

HHP/HPH COVID-19 Community Webinar Series

Monday, September 21, 2020
5:30pm – 6:30pm



Moderator – 09/21/20

Andy Lee, MD

Medical Director, *Hawai'i Health Partners*
Chief of Staff, *Pali Momi Medical Center*
Hawai'i Pacific Health

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- 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

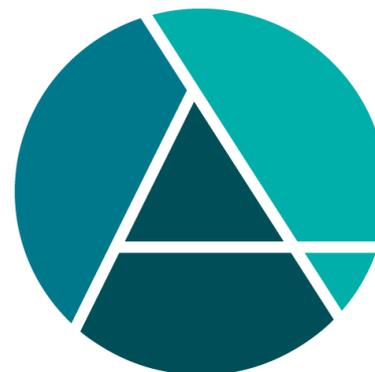
- You should have completed a brief questionnaire before joining today's live webinar.

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@hawaiiipacifichealth.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.



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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



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



Douglas Kwock, MD
Vice President of
Medical Staff Affairs



Gerard Livaudais, MD, MPH
Executive Vice President,
Population Health and
Provider Networks
Hawai'i Pacific Health

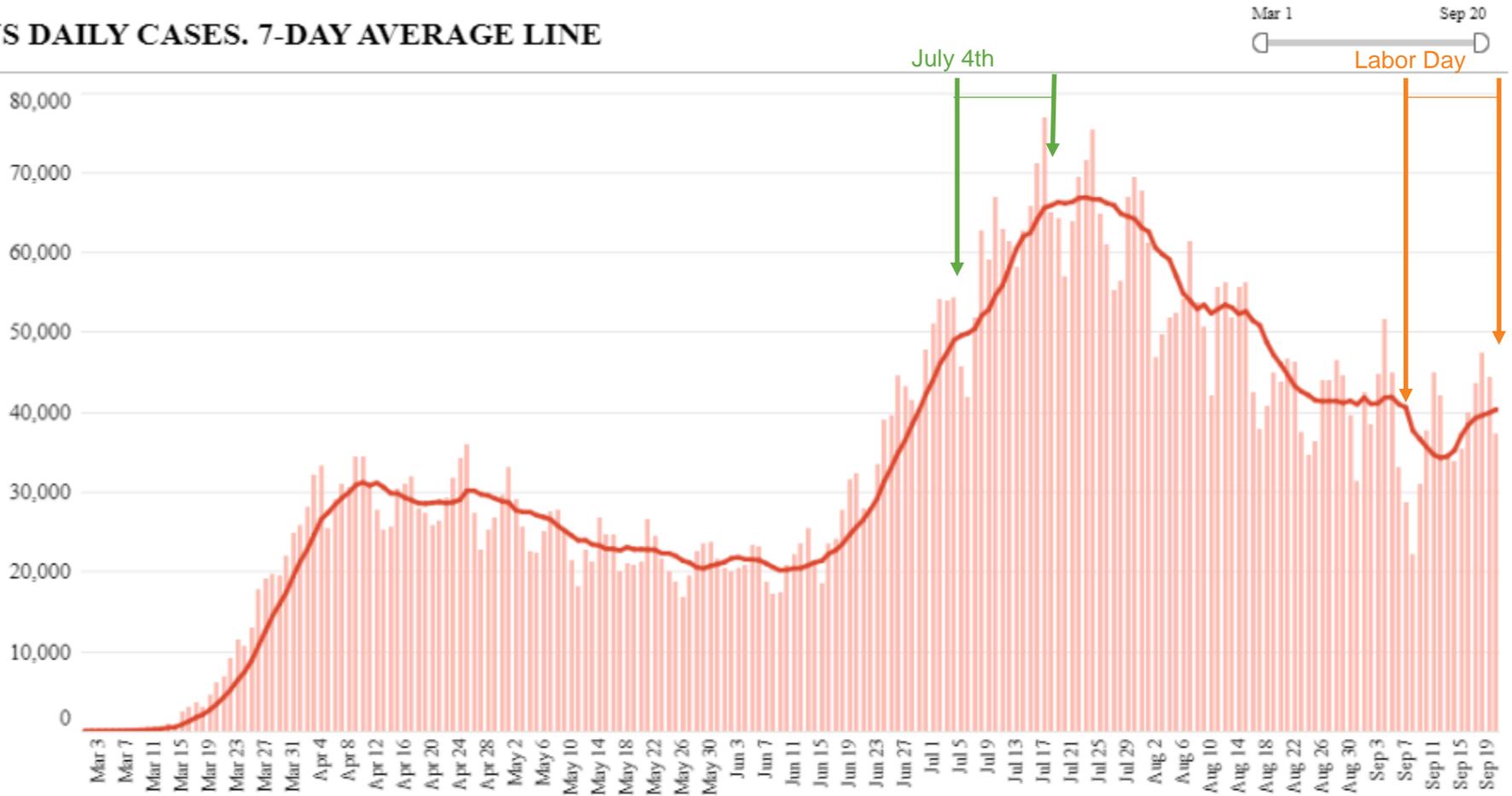


Shilpa Patel, MD
Pediatric Hospitalist,
Kapi'olani Medical Center
Physician Liaison,
Quality & Patient Safety
Hawai'i Pacific Health

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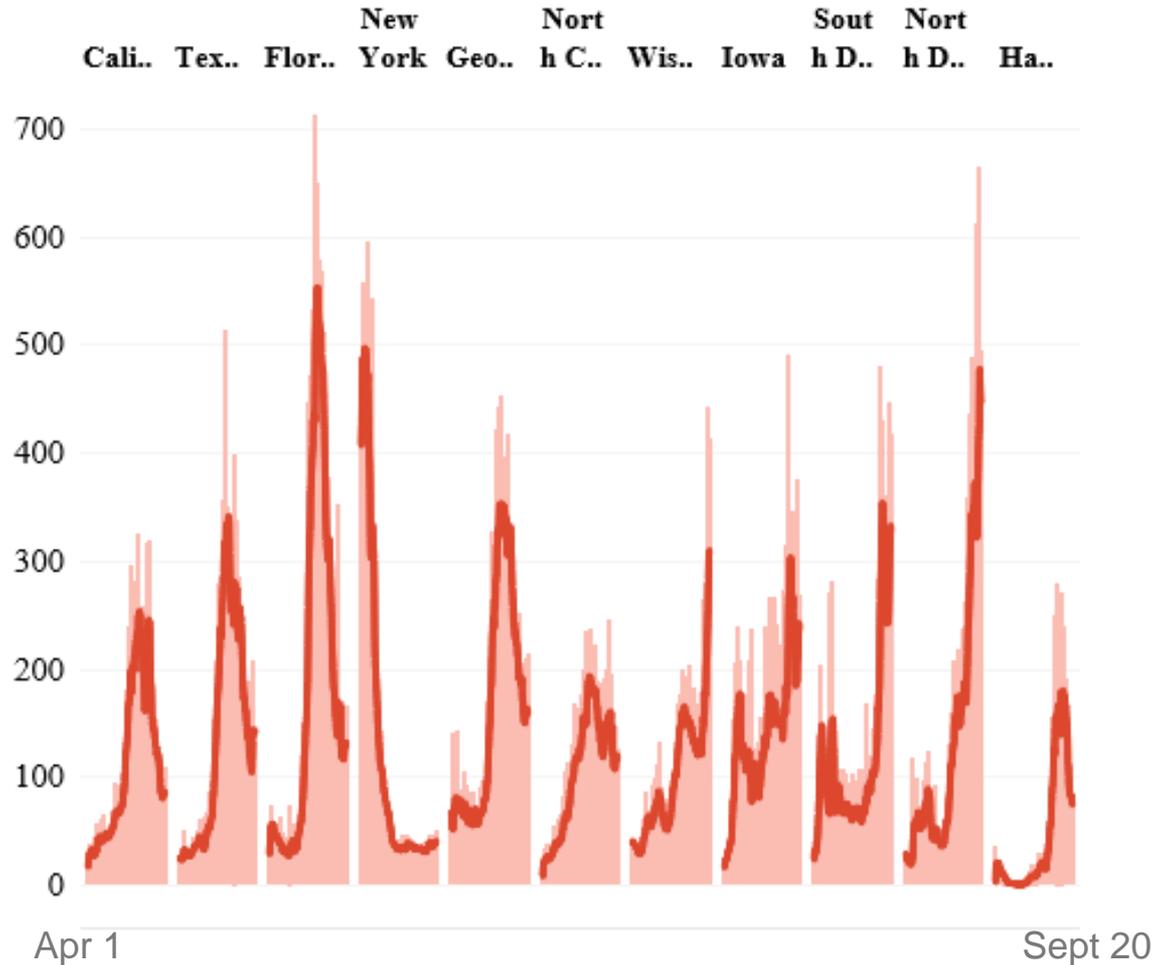
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US DAILY CASES. 7-DAY AVERAGE LINE



<https://covidtracking.com/data/charts/daily-cases-and-currently-hospitalized> accessed 09.20.20

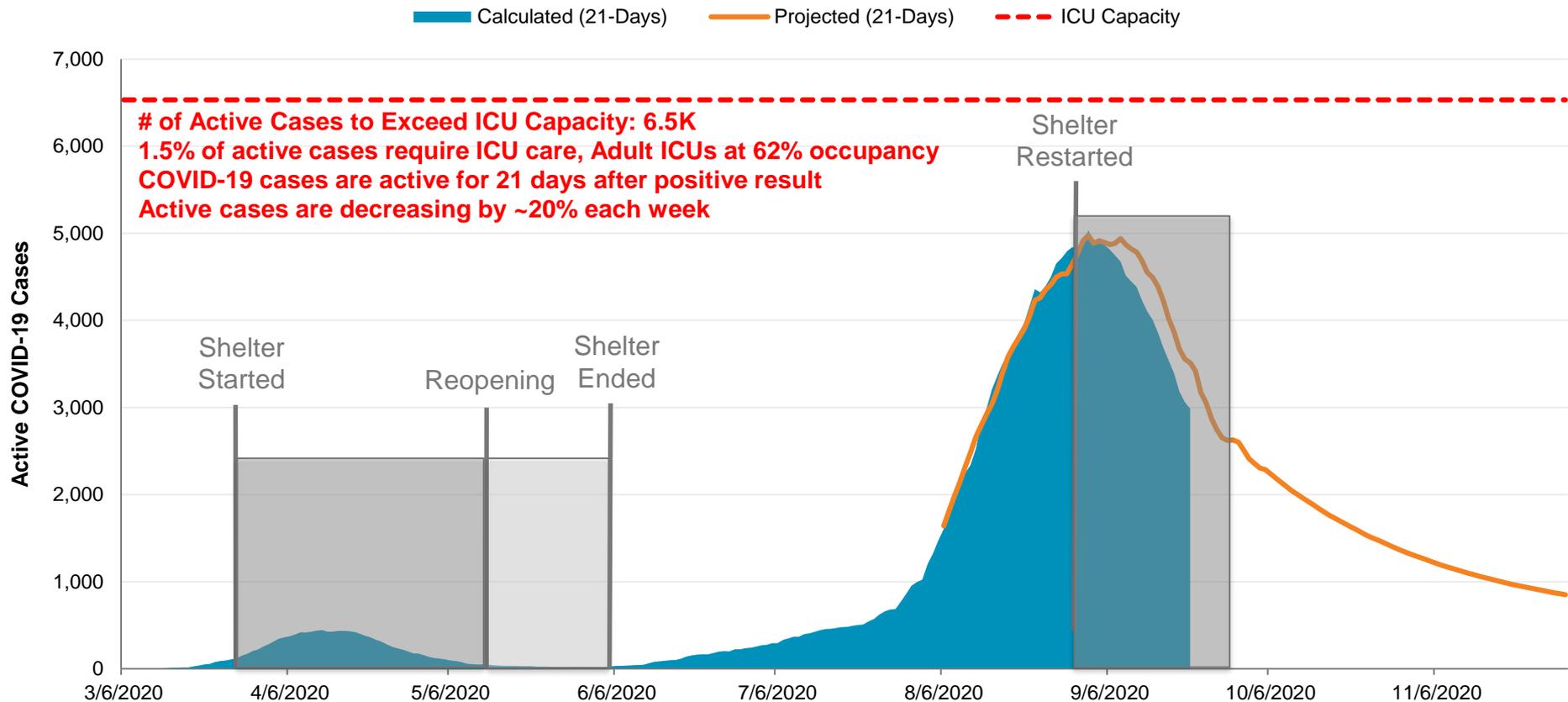
Daily cases per million with 7 day average



<https://covidtracking.com/data/charts/daily-cases-and-currently-hospitalized> accessed 09.20.20

Projected Active COVID-19 Cases

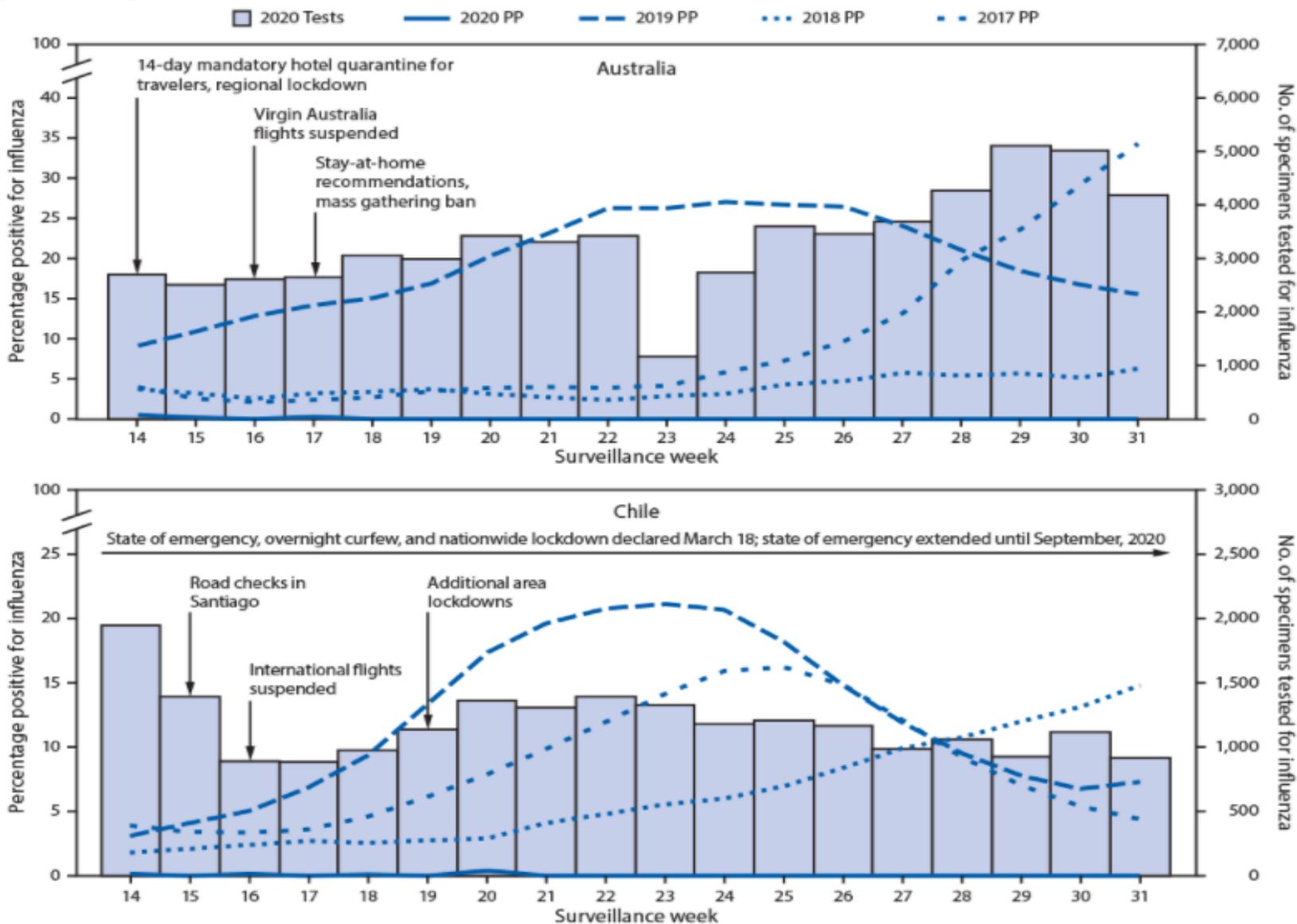
Hawaii Actual v. Projected Active COVID-19 Cases Updated 9/21/2020



As of 09/21/20	Total Census	ICU beds occupied	# Ventilators in use	# New Admissions w/ COVID-19 screening	# New Admissions w/ positive COVID-19	# Patients currently hospitalized w/ suspect or confirmed COVID-19	# Patients currently on a ventilator w/ suspect or confirmed COVID-19	# Patients currently in ICU w/ suspect or confirmed COVID-19
KMCWC	158	AICU: 0 NICU: 71 PICU: 6	AICU: 0 NICU: 18 PICU: 3 Wilcox: 0	0	0	S: 1 C: 1 (Peds)	S: 0 C: 0	S: 0 C: 1 (Peds)
PMMC	98	11	9	0	0	S: 0 C: 15	S: 0 C: 8	S: 0 C: 9
SMC	116	17	13	3	1	S: 0 C: 29	S: 0 C: 9	S: 0 C: 10
WMC	50	5	0	1	0	S: 1 C: 0	S: 0 C: 0	S: 0 C: 0

S = Suspected; C= Confirmed

Number of specimens tested and percentage testing positive for influenza - by year, April–August (weeks 14–31), 2017–20



Coronavirus Disease 2019 (COVID-19)



YOUR HEALTH

How COVID-19 Spreads

Updated Sept. 21, 2020

Languages ▾

Print



A draft version of proposed changes to these recommendations was posted in error to the agency's official website. CDC is currently updating its recommendations regarding airborne transmission of SARS-CoV-2 (the virus that causes COVID-19). Once this process has been completed, the update language will be posted.

