



Yale College
Class of 1971

“Hot Zone: Perspectives on the Pandemic”

Yale College Class of 1971 Virtual Reunion
Saturday, May 1, 2021 | 4:00 pm ET

Moderator: Richard Skolnik, MPA (BR) — Author, *Global Health 101*; Instructor for Yale Coursera course “Essentials of Global Health”; former Director for Health and Education for South Asia Region at World Bank

Panelists – *slides herein are in order presented*

James Rothman, PhD (BR) — Sterling Professor of Cell Biology and Chair of the Department of Cell Biology, Yale School of Medicine; Nobel Prize in Physiology or Medicine 2013; former Vice Chairman, Sloan Kettering Institute for Cancer Research

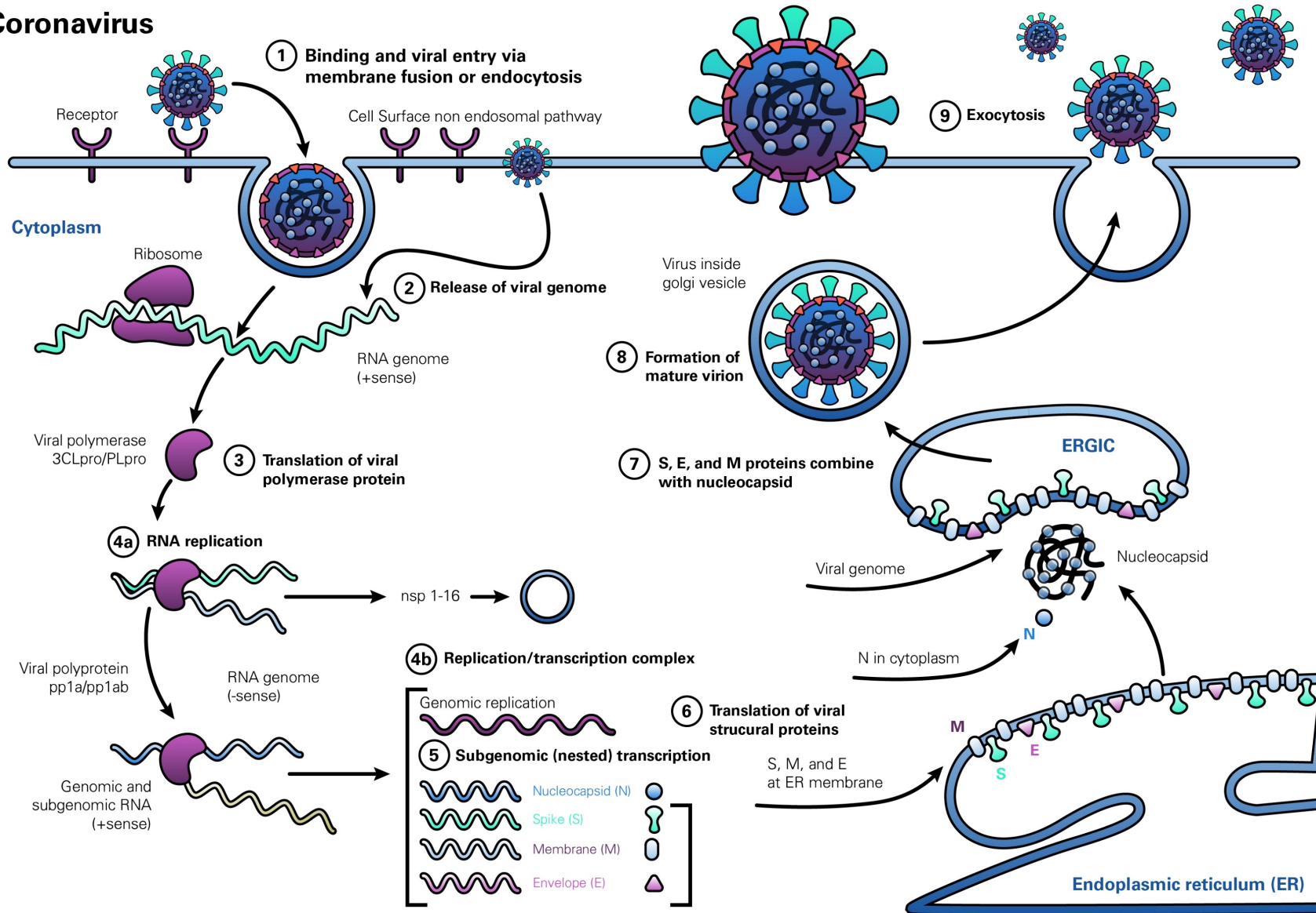
Dori Zaleznik, MD (BK) — Retired (all positions); Infectious Diseases Specialist; Associate Clinical Professor of Medicine, Harvard Medical School; bacterial vaccine research, Channing Laboratory; Hospital Epidemiologist; developer of Infectious Diseases section UptoDate™, Commissioner of Health & Human Services, Newton, MA

Andrew Wiesenthal, MD (SM) — Pediatric Infectious Diseases Specialist; Managing Director, Life Sciences and Health Care, Deloitte Consulting LLP; former Associate Executive Director, Permanente Federation; served on the Federal Health Information Technology Standards Committee and co-chaired its Precision Medicine Task Force.

Sten Vermund, MD, PhD — Dean and Anna M. R. Lauder Professor of Public Health, Yale School of Public Health; Professor of Pediatrics, Yale School of Medicine; infectious disease epidemiologist and pediatrician

