NAVIGATING UNCERTAINTY

FORECASTING THE EFFECTS OF COVID-19 THROUGH THE LENS OF VALUE PLURALISM

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EXECUTIVE SUMMARY

The Covid-19 pandemic continues to cause significant adverse effects to both individual and population health. In addition, other high consequence biological risks currently face us as a species: the possibility of H5N1 Highly Pathogenic Avian Influenza (HPAI) mutating to allow for efficient human to human transmission; the potential emergence of a new Variant of Concern (VOC) of SARS-CoV-2 that possesses vaccine escape properties and higher virulence; the possibility of a recombination occurring between SARS-CoV-2 and MERS, and the growing threat posed by the emergence of a fully antimicrobial resistant bacterial or fungal pathogen. To increase our individual, collective, and global resistance against all of these threats, the adoption of effective mitigation strategies, technologies, and systems is imperative. However, in order to maximise adoption of these strategies, technologies, and systems, lessons learned from the initial response to Covid-19 and the insights provided by value pluralism must be synthesised. Such a synthesis produces a set of value-neutral adoption criteria that should be applied to any proposed mitigation strategy, technology, or system in order to assess the likelihood of its successful adoption. These value-neutral adoption criteria are unobtrusiveness, non-restrictiveness, allowing for full control over one's material environment, informed consent, and the provision of accurate and transparent information. Forecasting the adverse health and population effects of the continued unmitigated transmission of SARS-CoV-2, at one year, two years, and five years from now provides the necessary impetus for urgent mitigation of transmission. In addition, the debate surrounding the origin of SARS-CoV-2 has emphasised the importance of regulating dual use research of concern (DURC) in the life sciences. A framework for mitigating SARS-CoV-2 and other airborne pathogens will only succeed if all of its components – increased population resilience, mitigation of near-field and far-field transmission, environmental biosensing and personal rapid testing, decentralised low-cost surveillance genotyping, and the deployment of effective 2nd generation blockers, therapeutics, and vaccines – fully meet value-neutral adoption criteria.

RECOMMENDATIONS

- Mitigations against airborne pathogens are most likely to be widely accepted and adopted if they meet value-neutral adoption criteria – unobtrusive, non-restrictive, allowing full control over one's material environment, informed consent, and the provision of accurate and transparent information.

- The threat of High-Consequence Biological Risks requires the urgent development, acceleration, and adoption of mitigation technologies that meet value-neutral adoption criteria.

- The accelerated development and commercial availability of inexpensive and accurate personal and point-of-care tests for Covid-19 is a priority infection risk mitigation strategy in 2025.

- The accelerated open-source design and global deployment of inexpensive and accurate genomic surveillance systems is a priority biological risk reduction strategy in 2025.

- Redouble efforts to ensure that all people living with HIV have easy access to antiretroviral therapy (ART).

- The accelerated development of simple and easily accessible tests for SARS-CoV-2 persistent infection and the accelerated development of treatments for persistent infection.

- The establishment of a trusted international multidisciplinary thought leadership organisation that can effectively develop mitigation strategies for SARS-CoV-2 and other airborne pathogens while simultaneously safeguarding individual liberty, economic prosperity, and human connection.

- In collaboration with national cancer screening programmes, design and fund studies to identify early warnings of increased cancer incidence related to SARS-CoV-2 infection.

INTRODUCTION

The COVID-19 pandemic has, and continues to have, highly significant and demonstrable effects on not only human health – both at the individual and population levels – but also on economies, politics, and, by extension, our global collective ability to confront future pandemic threats. With the spectre of H5N1 Highly Pathogenic Avian Influenza (HPAI) currently looming in North America, it is absolutely imperative that we develop robust mitigation strategies to not only significantly reduce the impacts of Covid-19, but also to create societies that are highly resilient against the danger posed by airborne pathogens. However, the SARS-CoV-2 virus, the causative pathogen of Covid-19, has not only been responsible for the deaths of millions of people since 2020, but our global response to mitigating it has both caused and fuelled political polarisation in many countries worldwide. In addition, the propensity of SARS-CoV-2 to not only cause acute infection but also medium to long-term adverse health effects – known as Long Covid (LC) or Post-Acute Sequelae of SARS-CoV-2 infection (PASC) – is increasing the prevalence of chronic disease and disability in the global population; this, in turn, is both increasing burdens on healthcare systems and hampering the ability of those affected to participate effectively in the workforce. Covid-19 vaccines, while effective at preventing severe disease and subsequent hospitalisation, do not provide significant protection against infection; even in highly vaccinated populations, in the absence of other mitigations, regular re-infection with the virus is now the norm. Since LC can develop after any infection or re-infection, it can easily be seen that in the context of unmitigated global transmission of SARS-CoV-2, global population health will inexorably worsen as time passes. However, due to the inherent properties of SARS-CoV-2, specifically its ability to transmit asymptomatically and the airborne nature of its transmission, mitigation against infection beyond the minimal protection provided by current vaccines is difficult, requiring diligent use of respirator masks to protect against near-field transmission. Masking, while effective, is a charged topic that has been highly politicised in many countries; masking may also adversely affect human connection, due to its inherent incompatibility with eating and drinking in public places. Technology to reduce the risk of far-field transmission – primarily High Efficiency Particulate Air (HEPA) filtration and Far UVC light – is available but has yet to be widely adopted and deployed. In addition, messaging to the general public from governmental public health agencies has been, in general, inadequate in conveying the risk posed by Covid-19; the downstream effect of this inadequate messaging is an utter lack of urgency in any national, institutional, or organisational attempt to mitigate transmission of SARS-CoV-2. However, in order to transform this pervasive inertia of mitigation, it is crucial to understand why it is occurring.

Fundamentally, we are collectively failing to mitigate transmission of SARS-CoV-2 for the following four reasons:

The initial phase of the pandemic – essentially before the widespread deployment of vaccines – was characterised by a set of non-pharmaceutical interventions (NPIs) that caused significant psychological trauma and economic hardship for many people. The stringency of these NPIs varied from country to country, but common themes are apparent across national boundaries: a high prevalence of Post Traumatic Stress Disorder (PTSD) amongst frontline healthcare workers[1]; social isolation[2]; increased substance abuse[3]; reduced earnings or unemployment; inability to visit elderly loved ones in residential nursing care; interruption in the education of school-age children and university students, and inability to participate in socially and psychologically important traditions or ceremonies, especially funerals. Access to routine healthcare was also limited in many countries during this period, leading to a reduction in preventative medicine, specifically cancer screening[4]. In short, many people deemed the effects of societal NPIs more damaging than infection with the virus. The overall effect of this collective psychological trauma is a pervasive psychosocial imperative to actively forget about Covid-19; this in turn disincentivises the deployment of existing mitigation technologies and also politicises them, since political parties understand that discussing Covid-19 is unpopular to a public that consciously or unconsciously wishes to forget it.

The brute-force nature of some of the NPIs used during the initial phase of the pandemic – specifically lockdowns and associated business closures – caused significant economic damage, characterised by stagnation of economic growth and consumer activity[5]. This led to some national governments being forced to balance mitigation of SARS-CoV-2 transmission with an imperative to maintain their own countries' economies. As a result of this, many policymakers now subscribe to a false dichotomy: that mitigating SARS-CoV-2 equates to economic damage, because, from a policy perspective, the concept of mitigation is now inextricably linked with lockdowns. Of course, this is absolutely not the

[1] S. Andhavaparu et al, 'Post-Traumatic Stress in healthcare workers during the Covid-19 pandemic: A systematic review and meta-analysis', *Psychiatry Research*, vol. 317, 2022.
[2] H. Tzung-Jeng et al, 'Loneliness and social isolation during the Covid-19 pandemic', *International Psychogeriatrics*, 2020, pp. 1217-1220.
[3] A. Roberts et al, 'Alcohol and other substance use during the Covid-19 pandemic: A systematic review', *Drug and Alcohol Dependence*, vol. 229, 2021.
[4] R. Shah et al, 'The global impact of the Covid-19 pandemic on delays and disruptions in cancer care services: a systematic review and meta-analysis', *Nature Cancer*, 2025.
[5] R. Chen et al, 'Analysing the impact of Covid-19 on consumption behaviours through recession and recovery patterns', *Scientific Reports*, vol. 14, 2024.

case; the transmission of SARS-CoV-2 can be effectively mitigated without adversely affecting economies.

The emergence of SARS-CoV-2 and subsequent responses to mitigating it rapidly became a conflict of values. Lockdowns undoubtedly saved many lives by preventing healthcare services from being overwhelmed, but also impinged on individual liberty. Vaccine mandates also undoubtedly saved lives but impacted individual human autonomy. The interruptions of long-standing societal traditions, such as religious services, deeply impacted those who valued tradition and faith. In short, the personal impact of NPIs was very strongly related to the values that any given individual held as prime.

Poor public health messaging and a lack of transparency regarding the efficacy of both NPIs and vaccines contributed to a lack of trust in public health agencies and governments. The initial emphasis on social distancing and hand washing rather than respiratory protection and ventilation – even though it was very clear from early 2020 that SARS-CoV-2 primarily transmitted via the airborne route – significantly contributed to this lack of trust; likewise, the messaging that vaccines prevented transmission, which was patently false, had the same effect[6]. This lack of accurate information regarding mitigations from governmental sources has, tragically, led to a current lack of trust in any suggested mitigation strategy.