COVID-19 is thought to spread mainly through close contact from person-to-person. Some people without symptoms may be able to spread the virus. We are still learning about how the virus spreads and the severity of illness it causes.

Person-to-person spread

The virus is thought to spread mainly from person-to-person.

- Between people who are in close contact with one another (within about 6 feet).
- Through respiratory droplets produced when an infected person coughs, sneezes, or talks.
- These droplets can land in the mouths or noses of people who are nearby or possibly be inhaled into the lungs.
- COVID-19 may be spread by people who are not showing symptoms.

School Reopening

Risk mitigation

- Schools and classrooms
 - Masks, Distance and Ventilation (vs. Hygiene Theater)
 - Testing, Isolation, Contact Tracing and Quarantine
- After school activities
 - Non-organized, social interactions
 - Organized activities and sports

Jones E, Young A, Clevenger K, Salimifard P, Wu E, Lahaie Luna M, Lahvis M, Lang J, Bliss M, Azimi P, Cedeno-Laurent J, Wilson C, Allen J. Healthy Schools: Risk Reduction Strategies for Reopening Schools. Harvard T.H. Chan School of Public Health Healthy Buildings program. June, 2020.



Hawai'i School Reopening based on Local Prevalence

Period: September 1 to September 14 (14 days)

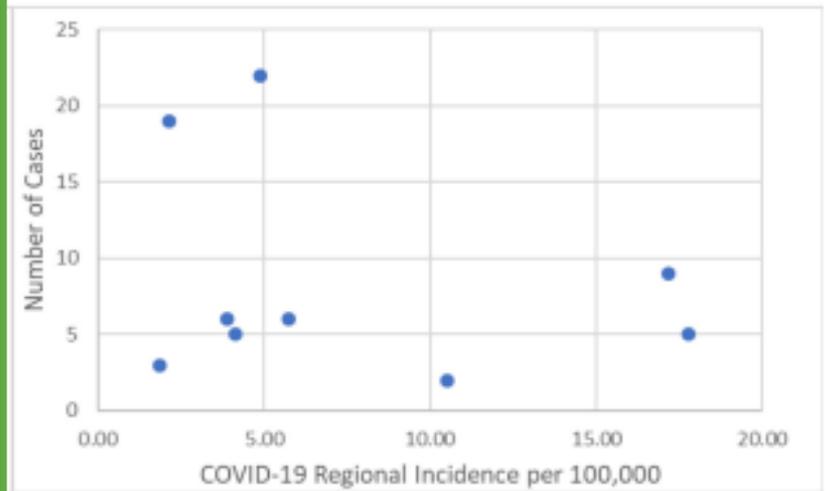
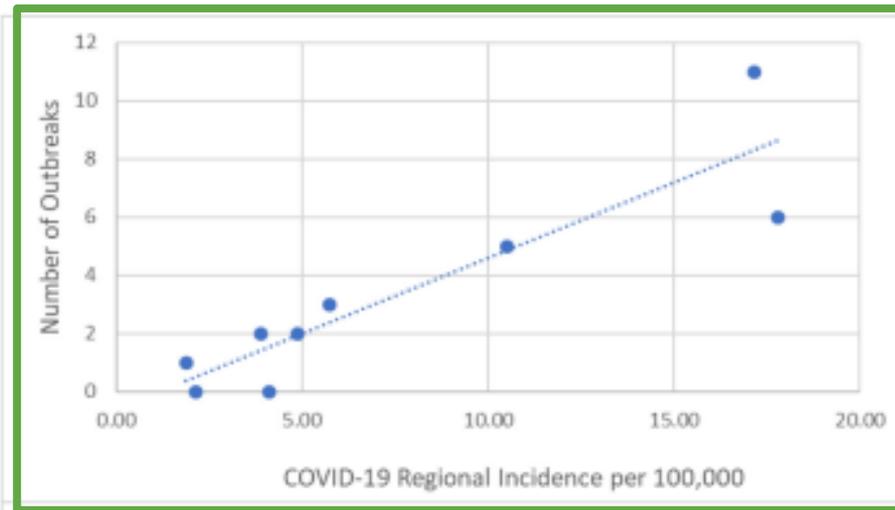
Island	Cases	Population	Cases per 10k	School Guidance
Oahu	1937	974,563	19.9	Elementary Blended / Secondary Blended
Molokai	9	7,345	12.3	Elementary In Person / Secondary Blended
Hawaii	216	201,513	10.7	Elementary In Person / Secondary Blended
Maui	29	144,444	2.0	In-Person (all students)
Lanai	0	3,135	0.0	In-Person (all students)
Kauai	1	72,293	0.1	In-Person (all students)

Metric Key		
Range	Elementary	Secondary
0-5.0	In Person	In Person
5.1-15.0	In Person	Blended
15.1-25.0	Blended	Blended
25.1-35.0	Blended	Learn-from-Home
35.1+	Learn-from-Home	Learn-from-Home



SARS-CoV-2 infection and transmission in educational settings: cross-sectional analysis of clusters and outbreaks in England

Settings	Numbers attending			Student Numbers			Rate per 100,000 students per day			
	Minimum	Maximum	average/d	Single	Coprimary	Outbreak	Single	Coprimary	outbreak	total
Early years	108,000	320,000	222,286	5	3	14	2.2 (0.73-5.3)	1.3 (0.28-3.9)	6.3 (3.4-10.6)	9.9 (6.2-15.0)
Primary	195,000	830,000	519,727	21	7	15	4.0 (2.5-6.2)	1.3 (0.54-2.8)	2.9 (1.6-4.8)	8.3 (6.0-11.1)
Secondary	78,000	126,000	101,417	2	0	0	2.0 (0.24-7.1)	0	0	2.0 (0.24-7.1)
	Numbers attending			Staff numbers			Rate per 100,000 staff per day			
Staff *			519,590	31	0	76	6.0 (4.1-8.5)	0	14.6 (11.5-18.3)	20.6 (16.9-24.9)



Age of COVID-19 Cases, Hawaii 2020

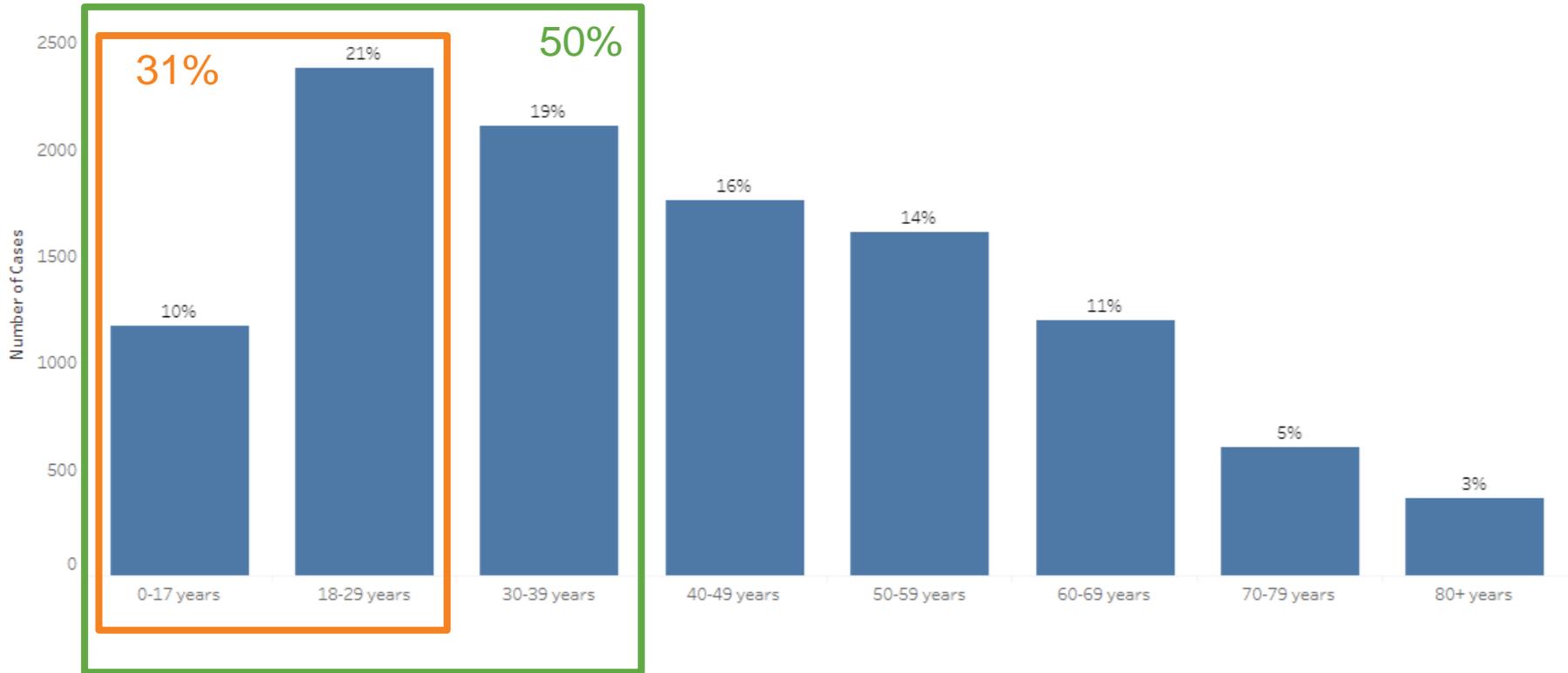
Includes all cases diagnosed in-state (excludes residents diagnosed out-of-state)
Last updated September 18, 2020 (updated weekly)

Total Cases: 11,189

Outcome Chart

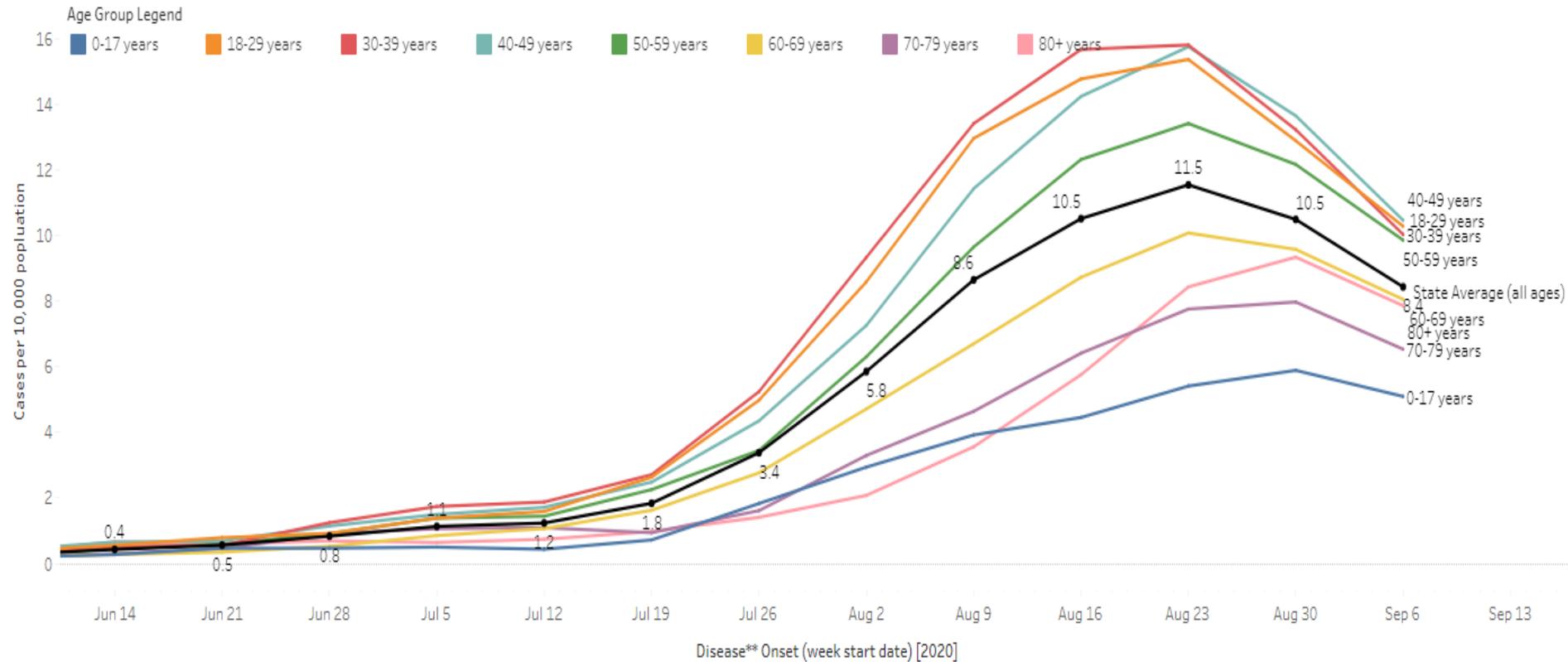
Gender Chart

Table View



https://experience.arcgis.com/experience/eb56a98b71324152a918e72d3ccdfe20/page/page_4/ accessed 09.20.20

New COVID-19 Cases* per Week by Age Group (per 10,000 population), Hawaii 2020

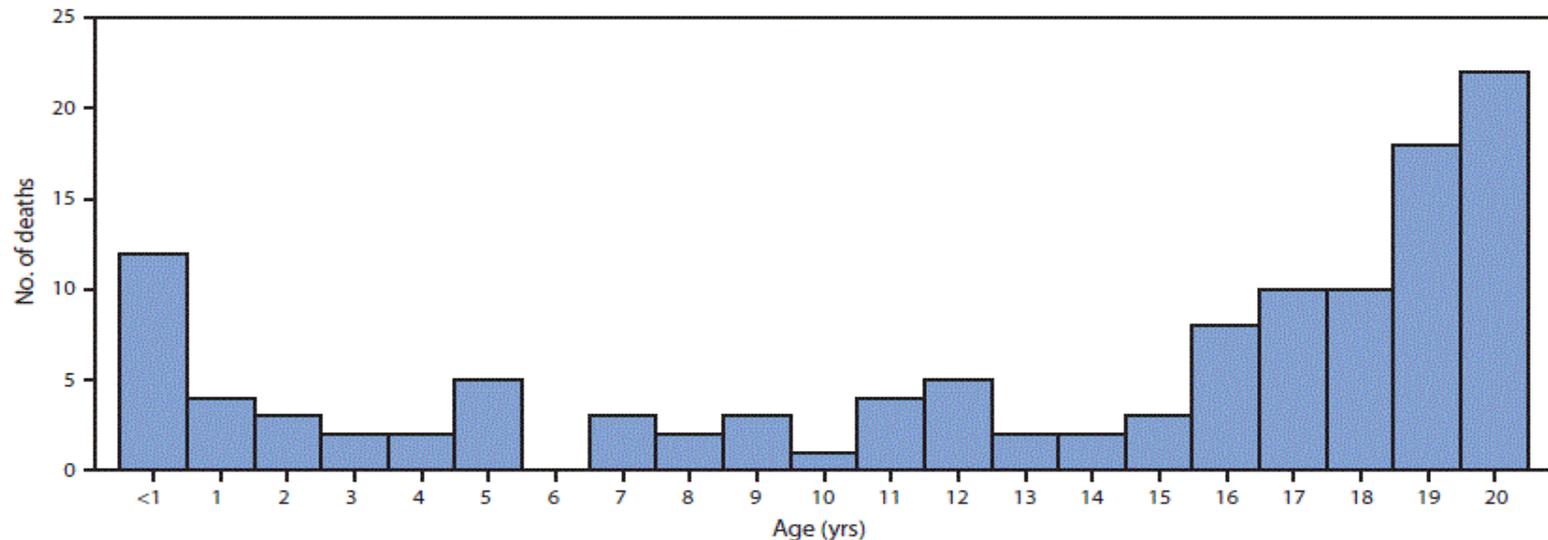


* Uses a 3-week moving average

** If symptom onset date is not available, date of test is used

https://experience.arcgis.com/experience/eb56a98b71324152a918e72d3ccdfc20/page/page_9/ accessed 09.20.20

