HHP/HPH COVID-19 Community Webinar Series

Thursday, February 18, 2021

5:30pm – 6:30pm

HAWAIʻI PACIFIC HEALTH | HAWAIʻI HEALTH PARTNERS

Moderator – 02/18/21

Andy Lee, MD
Medical Director, *Hawai‘i Health Partners*
Chief of Staff, *Pali Momi Medical Center*
Hawai‘i Pacific Health

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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

COVID-19 Updates

Gerard Livaudais, MD, MPH

Executive Vice President, Population Health and Provider Networks,

Hawai‘i Pacific Health

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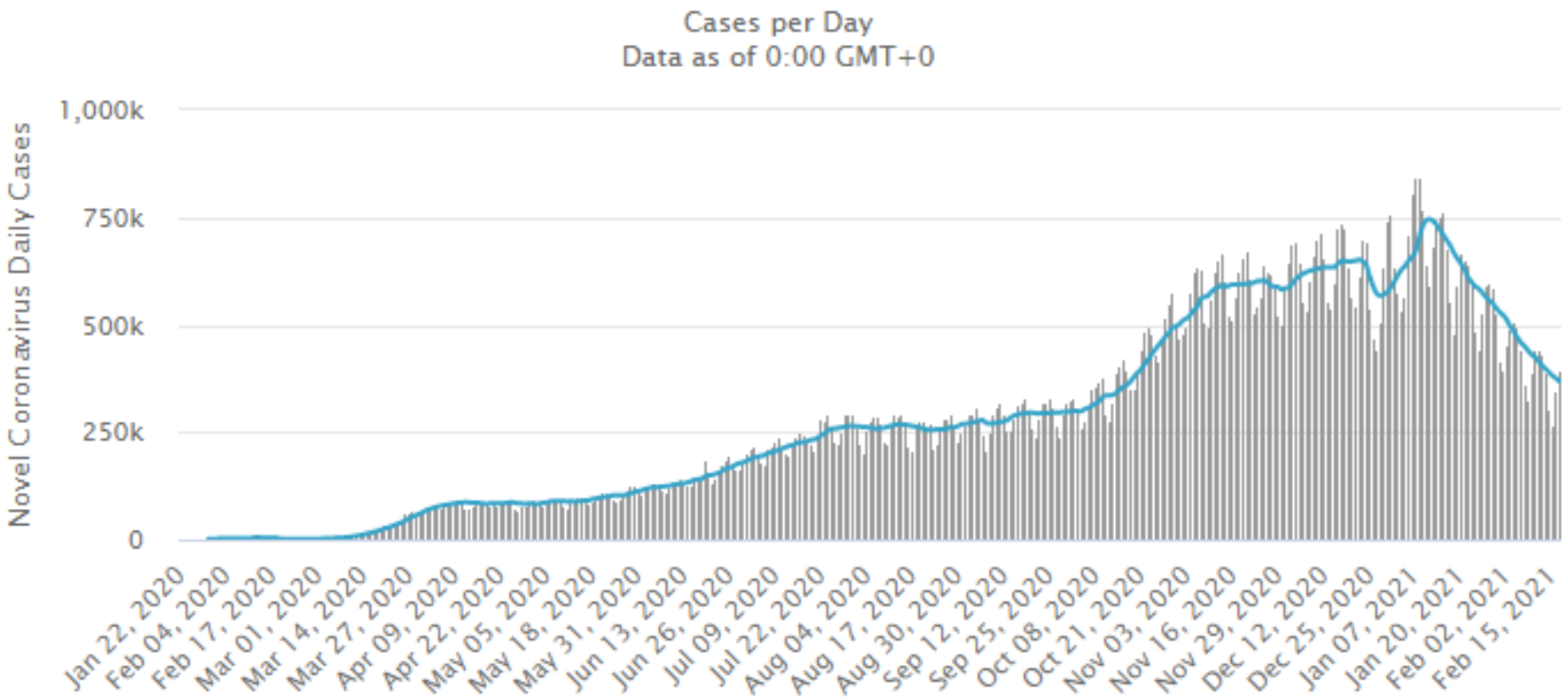
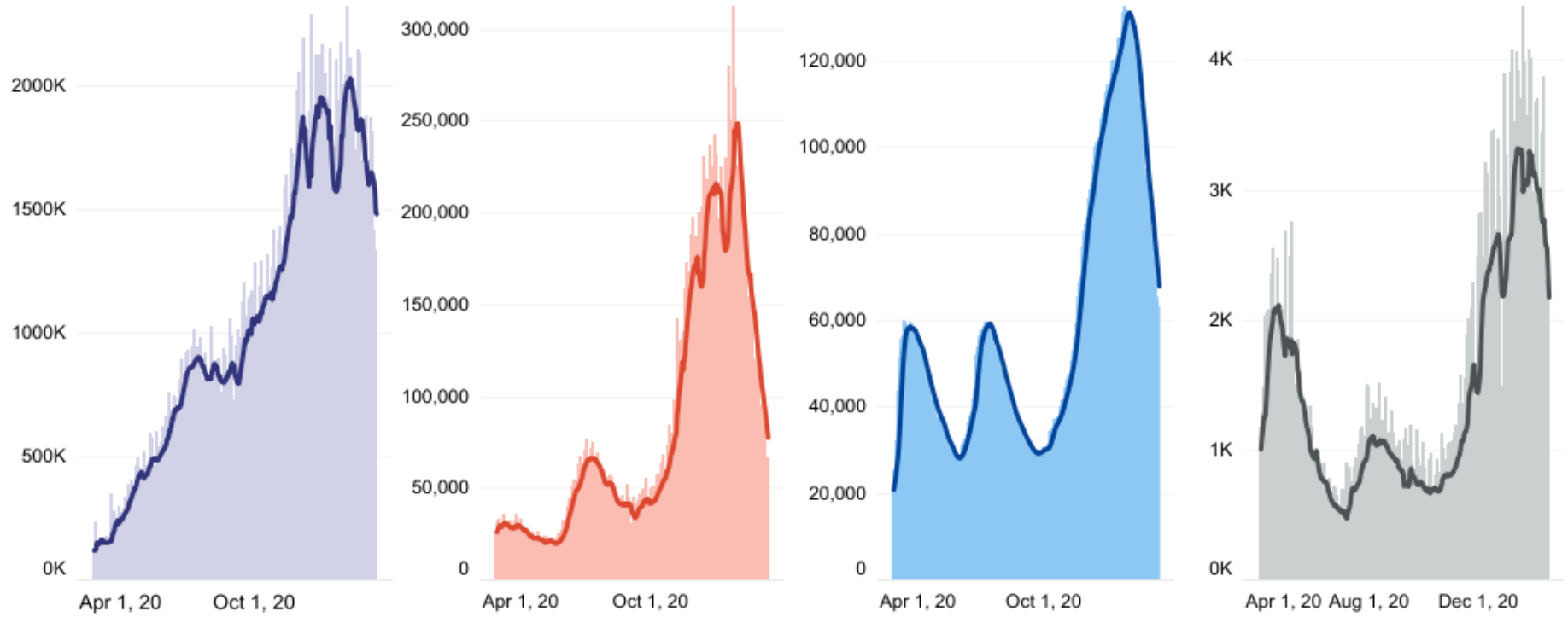
Daily New Cases



Source: **Worldometer** - www.worldometers.info

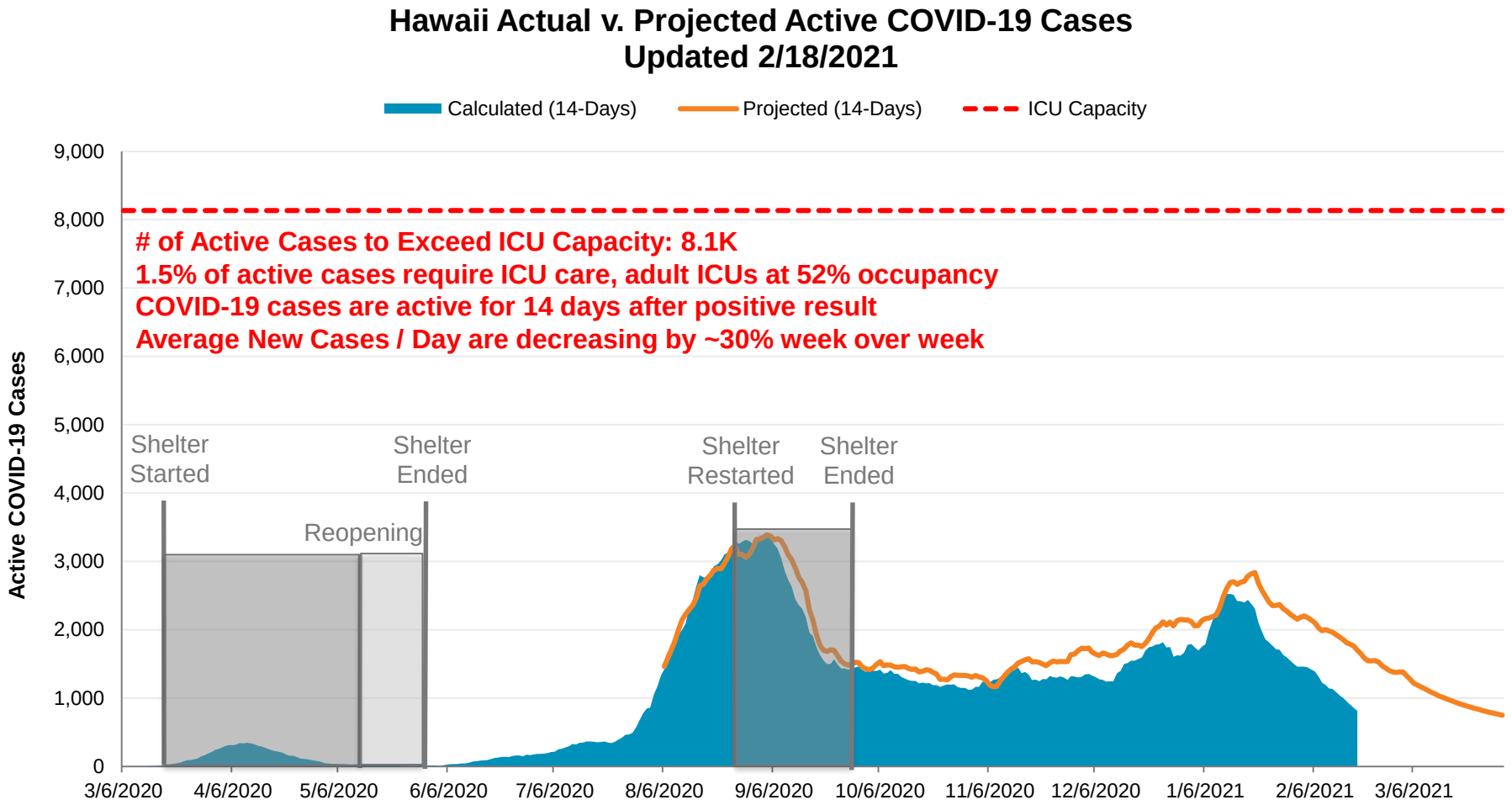
NATIONWIDE COVID-19 METRICS SINCE APRIL 1. 7-DAY AVERAGE LINES

Choose Census Region
All



The COVID Tracking Project

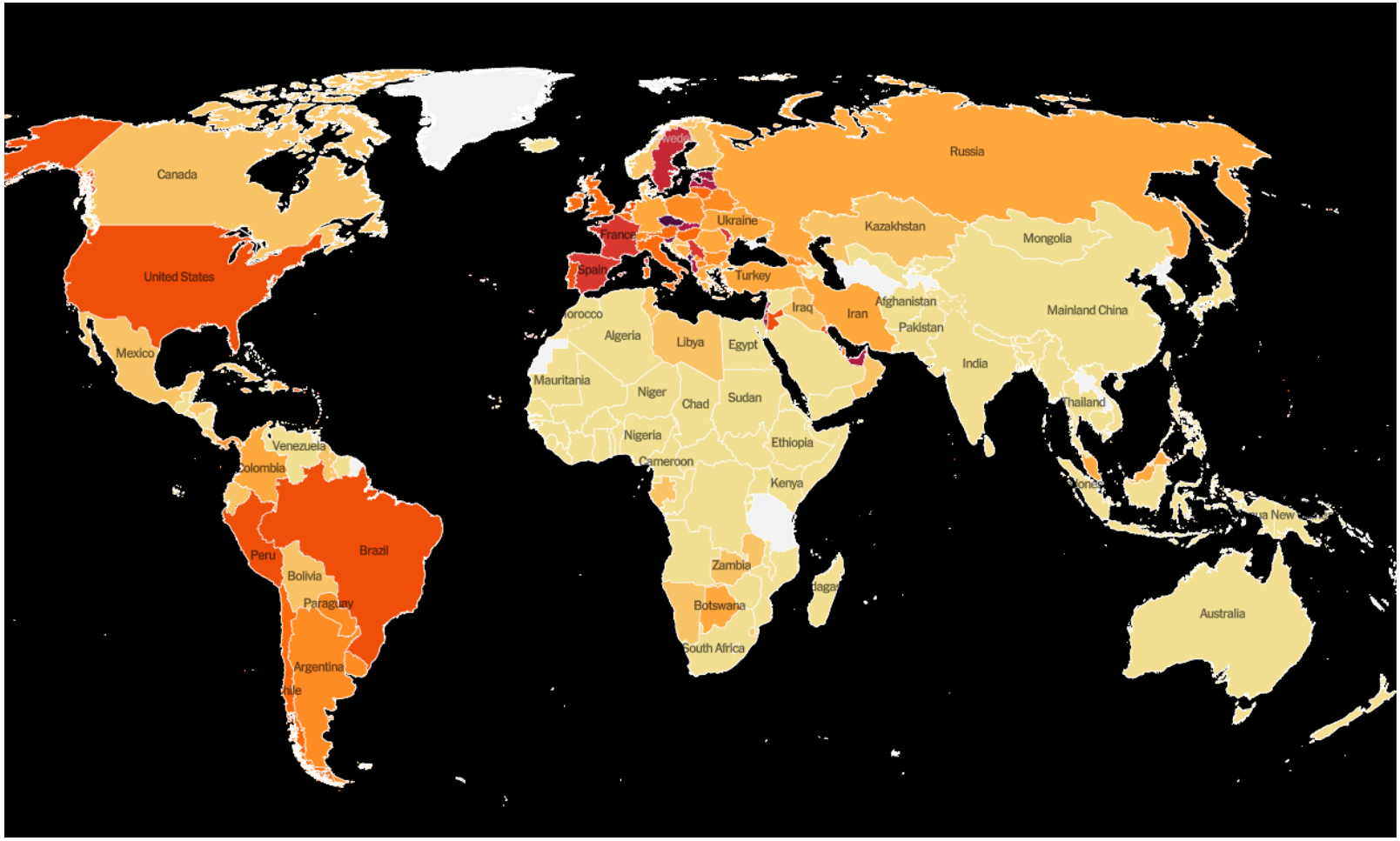
Projected Active COVID-19 Cases



As of 2/18/21	Total Census	ICU beds occupied	# Ventilators in use	# New Admissions w/ positive COVID-19	# Patients currently hospitalized w/ suspect or confirmed COVID-19	# Patients currently on a ventilator w/ confirmed COVID-19	# Patients currently in ICU w/ confirmed COVID-19
KMCWC	151	AICU: 0 NICU: 61 PICU: 9	AICU: 0 NICU: 16 PICU: 6	0	S: 0 C: 0	0	0
PMMC	112	4	3	1	S: 0 C: 4	0	0
SMC	132	10	8	0	S: 0 C: 3	1	1
WMC	48	6	2	0	S: 0 C: 1	0	0

