility: Outpatient, 40-80 years, COVID-19 positive and symptomatic in last 14 days
- **ACTIV-4c – Post-Hospitalization (Pending Activation)**
  - Apixaban (Eliquis) vs placebo orally x 30 days **after discharge**
  - Referral/recruitment during hospitalization

ACTIV-4b

- PI – Dr. Heidi Hillesland (WMH - Kauai),
  Sub-I - Dr. Brian Pien (Straub - Honolulu)

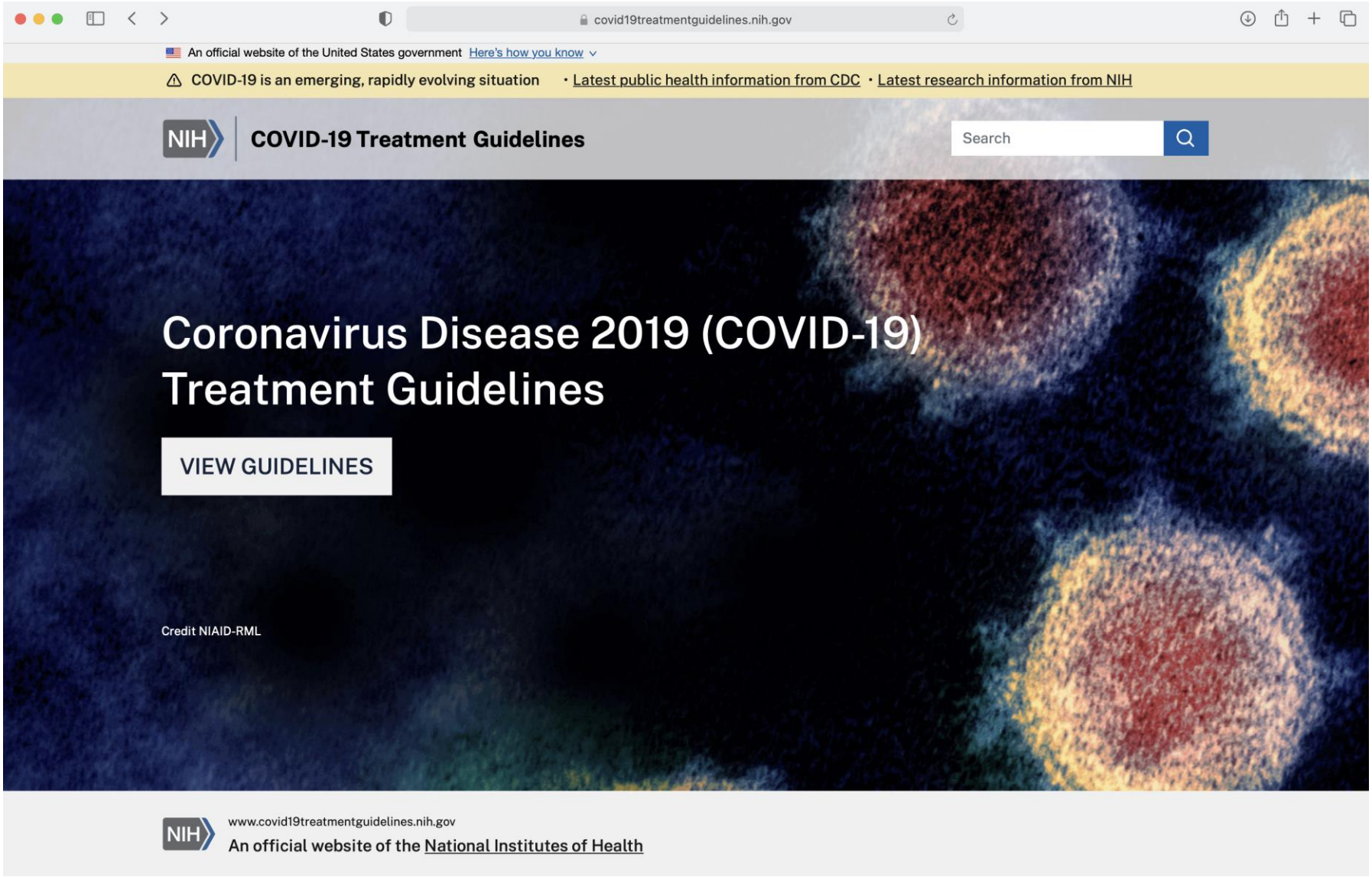
- To refer a patient send an email:

