Complex Adaptive Systems Initiative
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Diagnostic Tests: The Critical Element in Pandemic Control and Global Biosurveillance Against Infectious Threats

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BIOE 122: BioSecurity and Pandemic Resilience
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Virtual

Continuing Challenges in the COVID-19 Pandemic

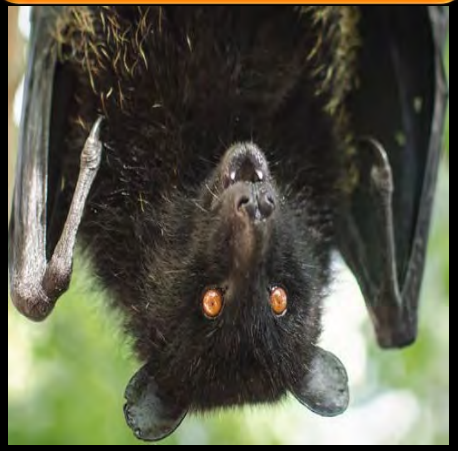
- improve control of disease spread
- more effective treatments for new COVID cases in 2021 (and beyond)
- better prediction/prognosis of disease severity in hospitalized patients and persistent chronic disease in COVID survivors
- lessons learned
  - how to better predict and manage future pandemic threats
- the imperative to rebuild international infrastructure for large scale biosurveillance (BSV)
  - earlier detection and mitigation of new threats from emerging pathogens (agent X)

Diagnostic Tests

- biosurveillance and early detection
- monitor disease prevalence and geographic distribution
  - contact tracing and isolation/quarantine of infected individuals
- prediction of disease severity and post-recovery complications
- immune responses and correlates of protection
- monitoring changes in pathogen biology
  - transmission and/or virulence
  - reduce accuracy of diagnostic tests
  - emergence of Rx/vaccine resistance
- real time situational awareness for national public policy actions for epidemic/pandemic control

The 2020 COVID-19 Pandemic: The “8-D’s” of Disaster

Danger (ignored)



Dispersal (global)

Deficient (CDC)

Disease (heterogeneity)

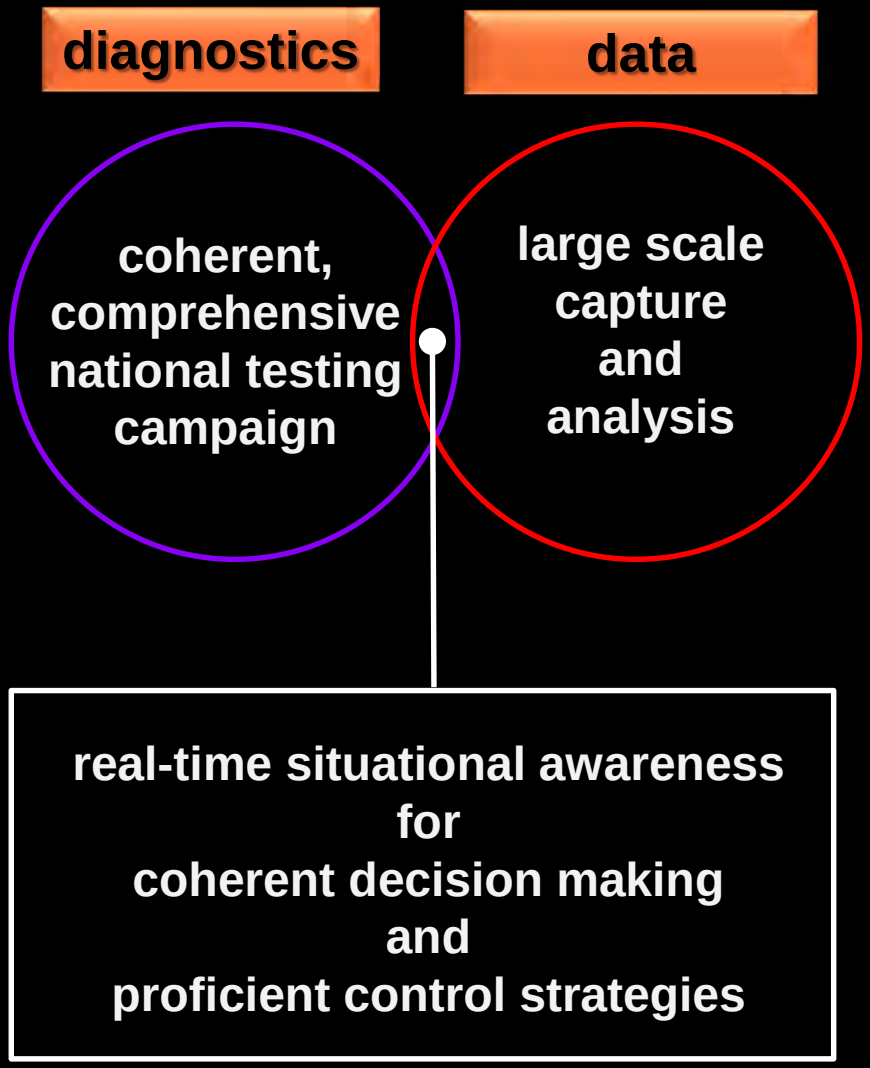
Disruption (socioeconomic)

Dissent (protests)

Disinformation (distrust)

Denial (disarray)

Two Missing Critical “D’s”



SPECIAL FOCUS

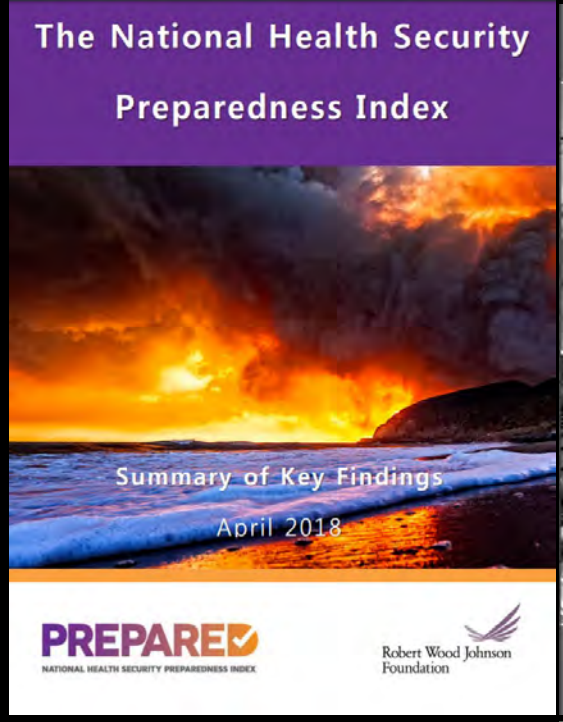
DIAGNOSTICS FOR BIODEFENSE

FLYING BLIND WITH NO PLAN TO LAND

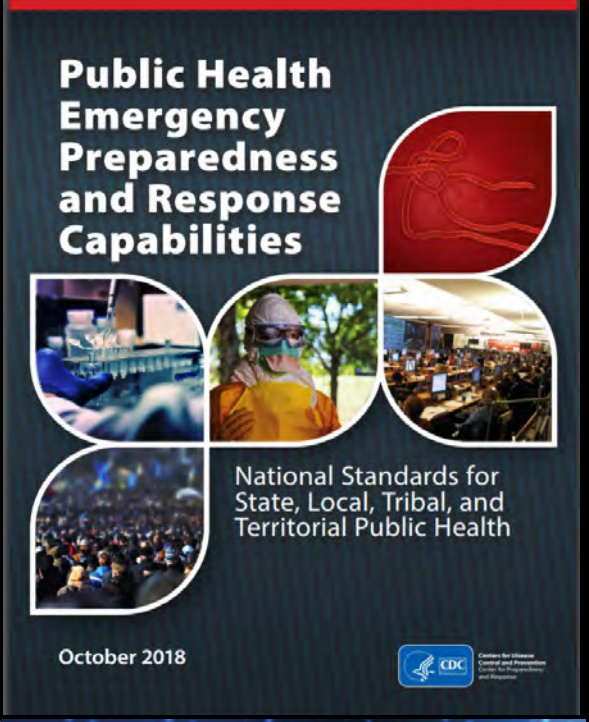
A REPORT BY THE
BIPARTISAN COMMISSION ON BIODEFENSE

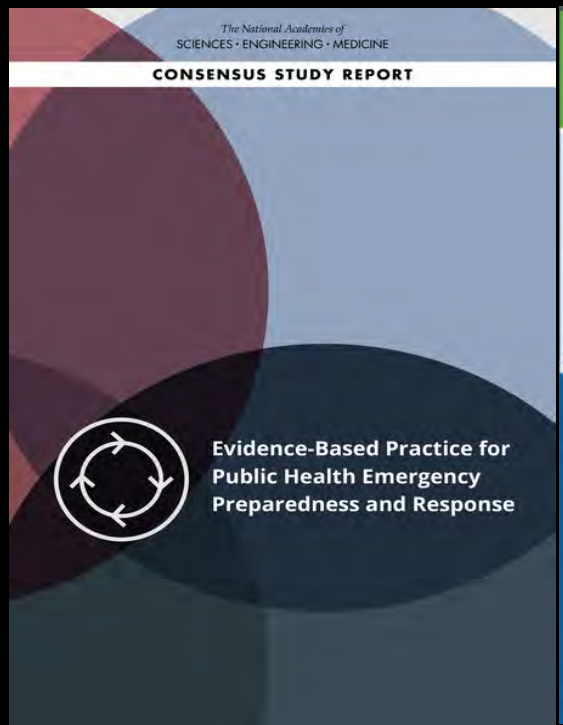
November 2020

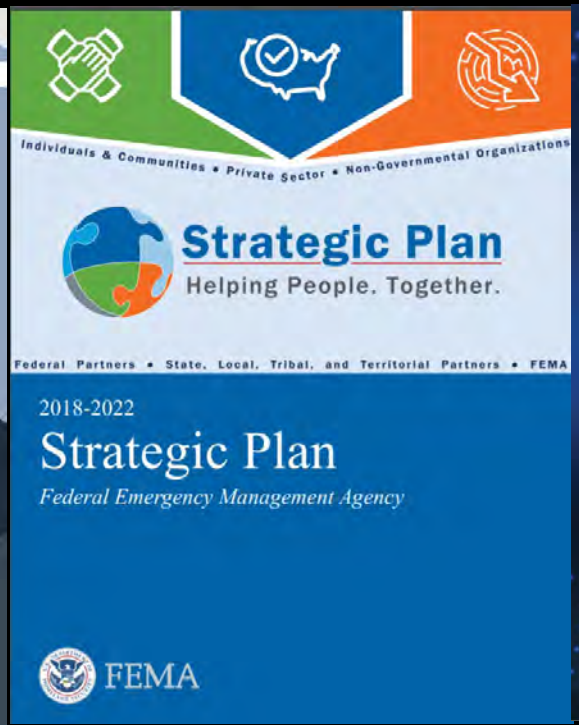
BIPARTISAN COMMISSION ON BIODEFENSE

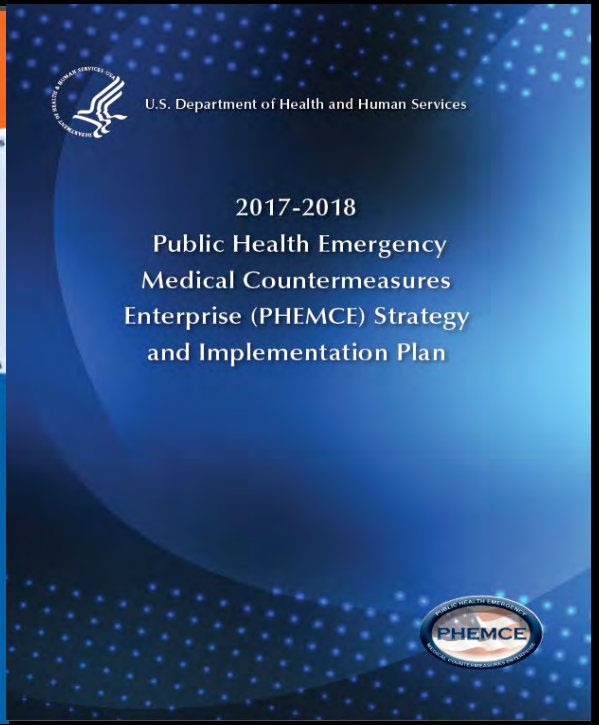

The National Health Security Preparedness Index
Summary of Key Findings
April 2018
PREPARE
NATIONAL HEALTH SECURITY PREPAREDNESS INDEX
Robert Wood Johnson Foundation


PUBLIC HEALTH
PREPAREDNESS AND RESPONSE
2018 NATIONAL SNAPSHOT
CDC
U.S. Department of Health and Human Services
Centers for Disease Control and Prevention


Public Health Emergency Preparedness and Response Capabilities
National Standards for State, Local, Tribal, and Territorial Public Health
October 2018
CDC


The National Academies of SCIENCES • ENGINEERING • MEDICINE
CONSENSUS STUDY REPORT
Evidence-Based Practice for Public Health Emergency Preparedness and Response

