

Delay, Detect, Defend

Preparing for a world in which thousands of individuals can ignite new pandemics

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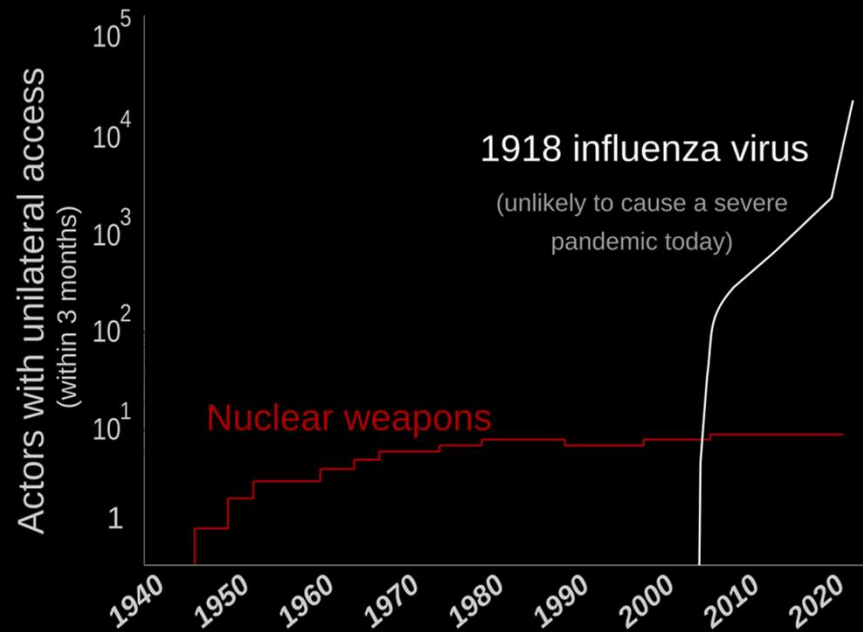
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Pandemic viruses can kill more people than any nuclear detonation



Like nuclear weapons, they cannot be blocked



Unlike nuclear weapons, they will become widely accessible...

unless we act

Proliferation cause #1: virus assembly protocols + the bioeconomy

~30,000 individuals can single-handedly assemble influenza viruses

(125 U.S. Virology PhDs per year) * (4 from other fields) * (3 for other countries) * (20 year career) = 30,000

“(Virus assembly) systems are available for virtually all virus families, and the rules of engagement for new virus creation are well-established... it is now a relatively straightforward matter to generate and test new virus configurations using what now amounts to the world’s best Lego set.”

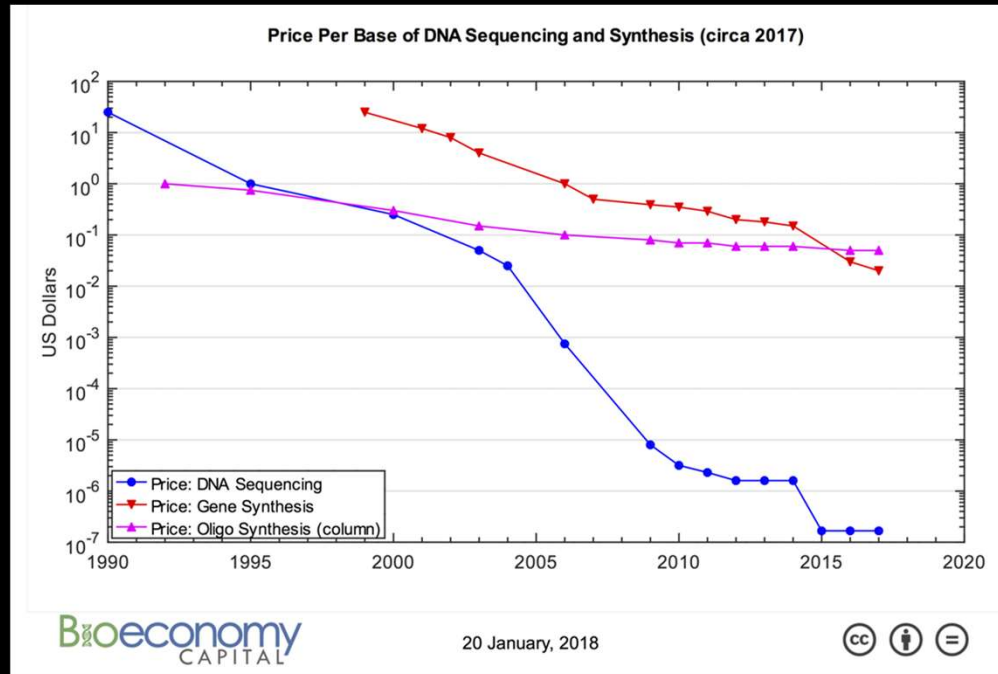
National Center for Science and Engineering Statistics. 2019. <https://nces.nsf.gov/pubs/nsf21308/data-tables>