Age at death among persons aged <21 years with SARS-CoV-2–associated deaths — United States, February 12–July 31, 2020



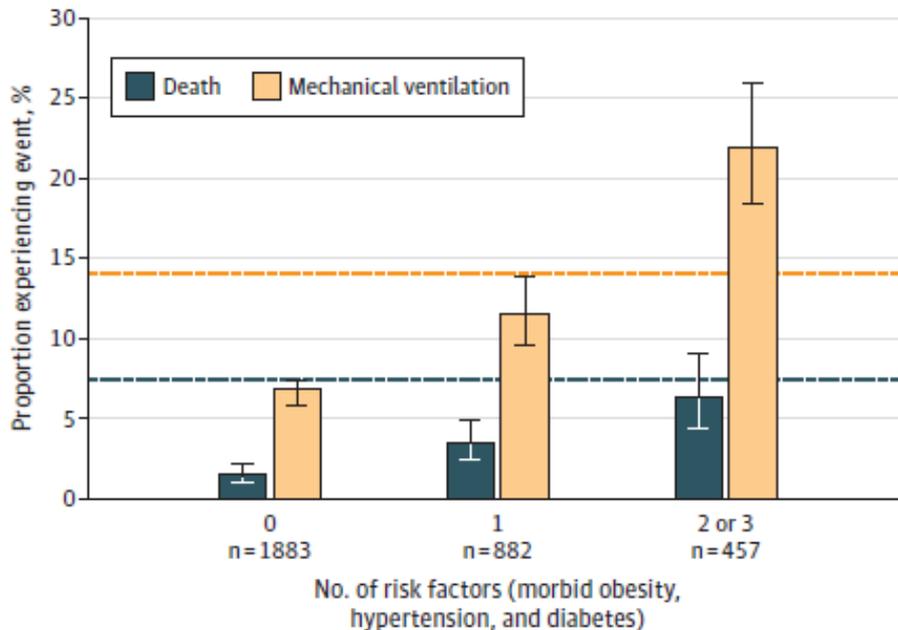
Of the 121 reported COVID deaths from 51 CDC jurisdictions

- 82% were Hispanic, black, native American or pacific islander
- 25% had no underlying health problems
- 13% died at home, 20% died in the ED
- 12% died from Multi-System Inflammatory Syndrome in Children (MIS-C)

Bixler D, Miller AD, Mattison CP, et al. SARS-CoV-2–Associated Deaths Among Persons Aged <21 Years — United States, February 12–July 31, 2020. MMWR Morb Mortal Wkly Rep 2020;69:1324–1329. DOI: http://dx.doi.org/10.15585/mmwr.mm6937e4external_icon.

Clinical Outcomes in Young US Adults Hospitalized with COVID-19 (Sept 9, 2020)

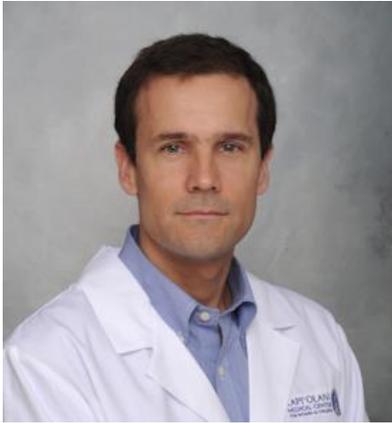
Figure. Death and Mechanical Ventilation in Young Adults With and Without Morbid Obesity, Hypertension, and Diabetes



Clinical Outcomes in Young US Adults Hospitalized With COVID-19. [Jonathan W. Cunningham, MD¹](#); [Muthiah Vaduganathan, MD, MPH¹](#); [Brian L. Claggett, PhD¹](#); [et al](#) [Karola S. Jering, MD¹](#); [Ankeet S. Bhatt, MD, MBA¹](#); [Ning Rosenthal, MD, MPH, PhD²](#); [Scott D. Solomon, MD¹](#) *JAMA Intern Med.* Published online September 9, 2020. doi:10.1001/jamainternmed.2020.5313

Study of 3222 young adults (18-34 years) required hospitalization for COVID-19 in the US between April 1 and June 30, 2020 (excluded 1600 pregnant women).

- 21% required intensive care, 10% required mechanical ventilation, and 2.7% died.
- In-hospital mortality rate is approximately double that of young adults with acute myocardial infarction.
- Morbid obesity, hypertension, and diabetes were common and associated with greater risks of adverse events.
- Young adults with more than 1 of these conditions faced risks comparable with those observed in middle-aged adults without them.
- More than half of these patients requiring hospitalization were Black or Hispanic



COVID-19 – Young Adults, Athletes, and Myocarditis

Andras Bratincsak, MD

Pediatric and Adult Congenital Cardiology,

Hawai'i Pacific Health Medical Group

Associate Professor of Pediatrics,

University of Hawai'i, John A. Burns School of Medicine

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New Online

Views **97,391** | Citations **0** | Altmetric **1084**



Viewpoint

ONLINE FIRST

FREE



May 13, 2020

More ▾

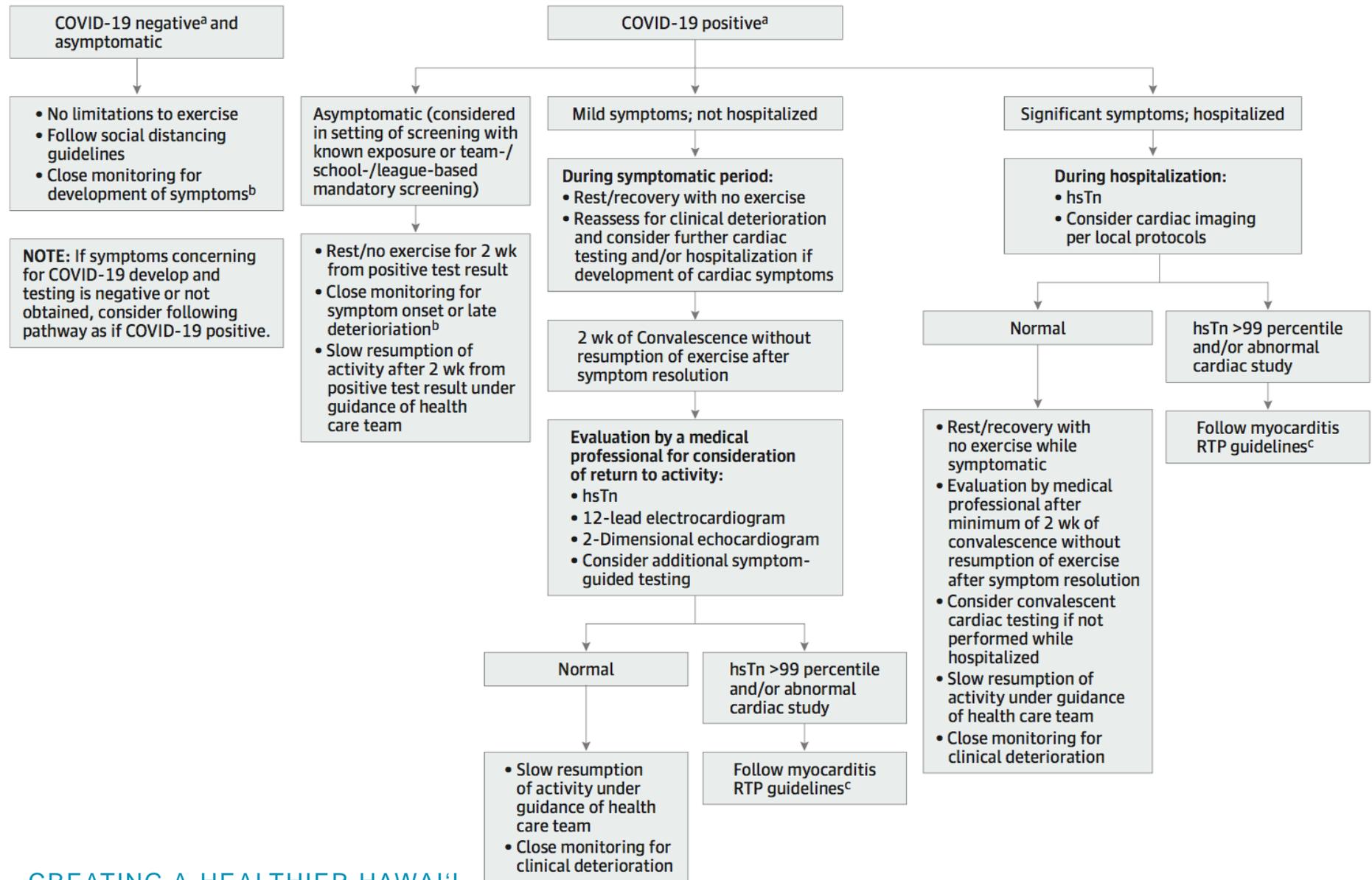
A Game Plan for the Resumption of Sport and Exercise After Coronavirus Disease 2019 (COVID-19) Infection

Dermot Phelan, MD, PhD¹; Jonathan H. Kim, MD, MSc²; Eugene H. Chung, MD, MSc³

» [Author Affiliations](#) | [Article Information](#)

JAMA Cardiol. Published online May 13, 2020. doi:10.1001/jamacardio.2020.2136

Figure. COVID-19 Return-to-Play Algorithm for Competitive Athlete and Highly Active People





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All Ty



Clinical Topics

Latest In Cardiology

Education and Meetings

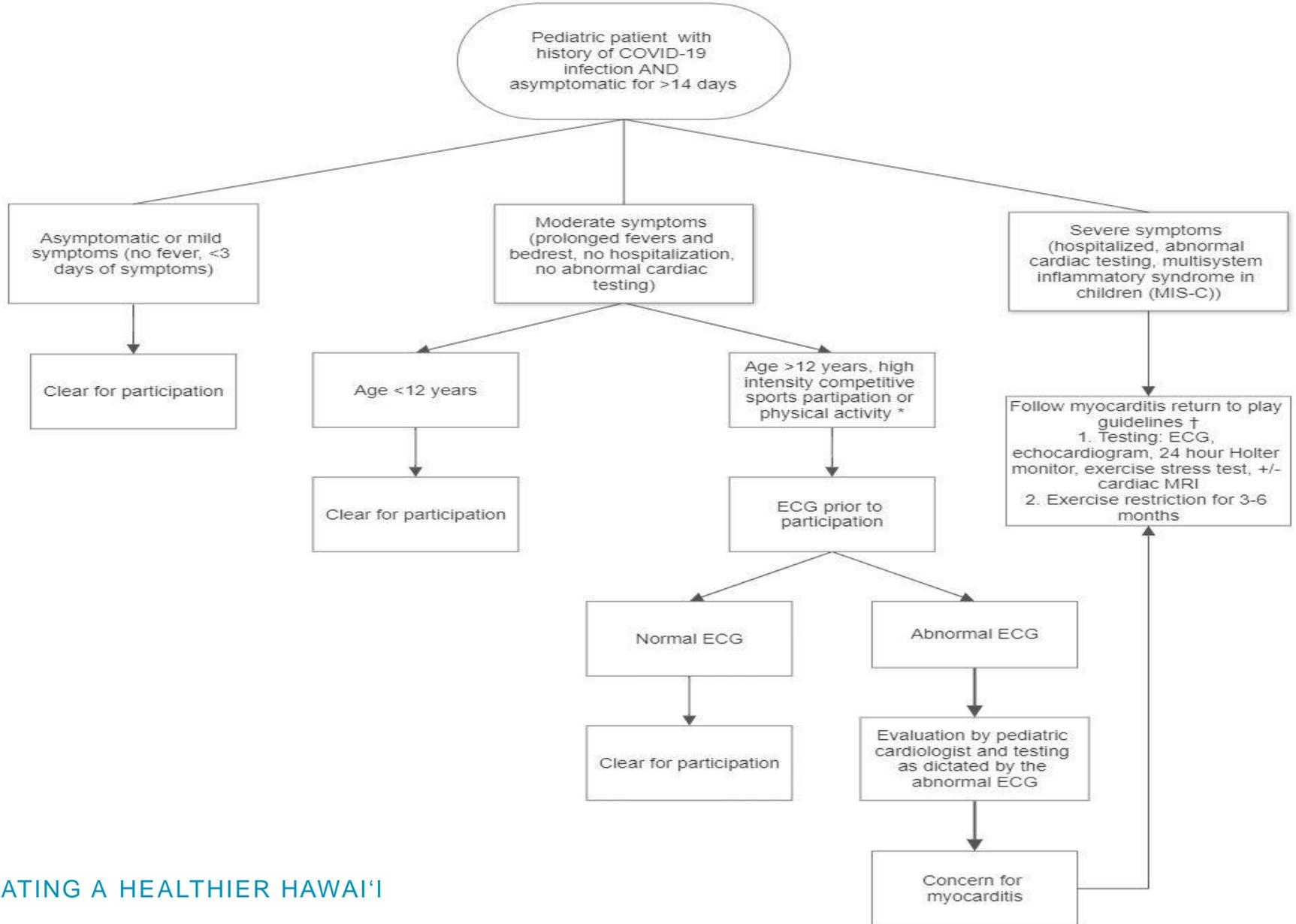
Tool

Returning To Play After Coronavirus Infection: Pediatric Cardiologists' Perspective

Jul 14, 2020 | [Peter N Dean, MD](#); [Lanier Burns Jackson, MD](#); [Stephen M. Paridon, MD, FACC](#)

Expert Analysis

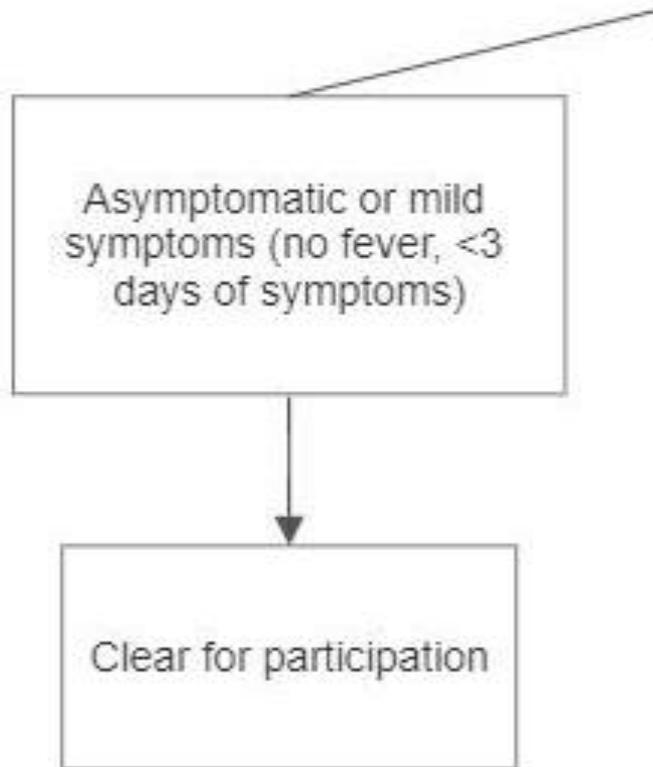
Return to Play After COVID-19 Infection in Pediatric Patients

