PUBLIC HEALTH COMMUNICATION CENTRE AOTEAROA

Long Covid in Aotearoa NZ: Risk assessment and preventive action urgently needed

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Amanda Kvalsvig, Anna ES Brooks, John D Potter, Mona Jeffreys, Julie Bennett, David Davies-Payne, Jonathan Kennedy, Dianne Sika-Paotonu, Carmen Timu-Parata, Jenene Crossan, Celia Hume, Lynne Russell, Paula Lorgelly, Michael Baker

Summary

Covid-19 can cause longer-term changes in health, collectively known as Long Covid. With only four years of follow-up time to observe this evolving new virus we cannot yet see the full picture of Long Covid, but its impacts are already substantial and measurable in individuals, sectors, and societies. Evidence consistently shows that Long Covid is common, affects all ages, and frequently results in prolonged illness that can be disabling. It occurs with first infections and reinfections and follows all virus variants. There is currently no cure, making prevention critical.

Three urgent recommendations to the NZ Government are:

1. Identify a proportionate response by conducting a comprehensive Long Covid risk assessment;
2. Rapidly reduce infection and reinfection rates by ensuring that public settings are safer to access; and
3. Expand Covid-19 vaccine eligibility and coverage (eg, to younger age groups) to benefit from the demonstrated ability of vaccines to reduce the risk of Long Covid.

This Briefing presents findings from a review of Long Covid to guide NZ's response to this public health threat. The author group includes researchers, clinicians, and people with lived experience of Long Covid. Statements in the Briefing are further discussed and fully referenced in the review, which is reproduced below for full transparency (Appendix 1).

Key findings to guide a multisectoral risk assessment and response

Changes in health status following SARS-CoV-2 infection are common and can occur at any age. Symptoms are frequently experienced for months or years and can increase over time.

- Several recent and well-designed cohort studies have reported central estimates ranging from 4 – 14% for ongoing symptoms per infection.
- Long Covid includes a full spectrum of severity from hidden effects through mild and transient symptoms to life-changing and life-limiting conditions such as heart attacks and strokes, diabetes, myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), and neurological disorders. Commonly experienced symptoms such as fatigue and cognitive dysfunction have a high impact on quality of life.
- Both SARS-CoV-2 infection and Long Covid are under-counted in children.
- There is no cure for Long Covid, and management options are currently extremely limited (Appendix 3). Vaccines substantially reduce Long Covid risk, but NZ eligibility settings are currently focused on protecting older adults against acute disease.

Future health impacts can be expected in addition to the effects that are already known and observed.

- Some people who are currently well post-Covid are already expressing biomarkers of risk for cardiovascular disease, neurodegenerative disorders, a range of autoimmune diseases, and cancers: conditions that typically have latency periods lasting years or decades.

- Early-life exposure to infections can have lasting impacts on developing tissues and organ systems. Already, several adverse effects of perinatal Covid-19 exposure have been described.
- Pre-pandemic evidence shows the adverse effects of inflammation on the developing brains of children and adolescents, which is concerning because neurological involvement is common even in mild SARS-CoV-2 infection.

Society, sector, and workforce effects of Long Covid are costly and disruptive, and they worsen existing inequities.

- Long Covid is associated with increased healthcare use, productivity loss, and workforce impacts, with implications for NZ workforces that experience high incidence of Covid-19 such as educators, healthcare workers, and prison workers.
- The frequency of (often undiagnosed) cognitive impairment after a mild infection indicates a need for risk assessment of impacts on occupational safety and performance. Occupations of particular concern because of safety implications include healthcare workers, airline pilots, electricians, truck drivers, and first responders.
- Covid-19 is a syndemic condition: it causes chronic disease, and chronic disease increases susceptibility to Covid-19 – a vicious circle for some. There are profound health-equity implications for Māori and Pacific Peoples and people with disabilities or underlying chronic conditions.

Because of rapid viral evolution, Covid-19 waves are not showing a consistent pattern of improvement over time. Without intervention to reduce cases, the prevalence of Long Covid is more likely to increase than to decrease.

- Ongoing exposure to new, highly transmissible variants – in combination with the high incidence of Long Covid per infection and the long duration of symptoms – drives up the population prevalence.
- Evolutionary biologists note that future variant scenarios include the possibility of both higher and lower disease severity with unpredictable impacts on Long Covid risk.
- Lack of seasonality increases risk exposure and reduces recovery time between infections.
- A high proportion of the NZ population has had Covid-19 at least once, and exposure to reinfection is continuing. Each infection is a ‘throw of the dice’.
- At four years into the pandemic, we are still well within the latency period of many chronic conditions. Biomarker evidence is a reminder that past Covid-19 variants can still cause future Long Covid cases.