As such, the success of any future mitigation strategy for SARS-CoV-2, and indeed, for any airborne pathogen, is highly contingent on addressing these issues. Successful mitigation therefore hinges on *unobtrusiveness*, so as not to invoke traumatic memories; *non-restrictiveness*, so as not to cause impingements on liberty, human connection, or economic damage; *informed consent*, so as not to impinge on human autonomy, and *accurate and transparent information*, to engender trust.

Forecasting of the short, medium and long-term effects of the unmitigated transmission of SARS-CoV-2 is necessary to provide the impetus for the adoption of mitigation strategies that meet the above criteria, while a profound recognition of *value pluralism* – the philosophical idea that there exists a multiplicity of values that while equally morally correct can also be in conflict with one another – is necessary to ensure that future mitigation strategies are morally acceptable and hence ethically adoptable by the greatest number of people possible.

[6] A. Sapienza & R. Falcone, 'The Role of Trust in Covid-19 Vaccine Acceptance: Considerations from a Systematic Review', *International Journal of Environmental Research and Public Health*, vol.20, 2022.

VALUE PLURALISM IN THE CONTEXT OF MITIGATION

To understand why recognising and integrating value pluralism into the design of any mitigation strategy for Covid-19 is crucial for its successful adoption, it is necessary to provide an explanation of the philosophical concepts that both define and underpin it. In everyday life, fundamental values are often in conflict. The question of course, is how do we resolve these conflicts? That is to say, how do we decide which fundamental value ranks above the other? One answer, of course, is the philosophical idea of *ethical monism*. This concept applies an ethical formula to the value conflict, and then uses that formula to rank the values in conflict in a preference order; in other words, application of a formula decides which fundamental value 'wins'[7]. In the context of mitigations against SARS-CoV-2, whether they be vaccines or NPIs, the most common ethical formula that was used was utilitarianism – the idea that the fundamental value that maximises utility to the greatest extent is ethically ranked the highest. Mitigations such as lockdowns were considered ethically justified through utilitarianism, with 'utility' tightly defined as 'that which is most effective at reducing illness and death from Covid-19'. However, this justification – while perfectly ethical from the standpoint of utilitarianism – in practice failed to consider that the value preferences of a great many people were in direct conflict to it. A good example of this is vaccine mandates: the *utility* of the mandate (*reducing illness and death by Covid-19*) directly conflicted with a large number of people whose value preference was that of *bodily autonomy*. But since the ethical formula in operation was utilitarianism, the value preference of this group of people was effectively overridden. This, of course, engendered entirely foreseeable resentment, which in turn led to negative consequences for future vaccine uptake and, more generally, increased political polarisation.

One philosophical solution to this problem is that of value pluralism, which posits that there is no single ethical formula to decide between competing fundamental values. This theory, primarily associated with the work of Isaiah Berlin, not only rejects ethical monism but also considers fundamental values to be 'incommensurable' with one another. That is to say, each fundamental value, be that liberty, or autonomy, or even utility (however it is defined in any particular situation) share no common measure by which they may be ranked and make ethical claims only in reference to themselves. As can be seen, however, the obvious problem at the core of Berlin's conception of value pluralism is that it is simply moral relativism. Berlin himself recognised this, but never really managed to answer this criticism effectively. Many philosophers have attempted to resolve this

[7] G. Crowder, *The Problem of Value Pluralism: Isaiah Berlin and Beyond*, New York, Routledge, 2021, p. 2.

problem at the heart of value pluralism, but, especially in the context of Covid-19 mitigations, the theoretical framework of *central capabilities* put forward by Martha Nussbaum[8] is most convincing. Nussbaum argues that there are ten core capabilities that are independent of one another and incommensurable; in short, they constitute ten fundamental values that cannot be ranked against one another (this, of course, is a value pluralist position). These fundamental values are:

- Life
- Bodily Health
- Bodily Integrity
- Senses, Imagination, and Thought
- Emotions
- Practical reason
- Affiliation
- Other Species (being able to live in relation to nature)
- Play
- Control over one's political and material environment

For the purposes of developing and deploying mitigations against SARS-CoV-2 in the future, the central capabilities that are most important contextually are life (being able to live a life of normal length), bodily health (being able to have good health), bodily integrity (being able to move freely and be secure against assault – especially non-consensual medical interventions), affiliation (especially being able to freely engage in social interaction), play (especially being able to enjoy recreational activities), and control over material environment (especially having the right to seek employment on an equal basis with others). It should also be noted here that the fundamental value of senses, imagination, and thought – which entails being able to think, reason, and guarantees freedom of expression – underscores the *validity* of the ongoing debate regarding the origin of SARS-CoV-2, and accompanying larger issues surrounding *dual use research of concern* (DURC)[9] in the life sciences.

[8] M. Nuusbaum, *Justice and the Capabilities Approach*, Routledge, 2012, pp 1-15.

[9] Dual Use Research of Concern (DURC) is research that is intended to provide a benefit, but which could easily cause harm if misapplied. This misapplication can be accidental or deliberate. An example would be modifying a pathogen to increase its virulence with the aim of producing a vaccine should a similar change occur in the pathogen naturally. However, should the modified pathogen be accidentally released from a research facility through a failure of biosafety protocols, the modified pathogen could infect and cause illness in humans. Another scenario using the same example would be the theft of the modified pathogen and its subsequent use as a biological weapon by state or non-state actors (biological warfare or bioterrorism). See https://oir.nih.gov/sourcebook/ethical-conduct/special-research-considerations/dual-use-research for a concise definition.

With this in mind, Nuusbaum's refined conceptualisation of value pluralism combined with the specific issues that must be addressed to ensure the widest adoption of mitigation measures provides us with a checklist for any proposed new mitigation strategy:

- Unobtrusive
- Non-restrictive (respecting bodily integrity, being able to freely engage in social interaction, and being able to freely enjoy recreational activities)
- Allowing full control over one's material environment
- Informed consent
- The provision of accurate and transparent information

From a pragmatic standpoint, this is not only an ethical framework, but also a framework for maximising adoption. By addressing the reasons that explain why we are not currently mitigating SARS-CoV-2, learning from them, and using the lens of value pluralism to ensure that all fundamental values – as defined by Nuusbaum's central capabilities – are taken into account, we have a recipe to develop and accelerate mitigation technologies and strategies that are most likely to be widely accepted by individuals and societies. The ideal mitigation strategy, technology, or system is one which maximises protection against infection from SARS-CoV-2 or any other airborne pathogen without coming into conflict with any other fundamental values. In effect, the lens of value pluralism, specifically as theorised by Nuusbaum, allows the design of mitigations that are essentially *value-neutral*; this has the potential to de-politicise, or at least reduce the politicisation, of mitigations against SARS-CoV-2. Shifting the concept of mitigations against airborne pathogens away from the extremes of politics and more towards a widely-accepted idea of a common good – such as clean drinking water – would serve to increase the acceleration of their adoption even further. The five criteria derived can therefore be termed *value-neutral adoption criteria*.

Recommendation 1: *Mitigations against airborne pathogens are most likely to be widely accepted and adopted if they meet value-neutral adoption criteria – unobtrusive, non-restrictive, allowing full control over one's material environment, informed consent, and the provision of accurate and transparent information.*

FORECASTING THE FUTURE EFFECTS OF COVID-19

In order to provide impetus for the implementation of mitigation measures against SARS-CoV-2 and other airborne pathogens, it is necessary to provide policymakers, public health agencies and other governmental institutions, industry, and the general public with a realistic set of scenarios that have a high probability of occurring should mitigations not be instituted at a widespread level across societies. These scenarios are as follows:

- Short-term (one year)
- Medium-term (two years)
- Long-term (five years)

These scenarios take into account the sum of our knowledge regarding SARS-CoV-2 at this point and extrapolate the cumulative effects of ongoing unmitigated global transmission of the virus. The scenarios also include the possible deployment of 2nd generation vaccines, therapeutics, and novel technologies that are currently in development, and, importantly, assess the likelihood of their adoption by referencing the value-neutral adoption criteria derived above. In addition, the scenarios attempt to position the ongoing global transmission of SARS-CoV-2 within a wider geopolitical context, since politics – especially the domestic politics of the United States – are likely to play a considerable role in the future in determining how SARS-CoV-2 and other airborne pathogens are mitigated.

However, it is important to note at this point that there also exists a set of serious biological risks that could occur *at any time*. As a result of this unpredictability, these risks will not be categorised into any of the scenarios but will rather be characterised as *high-consequence biological risks*. Each scenario therefore also includes the possibility of any or all of these risks occurring within the time period covered.

