Securing Civilisation Against Catastrophic Pandemics

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Executive summary

Pandemic security aims to safeguard the future of civilisation from exponentially spreading biological threats. Despite the world's failure to contain SARS-CoV-2, the existence of far more lethal and transmissible pathogens that afflict animals and growing access to increasingly powerful biotechnologies, no analyses of worst-case scenarios and potential defences have been published. Here we outline two distinct mechanisms by which pandemic pathogens transmissible between humans could cause societal collapse. In a "Wildfire" pandemic, the justifiable fear of a lethal and highly contagious respiratory agent released in multiple travel hubs leads to the breakdown of essential services. In a "Stealth" pandemic, a rapidly spreading virus with a long incubation period analogous to HIV infects most of humankind. We explain why current pandemic preparedness measures such as rapid vaccines and N95 masks will reliably fail against these threats and outline novel strategies and technologies capable of safeguarding civilisation.

Key takeaways

- Nations cannot yet contain natural, accidental or deliberate pandemics.
- Access to severe pandemics will expand with the ability to program biology.
- If too many essential workers die or refuse to work, societies will collapse.

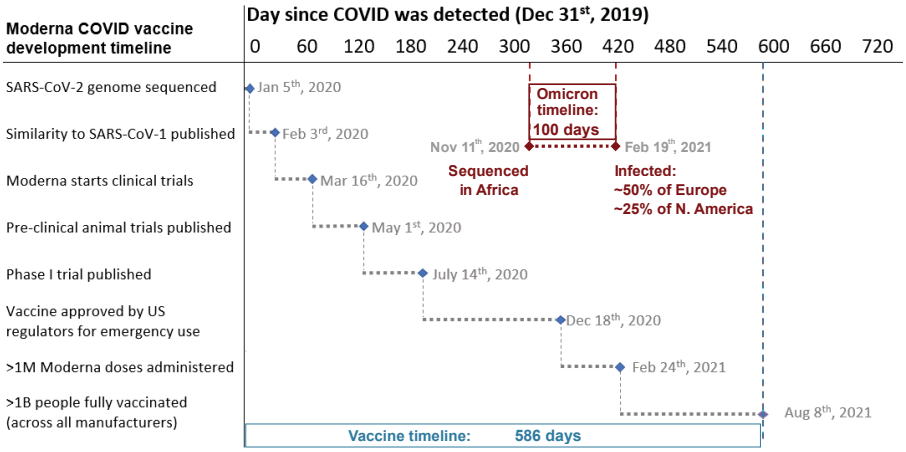
- A *Wildfire pandemic* is highly lethal and transmissible enough to infect most essential workers who are taking currently available precautions.
  - → Collapse can be prevented by providing essential workers with pandemic-proof personal protective equipment (P4E). (Essential workers are those who must deliver food, water, power and law enforcement without any interruptions.)
  - → Others can remain safely at home until P4E is available for everyone.
  - → Once the population is protected, the virus can be locally eradicated.
- A *Stealth pandemic* spreads widely with few symptoms and causes severe harm years later.
  - → Societal collapse can be prevented via early warning, credibility, cures, P4E and healthy buildings.
    - *Early warning:* deep metagenomic sequencing offers reliable detection.
    - *Credibility:* expert responders can assess threats and encourage action.
    - *Cures:* swift medical research can offer hope for the infected.
    - *P4E:* people will need protective equipment that they can trust to block transmission.
    - *Healthy buildings:* the use of germicidal lights and ventilation can prevent indoor infections.

I. Introduction

Biosecurity aims to protect humankind and current ecosystems from natural and deliberately released biological threats. Historically, the field has focused on non-transmissible agents such as anthrax. In the wake of COVID-19, there has been greater interest in preventing or mitigating pandemics arising from natural spillovers or accidents. Very little attention has been focused on the possibility of deliberately released pandemic agents, and none on plausible worst-case scenarios.

The world is currently unable to contain novel respiratory epidemics with any reliability. Nations demonstrably failed to halt SARS-CoV-2, initially a moderately transmissible agent (estimated R_0~2.79) introduced in one city.[1] Temporary lockdowns, travel bans, social distancing, contact tracing, masks and rapid diagnostics helped to limit its spread, but ultimately failed to stop the pandemic.[2] Even China, which employed severe lockdowns and mandatory testing to suppress widespread transmission for nearly three years, eventually buckled before the more-transmissible Omicron variant.[3] A less contagious pandemic agent that might be contained if it were introduced in a single region of a well-prepared nation would spread uncontrollably in low-income nations suffering from resource or organisational constraints, especially if released in multiple locations. As occurred with Omicron, ongoing selection in vulnerable populations can provide viruses with an opportunity to evolve transmissibility sufficient to overcome the defences of even the best-prepared nations.

Figure 1: Medical countermeasures are too slow to protect against rapid pandemics

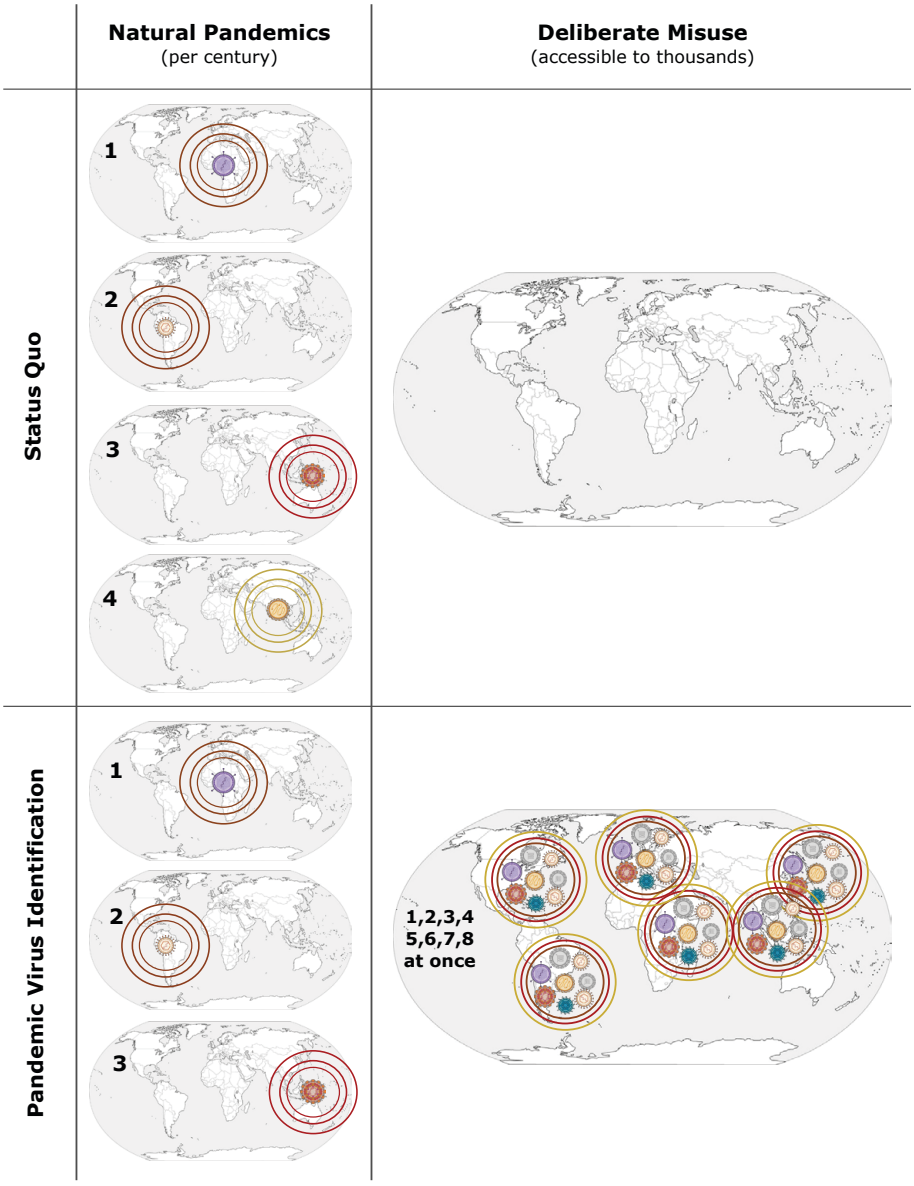


Vaccines for SARS-CoV-2 were developed and delivered to a billion people in 586 days. The US National Biodefense Strategy, described as a "moonshot", calls for vaccines to be widely available to residents within 130 days of sequencing a new pandemic agent. For comparison, the Omicron variant infected a quarter of North Americans and half of Europeans within 100 days of detection.

COVID-19 was a success story for biomedical countermeasures, which eventually mitigated its worst effects: vaccines saved an estimated 20 million people from dying of in 2021 alone.[4] However, they only became available in high-income countries a full year after the pandemic began (see Figure 1). Even if vaccines and therapeutics could be swiftly and reliably developed for every exponentially spreading pathogen, the logistics of production and distribution are too slow to match the speed of a highly contagious respiratory pandemic. Viruses spread by air travel can demonstrably outpace even the rosiest projections of vaccination: the Omicron variant of SARS-CoV-2 infected a quarter of North Americans[5] and nearly half of Europeans[6] within 100 days of being sequenced in South Africa. For comparison, the US National Biodefense Strategy moonshot calls for vaccines to be widely available to US residents within 130 days of sequencing.[7] Therefore, nations simply cannot afford to rely on medical countermeasures against severe pandemics.

Worse, ancestral SARS-CoV-2 and the Omicron variant both began to spread from a single geographic location, which is expected of natural spillover, evolution or laboratory accidents. A scenario in which pathogens were deliberately released could involve numerous pandemic-capable agents being introduced in multiple travel hubs, all of which would spread considerably faster than if they had been introduced in a single geographic location (see Figure 2). There would be less time to respond or develop countermeasures, and the challenge of defending against each of the agents would be multiplied.

Figure 2: The greater severity of deliberate pandemics



History suggests that natural pandemics causing at least a million deaths occur every ~33 years (upper left), but the current dearth of publicly credible pandemic-capable viruses limits accidents and precludes deliberate misuse. Pandemic virus identification may prevent one or more natural pandemics by targeting spillover prevention efforts (lower left), but would increase the risk of accidental pandemics because more laboratories would be working with pandemic-capable pathogens. It would also allow any of thousands of actors to seed more distinct pandemic viruses across multiple sites than would normally occur in a century (lower right), triggering more rapid spread, higher morbidity and mortality, and an increased likelihood of panic that will adversely impact services essential to civilisation.