Implications for Aotearoa New Zealand in 2024

When an infectious disease is common in the population, its long-term effects become common too. At a population level, modest-looking proportions of a post-infectious health risk readily translate into very large numbers; these are challenging for health systems and societies to absorb.

Our evidence summary strongly suggests that Long Covid is a major threat to individual health, societal wellbeing and economic performance. We recommend three immediate actions by Government to manage this threat:

1. **Identify a proportionate response by conducting a comprehensive Long Covid risk assessment** to estimate the current and future size of this threat and the

scale and targeting of an appropriate multisectoral response.
2. **Rapidly reduce infection and reinfection rates using well-established public health and social measures (PHSM)** to ensure that public settings are safer to access (Appendix 2).
3. **Expand Covid-19 vaccine eligibility and coverage.** Vaccination reduces Long Covid risk, indicating an urgent need to revise NZ's eligibility criteria. NZ should make vaccines available and accessible to younger age groups along with measures to encourage uptake and raise coverage levels, particularly among underserved groups and those at increased risk of infection (eg, those occupations highlighted above).

What this Briefing adds

Our evidence summary strongly suggests that Long Covid is a major threat to individual health, societal wellbeing and economic performance:

- Changes in health status following Covid-19 are common and can occur at any age. Symptoms are frequently experienced for months or years and can increase over time.
- It is clear that future health impacts can be expected in addition to effects that are currently known and observed.
- Societal and workforce effects are costly and disruptive, and they worsen existing inequities.
- Because of rapid viral evolution, Covid-19 waves are not showing a consistent pattern of improvement. Without intervention to reduce cases, the prevalence of Long Covid is more likely to increase than to decrease.
- There is currently no cure for Long Covid, and management options are extremely limited.

Implications for public health policy and practice

We recommend three urgent actions by the NZ Government to manage this threat:

- Identify a proportionate response using a comprehensive Long Covid risk assessment to estimate the current and future size of this threat and the scale and targeting of an appropriate multisectoral response.
- Rapidly reduce infection and reinfection rates using well-established public health and social measures to ensure that public settings are safer to access.
- Expand vaccine eligibility to younger age groups along with measures to raise coverage levels, particularly among underserved groups and those at increased risk of infection (eg, various occupational groups).

Patient information

Long Covid evidence overview: Radio New Zealand Prof “Danny Altmann: the burden of long COVID”: An interview with an international Long Covid expert who discusses current Long Covid evidence in non-technical language.

https://www.rnz.co.nz/national/programmes/saturday/audio/2018899512/prof-danny-altmann-the-burden-of-long-covid

Support for people with Long Covid: Long Covid Support Aotearoa https://longcovidsupport.co.nz/

Author details

Assoc Prof Amanda Kvalsvig, University of Otago Wellington | Te Whare Wānanga o Otāgo ki Te Whanga-nui-a-Tara

Dr Anna E. S. Brooks, University of Auckland | Waipapa Taumata Rau

Prof John D. Potter, Massey University | Te Kunenga ki Pūrehuroa

Assoc Prof Mona Jeffreys, Te Herenga Waka | Victoria University of Wellington

Dr Julie Bennett, University of Otago Wellington | Te Whare Wānanga o Otāgo ki Te Whanga-nui-a-Tara

Dr David Davies-Payne, Starship Children’s Hospital, Auckland

Dr Jonathan Kennedy, University of Otago Wellington | Te Whare Wānanga o Otāgo ki Te Whanga-nui-a-Tara

Assoc Prof Dianne Sika-Paotonu, University of Otago Wellington | Te Whare Wānanga o Otāgo ki Te Whanga-nui-a-Tara

Carmen Timu-Parata (Ngāti Kahungunu), University of Otago Wellington | Te Whare Wānanga o Otāgo ki Te Whanga-nui-a-Tara

Jenene Crossan (Ngāi Tahu), Long Covid Support Aotearoa

Dr Celia Hume, University of Otago Wellington | Te Whare Wānanga o Otāgo ki Te Whanga-nui-a-Tara

Assoc Prof Lynne Russell (Ngāti Kahungunu, Rangitāne, Kāi Tahu, Ngāti Porou), Te Herenga Waka | Victoria University of Wellington

Prof Paula Lorgelly, University of Auckland | Waipapa Taumata Rau

Prof Michael Baker, University of Otago Wellington | Te Whare Wānanga o Otāgo ki Te

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Appendices

Appendix 1: Evidence review and call to action

Overview

Epidemics and pandemics cast a long shadow of chronic ill-health that can persist for decades after they are over. Covid-19 has clinical and pathological features that indicate a relatively high potential to cause longer-term health consequences, collectively known as Long Covid (or Post-acute Sequelae of SARS-CoV-2 [PASC]). Worldwide and in Aotearoa New Zealand (NZ), impacts of Long Covid are undeniable. They include reduced quality of life, impaired ability to work and learn, increased healthcare use and costs, and workforce shortages in key sectors such as health and education.