HIGH-CONSEQUENCE BIOLOGICAL RISKS

1. H5N1 Highly Pathogenic Avian Influenza developing mutations that allow for efficient human to human transmission.

The A (H5N1) clade 2.3.4.4b virus is currently transmitting at very high levels in the United States and Canada. The vast majority of cases are in animals, particularly wild birds, poultry, and dairy cattle. However, there are a growing number of confirmed human cases, including two cases that have caused extremely severe illness in one patient and death in another (the former in British Columbia and the latter in Louisiana). The two severe human cases were infected with the D1.1 genotype of the H5N1 virus, whereas the mild to moderate human cases were predominantly infected with the B3.13 genotype. Concerningly, in both of the severe human cases, the virus mutated to allow for greater affinity to the upper respiratory tract[10]. These mutations occurred in a protein on the surface of the virus (akin to the spike protein of SARS-CoV-2); these proteins are normally optimised to bind to receptors in the respiratory tracts of birds, but the mutations observed in the two severe cases allowed the virus to bind to receptors in the human respiratory tract. Neither of these infected patients transmitted the virus to other people, but, regardless, the trajectory of mutation is worrying. In addition, with a high prevalence of seasonal influenza in North America, the possibility of a reassortment event – effectively seasonal influenza and H5N1 mixing in a co-infected patient to create a hybrid influenza virus – increases in direct proportion to the number of humans infected with H5N1 (which, according to a recent serological study conducted by the CDC[11], is likely far higher by several orders of magnitude than the official case count). If such a reassortment event occurred, especially between seasonal influenza and the D1.1 genotype, then a very dangerous new influenza pandemic could easily be the outcome. It is important to remember that as long as H5N1 is circulating at medium to high levels in North America, this could occur at any time. Should H5N1 spark a new pandemic, the concurrent global circulation of SARS-CoV-2 would worsen patient outcomes; co-infection with SARS-CoV-2 and a novel influenza would undoubtedly increase the likely case fatality rate (CFR). More importantly, currently available mitigations for a possible H5N1 pandemic consist of vaccines, antivirals, personal protective equipment (PPE) – including respirators – and similar NPIs to those enacted against Covid-19 in 2020 / 2021. Applying our value-neutral adoption criteria

[10] A. Jassem et al, ‘Critical Illness in an adolescent with Influenza A(H5N1) Virus Infection’, *New England Journal of Medicine*, 2024.

[11] A. Mellis, ‘Serologic Evidence of Recent Infection with Highly Pathogenic Avian Influenza A(H5) Virus Among Dairy Workers – Michigan and Colorado, June-August 2024’, *MMWR*, vol. 73, 2024, pp.1004 – 1009.

to these available mitigations, it can be seen that adoption of these mitigations would likely be less than optimal. Vaccine mandates would not meet the criteria of *non-restrictive*, by virtue of not respecting bodily autonomy; widespread respirator use would not meet the criteria of *unobtrusive*, and any lockdowns or stay at home orders would also not meet the criteria of *non-restrictive*, purely by the inherent nature of these NPIs. As such, many mitigations necessary to reduce the impact of a potential H5N1 pandemic would not be successfully implemented in many countries, especially the US and Canada.

2. The emergence of a new SARS-CoV-2 Variant of Concern (VOC) with potential vaccine escape that causes severe disease in a greater proportion of the population than has occurred thus far.

It is quite possible, through either point mutation or recombination, that a new SARS-CoV-2 VOC with a higher CFR and increased vaccine escape could emerge. SARS-CoV-2 is a highly mutable virus, which has demonstrated a highly significant ability to achieve fitness through immune evasion. Although all currently circulating sub-lineages of SARS-CoV-2 are fundamentally descendants of the Omicron VOC, there is no reason why a new VOC with increased virulence and immune evasion could not emerge at any time. Since SARS-CoV-2 is now essentially unmitigated globally, the sheer number of infections – especially chronic infections occurring in immunocompromised individuals – make such a mutation more likely than if transmission was being mitigated[12]. As with a potential H5N1 pandemic, a new SARS-CoV-2 VOC that evaded pre-existing immunity (whether natural, vaccine-derived, or both) could cause severe pressure on healthcare systems and increased morbidity and mortality worldwide until an updated vaccine could be formulated and deployed. Until such an updated vaccine was available, mitigation strategies (similar to those required for a potential H5N1 pandemic) would be necessary to reduce transmission. Once again, however, the application of our value-neutral adoption criteria suggests that many of these mitigation strategies would be unsuccessful.

[12] NERVTAG, '*Long term evolution of SARS-CoV-2*', 2022.

3. The potential for a recombination event between SARS-CoV-2 and MERS-CoV.

MERS-CoV is the causative pathogen of Middle East Respiratory Syndrome (MERS). MERS is a highly dangerous disease, with a CFR of approximately 30%. Although rare, it is present in many countries in or near the Arabian Peninsula and is typically acquired through direct or indirect contact with infected dromedaries. MERS can also transmit between humans, but, unlike SARS-CoV-2, this transmission seems to require prolonged contact, such as in households or hospital settings. Both SARS-CoV-2 and MERS-CoV are coronaviruses, and research has demonstrated the possibility of recombination of the viruses if a host was co-infected with them both[13]. This host could be a human, or potentially a dromedary. Such a recombination event could create a novel coronavirus with pandemic potential, possibly with a significantly higher CFR than SARS-CoV-2. Although vaccines for MERS are in development, and show significant promise, there is no guarantee that either a MERS vaccine or a Covid-19 vaccine would have any efficacy against a resultant recombinant pandemic virus. As with the two-preceding high-consequence biological risks, mitigation strategies would be likely sub-optimal, because the majority of those available do not meet value-neutral adoption criteria.

4. The potential for the widespread emergence of a fully antimicrobial resistant pathogenic bacteria or fungi with pandemic potential.

Rates of antimicrobial resistance (AMR) to common bacterial and fungal pathogens are increasing at an alarming rate; a recent study estimated that 4.95 million deaths were associated with bacterial AMR globally in 2019.[14]. Although a pandemic occurring as a result of a fully antimicrobial resistant pathogen occurring in the next five years is a very low probability event, the consequences would be devastating. AMR fungal pathogens are already rapidly becoming a significant biological risk in hospital settings in some parts of the US, with *C. auris* now considered a serious public health threat[15], and extensively drug-resistant tuberculosis (XDR-TB) is increasing in prevalence every

[13] A. Sajini et al, 'The Recombination Potential between SARS-CoV-2 and MERS-CoV from Cross-Species Spillover Infections', *Journal of Epidemiology and Global Health*, vol.11, 2021, pp. 155-159.
[14] R. Laxminarayan, 'The overlooked pandemic of antimicrobial resistance', *The Lancet*, vol. 399, 2022.
[15] M. Lionakis & A. Chowdhary, 'Candida auris Infections', *The New England Journal of Medicine*, vol. 391, 2024, pp. 1924-1935.

year[16]. As such, it is possible that a common bacterial or fungal pathogen could develop such a high degree of AMR that it could spark an epidemic or pandemic.

Recommendation 2: *The threat of High-Consequence Biological Risks requires the urgent development, acceleration, and adoption of mitigation technologies that meet value-neutral adoption criteria.*

SHORT-TERM FORECAST (JANUARY 2026)

Extrapolating from 2024 prevalence data[17], it is likely that there will be two or three significant waves of Covid-19 globally between January 2025 and January 2026. In the United States, it is unlikely but still possible that any of these waves will be greater than a peak of two million infections per day. However, it is important to remember that Covid-19 circulates year-round at relatively high levels; even during lulls, 150,000 infections per day in the United States is to be expected. Thankfully, mortality rates from acute Covid-19 are likely to stabilise at 2024 levels, or even decrease slightly. Of course, it is important to remember that SARS-CoV-2 is an extremely mutable virus, and should a variant emerge in a manner similar to BA.2.86 (the progenitor of JN.1) – through chronic infection in an individual – it is quite possible that such a variant, with a large number of mutations, could cause a surge of infections in excess of two million infections per day; this could occur at any time between now and January 2026. The key role that chronic infection plays in the emergence of these 'stepwise' highly transmissible variants cannot be understated. However, regardless of whether a JN.1 type variant emerges, the overall picture is still that of a very large number of infections globally in the course of the next year; this very large number of annual infections guarantees constant mutation of SARS-CoV-2, which in turn leads to increased immune evasiveness of the virus, which leads to further infections. In short, unmitigated global transmission of SARS-CoV-2 gives the virus the greatest chance to mutate at speed. It is this very speed of mutation that contributes to the fact there is no long-lasting immunity to infection by SARS-CoV-2; immunity, whether derived from infection, vaccination, or both, wanes very quickly indeed, allowing for multiple infections per year.

[16] M. Jassal & W. Bishai, 'Extensively drug-resistant tuberculosis', *The Lancet Infectious Diseases*, vol. 9, 2009, pp. 19-30.
[17] Data obtained from the *Pandemic Mitigation Collaborative*, pmc19.org, last accessed 04/01/2025.

The effects of Covid-19 from January 2025 to January 2026 will be similar to those from the previous year. A significant percentage of the global population will suffer from acute Covid-19 at least once during this period, leading to sickness absences from work, and / or reduced workplace productivity. School absences are also to be expected for the same reason. Schools and workplaces are often nodes of transmission in communities; reducing transmission in schools not only leads to reduced absences but also to a reduction of cases in the wider community[18]. Likewise, reducing transmission in workplaces leads to fewer employee absences and makes maintaining overall business productivity easier.