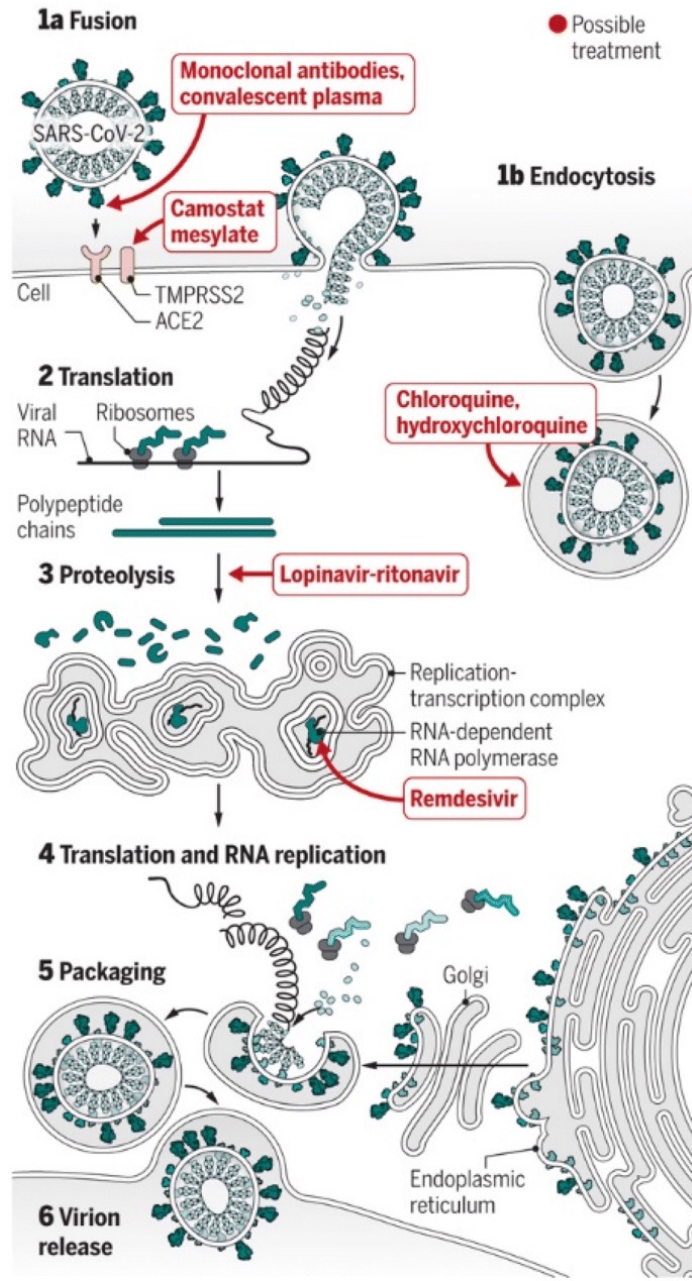
Decades of NIH investment in basic research allowed scientists to rapidly understand how SARS CoV-2 replicates itself

Coronavirus



Lines of attack

Experimental treatment strategies attempt to interfere with different steps (numbered) in the coronavirus replication cycle.



Our home-grown and world-leading biotechnology enterprise could pivot rapidly to deliver increasingly powerful options for testing and treatment

First attempts involved “re-purposing” existing drugs
→ Remdesivir and Dexamethasone can moderate disease

Next came manufactured “monoclonal antibodies”
→ Lilly and Regeneron “cocktails” can block disease progression when used early

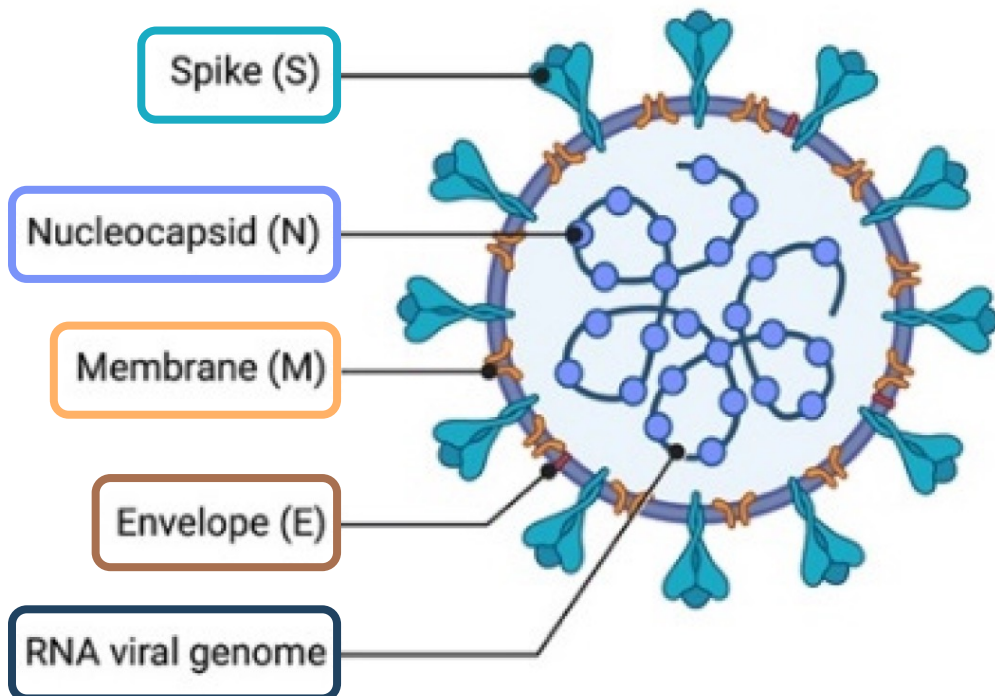
Next came the vaccines
→ Pfizer, Moderna, J&J et al. which strongly protect against infection and (in the case of known variants) sharply reduce hospitalizations and deaths by eliciting our bodies to manufacture our own “neutralizing” antibodies.

**Now we are waiting for totally new drugs that will block virus replication inside cells, analogous those developed for HIV.
→ Numerous candidates in pre-clinical and clinical trials will likely Take 3-5 years before available**

Vaccines work by safely duping the immune system into thinking we are infected

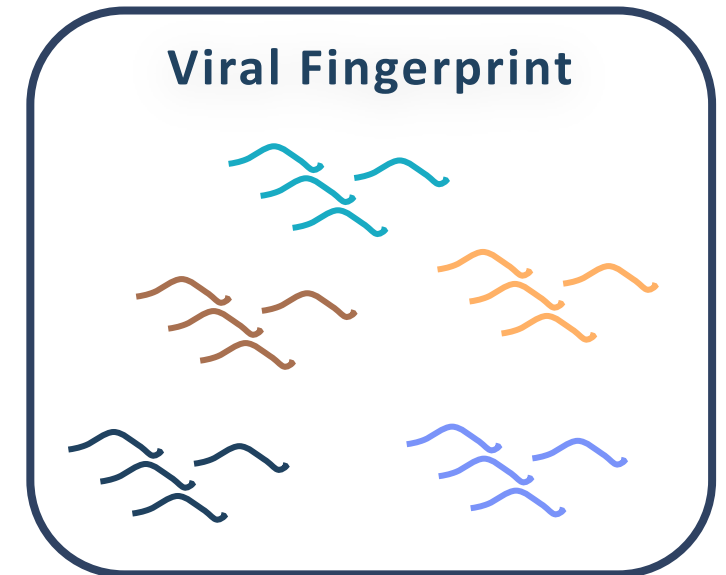
Immune cells normally break the virus proteins into tiny fragments (“antigens”) yielding a unique chemical “fingerprint” which the body remembers to wage the current battle and provide future protection