In addition to symptoms of Long Covid, mild Covid-19 disease episodes can generate persistent inflammatory and immune effects that are known predictors of later-life conditions such as neurodegenerative disorders, autoimmune conditions, and cardiovascular disease. Studies of infection during pregnancy have identified adverse effects on child health and development that may have long-term consequences. These findings are a reminder that we have experienced only the first four years of this new pathogen, a much shorter duration than the latency periods of many chronic diseases.

There is currently no cure for Long Covid, and management options are limited as there are no targeted pharmaceutical therapies. With Covid-19 circulating year-round in the NZ population and new variants continuing to appear, the cost of inaction is likely to be high.

In this report we identify key features of Long Covid that illustrate the need for a multisector risk assessment followed by a strategic and proportionate response. However, existing evidence is enough to show that NZ can benefit immediately from reducing the incidence of new Covid-19 cases: an achievable aim with many co-benefits.

Pandemic risk assessment

A new pandemic disease like Covid-19 presents a challenging risk-assessment problem for governments. Acute impacts such as hospitalisations and deaths due to the infection can be counted relatively early and easily in a pandemic, and NZ’s early pandemic response was appropriately focused on these metrics of immediate risk.

However, infectious diseases of public health significance cause longer-term health impacts beyond the acute infection phase.[1-6] When an infectious disease is common and widespread, these longer-term health impacts can become a public health concern in their own right. This is the mechanism through which major epidemics and pandemics can have

substantial and enduring cohort effects on population health.[7 8]

Infection with the SARS-CoV-2 virus has pathological features that are shared with the other severe coronaviruses (SARS and MERS) but not with common cold coronaviruses.[9-12] Such findings may explain why mild Covid-19 commonly causes longer-term effects, while colds usually do not. The rapidly growing evidence about these pathological effects is concerning, but it also reflects a tremendous opportunity not available in the pandemics of the past to assess and prevent harms to population health before they occur. NZ is well-positioned to demonstrate international leadership with a proactive response.

How common is Long Covid?

Symptomatic Long Covid

Long Covid functions as a broad umbrella term that encompasses a range of health impacts following Covid-19.[13] The pathophysiology of infection with the SARS-CoV-2 virus is complex and includes dysregulation of metabolic, immune, nervous, and cardiovascular systems.[14-16] Likely contributors to pathogenesis include altered immune cell function,[17] disruption to energy production in cells,[18-21] disrupted or dysregulated clotting pathways,[22] and persistence of the virus in body tissues after the initial infection has resolved.[23 24]

Because Long Covid is not a single health condition, estimates of incidence or prevalence per infection vary depending on what is being measured. Several symptom-based definitions have been proposed in an attempt to standardise measurement of Long Covid in populations,[12 25] but even with a standardised definition, pandemic context and methodological decisions introduce variability. Evidence is mixed as to whether there are meaningful differences between the Omicron and Delta variants,[26-29] or whether the anti-viral treatment nirmatrelvir (Paxlovid) reduces the risk of Long Covid.[30] However, vaccination does appear to reduce Long Covid risk[31-34] and, in a recent clinical trial, metformin showed promise as a potential risk reduction option.[35]

Despite these complexities, the evidence appears to be converging on a level that is well over the threshold of concern for population health impacts: several well-designed cohort studies have reported central estimates ranging from 4.5% to 13.2%[13 27 28 36 37] for Long Covid incidence per infection. One of these, a very large (n=198,096) recent study of Scottish adults,[28] reports that after adjustment for potential confounders, the estimated Long Covid prevalence following an infection was 6.6% at six months, 6.5% at 12 months, and 10.4% at 18 months, suggesting that Long Covid symptoms should not be assumed to decrease over time.

Measurement challenges mean that some symptoms are likely to be underestimated. Long Covid can occur at any age, but both SARS-CoV-2 infection and Long Covid are under-counted in children.[38 39] Neurological sequelae in children are a particular concern for their potential impacts on the developing brain, but they may be substantially under-diagnosed.[40-43] In adults, impacts that are well-recognised but are perceived as stigmatising, such as changes in sexual desire or capacity,[37 44] are also likely to be under-reported.