S = Suspected; C= Confirmed

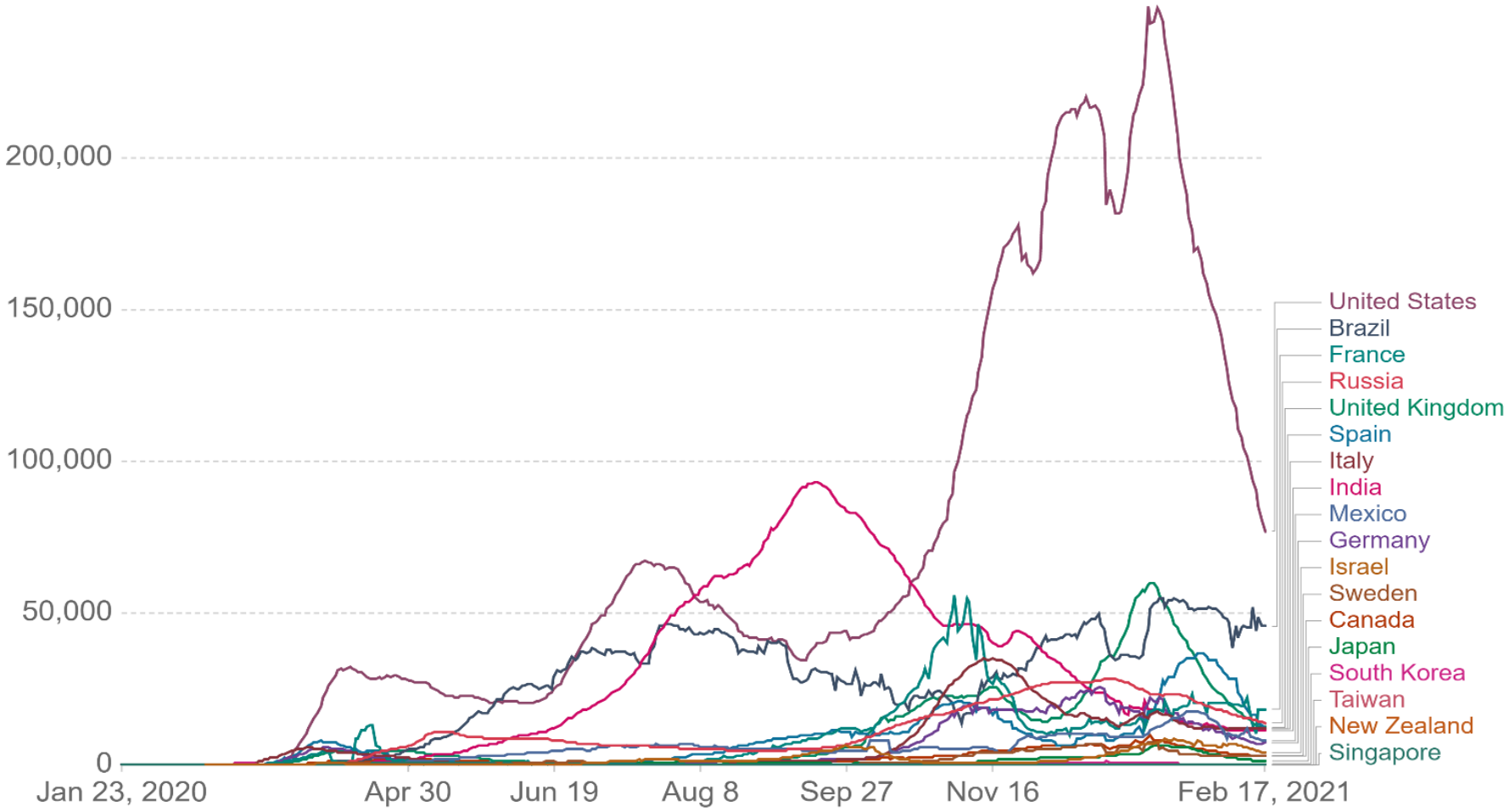
Hotspots are changing…



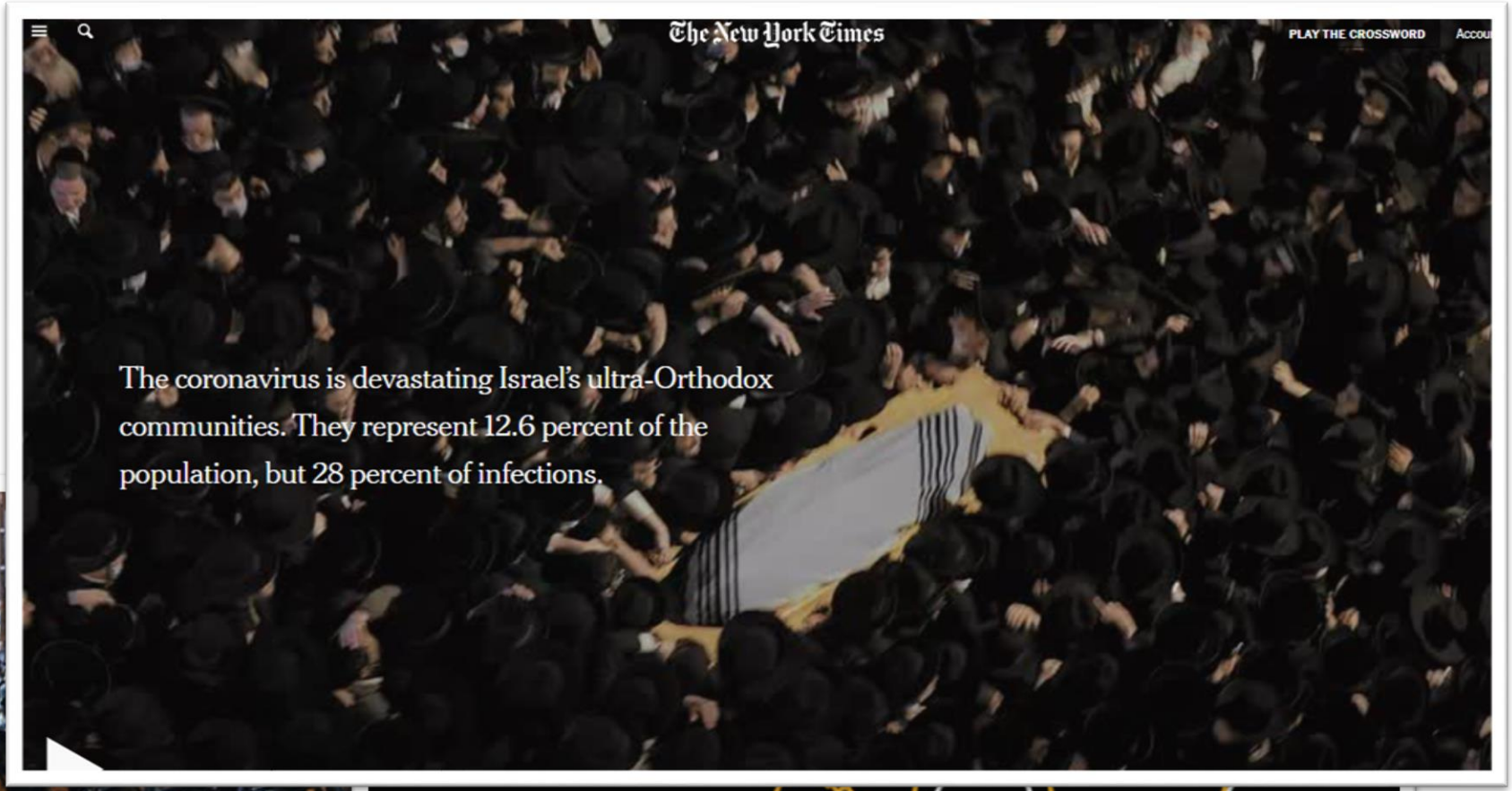
Daily new confirmed COVID-19 cases

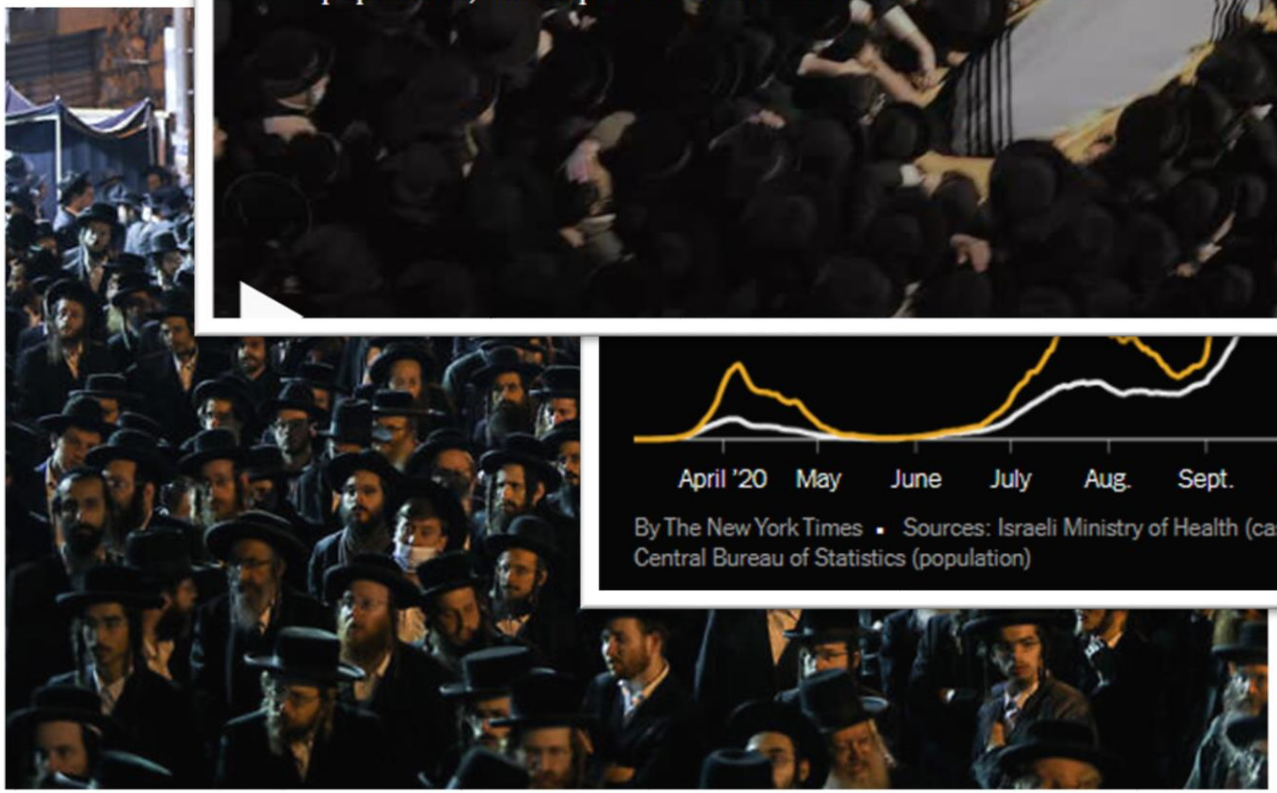
Shown is the rolling 7-day average. The number of confirmed cases is lower than the number of actual cases; the main reason for that is limited testing.

Our World in Data



Source: Johns Hopkins University CSSE COVID-19 Data – Last updated 18 February, 09:03 (London time)





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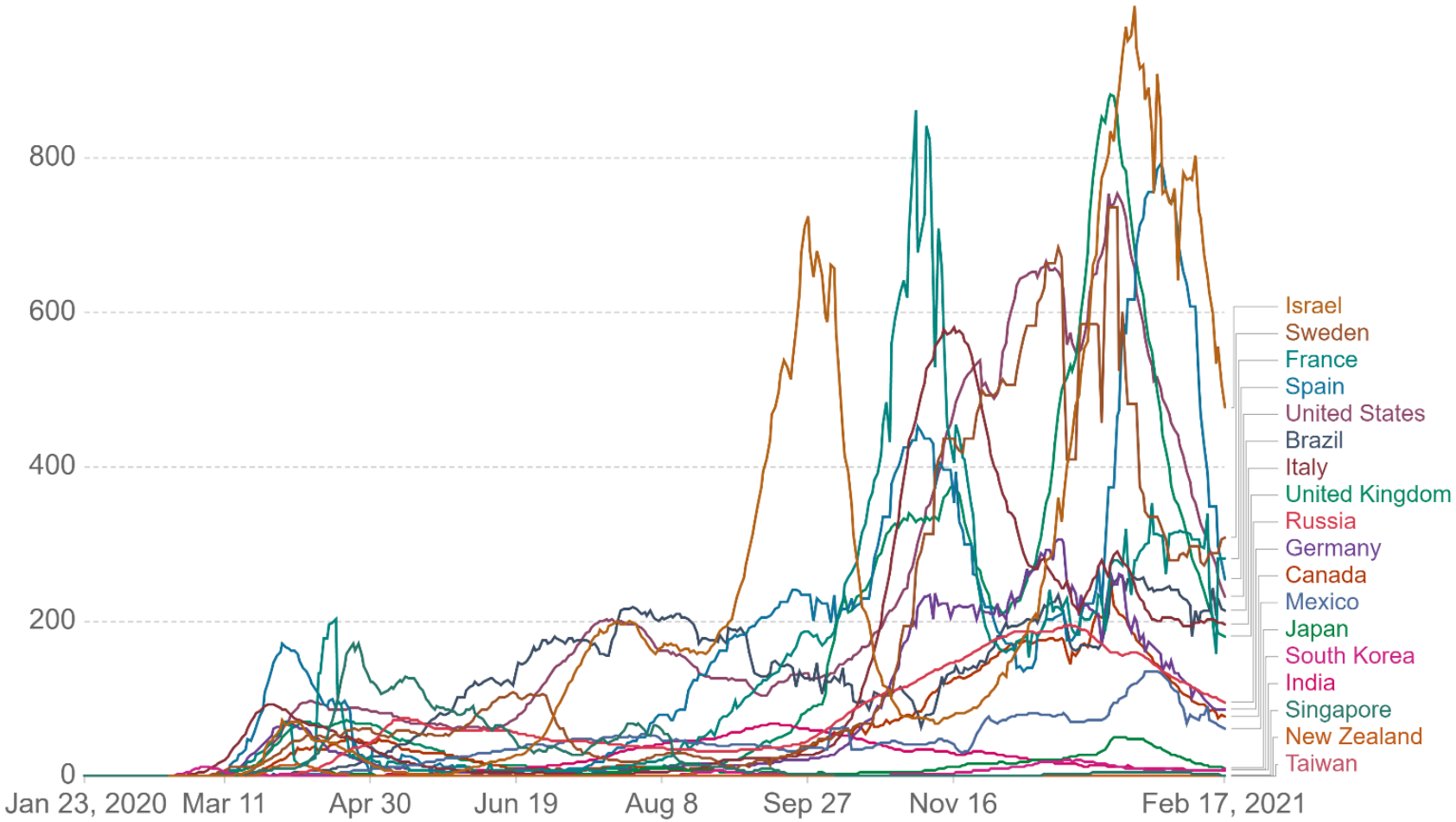
Daily new confirmed COVID-19 cases per million people

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.