The SARS-CoV-2 Viral Particle



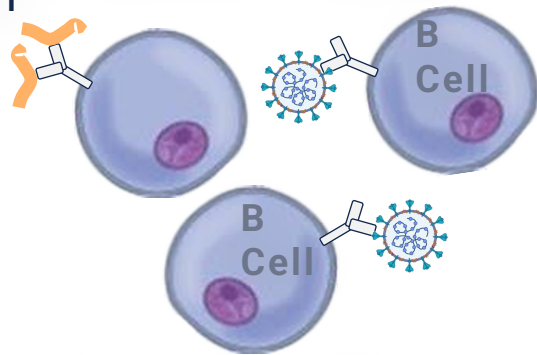
Processing by
The Immune System →

Antigens

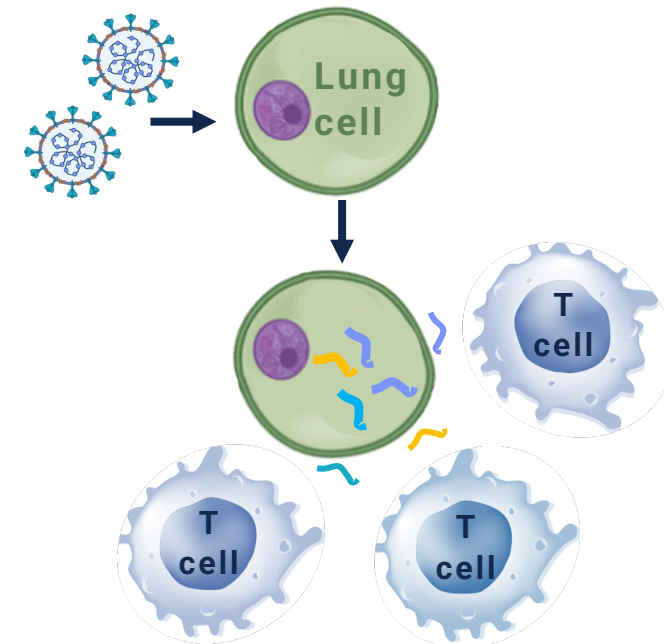
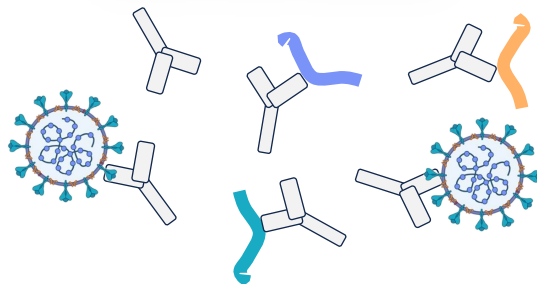


Antibodies and T Cells Recognize Different Parts (“Antigens”)

- **Antibodies (Ab)** directly target the virus in the blood before it enters our cells
- They only target the Spike (S) protein
- Virus “variants” easily dodge Ab by mutating their Spike proteins
- Antibodies are relatively short lived (months to a year) but rapidly re-appear after another infection
- **T Cells** can only see the virus when it has infected our cells
- Specialized “Killer T Cells” then kill that cell but spare uninfected cells
- T Cells mainly target many SARS CoV-2 proteins in addition to Spike protein so variants don’t easily evade them
- T Cell immunity can be very long-lasting (years) and may be key to controlling variants



Ab are made in B Cells and released into the blood



FULLY VACCINATED WHAT CAN YOU DO NOW?

OUTSIDE

- Alone – Moving around = No mask
- Safe distancing possible = No mask
- Small group, all vaccinated = No mask
- Crowds – Distancing not possible – Not moving around = Mask

WHAT CAN I DO NOW?

INSIDE

- Small group vaccinated = No mask
- Larger, mixed group = Mask
- Smaller room – less ventilated – present for >15 minutes = Mask

RULES OF THUMB

- Don't try to police other's behavior
- If situation feels uncomfortable, create more distance or leave

TRAVEL CONSIDERATIONS

- Prevalence of cases at destination
- Precautions during travel
- Precautions at destination
- Precautions on return
- Decision based on risk vs. reward

HOW LONG WILL IMMUNITY LAST?

BEST ANSWER —
NO ONE KNOWS YET

HOW LONG WILL IMMUNITY LAST ?

REASONS FOR OPTIMISM

- Few repeat cases of natural infection even with variants
- Few breakthrough cases among vaccinated
- Presence of memory B and T cells

HOW LONG WILL IMMUNITY LAST ?

- Need to follow breakthrough cases
- Possible need for booster vaccines

RISK OF ASYMPTOMATIC CARRIAGE AND TRANSMISSION AFTER VACCINATION?

- NOT HIGH!

Why?

- Need enough virus or variant
- Need high viral replication without symptoms
- Need close exposure, no precautions

WILL THIS PANDEMIC EVER BE OVER?

YES!!

WHAT DO WE NEED TO DO?

- Vaccinate, vaccinate
- Drive down the number of cases
- Need continued and improved testing
- Decrease circulating virus
- Detect cases and contacts
- Manage cases to reduce outbreaks

SOME CONCLUSIONS

- CONTROL POSSIBLE
- GLOBAL VACCINATION STRATEGY KEY
- COVID = ENDEMIC?
- IMPROVE MESSAGING
- REBUILD PUBLIC HEALTH → PREPAREDNESS

Health Care System Impacts

- Playing catchup
 - Deferred elective procedures
 - Deferred preventive care and health maintenance
 - Deferred screening
- Altering supply chain
 - On-shoring a proportion of materiel procurement
 - Revisiting just-in-time stock

Health Care System Impacts

- Permanent rise in virtual care—from video visits to tele-consultation, tele-critical care, robotic surgery, and hospital-at-home
 - Training implications
 - Licensure implications
 - Financial implications
 - Social/cultural implications
- Shift toward less bricks and mortar
- Shift away from fee-for-service and toward value-based care and health
- New, more dynamic relationship with public health

Hot Zone: Perspectives on the (Next) Pandemic

Sten H. Vermund, MD, PhD (sten.vermund@yale.edu)

Yale School of Public Health
(https://publichealth.yale.edu/profile/sten_vermund/)

How do we manage pandemics in the future?