By the end of 2022 SARS-CoV-2 had infected most of humankind and directly or indirectly killed perhaps 20 million people – an effective global fatality rate of 0.25% inclusive of reinfections.[8] Many viruses are far more lethal. Variola major, the causative agent of smallpox, killed approximately 30% of patients while maintaining high transmissibility (estimated R_0=3.5-6);[9] the virus was responsible for the deaths of 500 million people in the century before its eradication.[10] The 1971 Aralsk outbreak, which involved a potentially weaponised strain, was transmitted by vaccinated individuals and exhibited 100% lethality in the three unvaccinated patients.[11] More devastating pathogens exist in other animals that live in tight-knit groups: rabbit haemorrhagic disease virus (RHDV) is highly contagious, transmitted asymptomatically in young animals, and 80-100% lethal in adults.[12] If such a virus were to sweep the world anywhere near as quickly as the Omicron variant of SARS-CoV-2, billions would perish.

Even at the height of the Cold War, a city-targeting nuclear exchange would not have seriously threatened the viability of most nations in the southern hemisphere.[13] Given humankind's demonstrated failure to reliably contain the moderately transmissible SARS-CoV-2 virus and the dearth of large-scale subsequent investments aimed at halting pandemic transmission by any government, a sufficiently severe pandemic-class agent would threaten the stability of every unprepared nation. Today, this includes every country in the world. Thankfully, most of the technologies required to mount a reliable defence already exist. With dedicated preparations, many nations could become highly resistant to catastrophic pandemics – but only if they anticipate more severe threats than a reprise of COVID-19.[14]

Here we analyse two very different scenarios in which severe pandemics could trigger global societal collapse. We evaluate systemic vulnerabilities, analyse the primary sources of risk, and outline defensive measures capable of safeguarding civilisation.

II. Two scenarios for catastrophic pandemics

A. Scenario 1: "Wildfire" pandemic

One or more sufficiently debilitating and transmissible pandemic agents trigger civilisational collapse by interrupting the distribution of food, water, power and law enforcement.

COVID-19 demonstrated that some high- and middle-income nations may have the resources to temporarily contain pandemic agents by locking down their populations to limit human contact. However, maintaining a lockdown requires the continued distribution of essential goods and services such as food, water, power, and law enforcement. These are generated and provided by essential workers, many of whom were infected at particularly high rates during COVID-19.[15] The vast majority of these workers lack protective equipment beyond N95 masks, which theoretically block 95% of particles down to 0.3 um, but in practice have been found to block only 57-86% of coronavirus particles when worn loosely and 79-90% when worn correctly.[16] If a nation loses too many essential workers – whether to death, debilitation or refusal to work through fear of contagion – some households will fail to receive the food, water, heating, and protection they need to survive.[17] People forced to leave their homes in search of vital supplies will spread the virus and further disrupt essential services. As law and order increasingly break down, societies will collapse.

Figure 3: Artistic depiction of the consequences of a Wildfire pandemic

Pieter Brughel the Elder (c.1525-9 September 1569)

To qualify as a Wildfire agent, a highly lethal overt pathogen must be transmissible enough to infect most essential workers in high-income countries while the rest of the population locks down. If too many essential workers die or refuse to work, society will collapse. Comparable pathogens exist in other species and could be engineered in humans.

Crucially, a visibly severe Wildfire scenario and the spread of misinformation could trigger societal collapse even if the actual risk of infection is low. If essential workers perceive their own level of peril to be unacceptably high for any reason, they will reasonably decline to risk contracting an exceptionally deadly virus and carrying it home to their families. This may occur even if case numbers are falling among the population as a whole. Perception – at least among essential workers – is just as important as epidemiological reality.

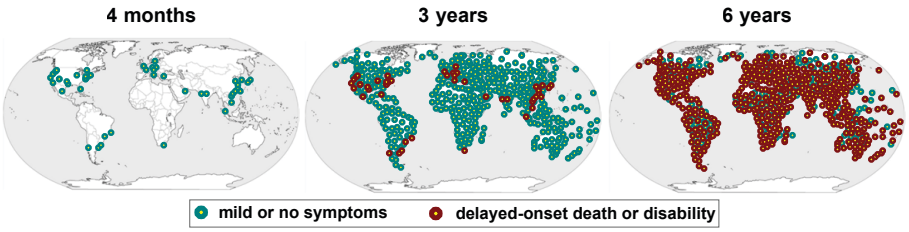
B. Scenario 2: "Stealth" pandemic

An initially mild or asymptomatic agent with a long incubation period infects most of humankind before its harmful effects become apparent.

SARS-CoV-2, tuberculosis and HIV killed more people in 2021 than any other pathogens.[18] All three exhibit some form of minimally symptomatic transmission or latency, but only SARS-CoV-2 spreads rapidly, and only HIV natively exhibits both a long incubation period and very high infection fatality rate. A lethal pathogen that combines these traits – colloquially, a "fast-spreading HIV-equivalent" – could infect much of humankind before anyone noticed its existence, then debilitate or kill most essential workers, triggering societal collapse. Today, such an event would almost certainly go undetected: since patients with common colds are rarely sequenced, no one would have cause to look for signs of adversarial engineering in the genome sequence of the pathogen.[19]

Even if a novel agent with a long incubation period could be detected early, SARS-CoV-2 also demonstrated that it is exceptionally difficult to contain a pandemic pathogen when a substantial fraction of the population does not believe that it poses a threat.

Figure 4: Timeline of a Stealth pandemic



A Stealth agent with transmissibility comparable to SARS-CoV-2 would rapidly spread across the world. With mild or non-existent symptoms, there would be no attempts to limit its spread until years later, when the first of those infected begin to suffer from debilitating illness or death. If too many people have already been infected and effective treatments cannot be developed in time, civilisation will collapse.

If no one is in hospital, no one has died, and only the scientific community is alarmed, will governments take politically costly actions to stop the transmission of a pandemic agent that might or might not be harmful?

With adequate preparation, much of the population might be persuaded that infection would entail (delayed) disability or death, but they may still struggle to protect themselves from being infected by people who do not believe that the pandemic is real. As more and more victims began to suffer the effects, people would come to understand that they had become infected and would likely suffer the consequences – as would almost everyone around them. How they would react is unclear. Perhaps they would come together to do what they can to preserve humankind's future, or they might withdraw in despair. Preserving hope in the form of newly devised treatments could be critical to maintaining order.

Either way, if most essential workers become infected and the scientific community cannot devise a treatment before they suffer debility or death, societies will collapse.

III. Estimating likelihoods

The magnitude of a risk is the product of severity and likelihood. A global collapse of modern civilisation would constitute the greatest disaster in human history. In addition to the direct casualties from Wildfire or Stealth pathogens, the loss of the essential workers who currently generate and distribute industrially produced fertiliser – to name just one essential process – would cause 3 billion people to starve.[20] Unlike comparably severe natural disasters such as major asteroid impacts and supervolcanic eruptions,[21] the likelihood of a civilisation-threatening pandemic is non-trivial and growing as access to advanced biotechnology increases.

In principle, a natural virus could exhibit the requisite combination of high transmissibility or stealth and high morbidity or mortality. However, accidental releases from state biological weapons programmes and deliberate releases by non-state actors are more probable sources of pandemic agents capable of triggering global collapse. Intelligent adversaries can identify and combinatorially exploit systemic weaknesses in ways that are extremely unlikely to be discovered by natural selection.

A. Estimating the likelihood of a Wildfire scenario

The Wildfire scenario requires the introduction of a lethal pandemic agent capable of spreading through populations of essential workers in every nation, even after they adjust their workflows to minimise human contact. The Omicron variant of SARS-CoV-2 plausibly sufficed. Drawing from data on its spread in previously naive Chinese populations in the months before and just after the relaxation of that country's zero-COVID policy, Omicron likely exhibits an R_0 between 4.0 and 5.5 with an upper bound of 6.8 (see Appendix 1). We therefore define a Wildfire pathogen as one exhibiting a case fatality rate above 20% and a basic reproduction number exceeding 5.5. Only one pandemic pathogen in the four thousand years in which densely populated cities and frequently used trade routes have been key features of civilisation,[22] i.e. the variola major virus that causes smallpox, has been both highly lethal (~30% case fatality rate) and could be sufficiently contagious (R_0=3.5-6.0).[23] Therefore, historical inference suggests that the annual chance of a natural Wildfire pandemic is somewhere between negligible and a theoretical maximum of 0.1% (see Appendix 1).

An accident involving a biological weapons programme working with a sufficiently dangerous pathogen could also trigger a Wildfire scenario. Rates of civilian laboratory-acquired infections and the history of accidental bioweapon releases yield estimated annual likelihoods mostly in the single-digit percentages conditional on a nation-state bioweapons programme working with a Wildfire agent (see Appendix 1). This includes the possibility of a rogue state building a system to deliberately cause a Wildfire pandemic as a dead-hand switch to

deter outside interference, which could accidentally leak. Given that the Soviet Union's bioweapons programme apparently aimed at enhancing variola major,[24] there are reasons to believe current and future programmes may pursue similar goals, particularly if other nations view a specific pandemic-class agent as a credible threat.

The last potential source of a Wildfire pandemic is a deliberate release. Zealots of many different ideologies aim to inflict mass death and civilisational collapse, from omnicidal cultists,[25] to apocalyptic terrorists,[26] anti-civilisation or suffering-focused ideologues,[27] deep ecologists,[28] nihilists,[29] and those who see no future for their own value system and way of life.[30] While the capabilities of these non-state actors are severely limited relative to those of nation states, civilian research will eventually provide widespread access to genomic blueprints: many well-meaning research programmes explicitly aim to identify credible pandemic pathogens and share their genome sequences and pathogen-specific reverse genetics protocols.[31] Even if they were to refrain from such activities, other advances in biotechnology and artificial intelligence will provide widespread access. Scientists will continue to seek to understand and program biology, including pandemics, and therefore will eventually learn to create them.

Thankfully, the vast majority of natural pandemic pathogens are not at the Wildfire level, sharply limiting the probability that any given deliberate release event would trigger a Wildfire scenario. Eventually, however, such an agent will be discovered or created, whether through advances in artificial intelligence,[32] increasingly powerful biological design tools,[33] or well-intended efforts to enhance the transmission of an already lethal virus.[34] If the genomic blueprints to such an agent become widely available and access to unscreened DNA synthesis[35] remains widespread,[36] the likelihood of a deliberate Wildfire pandemic will increase sharply. Under these circumstances, historical data suggests that the annual probability of a deliberate Wildfire release may substantially exceed that of an accidental release from a state programme, with likelihoods ranging from the low single to low double digits per year (see Appendix 1).