Long Covid biomarkers

Important though it is to understand symptoms because of their effect on people’s lives in the present, symptoms provide only a partial picture of health impacts. Advances in biomarkers, pathology, and imaging are important because this type of evidence generates

strategies for diagnosis and treatment. This information also provides a window of opportunity to identify and prevent future health impacts before they manifest within the population. Table 1 lists some examples of Long Covid biomarkers.

Severity and impact on quality of life

Long Covid includes a full spectrum of severity from hidden effects (tissue damage that does not initially cause symptoms)[17 45-47] through mild and transient symptoms to life-changing and life-limiting conditions such as heart attacks and strokes,[48 49] diabetes,[50] myalgic encephalomyelitis/ chronic fatigue syndrome [ME/CFS]),[51 52] and clinically significant neurocognitive events or dysfunction.[53]

Even when clinically mild, symptoms can have important impacts on everyday life. Cognitive impairment in adults and children can substantially affect daily functioning including work, education, and other complex tasks such as driving. Participants in NZ Long Covid studies report impairment of quality of life at levels similar to cancer patients, consistent with research outside NZ.[54 55] Table 1 lists some standardised measures of impact that aim to quantify these life-changing aspects of Long Covid.

How long does Long Covid last?

Nearly four years into the pandemic there is no predictable endpoint for Long Covid recovery: some people who became unwell in early 2020 are still unable to return to work or participate in education. Leaving aside effects such as heart disease and stroke which have clear endpoints of death or disability, substantial proportions of Long Covid patients report multiple, persistent symptoms one,[54 56] two,[57 58] and three[59] years after their initial infection, including experiencing symptoms that resolve and recur. Evidence from longitudinal cohorts suggests that the majority of people with Long Covid are still experiencing symptoms and disruption to everyday life two years later.[60 61] For the substantial sub-group meeting the criteria for ME/CFS, research on this condition has shown that recovery after 2-3 years is uncommon with ME/CFS and that most people have significant long-term disability.[7 62 63]

This phenomenon of persistent chronic pathology with slow or minimal recovery is to be expected from the pathophysiology of Long Covid. It highlights an important issue for risk assessment: long symptom duration acts in combination with high Covid-19 incidence and high incidence of Long Covid per infection to drive up the population prevalence, one of many examples of impact multipliers of Long Covid risk (Table 1).

Society, sector, and workforce effects

People with Long Covid require substantial healthcare resources for investigation and treatment and if Covid-19 case numbers are not reduced, NZ can expect to experience extensive long-term pressure on primary and secondary health services.[64 65]

Long Covid is also associated with substantial productivity loss.[66] Globally, there is concern about the workforce impacts of Long Covid.[67] There are additional implications for NZ workforces that experience high incidence rates of Covid-19, such as educators, healthcare workers, and prison workers.[68] The frequency of (often undiagnosed) cognitive impairment after a mild infection indicates a need for risk assessment of the impacts of deficits in memory, reasoning, or executive function on occupational safety and performance.[29 59 69 70]

Occupations of particular concern because of safety implications include healthcare workers,[71] airline pilots,[72] bus and train drivers, truck drivers, electricians, and first responders.

There are also health-equity implications for different population groups, particularly Māori and Pacific Peoples, who experience higher health and social impacts from Long Covid through the multiple interactions between higher burdens of other illnesses and pre-existing structural disadvantage.[73]

Table 1 has further examples of these population-level effects.

Assessing future Long Covid impacts

Virus factors

As the SARS-CoV-2 virus evolves, so do patterns of immune evasion and activation. Evolutionary biologists note that interactions between viral evolution and human epidemiology are too complex to allow confident prediction of the future evolutionary trajectory or clinical severity of the virus.[74] They also note that future variant scenarios include the possibility of both higher and lower disease severity, and that year-round infections and reinfections,[75] which are not a feature of influenza or RSV, increase the potential for higher public-health impact relative to seasonal infections.