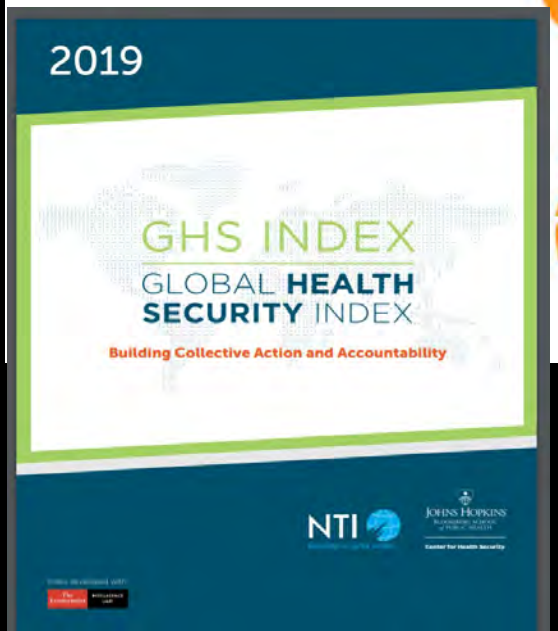

Individuals & Communities • Private Sector • Non-Governmental Organizations
Strategic Plan
Helping People. Together.
Federal Partners • State, Local, Tribal, and Territorial Partners • FEMA
2018-2022
Strategic Plan
Federal Emergency Management Agency
FEMA

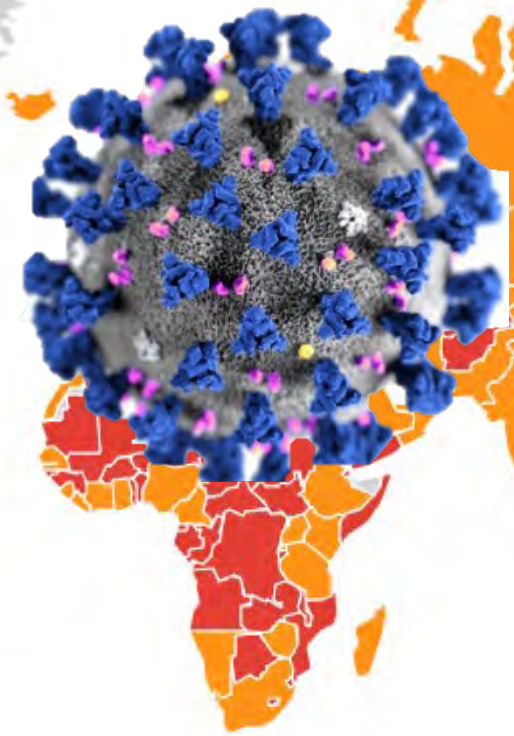

U.S. Department of Health and Human Services
2017-2018
Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) Strategy and Implementation Plan
PHEMCE

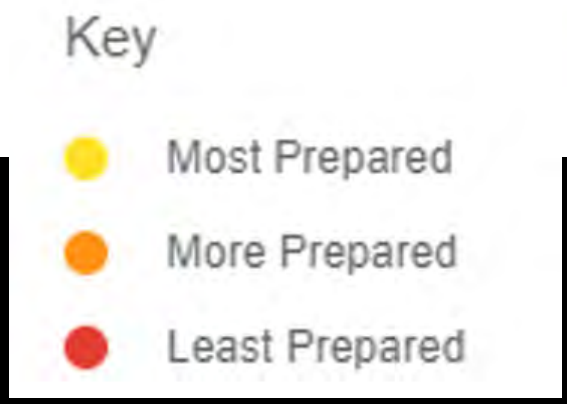
Global Preparedness for Major Bioincidents Deficits in 89% Countries

US ranked #1 as 'Most Prepared'

SADLY NOT !

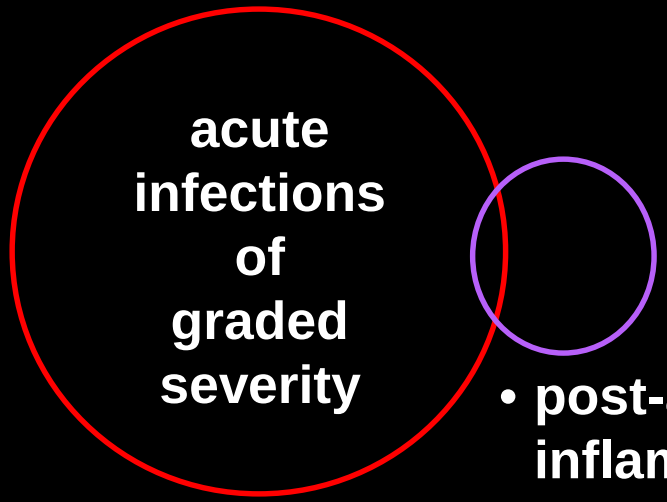






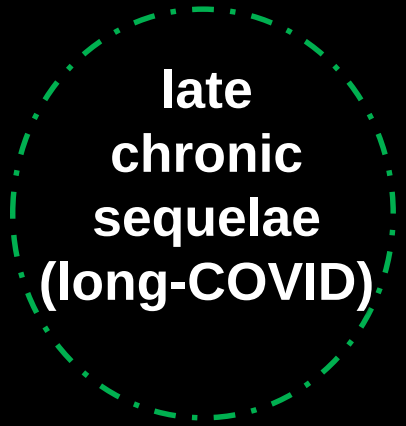
SARS-CoV-2: US Healthcare System Under Siege

The Disease Spectrum of SARS-CoV-2 Infections



- asymptomatic vs symptomatic
- diagnostic markers for prediction of disease severity and prognosis

- post-acute inflammatory illness
  - MIS-C
  - MIS-A



- prevalence?
- pathophysiological mechanisms?
- prognosis?
- duration?
- treatment?

The SARS-CoV-2 Diagnostic Landscape

acute infection	
• detection of viral nucleic acid and protein antigens • immune responses • differentiation from other RTI infections	• accuracy - low false positives and false negatives • contact tracing • population screening

The US Diagnostic Testing Infrastructure for SARS-CoV-2: A 'F' Report Card?

- failure of initial CDC RT-PCR test (Feb 2020) and six weeks lost for critical early control
- well documented capacity limitations of state public health laboratories to conduct large scale testing
- slow action by CDC (March 2020) to engage private sector testing capacity and scalability
- fragility of supply chains for testing reagents/supplies/PPE
  - states pitted against each other in bidding wars

SARS-CoV-2 Diagnostics

- detection of viral nucleic acids
- detection of viral antigens
- detection of viral antibodies
- utility (‘fit-for-purpose’) at different stages in the infection cycle

COVID-19 Testing Strategies

- individuals
  - symptomatic, at risk or known contact with positive case(s)
  - high sensitivity tests with low false negatives
- populations
  - detect asymptomatic/presymptomatic positive cases
  - high specificity tests to reduce false positives
  - lower sensitivity tests can produce false negatives but risk compensated by frequent, repeated testing

Still Unknown:
The Viral Load Threshold for Transmission

- load varies throughout the course of infection
- variable duration in different individuals
- critical benchmark for test sensitivity to identify infectious individuals
- biggest concern is false negatives from insufficiently sensitive tests
  - misplaced (re)assurance
- frequent testing reduces false negative risks by identification of cases previously missed

PCR Detection of Viral Nucleic Acid

- qualitative PCR
  - binary: ‘positive/negative’ result
- quantitative PCR
  - measurement of # viral genomes ml/sample (viral load)
  - viral load as surrogate for likely infectiousness
  - low LoD and detection of positive cases at early stage of infection when viral load is typically low
- threshold cycle (Ct) cut-points for rRT-PCR

The Nonsense of One-Time-Only Testing and the Delusion of Safety

- uncontrolled access overloads testing capacity and slows TAT
- meaningful negative status requires two negative tests 5-7 days apart
- non-quantitative PCR testing
  - useful for isolation recommendations
  - no data on viral load and potential individual infectiousness and super spreader risks

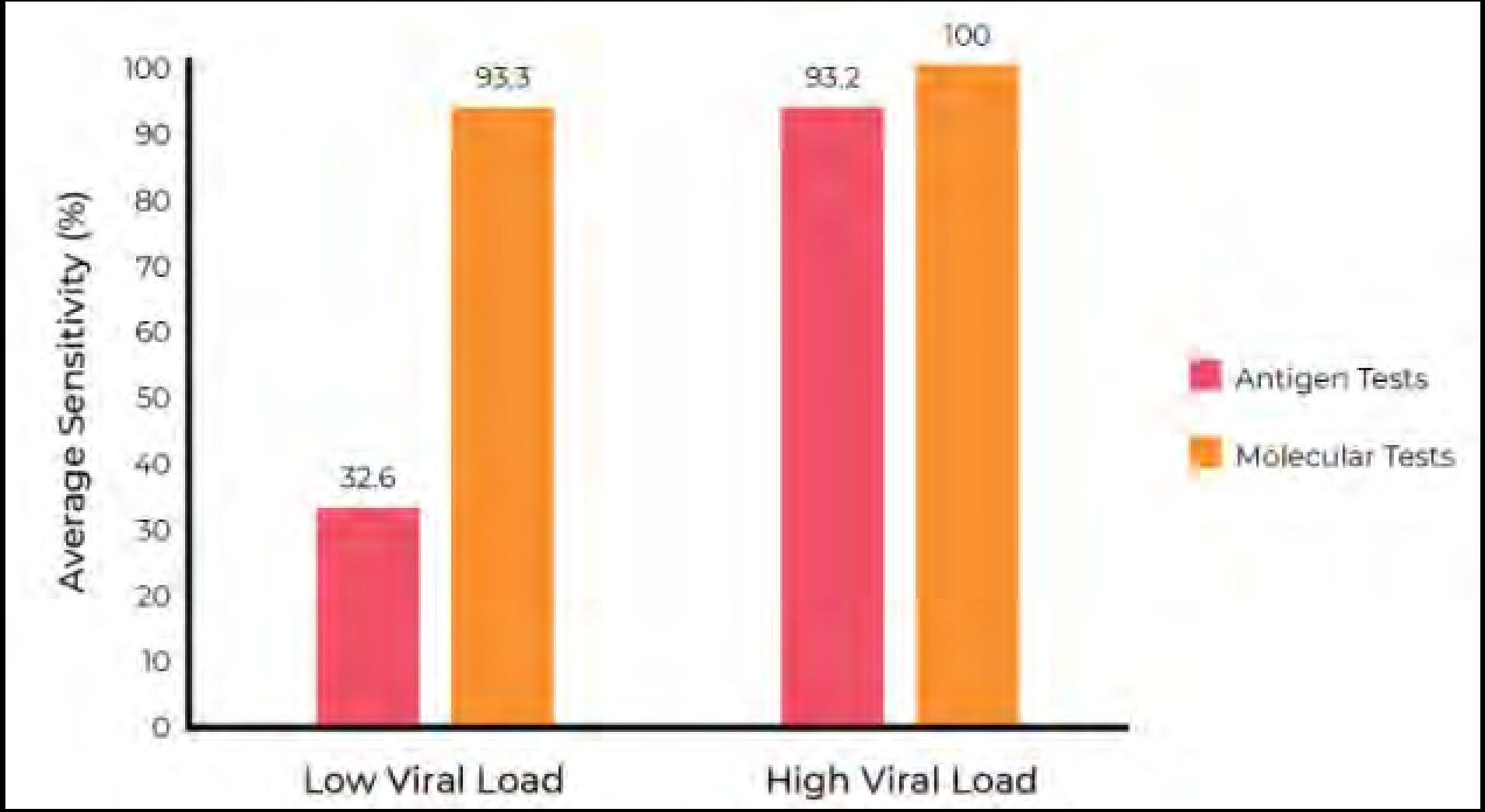
The RT-PCR Bottleneck in Individual Testing and Infection Tracking

- predominant reliance on large CLIA-certified reference laboratories with high volume throughput
  - capacity outstripped by demand leading to slow turnaround time (TAT)
- > 48 hr. reporting erodes willingness of asymptomatic individuals to self-isolate
- higher cost versus other test modalities as handicap to sustained widespread use
- catalyst to develop faster antigen detection tests and CLIA-waived POC/in-home antigen tests

Identification of Asymptomatic and Presymptomatic COVID-19 Cases: The Case for Large Scale Population Screening

- key contributors to virus spread and complicate ability to break transmission chains
- estimated 30- 40% infections are asymptomatic and may not be tested
- adoption of large-scale population screening
- schools, colleges, work facilities, military and in-home tests
- rapid, easy to use, low-cost tests
  - low false positive rates
  - lower sensitivity than PCR can be compensated for by frequency of testing to ID false negatives
  - link to mobile phone Apps for self-reporting

Test Sensitivity vs Sample Viral Load: PCR vs Antigen Detection



From: J. Dinnes et. Al (2020 Cochrane Database of Systematic Reviews Issue 8 DOI. 14651858CD013705

The Wild West of SARS-CoV-2 Diagnostics

- wide variation in performance, QC/QA of EUA tests
- sensitivity span of greater than 3 log 10
- Removal Lists of Tests that Should No Longer Be Used and/or Distributed for COVID-19 Testing
  - diagnostic tests
  - serological tests

- cease-and desist letters to 171 facilities testing without CLIA certification and/or compliance

Pending Innovations in High Accuracy POC Tests With Rapid TAT

- **CUE**
- **automated PCR cartridge**
- **20 - 30-minute TAT readout**
- **mobile phone reporting**
- **$481 million HHS contract for 100,000 tests/day (3/21)**
- **value for POC confirmation to eliminate false positives from antigen tests**

National Reporting of Aggregated COVID Testing Data

- patchwork of different testing platforms, instruments and data formats
- no uniform reporting mechanism or time deadline for individual states (electronic, fax, phone)
- requirements to report to county, state, CDC, CMS and HHS (FEMA sometimes)
- report both positive and negative assays
- HHS/CDC guidelines inconsistent for ‘required’ vs ‘requested’ data elements and CMS non-compliance penalties
- requirement to also report to state public health lab of an individual’s residence

