In the Age of Omicron and Beyond: Deploying Effective Shields and Swords to Protect and Defend the Hybrid Workplace

David Seftel, M.D., MBA (Harvard)

Track Physician: Golden Gate Fields, Berkeley, California
CEO and CMO: Enable Biosciences Clinical Reference Laboratory, South San Francisco, CA

Agenda

- Introduction
- Swords and Shields for optimal occupational health and safety
  - Sword – repurposed therapeutics – the Fluvoxamine story
  - Shield – vaccine effectiveness testing for safer, smarter more secure workplaces
- What we can do together
- New Rule: Occupational health is public health amplified and individualized for all

About

Education: Johannesburg, Harvard, Penn State, Loyola, UCSF

PI @ NIH: NIAID, NIDDK

NIH Immunololgy grant section reviewer

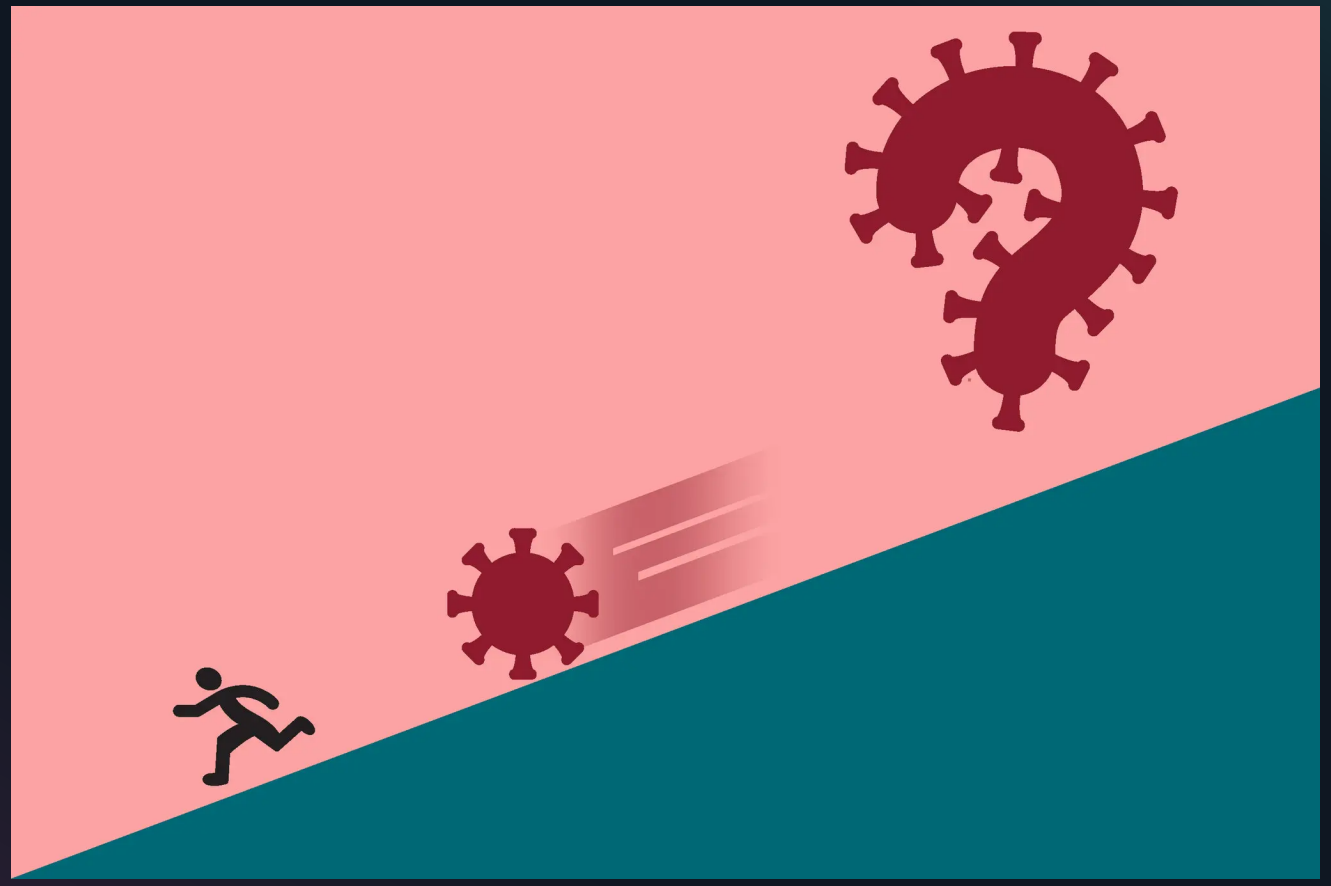
CEO: Enable Biosciences, clinical reference lab, South San Francisco, antibody detection specialty

Co-Investigator, Stanford Pediatric Endocrinology

Medical Director at Golden Gate Fields Occupational Urgent Care Clinic (16+yrs)

In the Age of Omicron

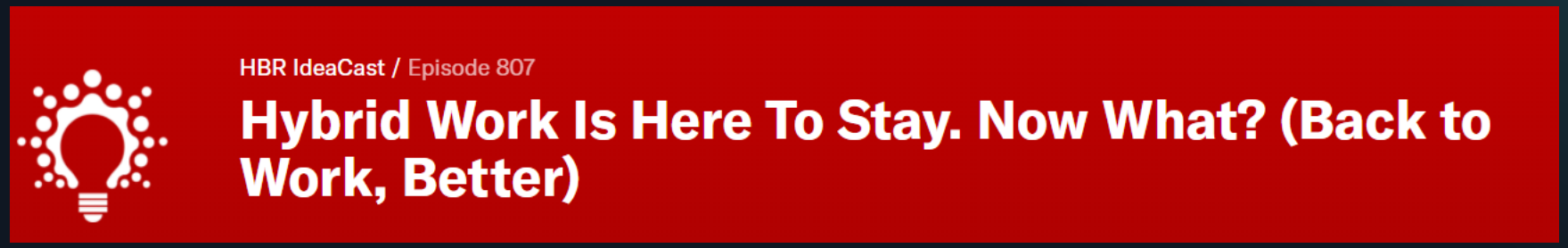
Uncertainty is the enemy

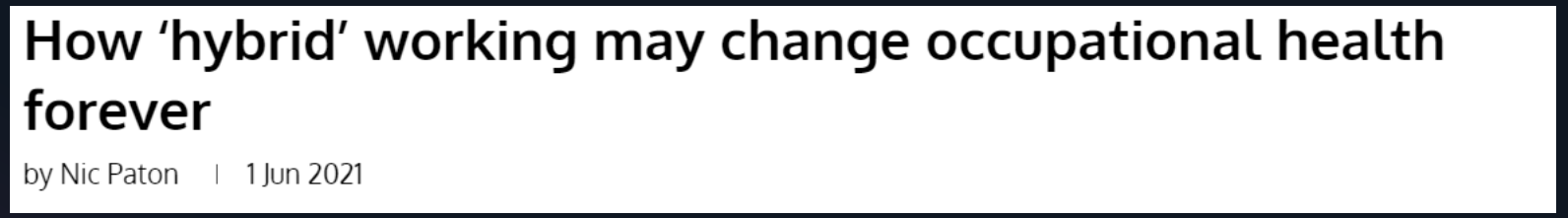


Vigilance, visibility, insight and responsiveness are essential

Graphic courtesy of NYTimes

Occupational Health Undergoes Dramatic Metamorphosis





Traditional Workplace is now a Warplace

- Inadequate ventilation is huge driver of infection
- CDC air exchange targets not met, or meetable without billions for retrofitting most buildings
- Without enforceable vaccine mandates, employee vaccination status invisibility creates considerable anxiety and risk
- Employee vaccination protection status uncertainty risks the health of all, but especially immunocompromised

Home Workplace can be Hellplace

Household Transmission of Severe Acute Respiratory Syndrome Coronavirus 2 in the United States: Living Density, Viral Load, and Disproportionate Impact on Communities of Color

FREE

Carla Cerami, Zachary R Popkin-Hall, Tyler Rapp, Kathleen Tompkins, Haoming Zhang, Meredith S Muller, Christopher Basham, Maureen Whittelsey, Srijana B Chhetri, Judy Smith ... Show more

Clinical Infectious Diseases, ciab701, https://doi.org/10.1093/cid/ciab701
Published: 12 August 2021 **Article history** ▾

"Household transmission really is the main place where most people are getting COVID," Lin says. "It's spreading from their family and friends, from people who are in their bubble and who they feel safe with.

"Household crowding in the context of high-inoculum infections may amplify the spread of COVID-19, potentially contributing to disproportionate impact on communities of color"

Original Investigation ONLINE FIRST FREE

October 8, 2021

Incidence Rates, Household Infection Risk, and Clinical Characteristics of SARS-CoV-2 Infection Among Children and Adults in Utah and New York City, New York

Fatimah S. Dawood, MD[1]; Christina A. Porucznik, PhD, MSPH[2]; Vic Veguilla, DrPH[1]; et al

» Author Affiliations | Article Information

JAMA Pediatr. Published online October 8, 2021. doi:10.1001/jamapediatrics.2021.4217

Immunocompromised are an occupational health challenge

Omicron-inspiring multi-mutation incubators

SARS-CoV-2 spike evolves during persistent infection to resist common antibodies

Intra-host evolution foreshadows mutations in circulating spike variants

Cell

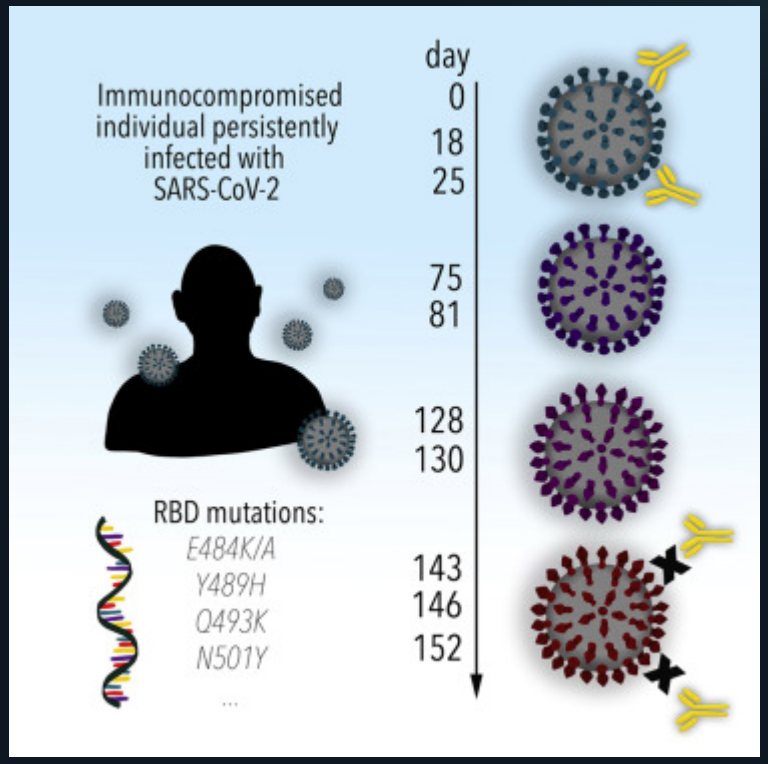
Volume 184, Issue 10, 13 May 2021, Pages 2605-2617.e18

CellPress

Article

SARS-CoV-2 evolution in an immunocompromised host reveals shared neutralization escape mechanisms