  activ4b@hawaiipacifichealth.org

- For more information:

  https://nhlbi-connects.org/activ4b

HAWAIʻI PACIFIC HEALTH | HAWAIʻI HEALTH PARTNERS

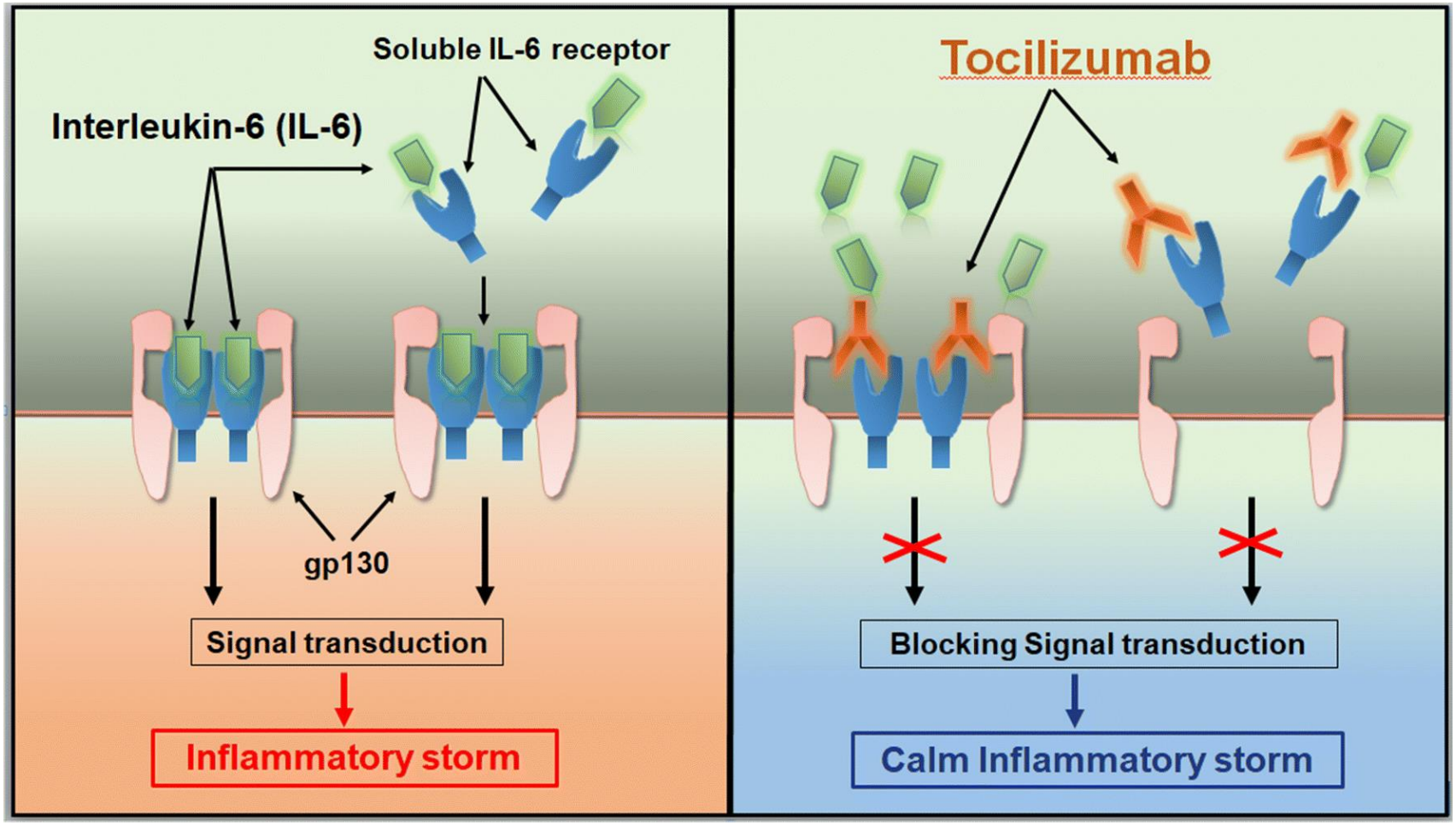

covid19treatmentguidelines.nih.gov
An official website of the United States government Here's how you know
COVID-19 is an emerging, rapidly evolving situation • Latest public health information from CDC • Latest research information from NIH
NIH
COVID-19 Treatment Guidelines
Search
Coronavirus Disease 2019 (COVID-19) Treatment Guidelines
VIEW GUIDELINES
Credit NIAID-RML
NIH
www.covid19treatmentguidelines.nih.gov
An official website of the National Institutes of Health

Turning Off Inflammation – IL-6 Inhibitors

- Interleukin (IL)-6 = pro-inflammatory cytokine
- Infection by the SARS-CoV induces a dose-dependent production of IL-6 from bronchial epithelial cells
- COVID-19-associated systemic inflammation and hypoxic respiratory failure can be associated with heightened cytokine release
  - elevated blood levels of **IL-6**, C-reactive protein (CRP), D-dimer, and ferritin
- It is hypothesized that **modulating the levels of IL-6 or its effects may alter the course of disease**
- Two FDA approved inhibitors
  - **Anti-IL-6 receptor monoclonal antibodies (sarilumab, tocilizumab)**
  - **Anti-IL-6 monoclonal antibodies (siltuximab)**