Contact Tracing: A Core Component in Historical Public Health Protocols for Epidemic Control

- test-trace-isolate
- rapid identification of emergent infection clusters (hots spots, sparks) to prevent unchecked spread (fire)
- backward tracing for previous 14 days: a formidable logistical hurdle in fast spreading bioincident
- resources: trackers, real time facile information transfer
- privacy concerns and societal trust/acceptance

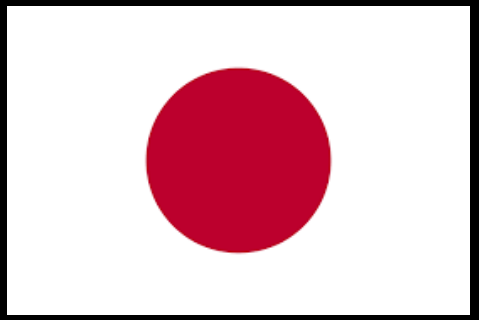
Contact Tracing

- **WHO benchmark is trace and isolate/quarantine 80% of close contacts within 3 days**
  - **very few countries achieve**

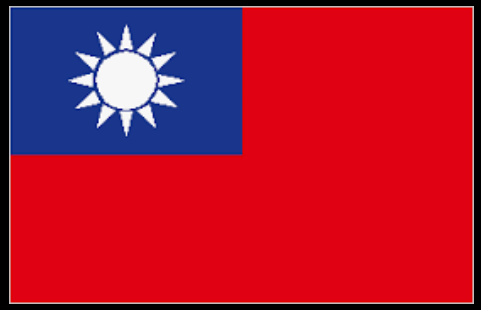
Contact Tracing:
A Foundational Historical Component in Epidemic Control
COVID-19 Success Stories

South Korea

Vietnam



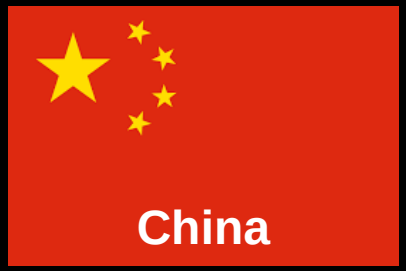
Japan



Taiwan

Singapore

New Zealand



China

US Contact Tracing in the COVID-19 Pandemic

- lack of preparedness, slow mobilization and loss of control from the outset
- high fraction of asymptomatic cases never tested so trace chain never launched
- high proportion of contacted individuals can't (won't) provide details of close contacts
- difficulty of tracing contacts > 48 hr before, particularly for users of public transportation or visits to large population venues
- no metrics on compliance of contacted individuals to isolate
- financial hardship for lower income households asked to isolate

Superspreading Events (SSE)

- **outsized contribution to overall transmission**
- **analysis of 60 SSE SARS-CoV-2 episodes***
  - **R_0 mean of 19.7 cases**
  - **extreme outlier of 187 cases in Hong Kong apartment**
- **logic for prevention of large gatherings of susceptible individuals and isolation/vaccination of select individuals for pandemic control**

*F. Wong and J. Collins (2020) PNAS 117, 29416

COVID-19: Perceptions of Contact Tracing
Institute of Global Health Innovation Global Report (2020)

- survey of 19 countries on public response to request for contact information
- % of population unwilling to provide
  - Vietnam 4%
  - Germany and USA 20%
  - France 25%
- shortcomings in public health messaging
- public trust, decline of social cohesion and political divisiveness
- distrust greater in US African American community (all aspects, including vaccination)

Individual Rights Versus Public Good

A Well Traveled Advocate for Mask Wearing

The SARS-CoV-2 Diagnostic Landscape

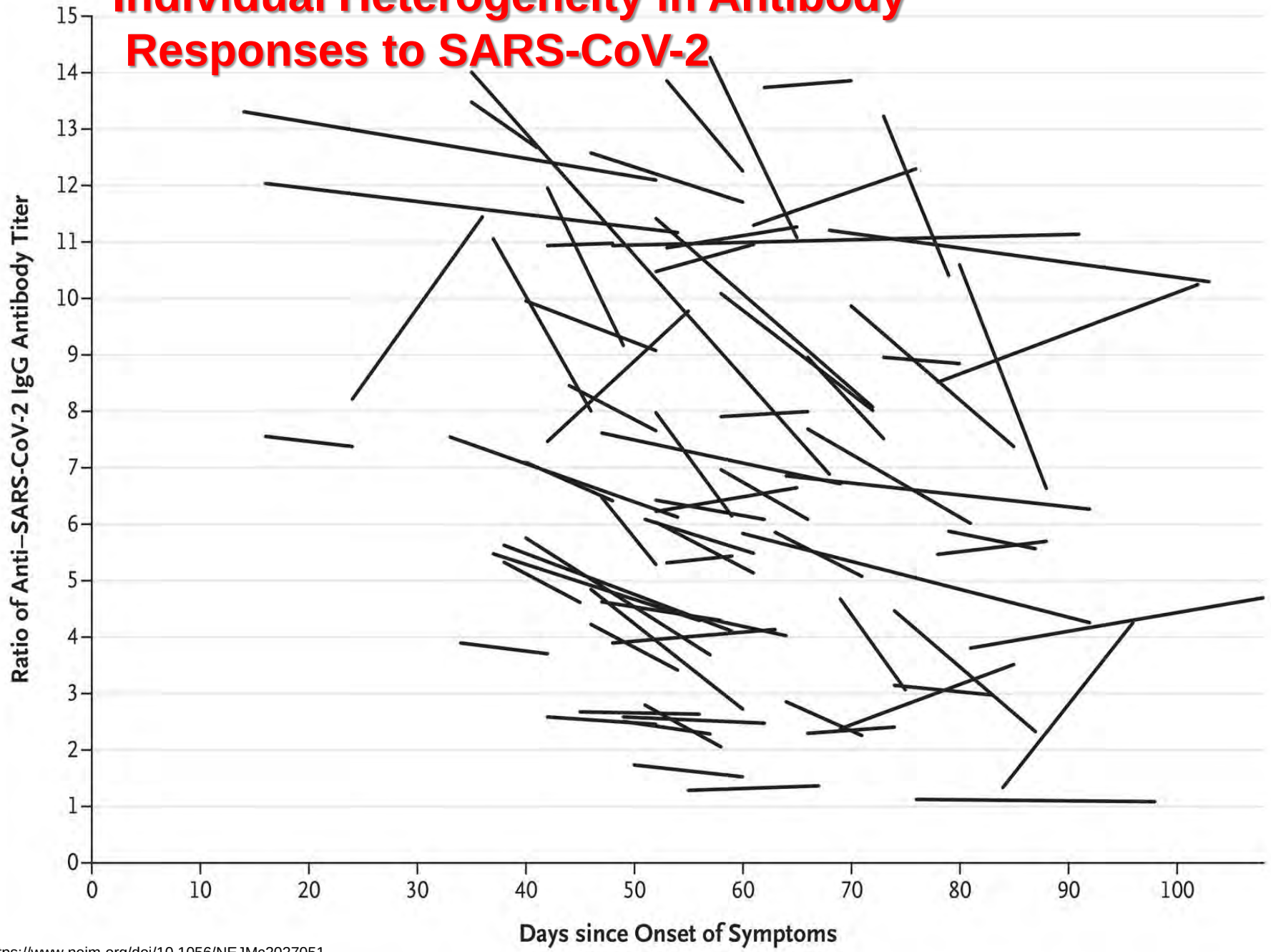
post-recovery and correlates of immune protection	
• infected and vaccinated individuals	• antibody detection - neutralizing antibody (Nab) titers and duration - ratio Nab:non-Nab • T cell responses - CD4, CD8 • inflammatory marker panels

Mobile Phone Apps, Contact Tracing and “Immune Passports”

“Vaccination (Digital) Passports”

- mobile phone-based QR validation of vaccination
- restore ease of international travel and other currently restricted activities (work, schools)
- trustworthy, traceable, verifiable and internationally recognized
- attractive but over simplified concept

Individual Heterogeneity in Antibody Responses to SARS-CoV-2



https://www.nejm.org/doi/10.1056/NEJMc2027051

Immunity Passports:
A Scientifically and Ethically Questionable Concept?

- ill-defined determinants of true immune protection
  - antibodies (neutralizing (Nab) vs non-Nab titers
  - T cell responses
  - duration of immune protection (natural vs vaccine)?
- risk from tests with inadequate specificity (false positives) and low sensitivity tests (false negatives with low antibody titer)

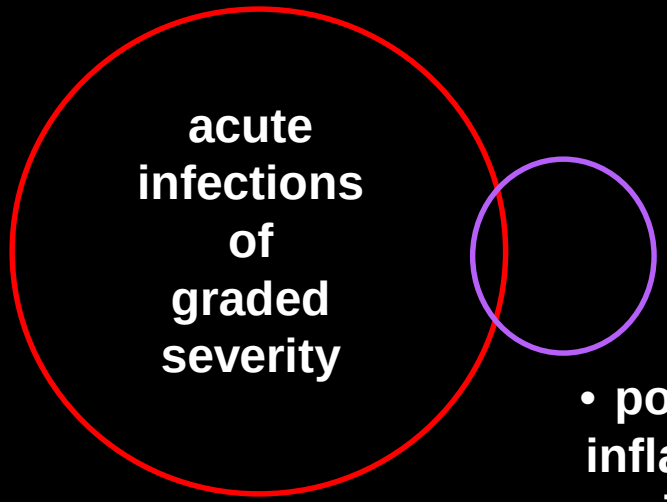
Vaccination (Digital) Passports

- extend to unvaccinated individuals with validated evidence of natural infection?
- antibody titers highly variable in both natural and vaccine-induced immune responses
  - protection threshold definition?
  - test standards for antibody measurements?
- duration of protective immunity and frequency of passport renewal?
- vaccines may reduce transmission but risk that some vaccinees may still be contagious?

Vaccination (Digital) Passports

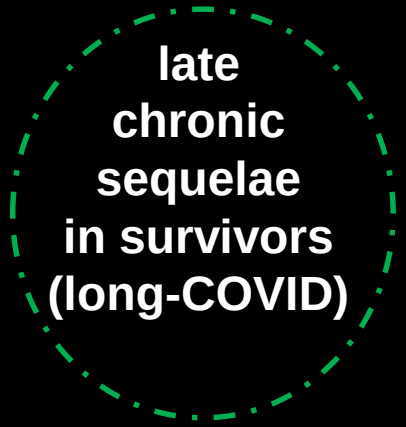
- creation of a discriminatory two-tier world of vaccination haves and have-nots?
  - delayed access to vaccines (risk categories, poorer countries)
- criminal black markets and other fraud risks

SARS-CoV-2 Infections:
Disease Spectrum, Prevalence and Extended Timelines



- asymptomatic vs symptomatic
- lack of biomarkers to predict disease severity
  - immunological
  - genetic
  - SDoH

- post-acute inflammatory illness
  - MIS-C
  - MIS-A



- prevalence?
- pathophysiological mechanisms?
- prognosis?
- duration?
- treatment?

Host Inflammatory and Immune Biomarkers and Prediction of Clinical Deterioration in Hospitalized COVID-19 Patients

- multiparameter clinical risk algorithms
- cytokine storms
- autoantibodies to IFN-I
- decoupling of CD4/CD8 T-Cell responses
- genetics
  - hypo-and hyper-inflammatory response genes
  - ACE2 receptor polymorphism
  - HLA genotypes
  - chromosome 3 Vindija 3.3.19 Neanderthal alleles?