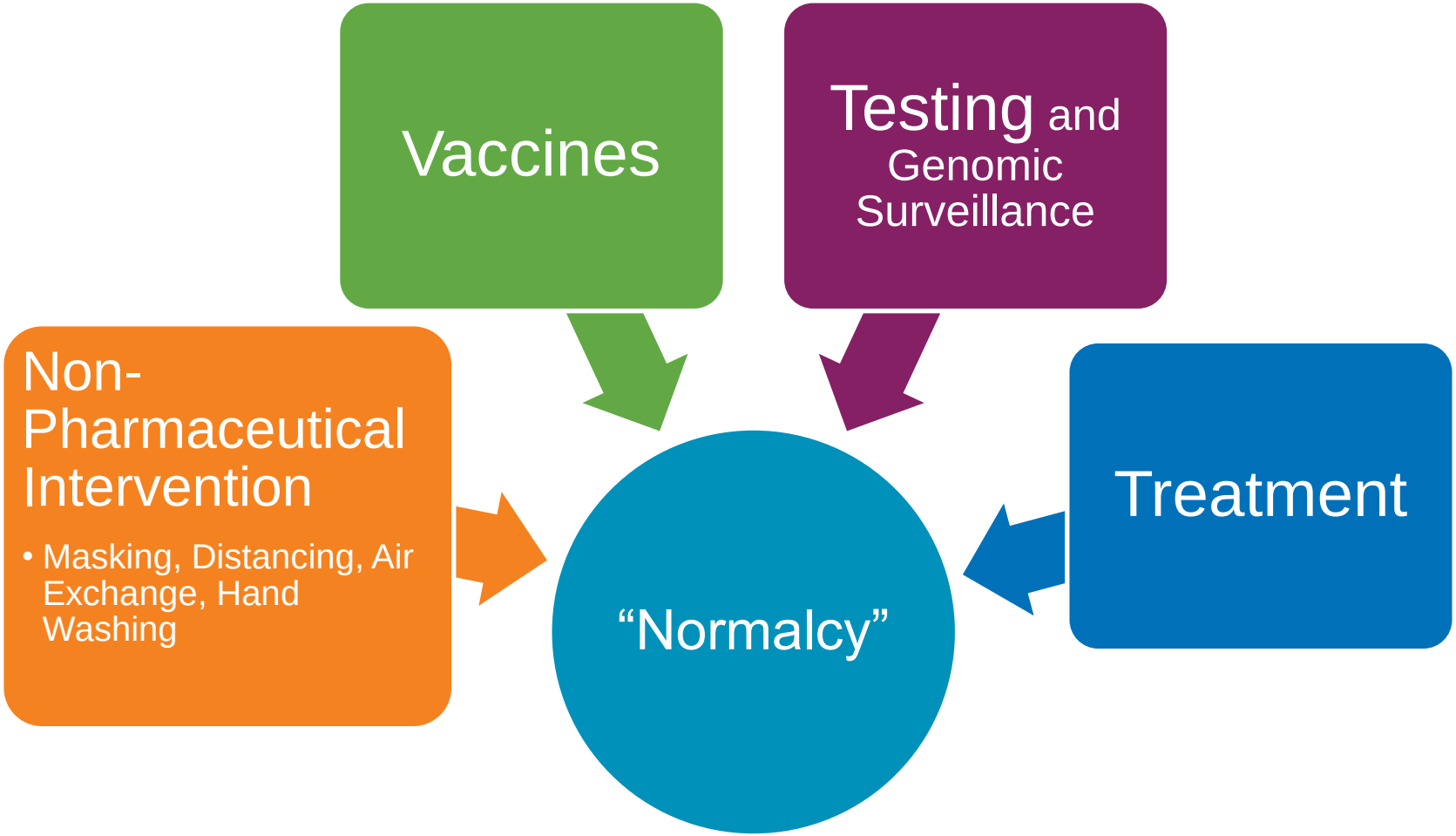
Our World in Data



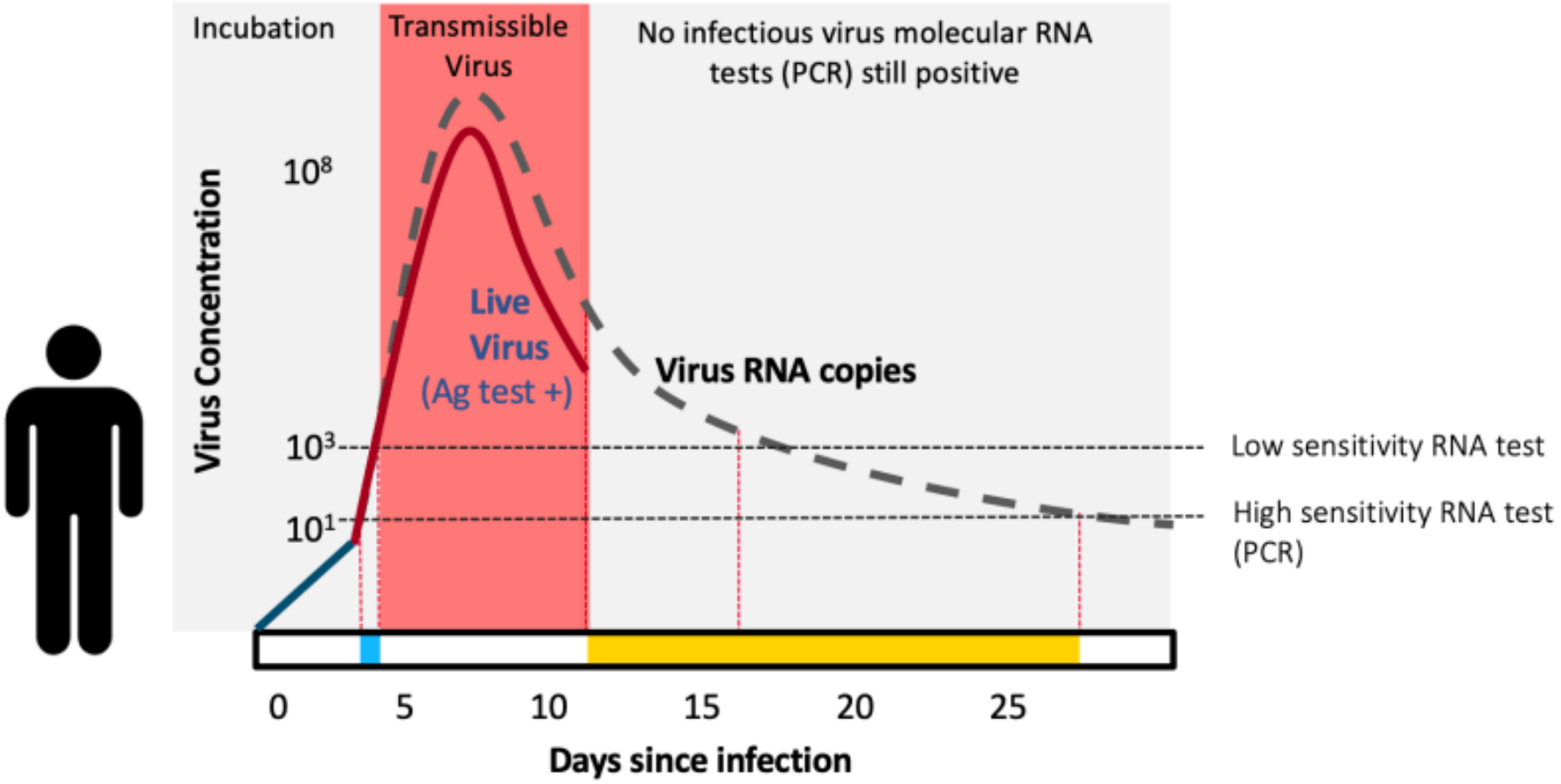
Source: Johns Hopkins University CSSE COVID-19 Data – Last updated 18 February, 09:03 (London time)

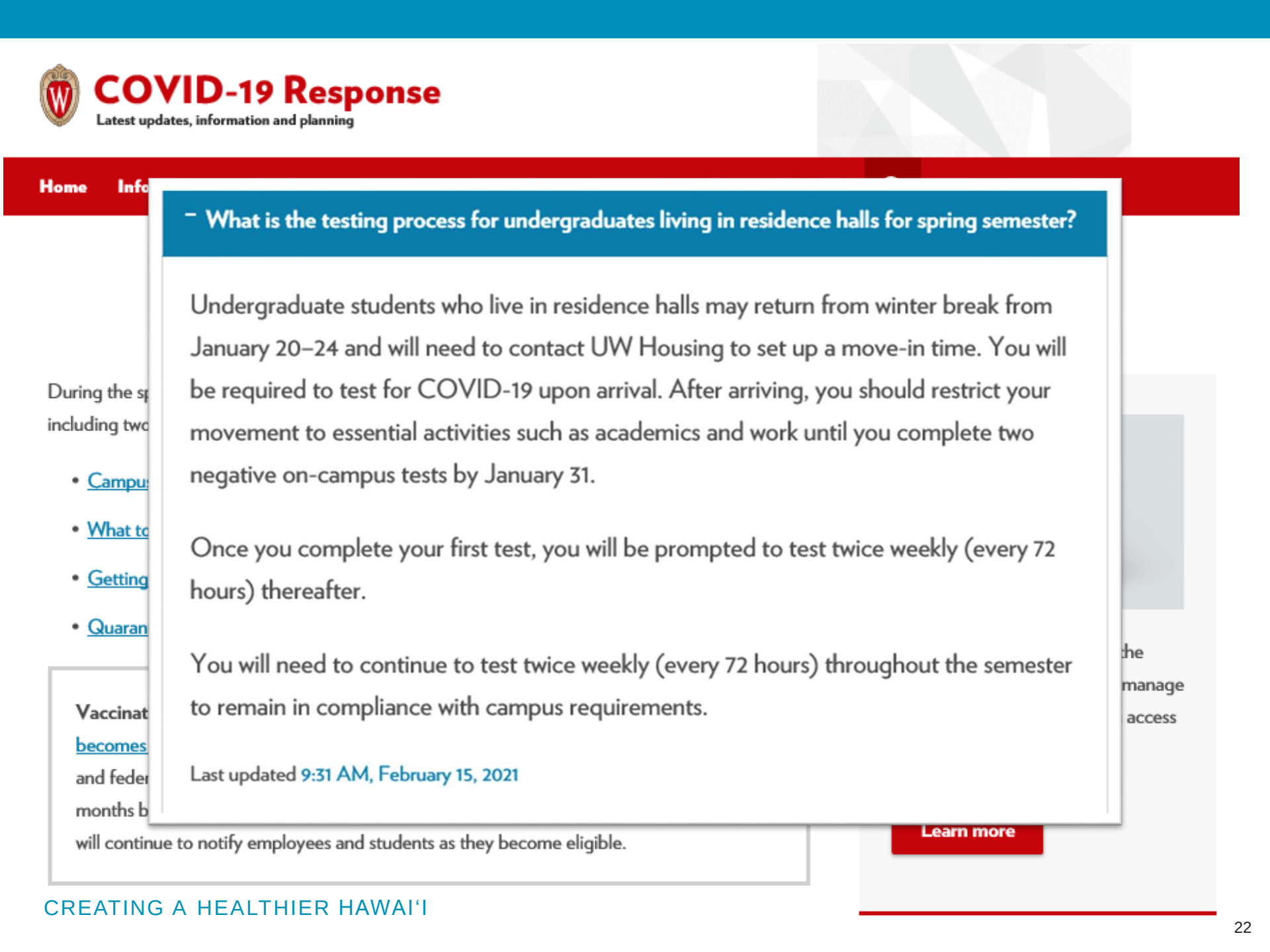
Evolving Variants of Concern…

Still the Winning Formula…



Still Missing the Opportunity with Testing…




COVID-19 Response
Latest updates, information and planning
Home
What is the testing process for undergraduates living in residence halls for spring semester?
Undergraduate students who live in residence halls may return from winter break from January 20–24 and will need to contact UW Housing to set up a move-in time. You will be required to test for COVID-19 upon arrival. After arriving, you should restrict your movement to essential activities such as academics and work until you complete two negative on-campus tests by January 31.
Once you complete your first test, you will be prompted to test twice weekly (every 72 hours) thereafter.
You will need to continue to test twice weekly (every 72 hours) throughout the semester to remain in compliance with campus requirements.
Last updated 9:31 AM, February 15, 2021
will continue to notify employees and students as they become eligible.
Learn more