Infection waves are not showing a consistent pattern of improvement. Four years on from the start of the pandemic, the JN.1 subvariant is causing a larger wave of infection than the one that preceded it, suggesting that we cannot rely on the intensity of infection to decrease over time. Several Long Covid experts propose that the continuing large number of infections and reinfections caused by Omicron variants compared with earlier ones and the long duration of Long Covid symptoms mean that the overall prevalence of Long Covid is more likely to increase over time than to decrease.[17 24 27 60]

Chronic diseases with a long latency period

Viral persistence and/or activated inflammatory pathways seen in Covid-19 infection[23 24] are pathological features that were known before the pandemic to increase the risk of chronic disease. Chronic conditions tend to have long latency times, longer than the duration of the pandemic so far. Examples of chronic conditions identified in biomedical research that may be triggered by Covid-19 inflammatory pathways include cardiovascular disease,[49] neurogenerative disorders,[76 77] a range of autoimmune diseases,[78] and cancers.[79 80]

Effects across the life-course

Early-life exposure to infection can have impacts on developing tissues and organ systems that are permanent or emerge decades after the original infection. The life-course health impacts for the 2020 pandemic generation remain to be seen. So far, reported adverse effects of perinatal Covid-19 exposure include premature delivery, impaired prenatal lung growth, respiratory distress and inflammatory changes, and altered early neurodevelopmental outcomes.[46 81-83] Further, and as outlined above, cognitive impacts in children and adolescents are well-recognised, and their long-term impacts are not yet known.

Summary and implications for Aotearoa New Zealand in 2024

When an infectious disease is common in the population, its long-term effects become common too. At a population level, modest-looking percentages of a post-infectious health risk can quickly translate into very large numbers; these are challenging for health systems and societies to absorb.

The size and complexity of the evidence that has accumulated after only four years of exposure to this new disease can be confronting. It appears to have had a paralysing effect on decision-makers in NZ and globally. As one global Long Covid expert observed in a landmark review: “The oncoming burden of Long Covid faced by patients, health-care providers, governments and economies is so large as to be unfathomable, which is possibly why minimal high-level planning is currently allocated to it”.[17]

Choosing to ignore potential harms is indefensible when the risk to New Zealanders can be reduced using a combination of new knowledge and well-established public-health approaches. In March 2024, three immediate actions by the NZ Government are needed to acknowledge and respond to the post-2019 reality.

First, the NZ Government needs to undertake a comprehensive Long Covid risk assessment that will guide an appropriate and proportionate response. In this Report, we highlight key features from the scientific literature that indicate the necessary scope and the multisectoral nature of this assessment, as well as the availability of quantitative evidence that can allow optimistic, pessimistic, and most-probable risk scenarios to be explored.

Second, as this Report also shows, what we already know is enough to warrant immediate preventive action. There is strong empirical evidence that person-to-person transmission of Covid-19 and many other respiratory infections can be substantially reduced using a multi-layered respiratory infection strategy. We have presented science-informed advocacy for an integrated strategy (see Appendix 1).[84-86] NZ is well-positioned to apply this knowledge to reduce the current high daily case count and hospitalisation count: an initiative that would have immediate and lasting benefits for New Zealanders.

Third, vaccine eligibility needs to be expanded. NZ’s current vaccine strategy focuses on protecting older age groups from the effects of acute Covid-19. Vaccination is now known to reduce Long Covid risk,[31-34] indicating an urgent need to revise NZ’s eligibility criteria and offer vaccines to younger age groups and to occupational groups at increased risk of infection.

Table 1. Features of Covid-19 infection and its sequelae to guide decisions around the structure and scope of a comprehensive risk assessment. This assessment should underpin NZ’s long-term Covid-19 strategy.

Characteristics of SARS-CoV-2 virus infection and acute Covid-19

The immunopathology of SARS-CoV-2 infection differs from other common respiratory viruses,[9-12] and it also has features that it shares with SARS-CoV, such as entering cells via angiotensin-converting enzyme 2 (ACE2) receptors.[87] These receptors are ubiquitous in the body, enabling the SARS-CoV-2 virus to affect multiple organ systems and immune pathways. As noted in the text of this Report, wide-ranging health consequences are occurring at levels high enough to have population-level effects.

The clinical severity of future variants is unpredictable, as is their propensity to cause chronic disease, a consideration that has not been factored into pandemic risk assessments to date. Immune evasion is the main driver of variability, and there is little evolutionary pressure towards reduced virulence. Risk assessment needs to include realistic future scenarios of high chronic-disease burden as a result of the population being exposed over many years to a year-round baseline of community transmission with sporadic variant waves.[74 75]

There is currently no cure for Long Covid, and treatment options are extremely limited (see Appendix 3 below). A preventive approach – achieving a substantial and sustained decrease in the incidence of Covid-19– is currently the only effective protection we have against Long Covid.