OECD graduates by field: https://stats.oecd.org/Index.aspx?DataSetCode=EDU_GRAD_FIELD

J Maroun, M Munoz-Alia, A Ammayappan, A Schulze, K Peng, S Russell (2017) *Future Virology*

Xie X, Lokugamage KG, Zhang X, Vu M, Muruato A, Menachery V, Shi P (2021) *Nature Protocols*

Proliferation cause #2: exponentially improving DNA/gene synthesis



1000x lower
since the first
virus assembly

Cost to make the DNA for infectious 1918 influenza virus: under \$1,000 USD

Cost to make the DNA for infectious SARS-1 virus: ~\$2,200 USD + manual assembly

Proliferation cause #3: pandemic virus identification (has not happened yet)

Q: How can we learn whether a newly isolated or engineered virus could cause a new pandemic?

A: Compare relevant traits to circulating human viruses of the same family

Do (immune-novel) animal or synthetic viruses...

- Infect relevant human primary cells >25% as well?
- Grow in relevant human primary cells >25% as well?
- Transmit between relevant animal models >25% as well?

Do (already-fit) engineered human viruses...

- Trigger <25% of the normal innate immune response?
- Trigger <25% of the normal humoral immune response?
- Trigger <25% of the normal cell-mediated immune response?

These experiments are the virological equivalent of nuclear testing

Credible pandemic virus identification will cause the number of actors capable of killing millions to rise >1,000-fold

Many well-meaning agencies and NGOs are actively trying to identify pandemic-capable viruses



Characterizing animal viruses to learn which could start new pandemics



Enhancing highly lethal agents to make them more transmissible
("gain-of-function" research)



Discovering and publicly listing all credible pandemic viruses in nature

Other recent funders (possibly not current): National Natural Science Foundation of China, China Mega-Project for Infectious Disease, Ministry of Science and Technology of China, Chinese Academy of Sciences, EU FP7 program EMPERIE, EU Human Frontier Science Program, Nederlandse Organisatie voor Wetenschappelijk Onderzoek, German Research Foundation

Expected value models suggest pandemic virus identification will cost >100x as many lives as it could possibly save

There are >100x as many pandemic-capable viruses in nature as will cause pandemics, so identifying one prevents at most 1/100 of a pandemic
That one virus will permit misuse, and a 1% annual chance equates to one expected pandemic

Pandemic virus identification does not accelerate vaccines as we can't run Phase II trials on a virus that hasn't infected a human

A roadmap to a world without pandemics

Delay

- Pandemic Test-Ban Treaty
- Liability+insurance for catastrophe
- Universal DNA synthesis screening

Detect

- Sequencing for reliable detection

Defend

- Sufficiently protective equipment
- Transmission-blocking infrastructure
- Societal pandemic resilience

Delay: Pandemic Test-Ban Treaty

Ban the virological equivalents of nuclear testing

- A Pandemic Test-Ban Treaty would be highly effective because it only needs to bind the well-meaning
- Rogue states and extremists claiming to wield pandemics *are not credible*: it's easy to fake the data

The banned experiments *do not help* vaccine and antiviral development; only a handful of labs perform them

Why is the Biological Weapons Convention insufficient?

- Article III: never to assist anyone... to manufacture or otherwise acquire biological weapons
- Article IV: take any national measures necessary... to prevent the acquisition of biological weapons within a State's territory
- Article X: have the right to participate in the fullest possible exchange of information for peaceful purposes

Article X arguably covers assisting 30,000+ actors in acquiring biological weapons capable of killing millions...