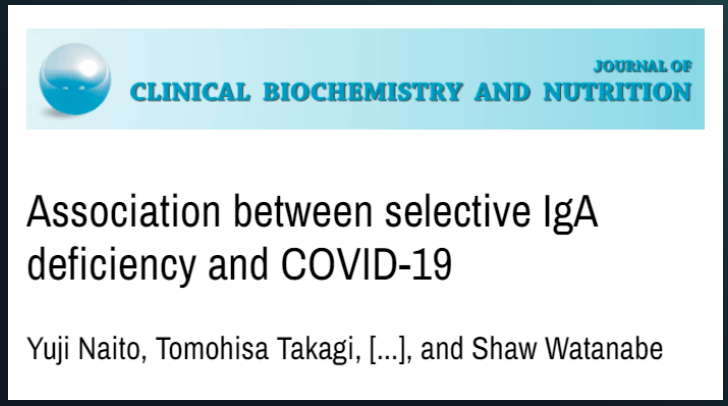
Sarah A. Clark [1, 6], Lars E. Clark [1, 6], Junhua Pan [1, 6], Adrian Coscia [1], Lindsay G.A. McKay [2], Sundaresh Shankar [1], Rebecca I. Johnson [2], Vesna Brusic [1], Manish C. Choudhary [3], James Regan [3], Jonathan Z. Li [3], Anthony Griffiths [2], Jonathan Abraham [1, 3, 4, 5, 7]



https://www.sciencedirect.com/science/article/pii/S009286742100355X

The Known and Unknown Immunocompromised

- Greater than "reported" 3% of the population, excludes those on chronic steroids
- Selective IgA deficiency incidence varies from 1:143 to 1:3000 in the US, higher death rates



Limited Swords

Figure 1. Therapeutic Management of NonHospitalized Adults With COVID-19

All outpatients with COVID-19 who enter the health care system should have in-person or telehealth follow-up visits. Symptomatic treatments, including hydration, antipyretics, analgesics, and antitussives, can be initiated as needed.

Patients should be counseled about symptoms that warrant re-evaluation by a health care provider (e.g., new onset dyspnea, worsening dyspnea [particularly dyspnea that occurs while the patient is resting or that interferes with daily activities], mental status changes). Home resources should be assessed before patients are discharged from a clinic, urgent care center, ED, or hospital; outpatients should have access to housing, proper nutrition, a caregiver, and a device that is suitable for telehealth. If patients are discharged while they are still receiving oxygen supplementation, they should receive oximetry monitoring and close follow-up soon after discharge.

PATIENT DISPOSITION	PANEL'S RECOMMENDATIONS
Not Requiring Hospitalization or Supplemental Oxygen, As Determined by a Health Care Provider During an ED, In-Person, or Telehealth Visit	Anti-SARS-CoV-2 mAb products are recommended for outpatients with mild to moderate COVID-19 who are at high risk of disease progression, as defined by the EUA criteria (treatments are listed in alphabetical order, and they may change based on circulating variants):[a] • **Bamlanivimab plus etesevimab**; *or* • **Casirivimab plus imdevimab**; *or* • **Sotrovimab** The Panel **recommends against** the use of **dexamethasone** or **other systemic glucocorticoids** in the absence of another indication **(AIII)**.[b]
Discharged From Hospital Inpatient Setting in Stable Condition and Does Not Require Supplemental Oxygen	The Panel **recommends against** continuing the use of **remdesivir (AIIa)**, **dexamethasone (AIIa)**, or **baricitinib (AIIa)** after hospital discharge.
Discharged From Hospital Inpatient Setting and Requires Supplemental Oxygen *For those who are stable enough for discharge but who still require oxygen*[c]	There is insufficient evidence to recommend either for or against the continued use of remdesivir, dexamethasone, and/or baricitinib. Review the text below when considering the use of any of these agents after hospital discharge.
Discharged From ED Despite New or Increasing Need for Supplemental Oxygen *When hospital resources are limited, inpatient admission is not possible, and close follow-up is ensured*[d]	The Panel recommends using **dexamethasone** 6 mg PO once daily for the duration of supplemental oxygen (dexamethasone use **should not** exceed 10 days) with careful monitoring for AEs **(BIII)**. There is insufficient evidence to recommend either for or against the use of remdesivir. When considering the use of remdesivir, review the text below for more information. The Panel **recommends against** the use of **baricitinib** in this setting, except in a clinical trial **(AIII)**.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Rating of Evidence: I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

[a] In laboratory studies, some CDC SARS-CoV-2 VOC, VBM, or VOI that harbor certain mutations have reduced susceptibility to certain agents. However, the impact of these mutations on a patient's clinical response varies, as do the proportions of these variants in different geographic regions. See Anti-SARS-CoV-2 Monoclonal Antibodies for more information. Updates on the distribution of bamlanivimab and etesevimab are available on the HHS Bamlanivimab/Etesevimab website.
[b] There is currently a lack of safety and efficacy data on the use of these agents in outpatients with COVID-19; using systemic glucocorticoids in this setting may cause harm.

...through telehealth, visiting nurse services, or in-person clinic visits.
..., it may be necessary to discharge an adult patient and provide an advanced ...receiving oxygen at home for the first time or are increasing their baseline ...g nurse services, telehealth, or in-person clinic visits.
...ion; ED = emergency department; EUA = Emergency Use Authorization; HHS = ...he Panel = the COVID-19 Treatment Guidelines Panel; PO = orally; VBM = ...rest

Therapeutic Management of Hospitalized Adults With COVID-19

Last Updated: August 25, 2021

Figure 2. Therapeutic Management of Hospitalized Adults With COVID-19 Based on Disease Severity

DISEASE SEVERITY	PANEL'S RECOMMENDATIONS
Hospitalized but Does Not Require Supplemental Oxygen	The Panel **recommends against** the use of **dexamethasone (AIIa)** or **other corticosteroids (AIII)**.[a] There is insufficient evidence to recommend either for or against the routine use of remdesivir. For patients at high risk of disease progression, remdesivir may be appropriate.
Hospitalized and Requires Supplemental Oxygen	Use one of the following options: • **Remdesivir**[b] (e.g., for patients who require minimal supplemental oxygen) **(BIIa)** • **Dexamethasone plus remdesivir**[b] (e.g., for patients who require increasing amounts of supplemental oxygen) **(BIII)** • **Dexamethasone** (when combination with remdesivir cannot be used or is not available) **(BI)**
Hospitalized and Requires Oxygen Delivery Through a High-Flow Device or Noninvasive Ventilation	Use one of the following options: • **Dexamethasone (AI)** • **Dexamethasone plus remdesivir**[b] **(BIII)** For recently hospitalized[c] patients with rapidly increasing oxygen needs and systemic inflammation: • Add either **baricitinib (BIIa)** or **IV tocilizumab (BIIa)** to one of the two options above[d] • If neither baricitinib nor IV tocilizumab is available or feasible to use, **tofacitinib** can be used instead of baricitinib **(BIIa)** or **IV sarilumab** can be used instead of IV tocilizumab **(BIIa)**.
Hospitalized and Requires IMV or ECMO	• **Dexamethasone (AI)** For patients who are within 24 hours of admission to the ICU: • **Dexamethasone plus IV tocilizumab (BIIa)** • If IV tocilizumab is not available or not feasible to use, **IV sarilumab** can be used **(BIIa)**.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Rating of Evidence: I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

[a] Corticosteroids prescribed for an underlying condition should be continued.
[b] If patients progress to requiring high-flow oxygen, noninvasive ventilation, mechanical ventilation, or ECMO, complete remdesivir course.
[c] For example, within 3 days of hospital admission.
[d] Drugs are listed alphabetically and not in order of preference. As there are no studies directly comparing baricitinib and tocilizumab for treatment of COVID-19, there is insufficient evidence to recommend one drug over the other. Treatment decisions should be determined by local guidance, drug availability, and patient comorbidities.

Key: ECMO = extracorporeal membrane oxygenation; ICU = intensive care unit; IMV = invasive mechanical ventilation; IV = intravenous; the Panel = the COVID-19 Treatment Guidelines Panel; PO = orally

NIH | COVID-19 Treatment Guidelines

https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/clinical-management-summary/

Vaccine vs Variant Vulnerability Variability Implies

- You can't fight a battle with just a shield. Must have a sword

- We must have effective, inexpensive therapies that are easy to manufacture, distribute and administer

Monitoring for Vaccine Escape Vital

Neutralizing antibody performance is the most important surrogate measure of clinical vaccine effectiveness, providing visibility into threshold of protection

Vaccine breakthrough (failure) should be closely monitored

Ramp up genomic sequencing for all positives, but especially for vaccinated cases with breakthrough infection

About Fluvoxamine

SSRI antidepressant
40 year safety history
28 years FDA approved
>10M people have used
12 manufacturers worldwide
Oral administration
No documented overdose deaths
$10 for 14-day course of treatment

University of Washington at St. Loius

Lenze Randomized Controlled Trial

- Published November 12, 2020 in JAMA
- JAMA Editors praised quality of the study methodology
- Chosen from > 10,000 COVID submissions

JAMA Network **November 12, 2020 Flv Phase 2 RCT** **100% SUCCESS RATE!**

QUESTION Does fluvoxamine, a selective serotonin reuptake inhibitor and σ-1 receptor agonist, prevent clinical deterioration in outpatients with acute coronavirus disease 2019 (COVID-19)?

CONCLUSION In this preliminary trial, outpatients with symptomatic COVID-19 treated with fluvoxamine, vs placebo, had a lower likelihood of clinical deterioration over 15 days; however, determination of clinical efficacy requires larger trials with more definitive outcome measures.

POPULATION

109 Women
43 Men

Adults with symptomatic, confirmed SARS-CoV-2 infection and O_2 ≥92%

Mean age: 46 years

LOCATIONS

Remote contactless trial in St Louis metropolitan area (Missouri and Illinois)

INTERVENTION

80
Fluvoxamine
50 mg, day 1
100 mg, 2 times daily for 2 days
100 mg, 3 times daily through day 15

72
Placebo
Equivalent dosing

(Study materials left at quarantined patients' homes)

PRIMARY OUTCOME

Clinical deterioration within 15 days: shortness of breath or pneumonia and O_2 <92% or supplemental oxygen

FINDINGS

Patients with clinical detorioration within 15 days

The between-group difference was significant:

8.7% (95% CI, 1.8% to 16.4%); *P* = .009

However, small sample size and short follow-up limit determination of efficacy

Lenze EJ, Mattar C, Zorumski CF, et al. Fluvoxamine vs placebo and clinical deterioration in outpatients with symptomatic COVID-19: a randomized clinical trial. *JAMA*. Published online November 12, 2020. doi:10.1001/jama.2020.22760

One week later...

massive COVID outbreak @ Golden Gate Fields Racetrack in Berkeley, CA

Context:

Saw FLV study in JAMA week earlier

Determined benefit>>risk

Offered FLV to all affected staff


HEALTH
BUILDING A BETTER BAY AREA
RACETRACK COVID-19 OUTBREAK
BERKELEY
abc 7
0:11 / 1:36
CC

CORONAVIRUS

More than 200 racetrack workers at Golden Gate Fields infected with COVID-19, Berkeley officials say

By Leslie Brinkley

Saturday, November 21, 2020

EMBED <> MORE VIDEOS

The track has suspended all live racing through the end of November.

BERKELEY, Calif. (KGO) -- COVID-19 cases in Berkeley are soaring, much of the sudden spike attributable to what appears to be a major outbreak among workers at Golden Gate Fields horse racing track, which is now shut down.