Impacts on the health and wellbeing of individuals

Changes in health status following Covid-19 are very common (the prevalence of symptomatic Long Covid is in the 4-14% range and around half of all cases experience individual symptoms following an infection). These health effects have variable (but frequently substantial) impacts on everyday life, including on work and educational attainment.[73 88 89]
A large United States (US) study reported that at two years post-infection, Long Covid contributed to a loss of 80.4 disability-adjusted life years (DALYs) per 1,000 persons in non-hospitalised patients, and 642.8 DALYs per 1,000 persons in hospitalised patients. (A DALY represents a year of healthy life lost to illness).[57] This is a large effect.
In one US household study, experiencing persistent Covid-19 symptoms was associated with a higher risk of economic hardship than having experienced a severe acute Covid-19 episode.[90]
These findings indicate a need to extend a NZ risk assessment beyond health data, making use of NZ's Integrated Data Infrastructure (IDI) to investigate patterns of income, employment, and uptake of benefits, and ensuring that quality of life data and metrics are captured.

Following a SARS-COV-2 infection there is an increased risk of morbidity or mortality from high-severity sequelae including cardiovascular and neurological events, as well as from chronic conditions such as new-onset diabetes (see text for details and references). These impacts need to be tracked systematically in health data.

Long Covid occurring in the form of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is debilitating and disabling, with long-term impacts on health and healthcare use.[51 52 63 91] SARS-CoV-2 may rapidly supersede other pathogens as the leading cause of ME/CFS.

Society, sector, and workforce effects

Post-infectious health impacts of Covid-19 occur in healthy people at any age, including before birth, and no-one is immune from this risk. However, risk is intensified for some, including people with chronic conditions, older adults, Māori and Pacific Peoples, whaikaha/people with disabilities, low-income workers, and specific occupations.[55 73]
Failure to address Long Covid risks for Māori is a failure to uphold obligations under Te Tiriti o Waitangi.[92]

The NZ health sector operates on small margins in terms of its capacity to increase service provision. A large United Kingdom (UK) study has reported provisional estimates that healthcare-associated costs for individuals with Long Covid increased almost fourfold in the two years following their initial illness compared with their previous healthcare use, and increased almost three times as much as age- and comorbidity-matched individuals.[64] A second UK matched cohort study has reported similarly substantial increases in healthcare utilisation and costs.[65] Increased pressure on primary and secondary care health services to investigate and treat Long Covid will challenge already stretched public health services, with the potential to increase inequality, as more wealthy private paying patients obtain investigations and treatment while those exclusively treated in the public health system may miss out.

Cognitive dysfunction is common in Long Covid and impaired occupational performance may have safety implications in some occupations, requiring additional resource to monitor and mitigate.[29 59 69-72]

Long Covid is associated with substantial and costly productivity loss.[66] Ongoing spread of SARS-CoV-2 in workplaces risks exacerbating existing shortages of skilled workers, including (but not limited to) education, healthcare, and prison workers.[68] Almost one in five UK doctors with Long Covid who responded to a workforce survey said that they were unable to work,[93] and hundreds of doctors are currently taking legal action against the National Health Service for failing to protect their health.[94]

Features that increase the likelihood of additional future health impacts

A recent large systematic review of Long Covid prevalence (194 studies and 735,006 participants) reported that on average, around 45% of Covid-19 survivors experienced at least one unresolved symptom. This finding suggests a need to monitor tissue- and organ-system impacts, a conclusion that is supported by research on biomarkers. Biomarker research indicates subclinical multiorgan damage with potential to become salient as people age: Brain injury biomarkers that predict cognitive deficits at 6 and 12 months,[95] immune system dysregulation,[95 96-98] disruption of metabolic pathways,[99] musculoskeletal involvement,[100] and dysfunctional mitochondria.[18-21 98 101] Cognitive dysfunction and MRI brain changes can be seen after mild infection in young, previously healthy adults.[29 53] Risk assessment in NZ should include biobanking to record and evaluate these measures of future impact.

Several features of Covid-19 including viral persistence and activated inflammatory pathways are recognised precursors of chronic disease in later life such as neurodegenerative disorders and heart disease (see text for details and references).

Infections early in life have potential life-long implications for health. Findings to date about cognitive impacts in children are concerning and raise questions about the long-term impact of ‘cognitive Covid’ on the developing brain and life chances of infants, children, and adolescents.[43 82 83]

Impact multipliers

Covid-19 is a syndemic condition: it causes chronic disease and chronic disease increases susceptibility to future Covid-19 infection. These pathways are amplified by structural determinants of health such as poverty and institutional racism in the health system. Long Covid is likely to further exacerbate health inequities experienced by Māori, Pacific Peoples, and other structurally marginalised populations.