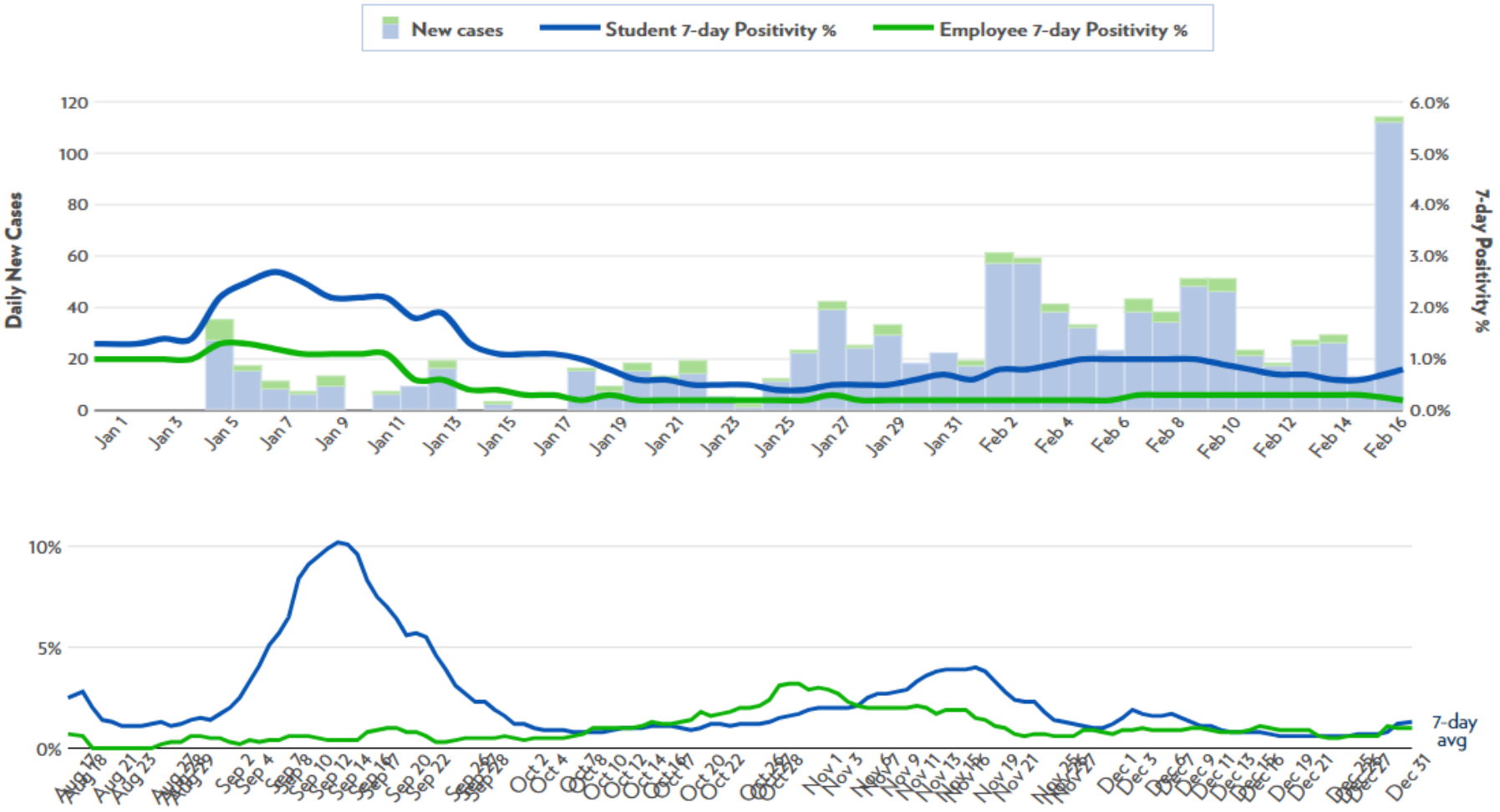
COVID-19 Response

Latest updates, information and planning

Home | Information for | Testing | Dashboard | FAQs | Campus Operations | Contact Us

Daily Cases and Percent Positivity 7-Day Average

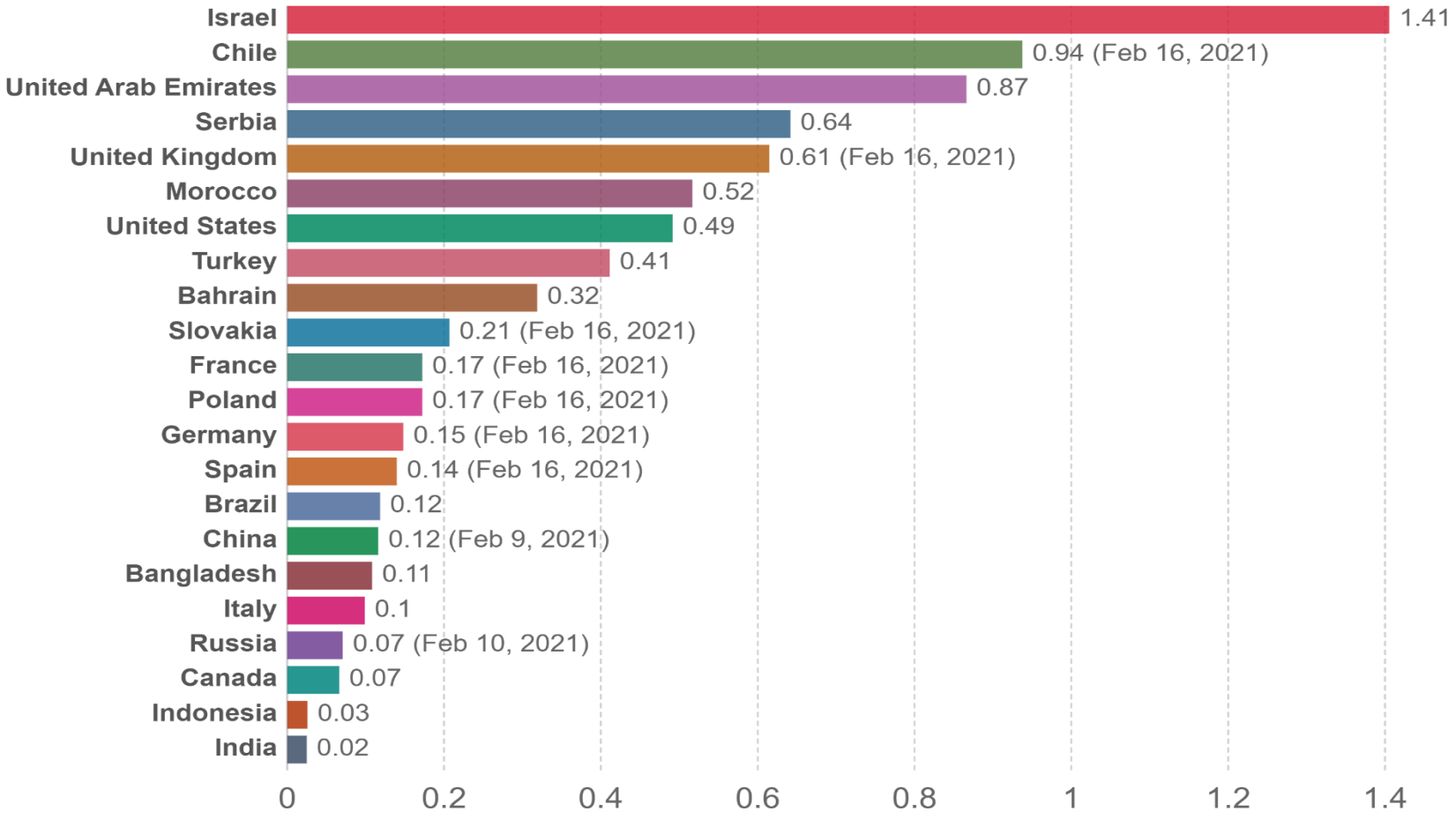
For testing performed on-campus



Daily COVID-19 vaccine doses administered per 100 people, Feb 17, 2021

Shown is the rolling 7-day average 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 – Last updated 18 February, 14:40 (London time)

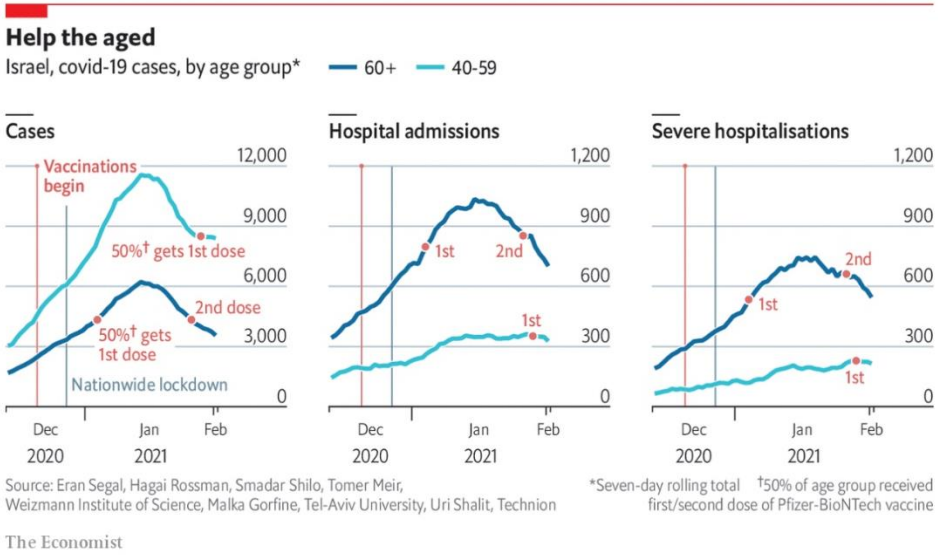
OurWorldInData.org/coronavirus • CC BY

Graphic detail

Daily chart

Israel's vaccine programme gives hope to the world

Hospital admissions among the old have fallen by a third since their peak



Feb 3rd 2021

OVER ONE-THIRD of Israel's population has received a vaccination against covid-19 since December 19th. Binyamin Netanyahu, the prime minister, has campaigned heavily for vaccinations, personally lobbying the boss of Pfizer, an American drugmaker, to secure early shipments of its vaccine. He was the first Israeli to be jabbed, live on television. He promised that

Date	Milestone
Dec 1	Covid-19 illness documented (unpublicized Nov 17th)
Jan 10	SARS-CoV-2 virus sequenced
Jan 15	NIH designs mRNA vaccine in collaboration with Moderna
Mar 16	Moderna Phase 1|2 trial begins
May 2	Pfizer/BioNTech Phase 1|2 trial begins
July 14	Moderna Phase 1|2 trial published in NEJM
July 27, 28	Moderna and Pfizer/BioNTech Phase 3 trial begins
Aug 12	Pfizer/BioNTech Phase 1|2 published in Nature
October 22,27	Enrollment in both Phase 3 trials complete; >74,000 participants
Nov 9	Pfizer/BioNTech announces interim analysis efficacy > 90%
Nov 16	Moderna announces interim analysis efficacy 94.5%
Nov 18	Pfizer/BioNTech announces 95% efficacy as final result
Nov 20	1st EUA submitted by Pfizer/BioNTech
Nov 27	Distribution of vaccine by UAL charter flights throughout US
Dec 10	FDA External review of Pfizer/BioNTech EUA
Dec 11	Phase 1a Vaccination begins for health care professionals*