More than 200 people living or working at the racetrack have tested positive, an official told ABC7 Saturday morning. This is accounts for half of the 400 that live there.

Our study: N=113 (p=.0049)

	FLV	No treatment
Number tested	65	48
Hospitalization/death rate	0%	12.5%
Long haulers	0%	25%

Table 1. Demographics and Outcomes in Prospective COVID-19 Cohort.

Group	Fluvoxamine	No Therapy	P-value [a]
N	65	48	
Men	50 (59%)	35 (41%)	.66
Age, years	44 ±15	43 ±15	.74
Age >65 years	5 (7%)	2 (4%)	
Age 50-64 years	17 (26%)	15 (31%)	
Race/Ethnicity			.001
Latino	61 (94%)	34 (71%)	
White, non-Hispanic	3 (5%)	13 (27%)	
African American	1 (1.5%)	0 (0%)	
Asian	0 (0%)	1 (2%)	
Chronic comorbidity	16 (25%)	18 (38%)	.15
Diabetes	11 (17%)	4 (8%)	
Hypertension	11 (17%)	17 (35%)	
Lung Disease	2 (3%)	1 (2%)	
Days for PCR confirmation	3.7 ±1.3	3.4 ±1.4	.25
Disease Status at time of testing			.064
Asymptomatic	25 (38%)	28 (58%)	
Mild	33 (37%)	24 (19%)	
Moderate/Severe	16 (25%)	11 (23%)	
Respiratory Rate, Day 1	17.7 ±2.9	17.7 ±3.4	.95
Respiratory Rate, Day 7*	12.9 ±1.6	15.1 ±4.1	.001
Hospitalized within 14 days	0	6	.005
ICU care and/or Death	0	2	--

Values are N (%) or mean (±SD). Abbreviation: ICU = intensive care unit.

[a] P-values are by Fisher's exact test for categorical variables and independent *t*-test for continuous variables.

[b] Six persons hospitalized had their day 1 value carried forward.

FLV cohort, although not random (patients got to choose with the healthier patients avoiding the drug as unnecessary), was objectively sicker and should have had worse results than the no treatment group.

The only attribute that might have given an advantage to the FLV group is that hypertension was lower in the FLV group. However, hypertension has an unclear link to hospitalization rate (older people have higher rates of hypertension and age is the big driver of hospitalization). Also, the hypertension was controlled with drugs so that their blood pressure was normal.

Therefore the FLV group should have fared **far worse** especially due to 27 more Latinos who have a 2.4x hospitalization rate once infected.

Our real-world evidence (RWE) trial validated the Lenze RCT

- 0% hospitalization in those who chose the drug (vs. 12.5% no treatment)
- Treatment group accepted all who opted in, regardless of disease stage
- Respiratory distress was rapidly reversed in all patients in the treatment cohort within days of administration of the drug
- Improved cognitive abilities
  Cohort was primarily Latino so was more challenging than the Lenze cohort (2.4x higher hospitalization rate once infected based on recent CDC data)

Of the 12.5% hospitalized on no treatment, one died, two were in ICU

The 15 long hauler symptoms assessed

1. persistent body aches, muscle or joint pain
2. brain fog, difficulty concentrating, or memory challenges
3. persistent, intermittent non-productive cough
4. fatigue
5. Headache
6. intermittent heart palpitations/tachycardia
7. insomnia
8. persistent anxiety
9. dizziness
10. diarrhea
11. elevated temperature
12. episodic chest tightness, pressure, or pain
13. inability to exercise
14. chills or sweats
15. shortness of breath or difficulty breathing

12 of the 48 non-fluvoxamine patients (25%) reported 5 or more symptoms consistent with COVID long-hauler syndrome concordant with the most commonly observed group outlined above vs. 0% in the treatment group

I could directly assess adverse events over time

Unlike in the RCT (which was remote and relied on self-reported adverse events and which did not report how those adverse events resolved over time), I had direct contact + observation of *every* patient

He observed that all 65 FLV patients resolved any virus-related symptoms within ~3 days after taking the drug. After the study was written up, I took on another 12 with exactly the same results.

To date, I've never had a single hospitalization in patients who took fluvoxamine

Update: Omicron efficacy in South Africa

Nicolas Hoertel's JAMA Invited Commentary

Invited Commentary | Infectious Diseases

November 15, 2021

Do the Selective Serotonin Reuptake Inhibitor Antidepressants Fluoxetine and Fluvoxamine Reduce Mortality Among Patients With COVID-19?

Nicolas Hoertel, MD, MPH, PhD[1,2]

» Author Affiliations | Article Information

JAMA Netw Open. 2021;4(11):e2136510. doi:10.1001/jamanetworkopen.2021.36510

Nicolas Hoertel, MD, PhD, PhD in JAMA

"Both fluoxetine (which is on the World Health Organization's Model List of Essential Medicines and has the greatest in vitro inhibitory effect on the ASM-ceramide system among SSRIs) and fluvoxamine (which has shown very encouraging results in 3 clinical trials) should be prioritized in large-scale phase 3 clinical trials at different stages of the disease, either alone or in combination with other medications."

Why:

1. Original multicenter, retrospective, observational study involving patients who were hospitalized for COVID-19 in Paris, France, indicated that antidepressant use—particularly fluoxetine use—was associated with reduced risk of intubation or death.

2. Second, several preclinical studies support a substantial in vitro efficacy of different SSRI- and non-SSRI antidepressants—particularly fluoxetine—against SARS-CoV-2 with different host cells (eg, Vero E6, Calu-1, Calu-3, HEK293T-ACE2-TMPRSS2) and human lung epithelial cells as well as with different variants of the virus.

3. 3 clinical trials, including 2 randomized, placebo-controlled trials, found an association between the use of fluvoxamine for 10 to 15 days and a reduced risk of clinical deterioration among outpatients with COVID-19.
   - Lenze et al - double-blind, randomized, placebo-controlled trial involving 152 outpatients with COVID-19, patients who were treated with fluvoxamine had a significantly lower risk of clinical deterioration over 15 days of treatment than those who received a placebo.
   - Seftel and Boulware - prospective, real-world evidence study of 113 outpatients with COVID-19 – 12.5% vs 0 hospitalization for untreated group.

4. Results of the multicenter randomized placebo-controlled TOGETHER trial showed a significant and substantial reduction in risk of hospitalization or retention in a COVID-19 emergency setting due to COVID-19 associated with fluvoxamine use vs placebo in 1472 outpatients with COVID-19 who were at a high risk for developing severe complications.

https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2786140

Fluvoxamine interest rises

Association of Northern California

The Washington Post
Democracy Dies in Darkness

Science Space Animals Health

Health

What is fluvoxamine, the antidepressant drug that shows promise in treating covid-19?

Lenze and Seftel Studies Affirmed by Large Brazil Trial Sponsored by Stripe CEO Patrick Collison's Fast Grants and Rainwater Fund

Cheap, generic anti-depressant may reduce severe Covid-19 disease, study finds

By Maggie Fox, CNN

Updated 5:39 AM ET, Thu October 28, 2021

Dr. David Seftel

But there are few early treatment options for COVID. The handful of drugs that have been approved are for high risk patients and must be delivered intravenously, often in a hospital.

Dr. David Seftel: When I looked at this community, I said I know the numbers, I know the stats. There are gonna be deaths and there's gonna be disability unless I take action.

CBS News / CBS Evening News / CBS Mornings /

60 MINUTES

FINDING A POSSIBLE EARLY TREATMENT FOR COVID-19 IN A 40-YEAR-OLD ANTIDEPRESSANT

Sharyn Alfonsi reports on the unusual path fluvoxamine, a drug commonly used to treat obsessive-compulsive disorder, has had to becoming an early treatment candidate for COVID-19.

TOGETHER TRIAL – fluvoxamine slices severe disease

THE LANCET
Global Health

ARTICLES | ONLINE FIRST

Effect of early treatment with fluvoxamine on risk of emergency care and hospitalisation among patients with COVID-19: the TOGETHER randomised, platform clinical trial

Gilmar Reis, PhD • Eduardo Augusto dos Santos Moreira-Silva, PhD • Daniela Carla Medeiros Silva, PhD • Prof Lehana Thabane, PhD • Aline Cruz Milagres, RN • Thiago Santiago Ferreira, MD • et al. Show all authors • Show footnotes

https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(21)00448-4/fulltext

How well are our shields working?

Developing, validating and deploying longitudinal vaccine effectiveness testing

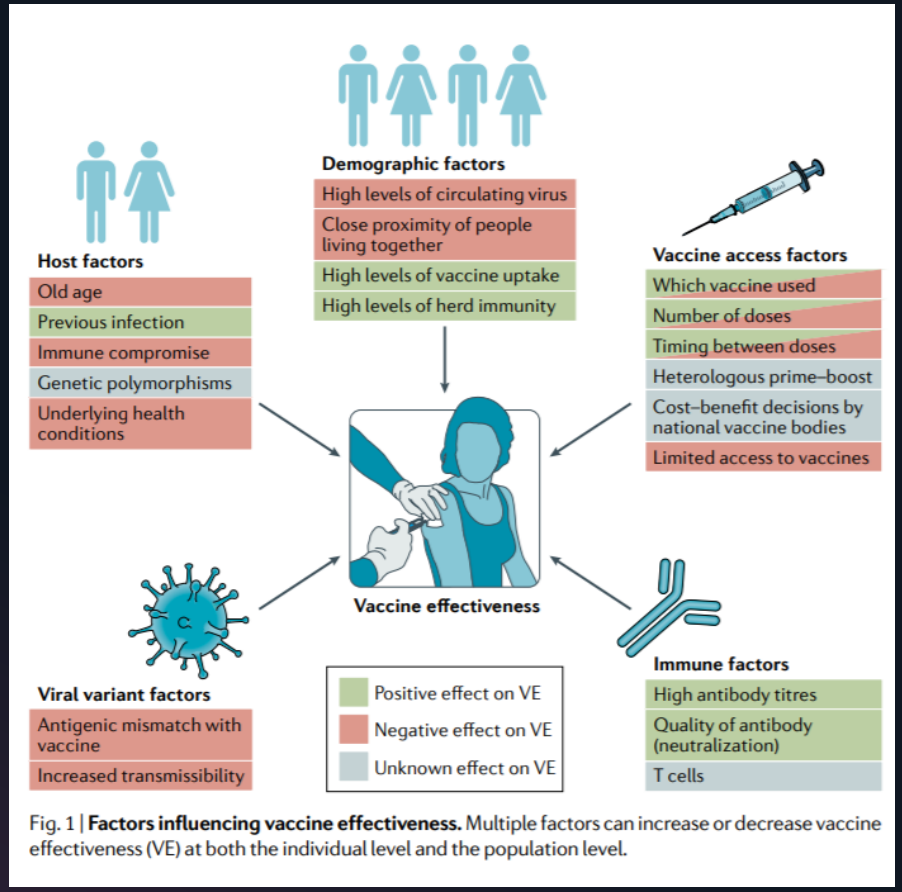


Fig. 1 | **Factors influencing vaccine effectiveness.** Multiple factors can increase or decrease vaccine effectiveness (VE) at both the individual level and the population level.

https://www.nature.com/articles/s41577-021-00592-1.pdf

ENABLE
BIOSCIENCES

Enabling accessible, accurate and actionable COVID vaccine effectiveness testing for all

Enabling safer, smarter homes, schools, workplaces and playspaces

Who: Enable is a NIH/NSF supported diagnostics company recognized for transformational next generation antibody detection technology and products