B. Estimating the likelihood of a Stealth scenario

Many natural pathogens exhibit quasi-asymptomatic transmission, but only a few inflict severe harm months or years later. The most obvious example is HIV, which is often associated with extremely mild or non-existent acute symptoms, but typically progresses to symptomatic AIDS and death after eight to ten years without treatment.[37] Tuberculosis is asymptomatically present and immunologically suppressed in an estimated two billion people, but reactivates to kill over a million each year.[38] The herpesvirus varicella zoster causes chickenpox upon initial infection and erupts into shingles after decades of latency.[39] Many other herpesviruses, adenoviruses and polyomaviruses also establish latent infections, some of which can culminate in relatively severe symptoms in a very

small fraction of patients.[40] However, none of these pathogens combines the ability to infect most people in less than a decade with a high rate of eventual morbidity and mortality, and they therefore do not qualify as Stealth agents capable of threatening civilisation. Without any historical examples, we can only estimate a very low upper bound on the likelihood of a Stealth scenario resulting from natural spillover (see Appendix 2).

In contrast, intelligent and highly competent adversaries seeking to build maximally devastating agents are likely to aim for Stealth pathogens precisely because they would be difficult to defend against. Even pandemic-themed games highlight the particular dangers of pathogens that exhibit a lengthy incubation period before killing their hosts:[41] SARS-CoV-2 underscored the difficulty of controlling a pandemic that a substantial minority does not believe exists. The question is when it will become possible for such an agent to be engineered. A viable conceptual design could be publicly articulated by anyone, even non-scientists or large language model chatbots that were open sourced or otherwise have not been subjected to adequate safety evaluations.[42] This initial disclosure could plausibly put Stealth agents within reach of bioweapons programmes and even sophisticated non-state actors capable of performing research to build and optimise such an agent.

Once publicly disclosed, controversy over whether or not the concept would work in practice will induce well-meaning scientists to perform experiments to test the hypothesis. Current norms in the life sciences support discovering and disclosing genome sequences and reverse genetics protocols for viruses thought capable of causing pandemics.[43] The publication of credible evidence that such an agent would function as intended would make Stealth pathogens accessible to individuals with substantially fewer skills and resources than the scientists who initially discovered or developed the agents.[44]

Unlike Wildfire agents, which must be highly transmissible to spread through populations of essential workers taking precautions, Stealth agents need only be transmissible enough to spread through populations behaving relatively normally. Since most viruses do not meet the Wildfire threshold for contagiousness, the typical Stealth agent will be substantially less transmissible than a Wildfire agent. This lower transmissibility substantially reduces the likelihood that a laboratory-acquired infection will trigger an accidental pandemic, and somewhat decreases the chance that terrorists or zealots will be able to deliberately start a Wildfire pandemic (see Appendix 2).

IV. Defences

Surprisingly modest investments can prepare nations to withstand the worst pandemic scenarios.[45] The cost of defence increases with the number of essential workers that need to be protected, although low-trust nations where residents are unlikely to cooperate may need to invest considerably greater sums in passive protective measures against Stealth agents.

Box 1: Key questions for a Wildfire scenario

How likely are essential workers to risk their lives in order to keep society functioning?

What is the relationship between the fatality rate and essential workers' willingness to continue to work?

What is the relationship between the transmission rate and essential workers' willingness to work?

How will social media impact essential workers' willingness to take risks for the greater good?

A. Preparing for a Wildfire pandemic

Protective equipment

To defend against a Wildfire scenario, nations must show that they can protect essential workers from infection (see Box 1). If workers who provide essential services are given credible pandemic-proof personal protective equipment (P4E) at the onset of a Wildfire event, the rest of society can and will lock down until they can be similarly protected or the threat has been locally eradicated.

P4E must not only protect essential workers, but give them confidence that they can do their jobs with negligible risk of infection (see Box 2). A reasonable minimum level of protection is provided by exclusively breathing air treated by HEPA filtration, which reduces infection risk by nearly 10,000-fold.[46] Unfortunately, elastomeric respirators cannot offer most users even a ten-fold reduction because they require fit testing, which is not feasible for large populations of essential workers. Moreover, fit testing is often unsuccessful,[47] and tightly sealing masks cause adverse skin reactions and headaches in over 90% of users who wear them for extended periods.[48]

Therefore, most sufficiently protective P4E designs will need to maintain positive pressure by pumping sterile air into an enclosed volume surrounding the wearer's face, preventing infectious particles from accessing the mucus

membranes in the nose, mouth and eyes. Sterilisation can be achieved using any of several methods, including filtration, germicidal ultraviolet light, plasma and heat. Current powered air-purifying respirators using HEPA filters fulfil these requirements, but are expensive, noisy and often uncomfortable.[49] Sterilisation methods that do not rely on a thick filter would require a much less powerful and energy-hungry fan, potentially reducing the noise, weight and cost. However, regulators currently assess device function by quantifying filtration efficacy, and will need to develop alternative metrics to evaluate sterilisation.

Again, workers must be extremely confident that P4E will protect them. Even if the number of cases begins to fall, widely viewed stories of people becoming infected and inadvertently killing their families by bringing the pathogen home would cause many others to think twice about taking the risk of going to work. These stories would certainly be circulated no matter the level of protection, but people will judge them to be more compelling if many are verified by credible observers.

Box 2: Requirements for P4E

Core requirements:

1. *Ready to wear:* no fit testing or training required for >90% of users;
2. *Highly protective:* as good as HEPA filters = >99.97% infectious particle removal;
3. *Comfortable:* can be worn for long hours every day for months;
4. *Cost effective:* cost parity with N95 masks on an annualised basis (~US$200 each);
5. *Regulator-approved:* meets NIOSH requirements for positive pressure devices;
6. *Viewing friendly:* unobstructed field of view with the full face visible to others.

Suggested features:

7. *Minimal noise:* air pump should not be too loud to converse.
8. *In-use sterilisation:* the capacity to eliminate any surface contamination before removing.

Awareness campaigns to build confidence in the assessments of expert responders and the scientific community should begin well before the next pandemic, ideally featuring trusted community leaders and public figures. Unusual but potentially effective ideas should be considered. Once a pandemic emergency has begun, people will view the resulting videos and come to their own conclusions.

Identifying essential workers

Nations should identify which services can least afford disruption *before* a Wildfire pandemic occurs so that P4E can be delivered to them in advance.

"Primary essential" sectors are those that, when disrupted, result in societal breakdown. Technologically advanced societies that fail to provide residents with food, water, power and law enforcement will not survive. Other sectors of similar importance can be identified by evaluating the time before unrest breaks out following disruption and the fraction of the typical workforce required to maintain essential operations.

All workers who provide primary essential services, including those who deliver and distribute goods and services and those who will produce more P4E units, must be immediately supplied with P4E at the onset of a Wildfire pandemic. This will require nations to maintain up-to-date lists of all such workers and their respective organisations. Military personnel can perform law enforcement duties during the emergency.

"Secondary essential" sectors provide services or produce goods that are not immediately necessary, but are required for the extended operation of primary essential services. Each primary sector relies on equipment that will gradually break down and supplies that will run out. At some point, repairs must be made and new parts and supplies manufactured to sustain operations.

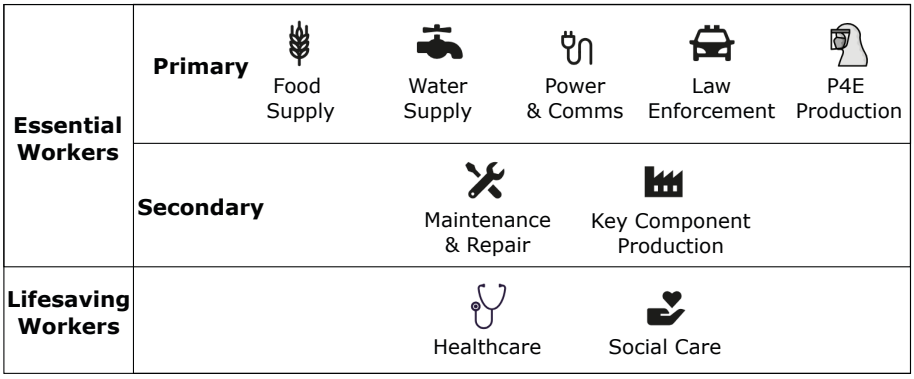
Secondary essential workers must be provided with P4E and given sufficient time to manufacture key components before any primary sectors fail. This underscores the importance of rapid P4E production if there are not enough units at the onset of the pandemic. A detailed understanding of the supply chain may allow spare parts and components to be stockpiled, potentially changing how soon the various secondary essential sectors must become operational and providing more time to produce sufficient P4E. It is safe to assume that most international trade will come to a complete standstill during a Wildfire pandemic. Therefore, nations should ensure that they possess reliable local P4E-manufacturing capabilities and stockpiles of the necessary materials. Verifying that this is the case is likely to require a comprehensive supply chain analysis.

"Life-saving" workers are those whose efforts will save lives, but are not strictly essential because their absence does not lead to societal breakdown. For example, if all healthcare workers stay home, everyone requiring urgent medical care will die, but most people would survive. This would not be the case if food or water were no longer available. Ideally, all life-saving workers will also receive P4E at the beginning of a Wildfire pandemic, but if the supply is insufficient, more lives will be saved by providing available units first to primary essential workers and then to secondary essential workers.

Preparing the workforce and supply chain

Importantly, workers who can perform their jobs without any contact with other humans or without entering rooms vacated by another human less than four to six hours beforehand should not require P4E. For example, maintaining and repairing cables is essential to the continued availability of electricity and communications, but typically does not require workers to share space with other people. Therefore, careful planning and increased automation can reduce the number of P4E units required to preserve civilisation. The more readily a society can produce and distribute essential goods and services without workers coming into contact with one another, the more resilient to Wildfire pandemics it will become.

Figure 5: Identifying essential and life-saving workers



People require food and water to live, while power is essential to the continued delivery of vital supplies. Law enforcement is needed to prevent unrest from desperate individuals or troublemakers. The workers needed to produce and distribute food, water, power and law enforcement are "primary essential": without them, society will break down. Those workers who produce, maintain or repair the supplies and equipment needed to maintain these key services are "secondary essential": while not required immediately, they will become essential within a period of weeks to months as stockpiles of essential components are depleted and machines break down. Finally, healthcare and social workers are "life-saving": without them, many people will die, but their absence would not cause civilisational collapse, although it may discourage essential workers from taking perceived risks.