- **Tackle at the source (e.g., Ebola in West Africa; Coronavirus in China)**
 - **Reform & revitalize international agencies, e.g., WHO, UNICEF, PAHO**
 - **Global viral surveillance and local response (capacity building)**
- Revitalize public health infrastructures & workforces, esp. CDC & state DPH
 - Coordinate emergency responses, as for natural disasters like fire
 - Improve logistics and supply chains for vital consumables
 - Address social determinants of risk
- Take warnings seriously for vaccine development (e.g., Ebola, SARS)
- Attend to climate change (zoonotic diseases) & unmet need for contraception (unwanted pregnancies)

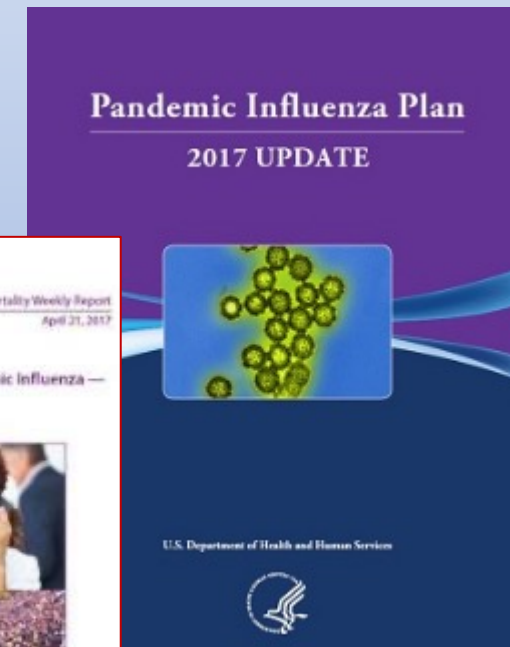
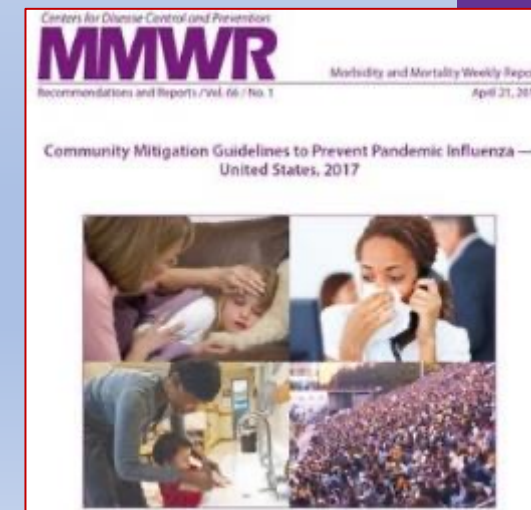
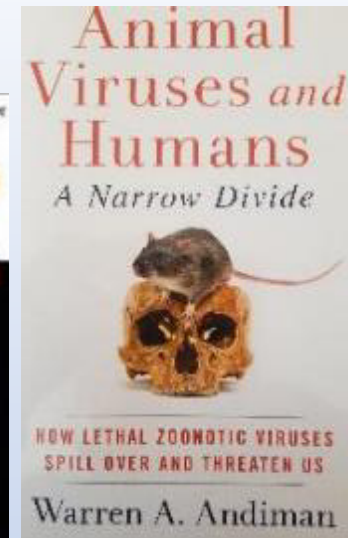
sten.vermund@yale.edu

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Prepare for & mitigate pandemic threats

Recent events were not surprises...

- 1918-1919 Spanish influenza → subsequent flu pandemics (1957, 1968, 2009)
- CoV cold viruses x4, then SARS, then MERS
- Ebola of 2014-2015 was one of 22 outbreaks from 1976 through 2021 (19 countries)
<https://www.cdc.gov/vhf/ebola/history/chronology.html>
- Public health financing in India ≈1.5% of GDP, so capacity to respond is minimal
- 100s of reviews of pandemic threats, e.g., Fedson DS. **Pandemic influenza and the global vaccine supply.** *Clin Infect Dis* 2003