- Enable Biosciences ("Enable") is a 6-year-old San Francisco-based diagnostics company commercializing licensed and patented technology from legendary translational biochemist Prof. Carolyn Bertozzi at UC Berkeley and Stanford
- Enable develops immunoassays that are triple advantaged - ultrasensitive, highly specific and supportive of easier sample collection - to help diagnose diseases at their earliest stages using saliva, dried bloodspot or serum samples
- The company provides a wide range of services to blue-chip academic and commercial clients, including:
  - Clinical and research testing in its high complexity Federal and State certified CLIA laboratory in South San Francisco
  - Turnkey deployment of customized Hamilton Robotics ADAP Star test analyzers utilizing Enable reagents for high volume and specialty clinical laboratories outside of US
  - Customized web test-ordering portal and logistics system available under "white-label" (e.g. CalScope serosurvey project)
  - Custom rapid antibody assay development services with a 7-to-14-day turnaround

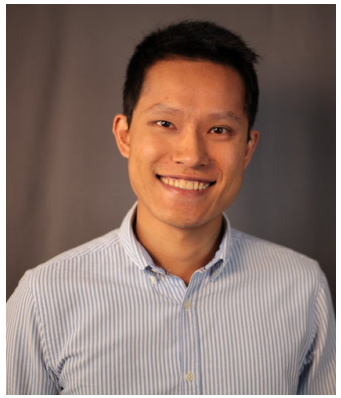
Leadership Team

David Seftel, MD, MBA
Chief Executive Officer, CMO
Harvard
President for Strategic Initiatives Harvard Business School Alumni (HBSANC)

Peter Robinson, PhD
Chief Operating Officer
UC Berkley/Stanford
Amgen Fellow@Stanford

Lynette Sawyer, DPH
Clinical Laboratory Director
UC Berkeley
30 years+ of clinical testing management

Carolyn Bertozzi, PhD
Chair of Scientific Advisory Board
Professor/Director, Stanford ChEM-H
Fellow of NAS, AAAS



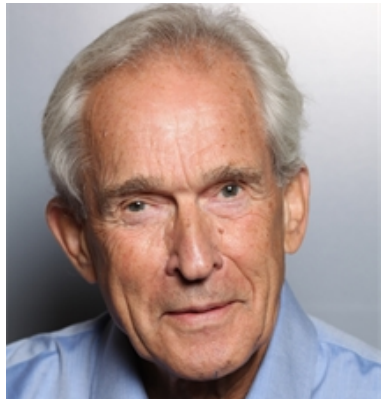
Jason Tsai, PhD
Chief Technology Officer
UC Berkley/Stanford
Gold Medalist @Chemistry Olympiad

Jerry Hurst
Clinical Supervisor
Former Chief Inspector of CLIA
40 years+ of clinical testing compliance and regulation

ENABLE BIOSCIENCES

Key Opinion Leading Collaborators And Clients

Darrell Wilson, MD
Former Chief of Stanford Pediatrics Endocrinology Department

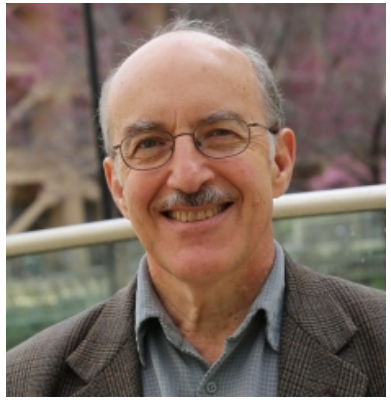


Ake Lernmark, MD/PhD
Director, Diabetes Unit, Lund University

David Maahs, MD
Chief of Stanford Pediatrics Endocrinology Department

CDC
Zoonotic Disease Division

Mark Pandori, PhD
Director of Nevada Public Health



Stephen Galli, MD
Former Chair of Stanford Pathology Department

Kari Nadeau, MD
Director of Stanford Sean Parker Allergy Center
Chief Innovation Officer, FARE

Carl Hansen, PhD
Chief, California Department of Public Health

Select Achievements and Awards

- 6 NIH/NIAID/NIDDK SBIR awards
- 4 NSF SBIR awards
- Judged best assay performance by the Immunology of Diabetes Society International Islet Autoantibody Standardization(IASP) workshop in both 2018 and 2020
- Stanford Diagnostics and Prognostics Accelerator Award (SPADA)
- Stanford SPARK / NIH Translational Medicine award
- American Association of Clinical Chemistry (AACC) award
- T1D Exchange and American Diabetes Association Global Diabetes Innovation Award
- Gates Foundation translational science grant via Stanford
- J&J award-winning JLABS incubator company
- Winner – Harvard Business School Northern California New Venture Competition

Stanford MEDICINE

Johnson & Johnson INNOVATION — JLABS —

HARVARD BUSINESS SCHOOL

SPARK AT STANFORD

Affiliations, Collaborators and Partners

Hospitals

- Schneider Childrens Hospital (Israel) since 2019
- Mayo Clinic – Multiple projects
- Royal Melbourne Hospital (Australia) since 2019

Type 1 Diabetes

- JDRF (Juvenile Diabetes Research Fund) – Multiple projects, including 47 State T1Detect home-collected sample screening in children
- Joslin Diabetes Center at Harvard - multiple projects
- Stanford Diabetes Immune Monitoring Core (DIMC)

Public Health

- Centers for Disease Control (CDC) – 4 contracts
- California Department of Public Health (CDPH) – 4 projects/contracts

Other

- J&J / Janssen Pharmaceuticals – wide range of services across several verticals
- Stanford Immunology – Prof. PJ Utz and colleagues
- Stanford Pediatric Allergy – Sean Parker Allergy Center – Prof's Kari Nadeau and Stephen Galli
- Hamilton Robotics – multiple US and international joint sales

The Royal Melbourne Hospital · Joslin Diabetes · JDRF · California Department of PublicHealth · CDC · CalScope

Contextual Updates

NYTimes

As concerns over omicron variant grow, experts say don't wait to get a booster

Experts are urging Americans to get vaccinated as soon as possible.

November 30, 2021 | 1 min read SAVE

Citing omicron variant, CDC says all adults should get COVID-19 booster

ADD TOPIC TO EMAIL ALERTS

The CDC has strengthened its recommendation for COVID-19 booster shots, saying all adults should get one, when eligible.

Rochelle P. Walensky

"The recent emergence of the omicron variant further emphasizes the importance of vaccination, boosters, and prevention efforts needed to protect against COVID-19," CDC Director **Rochelle P. Walensky, MD, MPH**, said in a statement. "Early data from South Africa suggest increased transmissibility of the omicron variant, and scientists in the United States and around the world are urgently examining vaccine effectiveness related to this variant."

Can communities and individuals be, and stay ahead of the curve with more accurate and actionable information on immunity and protection capability

Functional performance data on immunity can permit booster authorization on an individual basis that in turn optimally protects homes, schools **workplaces, the supply chain and enterprises**

Nike could run out of sneakers made in Vietnam as Covid crisis worsens, S&P Global warns

PUBLISHED MON, JUL 19 2021•9:52 AM EDT | UPDATED MON, JUL 19 2021•12:42 PM EDT

Lauren Thomas
@LAURENTHOMAS

SHARE

KEY POINTS

- Nike is at risk of running out of sneakers made in Vietnam as the Covid crisis worsens around the global, according to a new report.
- The warning comes after two of Nike's suppliers in Vietnam, Chang Shin Vietnam Co. and Pou Chen Corp., recently halted production due to a rapidly growing Covid outbreak in the region.
- A new analysis from Panjiva, a business line of S&P Global Market Intelligence, found Vietnam accounted for 49% of U.S. seaborne imports linked to Nike and its products in the second quarter of 2021.