Performing sector and supply-chain analyses to minimise the number of primary and secondary essential workers, establishing and regularly updating records detailing who they are and where they live, and ensuring that P4E will be delivered to them when needed — all with suitable margins of error – will be a major analytical undertaking. Nations should work with shipping and delivery firms to choose accessible P4E stockpile locations, ensure that adequate stocks of other key materials are located near production facilities, and sign contracts in advance to guarantee P4E distribution at very short notice. Establishing first-in, first-out inventory management systems to distribute stockpiled P4E

and materials to the market before they expire can refine protocols and ensure that distribution channels are functioning properly, while reducing costs.

B. Preparing for a Stealth pandemic

Reliable early detection

The best way to defend against a Stealth pathogen is to detect it as early as possible. An ideal monitoring system will flag every possible human-to-human threat before it spreads to more than a tiny fraction of the population. While early versions could privately search for sequences or molecular signatures of known or theoretical pathogenic threats or apply genetic engineering detection algorithms, highly competent adversaries might be able to work out which signatures are being used and build an agent that would not be detected.

Fortunately, to be able to spread around the world, every possible pandemic-class agent must exhibit a characteristic pattern of rapid growth. Therefore, any monitoring system capable of detecting nucleic acid fragments exhibiting such a growth pattern can provide reliable early warning of every new viral variant and endemic human pathogen, including Stealth agents[50] (see Figure 6, part a).

For example, deep metagenomic sequencing of DNA and RNA in wastewater and sewage from aircraft and/or major travel hubs can detect sequence fragments that are becoming increasingly common across a network of monitoring stations. By recording every biological variant, pathogen or genetic construct exhibiting quasi-exponential growth, a nucleic acid observatory can ensure that any biological sequence spreading in travel hubs will be detected and scrutinised, and will trigger an appropriate response. Publicising the system and explaining that it is built to detect a future respiratory HIV-equivalent pathogen before it infects too many people can help ensure that populations take the warning seriously, while reliable detection can deter adversaries from developing Stealth pathogens.

Expert responders for credible assessment and preliminary warning

Once a candidate Stealth threat has been identified, nations will need to quickly reach a preliminary consensus on its probable nature and severity. If warranted, they can alert the world, then map the extent of spread, confirm the predicted activity in infected individuals, and marshal a credible response as quickly as possible.

To deliver a rapid and credible assessment, nations can assemble a network of influential scientists and physicians willing to serve as “expert responders”. Their testimony, which must be delivered within days of initial threat detection, will be invaluable for policymakers and defence establishments – both of which will need to make difficult decisions on the basis of limited clinical evidence – as well as for the greater challenge of persuading the general public to begin taking precautions.

The difficulty of the task facing expert responders will depend on the degree to which the nature of the Stealth pathogen is apparent to expert inspection. If the genome sequence of the Stealth agent clearly indicates that it was adversarially engineered and makes apparent its mechanism of action, expert responders can quickly and unanimously determine that a maliciously engineered pandemic is under way. They can convincingly assert that the agent was intended to cause mass harm, knowing that virtually the entire scientific community will back their assessment. While it is possible that the agent will not function as intended, a preliminary warning is clearly justifiable, given adversarial intent. Less obvious cases will require deeper investigation, potentially warranting a much more tentative warning until more is known (see Table 1).

Table 1: Possible versions of Stealth pathogens detected by a monitoring system

Threat visibility	Consensus	Preliminary warning	Likelihood
Obvious	Immediate	"A maliciously engineered pandemic threat similar to a fast-spreading HIV"	Very high
Ambiguous	Not yet	"An engineered virus that may be harmful"	Low
Quasi-natural	No	"An unusual pathogen with few symptoms"	Very low

Warning key entities and institutions in advance could improve credibility. For example, defence establishments can be incentivised to pay heed to potentially adversarial threats and take precautionary actions to protect military personnel, who can function as primary essential workers by helping to maintain law and order in a crisis. If defence agencies order military personnel and their families to take extreme precautions to avoid infection, most of society will take note. Elite scientific and medical voices can help to persuade educated demographics, faith leaders can influence their respective flocks, and cultural influencers can sway others. Contacting key representatives of these groups in advance and preparing them for the possibility of a Stealth pandemic could markedly increase the impact of any eventual preliminary and confirmatory warnings.

Credible threat verification

Once a potential Stealth threat has been detected and a preliminary warning has been issued, nations must swiftly identify infected people so that they can be medically evaluated. To narrow the search area, existing monitoring systems can use primers or probes specific for the new agent to map the extent of spread and identify the greatest concentrations of patients, who are most likely to be frequent air travellers, flight crews or airport staff. Ideally, asking people for nasal swabs or saliva samples will already be routine in airports; offering compensation and genome privacy guarantees can increase the positive response rate.

Samples from high-likelihood populations can be tested for the newly identified agent by PCR or other sequence-specific assays using targeted primers or probes optimised on wastewater and sewage samples. Those testing positive should be contacted and tested by expert responders for anticipated physiological symptoms consistent with the predicted effects of the Stealth pathogen. If possible, nations should set aside funding and obtain legal permission for sampling, testing, and medical examinations in advance.

The question of when and how to convey the results of these examinations is difficult to predict. Many people, alarmed by the preliminary warning, will be taking precautions and waiting for diagnostic tests while they anxiously await further information. Others will be dismissive or view the event as a conspiracy. Because there is presumably a tradeoff between speed and credibility, it may be worth delaying dissemination of the medical analyses in order to achieve a near-consensus among expert responders in the medical community, which may be the only testimony sufficient to sway democratically elected officials. Unfortunately, elected representatives are among the least likely to take action: if no one is in hospital and no one has died, asking such representatives to risk their political careers by ordering costly and divisive actions to prevent a catastrophe that is only predicted to manifest once they have left office is a tall order.

Whether or not governments are willing to act, expert responders who are convinced of the threat must provide the most convincing possible evidence to the general public. This will pose a communications and misinformation problem of the highest order, one that will be at its worst in already low-trust societies. Communication specialists can make advance plans to maximise credibility and minimise political framings in each nation, although much will depend on the Stealth agent(s) in question and the findings of the expert responders. However, even the best messaging campaigns in high-trust populations will not persuade everyone to respond appropriately. Widespread scepticism regarding the public health establishment, the rapid spread of misinformation, and the fragmentation of the media landscape will collectively ensure that many people deny the existence of the threat. The challenge will be to save as many lives as possible, whether or not people believe that a problem exists.

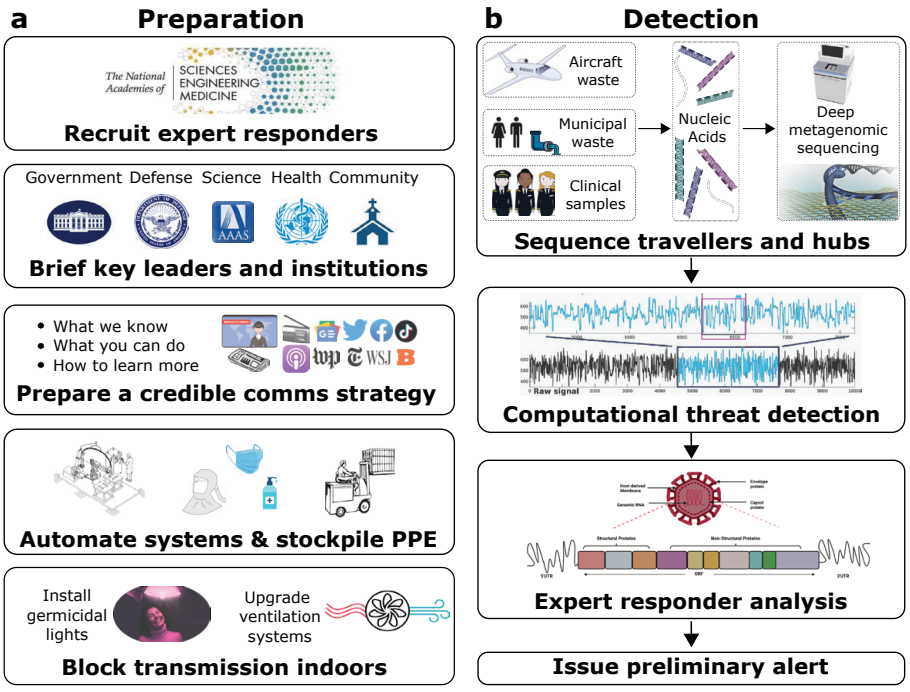
Developing medical countermeasures

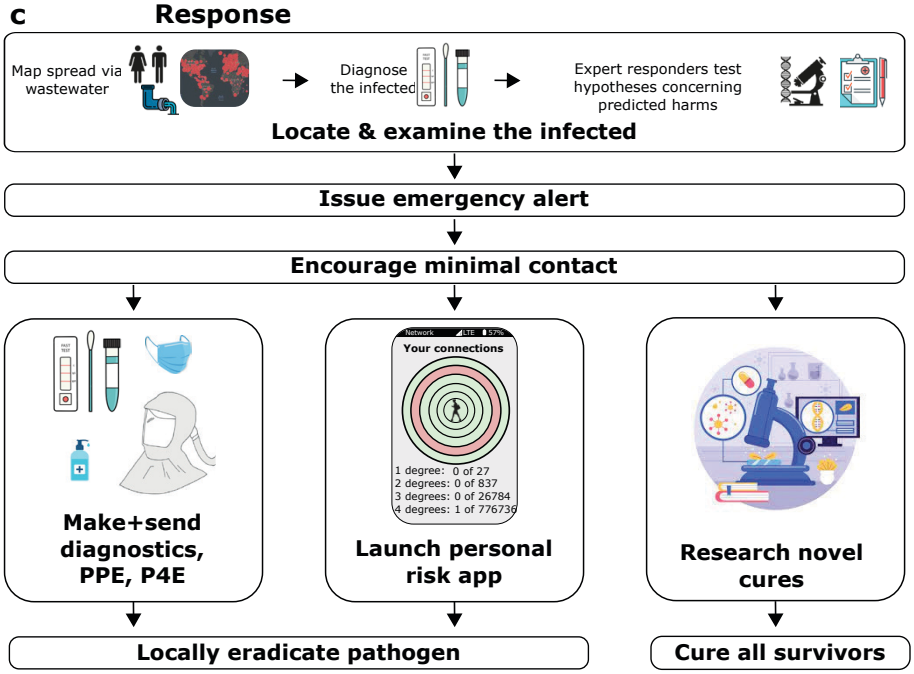
People who have tested positive for the Stealth agent will face a terrible choice: they can deny the expert responders' prediction of terrible harm, come to terms with the dire personal consequences, or hope for a cure. That flicker of hope may be warranted – and must be nurtured. With at least a year until the delayed effects begin to appear, the biomedical research enterprise will have time to seek therapeutics that can control or prevent the infection, much as antiretroviral drugs have indefinitely staved off AIDS. Given that much of the scientific community will certainly take the threat seriously, there will be no need to persuade researchers to make the attempt, but many scientists will be

reluctant to work close together in laboratories without adequate protective equipment. Nations can help by installing germicidal lights and ventilation systems in laboratories and planning to prioritise P4E delivery to researchers, as well as quickly offering so-called emergency "fast grants" to pursue every potentially promising therapeutic approach.[51] Given that there are fewer than 200,000 biomedical scientists in the United States,[52] protecting the biomedical enterprise will require many fewer P4E units than will be needed to protect all primary essential workers.