*Provisional on positive external review

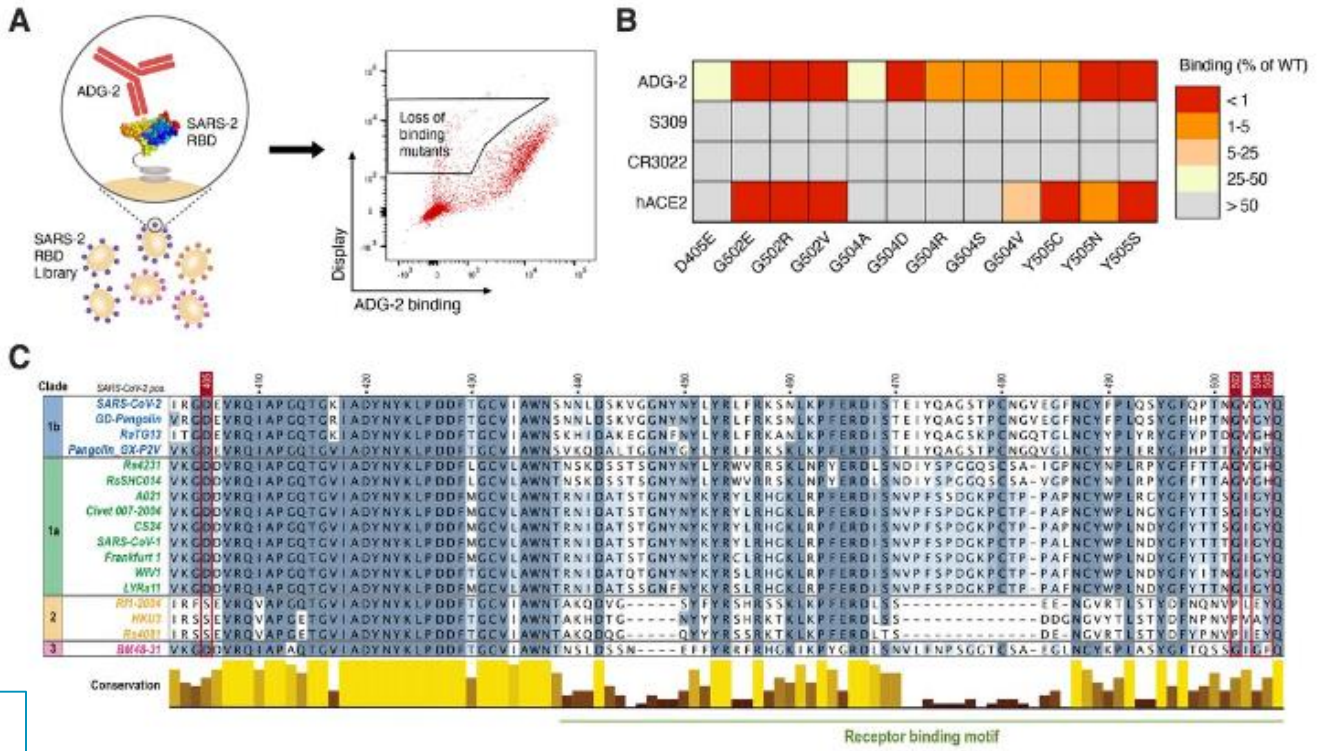
AAAS

Science Conte

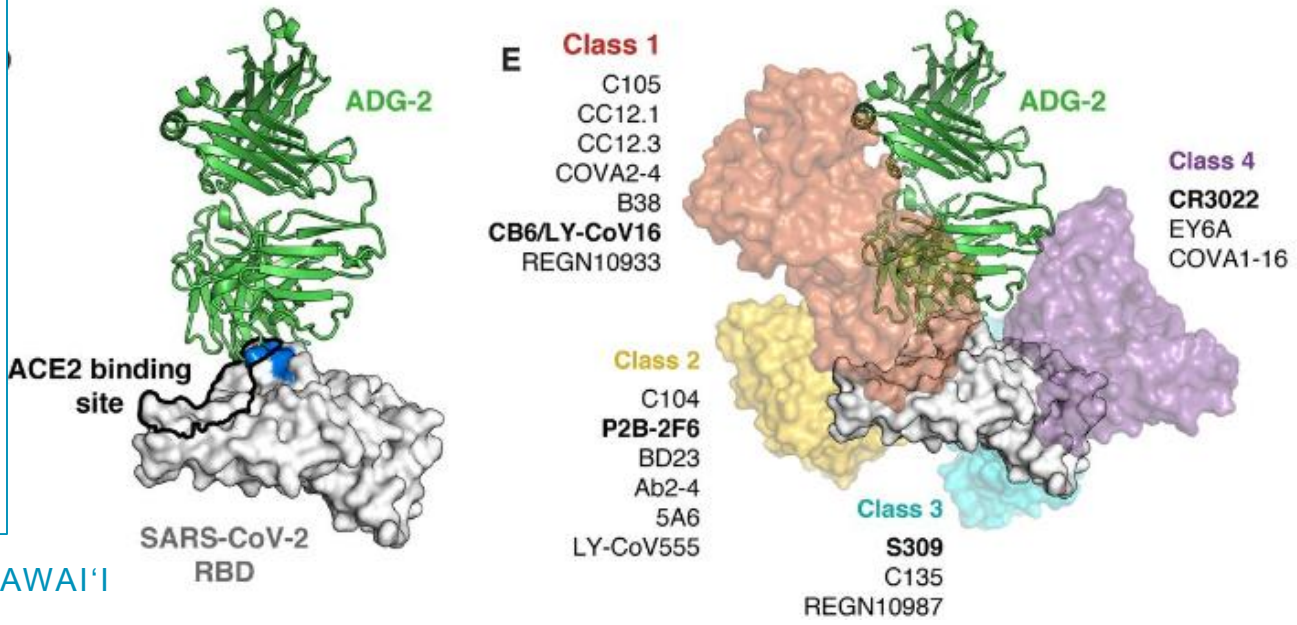
Broad and potent a
an engineered hum c

C. Garrett Rappazzo[1,*], Longping V.
+ See all authors and affiliations

Science 25 Jan 2021:
eabf4830
DOI: 10.1126/science.abf4830



ADG-2 employs a distinct angle of approach to recognize a highly conserved epitope overlapping the receptor binding site. This epitope represents an Achilles' heel for clade 1 sarbecoviruses and hence is an attractive target for the rational design of "pan-SARS" vaccines that aim to elicit similar broadly protective antibodies.



Science

REPORTS

Cite as: A. A. Cohen *et al.*, *Science* 10.1126/science.abf6840 (2021).

Mosaic nanoparticles elicit cross-reactive immune responses to zoonotic coronaviruses in mice

Alexander A. Cohen[1], Priyanthi N. P. Gnanapragasam[1], Yu E. Lee[1], Pauline R. Hoffman[1], Susan Ou[1], Leesa M. Kakutani[1], Jennifer R. Keeffe[1], Hung-Jen Wu[2], Mark Howarth[2], Anthony P. West[1], Christopher O. Barnes[1], Michel C. Nussenzweig[3], Pamela J. Bjorkman[1]*

[1]Division of Biology and Biological Engineering, California Institute of Technology, Pasadena, CA 91125, USA. [2]Department of Biochemistry, University of Oxford, Oxford OX1 3QU, UK. [3]Laboratory of Molecular Immunology, The Rockefeller University, New York, NY 10065, USA.

***Corresponding author. Email: bjorkman@caltech.edu**

Protection against SARS-CoV-2 and SARS-related emergent zoonotic coronaviruses is urgently needed. We made homotypic nanoparticles displaying the receptor-binding domain (RBD) of SARS-CoV-2 or co-displaying SARS-CoV-2 RBD along with RBDs from animal betacoronaviruses that represent threats to humans (mosaic nanoparticles; 4-8 distinct RBDs). Mice immunized with RBD-nanoparticles, but not soluble antigen, elicited cross-reactive binding and neutralization responses. Mosaic-RBD-nanoparticles elicited antibodies with superior cross-reactive recognition of heterologous RBDs compared to sera from immunizations with homotypic SARS-CoV-2–RBD-nanoparticles or COVID-19 convalescent human plasmas. Moreover, sera from mosaic-RBD–immunized mice neutralized heterologous pseudotyped coronaviruses equivalently or better after priming than sera from homotypic SARS-CoV-2–RBD-nanoparticle immunizations, demonstrating no immunogenicity loss against particular RBDs resulting from co-display. A single immunization with mosaic-RBD-nanoparticles provides a potential strategy to simultaneously protect against SARS-CoV-2 and emerging zoonotic coronaviruses.

COVID-19 Vaccine Updates

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

Shilpa Patel, MD
Pediatric Hospitalist, Kapi‘olani Medical Center
Physician Liaison, Quality & Patient Safety
Hawai‘i Pacific Health Medical

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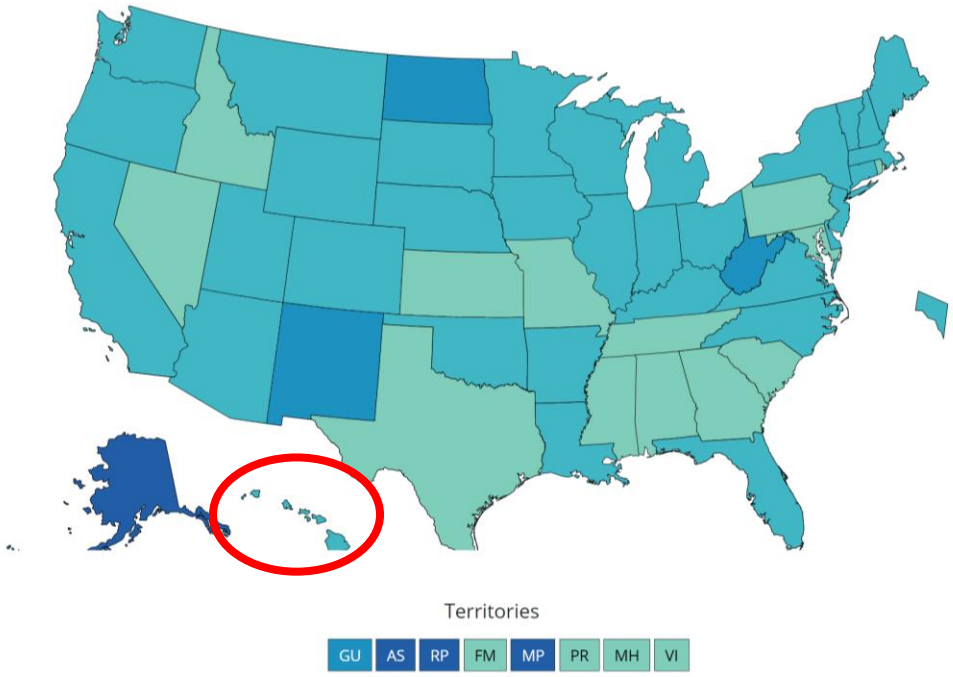
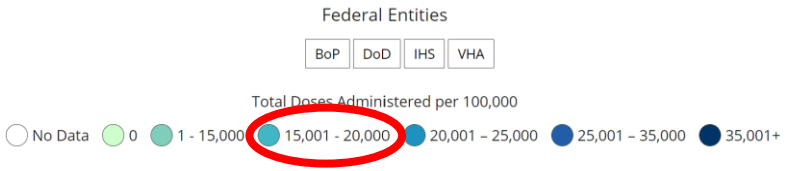
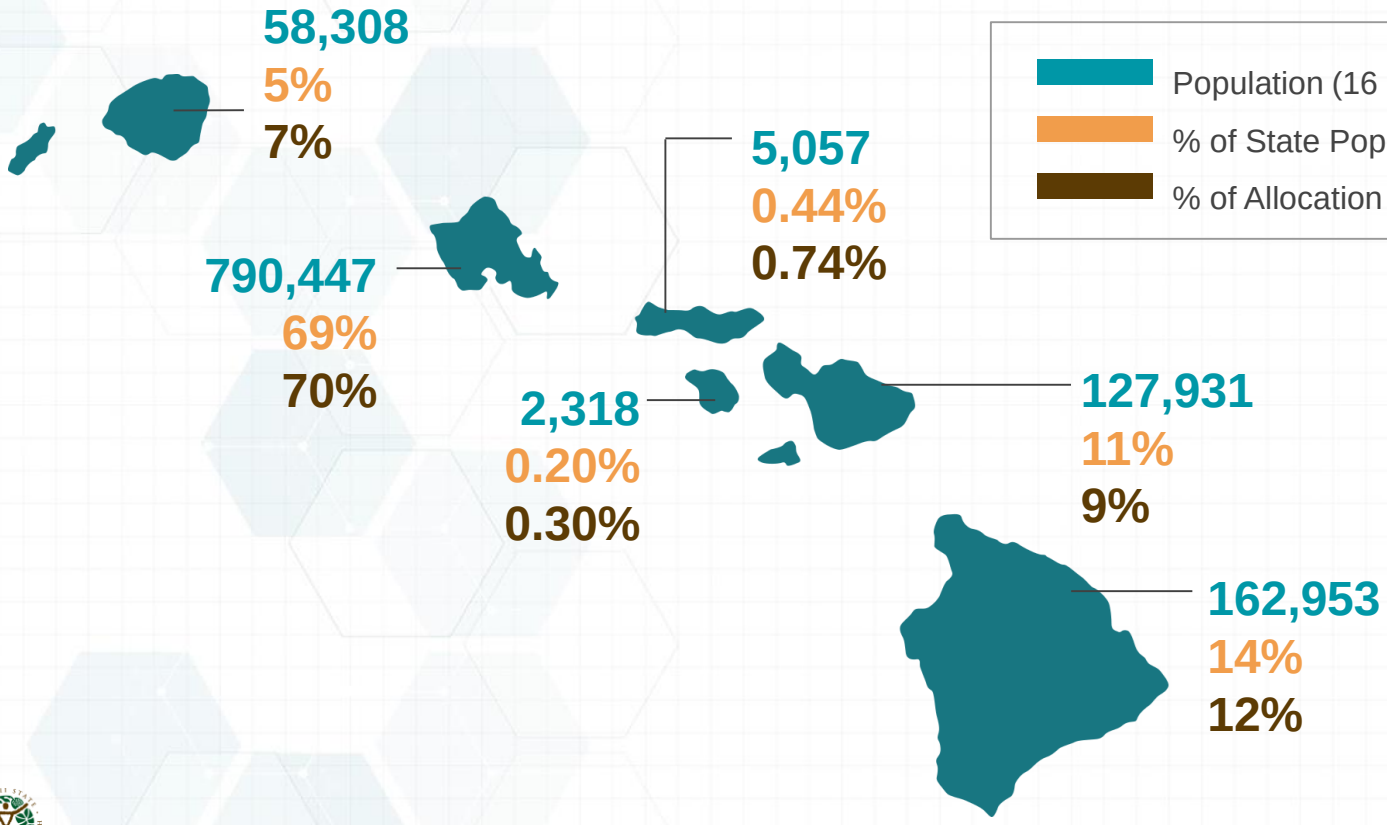
Total Doses Administered Reported to the CDC by State/Territory and for Selected Federal Entities per 100,000





Slide from Sarah Kemble 2/18/2021

Allocations by Population % (as of 2/17/21)



Slide from Sarah Kemble 2/18/2021

Weekly Hawaii COVID-19 Vaccine Summary

Last Updated on Wednesday, February 17, 2021

(includes all doses entered in the Vaccine Administration Management System, VAMS) ***Click INFO icon for notes on this data***

† Note: Counts for Doses Ordered and Doses Received previously included doses that will be ordered and received later in the week.

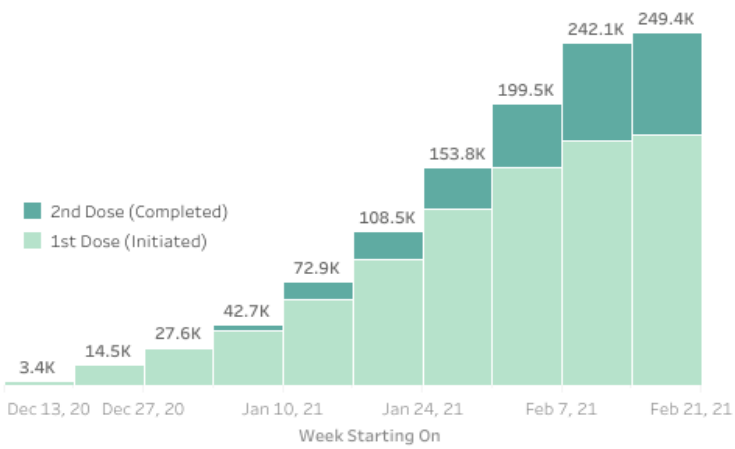
ORDERED†	RECEIVED†	ADMINISTERED		
Vaccines awarded	Shipments arrived	Vaccines given to individuals		
335,250	315,900	268,428	PUBLIC (reported in VAMS): 249,390	FEDERAL PHARMACY: 19,038

Public Doses Tracking

Percent of Total Population with at least 1 dose

12.5%

Cumulative Total of Vaccines Administered by Week



DISTRIBUTION PROGRESS

Vaccine Tracking Progress

% Administered (out of received)	% Received (out of ordered)	Total Ordered
79%	94%	335,250

AGE *

Percent of 75+ population with at least 1 dose

Percent 75+ with 1 dose	75 and older with 1 dose	Pop est over 75yrs
55%	58,971	107,600

55%

** This percentage is based on public doses counted in VAMS, not those administered through Federal Pharmacy Program and Federal Agencies, which includes some long term care facilities.*

https://health.hawaii.gov/coronavirusdisease2019/what-you-should-know/current-situation-in-hawaii/

Vaccine Completion Rates at HPH

All O‘ahu Sites*	Yesterday 2/17/21	Cumulative
Total # of vaccinations completed	1,523	58,165
Total # of 2nd doses completed	1,517	19,456
Pier 2 Vaccination Center		
Total # of vaccinations completed	1,523	44,100
Of those completed, # of 75+	967	21,198
Of those completed, # in phase 1a and 1b**	556	22,902
Total # of appointments scheduled (both first and second doses) but not yet administered		18,825
Total # of patients who requested an appointment and are awaiting outreach to be scheduled	2,198	

*includes vaccines administered at all HPH sites on O‘ahu including Pier 2 and vaccines clinics based at HPH facilities