Delay: Liability

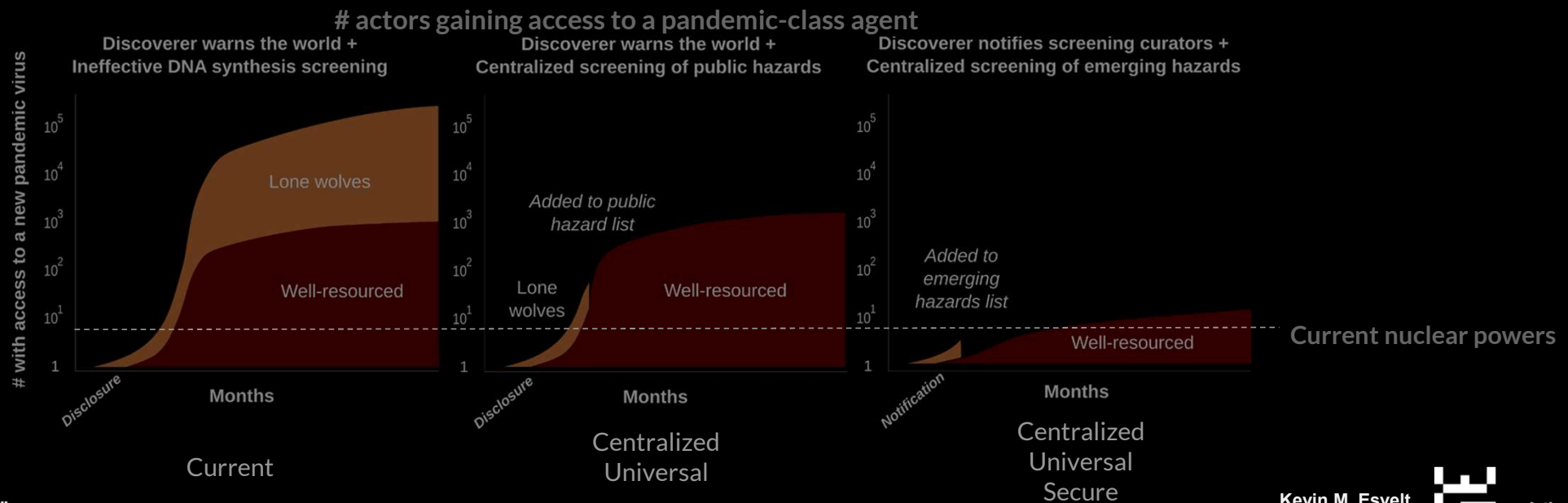
Make those who disclose key information liable & require insurance for catastrophic misuse

- To avoid harming research, set a threshold at which liability kicks in (e.g. 1 million casualties globally)
- Invite the insurance industry to model catastrophic risks and charge for foreseeable externalities

Delay: Secure and Universal DNA Synthesis Screening

Require commercial providers and device manufacturers to screen as soon as a free solution is available

- It must be possible to update the screening system immediately when a new pandemic-class agent is identified
- The screening system must not be located solely on the device (or it can be bypassed too easily)

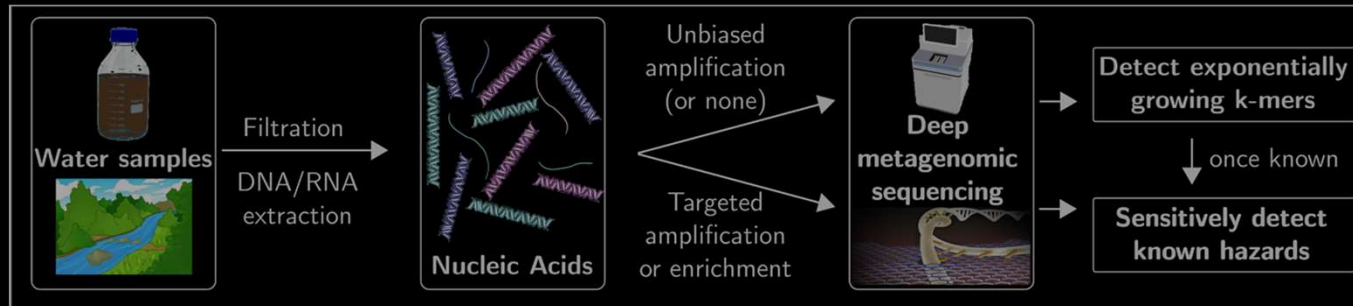


Detection: Reliably Identify Every Threat

Sequence all nucleic acids in travel hubs and look for exponential growth

- Does not assume there will be any clinical signs or symptoms of infection
- Does not assume agents could be detected by any set of targeted probes

A Nucleic Acid Observatory for wastewater, air filters, and waterways can reliably detect *all* hazards



Sequence air traffic hubs, plane lavatories, flight crews, waterways

An Observatory could reliably detect a respiratory HIV pandemic

“A Global Nucleic Acid Observatory for Biodefense and Planetary Health” (2021) *arxiv2108.02678*

Defense

The only reliable defense against pandemic-class agents is to avoid infection

Medical countermeasures such as vaccines are *unreliable*: we still don't have one for HIV

Vaccines are also *too slow*: omicron infected >25% of the U.S. within 100 days of genome sequencing

Assume biotech cannot reliably defend against biotech

Defense: Maintain Essential Services (during an 80% lethality pandemic)

Sufficiently protective equipment for all essential workers



All air touching mucus membranes must be sterile

- Comfortable, stylish, lightweight, durable, easy-to-use
- Visible face for “normal” social interaction
- Exceptionally reliable with a long battery life



Must be *believable*: essential workers must be willing to continue doing their jobs despite a 90% lethality measles-equivalent