Communicating the status of the biomedical efforts will be tremendously important to raise morale. Without hope of a cure, the well-documented psychological desire to remain ignorant of a lethal diagnosis could discourage people from getting tested in order to help control ongoing transmission.[53] Clear and frequent updates on the development of countermeasures will offer reassurance to those who are infected, to their loved ones, and to the essential workers keeping everyone else alive.

Figure 6: Defending against a Stealth pathogen





Nations that are prepared for a Wildfire pandemic could theoretically halt a Stealth agent, but only if they are aware of the threat, their populations recognise its severity, and most residents are willing to cease human contact outside the home unless they are wearing P4E. None of these things will happen without extensive preparation.

(a) The first step is to build a detection system and recruit expert responders to evaluate potential Stealth agents and communicate their findings. This includes briefing civil and military institutions in advance, making plans to persuade the various segments of the population of the reality of the threat, and underscoring the importance of automation and distancing to protect essential workers. In an ideal world, P4E stockpiles will be sufficient for everyone who wants protection. Failing that, essential and then life-saving workers should receive priority. Other protective equipment, including less effective masks, can be stockpiled and distributed to people who are unwilling to cease human contact but open to taking precautions. Installing germicidal lights and upgrading ventilation systems can help prevent or even completely block transmission indoors, especially in public buildings and essential facilities.

(b) Monitoring systems based on metagenomic sequencing can search for anomalies in wastewater and sewage samples from aircraft or travel hubs. Cataloguing all nucleic acid fragments exhibiting rapid growth will pick up all new variants of known public health threats and reliably detect Stealth pathogens, which are likely to exhibit signs of adversarial engineering that will be visible to expert responders.

(c) To confirm that the Stealth agent is functioning as predicted, infected patients can be located with diagnostic testing and examined by physician expert responders who can confirm the anticipated physiological signs. Once confirmed, the general public should be warned of the severity of the threat and advised how to best protect themselves and their loved ones while the scientific community develops cures. Once sufficient P4E units are available, the pathogen can be eradicated from the nation.

Slowing the spread

Since medical countermeasures may be difficult to develop, prudent nations should aim to minimise the number of people infected by potential Stealth pathogens. COVID-19 was a practice run for the challenge of controlling a virus that many people do not believe exists;[54] a Stealth pandemic will be much more difficult to control because there will be no obvious signs that anything is wrong. Without extreme government coercion, current technologies and control measures will be inadequate to the challenge. Success will require nations to learn from past mistakes and combine the best of the COVID-19 response with new innovations.

The most reliable way to prevent infection by respiratory pathogens is to limit time spent indoors in public spaces, especially in groups. Nations can support those who wish to isolate themselves, actively encourage people to work from home or outdoors, and require institutions to make plans that would minimise potential exposures by adjusting worker schedules and responsibilities in advance. For example, parents who wish to switch their children to outdoor or remote learning environments, ideally assisted by educational artificial intelligence,[55] should be accommodated by school districts reassigning their more cautious teachers to teach remotely.

When interactions are unavoidable, people can meet outdoors or in buildings engineered to minimise transmission. Very few COVID-19 superspreading events occurred on aircraft, presumably due to their exceptionally high ventilation rates.[56] Germicidal lights, which are discussed in more detail in the next section, are considerably more potent.

Perhaps most importantly, nations should stockpile P4E and provide it to all primary essential workers, just as they should in a Wildfire pandemic. Unlike in the latter scenario, they should offer incentives to use it, because many will not see the need. But if the expert responders are persuasive, there will not be enough P4E for everyone who wants it, even in nations with enough supplies stockpiled for all essential and life-saving workers.

Lesser forms of personal protection are better than nothing. Despite controversies over mandates,[57] there is no doubt that voluntarily wearing an N95-class mask substantially lowers the rate of infection by respiratory and surface-borne pathogens. There is more transmission to block indoors, but masks are particularly helpful outdoors and in buildings that guard against aerosol transmission because they protect people from sprays of respiratory droplets and physical contact with mucus membranes. While masks alone cannot reliably prevent a pathogen as transmissible as the Omicron variant of SARS-CoV-2 from spreading through the population(PLEASE ADD CITATION: “Gryphon Scientific, unpublished communication, 2023”), they will substantially slow transmission even if many people do not use them. Thus, while nations should preferentially invest in P4E, there will still be demand for N95s and surgical masks unless nations stockpile enough P4E for the bulk of their populations.

Sadly, many people will refuse to use protective equipment. No matter how persuasive the expert responders are, a substantial fraction of the population will view any alarm concerning an alleged Stealth pathogen to be a conspiracy,[58] if not an outright plot to seize power by their political opponents. They are unlikely to take any positive actions, and at best they will not actively interfere with protective steps taken by others. Others might intellectually accept the threat as real, but in the absence of any vivid pictures of hospitalisations and reminders of a growing death toll, they will struggle to remain vigilant and protect themselves, especially as the situation drags on. New technologies can help.

New technologies to halt spread

The most reliable way to prevent engineered biology from causing mass harm is to end infectious disease transmission entirely. If nations can block the spread of unwanted biological information by preventing viruses, microbes, and other vehicles from delivering nucleic acids without permission, their residents cannot be harmed by Stealth agents.

Social distancing contributed to virtually halting the spread of every endemic human virus during COVID-19, including influenza.[59] However, many populations quickly tired of lockdowns, distancing and mask mandates, many of which subsequently proved to be premature for their particular circumstances. People living in the same city faced very different risks of infection depending on their neighbourhoods and social circles.[60] Rapid diagnostics, contact tracing and exposure notification could not warn people when they themselves needed to be especially vigilant. This can and should be remedied.

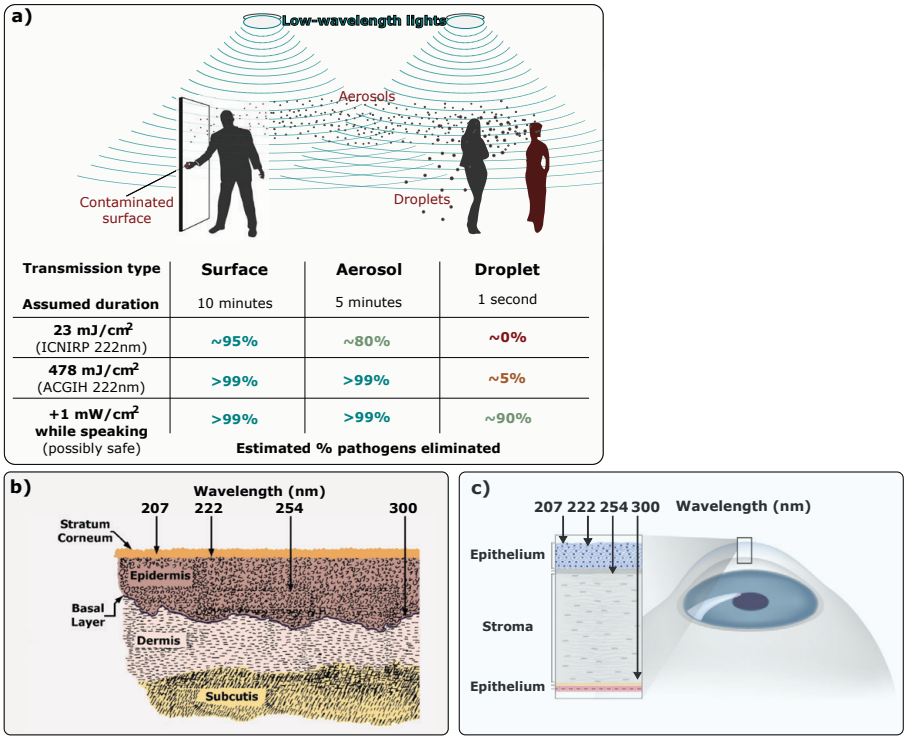
To bolster the psychological resilience of their populations against pandemic fatigue, nations can work with the makers of smartphone operating systems and electronic privacy advocates to build a privacy-preserving system that will provide everyone who does not opt out of taking preventive measures with customised advice based on their social contacts.[61] Whenever a person anonymously reports that someone they know has been infected, the risk level of everyone within five connections will robustly update to reflect their new risk level, helping everyone to decide when to take appropriate precautions.

Most rapidly spreading pathogens that could threaten civilisation are likely to be transmitted via respiratory and/or surface-borne routes; i.e., through the environment. The key to halting their transmission is therefore to engineer the built environment to eliminate pathogens while remaining safe for humans. The importance of ventilation for the control of aerosolised pathogens is now widely understood, but the efficacy of germicidal lights is unappreciated. In the 1940s, ultraviolet 254nm lamps installed well above head height in schools with high ceilings succeeded in helping to suppress the spread of tuberculosis and possibly chickenpox, a pathogen with an estimated R_0 of ~7.[62] But suppression was much less effective when children travelled in buses without 254nm lights, underscoring the importance of protecting all shared indoor spaces.

Most public buildings could benefit from this form of upper-room germicidal light, which can now employ cheaper 265nm LEDs.

Lower wavelengths of light can be even more effective because they appear to be extremely safe for humans.[63] Proteins strongly absorb light below ~235 nanometers, which is called "low-wavelength light" or "far-UVC". Photons that readily penetrate and destroy viruses and bacteria are typically absorbed before they can reach the DNA of much larger human cells; any that do pass through the outer layers of human skin and eyes do not come close to reaching the replicating stem cells protected below.