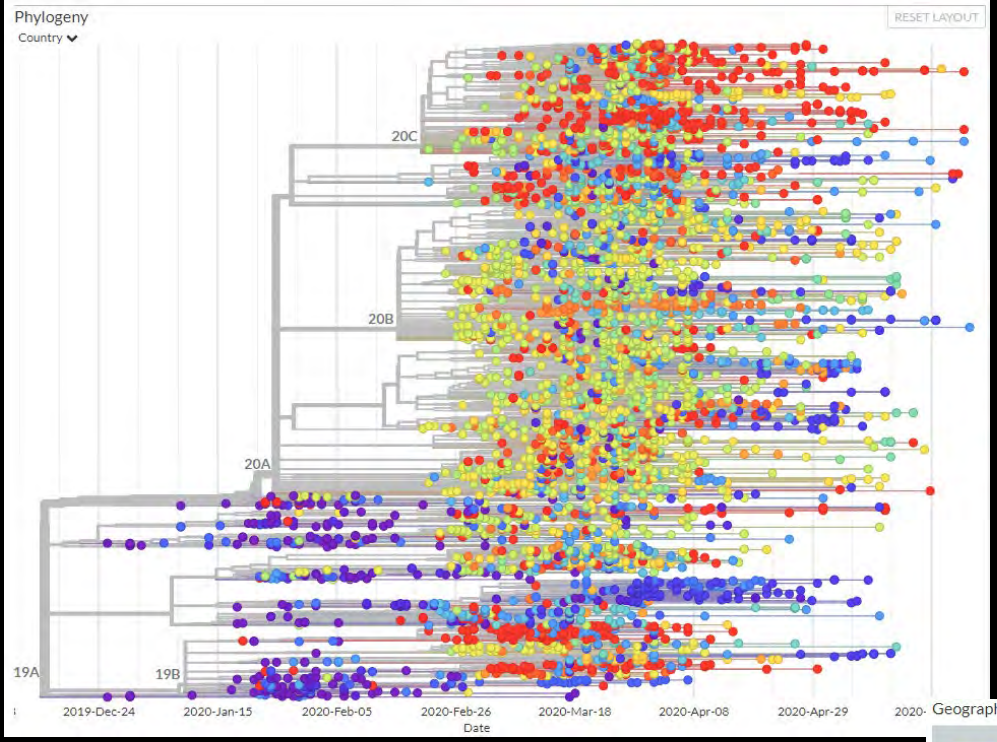
“Long/Long-Hauler” COVID Patients

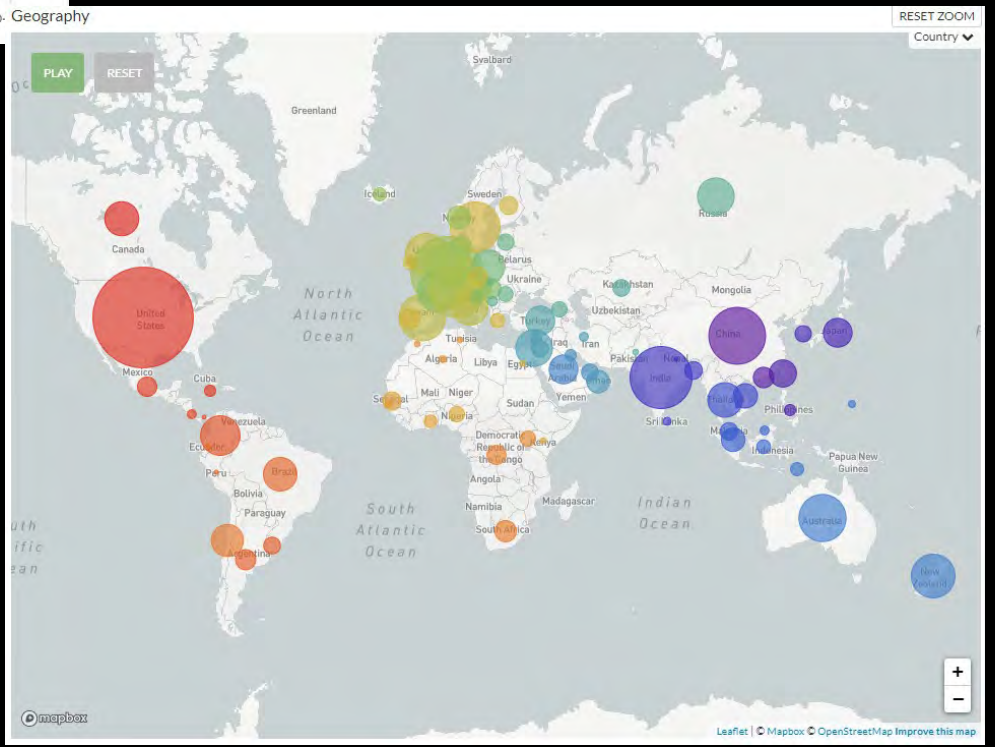
- CDC estimate
  - 30-35% patients with persistent symptoms
  - 1 in 10 with multi-organ symptoms lasting 12 weeks or longer
  - higher in women than men
- manifest in all age cohorts
  - relapsing and remitting clinical course
- ‘syndromic’ constellation of symptoms defies uniform COVID-related diagnosis
- new dedicated recovery clinics and patient registries

Chronic Disease in Post-Acute COVID Infections: "Long/Long-Hauler" Patients

- multi-organ involvement but high inter-patient variation
- cardiovascular, pulmonary and renal effects
- "neuro-COVID"
  - higher incidence in older, severe infection recovery with comorbidities
  - mental fog, impaired memory, anxiety, depression, fatigue
  - risk of myalgia encephalomyelitis/chronic fatigue syndrome (ME/CFS)
- delayed neurologic sequelae in other viral infections
  - SARS-CoV-1, MERS, HIV, Ebola, polio, H.zoster

Global Tracking of Mutational Changes in SARS-COV-2 Samples

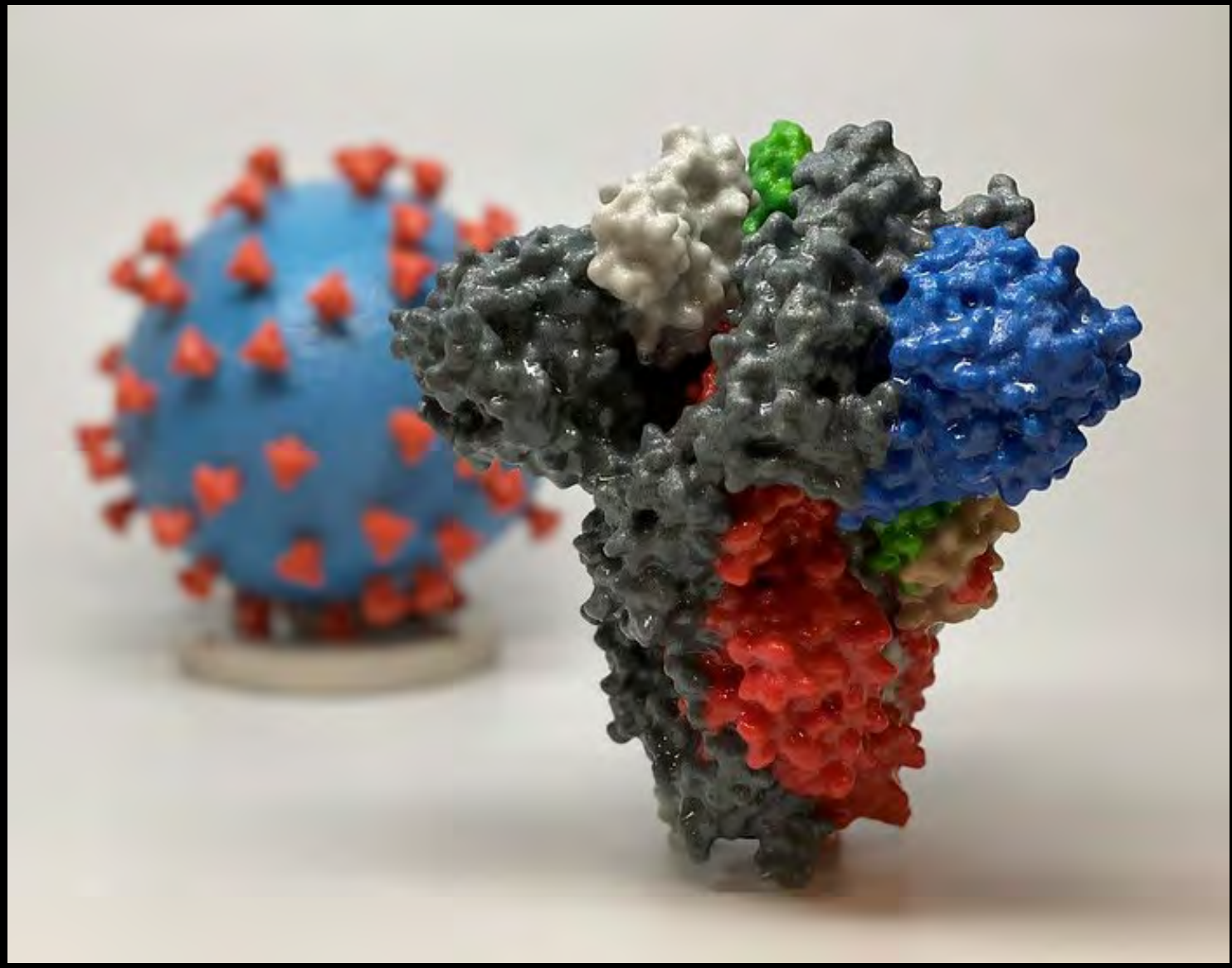




The Need for Coordinated National/International Campaigns for Large Scale Genome Sequencing to Identify and Track New SARS-CoV-2 Variants

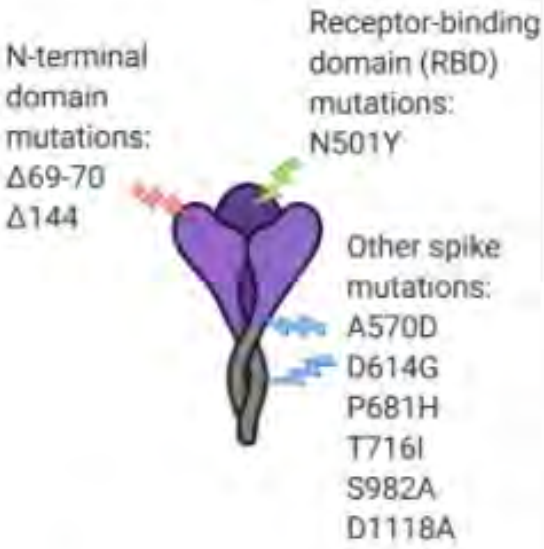
- altered transmissibility and/or virulence
- contact tracing and containment actions
- accuracy of Dx and serology tests
- evasion and/or reduced efficacy of Rx (Mabs) and vaccines

Global Biosurveillance of Mutations in SARS-CoV-2 Spike Protein Implications for Increased Transmission and/or Reduced Vaccine Efficacy



Effect of SARS-CoV-2 mutations on vaccines and therapies

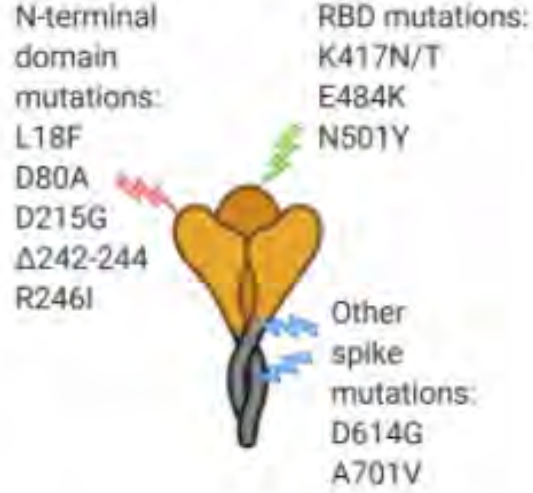
U.K. variant (B.1.1.7 lineage, 501Y.V1)



Impact on efficacy

- ✔ Likely little (vaccines)
- ✖ Possibly high (some mAbs)

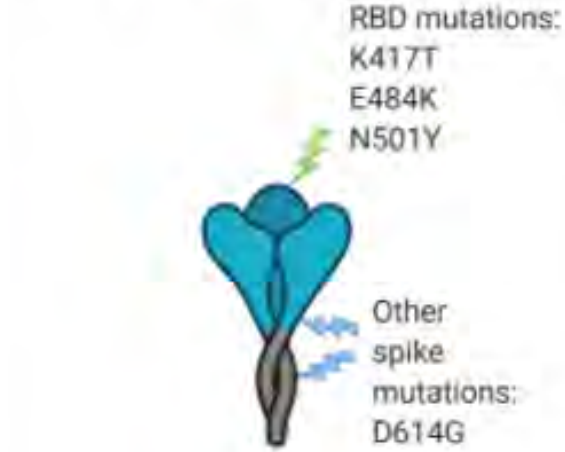
S. African variant (B.1.351 lineage, 501Y.V2)



Impact on efficacy

- ✖ Low to moderate (vaccines)
- ✖ High (some mAbs)

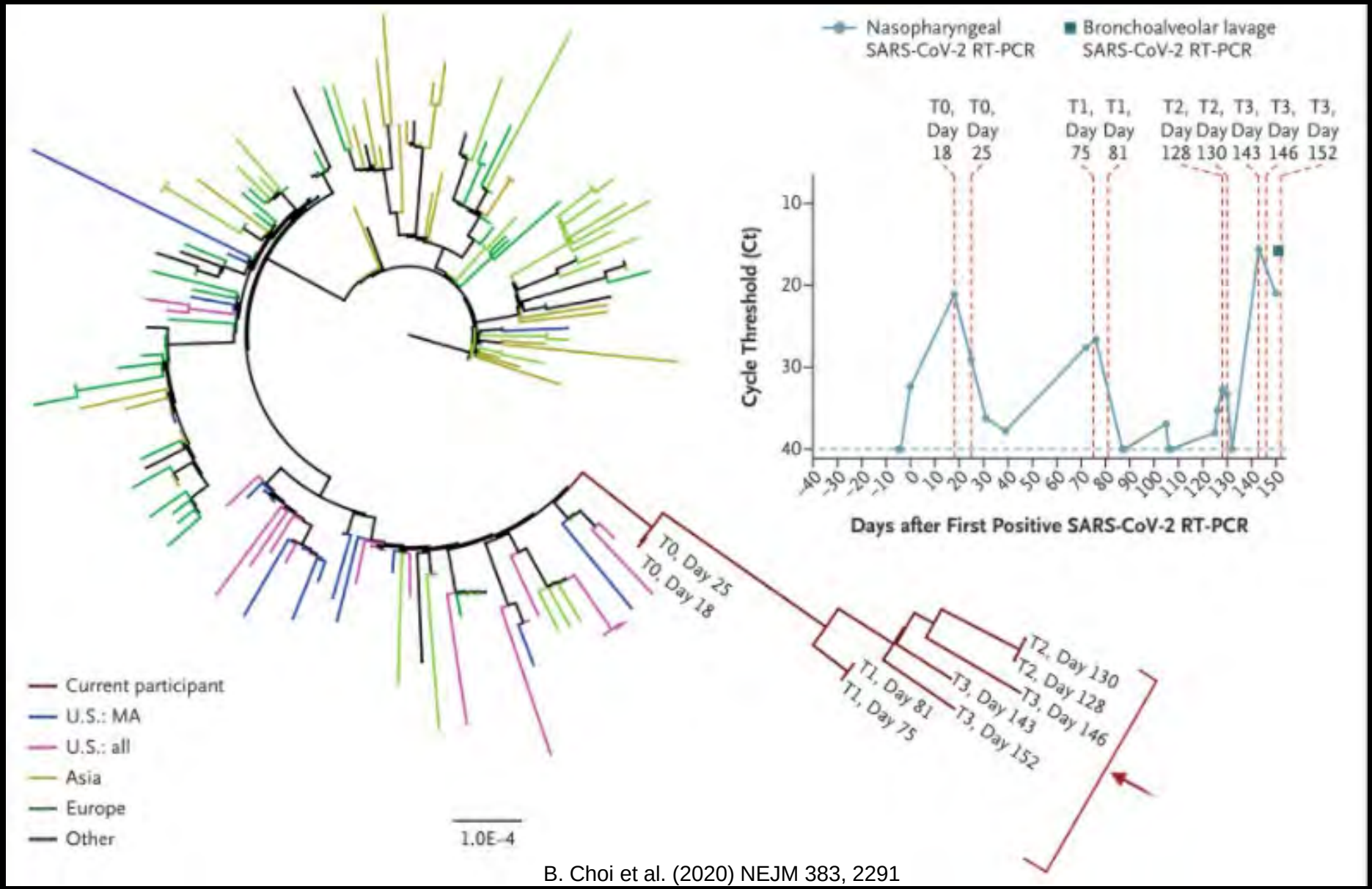
Brazilian variant (B.1.1.28 lineage, 501Y.V3)