Defense: Passively Prevent Indoor Infections

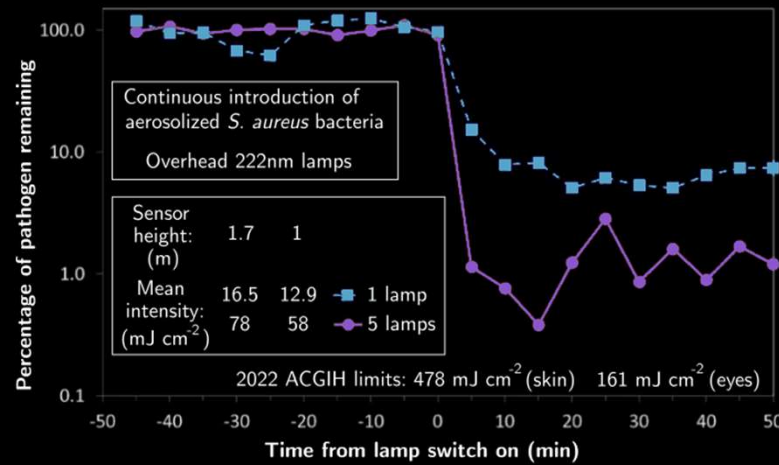
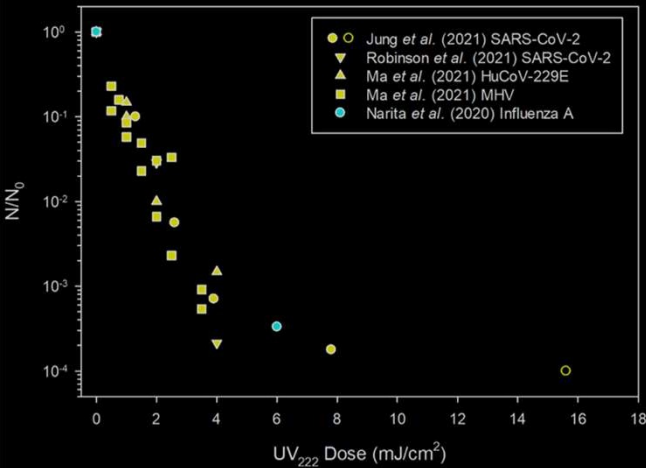
Equip all buildings with 220nm lights

Protects people regardless of what they do or believe

- Eliminates ~90% of pathogens per 1 mJ cm⁻² (~1 min)
- ACGIH limit: 478 mJ cm⁻² per day for skin
- Studies suggest much higher levels may be safe

Could adaptively strengthen upon sensing cough/sneeze/voice

- Requires development of better LEDs

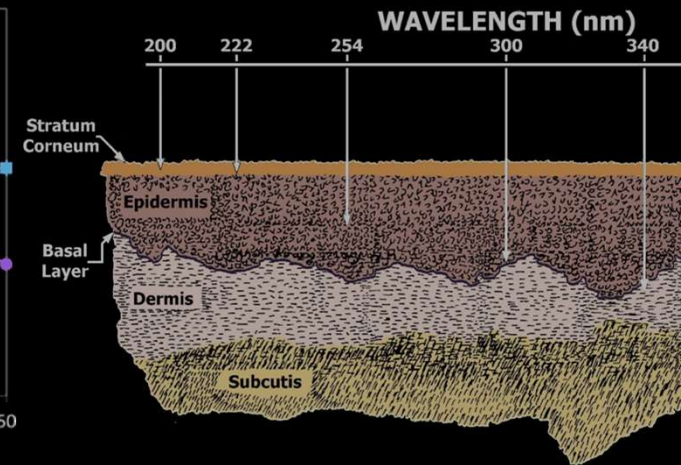


Pandemic defense

- SARS-CoV-2 ($R_0 = 4$ to 7) spreads primarily via aerosols
- ACGIH-permitted levels would likely have stopped it
- Higher/adaptive levels could suppress measles ($R_0 = 18$)

Economics and Public Health

- U.S. lost \$530 billion to illness and sick leave in 2019
- 50-60% is due to infectious disease
- At <\$30k per 100 m², employers would leap to install this



Blatchley et al (2022) *Crit Rev. Env. Sci. Tech.*
Integrated Benefits Institute: Full Cost Estimator 2022
Hansen, Zimmerman, & van de Mortel (2018) *J Infect. Prev.*

Eadie et al (2022) *Nature Communications*
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Welch et al (2022) *bioRxiv* 10.1101/2022.03.16.484636

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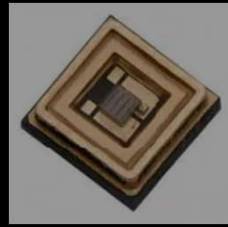


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Defense: Resilience

Prepare agencies for a world in which tens of thousands can unleash new pandemics

- Create detailed plans and be sure they are understood
- Ensure diagnostics will be available quickly
- Give individualized early warning (e.g. NOVID app)
- Plan for severe supply chain disruptions from lockdowns



Pandemic proliferation is a solvable problem

We can render our societies proof against pandemic-class events

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