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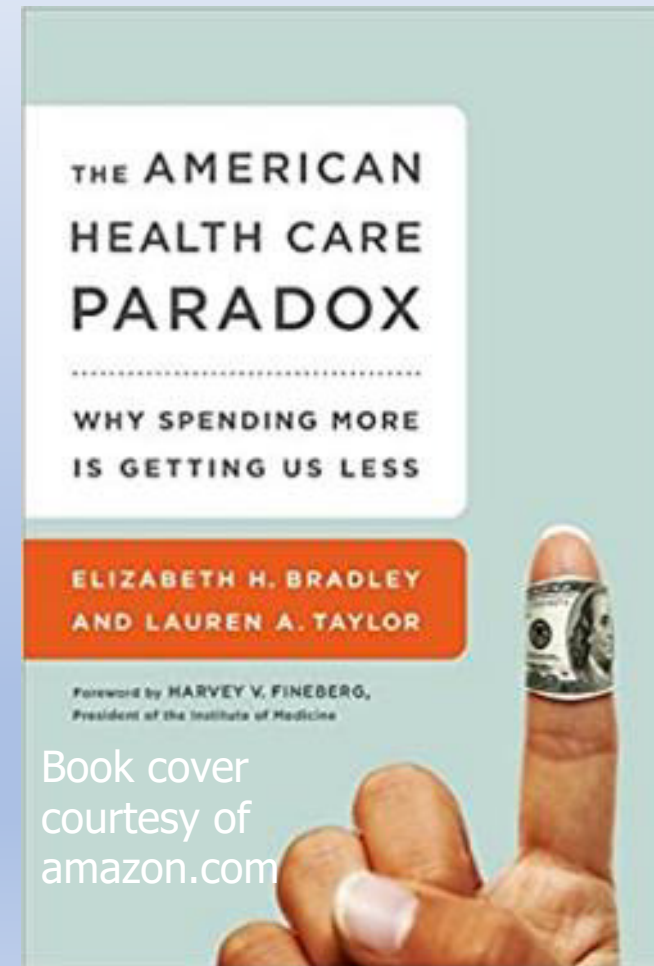
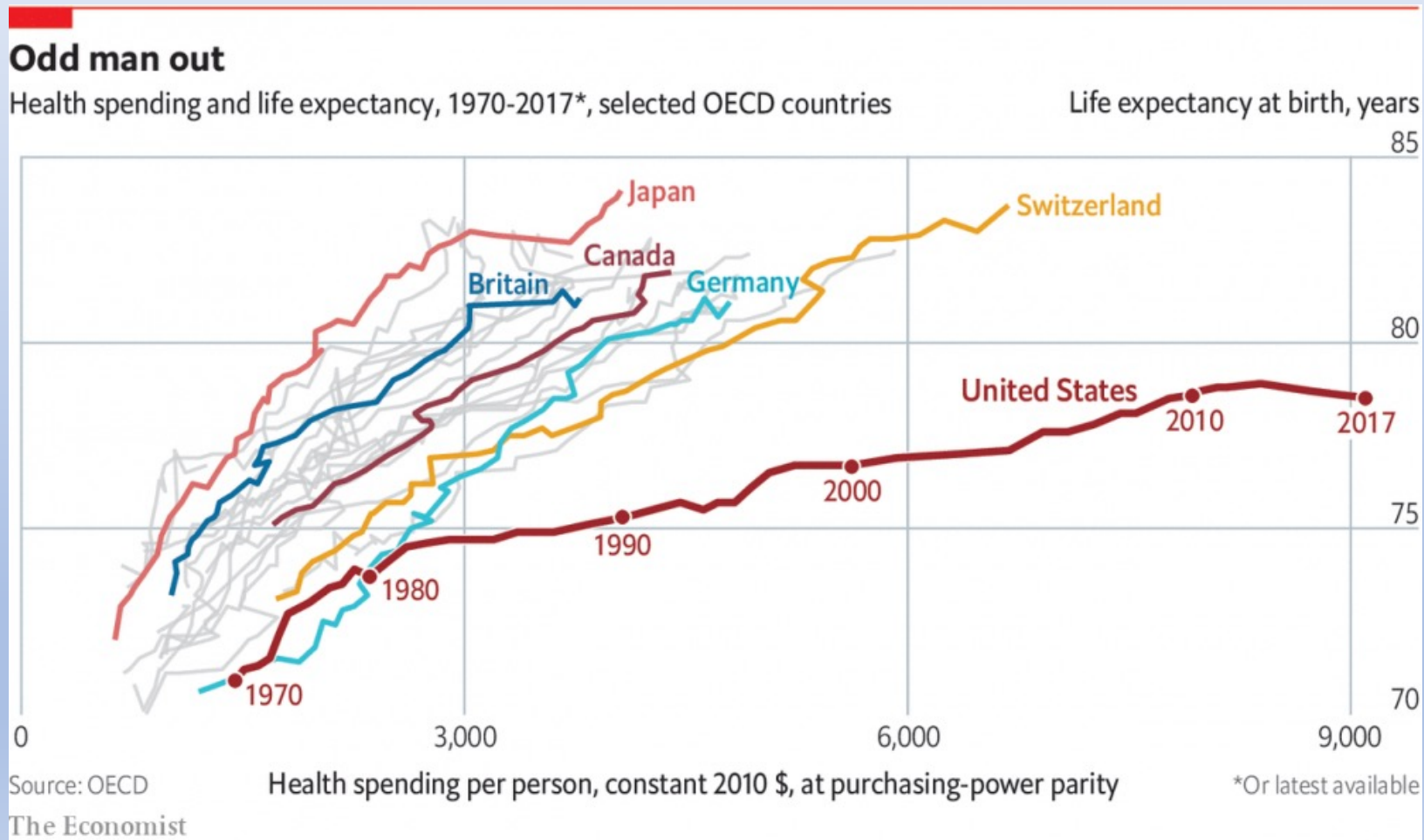
Intelligent policymaking in lieu of partisanship



- USSR & USA spearheaded global smallpox eradication in the 1950s
 - Global investment of \$300 million saved \$1 billion/yr smallpox vaccination costs in USA alone, when vaccinations ceased in 1980s, a fantastic ROI
- In 2003-2004, a broadly bipartisan bill to support the U.S. President's Emergency Plan for AIDS Relief was signed by President George W. Bush
 - Now with >\$90 B spent, it is the largest ever global public health investment
- Political vs. Partisan in Science
 - Political: influence legislation & regulation through public affairs for the community
 - Partisan: activities have a firm adherence to a party, faction, or person
 - 2003 House PEPFAR vote was 375 – 41; Renewal Senate vote in 2008 was 80-16



Bipartisan U.S. healthcare reform needed to highlight prevention and relevant social investments to improve a comparatively inefficient & ineffective system



Est. shortfall in the U.S. public health workforce

- “The Public Health Workforce Shortage: Left Unchecked, Will We Be Protected?” American Public Health Association in 2006
- Updated April 5, 2020: “A deficit of more than **250,000** public health workers is no way to fight Covid-19”
<https://www.statnews.com/2020/04/05/deficit-public-health-workers-no-way-to-fight-covid-19/>
- Yale School of Public Health is one of 60 accredited schools in the US (4 in New England) vs. 180 medical schools
- Endowment supports 13% of budget vs. 50% for all Yale schools
- Student demand exists, but limits in affordability (generalizable to other schools of public health, but some mitigation with naming gifts)

How do we manage pandemics in the future?