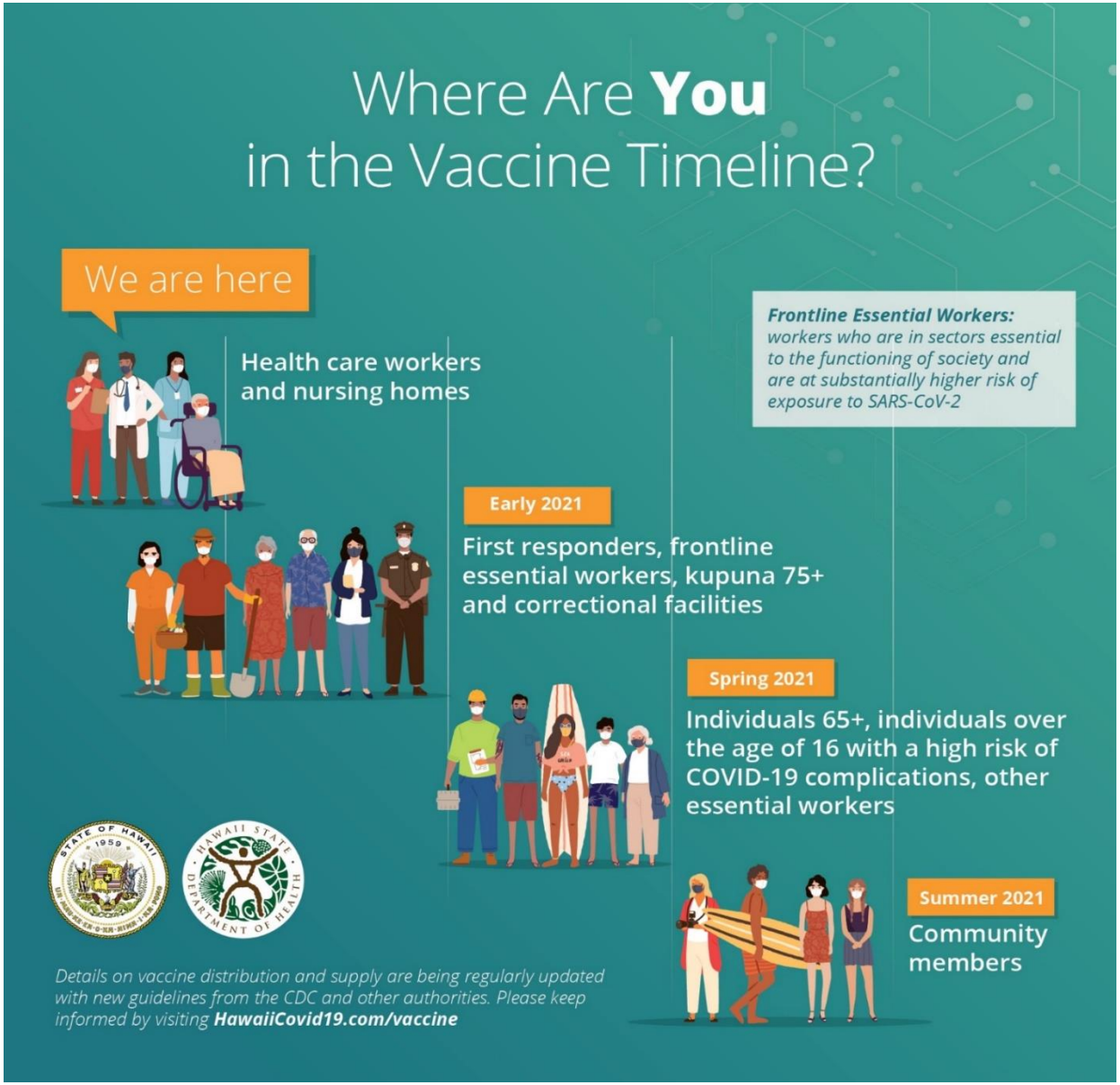
**includes identified priority groups of health care workers, first responders, and other essential frontline employees as designated by the Hawai‘i State Department of Health. The cumulative figure includes caregivers of those 75+ (no vaccinations provided to this group after 1/27/2021).

Pier 2

- 4 pods, 375 vaccines/pod/day currently → 500
- Operating with ~ 195 people per day
  - 147 directly supporting the clinics (e.g., vaccinators, monitors, schedulers and medical management)
  - Others assisting with parking, security and information services support
- ~120 Volunteers – data entry mostly (VAMS)
  - HPH
  - Docs
  - PSQS, IT, other
  - Community

Reactions to Vaccine – Pier 2

- 158 medical reports (primarily vasovagal or anxiety reactions: stuff like lighted headedness, dizziness, numbness, tingling, feeling flush, …)
- 91 addressed in Pod and sent home after observation period
- 67 addressed in medical management area
  - 61 sent home from pier after observation and monitoring
  - 3 EMS transfers
    - 1 for syncope, discharge from ED
    - 1 for hypotension, discharged from ED
    - 1 for head injury prior to receiving vaccine, discharged from ED
  - 3 referred to ED by private car
    - 1 for chest pain, medically stable in med management area
    - 1 for fall and face hematoma prior to receiving vaccine
    - 1 for fall and eye hematoma prior to receiving vaccine
- No serious reactions
- No deaths associated with vaccination

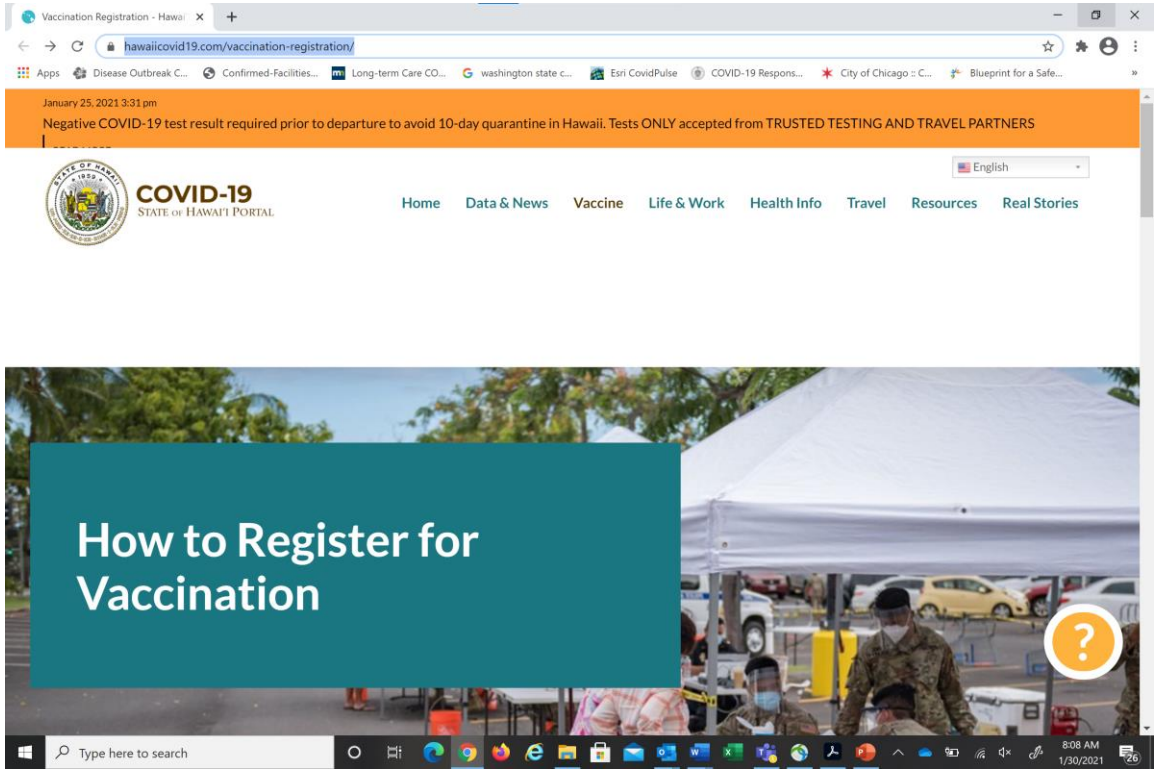


https://hawaiicovid19.com/vaccine/

Phases

- Phase 1a:
  - Long-term care facilities: CVS and Walgreens (Moderna)
  - Hospitals: Pfizer
    - Easiest to reach employees and others at clinical care sites, then affiliated, then non-affiliated (managed by HDOH and HAH)
  - First responders
- Phase 1b: 75+ and critical staff in essential worker roles
- Phase 1c: 65+, under 65 with comorbid conditions

How to Get Registered



Kupuna Registration

Adventist Health Castle
https://www.adventisthealth.org/castle/vaccine/
For questions about online registration: (808) 263-5002

Hawai'i District Health Office Vaccination Sites
Phone assistance for registration for adults 75+
Call (808) 300-1120, Mon. – Fri., 9 a.m. – 3 p.m.

Hawaii Health Systems Corporation
https://www.hilomedicalcenter.org/covid-19-vaccine-sign-up-information/

Hawaii Health Systems Corporation (Kaua'i)
kauai.hhsc.org

Hawaii Pacific Health
https://www.hawaiipacifichealth.org/hph-covid-19-updates/vaccine-update/

Hawaii Pacific Health (Kaua'i)
https://www.hawaiipacifichealth.org/surveyor/i2yon3cyqtvuyc6re5oq

Hilo Medical Center Helpline
For assistance with online registration call (808) 932-3000 and press 8 (weekdays during business hours)

Kaiser Permanente
https://healthy.kaiserpermanente.org/hawaii/health-wellness/coronavirus-information/covid-vaccine
If you're unable to schedule your appointment online, call (808) 432-2000 (TTY 711), Mon – Fri, 8 a.m. to 5 p.m.

Kona Community Hospital
For registration and appointments, call (808) 322-4451 Mon. – Fri. 8 a.m. – 12 p.m.

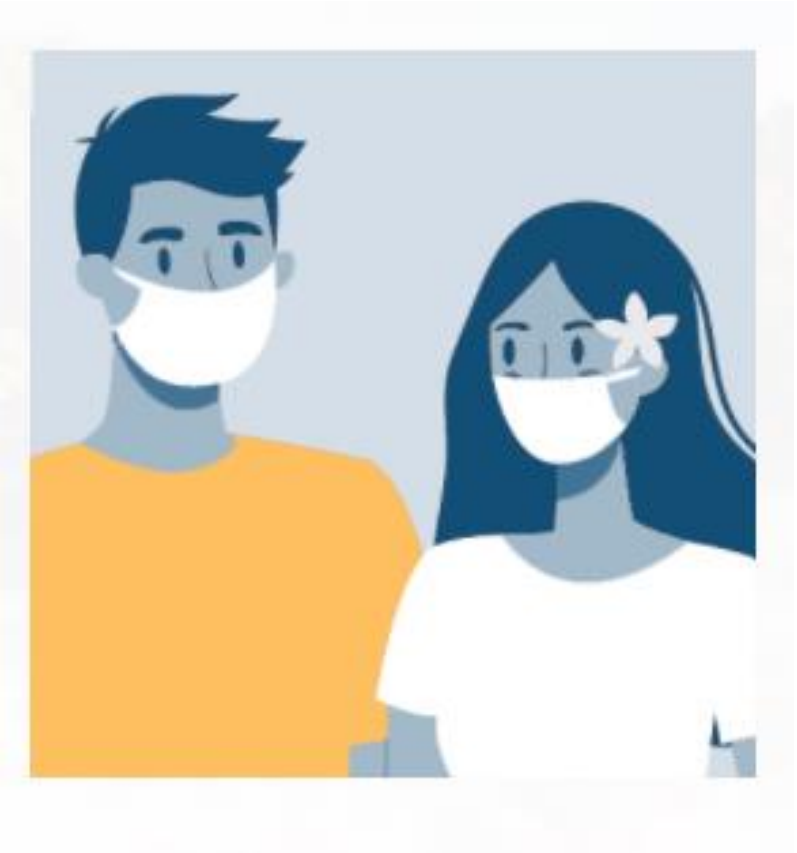
https://hawaiicovid19.com/vaccination-registration/

Slide from Sarah Kemble 2/18/2021

Will I Still need to wear a Mask?

YES !

Similar to other vaccines, a large number of people in the community will need to get vaccinated before transmission drops enough to stop the use of masks



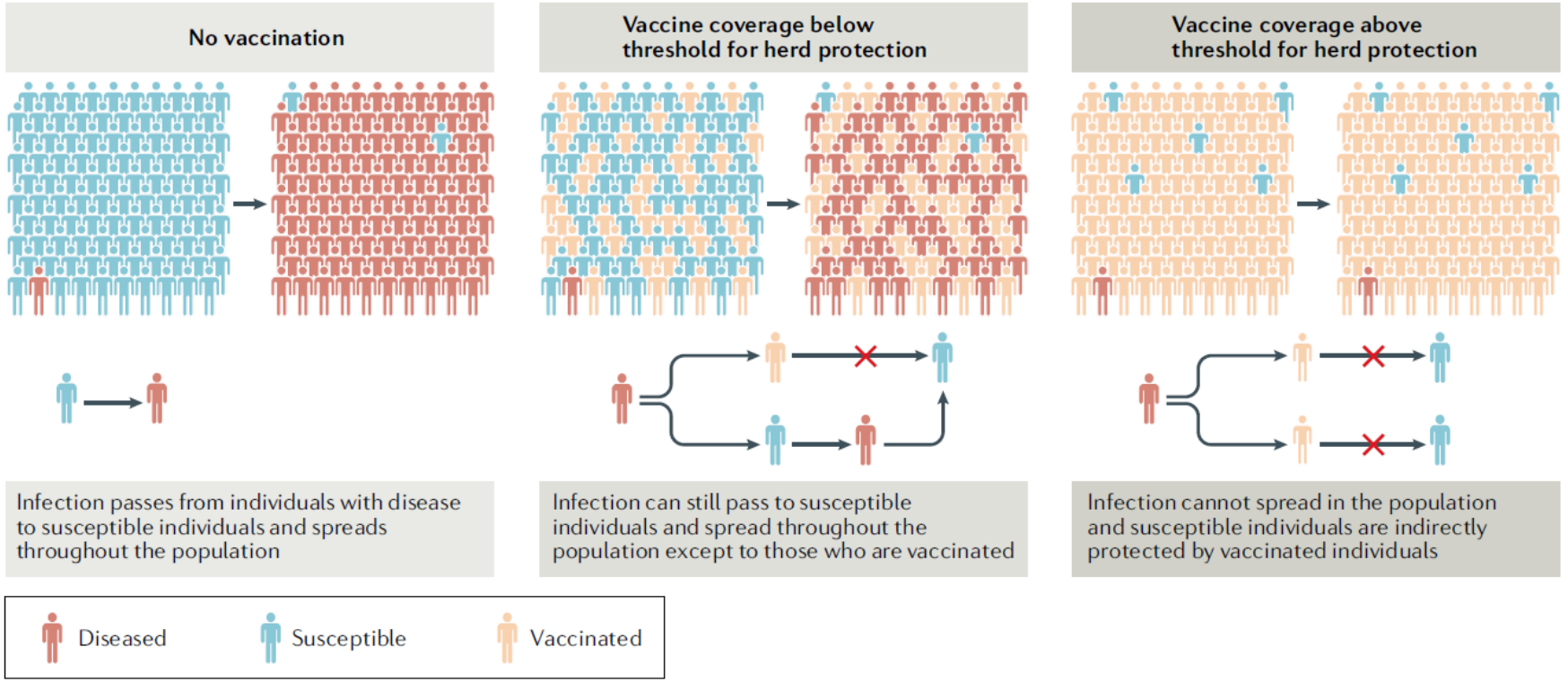
Slide from Sarah Kemble 2/18/2021

COVID-19: Vaccine Rollout and Effect of SARS-CoV-2 Mutants

Dr. rer. nat. Axel T. Lehrer, Associate Professor

Department of Tropical Medicine, Medical Microbiology and Pharmacology,
John A. Burns School of Medicine
University of Hawai'i at Manoa
Honolulu, Hawaii

Can we reach Herd Immunity?