Ad by

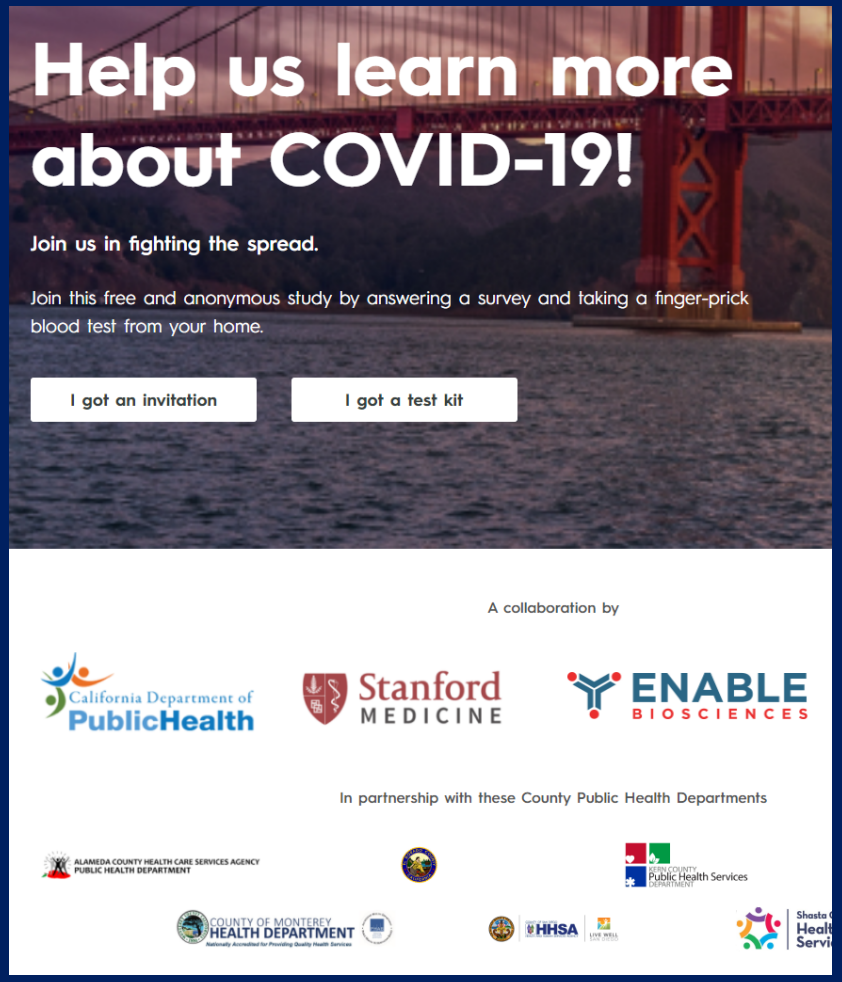
Report

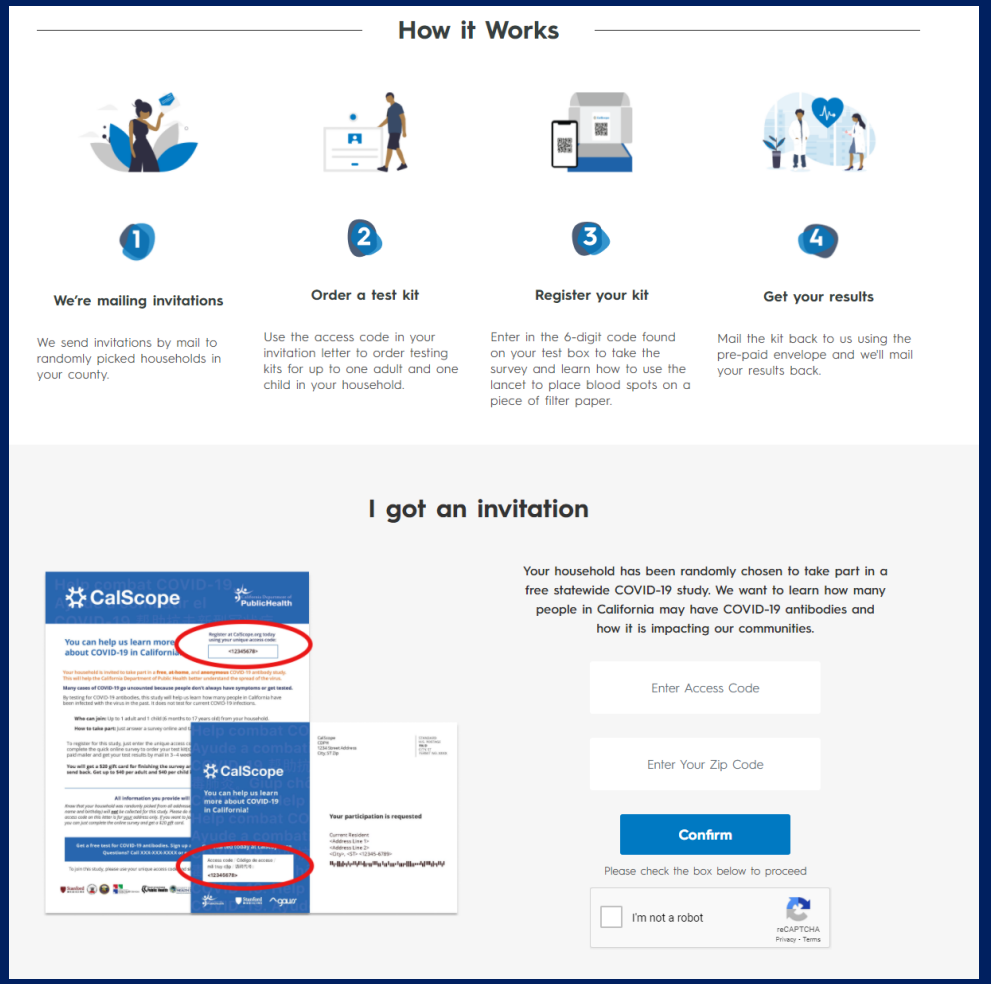
Ad cho

What ?

Enable is rolling out the California Department of Public Health's CDC-supported choice for remote-acquisition COVID vaccine effectiveness assessment via neutralization antibody testing

www.calscope.org





I got a test kit

Please enter the activation and zip code below.

Enter Activation Code

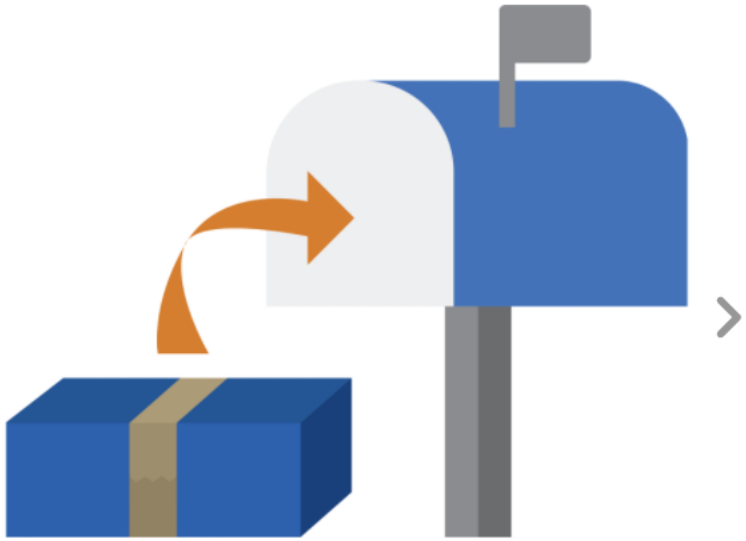
Enter Your Zip Code

Confirm

Please check the box below to proceed

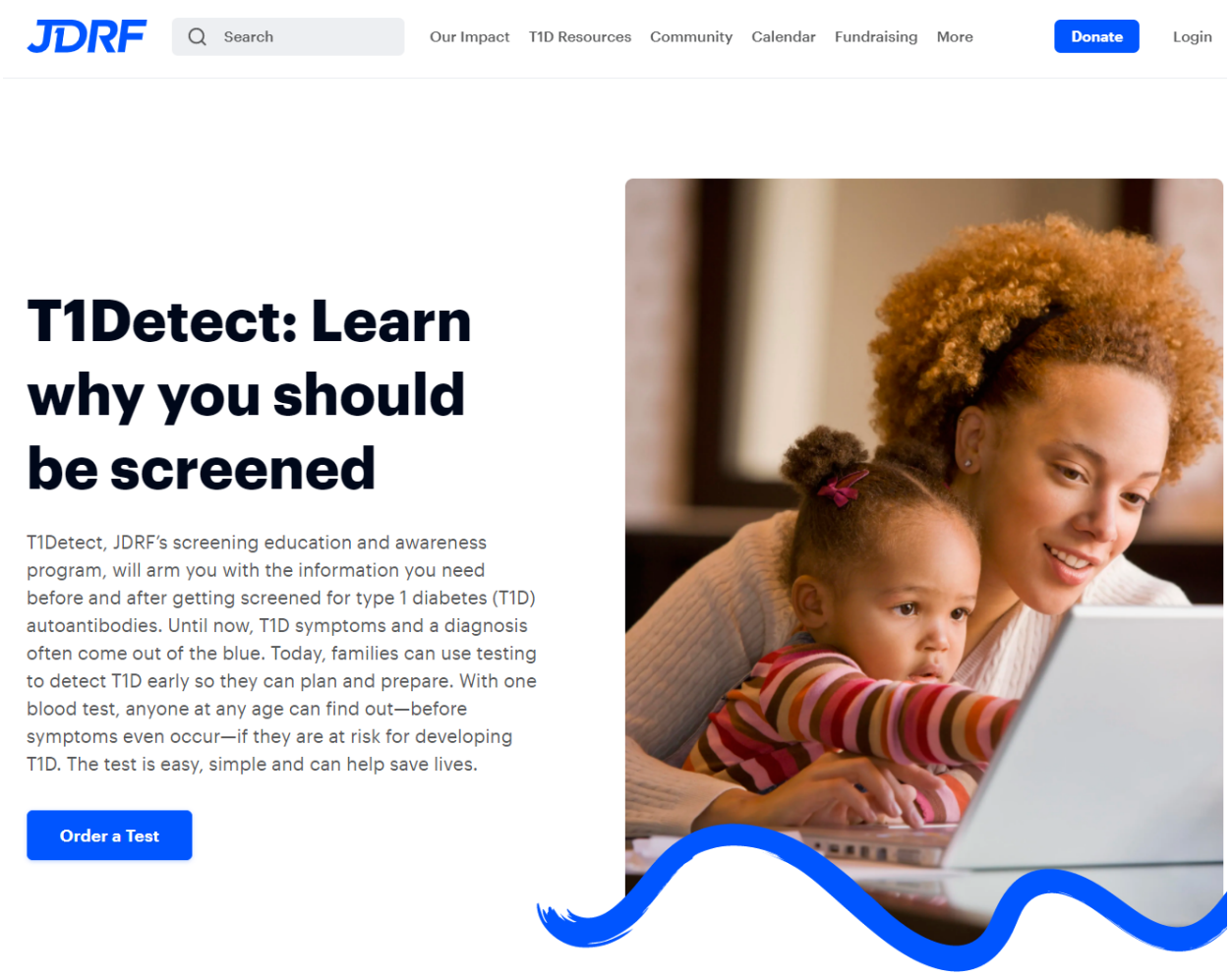
I'm not a robot

reCAPTCHA
Privacy - Terms



Login to your personal portal account for results

Not just COVID – another world first – T1Detect – a 47 state Type I diabetes detection program with the Juvenile Diabetes Research Fund (JDRF) https://www.jdrf.org/t1d-resources/t1detect/



Return to schools and the workplace with confidence

ADAP testing was selected by the State of California and funded by the CDC for triple testing in a State-wide initiative - total native infection induced, post vaccination and neutralizing antibody testing

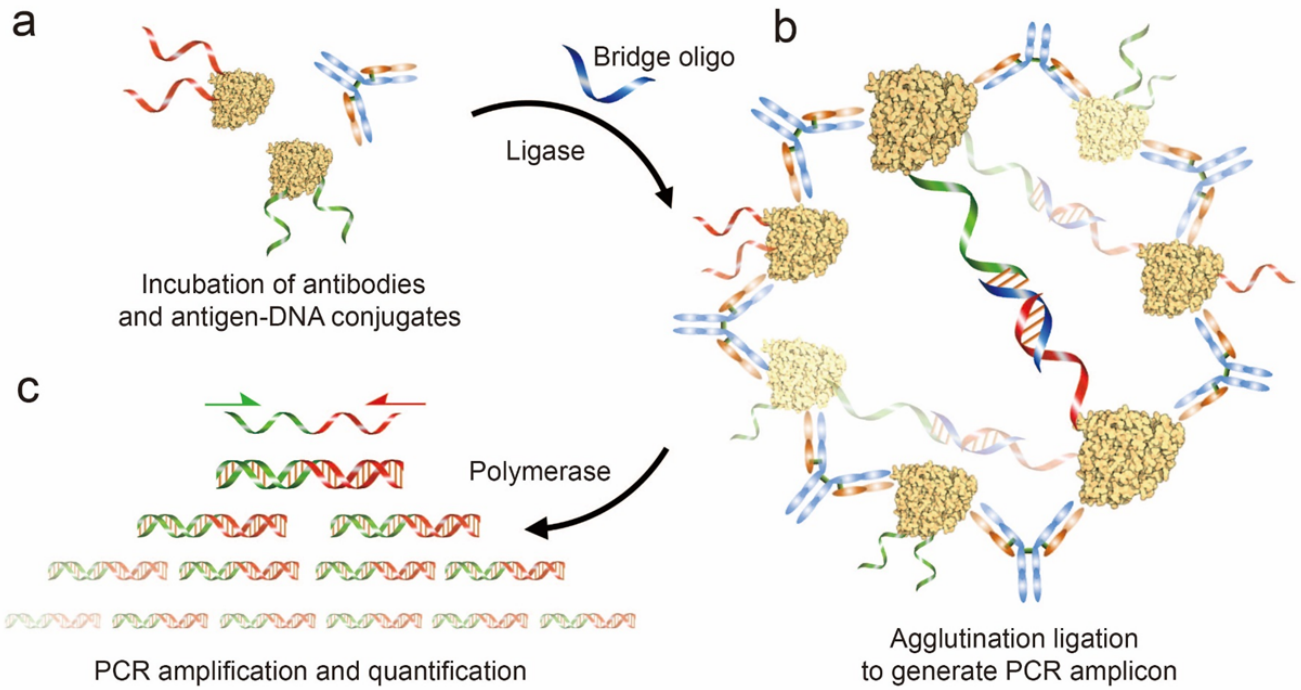
- Help overcome vaccine hesitancy with facts not fiction
- Test from home
- Test from schools
- Test at the office
- Better inform institutional workflows for maintaining the health and safety of individuals, students and employees

The Opportunity for Improved Institutional Health Security is Significant

1. Vaccine Proof-of-Function via antibody testing with quantification is now required to allow travel to certain countries such as Israel, more may follow.
2. Vaccine neutralizing capacity adds significant value.
3. Regular assessment for waning immunity can better guide vaccine booster timing and type
4. Real world vaccine effectiveness testing via reliable and accurate functional neutralization assays is increasingly important to individuals, public health officials and corporations:
   - Early detection of "vaccine escape" due to new variants
5. Assessing vaccine protection in people with varying degrees of immunocompromise – more than 10 million or 3.6% of US population have know immunocompromise and may need earlier boosters.