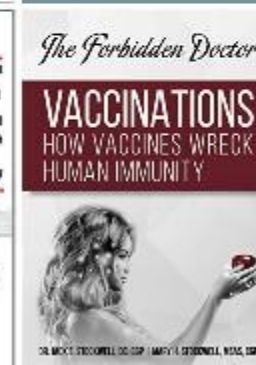
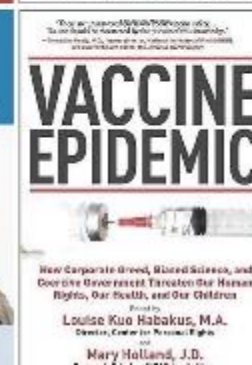
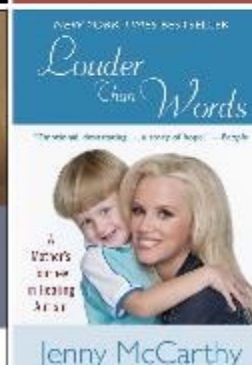
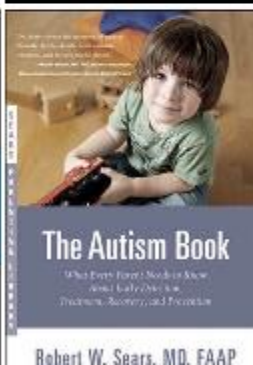
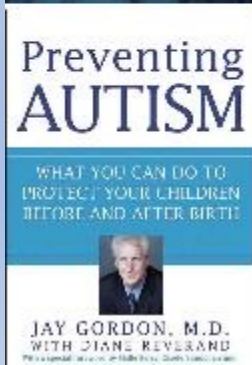
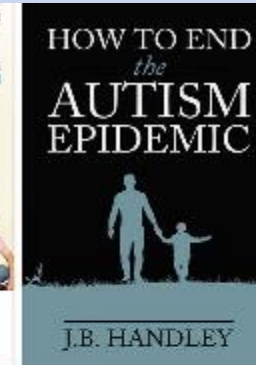
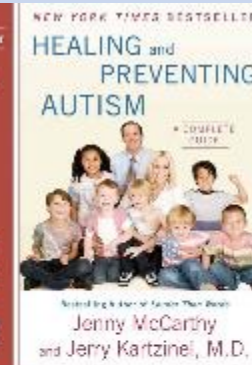
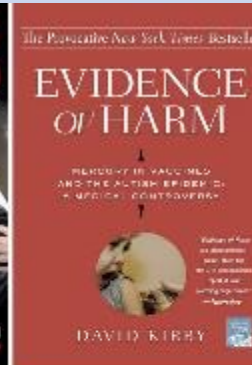
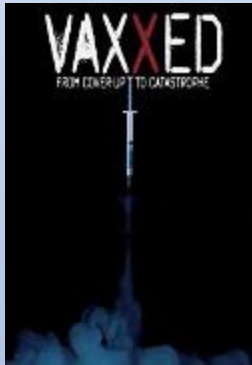
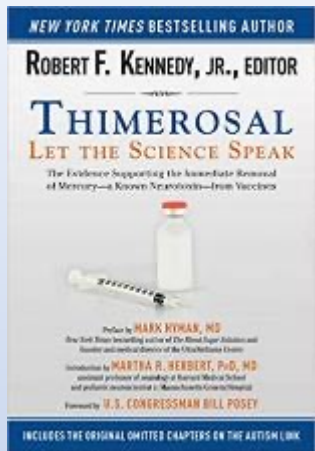
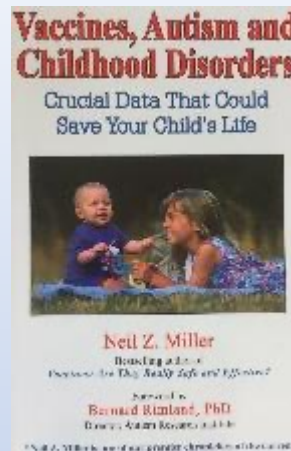
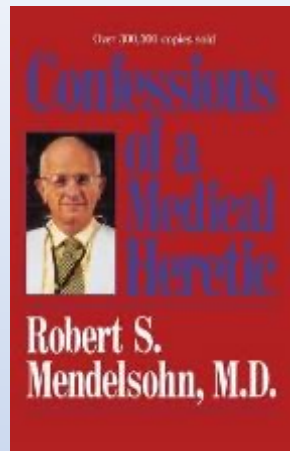
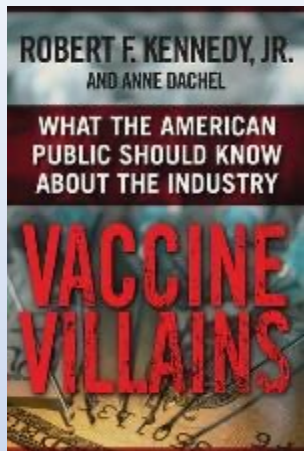
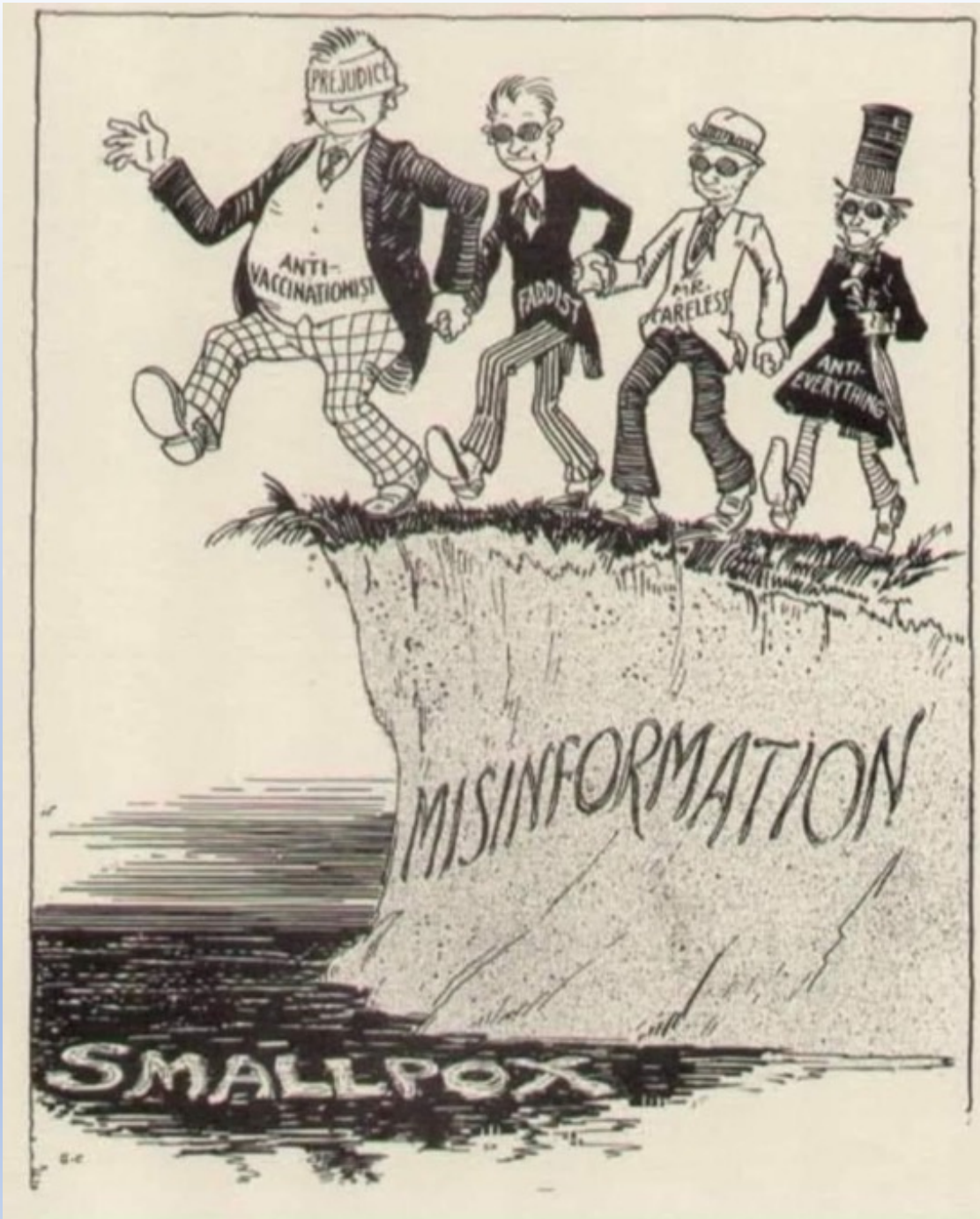
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We left promising vaccines on the shelf until AFTER the crises began