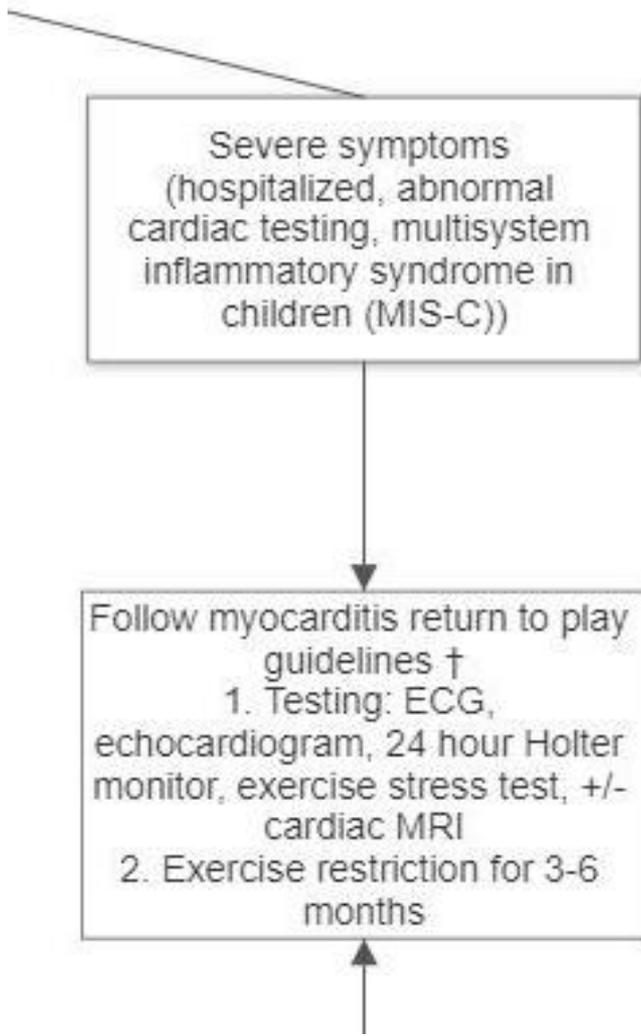


No symptoms 2 weeks
after + SARS-CoV-2 PCR



Return to sports
without further ado

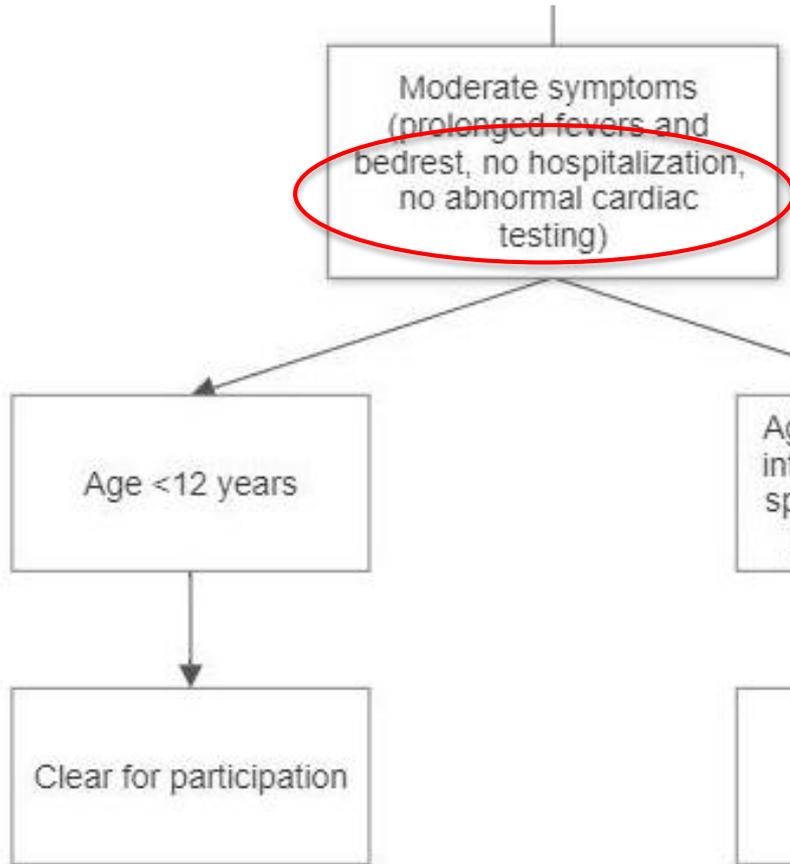




Severe symptoms likely diagnosis of MIS-C



Strict staged return overseen by cardiology

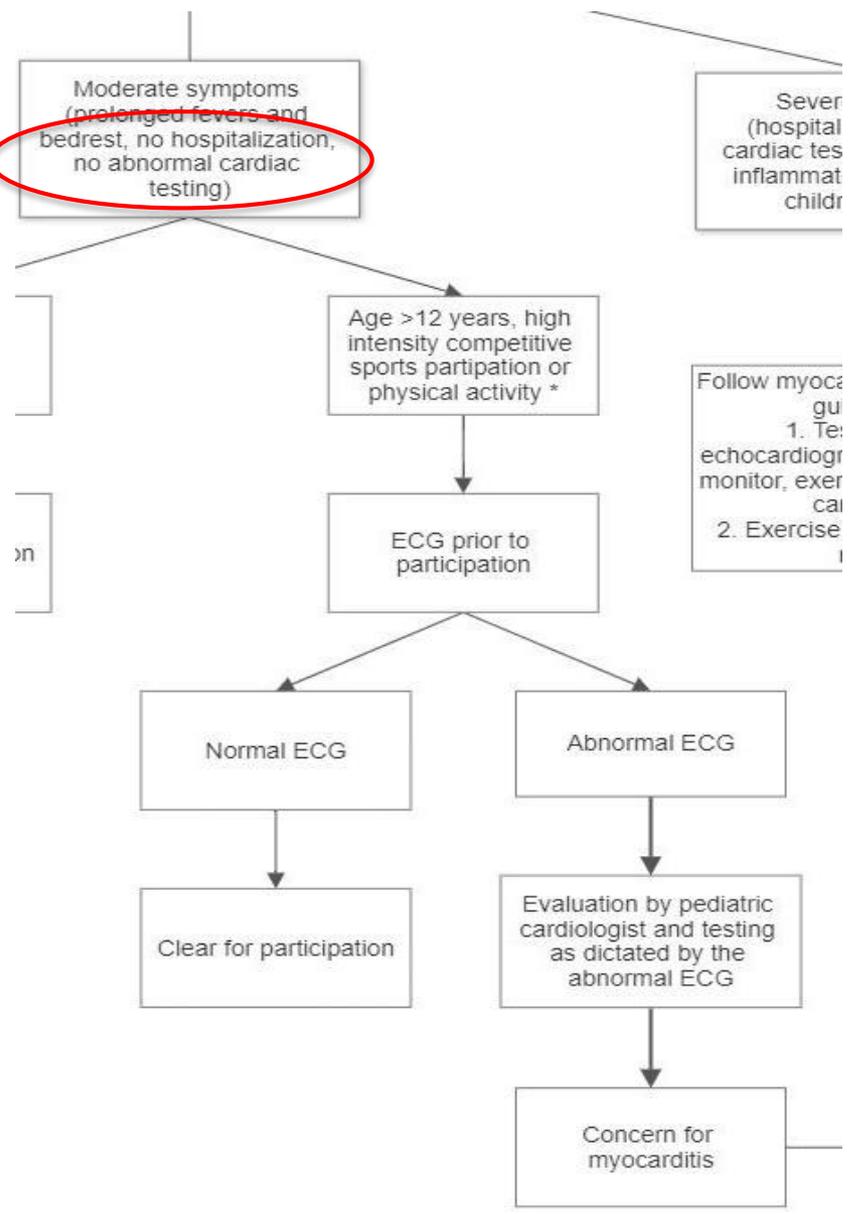


Moderate symptoms
but ECG, echo, Tn normal



Ok to go back after 2
weeks if no symptoms
(for younger than 12 years)

Suggested modification:
1) recreational sports,
not age



Moderate symptoms
but ECG, echo, Tn normal



Ok to go back after 2 weeks
if no symptoms and
if ECG normal
(for 12 years and older)

Suggested modification:
 1) competitive sports, not age
 2) ECG has very poor predictive value
 Consider echo, or cardiology consult

Pediatric patient with history of COVID-19 infection AND asymptomatic for >14 days

Asymptomatic or mild symptoms (no fever, <3 days of symptoms)

Clear for participation

Moderate symptoms (prolonged fevers and bedrest, no hospitalization, no abnormal cardiac testing)

Recreational sports

Clear for participation

Competitive sports

Consider echo or cardiology consult

normal

abnormal

Severe symptoms (hospitalized, abnormal cardiac testing, multisystem inflammatory syndrome in children (MIS-C))

Follow myocarditis return to play guidelines †
1. Testing: ECG, echocardiogram, 24 hour Holter monitor, exercise stress test, +/- cardiac MRI
2. Exercise restriction for 3-6 months

Hawai'i Pacific Health Research Institute (HPHRI): COVID-19 Therapies in Development



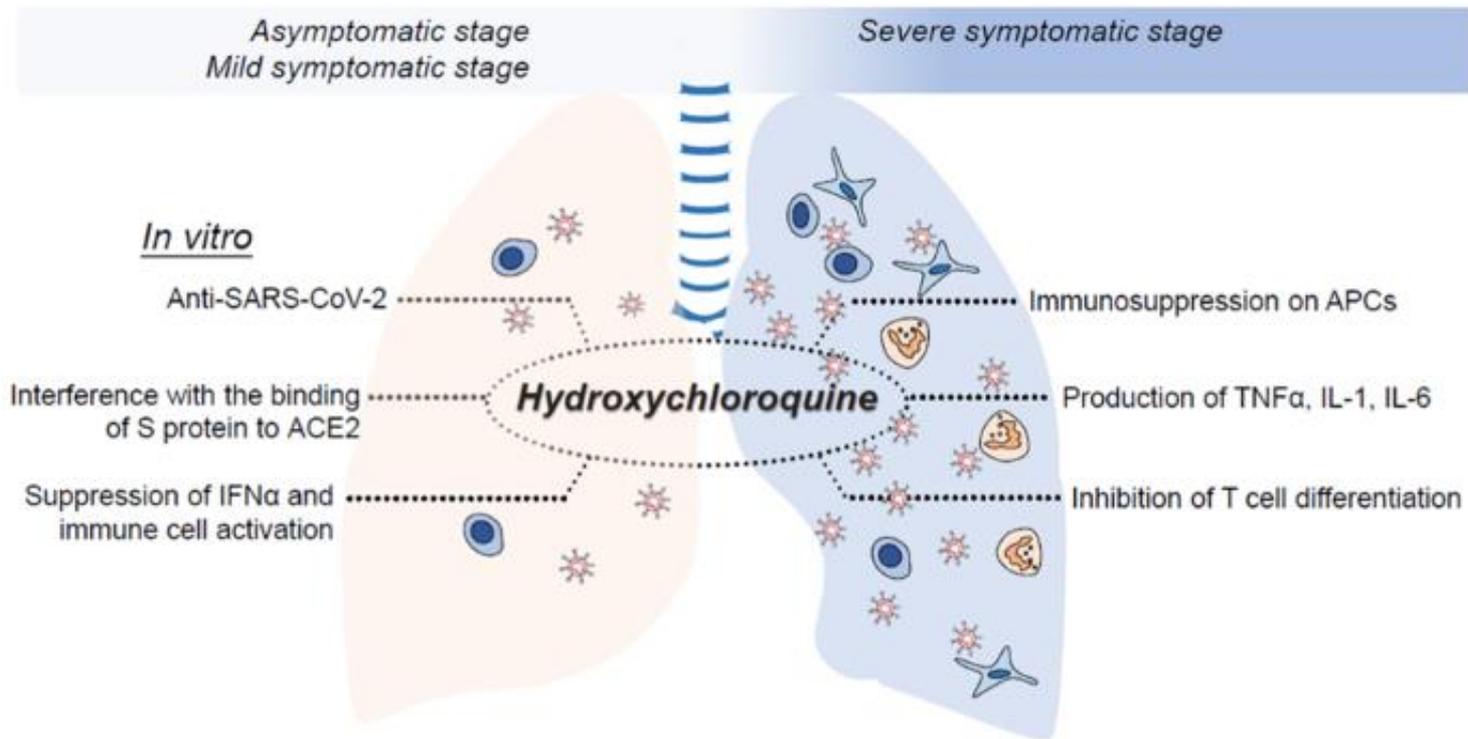
Wade Kyono, MD

*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*

HPH Research Institute COVID-19 Activities

- Identify and prioritize COVID-19 Research Initiatives
 - **Current (Past) Therapeutics**
 - Hydroxychloroquine
 - Convalescent plasma (Expanded Access Program -> Emergency Use Authorization)
 - Remdesivir (Emergency Use Authorization)
 - **Search for New Therapeutics**
 - Monoclonal antibodies (Regeneron, Eli Lilly)
 - Novel treatment – Brilacidin (Innovation Pharmaceutical)
 - Ongoing search for agents
 - **Prevention/Vaccines**
 - Moderna, AstraZeneca, Pfizer all approached for involvement in Phase III vaccine trials

Hydroxychloroquine



Hydroxychloroquine – A Cautionary Tale



F.D.A. Revokes Emergency Approval of Malaria Drugs Promoted by Trump

The agency said that a review of some studies showed that the drugs' potential benefits in treating Covid-19 did not outweigh the risks.



The Food and Drug Administration said that hydroxychloroquine was “unlikely to be effective” in treating the coronavirus. George Frey/Agence France-Presse — Getty Images

By Katie Thomas

June 15, 2020



Hydroxychloroquine – A Cautionary Tale

Hydroxychloroquine or chloroquine, a treatment for malaria, lupus erythematosus, and rheumatoid arthritis, has been under study as a possible treatment for COVID-19. Current data shows that this drug does not reduce deaths among hospitalised COVID-19 patients, nor help people with moderate disease.*

The use of hydroxychloroquine and chloroquine is accepted as generally safe for patients with malaria and autoimmune diseases, but its use where not indicated and without medical supervision can cause serious side effects and should be avoided.



World Health
Organization

#Coronavirus

#COVID19

**More decisive research is needed to assess its value in patients with mild disease or as pre- or post-exposure prophylaxis in patients exposed to COVID-19.*

FACT:
Studies show
hydroxychloroquine
does not have clinical
benefits in treating
COVID-19.



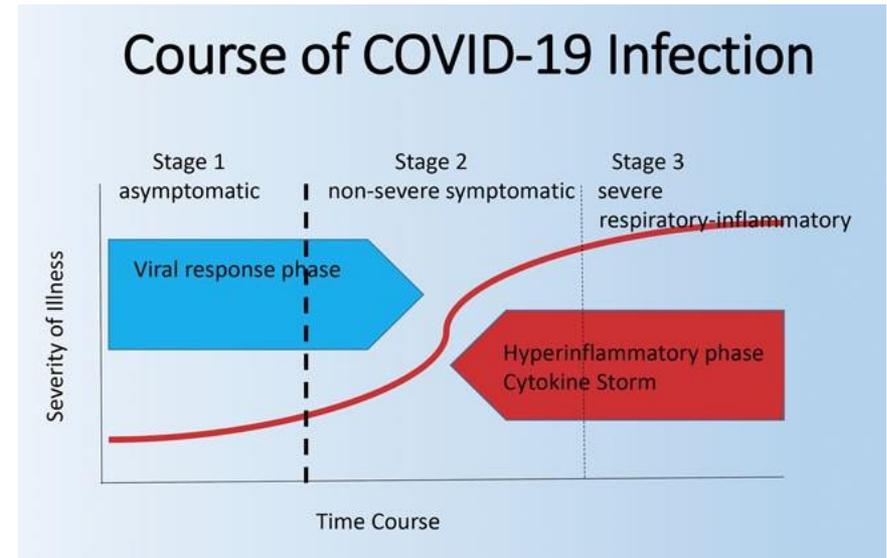
31 July 2020

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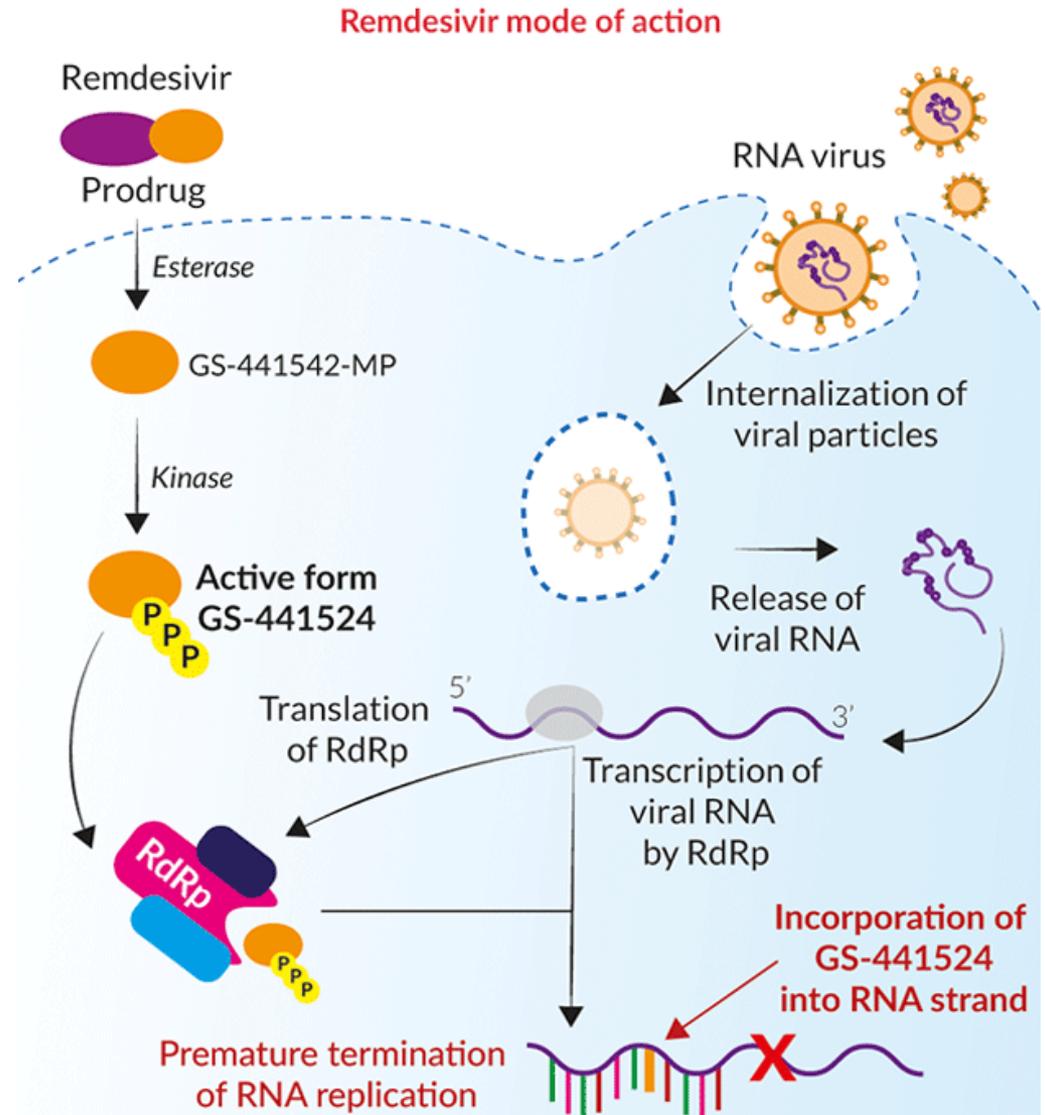
What We Are Doing . . .