Impact on efficacy

- ✖ Low to moderate (vaccines)
- ✖ High (some mAbs)

Global SARS-CoV-2 Phylogenetic Trees and Rapid Evolution in an Immunocompromised Patient *



B. Choi et al. (2020) NEJM 383, 2291

Comprehensive Biosurveillance of Potential New Zoonotic SARS-CoV-2 Reservoirs and Novel Mutational Drift

- cull of 17 million mink (Denmark) due to emergence of new SARS-CoV-2 variant (“cluster 5”)
  - suspected human to mink transmission (spill-back)
- six countries (5EU, USA) reported mink infections to WHO

Evolution or Deliberate Design of SARS-CoV-2 Variants: Challenges for Future Vaccine Design and an Expanded Bioterrorism Threat

Increased Dual-use Risk from Open Literature Publications?

Rapid reconstruction of SARS-CoV-2 using a synthetic genomics platform

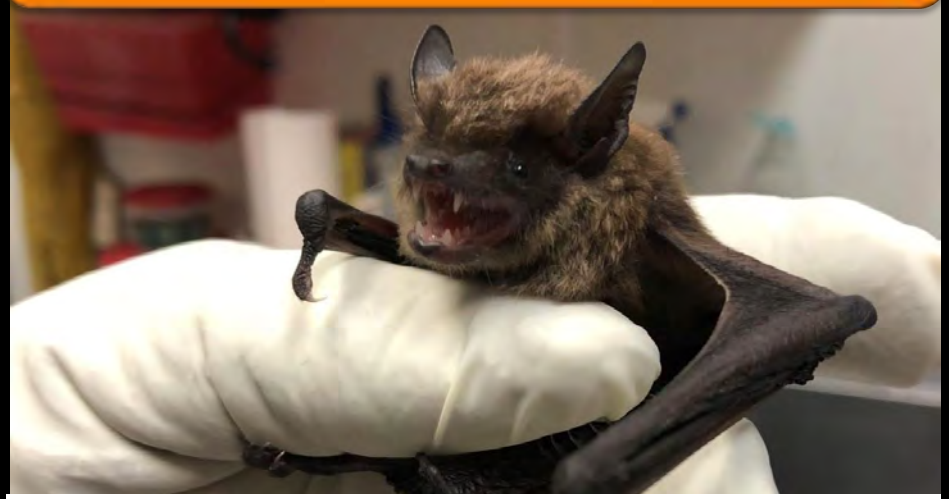
Tran Thi Nhu Thao, Fabien Labroussaa, [...], Volker Thiel *Nature* **582**, 561–565(2020)

Diagnostic Tests:
Forensic Analysis and Attribution of Infectious Episodes of Suspicious Origin

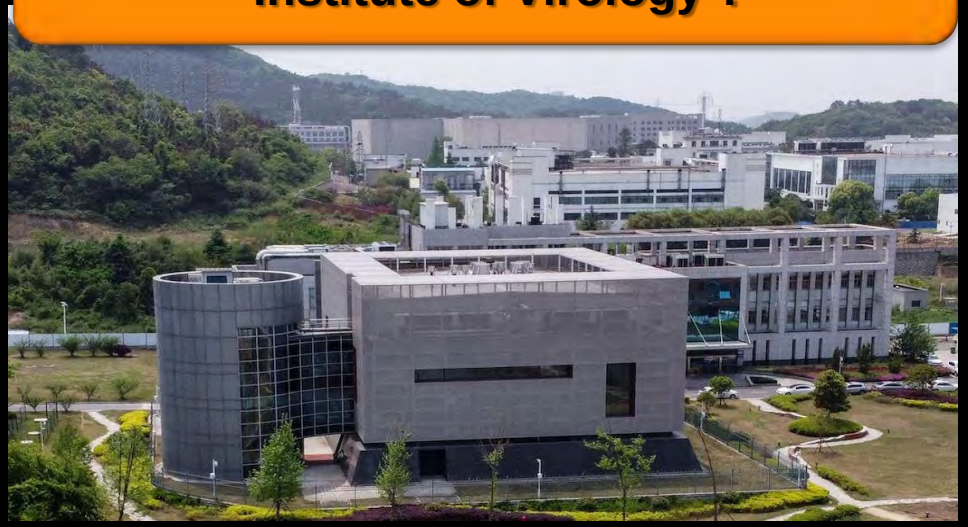
- biowarfare (nations states)
- bioterrorism (substate actors but may have national sponsors)
- bioerror (containment breaches)

The Origins of SARS-CoV-2

Bat-Derived Zoonose?
Additional Intermediate Host ?



Biocontainment Breach at Wuhan Institute of Virology ?



Wuhan Visit by WHO Panel (1/21)

2021 Intensified Chinese State Media Propaganda of US Origin

Social Media Conspiracy Theories: Chinese and Russian Campaigns to Undermine COVID-19 Vaccination Programs

- highlight ‘deaths’ (Norway) and ‘side effects’ for Pfizer/BNTech, Moderna and AZ/Oxford vaccines
- Russia
  - expansion of prior anti-Vaxx propaganda
- China

  - increased disinformation efforts after SinoVac vaccine only achieved 50.4% efficacy
- cyberattacks on US/EU vaccine companies and EU regulatory agencies

  - industrial espionage

A Critique of the US Response to COVID-19

- politics plus science = politics = consistent inconsistency
- lack of coherent national policies and assignment to individual states
  - erratic and policies and variable implementation of testing and ‘lock downs’
  - states forced to compete for purchase of critical PPE and diagnostic resources
- ambivalent Federal and State actions on value of face masks and social divisions
- conflict and confusion in USG messaging plus proliferation of disinformation on social media
- failure of top USG officials to model best practices

- what went wrong?
- how can control measures be improved rapidly to address persistent problems?
- how do we develop robust preparedness against an inevitable future pandemic?
- evaluation of public policy and institutional competencies, infrastructure and investment in preparedness

Enhanced Biosecurity: Will COVID-19 Be The Much-Needed Wakeup Call?

- biosecurity must be prioritized by governments as having equivalent status to macroeconomic and trade policies, foreign affairs and military threat doctrines in national security policy
- implementing this objective may be the most important challenge of the next quarter century
- radical institutional reforms and sustained investment
- need for greater sophistication and technical knowledge among political leaders

The Threat from Pandemic Influenza Remains!

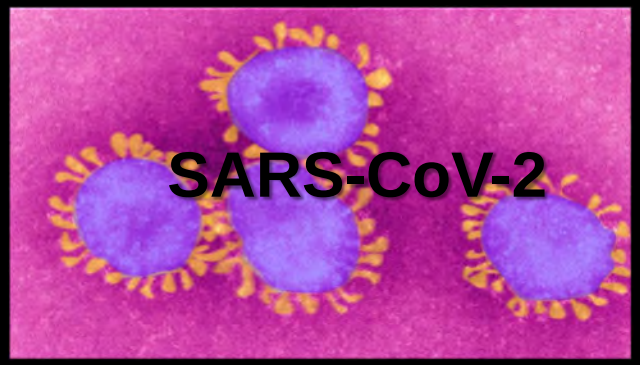
From Oct. 5, 1918.