Figure 7: Penetration of 222nm light in skin, eyes and pathogens



Transmission type	Surface	Aerosol	Droplet
Assumed duration	10 minutes	5 minutes	1 second
23 mJ/cm² (ICNIRP 222nm)	~95%	~80%	~0%
478 mJ/cm² (ACGIH 222nm)	>99%	>99%	~5%
+1 mW/cm² while speaking (possibly safe)	>99%	>99%	~90%
	Estimated % pathogens eliminated		

High protein absorption limits the exposure of nuclear DNA in large eukaryotic cells, while non-replicating cells at the surface layers of eyes and skin protect the DNA of replicating cells. Pathogens, which are much smaller and unicellular, have no such protection. Intense exposure levels can inactivate most aerosolised pathogens before they move between individuals engaged in conversation. If experiments can show that high intensities are safe and new-generation methods can reduce costs, their global installation in public spaces could block the transmission of nearly all infectious disease, including Stealth and possibly Wildfire pandemics.[64]

In North America, threshold levels of 222nm light currently designated as safe for use in the workplace can inactivate 90% of aerosolised viruses within a minute,[65] which is roughly nine times as effective as aircraft ventilation systems that accomplish one complete air exchange every three minutes. Preliminary experiments suggest that even higher levels of 222nm light may prove to be safe.[66] Installing these lights, especially in combination with upper-room 254nm or 265nm UV in rooms with high ceilings, and improving ventilation systems in all public spaces can block the spread of airborne pathogens between people in conversation and substantially reduce the transmission of surface-borne viruses and bacteria.[67]

Since US employers suffer an estimated US$300 billion in productivity losses to infectious disease each year,[68] businesses have a strong incentive to install protective lights once they are demonstrated to be safe and sufficiently effective against routine pathogen transmission. Because higher intensities are more effective at eliminating pathogens, nations can support research to determine what level of intensity is safe, taking care to invite and thoroughly address concerns and criticism from experts and the general public. Similarly, efficacy trials of intensities matching current levels can quantify transmission in areas where people only interact in protected areas. Research into solid-state and LED generation methods could lower costs enough to allow global installation, potentially abolishing most respiratory diseases and providing an effective defence against even highly transmissible future pandemics.[69]

V. Conclusion

Despite biomedical advances, nations remain profoundly vulnerable to pandemics. Even if every SARS-CoV-2 vaccine and therapeutic known at the time of writing had already been developed and approved at the beginning of the COVID-19 pandemic, the world would still have suffered millions of casualties due to the logistical challenges of manufacturing and distribution. As of 2023, no nation can plausibly keep a highly lethal and transmissible pandemic from bringing down society by threatening to infect the essential workers responsible for distributing food, water, power and law enforcement.

Our analysis suggests that while civilisation-threatening Wildfire and Stealth pandemics are extremely unlikely to emerge from nature, accidental or deliberate release is disturbingly likely as a result of their development by a biological weapons programme or the dissemination of credible genomic blueprints by well-meaning scientists. Neither possibility can be ruled out. The Soviet Union attempted to weaponise smallpox even though the virus would also have devastated its own population. And as the physicist Richard Feynman famously remarked, "What I cannot create, I do not understand".[70] Given that researchers aim to understand and program biology, the life sciences community typically shares all its results through publication,[71] the relevant harmful traits exist in natural pathogens, and artificial intelligence is widely expected to accelerate the rate of discovery, it would be surprising if humankind did *not* learn to build Wildfire and Stealth agents.

Defence and health agencies can protect their populations from both threats, as well as less severe pandemics, for a tiny fraction of their annual defence budgets. To defeat a Wildfire pandemic, nations can stockpile P4E and arrange for its delivery to primary and secondary essential workers while protecting supply chains. Against a Stealth pandemic, building a reliable early detection system, preparing credibility-enhancing expert responders to persuade the population that the threat is real, installing germicidal lights and ventilation in public buildings, and stockpiling sufficient P4E can prevent societal collapse, although not the deaths of those who do not believe that the threat is real.

Nations can therefore decisively stave off the worst consequences of catastrophic pandemics – but only if they anticipate and prepare for much more severe threats than they have faced in the past. Such preparations should commence immediately.

Appendix 1: Estimating the likelihood of a Wildfire pandemic

A. Epidemiological properties of a Wildfire pathogen

Basic reproduction number

1. In order to overwhelm developed nations with small populations of essential workers, a Wildfire pathogen must be at least as transmissible as the Omicron variant of SARS-CoV-2. The basic reproduction number (R_0, the number of people infected by a typical infected person in a naive population) of Omicron is hotly contested because immune evasion in populations exposed to older variants inflates naive transmissibility calculations. The best estimates consequently come from studies of its spread in China, where negligibly few individuals had been previously exposed and vaccines are ineffective against Omicron.
2. SEIR models of outbreaks in Chinese cities prior to the imposition of lockdowns estimated the effective reproduction number of Omicron (R_e) at ~3.4.[72] A more recent model analysing testing data from the period when "zero-COVID" lockdown controls were still in place but failing in November 2022 and also after their removal in December ("10 Measures") similarly estimated R_e at 3.13 after removal and 1.57 beforehand, consistent with the failure of zero-COVID measures at the time.[73] As the authors state, "the results indicate that the Omicron variant evolved a higher intrinsic transmission fitness by shortening the time needed for transmission to occur (and thus the generation interval), rather than generating more secondary infections (and obtaining a high reproductive number)".[74]
3. During this period, people in China were still wearing masks and taking precautions against infection, reducing the effective reproduction number relative to R_0. Estimates of the combined efficacy of typical non-pharmaceutical interventions across nations predicted R_e reductions of 62-77%;[75] the same studies predicted a two-fold transmission increase from lifting stricter measures, which is consistent with the increased estimated R_e following the relaxation of zero-COVID.[76]
4. We therefore estimate the benchmark R_0 of SARS-CoV-2 Omicron as roughly 4 to 5.5, and probably no more than 6.8 (double the estimated R_e).

Lethality

1. We do not know what degree of lethality is required to intimidate enough essential workers to stay home in order to cause civilisational collapse.
2. During the SARS-CoV-1 outbreak in 2002-2003, with just 10% lethality, some families sought to stop nurses from going to work and threatened

them with termination of the kin relationship.[77] Healthcare workers avoided contact with their families and were shunned by the general public; however, most still performed their duties. Therefore, it is reasonable to assume that a Wildfire pandemic requires a case fatality rate at least twice as high: 20%.

→ **A Wildfire pandemic requires R_0 > 5.5 and case fatality rate (CFR) > 20%.**

B. Likelihood of a natural Wildfire pandemic

1. Among historical human pathogens, clear candidates for Wildfire status include variola major (estimated R_0=3.5-6.0, ~30% lethal) and *Yersinia pestis* (estimated R_0=2.8-3.5, ~80% lethal).[78] Only variola clearly approaches the transmissibility of Omicron, although it lacks the presymptomatic and asymptomatic transmission characteristic of the latter and was likely less transmissible when it first spilled over.[79]
2. We thus have between zero and one example of a natural Wildfire pathogen in the ~4,000 years since the advent of dense cities and extensive trade networks, suggesting that the annual likelihood of a natural Wildfire pandemic is between 0 and 1/4,000 per year. If theories that variola major only evolved greater virulence after spillover are accurate,[80] the actual number is on the lower end of this range.
3. Climate change is hypothesised to increase the baseline spillover risk by up to four-fold.[81] Multiplying the above estimate by this factor, we come to an annual risk estimate for a natural Wildfire pandemic of between 0 and 1/1,000 per year.

→ **Estimated probability of a natural Wildfire pandemic = 0% to 0.1% / year**

C. Likelihood of an accidental Wildfire pandemic

Biological weapons programmes are a second and much more likely source of Wildfire pathogens. State actors broadly lack strategic incentives to develop pandemic agents as weapons of war because they are slow, indiscriminate and asymmetric compared to modern munitions. The Soviet Union's offensive biological weapons programme did so anyway, suggesting that modern states may also seek to develop exponentially spreading pathogens. A rogue regime might view pandemic agents as worth developing for deterrence reasons, although this strategy would only be effective if others first identified the agents as credible enough to fear.

While it is highly unlikely (although not impossible) that any biological weapons programme developing a Wildfire agent would deliberately release it and kill their own citizens, such an agent would be released by such a programme accidentally. Here we estimate the risk that such an accidental release would

cause a Wildfire pandemic using two methods: historical rates of laboratory accidents and historical outbreaks caused by known bioweapons programmes. In both cases we only estimate the probability of a Wildfire pandemic occurring, given that at least one laboratory/programme is working with a Wildfire agent; we do not attempt to estimate the probability of such an agent coming into any laboratory's/programme's possession.

Estimate 1: Laboratory accident rates

1. We do not know the laboratory-acquired infection rate for bioweapons laboratories. Only two major accidents involving the Soviet bioweapons programme were severe enough that attempted cover-ups failed; presumably other accidents occurred, but were never publicly documented.
2. For a base rate, we can look at the annual accidental infection rates of laboratories registered with the Federal Select Agent Program (0.246% per laboratory per year) and NIH-funded BSL-3 and BSL-4 laboratories (1.6% per laboratory per year).[82] The fact that the more tightly regulated Select Agent laboratories exhibited a 6.5-fold lower accidental infection rate strongly suggests that tighter regulations and more regular inspections improve safety.
3. We predict that the deep secrecy surrounding bioweapons laboratories, combined with the fact that accidents in them will typically take place outside highly developed countries with state-of-the-art biosafety systems, will result in accident rates several-fold higher than the known rates for US laboratories. We apply a flat five-fold multiplier to account for these effects, yielding estimated accident rates of roughly 1.23% to 8% per year.
4. Models suggest that a single individual infected with an agent exhibiting an R_0 of 5.5 is 50-99% likely to cause an outbreak, depending on the variance in the number of individuals infected by any given host (e.g. viruses that are mostly transmitted by rare "superspreaders" who infect very large numbers of people are more likely to randomly go extinct than viruses whose victims all typically infect at least one other person).[83] We use this as our estimate of the likelihood of a single laboratory-acquired Wildfire infection causing a Wildfire pandemic. Multiplying through by the estimated laboratory-acquired infection rate above gives a lower bound of 1.23×0.5=0.615% and an upper bound of 8×0.99=7.92% annual risk of a Wildfire pandemic, assuming that a single laboratory exists that is working with such an agent.