- Severe COVID-19
 - Dexamethasone
 - Remdesivir
 - COVID-19 Convalescent Plasma (CCP)



Remdesivir

- Phase 3 SIMPLE - Severe Study
 - 65% more likely to have improvement at day 11 (5 day dosing)
 - 74% vs 59% recovered by Day 14
 - Mortality 7.6% vs 12.5% at Day 14
- EUA - August 28th



COVID-19 Convalescent Plasma

- **Hawaii CCP Coalition**

- BBOH, Hawaii Hospitals, DOH, JABSOM, etc . . .
- Donors - 28 days after infection
- Mayo Clinic Expanded Access Program
 - HPHRI and HPH Investigator involvement
- 80% of units with high titer antibody levels
- 636 units distributed Statewide by BBOH

Here's the study patient data:

Approached	114
Enrolled	91
Declined	23
<u>By HPH Site:</u>	
PMMC	46
Straub	68

Convalescent Plasma



Expanded access program for convalescent plasma discontinues enrollment, as FDA authorizes its emergency use.

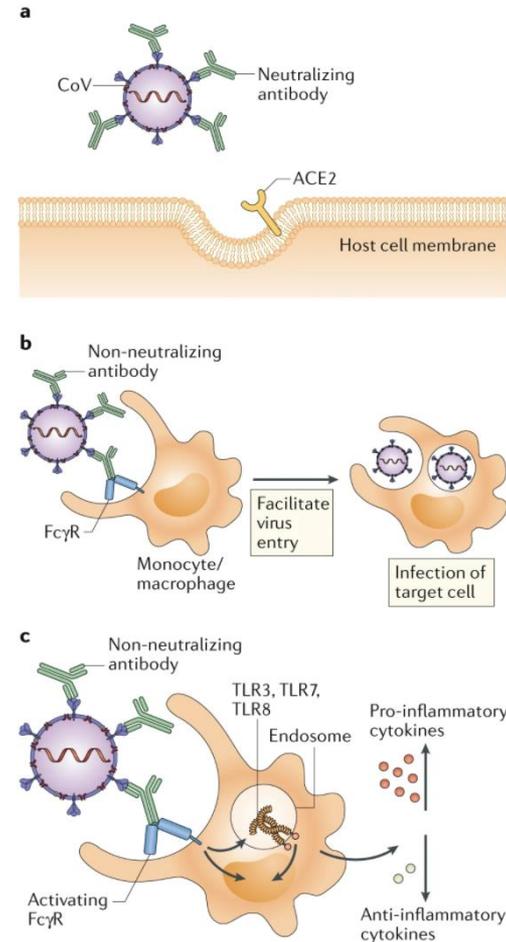
August 23, 2020

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Monoclonal Antibodies

- Want neutralizing antibody
 - High titer convalescent plasma
 - Manufactured monoclonal antibodies
 - Eli Lilly
 - Regeneron
- Non-neutralizing antibody may enhance infection or inflammation

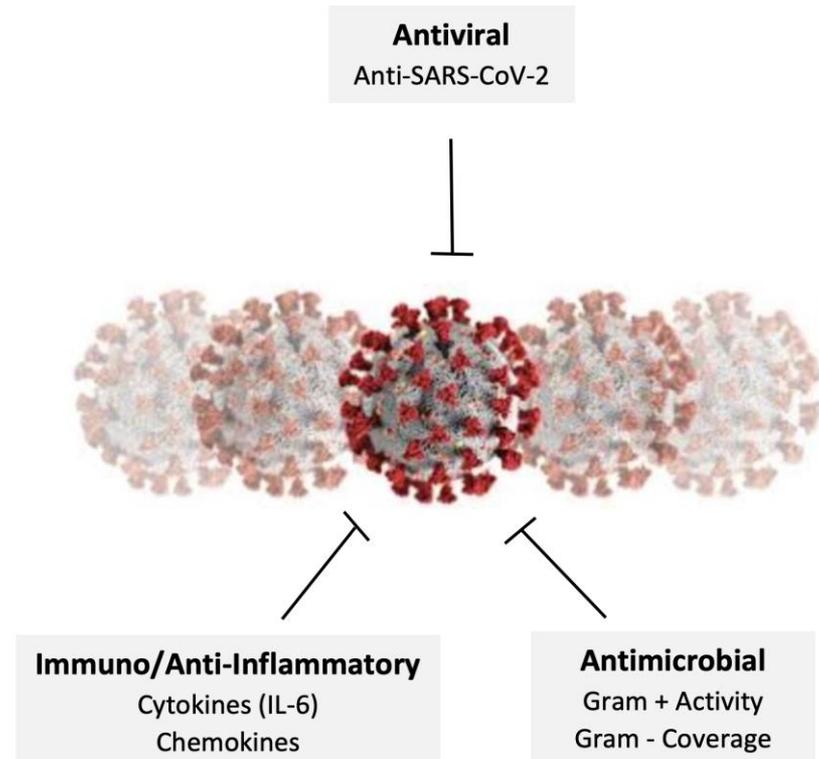


Novel Agent - “Swiss Army Knife”

- **Brilacidin**

- Defensin
 - Small antimicrobial particle widely expressed in animals
 - “First line of defense”
- Fully synthetic – smaller, more stable and more potent than natural defensins
- Heidi Hillesland (Wilcox ID) with initial Pharma contact
- Now with FDA IND filing, funding and protocol
- Will undergo HPHRI/ID Review

3-in-1 Combination of Therapeutic Properties



Innovation Pharmaceuticals: Mechanism of Action and Supporting Data for Brillacidin as a Potential Novel Coronavirus (COVID-19) Treatment (April 5, 2020)

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September 2020: Current Update on Development of COVID-19 Vaccines

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

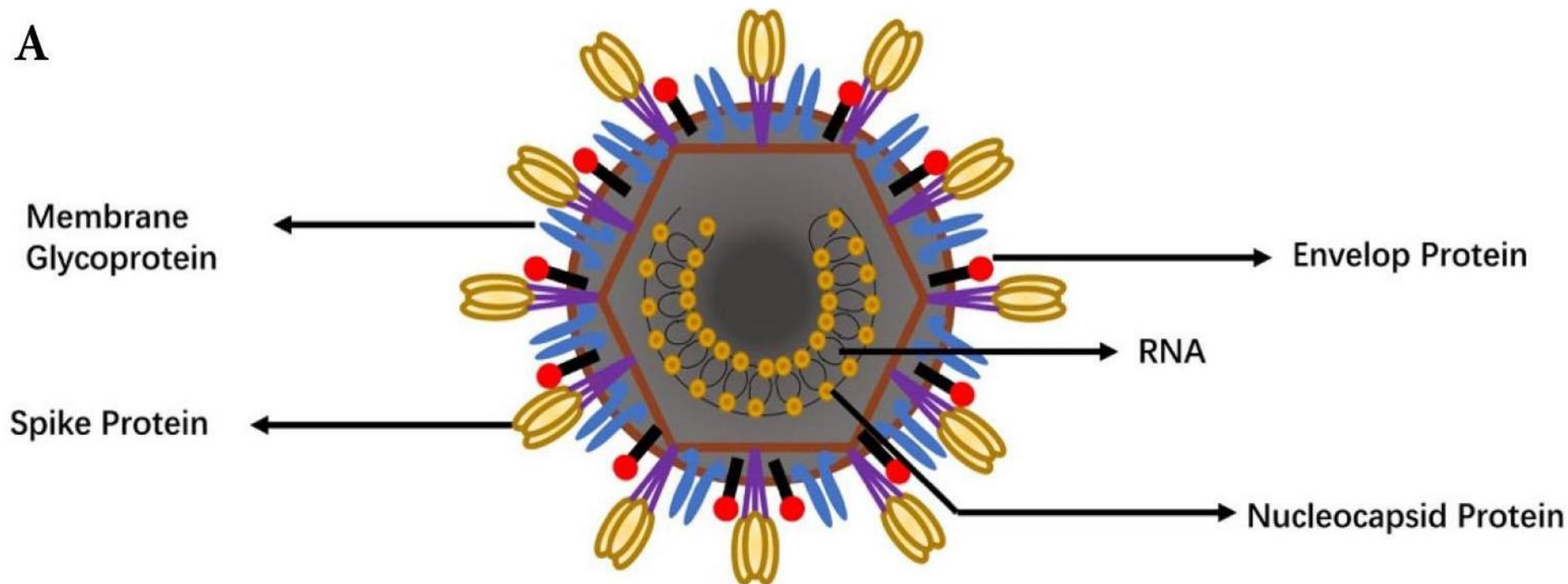




Antigen Selection (CoV)



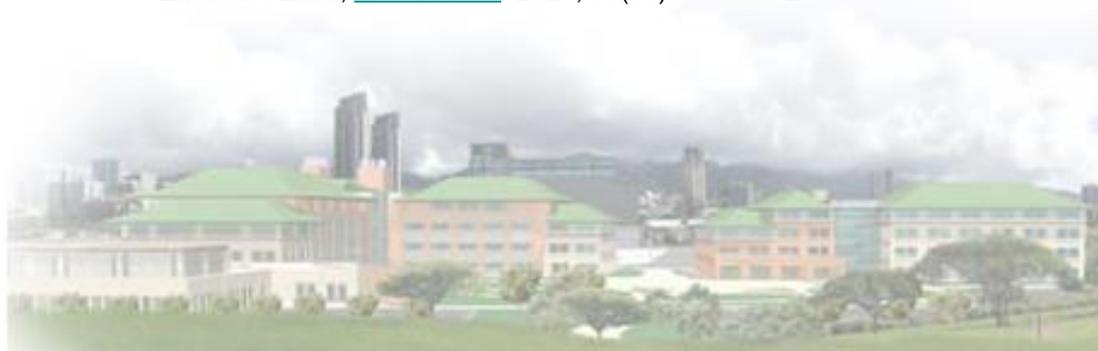
A



Spike protein function:

- Receptor binding
- Membrane fusion

Zhou and Zhao, [Int J Biol Sci.](#) 2020; 16(10): 1718–1723.

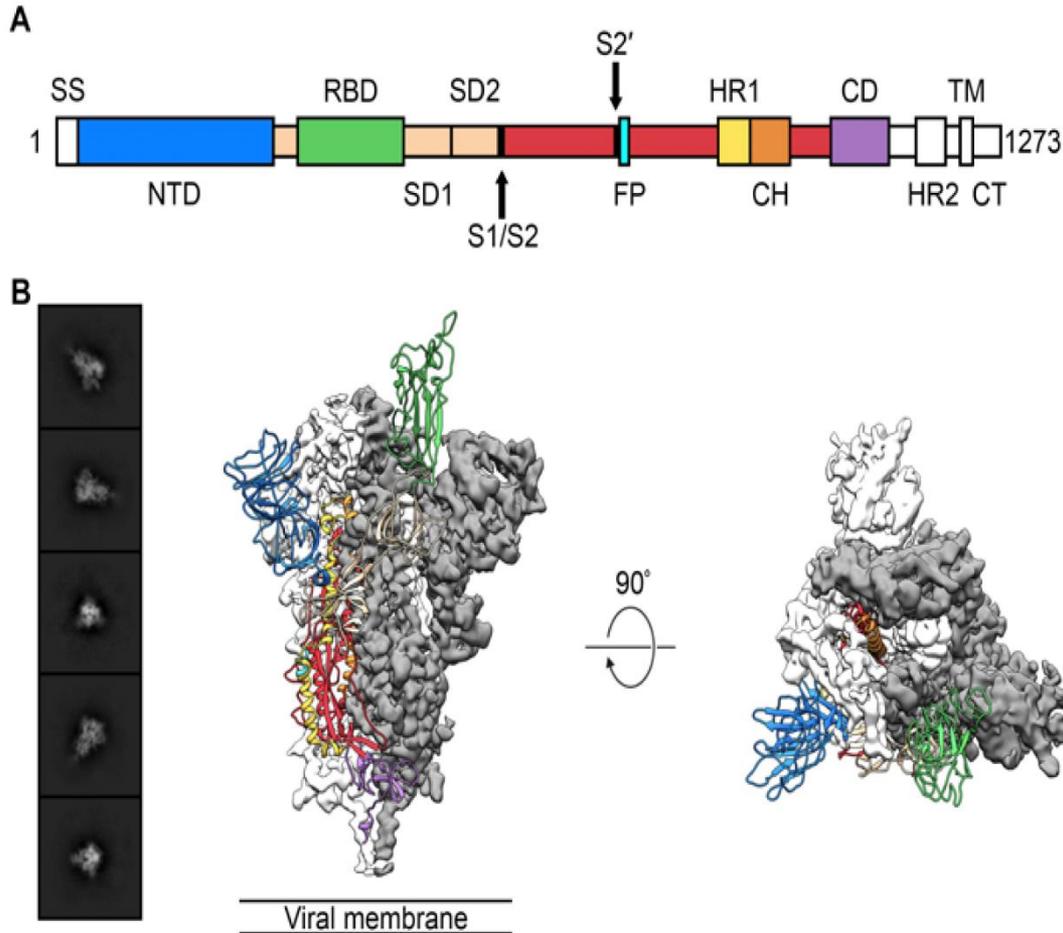




Spike Protein



SARS-CoV-2



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

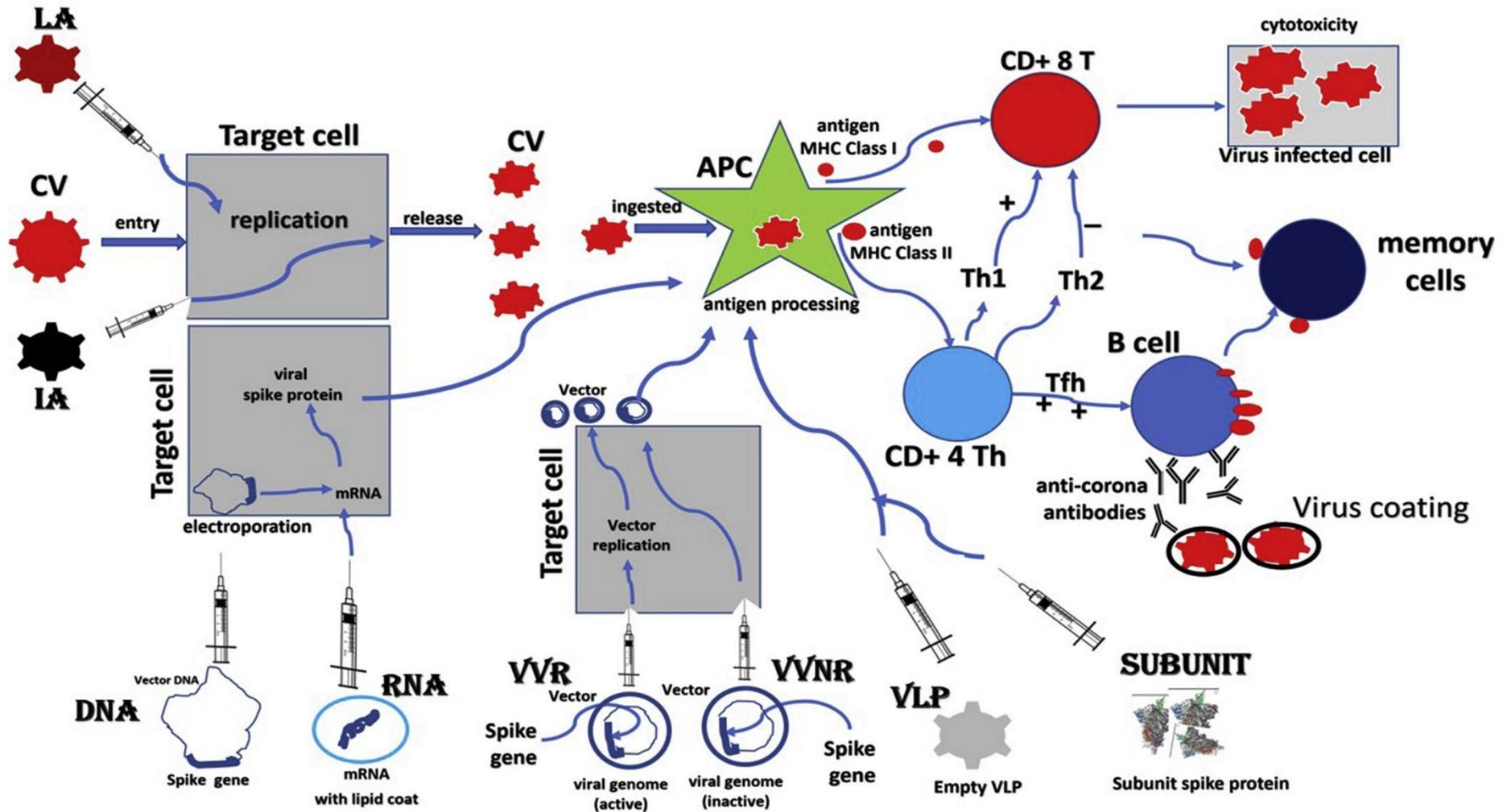
Conformation that undergoes a substantial structural rearrangement to fuse the viral membrane with the host cell membrane