The Relentless Ever-Changing Dynamics of Infectious Diseases

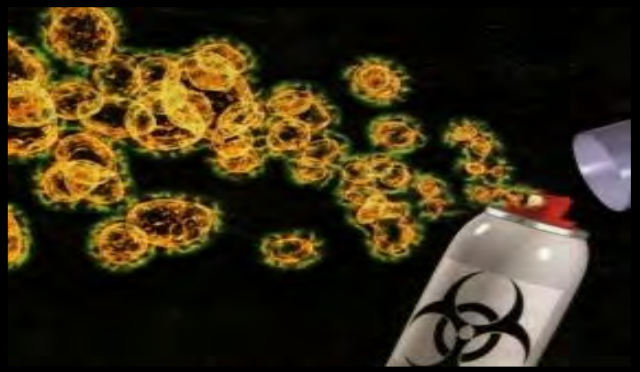
old foes resurgent: Rx – resistance

omnipresent pandemic threats

new foes: emerging infectious diseases



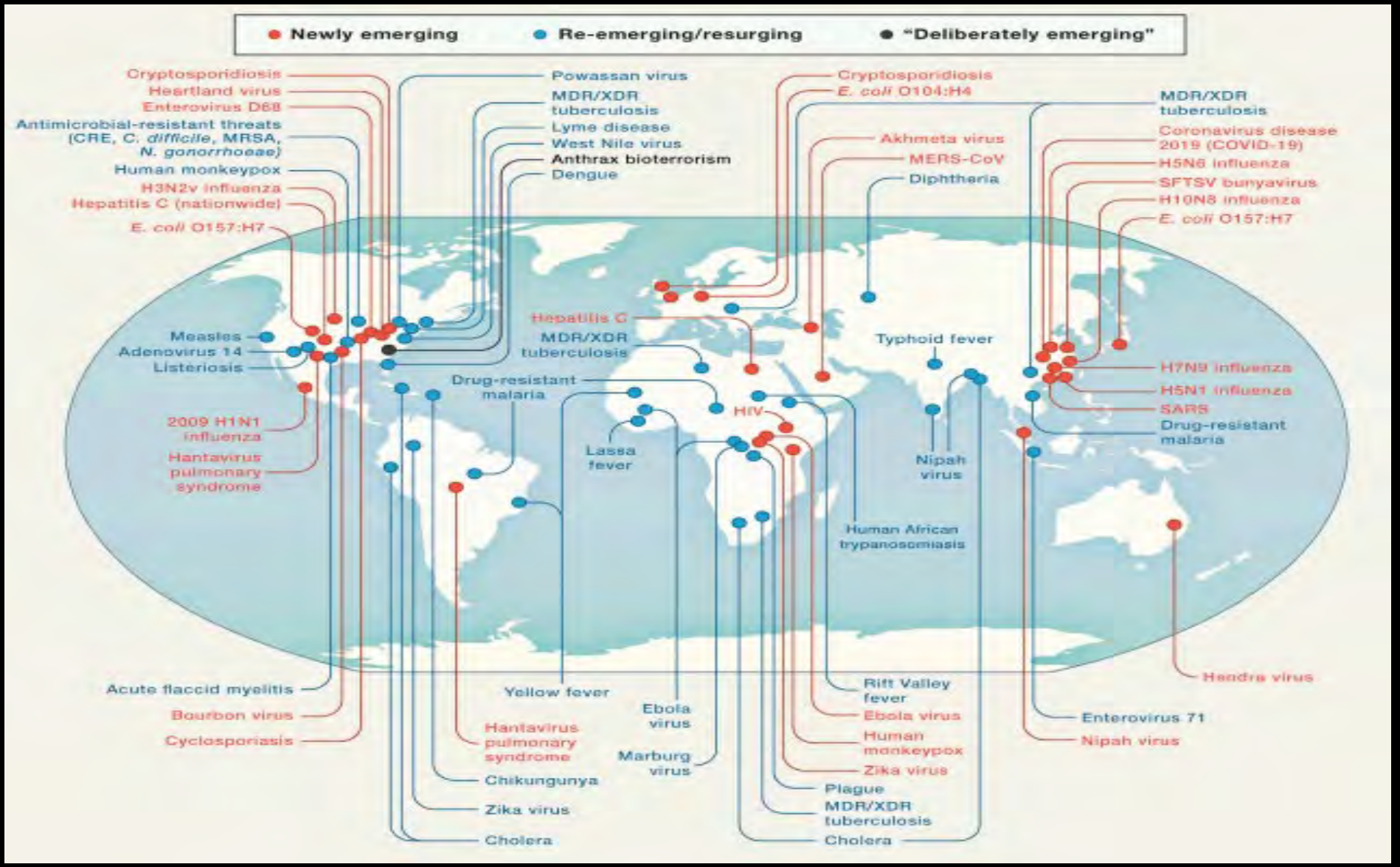
climate change and new vector ranges



bioterrorism and bioweapons

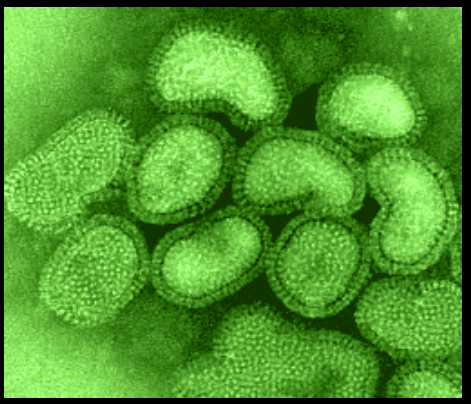
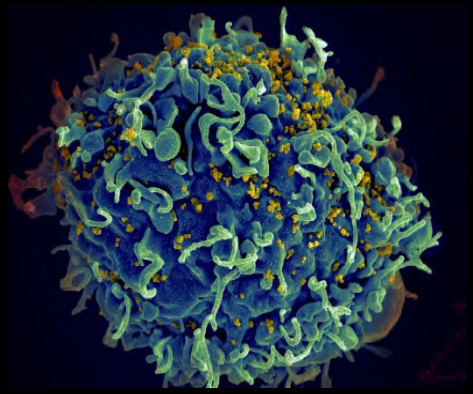
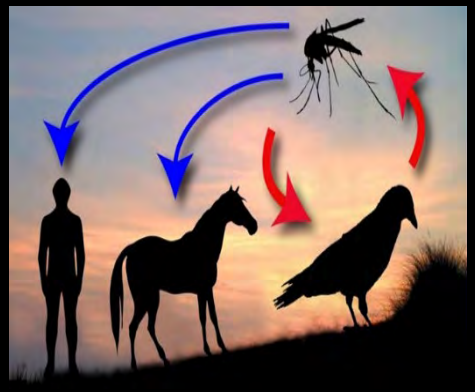
dual-use research of concern

Recent Emerging Infection Diseases



Cell 182, D. Morens, A. Fauci (2020), 1082 https://www.cell.com/cell/pdf/S0092-8674(20)31012-6.pdf

“One Health”- The Importance of Zoonotic Diseases as Human Health Threats: A Rich Reservoir for EIDs and Genetic Manipulation

pandemic (avian) influenza	HIV	West Nile virus	MERS- CoV
			
			
Ebola virus	bush meat food chain	Zika virus	what’s out there?

Urbanization and Mega-Cities in Developing Countries and the Increased Threat of Exotic Zoonotic Diseases

High Population Density With Inadequate Biosurveillance

Expanded Eco-niches and New Zoonotic Exposures/Risks

Major Gaps in Health Infrastructure and Rapid Disease Reporting

Anthropogenic Effects on Ecosystem Stability and Altered Patterns of Infectious Diseases

famine

contaminated water

no water and desertification

depletion of natural resources

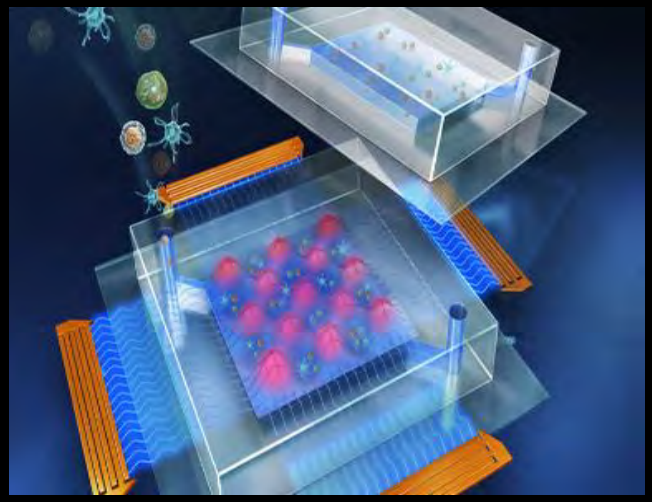
climate change and new vector ranges

new vulnerabilities

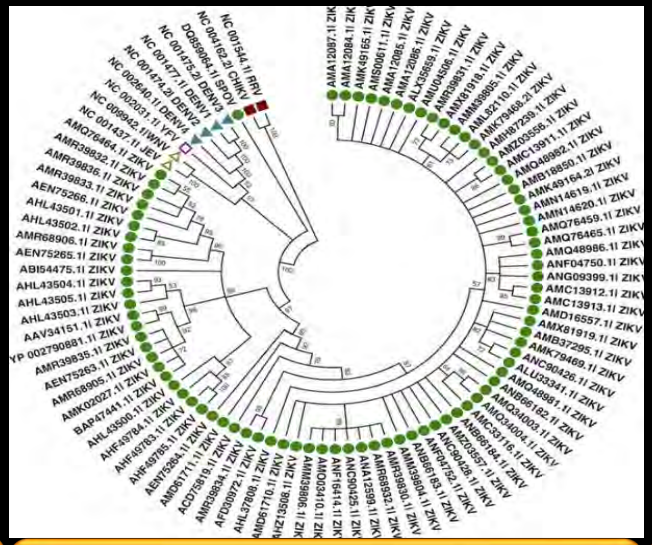
Faster Detection Saves Lives:
The Primacy of Diagnostics in Biosurveillance and Preparedness Mobilization

Profile:
signatures of infectious agents

Detect:
rapid automated PON/POC diagnostics



Act:
real-time situation awareness, decisions



surveillance
sans frontières

genomics of
pathogen evolution

dual-use research and
engineered biothreats

Proactive Investment in Preparedness

Public Sector Responsibilities and Private Sector Incentives

Large Scale Molecular Diagnostics, Therapeutics and Vaccines for COVID-19: Critical Dependence on Private Sector Innovation and Investment

Society's Love: Hate Relationship With the Biopharmaceutical Industry: Taking Innovation for Granted

- estimated two-decade lifetime expansion in lifespan from 1950 onwards
  - heart disease/diabetes
  - infectious diseases (antibiotics and vaccines)
- among the most technologically sophisticated and highest R&D investment of any industry
  - $1.5 to 2 billion per Rx/10-15 years R&D
  - 600-800million per vaccine/5-25 years R&D

‘Market Failure’
Lack of Incentives for Development of Medical Countermeasures (MCMs)

- new incentives for private sector to undertake high risk/high-cost R&D absent guaranteed markets and ROI
  - neglected diseases of the developing world
  - antibiotic resistance
  - MCMs for biowarfare select agents
  - emerging infectious diseases

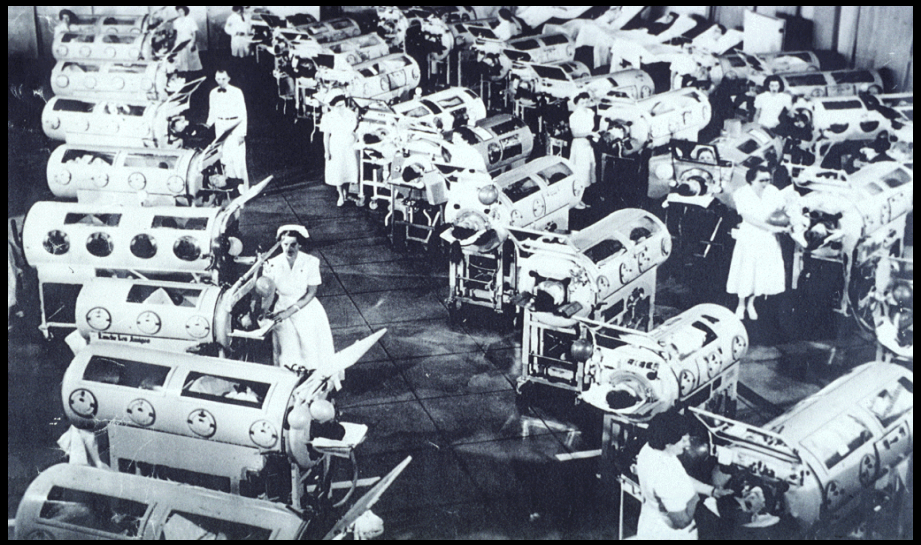
Unfortunate Truisms in Public Health: Comfort and Complacency Erode Robust Preparedness

Out-of-Sight, Out-of-Mind

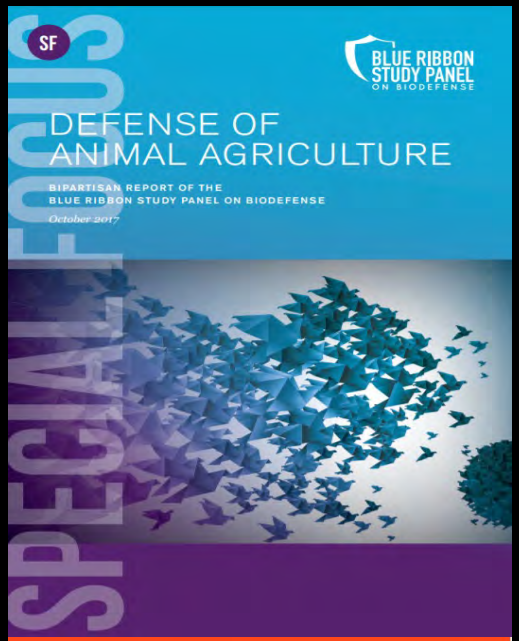
If Nothing Happens, the Preparedness Budget Gets Cut

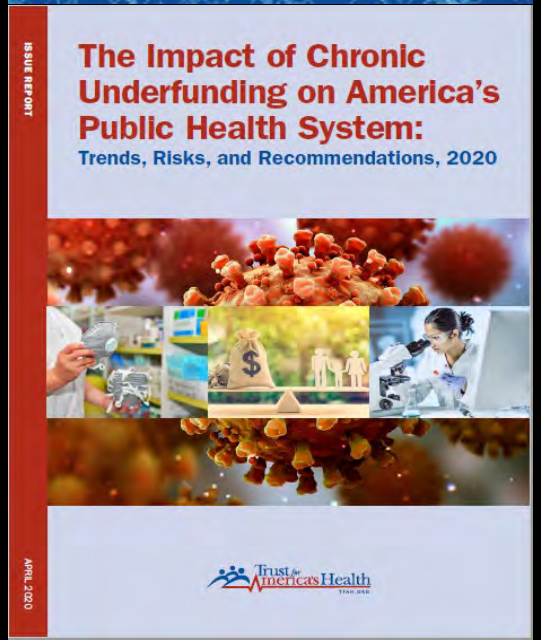
Why Don’t We Learn from History?

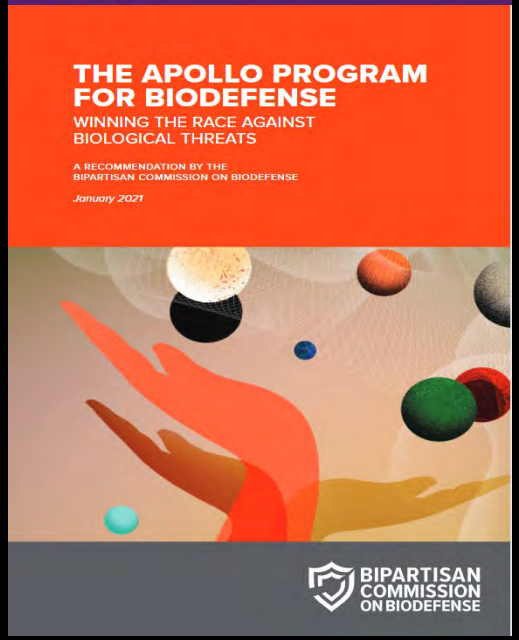
Comfort and Complacency: The Enemies of Vigilance and Preparedness



“Fits and Starts: Reactionary Biodefense”
From Complacency to Crisis and Back to Complacency







Presidential Encounters with Infectious Disease

WH Directives and Memoranda

- Presidential Policy (PPD)
- National Security (NSPD)
- Homeland Security (HSD)
- National Security Memoranda (NSPM)

- HIV

- Military Medicine: force protection and projection

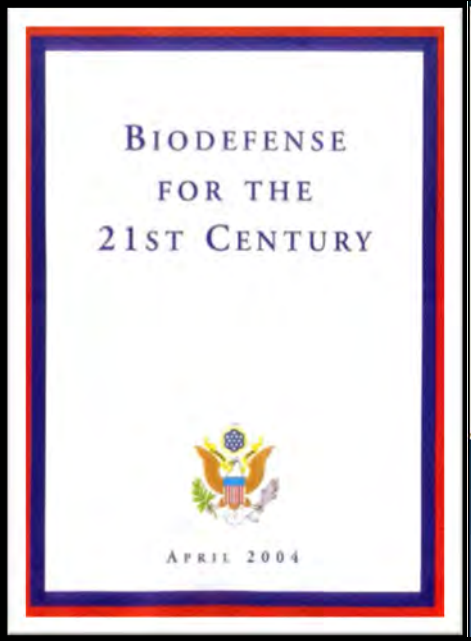
- West Nile
- PPD (x3)