However, even though acute Covid-19 will continue to cause deaths and hospitalisations over the next year, rates of LC will continue to rise. While the incidence of LC following acute infection is contested, a conservative estimate of incidence is between 10-30% of non-hospitalised unvaccinated cases, 50-70% of hospitalised cases, and 10-12% of vaccinated cases[19]. When patients develop LC, full recovery is uncommon – approximately 15-20% of patients recover fully, 10% show no improvement, even over years, and the remaining 70-75% show some improvement, but do not return to baseline (the level of health they had before the acute SARS-CoV-2 infection that triggered their LC). Re-infection with SARS-CoV-2 can also worsen LC patients' symptoms or cause new ones[20]. With only 15-20% of LC patients recovering fully, it can easily be seen that the global cumulative incidence of LC – currently estimated at approximately 400 million individuals[21] – will likely increase significantly by January 2026. This increasing prevalence of LC from January 2025 to January 2026 will inexorably lead to an increased number of people unable to work due to their illness, and will also place further stress on healthcare systems worldwide – especially from those LC patients who develop new-onset cardiovascular disease, new-onset diabetes, new-onset autoimmune disease, and new-onset cognitive impairment. Likewise, as the number of patients with cardiovascular-type, endocrine-type, and autoimmune-type LC inexorably rises, so too will the aggregate number of more serious acute Covid-19 infections. This is because all of these conditions are themselves risk factors for acute Covid-19 infection. Covid-19 is a unique disease in one very pernicious sense: the risk factors that predispose an individual to a more severe initial acute infection

[18] L. White et al, 'The role of schools in driving SARS-CoV-2 transmission: Not just an open-and-shut case', *Cell Reports Medicine*, vol. 3, 2022.
[19] H. Davis et al, 'Long COVID: major findings, mechanisms and recommendations', *Nature Reviews Microbiology*, vol. 21, 2023, pp. 133-146.
[20] J. Ducharme, 'Long COVID Recovery Remains Rare. Doctors are Struggling to Understand Why', *Time*, August 29, 2023.
[21] Z. Al-Aly et al, 'Long COVID science, research and policy', *Nature Medicine*, vol. 30, 2024, pp. 2148-2164.

can also be caused as a result of an initial acute infection. Because of its propensity to reinfect, Covid-19 can therefore create an inexorable downward spiral of health in individuals thus affected.

Domestic politics in the United States could potentially have adverse effects on the availability and / or accessibility of Covid-19 vaccines there, and potentially, via a ripple effect, to other countries in the world. Since vaccination is the only intervention we possess that is conclusively proven to reduce the risk of LC, any reduction in vaccine availability is likely to increase rates of LC. Conversely, should the incoming administration seriously address the root causes of the high prevalence of chronic disease in the US population, this could begin the process of reducing the overall risk of hospitalisation for acute Covid-19, by reducing the prevalence of underlying risk factors. In addition,

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if new public health policies were adopted to reduce the prevalence of cardiovascular disease, diabetes, obesity, hypertension, chronic obstructive pulmonary disease (COPD), and physical inactivity, this would have the potential to increase population resilience against acute Covid-19[22] and possibly any future airborne pandemic pathogens. Any potential legislation that reduces access to current Covid-19 vaccines or limits research and development into 2nd generation therapeutics or vaccines constitutes a significant risk to the population health of the United States. It would also constitute an overall *reduction* in mitigation and hence could not be considered a value-neutral policy decision by our definition, since it would not fulfil the criteria of *non-restrictive* and *control over material environment*. On the other hand, if the incoming administration communicated the risks and benefits of vaccination more clearly, this would constitute a value-neutral policy decision, as it would increase both *informed consent* and the *provision of accurate and transparent information* to the general public.

[22] J. Zhang, 'Risk and Protective Factors for Covid-19 Morbidity, Severity, and Mortality', *Clinical Reviews in Allergy and Immunology*, vol. 64, 2022, pp, 90-107.

‘…if new public health policies were adopted to reduce the prevalence of cardiovascular disease, diabetes, obesity, hypertension, chronic obstructive pulmonary disease (COPD), and physical inactivity, this would have the potential to increase population resilience against acute Covid-19 and any future airborne pandemic pathogens’

In 2024 testing for SARS-CoV-2, both by the public and in healthcare settings continued to decrease to considerably lower levels than occurred earlier in the pandemic; this trend will likely continue in the following year. Testing is a *crucial* component of any mitigation strategy; without easy and inexpensive access to accurate testing, members of the public will be unable to determine their infection status, and healthcare systems, especially in low-resource countries, will be unable to test patients in an accurate and timely manner. Access to accurate, low-cost testing also empowers individuals to make informed decisions about their own health. Currently available rapid antigen tests (RATs) have a sensitivity of 47% compared to PCR in asymptomatic and presymptomatic acute Covid-19, only rising to 80% at two to three days from onset of symptoms[23] ; most people cannot afford to serially test, so this low accuracy leads to not only missed diagnoses of symptomatic Covid-19, but also essentially fails entirely to reliably detect asymptomatic or presymptomatic disease. Since transmission – including superspreading events – is often driven by individuals who are asymptomatic, this lack of accurate low-cost testing significantly hinders mitigation. Much more accurate home and point-of-care nucleic acid tests (NATs) are commercially available, but relatively expensive; this places them out of the reach of most people. Widely available, accurate, and affordable personal testing is therefore a pressing global need to mitigate the transmission of SARS-CoV-2, and also meets value-neutral adoption criteria. It is unobtrusive, non-restrictive, allows full control over one’s material environment, entails informed consent, and provides accurate and transparent information to the user. As such, affordable and accurate testing would likely be widely adopted if available. Novel testing technologies that do not involve nasal swabbing are already available or currently at the prototype stage; Forced Cough Vocalization (FCV), pioneered by RAIsonance AI, utilises machine learning technology to analyse cough signatures and diagnose respiratory illnesses with a high degree of accuracy, using only a smartphone with an internet connection[24]. Likewise, technology has been developed to diagnose SARS-CoV-2 infection through

[23] S. Smith-Jeffcoat et al, ‘SARS-CoV-2 Viral Shedding and Rapid Antigen Test Performance’, *Respiratory Virus Transmission Network*, CDC, 2022-2023.
[24] https://raisonance.ai/ , last accessed 06/01/2025.

breath sampling[25]. These non-invasive testing methods should be accelerated, as they both fully meet value-neutral adoption criteria.

Recommendation 3: *The accelerated development and commercial availability of inexpensive and accurate personal and point-of-care tests for Covid-19 is a priority infection risk mitigation strategy in 2025.*

In concert with reduced testing, global surveillance for new variants and sub-lineages of SARS-CoV-2 continues to decline[26]; this concerning trend will likely not be reversed in 2025. Genomic surveillance of SARS-CoV-2 is absolutely vital to detect potential new VOCs as early as possible, allowing for prompt assessment of current vaccine effectiveness. Comprehensive global genomic surveillance of SARS-CoV-2 would also provide a vastly increased amount of data to train existing AI systems to predict viral evolution[27]; this technology has the potential to design vaccines for high-consequence mutations before they occur. However, sequencing of SARS-CoV-2 is relatively expensive, and is now rarely performed in low- and medium-income countries; even in high income countries, sequencing rates have decreased. Although the cost of sequencing has decreased significantly in the last decade, it is still technically, financially, and logistically challenging in resource-limited settings[28]. As such, there exists a pressing need to rapidly expand our global genomic surveillance capability for both SARS-CoV-2 and other pathogens with pandemic potential (such as H5N1) through the accelerated development of low-cost and high-efficiency genomic surveillance systems. Open-source design of such systems would, of course, reduce the cost even further, allowing for utilisation in even the most resource-limited geographical regions of the world.

Recommendation 4: *The accelerated open-source design and global deployment of inexpensive and accurate genomic surveillance systems is a priority biological risk reduction strategy in 2025.*

[25] R. Myers et al, ‘Breath testing for SARS-CoV-2 infection’, *eBioMedicine – The Lancet*, vol. 92, 2023.
[26] Covid-19 Surveillance’, *WHO Policy Brief*, December 2024.
[27] N. Pasquini, ‘Predicting Viral Variants and Vaccine Cures’, *Harvard Magazine*, December 2024.
[28] Y. Furuse, ‘Genomic sequencing effort for SARS-CoV-2 by country during the pandemic’, *International Journal of Infectious Diseases*, vol. 103, 2021, pp. 305-307.

In a similar manner to personal and point-of-care testing, low-cost genomic surveillance also meets value-neutral adoption criteria as a mitigation strategy.

In North America and the European region, it is very unlikely indeed that 2nd generation mucosal Covid-19 vaccines will be deployed before January 2026. Project NextGen is currently only supporting three programs for nasal vaccine candidates, and none of these candidates will be approved this year. Castlevax's nasal vaccine candidate is currently only in Phase 1 trials, while CyanVac's and Codagenix's nasal vaccine candidates are still in Phase 2 trials[29]. However, a 2nd generation nasal vaccine – iNCOVACC, developed by Washington University and Bharat Biotech[30] – has been approved and rolled out in India as a heterologous booster for those who have already received at least two doses of a 1st generation vaccine. This is frustrating, as a landmark study[31] conducted in animal models in July 2024 showed that another candidate nasal vaccine both blocked transmission of SARS-CoV-2 and reduced viral titres following exposure by 100 in the upper respiratory tract and 100,000 in the lower respiratory tract[32]; this of course raises the very real possibility that a human vaccine based on this platform could have a significantly higher efficacy against symptomatic disease than any currently available vaccine.