Pallesen et al. PNAS 2017

Wrapp and Wang et al. Science 2020



Immunity to SARS-CoV-2



*Journal of Clinical and Experimental
Hepatology* DOI: (10.1016/j.jceh.2020.06.003)



Overview - COVID-19 Vaccines



- Total number of (known) Vaccine Candidates under development: 209 (19: unknown platform used)
- **Conventional:** 14 (inactivated), 4 (live-attenuated)
- **Virally vectored vaccines:** 25 (non-rep), 18 (rep)
- **Genetic vaccines:** 16 (DNA), 27 (RNA)
- **Recombinant subunits:** 70 (protein), 16 (VLP)
- **Passive Immunization** - convalescent serum and antibody therapies: 51

Source: Milken Institute COVID-19 tracker

Accessed 09/11/2020





COVID-19 Vaccines – Clinical Status



Platform	Pre-clinical	Phase I	Phase II	Phase III
Inactivated	9		2 ?	3
live attenuated	4			
protein subunits	61	5	4 ?	
VLP	14	1	1	
DNA	12		4 ?	
RNA	21	2	2 ?	2
non-replicating viral vector	20	1	3 ?	1
replicating viral vector	18			

Source: Milken Institute COVID-19 tracker

Accessed 09/11/2020





Operation Warp Speed (HHS)



August 31st, 2020
Update (hhs.gov)

Fact Sheet: Explaining Operatio X +

Fact Sheet: Explaining Operatio X +

https://www.hhs.gov/coronavirus/explaining-operation-warp-spe

evidence, the FDA determined convalescent plasma may be effective in lessening the severity or shortening the length of COVID-19 illness in hospitalized patients, and that the known and potential benefits of the product outweigh the known and potential risks. The EUA authorizes the distribution of convalescent plasma in the U.S. as well as its administration by health care providers, as appropriate, to treat suspected or confirmed cases of COVID-19. [Learn more about EUAs.](#)

As announced on May 15, the vaccine development plan is as follows, subject to change as work proceeds:

- Fourteen promising candidates have been chosen from the 100+ vaccine candidates currently in development—some of them already in clinical trials with U.S. government support.
- The 14 vaccine candidates are being narrowed down to about seven candidates, representing the most promising candidates from a range of technology options (nucleic acid, viral vector, protein subunit), which will go through further testing in early-stage clinical trials.
- Large-scale randomized trials for the demonstration of safety and efficacy will proceed for the most promising candidates.

Manufacturing

The federal government is making investments in the necessary manufacturing capacity at its own risk, giving firms confidence that they can invest aggressively in development and allowing faster



Operation Warp Speed (HHS)



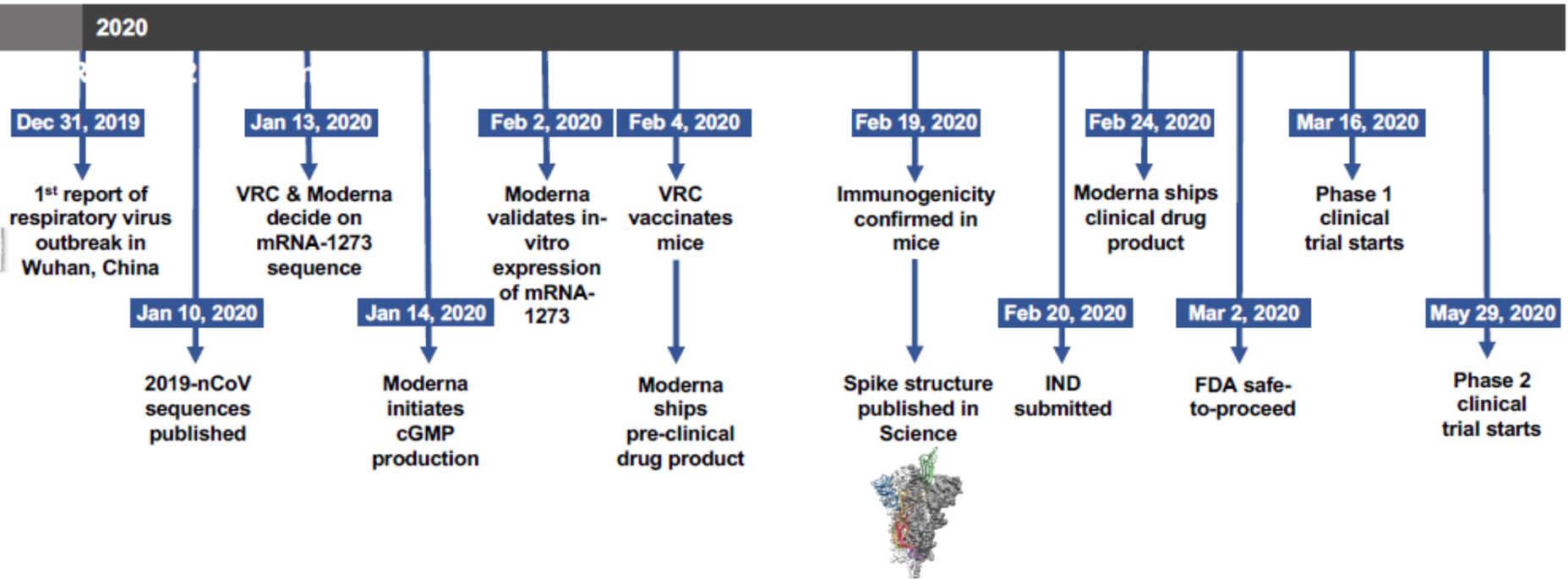
Technology Platforms funded:

- Nucleic acid: mRNA – Moderna, Pfizer/BioNTech
- Viral vector: Adenovirus – AstraZeneca (ChAdOx), Johnson & Johnson (Ad26)
- Protein subunit: Novavax (Matrix-M adjuvant), Sanofi/GSK (AS03 adjuvant)
- Expected additional candidate: rVSV (replicating viral vector, Merck)





Moderna – RNA Vaccine Candidate



Corbett et al. 2020, bioRxiv preprint doi:
<https://doi.org/10.1101/2020.06.11.145920>.

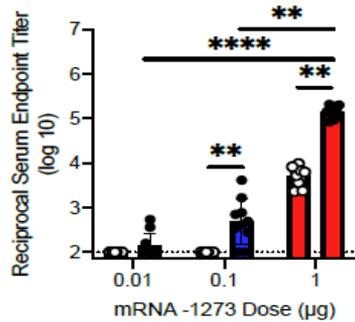




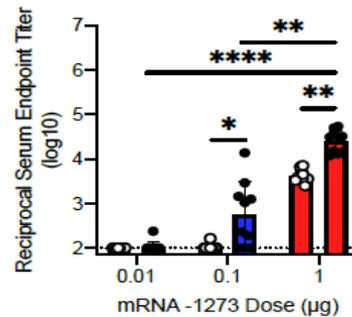
RNA: Mouse Immunogenicity



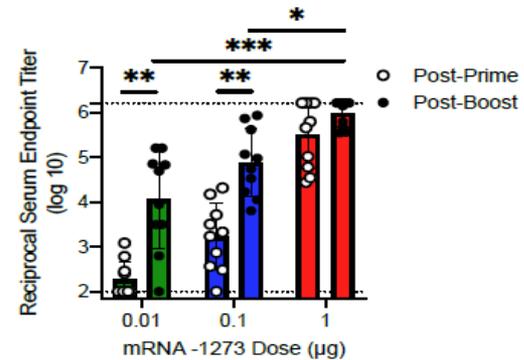
a Binding Antibodies
mRNA-1273 Immunized BALB/c



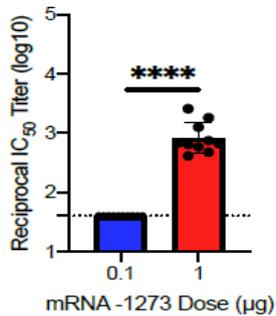
b Binding Antibodies
mRNA-1273 Immunized C57BL/6



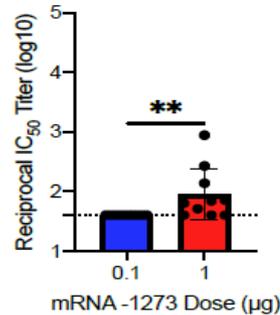
c Binding Antibodies
mRNA-1273 Immunized B6C3



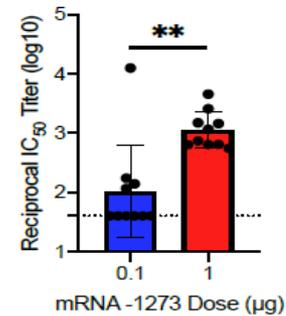
d Neutralizing Antibodies
mRNA-1273 Immunized BALB/c



e Neutralizing Antibodies
mRNA-1273 Immunized C57BL/6



f Neutralizing Antibodies
mRNA-1273 Immunized B6C3



Corbett et al. 2020, bioRxiv preprint doi:
<https://doi.org/10.1101/2020.06.11.145920>.