About Antibody Detection by Agglutination-PCR (ADAP) Technology

A breakthrough DNA-barcoding, solution-phase homogenous assay with zeptomolar sensitivity and ultra-specificity unlocks the amplification power of PCR for early antibody detection



ADAP advantages: strong technical merits

- Ultra-sensitivity **Up to 10,000x**
- Low sample consumption **1-2 µL**
- Highly multiplexable **18-plex or above**

ADAP advantages: wide applicability

- **Compatible with diverse sample types**
- Low reagent costs
- Common qPCR readout

ACS Cent Sci. 2,139-147 (2016) *PNAS 115, 1250-1255 (2018)*

J Allergy Clin Immunol 141, 1901-1904 (2018) *SLAS Technol.25(6): 545–552 (2020)* *Scientific Reports 10, 20188 (2020)* *PLoS One15, e0242049 (2020)*

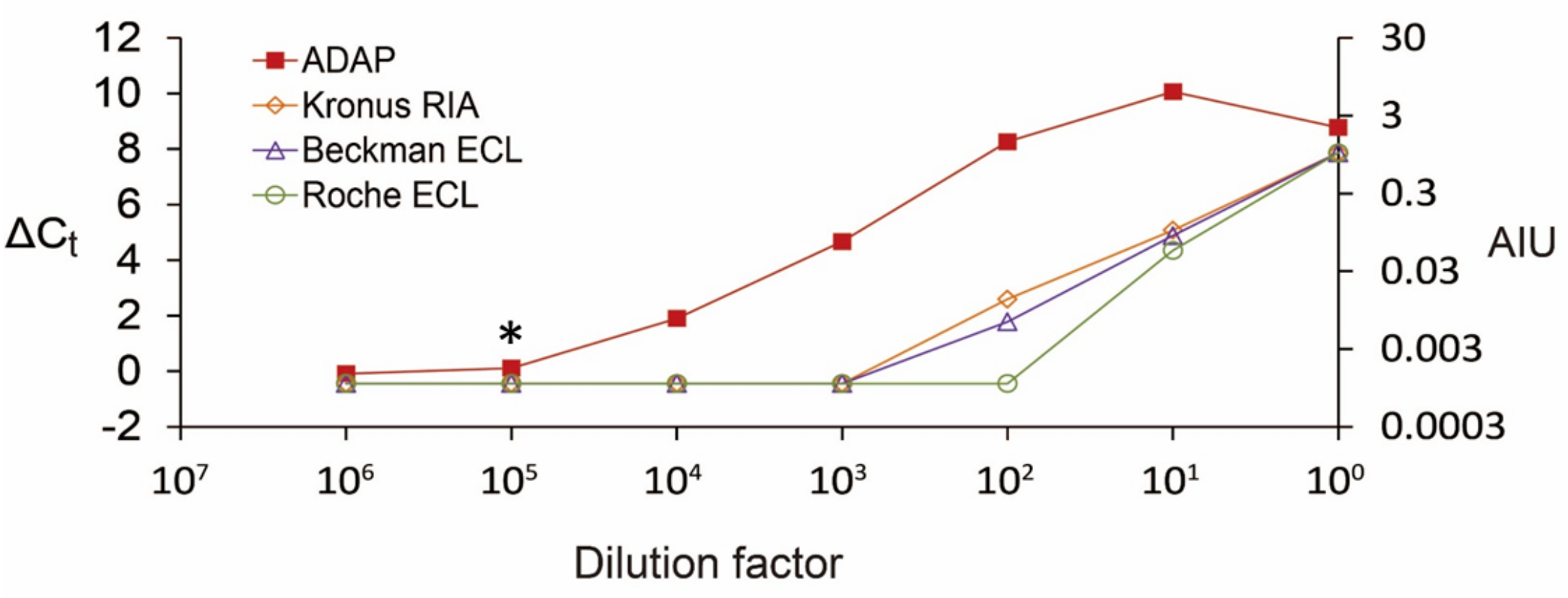
ENABLE BIOSCIENCES

Enable Biosciences: the Core ADAP Technology

Ultra-sensitivity **Up to 10,000x**

ADAP advantages: strong technical merits

Significantly outperforms other commercial assays (e.g. anti-thyroglobulin)



Enable Biosciences is a leader in highly accurate COVID-19 serological tests

Enable's unique at-home-collected COVID-19 antibody tests can answer key questions:

Multiplex Total Antibody Assay	
Are my antibodies from vaccination or past infection?	SLAS Technol.25(6): 545–552 (2020), Nature: Scientific Reports 10, 20188 (2020) Deployed for CDPH/CDC in CalScope
SARS-CoV-2 Single Variant Neutralizing Antibody Assay	
Am I immune? Did my vaccine work? Am I still immune over time?	medRxiv 2, 20105692 (2020) Blood, submitted, Developed and validated in-house at Enable, deployed for California Department of Public Health (CDPH) under CDC funding – CalScope
New Variant of Concern (VoC) Multiplex Neutralizing Antibody Assay	
Does the vaccine work to protect me against new strains? Do I need a booster vaccine shot? Will I need an updated vaccine to deal with variants?	Developed and validated with the CDPH, deployed for California Department of Public Health under CDC funding in the Calscope program

ENABLE BIOSCIENCES

Enable's unique neutralizing antibody relative performance test can accurately guide the assessment COVID vaccine effectiveness for all major variants of concern

The Problem

- Who is immune to COVID?
- Pfizer vaccine – some studies showed only 16% efficacy against infection after 6 months
- Vaccine protection is closer correlated with **neutralizing** antibodies versus total antibodies
- What populations are vulnerable and require boosters?

The Solution

- Enable offers both standard **and** neutralizing antibody titers to determine vaccine adoption and efficacy
- Determine what geographical regions require additional support for vaccine outreach
- Inform individuals of their post-vaccination risk for COVID
- Saliva or dried blood spot options for at-home testing

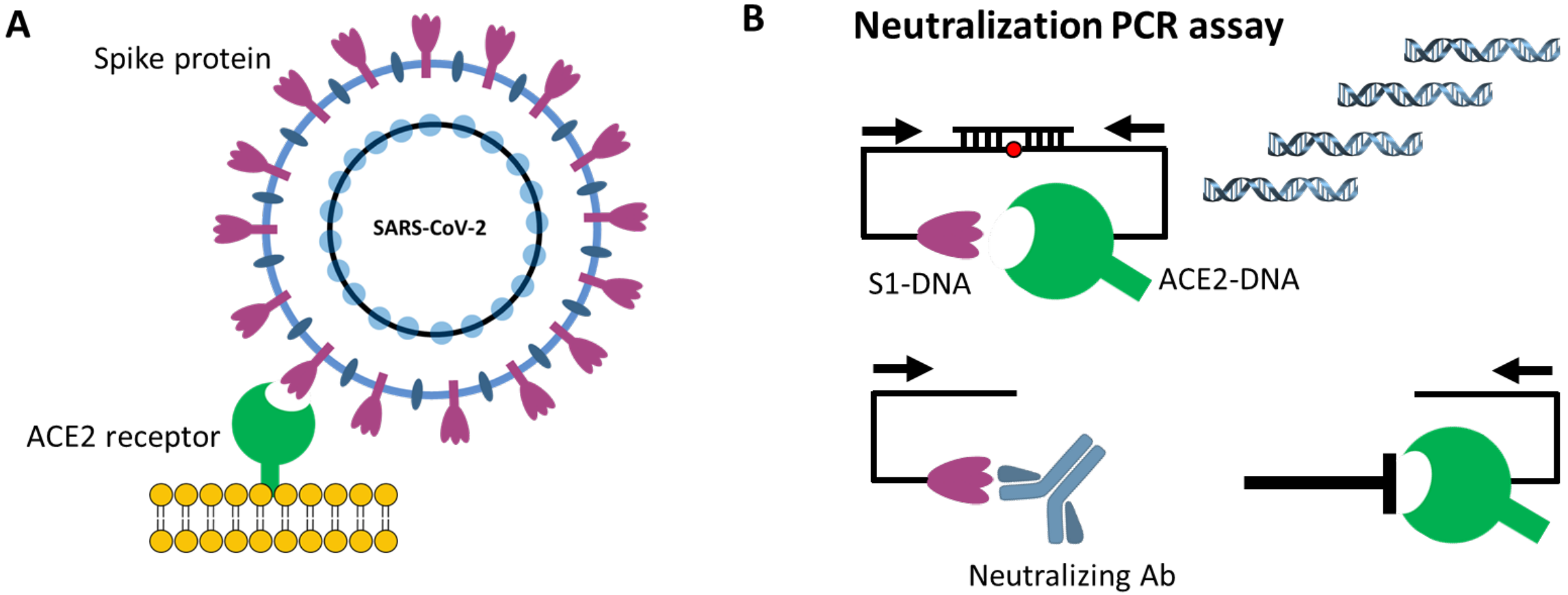
The Opportunity

- Protective titers from vaccination may wane every 6 months
- Only 53% of the US population currently fully vaccinated
- Enable offers the **only multivariant-of-concern** (VOC) neutralizing antibody panel with at-home **dried blood spot** sample collection

Enable is the logistics and lab partner for CalScope - California's state-wide serosurvey. Over 200,000 households are engaged for participation

ADAP Neutralization Assay Principle

a unique quantitative soluble ACE-receptor competition assay provides continuous variable scale performance data



medRxiv 2, 20105692 (2020)

ENABLE BIOSCIENCES

ADAP neutralization is the world's only multiplex, dried blood spot capable test with quantitative output

	Plaque Reduction Neutralization Testing	Spike antibody assay	Surrogate ELISA (e.g. Genscript)	Enable SARS-CoV-2 Neutralization Assay
Probes	Virus/Cells	Spike protein or RBD	RBD/ACE2	Spike Protein/ACE2
Relevance to neutralizing capacity	High	Low	High	High
Biosafety Lab Level 3 requirement	BSL3	Not	No	Not required
Variant **mutiplexability** (e.g. B1.351, B1.1.7)	No	No	No	Yes
Dried blood spot compatibility	No	No	No	Yes

A quickly adaptable assay with at-home collection capability to cover all variants-of-concern (VOC)

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ADAP neutralization assay has outstanding concordance with the labor intensive and biolevel 3 lab-requiring live virus plaque reduction neutralization test (PRNT)

Validation with samples from the Mayo Clinic

Titer by Cell-Based Assay	Average NAb signals	Number Positive by NAb ADAP assay	Number of samples	Agreement
Pre-COVID	0.07	0	43	100%
80	3.44	31	32	97%
160	4.33	34	34	100%
320	4.83	37	37	100%
640	5.10	26	26	100%
1280	4.98	14	14	100%
2560	6.15	3	3	100%

Positive Agreement	Negative Agreement	Overall agreement
99% (145/146)	100% (43/43)	99% (188/189)