NIH | COVID-19 Treatment Guidelines

Tocilizumab

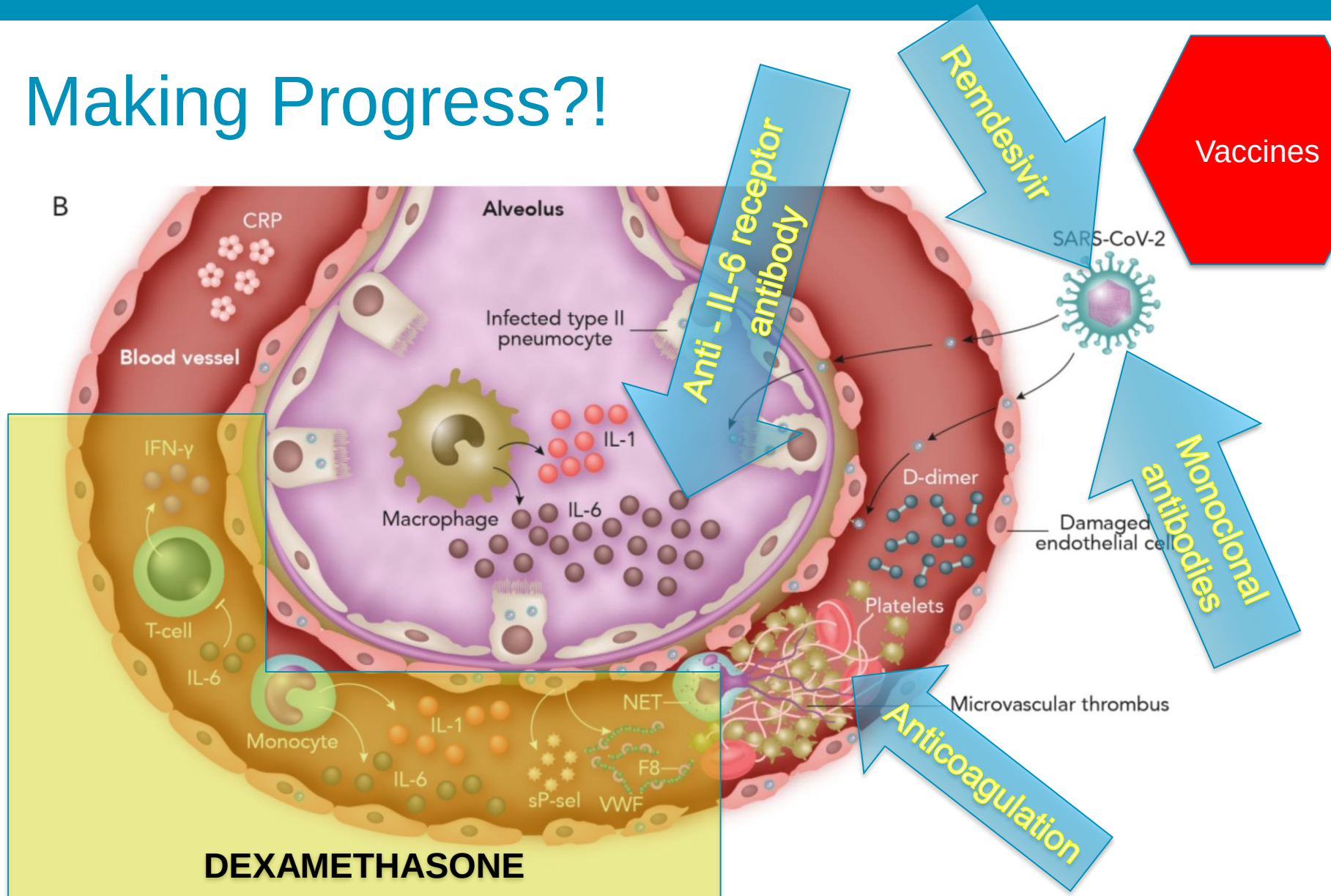


Use of Tocilizumab – Update 3/2021

- ***Evidence*** *from the Randomized, Embedded, Multifactorial Adaptive Platform Trial for Community-Acquired Pneumonia (REMAP-CAP) and Randomized Evaluation of COVID-19 Therapy (RECOVERY) trials* ***supports****:*
- ** The Panel recommends the use of **tocilizumab** (single intravenous dose of 8 mg/kg, up to 800 mg) **in combination with dexamethasone** (6 mg daily for up to 10 days) in certain hospitalized patients who are exhibiting rapid respiratory decompensation due to COVID-19 **
  - **Patients admitted to the ICU within the prior 24 hours who require invasive mechanical ventilation, noninvasive mechanical ventilation (NIV), or high-flow nasal canula (HFNC) oxygen;** ***or***
  - **Recently hospitalized patients (not in the ICU) with rapidly increasing oxygen needs who require NIV or HFNC and have significantly increased markers of inflammation (CRP ≥75 mg/L)**
- **Insufficient evidence to use tocilizumab** for hospitalized patients with hypoxemia who require conventional oxygen supplementation, instead use: **remdesivir, dexamethasone plus remdesivir**, or **dexamethasone alone**
- *https://www.covid19treatmentguidelines.nih.gov/statement-on-tocilizumab/*

NIH | COVID-19 Treatment Guidelines

Making Progress?!



Q&A

HAWAIʻI PACIFIC HEALTH | HAWAIʻI HEALTH PARTNERS

Next Webinar:

HHP Care Model and Disease Management Webinar:

Heart Failure (webinar #2 in CHF series)

Dr. Carol Lai & Dr. Rajive Zachariah

Thursday, April 29, 2021

5:30pm – 6:30 pm

Thank you!

- A recording of the meeting will be available afterwards.
- Unanswered question?
  - Contact us at Covid19Bulletin@hawaiipacifichealth.org

CREATING A HEALTHIER HAWAIʻI

HAWAIʻI PACIFIC HEALTH | HAWAIʻI HEALTH PARTNERS