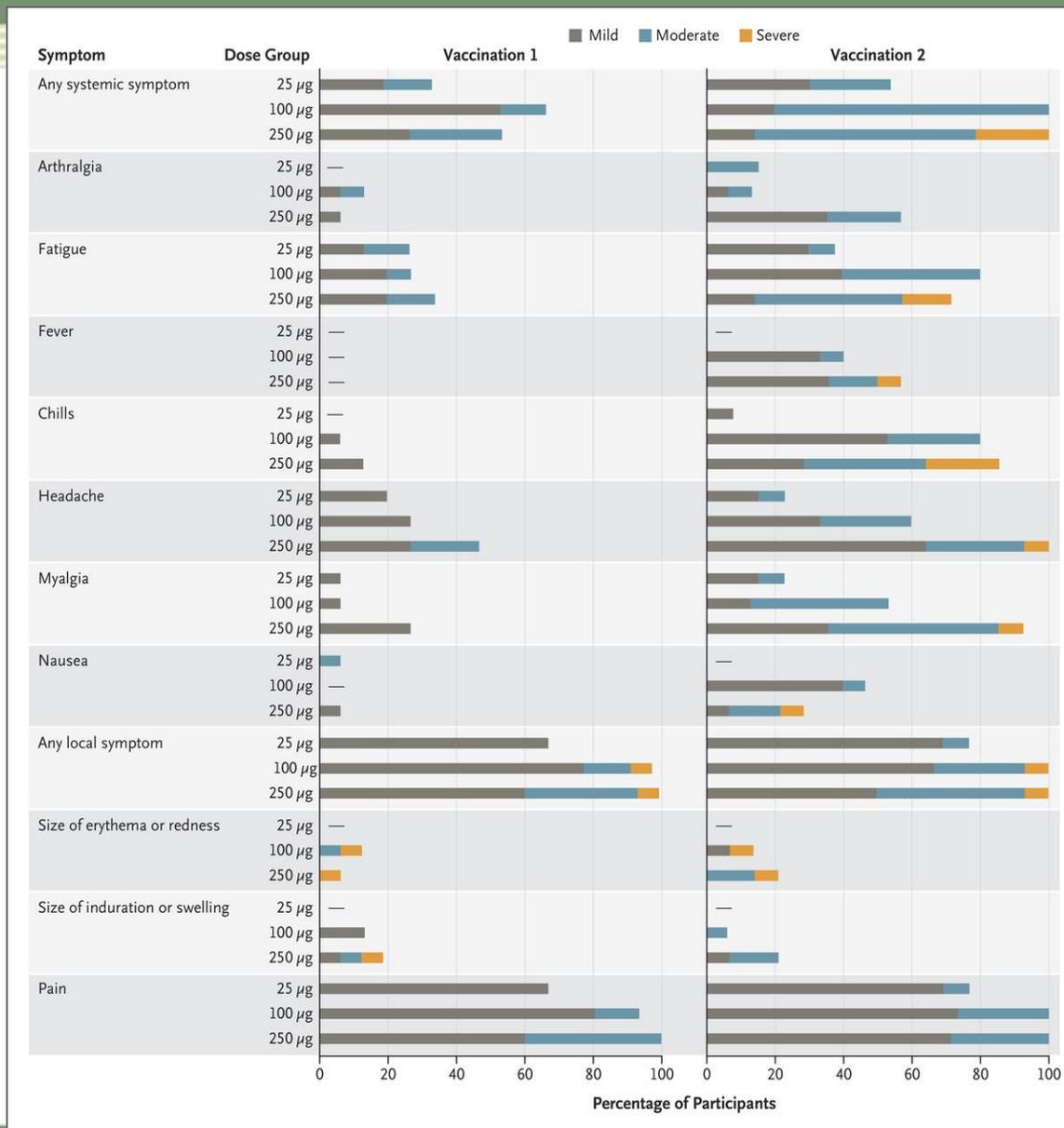




Moderna RNA – Phase I: Systemic and Local AE's



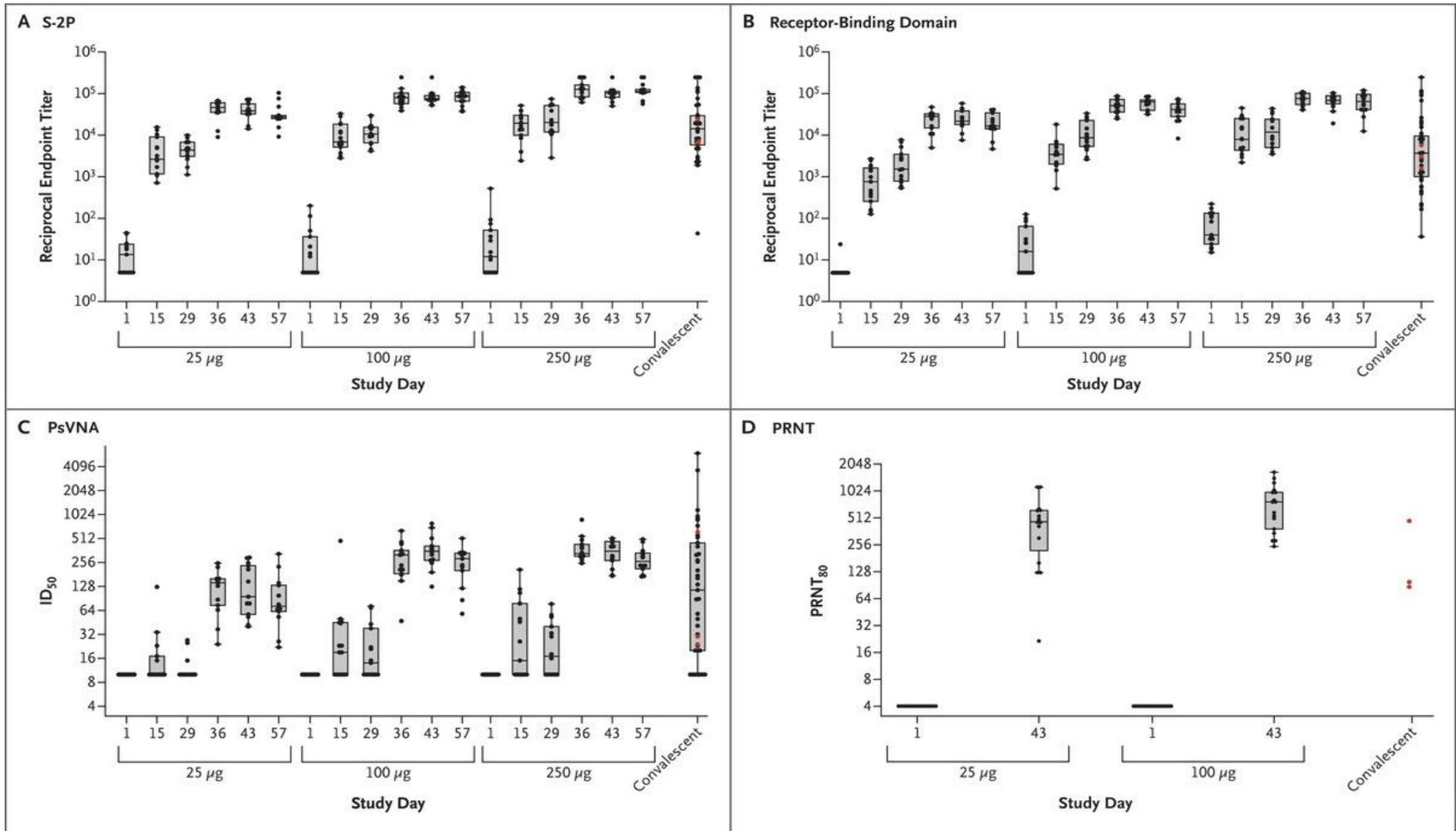
➤ Continued with 100µg dose level



LA Jackson et al. N Engl J Med 2020.
DOI: 10.1056/NEJMoa2022483



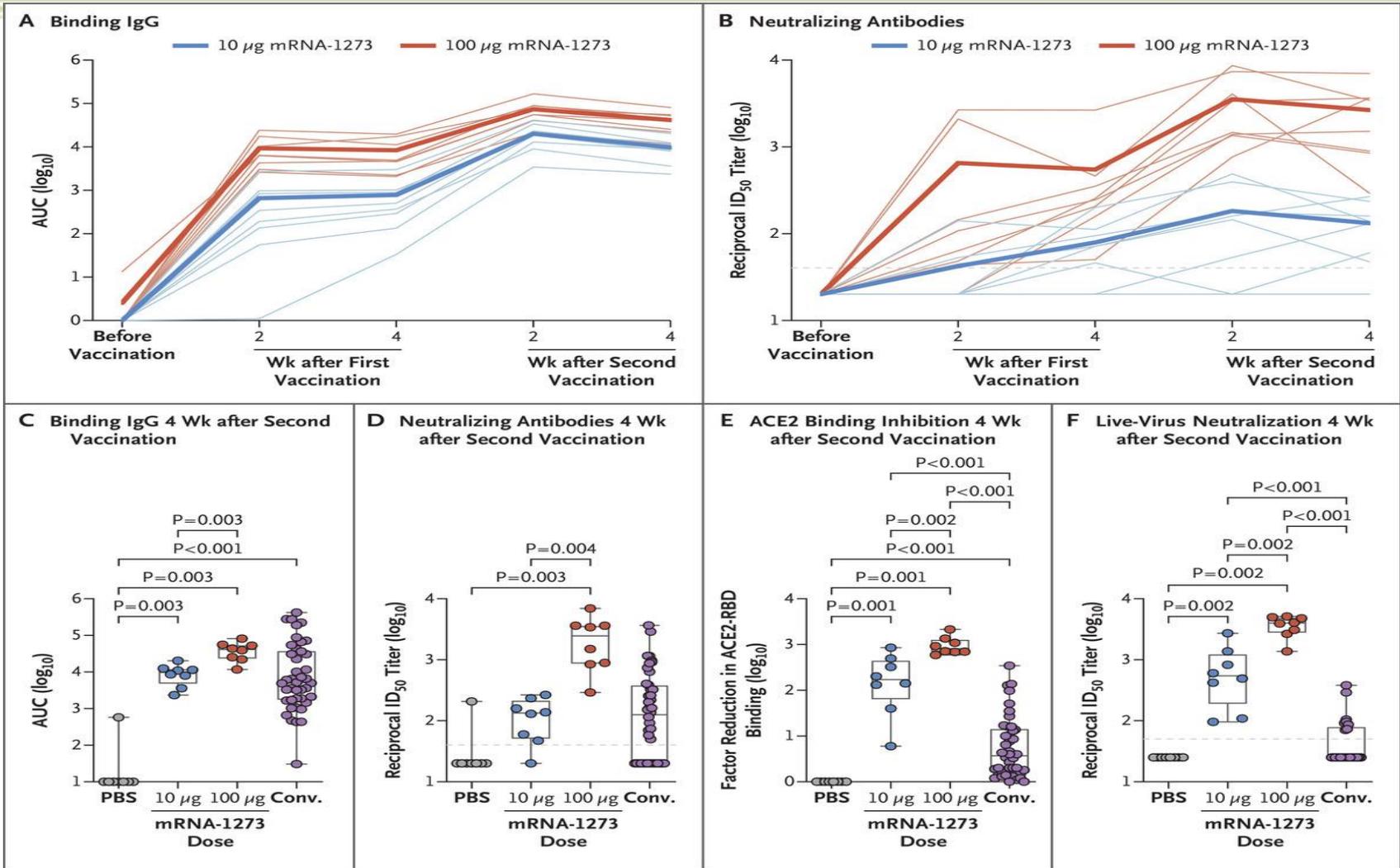
mRNA: Antibody and Neutralization Responses



LA Jackson et al. N Engl J Med 2020.
DOI: 10.1056/NEJMoa2022483



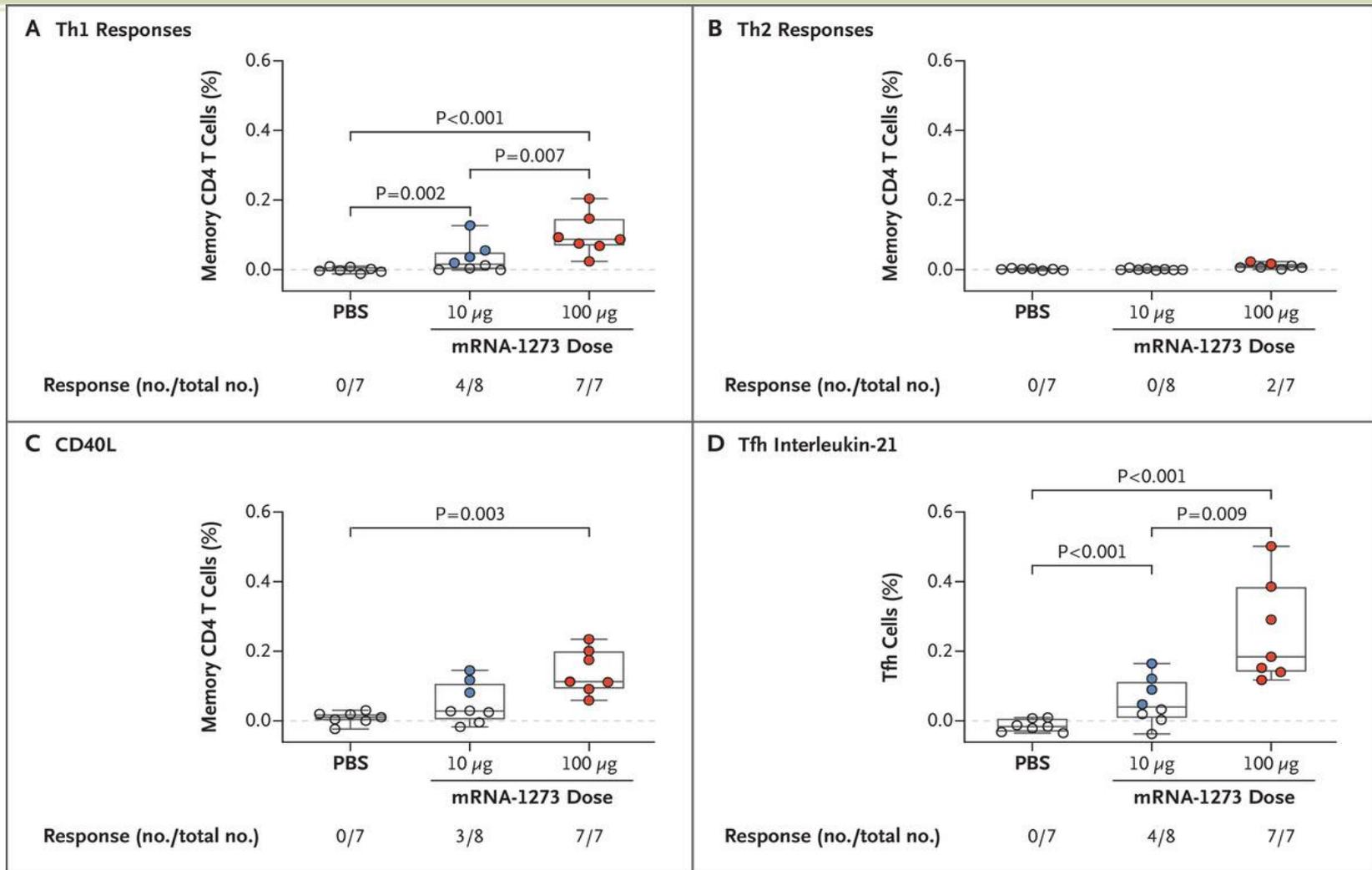
Antibody Responses in Rhesus Macaques (mRNA)



KS Corbett et al. N Engl J Med 2020.
DOI: 10.1056/NEJMoa2024671



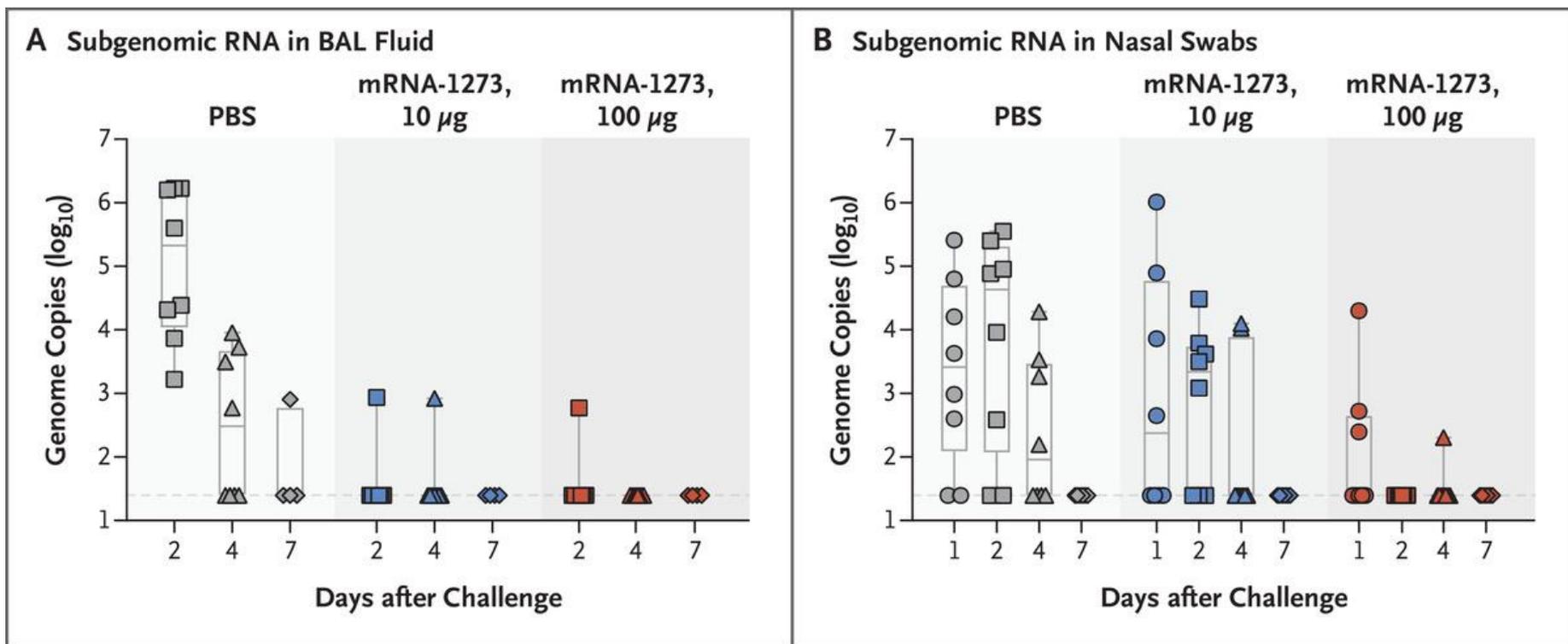
T-Cell Responses after mRNA-1273 Vaccination



KS Corbett et al. N Engl J Med 2020.
DOI: 10.1056/NEJMoa2024671



Efficacy: Upper/Lower Respiratory Viral Load (mRNA)



KS Corbett et al. N Engl J Med 2020.
DOI: 10.1056/NEJMoa2024671





Summary: Moderna Vaccine



- Good immunogenicity after two doses in mice, NHP's and humans
- Balanced responses show that delivery seems efficient for this candidate
- Potent virus neutralization shown
- Reduction in viral loads in Rhesus model – lower and upper respiratory tract
- Durability of immunity?
- Adverse reactions and exclusion criteria?
- Efficacy after only one dose and kinetics of immune response?





Adenovirus-vectored Candidates



nature
medicine

LETTERS

<https://doi.org/10.1038/s41591-020-1070-6>

Check for updates

OPEN

Ad26 vaccine protects against SARS-CoV-2 severe clinical disease in hamsters

Lisa H. Tostanoski^{1,10}, Frank Wegmann^{2,10}, Amanda J. Martinot^{1,3,10}, Carolin Loos^{4,5,10}, Katherine McMahan^{1,10}, Noe B. Mercado^{1,10}, Jingyou Yu^{1,10}, Chi N. Chan⁶, Stephen Bondoc⁶, Carly E. Starke⁶, Michael Nekorchuk⁶, Kathleen Busman-Sahay⁶, Cesar Piedra-Mora^{1,3}, Linda M. Wrijil³, Sarah Ducat³, Jerome Custers², Caroline Atyeo^{4,7}, Stephanie Fischinger^{4,7}, John S. Burke⁴, Jared Feldman^{4,7}, Blake M. Hauser^{4,7}, Timothy M. Caradonna^{4,7}, Esther A. Bondzie¹, Gabriel Dagotto^{1,7}, Makda S. Gebre^{1,7}, Catherine Jacob-Dolan^{1,7}, Zijin Lin¹, Shant H. Mahrokhian¹, Felix Nampanya¹, Ramya Nityanandam¹, Laurent Pessaint⁸, Maciel Porto⁸, Vaneesha Ali⁸, Dalia Benetiene⁸, Komlan Tevi⁸, Hanne Andersen⁸, Mark G. Lewis⁸, Aaron G. Schmidt^{4,7,9}, Douglas A. Lauffenburger⁵, Galit Alter^{4,9}, Jacob D. Estes⁶, Hanneke Schuitemaker², Roland Zahn^{1,2} and Dan H. Barouch^{1,4,7,9} ✉

Coronavirus disease 2019 (COVID-19) in humans is often a clinically mild illness, but some individuals develop severe pneumonia, respiratory failure and death¹⁻⁴. Studies of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in hamsters⁵⁻⁷ and nonhuman primates⁸⁻¹⁰ have

vector-based vaccine¹⁹ encoding a stabilized SARS-CoV-2 spike (S) in this stringent model.