- Ebola vaccine available before 2009 responding to DRC outbreaks, but not tested in earnest until 2015 West African crisis in Guinea, Liberia, and Sierra Leone
 - Jack Rose at Yale: <https://www.statnews.com/2020/01/07/inside-story-scientists-produced-world-first-ebola-vaccine/>
 - Est. investment in West Africa \$300 million; spent in US response >\$2 billion
- SARS and MERS coronavirus vaccines developed in the 2004-2016 period.
 - None tested or completed until SARS-CoV-2 pandemic led to emergency vaccine work
 - SANOFI vaccine dropped due to business considerations, for ex. Need for public-private partnerships.
Why do SARS-COV vaccines not exist? The pharma scientific intelligence and business model must be revisited!
Boudjelal M et al. *Expert Opinion on Drug Discovery* 2020; DOI: 10.1080/17460441.2020.1777980
- Also left on the shelf were surge capacity plans for:
 - Personal protective equipment (e.g., masks), ventilators, MERV 13 air filters
 - Workforce for nursing homes, hospitals, and contact tracers
 - Reminds us of Hurricane relief failures (Katrina and others)

Not just the vaccines themselves; Vaccine confidence essential



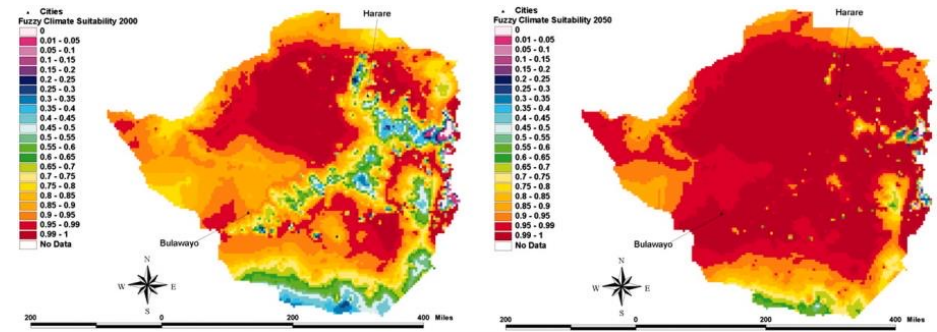
Continuing pandemic risks emerge from population pressures > Global pop 2.4 B in 1954, now 7.8 B

Massive unmet need for contraception among women who want it



Spread of vector-borne diseases favored by warmth, moisture

- Water-borne diseases like cholera
- Mosquito-related infections
 - Malaria, Dengue Fever, Yellow Fever, Zika virus, many other arboviruses
- Other vector-related infections
 - Filariasis/Onchocerciasis, Schistosomiasis, Hantaviruses, Trypanosomiasis, Rickettsiosis
- Drought-flood cycles, hunger, climate refugees



Malaria projections in Zimbabwe due to warming, 2000-2050



Future pandemics are a certainty

- **Must fill gaps** in public health supply chain and workforce, both in the USA and globally
- Disproportional attention to curative medicine is inefficient; we must **prevent** root causes of disease and **mitigate** risk
- Rapid response planning is essential with **public-private partnerships**
- A **longer view** of public health is needed (not “problem-of-the-week”)
- **Global equity** to prevent and/or respond to the next pandemic
 - Human rights and humanitarian rationale
 - Build the global reputation of the USA
 - Save us trillions of dollars and massive human suffering in the long run

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Q&A if vaccine hesitancy arises from audience

Vaccine enthusiasm vs. hesitancy:

Now a partisan issue, surprisingly

- If a coronavirus vaccine is determined to be safe by scientists and is available for free to everyone who wanted it, would you get it? --definitely, --probably, --probably not, --definitely not?
- What are the predictors of vaccine hesitancy (wait & see) & vaccine opposition (only if required or definitely not)?