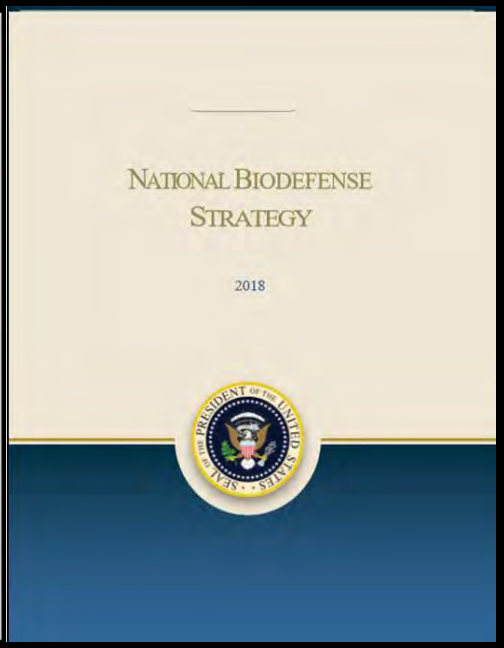
- Anthrax
- PEPFAR
- SARS
- HSD 4,10,18, 21
- NSPD 17,33
- PPD 10

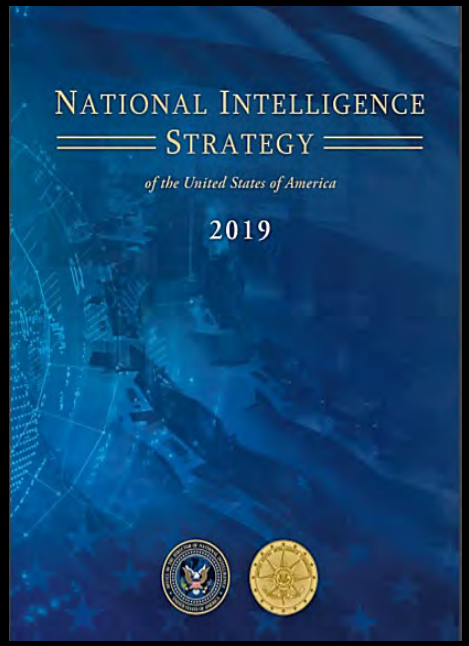
- H1N1 influenza
- MERS
- Ebola
- Zika
- Chikungunya
- HSPD 17
- PDD (X2)

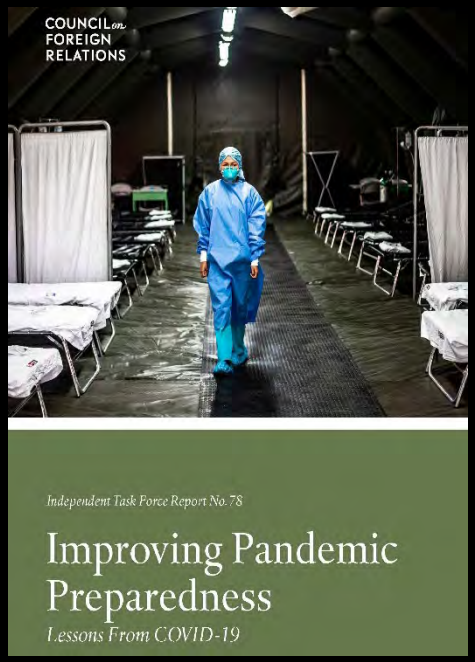
- NSPM 7, 14
- PRC - espionage
- SARS-COV-2
- ???

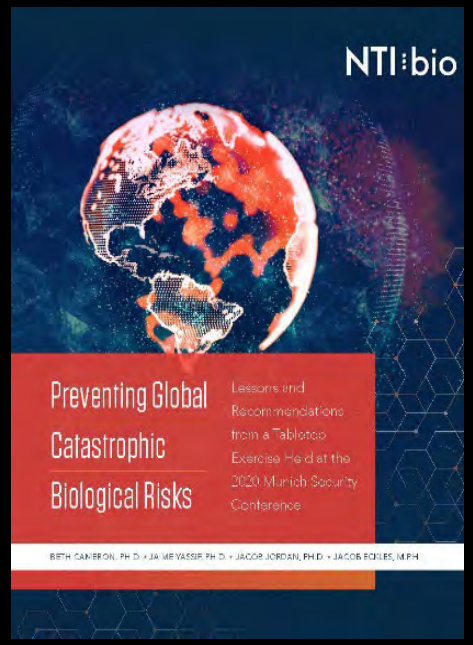
U.S. National Security Policy and Biodefense

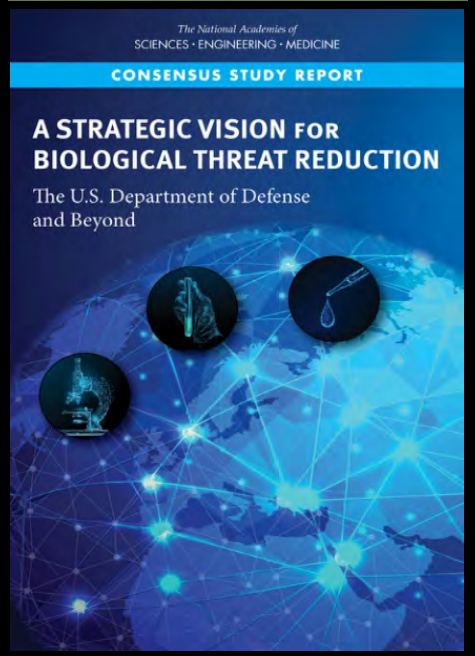












U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
OFFICE OF THE ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

CRIMSON CONTAGION 2019 FUNCTIONAL EXERCISE AFTER-ACTION REPORT

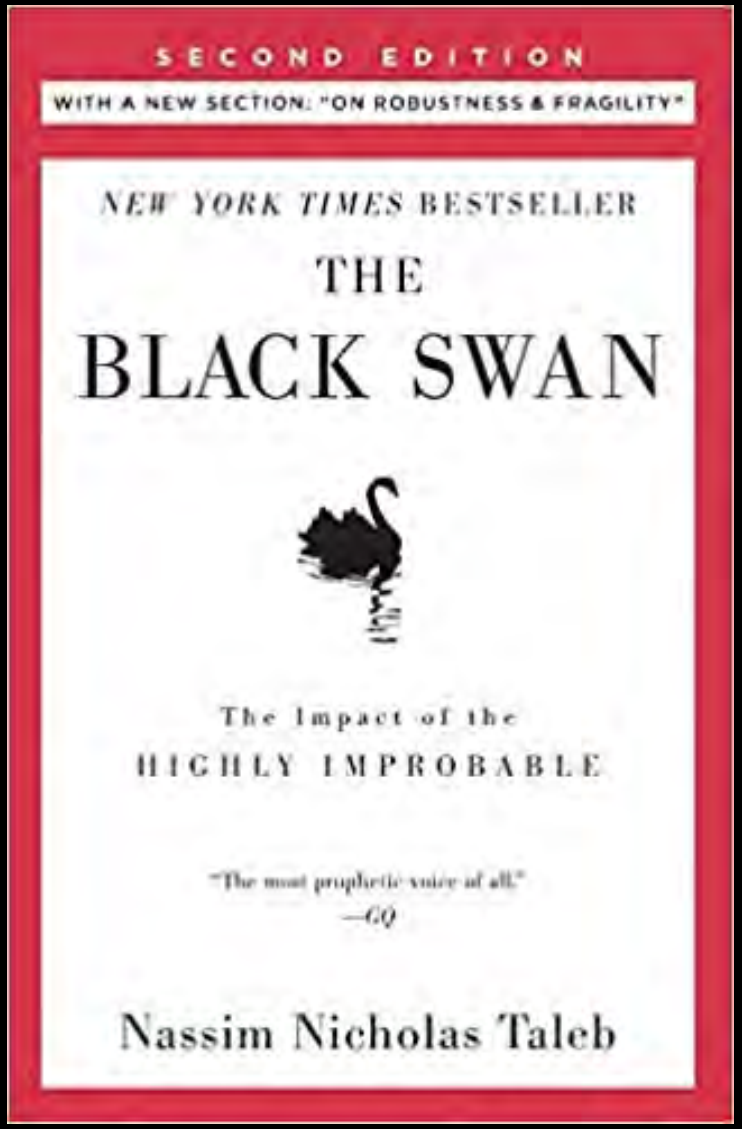
JANUARY 2020

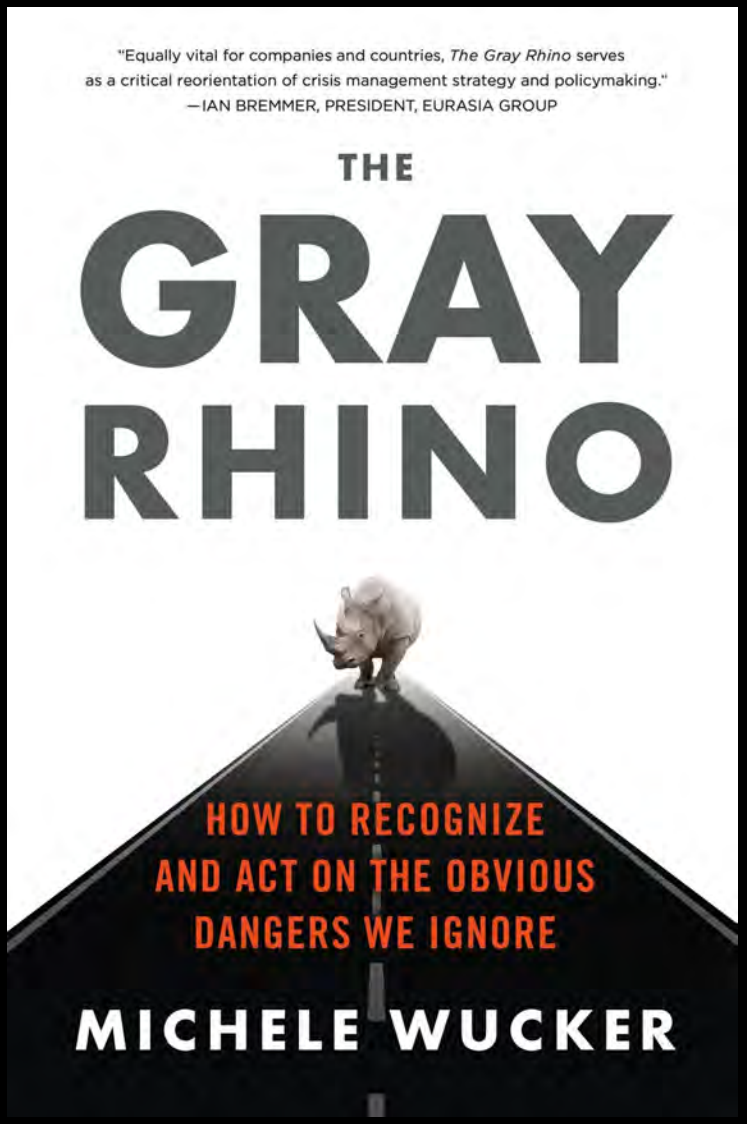
PRESIDENT JOSEPH R. BIDEN, JR.

National Strategy for the COVID-19 Response and Pandemic Preparedness

JANUARY 2021

Risk Awareness and Risk Perception: Black Swans Versus Gray Rhinos





‘Black Swans’

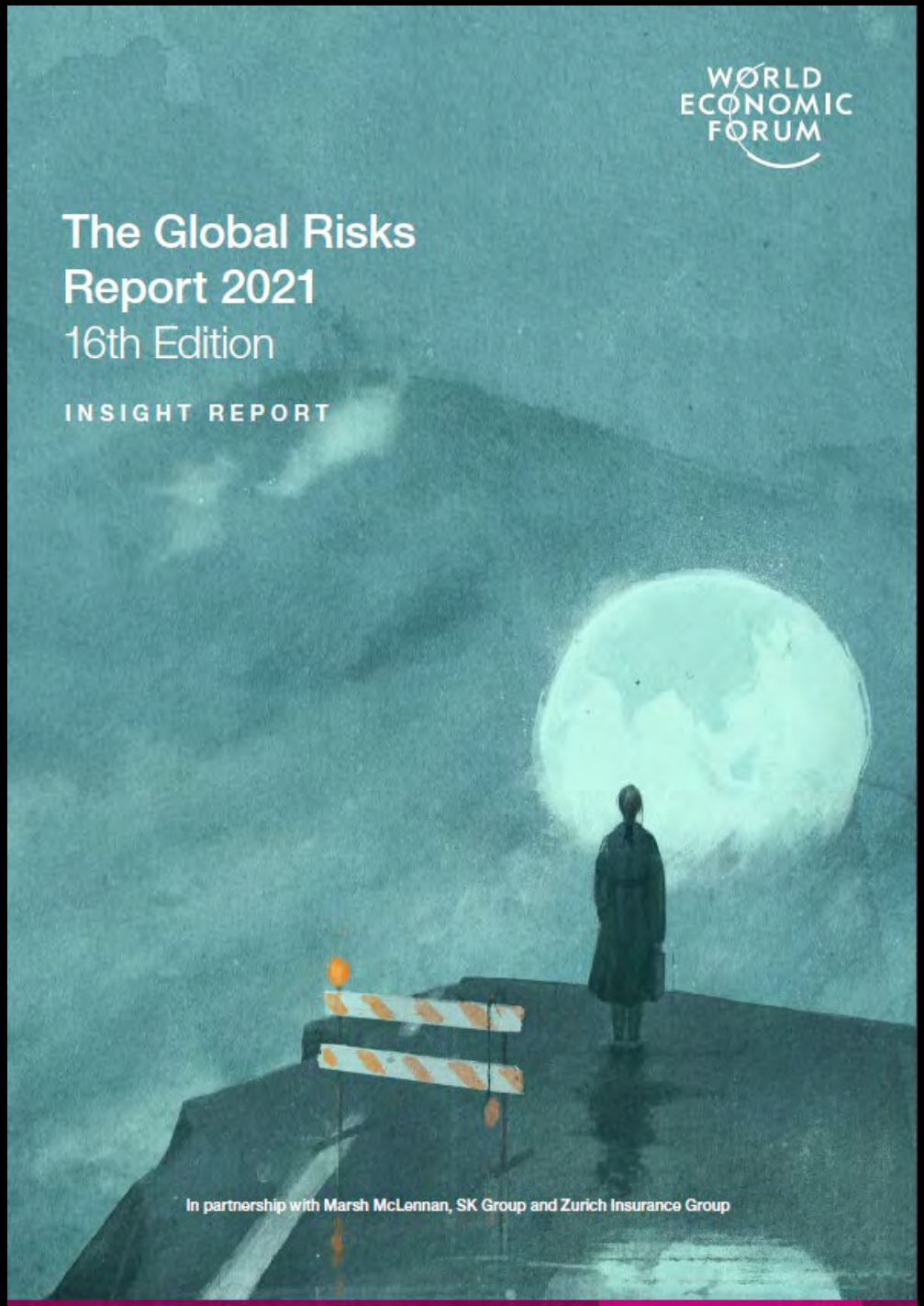
- highly improbable and/or unimaginable events
- no apparent ‘prodromal’ warning sings
- intellectually lazy and disingenuous excuse that nothing can be done to prepare
- warning signals always there but widely ignored and/or denied
  - 2008 financial crash: derivatives; sub-primes
  - escalating cyber attacks by Russia and PRC
  - intensity of PRC industrial espionage and IP theft