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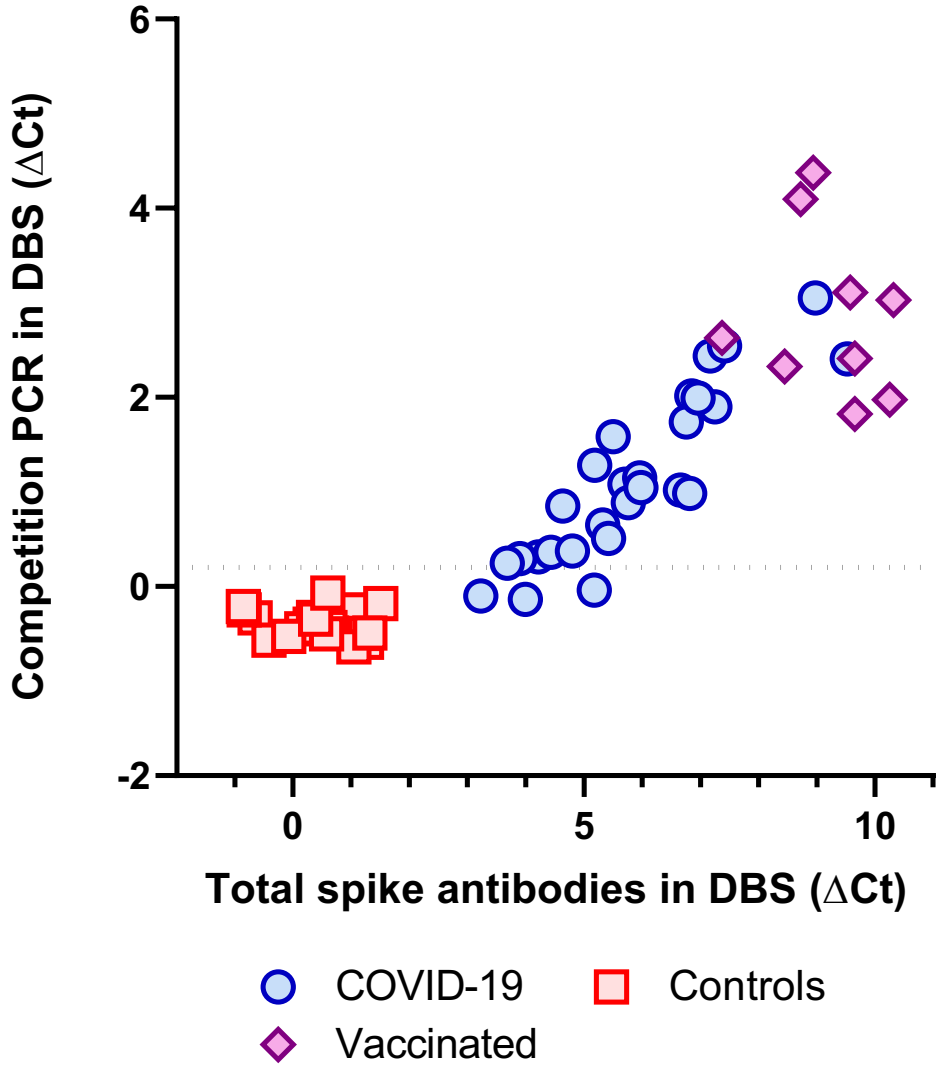
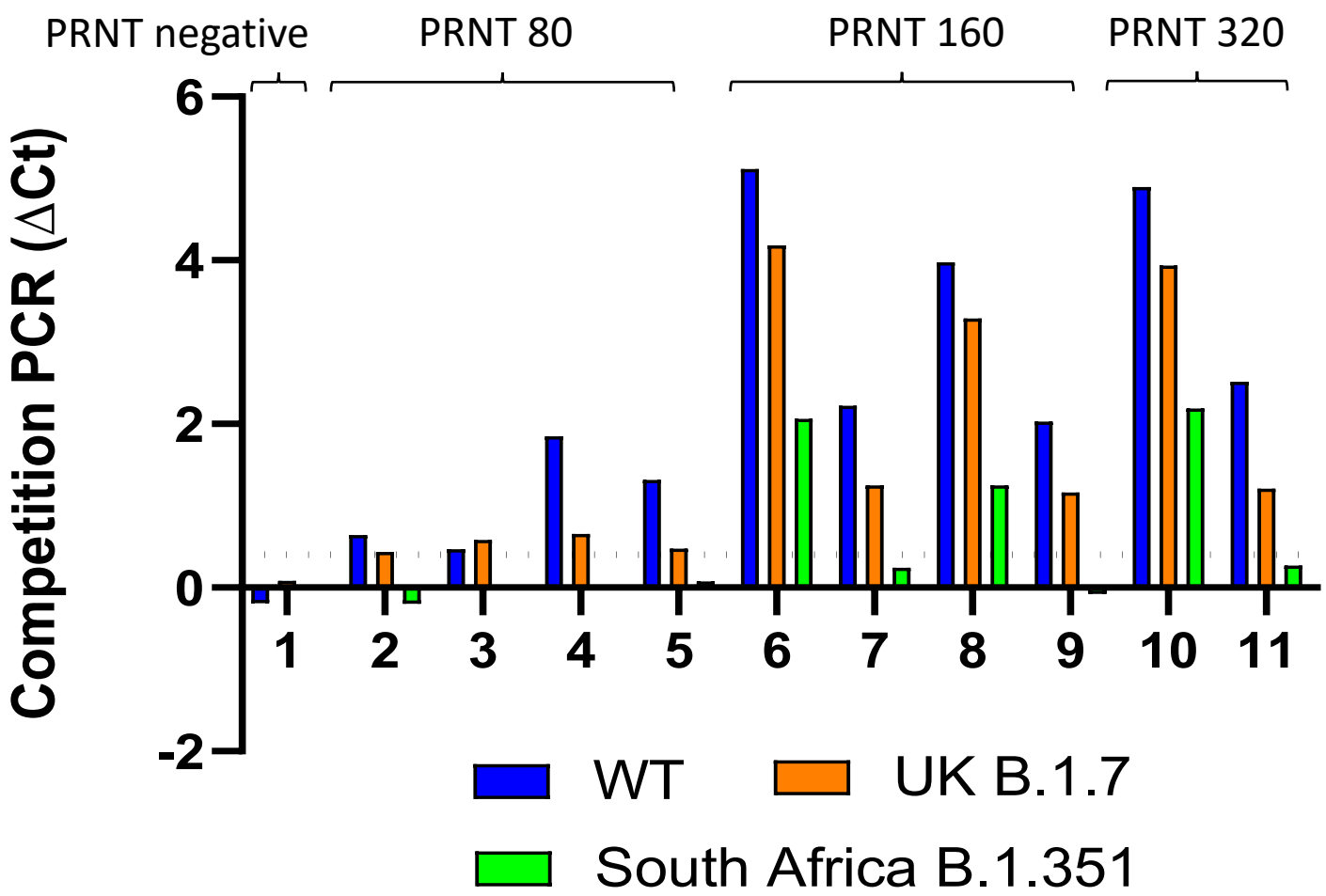
ADAP Neutralization Assay has been validated for Dried Blood Spot samples too

Validation with finger-prick elicited DBS samples

Patient Group	NAb positive rates in DBS
Controls	0/20
COVID-19 infection	24/27
Vaccination	9/9



ADAP multiplex neutralization assay shows the quantitative performance of a persons SARS-CoV2 antibody neutralization versus common SARS-CoV2 Variants of Concern



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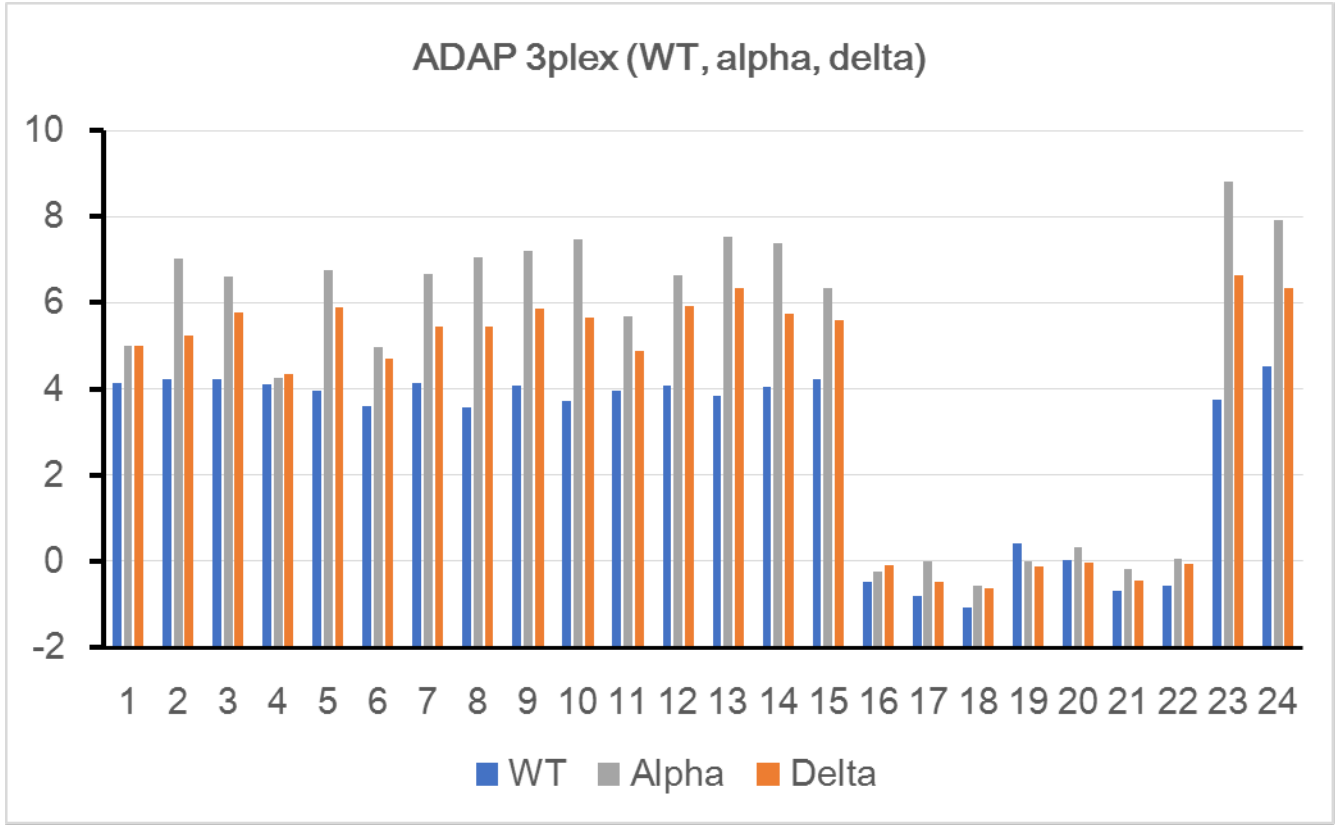
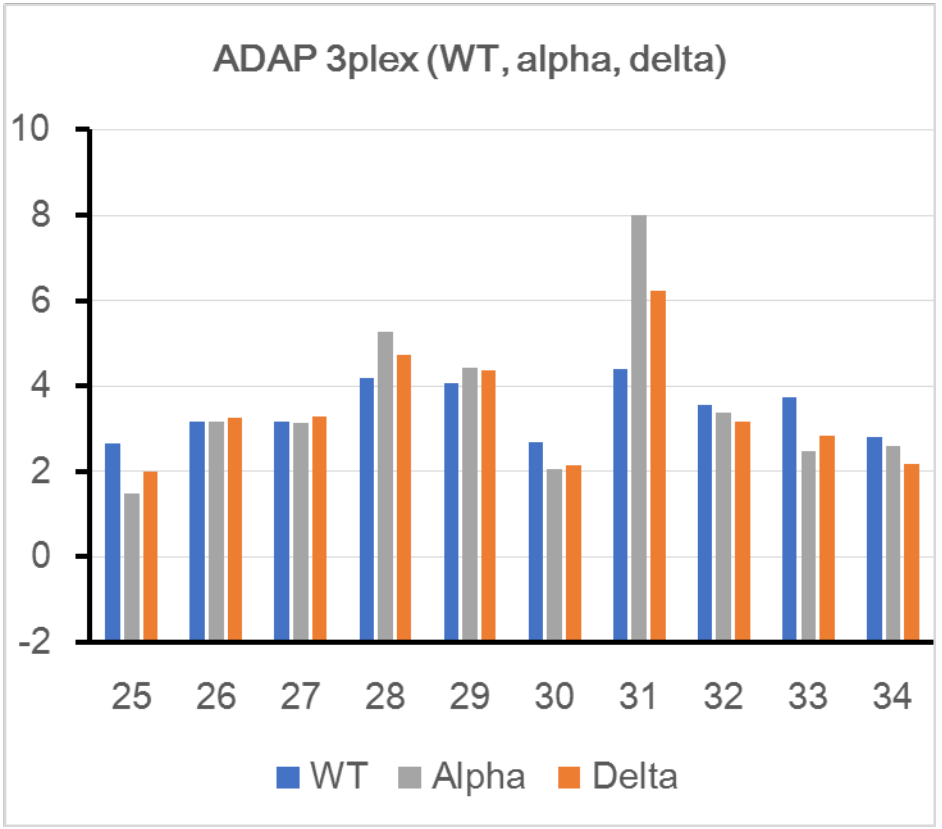
Multiplex ADAP Neutralization Assay is validated for Delta, deployed for CalScope