KFF COVID-19 Vaccine Monitor

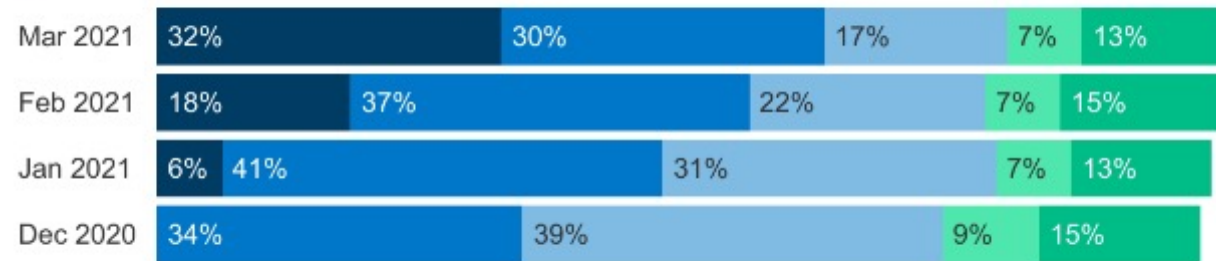
<https://www.kff.org/6787d74/>

% definitely or probably will get a vaccine if deemed safe by scientists & available for free <https://www.kff.org/6787d74/>

Figure 1 One-Third Report Having Received At Least One COVID-19 Vaccine Dose; Share Wanting To "Wait And See" Continues To Shrink

Have you personally received at least one dose of the COVID-19 vaccine, or not? When an FDA authorized vaccine for COVID-19 is available to you for free, do you think you will...?

Legend:
■ Already gotten
■ As soon as possible
■ Wait and see
■ Only if required
■ Definitely not



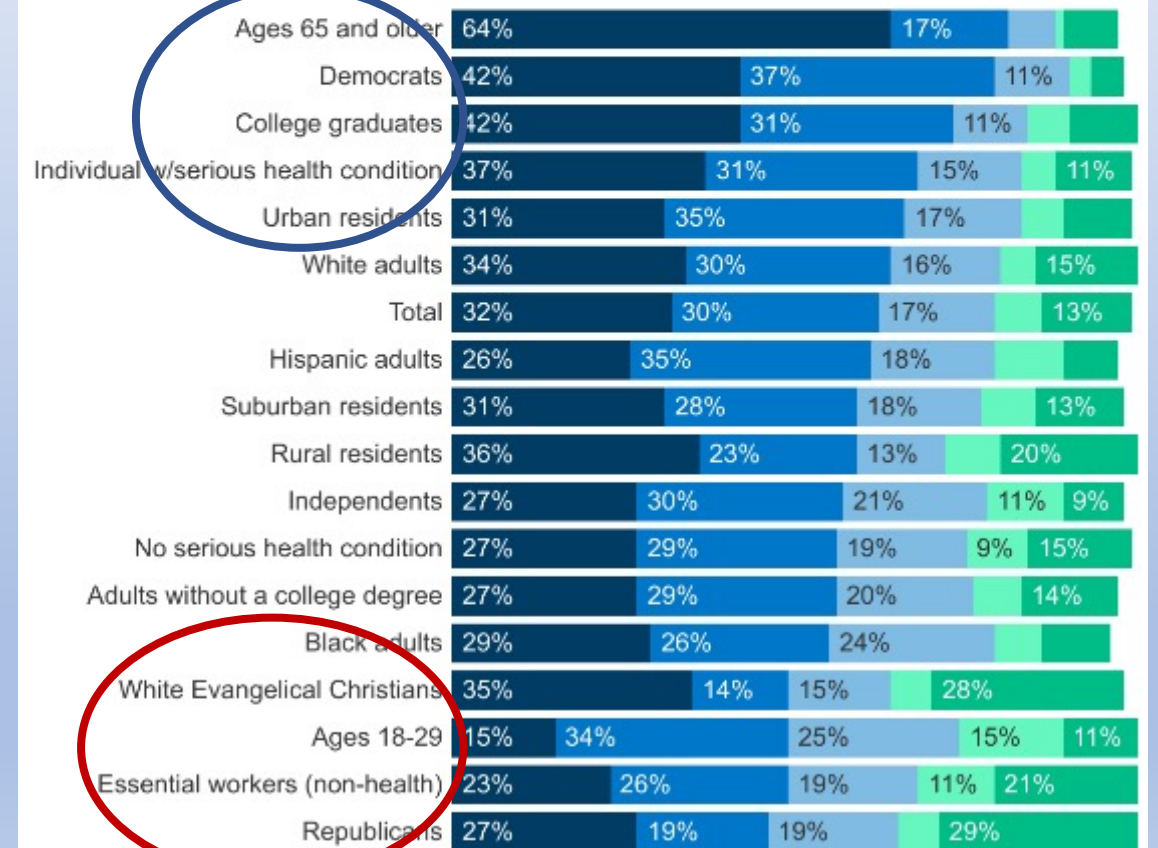
NOTE: December 2020 survey did not have an option for respondents to indicate they had already been vaccinated. See topline for full question wording.
 SOURCE: KFF COVID-19 Vaccine Monitor (March 15-22, 2021)

KFF COVID-19 Vaccine Monitor

Older Adults Most Likely To Say They've Been Vaccinated Or Want To Right Away, Republicans And White Evangelicals "Most Likely To Say Definitely Not"

Have you personally received at least one dose of the COVID-19 vaccine, or not? When an FDA authorized vaccine for COVID-19 is available to you for free, do you think you will...?

Legend:
■ Already received at least one dose
■ Get vaccinated ASAP
■ Wait and see
■ Only if required
■ Definitely not



NOTE: See topline for full question wording.
 SOURCE: KFF COVID-19 Vaccine Monitor (March 15-22, 2021)

KFF COVID-19 Vaccine Monitor

Personality, Partisanship, & COVID-19 Protection

- ✓ Individuals who eschew masks are twice as likely to resent authority and to believe the truth about CoV is being kept from the public
- Morgan Freeman PSA, targeting the “wait and see” audience:
<https://www.youtube.com/watch?v=RU43V0Zt2gA>
- Dolly Parton’s contribution for a “no vaccine” audience:
<https://www.youtube.com/watch?v=OjbSWebA3Ko>

Resnicow K, et al. **Novel Predictors of Coronavirus Protective Behaviors among US adults: The role of trait reactance, conspiracy beliefs, and belief in the apocalypse.** *J Med Internet Res.* 2021 Apr 6. doi: 10.2196/23488. Epub ahead of print. PMID: 33835930.