A high proportion of the NZ population has had Covid-19 at least once (possibly twice), and exposure to infection and reinfection is ongoing. Each infection represents a ‘throw of the dice’ for that individual and risk of Long Covid persists with each episode. Some studies have shown an increasing risk pattern for Long Covid as might be expected from its pathophysiology,[75] [102] but lack of testing is making this phenomenon difficult to study and there may be high individual variation in reinfection risk.
Transmissibility, rather than virulence, is a key characteristic to model. A variant with high immune-evasive capability but relatively low virulence can generate substantial population health impacts because larger absolute numbers of people are affected, introducing stressors on public systems with finite capacity.
Recovery is not straightforward: as discussed in the text of this Report, Long Covid health effects are commonly experienced for months or years and can increase over time. Recovery can be episodic, with periods of improvement and relapse, while in some cases, symptoms may persist long term.
Even a relatively short duration of illness can have a major life-course impact. Inability to work is common, and few low-income workers can easily afford to be unable to work for a month or two. For children and young people at key developmental or life stages, being unwell for a short time may be highly disruptive to their social development and learning, for example if the illness coincides with the start of primary or secondary school, or with major assessments or exams.
Lack of seasonality increases risk exposure and reduces recovery time between infections.
Relative lack of public health messaging and low level of perceived risk may act as impact multipliers, reducing protective behaviours including testing. Reduced testing leads to under-ascertainment of cases, further reinforcing low levels of perceived risk and leading to under-prevention and then under-diagnosis of Long Covid, as people may not be aware of the infection that triggered a new-onset health condition.
Interactions between SARS-CoV-2 virus infection and infections from other pathogens continue to emerge, including reported associations with Group A Streptococcus,[103] [104] RSV,[105] and overall infection incidence.[106] SARS-CoV-2 infection can reactivate several common latent viruses including Epstein-Barr virus (EBV), human herpesvirus 1 (HHV-1), and cytomegalovirus (CMV)[23] [107] with secondary health effects that include increased severity of infection as well as post-viral fatigue following reactivation of EBV.[108]

Appendix 2: Prevention

Because Long Covid is a consequence of acute infection with SARS-CoV-2, a central element in the prevention of Long Covid is prevention of acute infection.

Responding to COVID-19: The need for a national strategy

The NZ Government needs to introduce a comprehensive respiratory infection strategy.[85] [86] This strategy would apply a proactive and integrated approach to reduce NZ’s high burden of serious respiratory infections.

Adding to actions we have proposed in a previous NZMJ article,[85] key aspects of the strategy would include:

1. Choose and articulate an optimal and equitable response strategy: Given the large health impact of COVID-19, a continuing mitigation strategy is justified. There are large efficiency gains in having an integrated strategy that includes influenza and other seasonal respiratory infections such as RSV.

2. Develop and implement an integrated respiratory infection programme to reduce disease transmission, including:

- Support for self-isolation of infected cases, such as improved sick leave entitlement.
- Improve indoor air quality to reduce transmission, notably improved ventilation and indoor air quality standards.
- Maintain mask use in high-risk indoor environments such as health care settings.[119]
- Implement strategies to limit transmission in shared environments like schools.[84]

3. Achieve and maintain high and equitable vaccine coverage:

- Widen current vaccine eligibility criteria, which are currently focused on reducing risks from acute infection in older adults, to recognise that vaccines can reduce Long Covid risk and that Long Covid can be experienced at any age.
- Continue to refine the COVID-19 vaccine schedule, notably timely introduction of new vaccines better adapted to currently circulating strains.
- Intensify efforts to achieve high and equitable vaccine coverage, especially for Māori, Pacific Peoples, people with disabilities or underlying chronic conditions, and occupation groups at increased risk.

4. Enhance health services capacity to manage respiratory infections:

- Review and enhance equitable delivery of essential respiratory infection management interventions such as antivirals (notably Paxlovid).

5. Improve public communication about respiratory infections:

- Provide effective and culturally appropriate communication for informing the public about risk of infection (particularly at the start of new pandemic waves and at the start of winter for conditions such as influenza and RSV) and about actions that they can take.
- These systems would include resourcing community-led initiatives by Māori and Pacific providers to embed and extend the public health information services they provided during the early stages of the COVID-19 pandemic.[120]

6. Improve surveillance and research to inform our response:

- Continue to improve current surveillance systems, including filling important gaps such as sentinel surveillance and surveillance of Long Covid, including biobanking to understand unique aspects of COVID-19 in NZ and to support long-term follow-up of Long Covid cases.
- Develop a research agenda to fill key gaps in knowledge about COVID-19 and its management, including ongoing reviews of the international literature, analysis of the cost-effectiveness of interventions (eg, vaccination, ventilation upgrades) and identifying ways of improving the equity and sustainability of the response to all major

respiratory infections.