The United States Advanced Research Projects Agency – Health (ARPA-H) launched its BREATHE (Building Resilient Environments for Air and Total Health) project in April 2024[33]. The focus of the project is the monitoring and improvement of indoor air quality through the utilisation of biosensors, respiratory risk analysis software, and the installation of systems in buildings to deliver healthier air. This project has significant promise to develop systems that will dramatically reduce the transmission of SARS-CoV-2 and other airborne pathogens inside buildings and will likely show results by the end of 2025. Improving indoor air quality, is, of course, a crucial element of mitigating SARS-CoV-2; the technology and systems that will be developed by BREATHE will have the potential for widespread adoption.

Sadly, 2025 may well see increasing political support for mask bans, especially in the United States. Mask bans tend to have a *surface* justification rooted in the prevention of crime or protests – surgical

[29] https://medicalcountermeasures.gov/nextgen , *BARDA*, last accessed 05/01/2025.
[30] https://medicine.washu.edu/news/worlds-first-nasal-covid-19-vaccine-approved-in-india-based-on-washington-university-technology/ , last accessed 05/12/2025.
[31] T. Darling et al, 'Mucosal immunization with ChAd-SARS-CoV-2-S prevents sequential transmission of SARS-CoV-2 to unvaccinated hamsters', *Science Advances*, vol. 10, 2024.
[32] E. Topol, 'The Indomitable Covid Virus', https://erictopol.substack.com/p/the-indomitable-covid-virus , last accessed 05/12/2025.
[33] https://arpa-h.gov/research-and-funding/programs/breathe , last accessed 05/12/2025.

masks or respirators obviously cover at least part of the face, thus partially concealing identity – but a more *deeper and accurate* explanation for the likely increasing rate of mask bans in the US (and also potentially in the European region) as 2025 progresses is both psychosocial and political. When former CDC Director, Rochelle Walensky, declared in late February 2022 that, 'the scarlet letter of this pandemic is the mask… it reminds us that we're in the middle of a pandemic'[34], she – perhaps inadvertently – spoke directly to the widespread psychosocial phenomenon (detailed in the introduction of this report) of society wishing to actively forget the Covid-19 pandemic, which of course underpins the value of *unobtrusiveness* in the adoption of mitigation strategies. Masking has also become deeply political, being strongly associated with the political left. Ironically, in the United States, the *extreme* politicisation of masks did not begin with the political right, but rather was sparked by the political left's reaction to mask refusal[35]. Regardless, masks have now become political symbols and are likely to remain so for the foreseeable future; as a result, this will further reduce individuals' ability to protect themselves from infection and from infecting others. In addition, the politicisation of masks and the likely proliferation of mask bans in the US in 2025 may well have significant adverse downstream effects on the introduction and adoption of other technologies specifically designed to mitigate the transmission of SARS-CoV-2.

> *'…masks have now become political symbols and are likely to remain so for the foreseeable future; as a result, this will further reduce individuals' ability to protect themselves from infection and from infecting others'*

MEDIUM-TERM FORECAST (JANUARY 2027)

Preceding from the assumption that transmission of SARS-CoV-2 still remains effectively unmitigated globally by this point, rates of acute infection will likely remain similar to those estimated in the previous scenario. However, the possibility of the emergence of a VOC with an impact similar to the emergence of the Omicron VOC in late 2021 is likely by this point. This could lead to an extremely large and disruptive wave of infections, potentially reaching a peak of five million infections per day in the United States. Such a VOC is very likely to emerge as a result of a

[34] A. Slavitt, 'What the CDC Director Really Wants You to Know', 2022, https://podcasts.apple.com/us/podcast/what-the-cdc-director-really-wants-you-to-know/id1504128553?i=1000551739869 , last accessed 05/01/2025.
[35] C. Scoville et al, 'Mask Refusal Backlash: The Politicization of Face Masks in the American Public Sphere during the Early Stages of the Covid-19 Pandemic', *Socius: Sociological Research for a Dynamic World*, 2022.

long-term chronic infection in an immunocompromised individual[36]. The SARS-CoV-2 virus can undergo extensive evolution in the context of persistent infection in an immunocompromised host[37], leading to significantly altered virus phenotypes; these altered phenotypes can confer both antigenic escape and enhanced ACE2 receptor binding affinity. Extensive SARS-CoV-2 evolution has already been observed in patients with advanced HIV and is also likely to occur in patients with B-cell deficiencies[38]. Since patients with advanced HIV are, by virtue of their severe immunocompromised status, at high risk of developing persistent SARS-CoV-2 infections, it is vital that *all* patients with HIV have access to antiretroviral therapy (ART) to reduce their viral load to undetectable. This is not only a worthy goal in and of itself, but by increasing efforts to treat all HIV patients with ART, the probability of a new SARS-CoV-2 VOC emerging would be reduced. Currently, only 77% of all people living with HIV have access to regular ART[39]; in the contexts of both advancing human health and reducing the risk of the emergence of SARS-CoV-2 VOCs, every effort should be made to increase this percentage to as close to 100% as possible. The relationship between one pathogen – HIV – increasing the likelihood of significant evolution of another pathogen – SARS-CoV-2 – is an example of pathogen-pathogen interaction (PPI)[40], and, as such, HIV and SARS-CoV-2 can be considered to be *syndemic*.

Recommendation 5: *Redouble efforts to ensure that all people living with HIV have easy access to antiretroviral therapy.*

Persistent SARS-CoV-2 infection is surprisingly common, with a prevalence of approximately 0.1 – 0.5%[41] and is associated with the development of LC. As such, persistent infection is an individual risk factor (the development of LC) and a population risk factor (the potential for in-host evolution of a VOC). However, many individuals with persistent SARS-CoV-2 infection may be asymptomatic, and hence unaware of their condition[42]. Even following acute Covid-19, a negative

[36] PV. Markov et al, ‘The evolution of SARS-CoV-2’, *Nature Reviews Microbiology*, vol. 21, 2023, pp. 361-379.
[37] B. Choi et al, ‘Persistence and evolution of SARS-CoV-2 in an immunocompromised host’, *New England Journal of Medicine*, 2020.
[38] H. Machkovech et al, ‘Persistent SARS-CoV-2 infection: significance and implications’, *The Lancet Infectious Diseases*, vol. 24, 2024.
[39] https://www.hiv.gov/hiv-basics/overview/data-and-trends/global-statistics , last accessed 06/01/2025.
[40] M. Singer, ‘Pathogen-pathogen interaction: A syndemic model of complex biosocial processes in disease’, *Virulence*, vol. 1, 2010.
[41] M. Ghafari, ‘Prevalence of persistent SARS-CoV-2 in a large community surveillance study’, *Nature*, 2024.
[42] M. Spinicci et al, ‘Long-term SARS-CoV-2 Asymptomatic Carriage in an Immunocompromised Host: Clinical, Immunological, and Virological Implications’, *Journal of Clinical Immunology*, vol. 42, 2022, pp. 1371-1378.

RAT does not constitute evidence that a persistent infection is not present, and, as such, it is difficult to identify individuals with persistent infection outside of clinical studies. Considering the individual and population health implications of persistent SARS-CoV-2 infection, it is imperative that easily accessible testing and treatment[43] be accelerated. In addition, the common medication, metformin, when used for acute Covid-19, appears to significantly reduce the risk of persistent infection[44]; it is likely that by January 2027, metformin will be routinely prescribed for acute SARS-CoV-2 infection.