We inoculated 20 Syrian golden hamsters (10–12 weeks old) with 5×10^4 50% tissue culture infective dose (TCID₅₀) ($n=4$; low-dose) or 5×10^5 TCID₅₀ ($n=16$; high-dose) SARS-CoV-2 by the intranasal

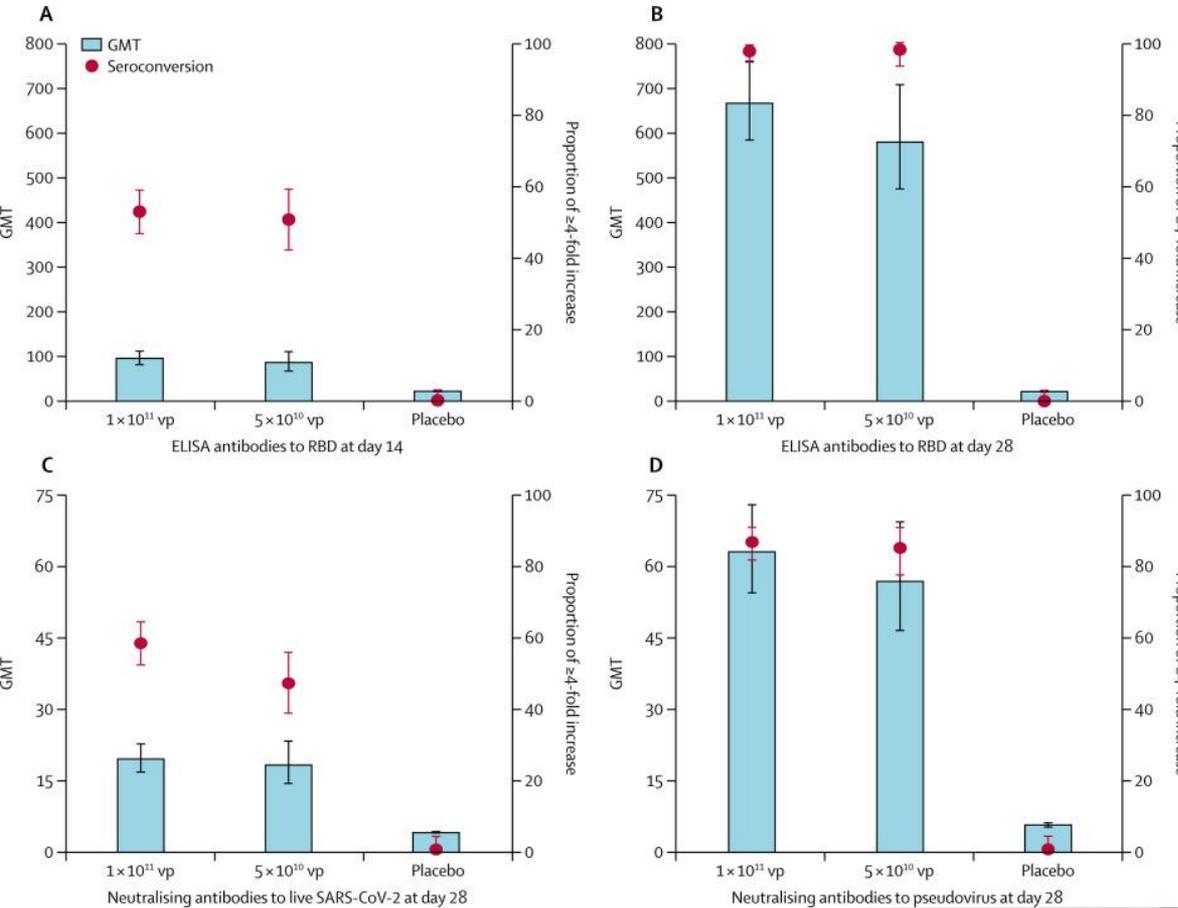
September 3, 2020 – Demonstrate utility of a COVID-19 pathology model and show that a single dose of Ad26-vectored vaccine reduces viral loads and eliminates pathology. Selects version of the Spike protein that generates better vaccine efficacy.

(Johnson&Johnson/Janssen)





Ad5-vectored Platform (CanSinobiologics)



Specific antibody responses to RBD, neutralising antibodies to live severe acute respiratory syndrome coronavirus 2 and pseudovirus post vaccination

Zhu et al. 2020. The Lancet.

[https://doi.org/10.1016/S0140-6736\(20\)31605-6](https://doi.org/10.1016/S0140-6736(20)31605-6)

➤ Single (high) dose – problem: pre-existing immunity to vector



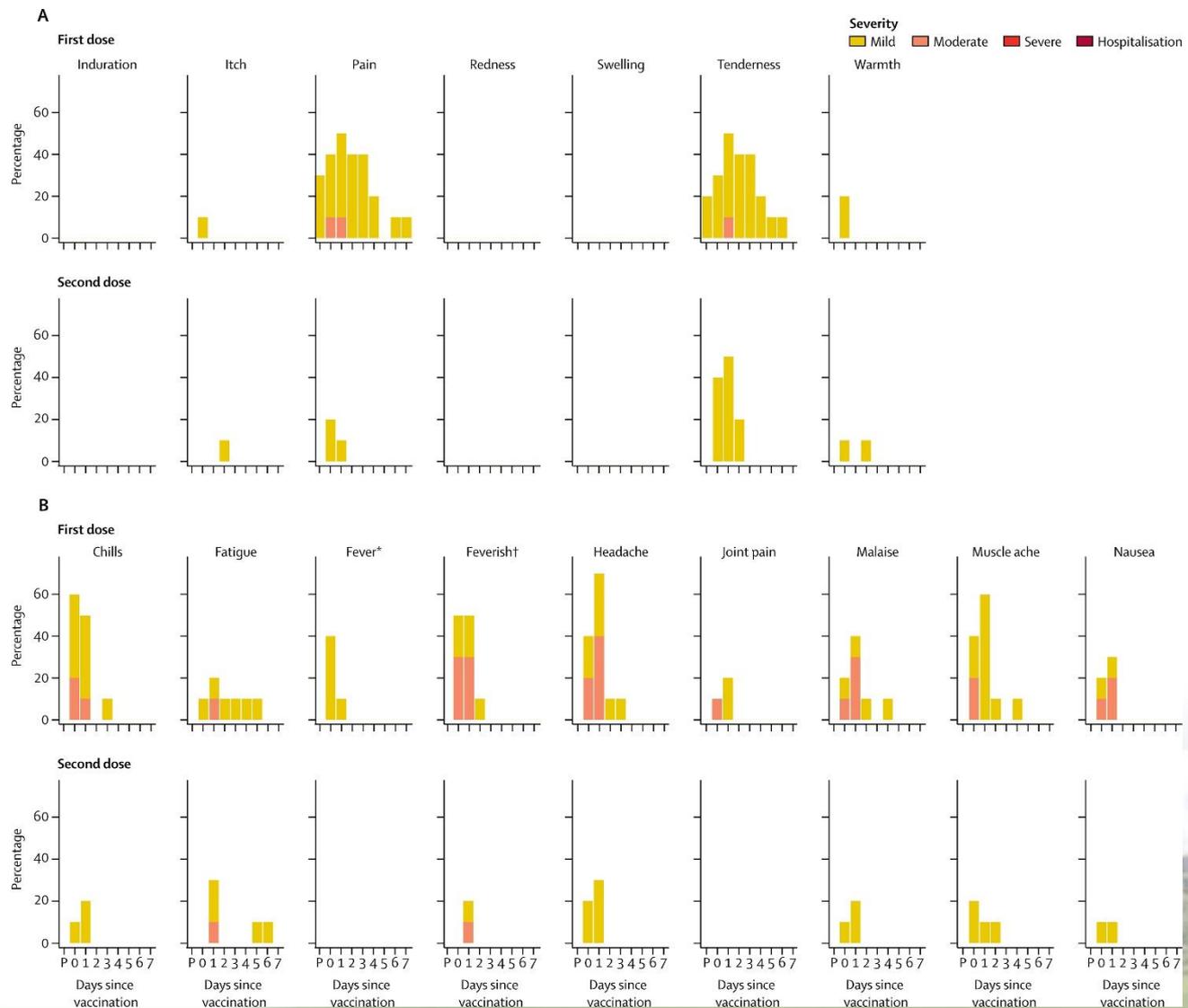


ChAdOx Platform – Human Clinical Testing



Safety Data

Commercial Developer:
AstraZeneca



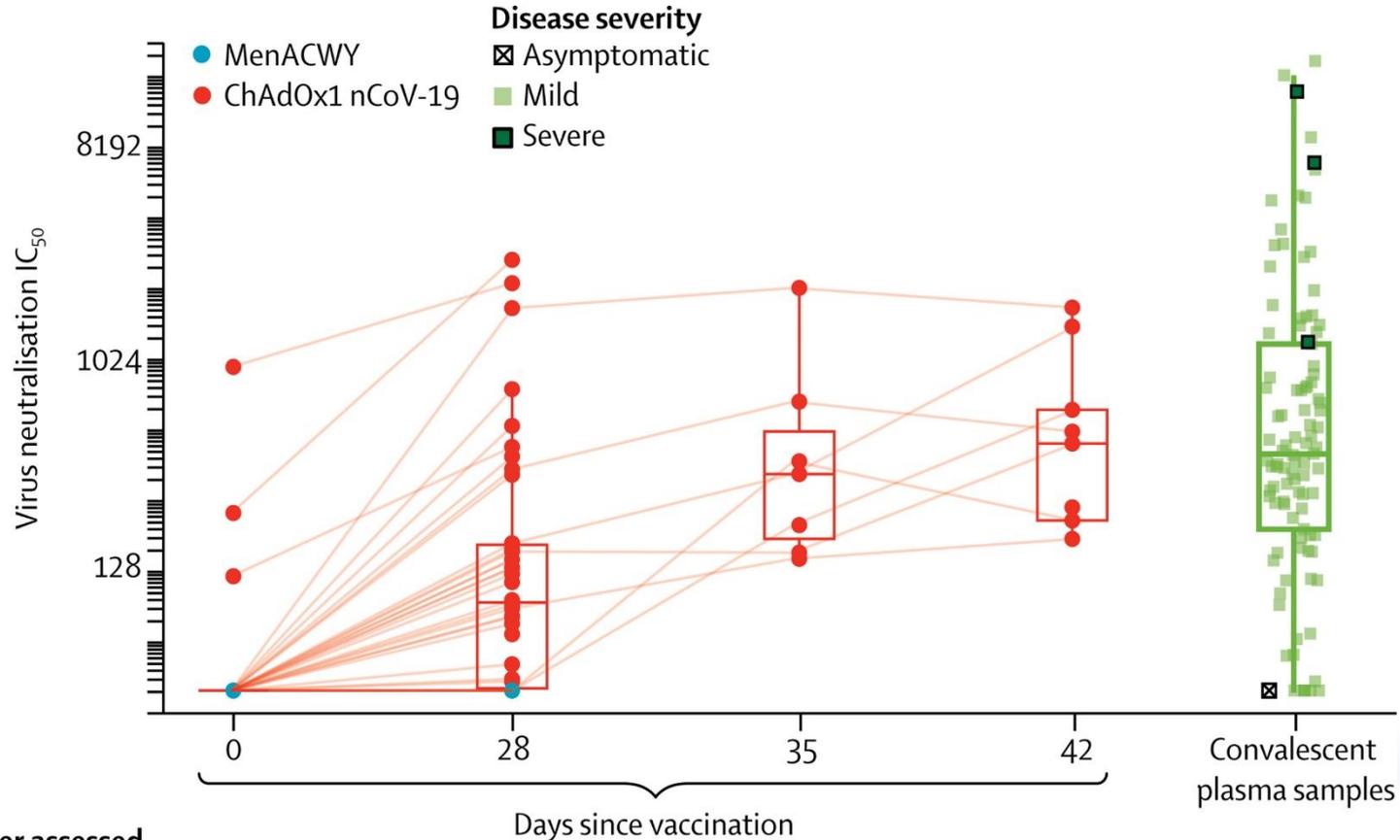
Folegatti et al. 2020.
The Lancet DOI: (10.1016/S0140-6736(20)31604-4)



ChAdOx Platform – Human Clinical Testing



Need for **2 doses** to achieve consistent seroconversion (based on **virus neutralization**)



	Number assessed			
ChAdOx1 nCoV-19	39	38	10	9
MenACWY	30	30	0	0

Folegatti et al. 2020
The Lancet DOI: (10.1016/S0140-6736(20)31604-4)



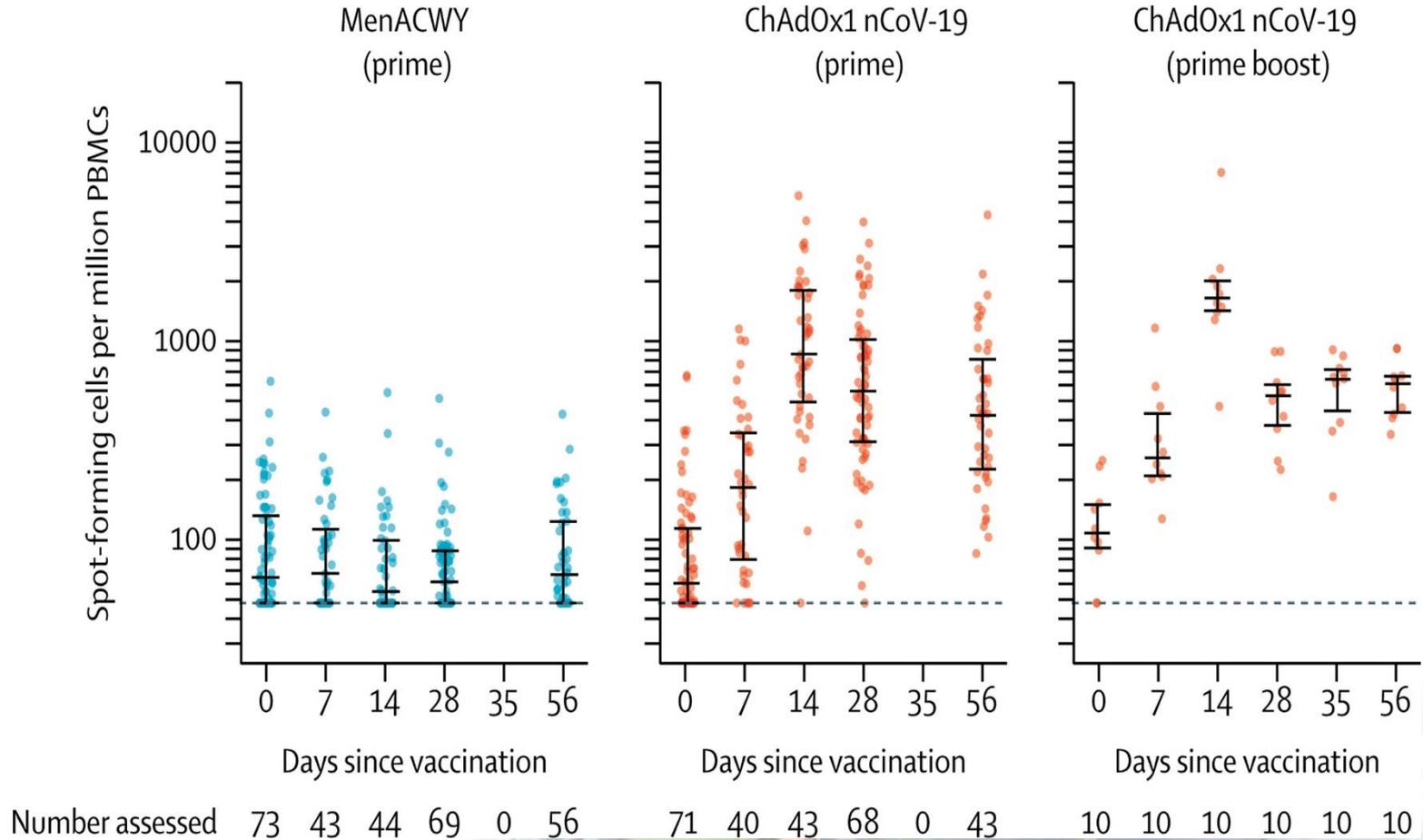


ChAdOx Platform – Human Clinical Testing



Potent cell-mediated immunity

(already after single dose)



Folegatti et al. 2020

The Lancet DOI: (10.1016/S0140-6736(20)31604-4)



Summary: Adenovirus-vectored Vaccines



- Potent immunogenicity after single doses of vaccine seen for Ad5 and Ad26-vectored candidates given at very high dose levels, ChAdOx seems to require two doses to get consistent seroconversion
- Balanced immune responses shown
- Potent virus neutralization shown
- Animal efficacy data not conclusive – mostly just reduction in viral load shown
- Cause of Adverse Reactions that resulted in pauses in clinical trial of ChAdOx?
- Durability of immunity?
- Adverse reactions and exclusion criteria?
- Efficacy of Russia's prime-boost approach with Ad26/Ad5 combination?





Clinical Endpoints – Phase III Trials



Developer	Participants	Definition of efficacy	Threshold of cases to determine efficacy	Platform	Storage Temperature
Moderna mRNA-1273	30,000	Prevention of cases a minimum of 2 weeks after 2 nd dose	151 (60% VE) Interim analysis: 53 cases (73%) and 106 cases	mRNA	-20°C
Pfizer	44,000	Prevention of Cases a minimum of one week after 2 nd dose	164 (60% VE) Interim analysis: 32 cases (77%) and 2 more points	mRNA	-70°C
AstraZeneca AZD1222	30,000	Prevention of cases a minimum of 15 days after 2 nd dose	150 (60% VE) Interim analysis: 75 cases (75%)	chAdOx	2-8°C ?
Johnson & Johnson	60,000?	?	?	Ad26	xx°C



Q&A

Save the Date! HHP 7th Annual Membership Meeting

- Saturday, November 7, 2020
 - 8:00 a.m. to 12:30 p.m.
- Physician Planning Committee
- Virtual meeting
- Community giveback project
 - Blood Bank of Hawai'i
 - Hawai'i Food Bank
 - Aloha United Way
 - Child & Family Services
- Details & updates forthcoming:
 - HHP website under “For Providers/Events Calendar”
 - HPH eConnect, “Hawai'i Health Partners” channel
 - Emailed via Info@hawaiihealthpartners.org

Thank you!

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