From: A guide to vaccinology: from basic principles to new developments. Pollard and Bijker, Nat. Rev. Immunol. (2020)

A little bit of Luck…

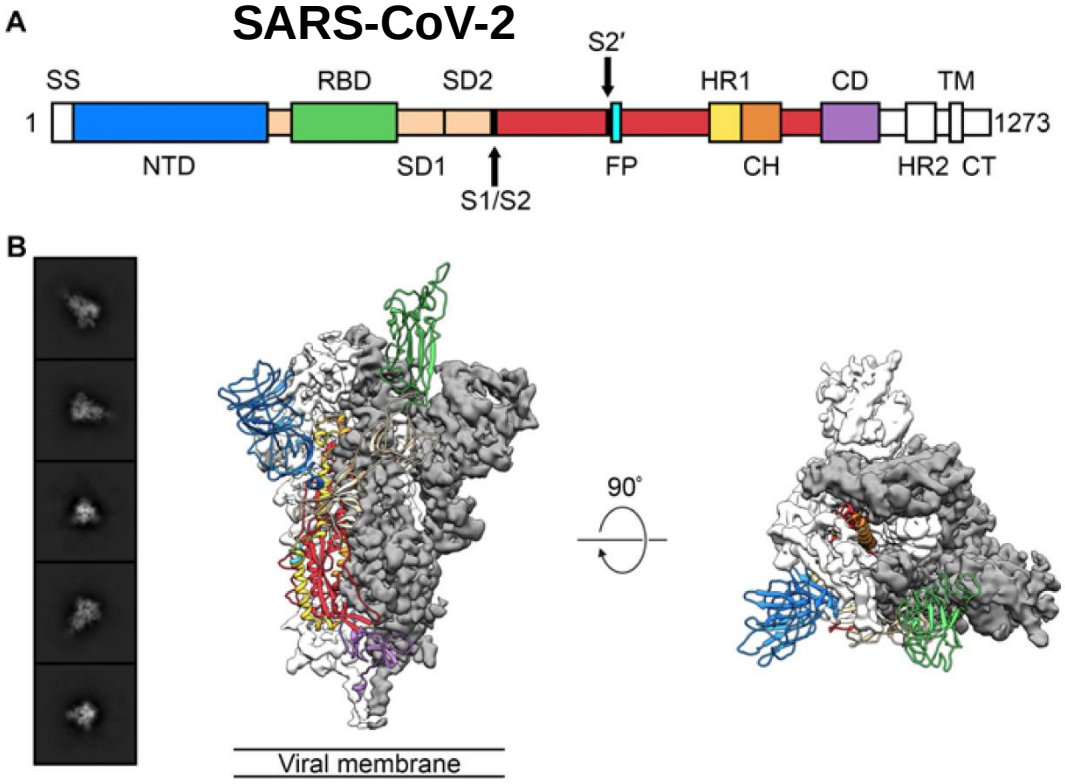
- Outbreak of SARS in 2003 sparked development of Coronavirus vaccines giving basic blueprint of “what works”
- Bird flu in 2005 triggered an effort to prepare for pandemic flu and other viruses with pandemic potential
- MERS cases are first reported in 2012 – triggers accelerated vaccine programs and allow to validate the previously developed technology for Coronavirus vaccines
- West African outbreak of Ebola virus pushes replication incompetent adenovirus-vectored vaccines into late stage development

A little bit of Luck… continues

- Continued clinical development of virally vectored Ebola virus vaccines leads to approval of two “first-in-class” vaccines: Ervebo and Ad26/MVA prime boost vaccine by J&J

- Zika virus outbreak in 2015/16 in South America sparked the development of mRNA based vaccines and further honing of production and delivery technologies

Spike Protein



Wrapp and Wang et al. Science 2020

Class I fusion glycoprotein on the surface of the virus responsible for to gain entry into host cells.

The S protein is a trimeric protein that exists in a metastable prefusion

~180 kDa if fully glycosylated, 22 glycosylation sites

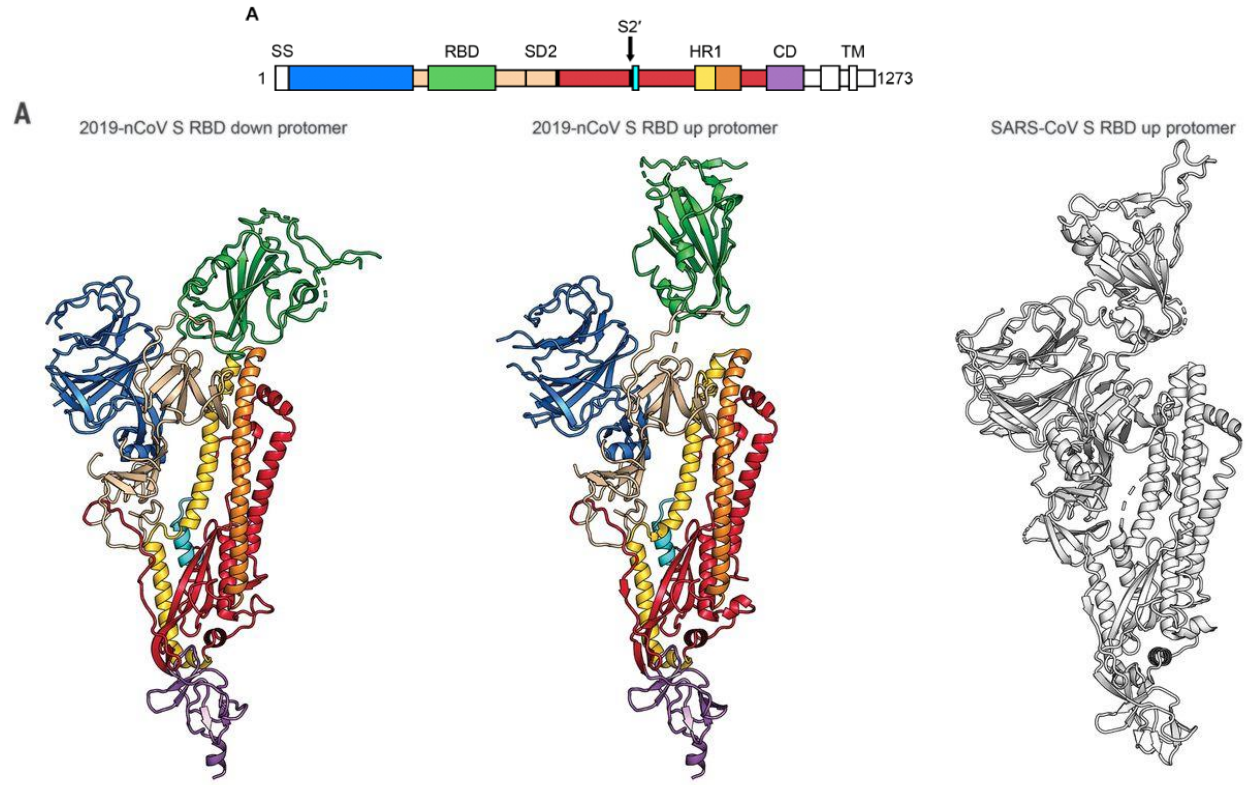
The monomer consists of S1 and S2 subunit that are associated non-covalently

S1 subunits forming an interwoven cap that rests atop the spring-loaded S2 stem

Conformation that undergoes a substantial structural rearrangement to fuse the viral membrane with the host cell membrane

Pallesen et al. PNAS 2017

Spike Protein



Wrapp and Wang et al. Science 2020

S1 subunit contains the RBD and responsible for receptor recognition

S2 subunit responsible for membrane fusion

The SARS-CoV 2 S shares 76% aa homology with SARS-CoV

Ou et al. Nat Comm 2020

S1 homology is about 64%
RBD homology is about 74%

Ou et al. Nat Comm 2020

RBD domain exhibits hinge like motion switches between several open and one closed formation

Receptor (Ab) binding is only possible when RBD is in open position

Mutants of SARS-CoV-2

- ssRNA virus, ~30kb genome
- Approximately 1-2 nucleotide mutations/month
- Due to exoribonuclease ExoN: Half the rate of influenza, a quarter of HIV

> relatively slow to mutate

- Additionally: most relevant mutations have to **occur within the Spike protein gene AND lead to amino acid changes**

Further reading: https://asm.org/Articles/2021/February/SARS-CoV-2-Variants-vs-Vaccines

Mutants of SARS-CoV-2

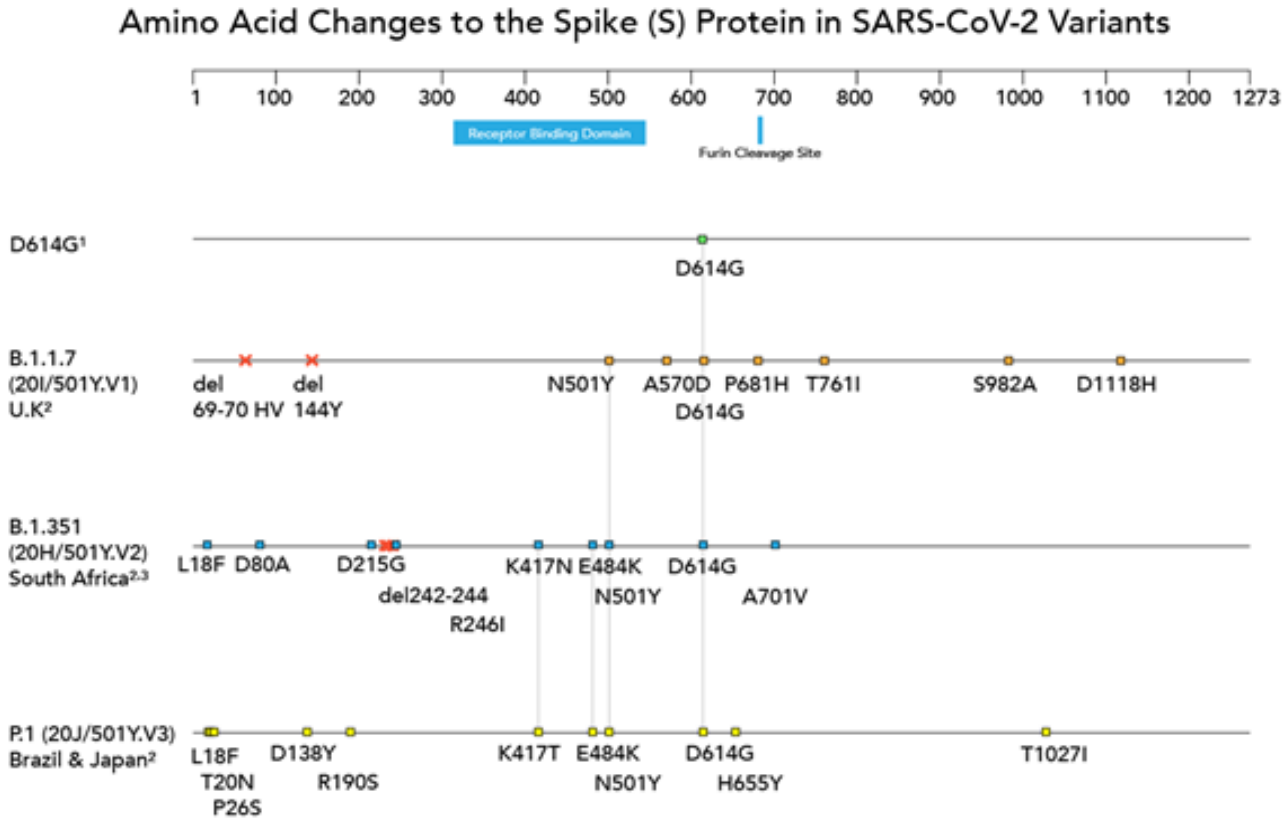
Wuhan strain Hu-1

“Original” mutant Spring 2020

UK variant

South Africa variant

Brazil variant



[1]https://www.cell.com/cell/fulltext/S0092-8674(20)31229-0?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0092867420312290%3Fshowall%3Dtrue
[2]https://www.cdc.gov/mmwr/volumes/70/wr/mm7003e2.htm?s_cid=mm7003e2_w#T1_down
[3]https://doi.org/10.1101/2021.01.25.428137

What do we know about vaccines?