Recommendation 6: *The accelerated development of simple and easily accessible tests for SARS-CoV-2 persistent infection and the accelerated development of treatments for persistent infection.*

Cases of LC will continue to increase globally over this scenario period. Individuals with LC will be increasingly likely to experience re-infection purely by virtue of probability; since there is significant evidence that re-infection can worsen LC symptoms[45], the sub-set of individuals with highly disabling LC will, tragically, also increase. As a result of this, by January 2027, the negative impacts of LC on both workforce participation and disability prevalence will prove much more difficult for policymakers worldwide to ignore. In the last four years, the number of Americans claiming disabilities has risen by approximately 35%[46], to a total of 38,844,000 people; extrapolating this figure to January 2027 suggests that by the end of this scenario period, this figure could easily rise to approximately 43 million Americans claiming disabilities. In the UK, the current economic cost of LC – driven predominantly by productivity losses – averages £931 ($1164 USD) per patient per month; with a current LC prevalence of two million people in the UK, this current cost to the UK economy is approximately £20 billion per year[47]. Remembering both the negative impact of re-infections, and the previously noted fact that only 15-20% of patients with LC recover fully, it is not difficult to see that by January 2027 both the global prevalence of LC and its already-staggering economic cost will have increased substantially. Although political responses are difficult to predict,

[43] An extended course of Paxlovid is showing some benefit in this regard, see A. Cohen et al, 'Impact of extended-course oral nirmatrelvir/ritonavir in established Long COVID: a case series'. *Nature*, vol. 372, 2025.
[44] M. Scoullar et al, 'Towards a cure for long COVID: the strengthening case for persistently replicating SARS-CoV-2 as a driver of post-acute sequelae of COVID-19', *The Medical Journal of Australia*, 2024.
[45] P. Joi, 'New survey suggests reinfection worsens Long COVID', *Gavi: The Vaccine Alliance*, 2022.
[46] https://insurancenewsnet.com/innarticle/disability-claims-skyrocket-raising-new-puzzle-alongside-excess-mortality , last accessed 06/01/2025.
[47] J. Wang et al, 'Trajectories of functional limitations, health-related quality of life and societal costs in individuals with long COVID: a population-based longitudinal cohort study', *BMJ*, vol. 14, 2024.

it is probable that during this scenario period, there is likely to be renewed interest amongst policymakers in addressing LC more effectively than they currently are; inexorably rising disability rates and the accompanying adverse economic effects will prove increasingly more difficult to blame on nebulous 'lockdown effects' or 'sick-note cultures'[48]. In essence, by January 2027, many governments will have learned that disability caused by Long Covid cannot either be wished or instructed away. This growing political realisation of the economic damage of LC will likely lead to a slow but steady increase in governmental funding towards addressing the condition.

'… by January 2027, many governments will have learned that disability caused by Long Covid cannot either by wished or instructed away'

This increase in government funding will be accompanied by an increased tempo of translational medicine surrounding both acute Covid-19 and LC; this will begin the process of formalising the treatment of LC in general practice and re-categorising certain medications used by LC specialist physicians – such as low-dose naltrexone (LDN) and tocilizumab[49] – from off-label use to fully approved. However, opposition to mitigation technologies against acute Covid-19 and other airborne pathogens will likely remain, due to the four reasons detailed in the introduction of this report. As a result, trusted international thought leadership will be required to connect governments, industry, academia, and entrepreneurship in order to advance the idea that mitigation of airborne pathogens is both possible and desirable without disrupting society, economies, or human connection. Known as an epistemic community[50] in political science, such an organisation would have significant policy influence[51], and, as such, could effect real change in increasing the resilience of populations to the threat posed by SARS-CoV-2 and other airborne pathogens while simultaneously safeguarding individual liberty and economic prosperity. This, of course, would be made possible by only developing and recommending mitigation systems and strategies that fulfil the *value-neutral adoption criteria* derived earlier in this report.

[48] E. Church, 'Controversial sick note consultation splits healthcare opinion', *Nursing Times*, April 2024.
[49] For a list of all medications currently being trialled for Long Covid, see H. Bonilla et al, 'Therapeutic trials for long COVID-19: A call to action from the interventions taskforce of the RECOVER initiative', *Frontiers in Immunology*, vol. 14, 2023.
[50] See https://www.britannica.com/topic/epistemic-community for a basic description of the concept of an epistemic community.
[51] P. Haas, 'Introduction: Epistemic Communities and International Policy Coordination', International Organization, 1992, pp. 1-35.

Recommendation 7: *The establishment of a trusted international multidisciplinary thought leadership organisation that can effectively develop mitigation strategies for SARS-CoV-2 and other airborne pathogens while simultaneously safeguarding individual liberty, economic prosperity, and human connection.*

It is likely that during this scenario period at least one 2nd generation nasal vaccine for Covid-19 will be approved and potentially deployed in one or more countries. As noted in the previous scenario, the mucosal immunity elicited by these 2nd generation vaccines has the potential to provide high protection against symptomatic infection and also block transmission[52], a huge improvement in efficacy over current vaccines. However, the problem will not be the effectiveness of the vaccine, the problem will be *uptake*. During this scenario period, it is highly likely that vaccine hesitancy and anti-vaccine activism will continue to grow in many countries worldwide. Elements of these viewpoints have already been making inroads into governmental policy in the United States, in both Louisiana[53]and Idaho[54], and this trend will likely increase with the new US administration. Vaccine hesitancy and anti-vaccine activism is not new but increased significantly across the globe following the deployment of the first Covid-19 vaccines. As explained in the introduction to this report, the most effective method to increase uptake of a 2nd generation nasal vaccine would be to be guided by the value-neutral adoption criteria – especially *the provision of accurate and transparent information* and *informed consent*. The widespread uptake of a 2nd generation nasal vaccine would entail public messaging that is ruthlessly honest in terms of risks and benefits of vaccination, with absolutely no coercion of any form to be vaccinated. Vaccine hesitancy and anti-vaccine activism was fuelled in

'The widespread uptake of a 2nd generation nasal vaccine would entail public messaging that is ruthlessly honest in terms of risks and benefits of vaccination, with absolutely no coercion of any form to be vaccinated'

[52] B. Sun et al, 'An intranasally administered adenovirus-vectored SARS-CoV-2 vaccine induces robust mucosal secretory IgA', *Clinical Research and Public Health*, 2024.
[53] https://www.wafb.com/2024/12/20/louisiana-department-health-is-no-longer-publicly-promoting-flu-vaccines/ , last accessed 06/01/2025.
[54] https://www.opb.org/article/2024/11/21/idaho-health-department-covid-19-vaccines-counties-bordering-oregon/ , last accessed 06/01/2025.

2020 / 2021 by policies that utilised coercion to be vaccinated, and public health messaging that failed to provide accurate information about the risks and benefits of vaccination; it would be extremely counter-productive to try the same deeply flawed approach again.

It is also likely during this scenario period that at least one antibody-based nasal spray will become available as a preventative against infection. Sinovac Biotech has already produced and deployed a nasal spray of this type – based on the SA55[55] antibody – to around 300,000 people in China under compassionate use regulations. The spray is also entering a large Phase 3 trial[56], but is already showing impressive results, with an approximate 80% efficacy at blocking infection. These types of nasal preventatives will likely have a much higher adoption rate than 2nd generation nasal vaccines because novel preventatives and therapeutics are not viewed with anywhere close to the same level of suspicion by anti-vaccine advocates. This was strongly evidenced in 2020 / 2021, when monoclonal antibody therapy was readily embraced by many of those opposed to vaccines.[57]

Cognitive dysfunction (erroneously named, 'brain fog') is both a symptom of acute Covid-19 and of LC. In this scenario period, it is likely that the effects of widespread cognitive dysfunction will become much more obvious at a societal level. Cognitive dysfunction is common in LC, with a prevalence of approximately 27%[58], and temporary cognitive issues are also common in acute Covid-19. The effects will be clearest in children and young adults in education, as cognitive dysfunction is most obvious in those individuals who are engaged in learning[59]; this of course has significant adverse implications for the future employment prospects of children and young adults thus affected.

[55] C. Hu et al, 'Safety and Intranasal Retention of a Broad-Spectrum Anti-SARS-CoV-2 Monoclonal Antibody SA55 Nasal Spray in Healthy Volunteers: A Phase 1 Clinical Trial', *Pharmaceutics*, vol. 17, 2024.
[56] J. Cohen, 'COVID 5 years later: Learning from a pandemic many are forgetting', *Science*, vol. 387, 2025.
[57] https://www.nytimes.com/2021/09/18/health/covid-antibody-regeneron.html , last accessed 06/01/2025.
[58] V. Serrano et al, 'Brain and cognitive changes in patients with long COVID compared with infection-recovered control subjects', *Brain*, vol. 147, 2024.
[59] Z. Al-Qahtani et al, 'Memory, Attention, and Concentration Dysfunction Post-COVID-19 Among College Students in Saudi Arabia: A Case-Control Study', *Cureus*, vol. 15, 2023.

LONG-TERM FORECAST (JANUARY 2030)

Continuing with the base assumption that SARS-CoV-2 continues to transmit effectively unmitigated to the end point of this forecast, it is highly likely that at least one new VOC will have emerged at this point, possibly two. As noted in the previous scenario, if these new VOCs are Omicron-type events[60], very high initial waves of infection could be expected as a result. A VOC with increased ACE2 receptor binding and high immune evasiveness would cause explosive global spread; increased virulence could also be a possibility. Of course, even if a new VOC does not emerge during this period, regular waves of SARS-CoV-2 infections would still occur two to three times per year. There is no current evidence to suggest, contrary to many reports in the media, that SARS-CoV-2 will settle into a pattern of only surging during the winter; rapidly waning immunity and accompanying rapid viral evolution makes such an outcome extremely unlikely[61].