Samples from 2021



Samples from 2020



A shift has been noted in neutralizing antibody signals, likely associated with the emergence of Variants of Concern (VOC)

ENABLE BIOSCIENCES

Updated longitudinal vaccine performance data empowers

- Greater return to work protection confidence
- Improved employee productivity and reduced sickout time
- Reduction of in-office and other facility spread
- Predictive planning for booster vaccination timing
- Predictive planning for variant vaccine update recommendations
- Reduction in new variant surge disruption throughout the community through generation of pre-emptive intelligence to guide mitigation steps
- Guidance to improve site-level protection for immunocompromised person

Test supply options

- Dried blood spot cards returned via USPS, Fedex, UPS, DHL

- Bulk test kits
- Individual home orders via web portal like CalScope (launching soon)

Results reporting and analytics options

- Secure online individual account and portal
- Aggregate anonymized performance ratings data reporting by geography

Testing timing

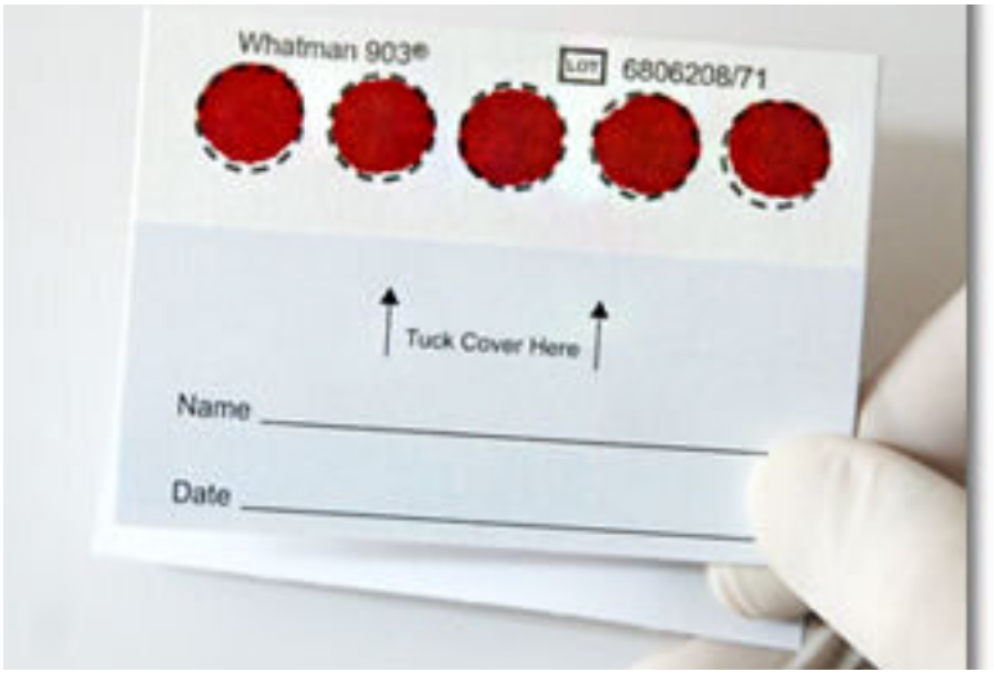
- Every 3 months
- When a new variant of concern is spreading
- On-demand
- As directed by institutional health security leadership

Recap: For schools, colleges and companies – Enable can help achieve greater institutional health security and proactively predict and mitigate future COVID driven institutional disruption

- What we know – everyone responds to vaccination differently
- Some generate a strong neutralizing antibody response, and some don't
- More than 15 million in the US have known immunocompromise and need boosters earlier
- Many millions more don't know they are mildly to moderately immunocompromised and will have inadequate or wanning immunity sooner
- The only way to tell is to regularly measure individual level neutralizing antibody performance vs the current variant of concern
- When a new variant of concern like Omicron emerges, one needs to test against it
- Vaccine effectiveness performance data enables a smarter, safer return to in person activities of all types

Enabling occupational health with accurate personal and institutional COVID vaccine protection visibility

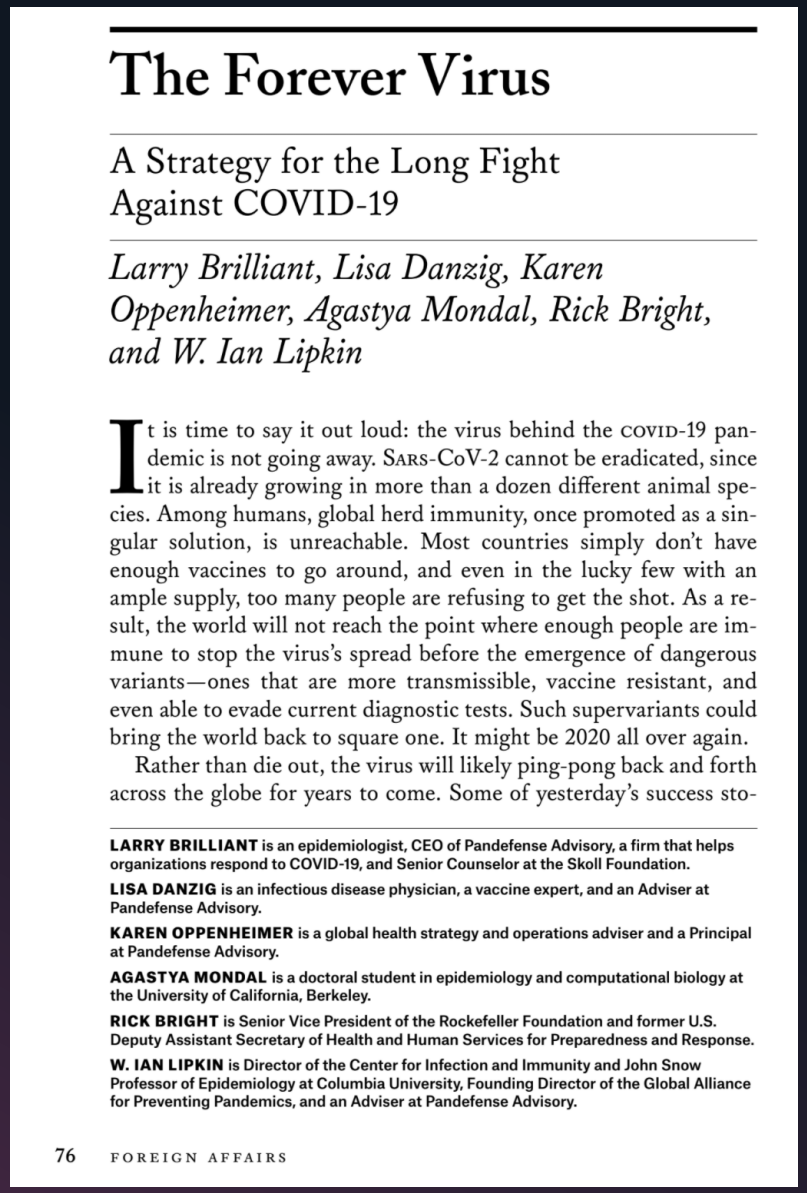
UCSF Health Awards 2021: Breakthrough COVID-19 Technology Finalist



Enable Biosciences to Support California Department of Public Health's Calscope Program to Survey Covid-19 Antibodies from Infection and Vaccination

Contact: David Seftel, MD at dseftel@enablebiosciences.com

What we know > how we plan



The Forever Virus

A Strategy for the Long Fight Against COVID-19

Larry Brilliant, Lisa Danzig, Karen Oppenheimer, Agastya Mondal, Rick Bright, and W. Ian Lipkin

It is time to say it out loud: the virus behind the COVID-19 pandemic is not going away. SARS-CoV-2 cannot be eradicated, since it is already growing in more than a dozen different animal species. Among humans, global herd immunity, once promoted as a singular solution, is unreachable. Most countries simply don't have enough vaccines to go around, and even in the lucky few with an ample supply, too many people are refusing to get the shot. As a result, the world will not reach the point where enough people are immune to stop the virus's spread before the emergence of dangerous variants—ones that are more transmissible, vaccine resistant, and even able to evade current diagnostic tests. Such supervariants could bring the world back to square one. It might be 2020 all over again.

Rather than die out, the virus will likely ping-pong back and forth across the globe for years to come. Some of yesterday's success sto-

LARRY BRILLIANT is an epidemiologist, CEO of Pandefense Advisory, a firm that helps organizations respond to COVID-19, and Senior Counselor at the Skoll Foundation.

LISA DANZIG is an infectious disease physician, a vaccine expert, and an Adviser at Pandefense Advisory.

KAREN OPPENHEIMER is a global health strategy and operations adviser and a Principal at Pandefense Advisory.

AGASTYA MONDAL is a doctoral student in epidemiology and computational biology at the University of California, Berkeley.

RICK BRIGHT is Senior Vice President of the Rockefeller Foundation and former U.S. Deputy Assistant Secretary of Health and Human Services for Preparedness and Response.

W. IAN LIPKIN is Director of the Center for Infection and Immunity and John Snow Professor of Epidemiology at Columbia University, Founding Director of the Global Alliance for Preventing Pandemics, and an Adviser at Pandefense Advisory.

"The psychiatrist Elisabeth Kübler-Ross famously and controversially outlined the stages of grief that people go through as they learn to live with what has been lost: denial, anger, bargaining, depression, and acceptance. **Almost everyone has experienced at least one of these stages during the pandemic, although in many ways, the world is still stuck in the first stage, denial,** refusing to accept that the pandemic is far from over.

To these five stages, the bioethicist David Kessler has added one more that is crucial: finding meaning. **From the devastation of covid-19, the world must work together to build an enduring system for mitigating this pandemic and preventing the next one. Figuring out how to do that might be the most meaningful challenge of our lifetime."**

Occupational Health Renaissance
Central to Everyone Now

Questions