→ **P(accidental Wildfire pandemic) ≈ 0.62% to 7.9% / year / laboratory (Method 1)**

Estimate 2: Programme-caused outbreaks

1. A second way to estimate the likelihood of accidents is to analyse the number of outbreaks per year from known programmes working with potential Wildfire agents. We know of a single accidental outbreak involving

such a pathogen, the Aralsk incident of 1971,[84] in which a hypothesised Soviet aerosol delivery test of a smallpox strain on Vozrozhdeniye Island infected a vaccinated individual on a vessel several kilometres offshore. A small outbreak ensued, with allegedly high levels of transmission from infected individuals that are suggestive of an engineered strain; all three unvaccinated patients died.[85] Lone infections and smaller outbreaks presumably occurred, but were successfully covered up; for the purposes of this exercise, we estimate a total of 0 to 2 such unknown outbreaks, for an overall total of 1 to 3.

2. The biological weapons programme of the Soviet Union (and then the Russian Federation) is certain to have worked with smallpox for the 35 years between 1956 and 1991, and may have done so from ~1950 to ~2020 (70 years), providing outside bounds on the historical period during which an accident may have occurred.[86]
3. Dividing the estimate of the number of accidents by the number of years with which a known programme worked with a possible Wildfire agent yields a lower bound for the annual risk of 1/70=1.4%, and an upper bound of 3/35=8.6%.

→ **P(accidental Wildfire pandemic) ≈ 1.4% to 8.6% / year / programme (Method 2)**

D. Likelihood of a deliberate pandemic release that infects at least one person

Before estimating the likelihood of a deliberate Wildfire pandemic, it is useful to assess the annual probability that a credibly identified pandemic-capable virus, whether or not it is Wildfire-level, will be deliberately used to infect at least one person, conditional on the availability of genomic blueprints and a working reverse genetics protocol.

Accessibility of virus assembly

Numerous civilian research projects hoping to mitigate natural outbreaks aim to find[87] or create[88] new pandemic-capable agents and share their genome sequences and step-by-step virus assembly protocols.[89] No novel research and little tacit knowledge is required to successfully follow a well-defined step-by-step experimental protocol; indeed, protocols journals are intended to enable researchers from diverse fields to successfully perform techniques on their first attempt. Hence, successful pandemic virus identification will make pandemic agents accessible to individuals capable of following the reverse genetics protocol who have access to the necessary resources: a laboratory and the necessary reagents, equipment, and unscreened synthetic DNA.

Most individuals with the relevant skills will presumably have access to a laboratory. For those without current laboratory access, approximately

US$50,000 can purchase used equipment, reagents, an incubator and a tissue culture hood. The price of synthetic DNA varies with the virus in question, but seldom rises above US$0.25 per base pair, or US$7,500 for a 30,000 base pair virus. For non-influenza viruses or to evade DNA synthesis screening, the cost is likely to be higher because of the need to assemble the pieces and confirm the final reverse genetics construct(s) by sequencing. At the time of writing, presumably unscreened synthetic genes can be readily obtained from any of the 45 companies that are not included among the 15 publicly listed members of the International Gene Synthesis Consortium – as chatbots now clearly explain.[90] Of these firms, 30 are based in the United States, ten in China, five in the UK, three in France and Korea, and the remainder in other nations, providing a diversity of options. For segmented viruses such as influenza, no additional assembly is needed, whereas non-segmented viruses require several thousand additional dollars in cost for molecular cloning and sequencing. For estimation purposes, we assume this level of access to unscreened synthetic DNA will continue.

It therefore seems plausible that funding in the range of US$20,000-100,000 will be sufficient for a suitably skilled individual to assemble a known pandemic virus. For comparison, the apocalyptic cult Aum Shinrikyo, which was responsible for multiple mass-murder attempts, allegedly possessed a weapons development budget exceeding US$10 million per year.[91]

These numbers serve to confirm that many types of viruses with public genome sequences are accessible to skilled individuals. However, they cannot estimate how many would use this knowledge maliciously.

Number of motivated and capable individuals

1. The number of people who could credibly attempt to cause a pandemic (given publicly available genome blueprints, a reverse genetics protocol and unscreened synthetic DNA) is limited by the number who (i) possess or could reasonably acquire the laboratory training that a modern individual would need to acquire an infectious sample, and (ii) are motivated to attempt mass murder.
2. A lower bound on this number can be estimated by tabulating individuals who in fact both possessed the relevant skills and attempted mass murder:

    a. One historical mass murderer, Seiichi Endo of Aum Shinrikyo, clearly possessed both the requisite training and intent. Endo, a graduate-trained virologist from Kyoto University who specialised in genetic engineering, reportedly sought samples of Ebola to use against civilians and ultimately participated in the sarin gas attack in the Tokyo subways.[92] A modern individual with the same educational background could certainly obtain infectious viruses of many families from their genome sequences using available reverse genetics protocols. Therefore, the minimum number of known historical individuals

with the training and motivation to commit mass murder using a deadly virus is at least one.

b. Known additional mass murderers who may plausibly have possessed or readily acquired the relevant laboratory skills include two members of al-Qaeda with training in the life sciences who may or may not have assisted with the alleged biological weapons laboratory in Kandahar and expressed willingness to cause indiscriminate death to harm the West,[93] and the molecular neuroscience graduate student who opened fire in a crowded Colorado theatre in 2012.[94] We conservatively do not include Bruce Ivins, the US Army microbiologist and biodefence specialist allegedly responsible for the anthrax attacks of 2001, because there is no evidence that he was willing to kill indiscriminately. Therefore, a reasonable upper estimate of the number of such known historical individuals is four.

3. This empirical lower bound is necessarily an underestimate due to several factors. It does not account for the growing number of individuals receiving suitable training, or for the fact that some malicious individuals talented enough to acquire such training did not take advantage of their opportunity due to a lack of perceived options for causing harm, a limitation expected to change if blueprints for Wildfire or Stealth agents become public. It also omits skilled individuals with suitable motivation who did not attempt biological mass murder due to a lack of attractive options, or who did attempt it and were quietly prevented by authorities.

   a. Due to disputes over the level of training necessary to assemble different types of infectious virus today, it is challenging to determine how many more people currently possess the relevant skills than did so in the average historical year. Similarly, we cannot know how many historical individuals with suitable training would have attempted to cause a pandemic for ideological reasons had they been given the opportunity, and simply did not commit small-scale mass murder or otherwise come to our attention in its absence. However, we can attempt to estimate how many *would have* sought training if they were confident that doing so would allow them to cause a pandemic.

   b. The number of individuals with biological training is a tiny fraction of the total population with the capacity and discipline to acquire that training. For every doctorate in the life sciences, there are roughly 3.5 in other disciplines.[95] Some of these will also be motivated to commit mass murder. One historical example is the Berkeley mathematics professor Ted Kaczynski, known as the Unabomber, who wrote of "the immense power of biotechnology" in the 1980s and explicitly sought to bring down industrial civilisation.[96] Untrained members of the Rajneeshee cult – which used *Salmonella* as a biological weapon in 1984 — also attempted to obtain viruses to commit mass murder.[97]

   c. Given that many highly capable individuals do not seek doctoral training, the true ratio of capable individuals to trained individuals is presumably higher than that implied by the number of doctorates alone. On the other hand, arranging such a career transition is a substantial undertaking. How these two factors balance is very uncertain; for the purposes of this estimate, we will conservatively assume that for every malicious individual who already possesses the relevant skills, there are an additional 1 to 3 who will retrain, for a total multiplier of 2 to 4.

4. Multiplying the lower-bound estimate from known trained and malicious individuals by the adjustment factor in the previous paragraph, we obtain an estimate for the historical number of trainable and motivated individuals of (1 to 4) × (2 to 4) = 2 to 16 individuals. Note however that those who begin training will not gain access for a number of years.

Rate of successful attempts

1. Fifty years have passed since the dawn of recombinant DNA, the first time it became possible for an individual to be trained to create dangerous viruses from scratch (given a suitable protocol). Assuming each trainable and motivated individual would only make one serious attempt to start a deliberate pandemic before they are successful or caught, we can divide the number of such individuals by 50 to obtain an estimate of the annual rate of such attempts in the presence of a known pandemic agent: (2 to 16)/50 = 0.04 to 0.32 attempts per year.
2. Not every attempt at causing a pandemic will be successful. Historically, both obtaining lethal biological agents and delivering them have proven limiting for terrorists.[98] That said, successful delivery should be far easier for a pandemic agent. It is presumably dozens if not thousands of times easier to infect a handful of people with a transmissible agent than it is to produce and deliver the quantities needed to infect thousands, which was the historical bar for an effective biological attack with non-transmissible agents. This is particularly true if terrorists are willing to sacrifice their own lives, as some are. We therefore conservatively[99] assume that an individual in possession of an infectious Wildfire agent is 70% likely to succeed at infecting others.
3. Combining the estimate for the number of annual attempts with that for the rate of successful infection gives an estimate for the rate of successful attempts: (0.04 to 0.32) × (0.7) ≈ 2.8% to 22.4% per year.

→ **P(deliberate infection | publicly known pandemic agent) ≈ 2.8% to 22.4% /year**

E. Likelihood of a deliberately released Wildfire pandemic (known Wildfire pandemic agent)

1. While it is theoretically possible that a state actor would deliberately release a Wildfire pathogen developed as a deterrent, there are strong incentives against such drastic action. Thus, the third likely source of a Wildfire pandemic is deliberate release by a non-state actor. Performing novel research to identify or create a new Wildfire agent is currently beyond the capabilities of even a well-funded terrorist programme. However, it is possible that a deliberate Wildfire pandemic might occur when a non-state actor assembles and releases a highly contagious pandemic-capable virus identified by others. Historical patterns of scientific publication suggest that open disclosure in the literature is reasonably likely. Moreover, advances in generative artificial intelligence[100] are likely to eventually produce systems capable of disclosing how such an agent might be created by recombining key concepts in biology that are not obvious even to most or all human experts. Once public, there will be strong incentives for the scientific community to determine whether the design would function, thereby making it credible to terrorists.
2. The above section estimates the annual likelihood of a successful attempt to infect one person with a pandemic agent, assuming that genome sequences and reverse genetics protocols for one or more pandemic-capable viruses are in the public domain. Most zoonoses are not Wildfire-level agents; therefore, deliberate engineering is considerably more likely to produce a Wildfire agent. While it might be argued that scientists would not deliberately generate, characterise and publicise Wildfire-level agents, past enhancement efforts specifically focused on increasing the transmissibility of highly lethal viruses such as H5N1 influenza.[101]
3. As discussed above, models suggest that a single individual infected with an agent exhibiting an R_0 of 5.5 is 50-99% likely to cause an outbreak. Multiplying this range by the estimated annual risk of successful release given above, we find that the annual risk of a deliberate Wildfire pandemic, given available blueprints for one Wildfire agent, is (2.8% to 22.4%) × (50% to 99%) ≈ 1.4% to 28.5% per year.