By January 2030, not only will prevalence of LC increase to very high levels globally, but the long-term sequelae of acute SARS-CoV-2 infection will be very apparent in the global population. It is very important here to make a distinction between LC and the concept of acute Covid-19 being a *risk factor* for the development of other chronic illnesses. Although this distinction is contentious[62], for the purpose of this scenario, it is necessary in order to distinguish between patients who developed LC within weeks or months of the precipitating acute infection and those patients who recovered entirely from their acute infection but for whom the infection precipitated the development of chronic illness months to years later. A good analogy here is the causal role of Epstein-Barr virus (EBV)[63] in several cancers and potentially in the development of multiple sclerosis (MS)[64]; individuals infected with EBV can experience years of good health following resolution of the initial infection before any long-term sequalae of infection occur. As such, by January 2030, prevalence of the following chronic diseases will have significantly increased in the global population:

[60] M. Hoffman et al, ‘Omicron: Master of immune evasion maintains robust ACE2 binding’, *Signal Transduction and Targeted Therapy*, vol. 7, 2022.
[61] https://www.cdc.gov/ncird/whats-new/covid-19-can-surge-throughout-the-year.html , last accessed 07/01/2025.
[62] D. Munblit et al, ‘Long COVID: aiming for a consensus’, *Lancet Respiratory Medicine*, 2022.
[63] It is worth noting that Long Covid can also cause reactivation of EBV in infected individuals, see J. Rohrhofer et al, ‘Association between Epstein-Barr Virus reactivation and development of Long-COVID fatigue’, *Allergy*, 2022.
[64] S. Soldan et al, ‘Epstein-Barr virus and multiple sclerosis’, *Nature Reviews Microbiology*, vol. 21, 2023.

1. Autoimmune diseases

Acute SARS-CoV-2 infection is an established risk factor for the development of autoimmune diseases[65], including rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), vasculitis, inflammatory bowel disease, and type 1 diabetes mellitus. In addition to causing significant loss of quality of life and disability to patients, autoimmune disease incurs a large financial cost to healthcare systems; the cost of treating autoimmune disease in the US in 2023 was approximately $100 billion annually[66]. Autoimmune diseases currently affect approximately one in ten individuals[67]; considering that by the end point of this forecast it is highly likely that the majority of the global population could well have been infected with SARS-CoV-2 at least *eight times*, that figure could easily double to one in five individuals globally suffering from autoimmune disease.

2. Cardiovascular disease

Acute SARS-CoV-2 infection is associated with a significant risk of major cardiovascular events in both unvaccinated[68] and vaccinated[69] individuals. While the risk is lower in vaccinated individuals, Covid-19 disease increases the risk for future heart attacks, strokes, and premature cardiovascular-related mortality for *at least* three years following resolution of acute SARS-CoV-2 infection. With the average individual having Covid-19 at least once per year, it can be seen that this elevated risk of cardiovascular disease is essentially an ongoing one; in fact, re-infections could well be cumulative in terms of increasing risk. Cardiovascular diseases are the leading cause of death globally, with an estimated 17.9 million people dying as a result in 2019[70]; by 2030 this figure will increase significantly as a result of the unmitigated transmission of SARS-CoV-2.

[65] C. Sharma, 'High risk of autoimmune diseases after COVID-19', *Nature Reviews Rheumatology*, vol. 19, 2023.
[66] https://www.npr.org/sections/health-shots/2023/11/18/1213946352/autoimmune-disease-patients-hit-hurdles-in-diagnosis-costs-and-care , last accessed 07/01/2025.
[67] N. Conrad et al, 'Incidence, prevalence, and co-occurrence of autoimmune disorders over time and by age, sex, and socioeconomic status: a population-based study of 22 million individuals in the UK', *The Lancet*, 2023.
[68] J. Hilser et al, 'COVID-19 is a Coronary Artery Disease Risk Equivalent and Exhibits a Genetic Interaction with ABO Blood Type', *Arteriosclerosis, Thrombosis, and Vascular Biology*, vol. 44, 2024.
[69] E. Harris, 'COVID-19 Vaccination Linked with Lower Risk of Cardiac Problems', *JAMA*, vol. 331, 2024.
[70] https://www.who.int/health-topics/cardiovascular-diseases#tab=tab_1 , last accessed 07/01/2025.

3. Neurological diseases

There is already an established causative link between both the development of new-onset dementia[71][72][73] (including Alzheimer's Disease[74]) and the worsening of pre-existing dementia[75] following Covid-19. Vaccination decreases the risk of both but does not eliminate it[76]. As with other long-term sequelae, it is uncertain if re-infection causes a cumulative risk for these effects, but, regardless, it is highly probable that by 2030, the global burden of dementias will be significantly increased, with the very real potential for a higher incidence of young-onset dementias[77]. We should not be surprised by this; following the Spanish Flu of 1918-1920, more than one million individuals subsequently suffered from encephalitis lethargica, characterised by fatigue, movement disorders, and, for some, the development of postencephalitic parkinsonism[78]. That is to say, long-term neurological disease has already been documented following a pandemic.

4. Cancer

There is currently growing evidence that suggests SARS-CoV-2 may well have oncogenic potential[79]. While this is still not a certainty, mounting research is demonstrating that cellular mechanisms associated with SARS-CoV-2 infection increase the likelihood of carcinogenesis; downregulation of gene expression of p53[80], reduction of CD4+ / CD8+ cells, a reduced number of natural killer (NK) cells[81], and the triggering of inflammatory cascades by enhancing cytokine production[82]. In addition, SARS-CoV-2 infection has been associated with specific cancers –

[71] G. Clews, 'Increased risk of dementia and brain fog after Covid-19 infection', *Nursing Times*, August 2022.
[72] 'COVID survivors may develop dementia', *Nature India*, 2024.
[73] D. Shan et al, 'Temporal Association between COVID-19 Infection and Subsequent New-Onset Dementia in Older Adults: A Systematic Review and Meta-Analysis', *The Lancet*, 2024.
[74] L. Wang et al, 'Association of COVID-19 with New-Onset Alzheimer's Disease', *Journal of Alzheimer's Disease*, vol. 89, 2022.
[75] S. Dubey et al, 'The effects of SARS-CoV-2 infection on the cognitive functioning of patients with pre-existing dementia', *Journal of Alzheimer's Disease Reports*, vol. 7, 2023, pp. 119-128.
[76] M. Catala et al, 'The effectiveness of COVID-19 vaccines to prevent long COVID symptoms', *Lancet Respiratory Medicine*, vol. 12, 2024.
[77] E. Herrera et al, 'Cognitive impairment in young adults with post COVID-19 syndrome', *Scientific Reports*, vol. 13, 2023.
[78] A. Giordano et al, 'COVID-19: can we learn from encephalitis lethargica?', *The Lancet Neurology*, vol. 19, 2020.
[79] A. Jaiswal et al, 'Oncogenic potential of SARS-CoV-2 – targeting hallmarks of cancer pathways', *Cell Communication and Signalling*, vol. 447, 2024.
[80] A. Gomez-Carballa et al, 'Is SARS-CoV-2 an oncogenic virus?', *Journal of Infection*, 2022.
[81] N. Ogarek et al, 'SARS-CoV-2 infection as a potential risk factor for the development of cancer', *Frontiers in Molecular Biosciences*, 2023.
[82] K. Jahankhani et al, 'Possible cancer-causing capacity of COVID-19: Is SARS-CoV-2 an oncogenic agent?', *Biochimie*, vol. 213, 2023, pp. 130-138.

pancreatic cancer[83] and lymphomas.[84] Since cancer generally takes years to develop, it is likely that during this scenario period we will begin to see the first increases in prevalence of cancers amongst those predominantly infected early in the pandemic; this trend will then likely continue beyond 2030.

Significant increases in autoimmune diseases, cardiovascular disease, neurological disease, and possibly cancers will, obviously, lead to a substantial increase in the global burden of chronic disease, and will, as a result, increase morbidity and mortality worldwide. Accompanied by an ever-growing population of individuals with Long Covid, this paints a dire picture of global population health by the end of 2030 and is why the development and adoption of effective mitigation technologies and systems is a matter of the utmost urgency. In addition, it is vital to be vigilant for any signals that may indicate increases in specific cancers resulting from SARS-CoV-2 infection; this data could be obtained from national screening programs for bowel cancer, breast cancer, cervical cancer, lung cancer, and Barrett's esophagus surveillance.

Recommendation 8: *In collaboration with national cancer screening programmes, design and fund studies to identify early warnings of increased cancer incidence related to SARS-CoV-2 infection.*

It is very likely that a number of 2nd generation nasal vaccines will be approved and fully deployed during this scenario period, and there is also a high likelihood of the approval and deployment of a pancoronavirus[85] vaccine close to 2030. Such a vaccine would be effective against all variants of

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[83] A. Sadrabadi et al, 'The risk of pancreatic adenocarcinoma following SARS-CoV family infection', *Scientific Reports*, vol. 11, 2021.
[84] U. Cartas et al, 'Lymphoma as a Complication of Recurrent COVID-19 Infection in Patients with Rheumatic Disease', *Annals of Case Reports*, 2022.
[85] For a detailed description of how a pancoronavirus vaccine could be developed, see S. Cankat et al, 'In search of a pan-coronavirus vaccine: next-generation vaccine design and immune mechanisms', *Cellular & Molecular Immunology*, vol. 21, 2024, pp. 103-118.

SARS-CoV-2, and other coronaviruses (including MERS-CoV), so could potentially end the Covid-19 pandemic. In addition, it is likely that during this period effective and phenotype-specific treatments will be discovered and deployed for LC (LC can be divided into five phenotypes: gastrointestinal, fatigue, cardiorespiratory, cognitive impairment, and depression / anxiety – phenotypes often overlap[86]).