- **Pfizer/BioNTech: mRNA, 2 doses**
- **Moderna: mRNA, 2 doses**

- **Johnson&Johnson/Janssen: Ad26, 1 dose or 2 doses**
- **AstraZeneca/Oxford: chAdOx1, 2 doses**

- **Novavax: Subunit + Matrix-M adjuvant, 2 doses**

Pfizer

Tested neutralization of deliberate mutants – bioRxiv Preprint

1 **Neutralization of SARS-CoV-2 spike 69/70 deletion, E484K, and N501Y variants by**

2 **BNT162b2 vaccine-elicited sera**

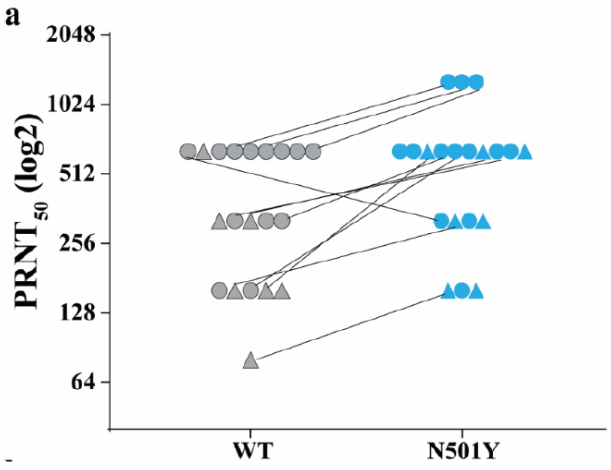
3 Xuping Xie[1,*], Yang Liu[1,*], Jianying Liu[2,3,*], Xianwen Zhang[1], Jing Zou[1], Camila R. Fontes-
4 Garfias[1], Hongjie Xia[1], Kena A. Swanson[4], Mark Cutler[4], David Cooper[4], Vineet D. Menachery[2,3],
5 Scott Weaver[2,3], Philip R. Dormitzer[4,#], Pei-Yong Shi[1,3,5,6,7,#]

6 [1]Department of Biochemistry and Molecular Biology, University of Texas Medical Branch,
7 Galveston TX, U.S.A.

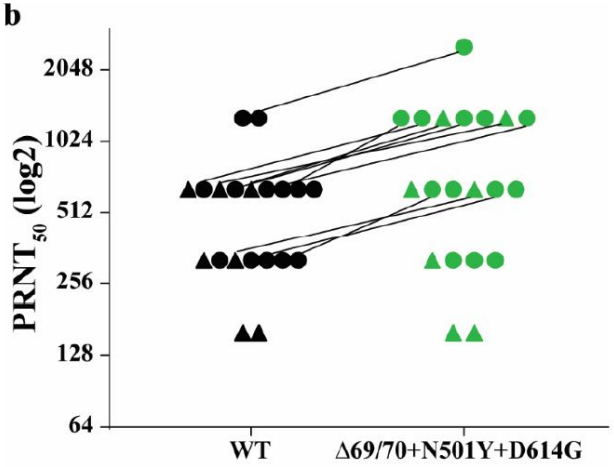
Pfizer - Neutralization

Tested neutralization of deliberate mutants representing major differences – bioRxiv Preprint

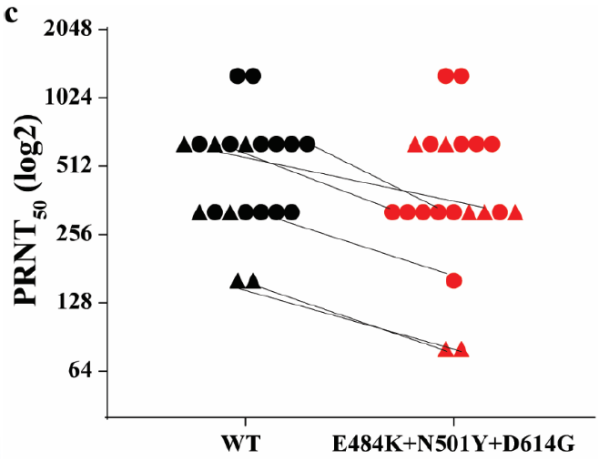
"Original" mutant



UK variant



"almost" South Africa



Pfizer - Neutralization

Plaque morphology

	“Original” mutant	UK variant	“almost” South Africa
WT	N501Y	Δ69-70+N501Y+D614G	E484K+N501Y+D614G

mRNA - Neutralization

- **Other preprints available that used pseudoviruses in surrogate neutralization tests (based only on variations in the Spike protein) – some concerns as neutralization was reported to be reduced up to ~4fold**

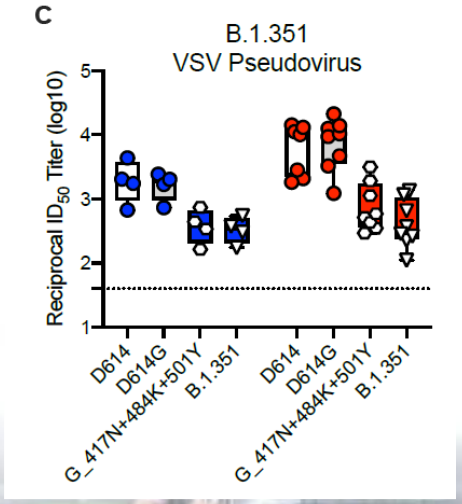
- **Analysis for Moderna vaccine has also been pre-published demonstrating neutralization with the current candidate both from human and NHP sera (using pseudovirions as well)**

mRNA-1273 vaccine induces neutralizing antibodies against spike mutants from global SARS-CoV-2 variants

Kai Wu[1]*, Anne P. Werner[2]*, Juan I. Moliva[2], Matthew Koch[1], Angela Choi[1], Guillaume B. E. Stewart-Jones[1], Hamilton Bennett[1], Seyhan Boyoglu-Barnum[2], Wei Shi[2], Barney S. Graham[2], Andrea Carfi[1#], Kizzmekia S. Corbett[2#], Robert A. Seder[2#], Darin K. Edwards[1#]

[1]Moderna Inc., Cambridge, MA, USA

[2]National Institutes of Health, National Institute of Allergy and Infectious Diseases, Vaccine Research Center, Bethesda, MD, USA



Status of other Vaccines

- **Johnson&Johnson: ~60% efficacy overall, ~72% efficacy in the U.S. trial, interim analysis (single shot)**

- **AstraZeneca: multi-country testing complicates situation, dosing error introduced the opportunity to give a smaller first dose followed by larger second dose or longer dosing interval; Lancet preprint speaks of single dose and well as delayed booster administration**

- **Novavax: UK data suggests ~90% efficacy after two doses, noteable: mostly UK variant found at the time of the trial (in placebo group). Suggests that the vaccine works against both UK and South Africa variants.**

- **NOTE: clinical trials for the different platforms/dosing regimens may use different metrics as the exclusion times vary from 14-28 days. This of course affects efficacy rates reported**

COVID-19 Testing Update

Owen Chan, MD, PhD
Medical Director
Clinical Labs of Hawai‘i
Pali Momi Medical Center

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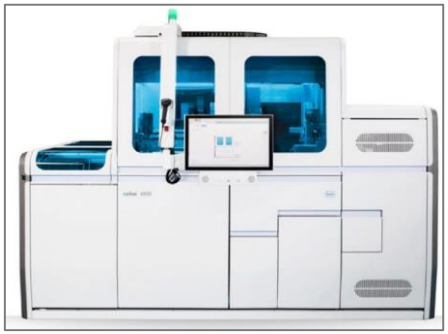
Detection of SARS-CoV-2 at Clinical Labs of Hawaii:

Nucleic Acid Amplification Test (NAAT)

Hologic Aptima SARS-CoV-2 Assay (Panther System):

- Technology: Isothermal nucleic acid amplification (transcription mediated amplification)
- FDA NAAT Detectable units / mL = 600
- Turnaround time: 24-48 hours



Roche cobas SARS-CoV-2 (cobas system)

- Technology: Reverse transcriptase polymerase chain reaction (RT-PCR)
- FDA NAAT Detectable units / mL = 1800
- Turnaround time: 24-48 hours
- Multiplex (SARS-CoV-2 and influenza)

Abbott ID NOW COVID-19

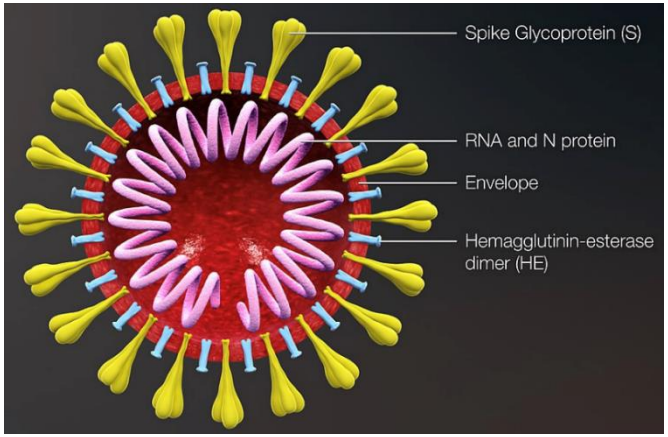
- Technology: Isothermal nucleic acid amplification
- FDA NAAT Detectable units / mL = 300,000
- Turnaround time: 20 minutes

Capacity: 10,000 specimens / day

https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-reference-panel-comparative-data

Detection of SARS-CoV-2 at Clinical Labs of Hawaii:

Viral Antigen Testing



***Several platforms exist**

***As of 2/18/21, none being conducted at CLH**

***Abbott BinaxNOW COVID-19 Ag**

- Technology: Immunochromatographic membrane
- Nasal swabbing
- Turnaround time: 15 minutes
- Released to the federal government and certain sectors
  - CLH approved to perform
  - Timeline: not available yet

COVID-19 Treatment Updates

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

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Outpatient NIH Anticoagulation Trial

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

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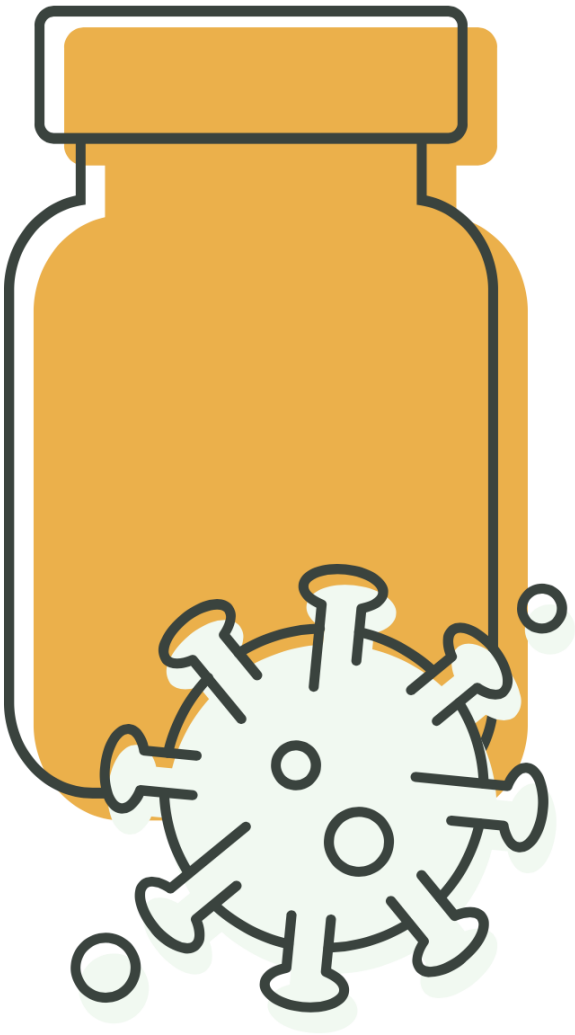
What is the ACTIV-4b Outpatient Study?



ACTIV-4b is a national study to determine if taking an FDA-approved and commonly prescribed blood thinner Eliquis (apixaban), or alternatively, taking baby aspirin is better than taking no blood thinner to prevent blood clots in people with COVID-19 who are recovering from their symptoms at home.

By participating in this study, you will help us learn more about COVID-19 and the best way to treat people newly diagnosed with COVID-19.

HHS

NIH National Heart, Lung, and Blood Institute

NIH National Institutes of Health
Turning Discovery Into Health

What is 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)
- D-dimer levels are highly abnormal in many COVID-19 patients
- Meta-analysis of studies in hospitalized patients with COVID-19
  - VTE prevalence of 14%
  - With ultrasound screening rates as high as 40%

Anticoagulation in **hospitalized** COVID-19

- NHLBI – sponsored ACTIV-4a, REMAP-CAP and ATTACC
  - Full-dose therapeutic anticoagulation (AC) is superior to prophylactic dosing in hospitalized but noncritically ill COVID-19 patients (moderately ill)
    - Requirement for organ support: Prophylactic AC 23%, Therapeutic AC 16%
  - Improved outcomes (OSFD) and a trend to improved survival
  - Reduces the proportion of patients progressing to mechanical ventilation and other vital organ support
  - **Only the 2nd treatment proven to provide a survival benefit for COVID-19 patients (other than dexamethasone)**
- 4200 Veterans Affair (UK) patients hospitalized with COVID-19
  - 84% started on prophylactic AC
  - 27% lower risk of death at 30 days, 31% lower risk of inpatient mortality

Who is a good fit for the ACTIV-4b study?

Someone who is:

- Between 40 - 80 yrs old
- COVID-19 positive in the last 14 days and is symptomatic
- Not pregnant
- Willing to have a blood test to confirm they can safely join the study
- Willing and able to take study pills every morning and evening for 45 days
- Willing to complete a survey to confirm their study pills were received
- Willing to complete 6 weekly check-ins, along with one call 75 days after starting, so study staff can assure safety and track their progress

Medication

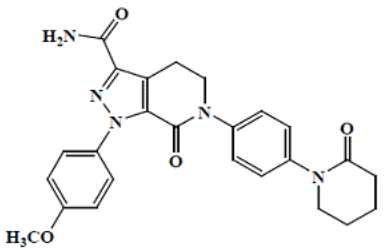
You would be randomly assigned by a computer (like flipping a coin) to one of four groups:

Group 1 - participants taking baby aspirin in the morning and then a placebo pill in evening

Group 2 - participants taking low dose Eliquis (apixaban) once in the morning and evening

Group 3 - participants taking high dose Eliquis (apixaban) once in the morning and evening

Group 4 - participants taking the placebo pills in the morning and evening



What happens during the study?

1 While at your local COVID-19 testing site or hospital involved in the ACTIV-4b study, a study team member will determine if you're eligible to participate. They will assist you in signing up.

Flyers at drive-through testing
REC and Virtual Clinics
Provider referrals

HPHRI research staff will contact patient and remote consent

2 Get your blood drawn at your testing site or with another service.

REC at Staub and WMH

3 Two days after entering into the study you will receive your study kit, including pills, by mail.

The study team will call you to confirm that you received your package and to answer any questions you may have.

4 Take your study pills, every morning and evening for the next 45 days.

5 Complete 6 weekly follow-ups via text / email or phone call *(you choose your preference)*.

6 Finish taking your pills and complete your week 6 check-in with the study team.

YOU'RE DONE!

Next steps

- Hope to activate study in the next 2-4 weeks
  - Dr. Heidi Hillesland and Dr. Brian Pien
- Will communicate through eConnect once activated
- https://nhlbi-connects.org/activ4b

Q&A

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CREATING A HEALTHIER HAWAIʻI

Next Webinar:

HHP Care Model and Disease Management Webinar:

Pediatric Neurology

Dr. Keith Abe & Dr. Justin Hino

Thursday, February 25, 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

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