→ **P(deliberate Wildfire | publicly known Wildfire agent) ≈ 1.4% to 22.2% / year**

F. Likelihood of a deliberately released Wildfire pandemic (known zoonotic pandemic agent)

1. Most credible pandemic viruses identified in nature will not be Wildfire agents. Hence, given one or more agents that have been credibly identified as pandemic-capable, but not established as Wildfire, a malicious actor has a non-zero, but much lower, probability of successfully causing a Wildfire event.

2. In the 130-year span from 1889 to 2019, five outbreaks have inflicted over a million casualties. Extrapolating over the past four thousand years yields an estimate of approximately 150 spillover events capable of causing a severe pandemic. If only variola major qualifies as a natural Wildfire agent, then about 1 in 150 natural severe pandemics are Wildfire-level agents.
3. Dividing the previous estimate by this factor gives an estimated rate of a successful Wildfire release of (1.4% to 22.2%)/150 ≈ 0.00009 to 0.0015.
4. Importantly, a malicious actor capable of obtaining infectious samples of one virus would almost certainly be able and motivated to simultaneously acquire and release several others. Consequently, in a world in which multiple characterised and presumed pandemic-capable agents originating from animals are publicly known and listed relatively accurately, the risk of a successful Wildfire release scales roughly linearly with the number of characterised agents.

→ **P(deliberate Wildfire | publicly known pandemic-capable agent) ≈ 0.009% to 0.15% / year / agent**

Table A1: Estimated likelihood of a Wildfire scenario

Source	Assumption	Low	High	Units	Basis of estimate
Natural Spillover	0-1 historical Wildfire-class pathogens (R_0 > 5.5, lethal)	Tiny	0.1%	Per year	Known pandemic Pathogens, estimated spillover risk change
Bioweapon accident	A bioweapons lab is developing a Wildfire agent	0.62%	7.9%	Per lab per year	FSAP/NIH lab infection rates, spread from 1 individual (R_0=5,5), 5x increase over civilian rate
Bioweapon accident	A bioweapons programme is developing a Wildfire agent	1.4%	8.6%	Per programme per year	Historical accident rate involving pandemic bioweapons
Deliberate	Credible blueprints for a known Wildfire pathogen are publicly available	1.4%	22.2%	Per year	Historical mass murderers with the skills to follow a reverse genetics protocol
Deliberate	Credible blueprints for N pandemic-capable pathogens unlikely to be Wildfire-level are available	0.009N%	0.15N%	Per year	Historical mass murderers with the skills to follow a reverse genetics protocol

Because Wildfire-class pathogens are rare in nature, the scenario is most likely to result from an accidental release from a biological weapons programme developing a Wildfire agent or a deliberate release by a non-state actor once blueprints for a Wildfire agent are publicly available. There is a small chance that a non-state actor deliberately releasing credible pandemic agents of unknown lethality would trigger a Wildfire event. Access restrictions such as DNA synthesis screening might be implemented upon credible identification, but the need for such screening to be universal has been apparent for 17 years without a single nation rendering it mandatory, even after the COVID-19 pandemic directly or indirectly caused 20 million deaths. Moreover, quickly securing all DNA synthesis equipment would be challenging. These estimates consequently assume that unscreened synthetic DNA will remain accessible.

Appendix 2: Estimating the likelihood of a Stealth pandemic

A. Likelihood of a natural Stealth pandemic

1. Unlike for Wildfire, for which variola major provides a credible historical example, there are no known examples of historical Stealth agents in humans or animals.

    a. The most obvious historical model of a Stealth agent is the human immunodeficiency virus (HIV), which often exhibits asymptomatic infection and causes death in most untreated patients after several years.[102] However, HIV does not spread quickly enough to threaten civilisation.

    b. Many other human pathogens exhibit few symptoms upon infection and have a long latent stage. These include numerous herpes viruses. Varicella zoster virus is noteworthy in exhibiting a highly infectious varicella stage that is responsible for chickenpox in young children (R_0 ~7), then becoming latent for decades before erupting in the zoster phase to cause shingles and transmit again.[103] This demonstrates that highly infectious natural viruses can undergo an extended latent phase before they are reactivated. Even so, reactivation typically occurs very late in life and is seldom lethal, so it does not qualify as a Stealth agent. Tuberculosis is also highly infectious, characterised by a latent period of many years, and kills more than a million people each year, but proves lethal to less than one in 500 carriers each year.[104]

    c. In animals, there are slow-acting lethal pathogens such as the HIV-like koala retrovirus[105] and the tuberculosis-like *M. avium* bacterium responsible for Johne's disease in cattle.[106] But the former does not spread quickly enough to qualify as a Stealth agent, and the latter is only lethal if calves are infected at a young age.

2. Based on our estimate for natural Wildfire pandemics given above, a single plausible historical example would produce an estimated likelihood of a natural Stealth pandemic of 0% to 0.1% / year. In the absence of such an example in either humans or animals, it seems reasonable to discount this estimate at least ten-fold, likely more.

→ **Estimated probability of a natural Stealth pandemic = 0% to <0.01% / year**

B. Likelihood of an accidental Stealth pandemic

Estimate 1: Laboratory accident rates

1. A national bioweapons programme may attempt to develop Stealth pathogens for the same (misguided) reasons that they might develop Wildfire pathogens. But Stealth pathogens need only be pandemic capable; they do not require a basic reproduction number around 6. This reduces the risk of a laboratory-acquired infection resulting in a pandemic: a single individual infected with an R_0=2 pathogen is only 10-60% likely to cause an extended outbreak, as compared to 50-99% for an R_0=6 pathogen.[107]
2. Taking the estimated risk of a laboratory-acquired infection at a bioweapon laboratory of 1.23% to 8% per year from our Wildfire estimate above, and multiplying by this reduced risk of such an infection causing a sustained outbreak, we obtain an estimate of (1.23% to 8%) × (10% to 60%) = 0.12% to 4.8% per year – assuming again that a single laboratory exists that is working with a Stealth agent.

→ **P(accidental Stealth pandemic) ≈ 0.12% to 4.8% / year / laboratory (Method 1)**

Estimate 2: Programme-caused outbreaks

1. We cannot directly use the historical base rate to estimate the likelihood of bioweapons programme accidents involving Stealth agents, because there are no known examples of such programmes working with these agents, let alone accidents.
2. However, if we assume that the primary relevant difference between Stealth and Wildfire agents is their expected contagiousness, we can use that to adjust the previously calculated historical base rate of accidents involving Wildfire agents per bioweapons programme as we did for individual laboratories above. For example, if the Aralsk incident had involved a less contagious pathogen, it may have failed to infect the index patient, or if it had, may not have been transmitted to others.
3. Assuming a Wildfire pathogen would exhibit an R_0 of 5.5 (50-99% chance of pandemic per infection) and that a typical Stealth pathogen exhibits an R_0 of 2.0 (10-60% chance per infection), we can make a crude adjustment to the estimated annual likelihood by multiplying by the ratios of these upper and lower bounds. Applying this adjustment yields a lower-bound annual likelihood of 1.4% × 10/50 = 0.28%, and an upper-bound likelihood of 8.6% × 60/99 = 5.2%.

→ **P(accidental Stealth pandemic) ≈ 0.28% to 5.2% / year / programme (Method 2)**

C. Likelihood of a deliberately released Stealth pandemic (single known Stealth agent)

Unlike for Wildfire, there are no known examples of Stealth agents arising in nature. For this and other reasons, the probability of successfully releasing a Stealth agent through the simultaneous release of multiple characterised pandemic pathogens is far lower than for Wildfire – low enough that we consider it to be negligible. Consequently, we only here consider the single scenario of a known and characterised Stealth agent. While the availability of credible blueprints for a Stealth agent may seem to invalidate the premise of a pathogen capable of undetectably infecting most of humankind before anyone begins to show severe symptoms, the rise of protein design models that can predict many sequences capable of performing a desired molecular function implies that it may not be possible to search for every possible functional equivalent of even a Stealth agent of known design. In this case, "blueprints" do not necessarily refer to an exact DNA sequence, but to functional instructions capable of generating one of many functional sequences with the desired properties.

Retaining from Appendix 1 the estimated annual likelihood of a deliberate pandemic release that infects at least one person (2.8% to 22.4% / year), and combining this with the likelihood of an initial infection causing a sustained outbreak from the accidental Stealth outbreak estimate above (10% to 60%), we obtain a rough estimate of the rate of successful deliberate Stealth releases per year, given the availability of a credible blueprint for a Stealth agent: (2.8% to 22.4%) × (10% to 60%) = (0.28% to 13.44%).

→ **P(deliberate released Stealth | publicly known Stealth agent) ≈ 0.28% to 13.4% / year**

As above, we do not formally model the likelihood that blueprints for such an agent will be made public, only the probability that a deliberate pandemic occurs once someone has done so. That said, we do not consider this an implausible scenario. Once the broad concepts permitting the construction of a Stealth agent are first proposed, discussion and disagreement over its feasibility will both increase the profile of the topic and incentivise further researchers and publications, eventually leading to the release of publicly available blueprints for a Stealth pathogen.

Table A2: Estimated likelihood of a Stealth scenario

Source	Assumption	Low	High	Units	Basis of estimate
Natural spillover	No historical Stealth pathogens (>1 year incubation, lethal)	Tiny	<0.01%	Per year	No known natural Stealth pathogens; spillover risk change
Bioweapon accident	A bioweapons lab is developing a Stealth agent	0.12%	4.8%	Per lab per year	FSAP/NIH lab infection rates, spread from 1 individual (R_0=2), 5x increase over civilian rate
Bioweapon accident	A bioweapons programme is developing a Stealth agent	0.28%	5.2%	Per programme per year	Historical accident rate involving pandemic bioweapons, adjusted for difference in reproduction number between Wildfire (5.5) and Stealth (2.0) scenarios
Deliberate	Credible blueprints for a Stealth pathogen are publicly available	0.28%	13.4%	Per year	Historical mass murderers with the skills to follow a reverse genetics protocol corresponding to a known genomic sequence

Stealth agents are expected to exhibit transmission rates more similar to typical pandemic viruses rather than Wildfire agents, reducing the likelihood of a pandemic per infected individual. Because there are no known Stealth-class pathogens in human history, only an upper bound can be established for a natural origin. Data on laboratory-acquired infections can estimate the likelihood of an accident involving a biological weapons programme conditional on its successful development of a Stealth agent. As with Wildfire, the publication of genomic blueprints would provide access to all those capable of following an existing protocol to assemble infectious samples using unscreened synthetic DNA.

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