‘Black Swans”:
The Delusion of the Inability to Plan for Known Risks

- encourages willful ignorance
- obfuscates accountability
- short-termism as major barrier to longer – term risk assessment and preparedness
  - governments, corporations, society

Gray Rhinos

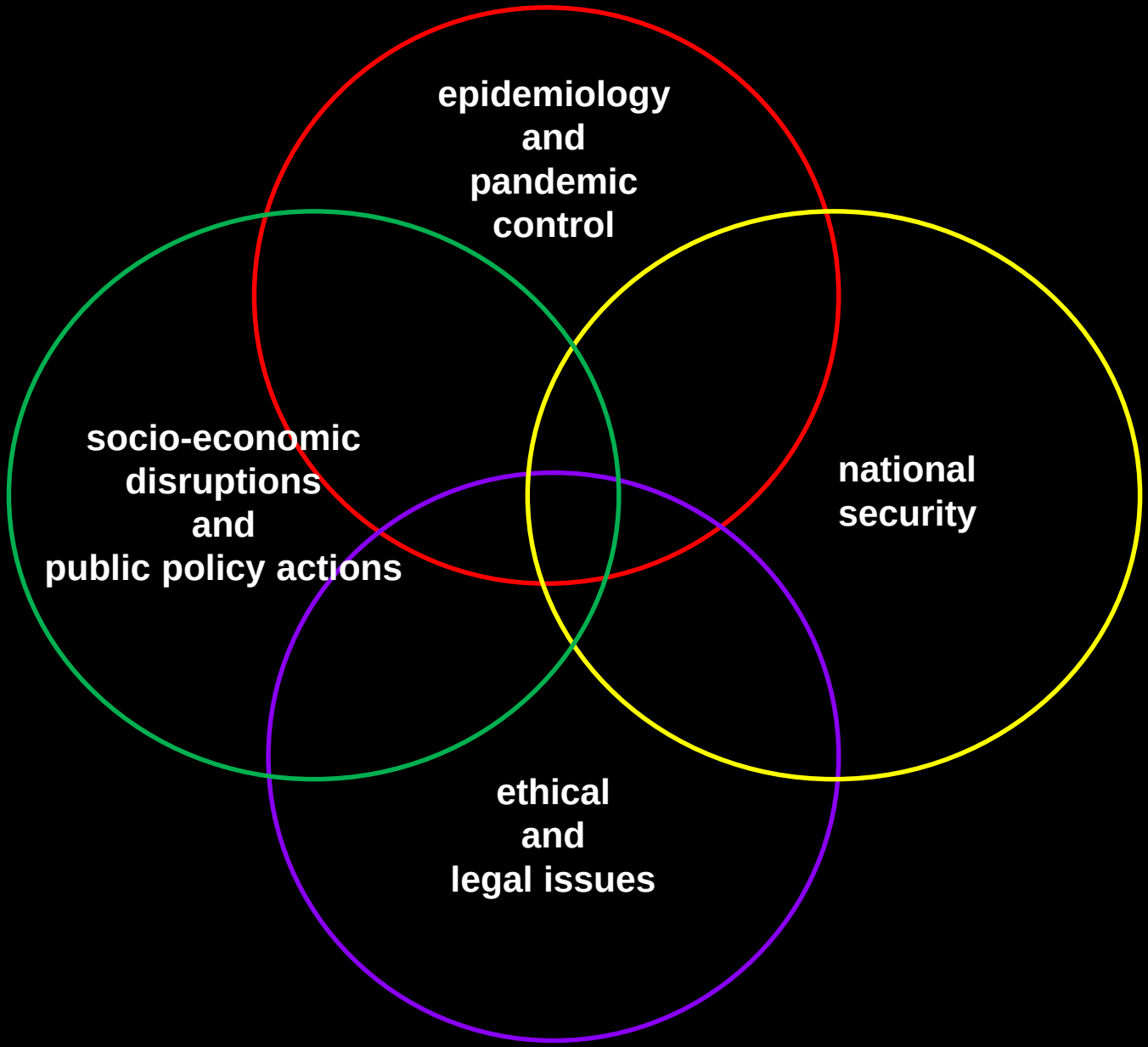
- slow moving but with the potential for profound disruption
- documented risk but typically dismissed incorrectly as low probability threats
- prior warning signs (acute or cumulative)
- resulting disruption reveals the stark consequences in public policy, preparedness and crisis management competences


WORLD ECONOMIC FORUM
The Global Risks Report 2021
16th Edition
INSIGHT REPORT
In partnership with Marsh McLennan, SK Group and Zurich Insurance Group

The Curse of Contemporary Governance: 'Quick Fixes' and the Retreat from Complexity

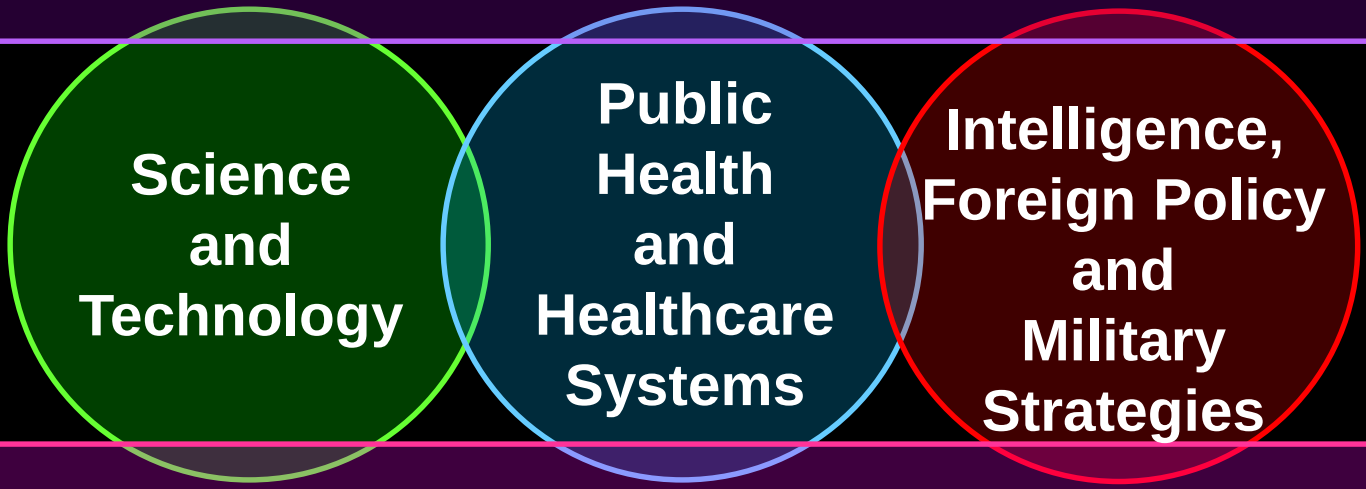
- false comfort and complacency
  - society increasingly "cocooned" from complexity and risk
- pervasive and dangerous scientific illiteracy among legislative and policy makers about biosecurity
- "quick fixes" unidimensional, short term policies that
  - do not address long term, multidimensional complexity
- public policy defined increasingly by length of legislative terms
- influence of media in shaping public policy priorities and potential compromise of operational preparedness

The Complex Landscape of Pandemic Disease



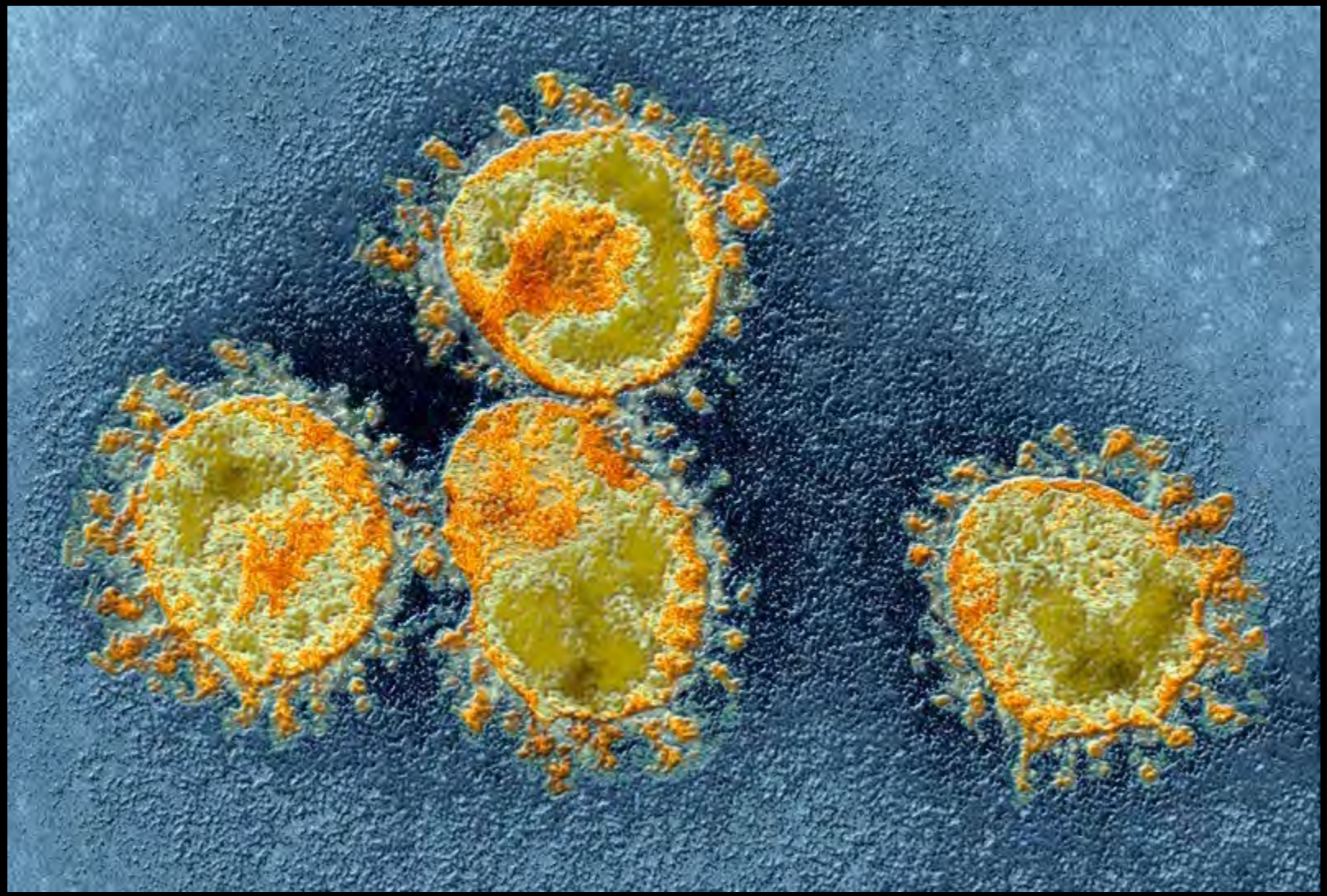
Biosecurity:
A Classic Complex System of Systems Challenge

- global perspectives
- biological, socio-economic, and political ecosystems



- societal priorities and cost of biosecurity
- proactive preparedness
- conflicting political ideologies, intents and capabilities (global and national)

A World Transformed By SARS-COV-2



**“There are decades where nothing happens
and there are weeks where decades happen.”**

Vladimir Lenin (1917)

**“Every few hundred years throughout Western history
a sharp transformation has occurred
In a matter of decades, society altogether rearranges itself
- its world view, its basic values,
its social and political structures,
its arts, its key institutions .”**

**Peter Drucker (1992)
Harvard Bus. Rev. Reprint 92503**

**“Politics is the art of the possible,
the calculated science of survival”**

Prince Otto von Bismarck

**“Survival owes little to the art of politics,
but everything to the calculated application
of science”.**

**Professor Rudolph Virchow
(in reply)**

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