Research during this scenario period into both acute SARS-CoV-2 infection and LC will inevitably lead to a growing understanding of the connection between pathogenic infection and chronic disease, which may well revolutionise how we prevent and treat both. However, it is still likely that in the absence of effective mitigation against SARS-CoV-2 – whether pharmaceutical or non-pharmaceutical - the world will be, on aggregate, unhealthier in 2030 than it is now.

REGULATING DUAL-USE RESEARCH OF CONCERN (DURC)

As noted earlier, the ongoing debate surrounding the origins of the SARS-CoV-2 virus is a valid one, specifically when viewed through the lens of value plurality. Evidence exists that supports both possibilities: a zoonotic origin[87] or accidental release[88] (popularly known as the 'lab leak' theory), but it seems unlikely that a conclusive answer will ever be arrived at[89]. However, there are two key points to be made here. First, honest, robust, public, and transparent debate regarding the origin of Covid-19 is important in and of itself, because it parallels the four reasons given previously in this report as to why we are failing to mitigate transmission of the virus: collective trauma, economic damage, value conflict, and a lack of transparency. The pandemic thus far has been responsible for the deaths of approximately 27 million people[90] and the disablement of millions more, with an economic cost roughly equivalent to 10.53% of global GDP[91]. The NPIs initiated by many governments worldwide caused a severe conflict of values between citizens, causing and exacerbating political polarisation[92], and transparency is lacking to this day, with the WHO very

[86] F. Liew et al, 'Large scale phenotyping of long COVID inflammation reveals mechanistic subtypes of disease', *medRxiv* (preprint), 2023.
[87] A. Crits-Christoph et al, 'Genetic tracing of market wildlife and viruses at the epicenter of the COVID-19 pandemic', *Cell*, vol. 187, 2024.
[88] O. Dwyer, 'Covid-19 originated in Wuhan lab, alleges Republican congressional report', *BMJ*, 2024.
[89] M. Looi, 'Will we ever know where covid-19 came from?', *BMJ*, 2024.
[90] https://ourworldindata.org/key-charts-understand-covid-pandemic , last accessed 07/01/2025.
[91] A. Faramarzi, 'The global economic burden of Covid-19 disease: a comprehensive systematic review and meta-analysis', *Systematic Reviews*, vol. 13, 2024.
[92] J. Kerr et al, 'Political polarization on COVID-19 pandemic response in the United States', *Personality and Individual Differences*, 2021.

recently calling for China to share data and access to better understand the origin of SARS-CoV-2[93]. As such, the ongoing debate encompasses all of the core capabilities that Nussbaum argues that all democracies should support: human life, human health, bodily integrity, to think and reason, to grieve and to have justified anger, to engage in practical reason, the protection of political speech, our concern for the natural world, our ability to enjoy recreational activities, and control over our political and material environment. As such, from the perspective of value plurality, the ongoing debate is *morally and ethically valid*. Second, regardless of whether the Covid-19 pandemic began as the result of a zoonotic event or the accidental release of a pathogen from a research laboratory, even the *possibility* that the latter could have occurred means that a crucial component of mitigating against any future pandemic is by significantly reducing the possibility that accidental release of a pathogen with pandemic potential could ever occur. This entails a commitment by all countries to:

- Enact national legislation that strictly regulates DURC and ensures fully independent oversight and funding reviews of any such research.[94]

- Act on the consensus amongst the biosecurity community worldwide[95] that the Biological Weapons Convention (BWC) should be modified to include provision for a multilateral mechanism to verify compliance among state parties[96], including routine on-site laboratory inspections (focussed especially on BSL4 and BSL3+ laboratories).

- Support current initiatives that track the ongoing global proliferation of BSL4 and BSL3+ laboratories.[97]

- Ensure that robust national legislation is enacted to protect whistleblowers involved in life sciences research.

[93] https://www.who.int/news/item/30-12-2024-milestone-covid-19-five-years-ago , last accessed 07/01/2025.
[94] The Risky Research Review Act is an example of such legislation: https://www.congress.gov/bill/118th-congress/senate-bill/4667 , last accessed 08/01/2025.
[95] J. Revill, ‘How the Biological Weapons Convention could verify treaty compliance’, *Bulletin of the Atomic Scientists*, 2024.
[96] N. Cropper et al, ‘A Modular-Incremental Approach to Improving Compliance Verification With the Biological Weapons Convention’, *Health Security*, vol. 21, 2023, pp. 421-427.
[97] For such an initiative, see: https://www.globalbiolabs.org/ , last accessed 08/01/2025.

- Enact robust national field biosafety standards, to protect researchers from being exposed to pathogens while collecting biomedical and environmental samples and when handling wild animals.[98]

Such an undertaking at the international level would be both politically difficult and reasonably expensive – adding a verification regime to the BWC would likely cost in the region of $200 million annually – but when compared to the economic damage inflicted globally by the Covid-19 pandemic thus far, it is a small price to pay to mitigate an extremely high consequence biological risk.

> *'…regardless of whether the Covid-19 pandemic began as the result of a zoonotic event or the accidental release of a pathogen from a research laboratory, even the possibility that the latter could have occurred means that a crucial component of mitigating against any future pandemic is by significantly reducing the possibility that accidental release of a pathogen with pandemic potential could ever occur'*

CONCLUSION: A DEVELOPMENT FRAMEWORK FOR MITIGATING SARS-CoV-2 AND OTHER AIRBORNE PATHOGENS

The forecasting scenarios detailed in this report demonstrate the absolute necessity of mitigating both the transmission of SARS-CoV-2 and the widespread individual and population adverse health effects that Covid-19 causes. Value-neutral adoption criteria, derived from value pluralism, provide a methodology for ensuring the highest possible chance of any proposed mitigation strategies, technologies or systems being adopted. In addition, these strategies, technologies, and systems also serve to not only mitigate the transmission and health effects of SARS-CoV-2, but also any future airborne pathogen. Adoption of technologies could also be increased using a *design thinking*[99] philosophy. The value-neutral adoption criteria are:

[98] F. Lentzos, G. Koblentz et al, 'Global BioLabs Report 2023', *King's College London & Schar School of Policy and Government*, 2023.
[99] For an excellent description of current design thinking philosophy, see: https://hbr.org/2015/09/design-thinking-comes-of-age , last accessed 08/01/2025.

- Unobtrusive: mitigation systems and technologies should integrate seamlessly with everyday life.

- Non-restrictive: mitigation strategies should not restrict the individual liberty of people.

- Allow individuals full control over their material environment: mitigation strategies should not adversely affect political participation, free speech and association, or employment prospects.

- Informed consent: mitigation strategies should centre the principle of informed consent, ensuring that individuals have full knowledge of the risks and benefits involved.

- The provision of accurate and transparent information: mitigation strategies, technologies or systems should always fully encompass accuracy and transparency in any information provided. This should be a dynamic process, with any new information being communicated immediately.

With these adoption criteria in mind, a framework for the mitigation of the transmission and adverse health effects of SARS-CoV-2 and other airborne pathogens is as follows:

1. Increase overall population health through accurate and transparent advice from both governmental public health agencies and trusted thought leadership sources. Reducing chronic disease[100] and encouraging physical activity[101][102] and healthy nutrition[103] builds population resilience to SARS-CoV-2 and likely other airborne pathogens.

2. The accelerated development of solutions that effectively mitigate near-field transmission of airborne pathogens without the need for utilising a respirator mask[104]

[100] P. Laires et al, 'The Association Between Chronic Disease and Serious COVID-19 Outcomes and Its Influence on Risk Perception: Survey Study and Database Analysis'. *JMIR Public Health Surveillance*, vol. 7, 2021.
[101] Only if medically appropriate – exercise is often contraindicated in Long Covid and ME/CFS.
[102] F. Cardoso et al, 'Physical fitness level and the risk of severe COVID-19: A systematic review', *Sports Medicine and Health Science*, vol. 5, 2023, pp. 174-180.
[103] J. Merino et al, 'Diet Quality and risk and severity of COVID-19: a prospective cohort study'. *Gut*, vol. 70, 2021.
[104] See https://xcmr.co/applications/ for an example of such technology , last accessed 09/01/2025.

3. The accelerated development of both established and novel solutions to mitigate far-field transmission, such as HEPA, Far-UVC, and other methods of safely eliminating pathogens in indoor air.

4. The accelerated development of biosensor technologies that detect and identify specific pathogens, such as SARS-CoV-2, but which also have threat-agnostic capability; these biosensors should additionally allow for adaptive control of indoor air.

5. The accelerated development of high accuracy personal and point-of-care rapid testing, incorporating a strict opt-in system for decentralised population health surveillance.

6. The accelerated development of effective preventative blockers, such as nasal sprays.

7. The accelerated development of effective therapeutics – including novel broad-spectrum candidates.[105]

8. The accelerated development of 2nd generation nasal vaccines and pancoronavirus vaccines.

9. The accelerated development and deployment of low-cost and decentralised genotyping systems for pathogen surveillance.

[105] See: https://maxwellbiosciences.com/ for an example of pathogen-agnostic candidate therapeutics.

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