7. Improve pandemic preparedness nationally and internationally:

- These measures against current respiratory infections also protect against new emerging pathogens before vaccines are available. The proposed integrated system would be a cornerstone of NZ's future pandemic preparedness.

Appendix 3: Treatment

As yet, there are no widely available and effective curative options for Long Covid, and although research is progressing this area it appears to be underfunded relative to need.

Immunological studies describing Long Covid immune profiles and vascular inflammation biomarkers[96-98 109] are a promising initial step towards definitive treatment. Repurposing existing medications may be helpful but definitive treatments may still be years away. The 'syndromic' type of Long Covid presentation that includes extreme fatigue, cognitive impairment ("brain fog"), and post-exertional malaise (PEM) has clinical and biological similarities with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS);[51 52 101] research on treatment options may benefit both of these groups of patients.

A breakthrough study recently published in *Nature Communications* revealed mitochondrial dysfunction as the pathophysiological cause of muscle damage associated with exercise intolerance.[21] This recent discovery builds on previous research identifying immune and mitochondrial disturbances associated with post-infection syndromes which is critical for identifying pathogenesis and mechanisms of disease. The accumulating evidence[16 110-114] also highlights the importance of clinically assessing for PEM in Long Covid and ME/CFS patients, and managing exertion appropriately, as Graded Exercise Therapy (GET) is contraindicated.[115]

Despite the complex nature of Long Covid symptomatology, there are known conditions, although poorly recognised, that can be diagnosed and managed. Research suggests autonomic dysfunction or dysautonomias,[16 91] including postural orthostatic tachycardia syndrome (POTS), are common and associated with reduced health-related quality of life.[116] There are anecdotal reports of difficulties in finding medical professionals familiar with diagnosing and managing POTS, therefore delaying, or preventing appropriate symptom management or treatment.

Mast Cell Activation Syndrome (MCAS) is another poorly recognised immune condition that is often associated with Long Covid symptoms, yet rarely clinically acknowledged, diagnosed, or treated.[117]

Clinical trials investigating treatment options for Long Covid are gaining traction, however, for now, supportive treatment is the mainstay of Long Covid management.

NZ's health services are already stretched, raising the question of how the health system will accommodate this extra burden, especially as healthcare workers themselves are affected by Long Covid. Staff at one NZ hospital have set up a Long Covid clinic for staff and extend this service to the public,[118] but without any additional funding must fit those referrals in within existing caseloads.

Useful, NZ-centred resources include:

- Clinical Rehabilitation Guideline https://www.health.govt.nz/publication/clinical-rehabilitation-guideline-people-long-covid-coronavirus-disease-aotearoa-new-zealand
- Flow chart for activity https://issuu.com/wboppho/docs/j000497_pnz_-_exercise_after_covid_flow_chart_v5_

Appendix 4: Current research in Aotearoa New Zealand

Long Covid research in Aotearoa NZ has been challenging due to funding limitations. Current and ongoing projects include the following (a non-exhaustive list):

- **Ngā Kawekawe o Mate Korona Victoria University Wellington**: national study of COVID-19 impact, those infected prior to December 2021 (pre-Omicron). Results have been published.[55]
- **Mātauranga Raranga | Long COVID Registry Aotearoa**, self-reporting symptoms of Long COVID: https://www.lcregistry.auckland.ac.nz/ . Findings indicate an estimated $140 million cost of additional GP visits annually attributable to Long Covid.
- **Evidence-based management of Long COVID**. Health Research council of New Zealand. Contact: Associate Professor Mona Jeffreys mona.jeffreys@vuw.ac.nz. https://www.hrc.govt.nz/resources/research-repository/evidence-based-management-long-covid.
- **COVID-19 and National Immunisation Programme research PROP-067**: Understanding the impact of vaccination on long-term health outcomes from COVID-19 in children and young adults. Results forthcoming. Contact: Dr Julie Bennett, julie.bennett@otago.ac.nz .
- **Immunology/biomarker discovery led by Dr Anna Brooks (University of Auckland)**: Characterising immune dysfunction associated with Long Covid and ME/CFS: Cellular and molecular studies of SARS-CoV-2 infection, post-viral conditions and COVID-19 vaccination.
- **HRC Programme SYMBIOTIC - Integrated prevention of infectious diseases and long-term conditions**. In progress. Contact: A/Prof Amanda Kvalsvig, amanda.kvalsvig@otago.ac.nz or Dr Celia Hume celia.hume@otago.ac.nz.

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