PUBLIC HEALTH COMMUNICATION CENTRE AOTEAROA

Long COVID: Century-old Lessons We Still Have Not Learned

29 June 2022

John D. Potter

This long-read blog updates what is known about long COVID – now informed by some very large studies and a meta-analysis. The two most concerning aspects of long COVID are its high prevalence (up to 30% of those infected) and, as reinfection is increasingly common, a dose-response relationship between the number of infections and the increased risk of harmful outcomes. Such findings reinforce the continuing need for government action and individual commitment to the core preventive measures of: vaccination, mask use inside public places, and physical distancing where possible.

Pandemics and Public-Health Measures

The Japanese adopted mask-wearing during the 1918-19 influenza pandemic – a time when it was the key public-health element of the short list of possible measures available. As Spinney noted in 2017 in her excellent coverage of the history of the pandemic that we have allowed to fade from memory, it “probably marked the beginning of the practice of

mask-wearing to protect others from one's own germs"[1]. In Japan, mask use was compulsory for some, such as the armed forces and police, and in some towns, people were not permitted on public transport or allowed to enter a theatre or cinema without a mask[2]. It is notable that Japan had the lowest death rate of all the Asian countries in this pandemic (and is looking close to the lowest cumulative mortality in the OECD for the COVID pandemic).

During the 1918-19 pandemic, the United States (US), unlike Europe, put considerable effort into public-health interventions. Bootsma and Ferguson explored whether differences in such measures across different cities explained the variation in epidemic patterns and mortality. Consistent with theory, they found that the interventions reduced total mortality by perhaps 10-30%, but that the impact was often limited because interventions were introduced late and shut down early. San Francisco, St Louis, Milwaukee, and Kansas City had the most effective interventions, reducing transmission rates by up to 30-50%. They also noted that individuals reactively reduced contact rates in response to high levels of mortality during the pandemic[3].

In Geoffrey Rice's *Black November*[4] and *Black Flu*[5] (together the most comprehensive coverage of the 1918-19 influenza pandemic in Aotearoa New Zealand), there are some photographs of people wearing masks and a reference to Dr Hastings in Temuka requiring "gauze masks" for shop keepers. However, there is little evidence to suggest that mask wearing was widespread or even much encouraged in Aotearoa. We have quite a number of photographs of the period, so it probably was rare, a conclusion supported by Professor Rice who said, "masks have left little trace in the written records from 1918" (personal communication June 22, 2022).

One of the central aspects of the official, increasingly laissez-faire, attitude towards the fact that we are still in the middle of a pandemic is that we do not take even those precautions over which, as autonomous individuals, we still have control, namely mask wearing, physical distancing, and choosing carefully whether we are in crowded settings. The consequences are not just a more-or-less steady daily number of cases – and deaths – but also the lurking and still, to most, barely visible burden of long COVID.

It is worth keeping in mind that SARS-CoV-2 is not unique in its ability to cause post-acute symptoms and organ damage; certain acute infections have long been associated with an unexplained chronic disability in a minority of patients, including Ebola, dengue, polio, the original SARS, West Nile Virus infection, and others including non-viral pathogens such as the cause of giardiasis (*Giardia lamblia*)[6]. What is different about the long-term consequences of infection with SARS-CoV-2 is the sheer size of the pandemic and, thus, the size of the long-COVID-affected population.

In previous discussions of long COVID (here, here and here), we have tried to pull in as much detail as possible from as many sources as possible so that readers could get a good sense of the wide spectrum of studies from around the world and the degree to which the studies were giving us more or less the same information. Here, we just focus on a few of the largest studies so we can understand the depth and breadth of the impact of long COVID in more uniform population and research settings, first across whole populations and then among the hospitalised. That is followed by brief discussions of the evidence regarding reinfection, vaccination, and variants on the risk of long COVID.

Long COVID: Larger Population Studies

Vedel Sørensen et al conducted a nationwide cross-sectional study in Denmark of 61,002 individuals aged ≥15 years with RT-PCR-confirmed COVID-19 (September 2020 – April 2021) and a corresponding test-negative group of 91,878. Web-based-questionnaire data were collected 6, 9, or 12 months after diagnosis. Six to 12 months after the test date, the risks of 18 of 21 physical symptoms were higher among those who tested positive and 29.6% of these people experienced at least one post-acute symptom. The largest risk differences were observed for loss of sense of smell (risk difference (RD) for prevalence = 10.9%); loss of sense of taste (RD=8.7%); fatigue/exhaustion (RD=8.4%); shortness of breath (RD=4.9%); and reduced limb strength (RD=4.7%). Over half (53.1%) of those who tested positive reported at least one of the following conditions: concentration difficulties (RD=28.3%); memory disturbance (RD=27.3%); sleep disturbance (RD=17.3%); mental exhaustion (RD=32.6%), or physical exhaustion (RD=40.5%) compared to 11.5% of those who tested negative. New diagnoses of anxiety (RD=1.2%) or depression (RD=1.0%) were also more common among those with a history of SARS-CoV-2 infection[7].

Whitaker et al reported on the REACT-2 study, involving 508,707 people in the community in England. The weighted prevalence of self-reported COVID-19 was 19.2% with 92,116 people reporting one or more of 29 specific symptoms, of whom 76,155 (82.7%) reported a valid date of symptom onset ≥12 weeks before their survey date. Over a third (37.7%) of these 76,155 symptomatic people experienced at least one symptom and 14.8% experienced three or more for ≥12 weeks. Nearly a third (30.5%) of people with at least one symptom lasting ≥12 weeks reported having had severe COVID-19 symptoms during their acute illness. The prevalence of persistent symptoms was higher in women than men (odds ratio (OR)=1.5) and higher at older ages. Obesity, smoking or vaping, hospitalisation, and deprivation were also associated with a higher probability of persistent symptoms; Asian ethnicity was associated with a lower probability. Two stable symptom clusters were identified for symptoms that persisted for ≥12 weeks: a larger cluster in which tiredness predominated and another with a high prevalence of respiratory symptoms[8].

Long COVID: Larger Studies of the Hospitalised

When we consider specifically those who were hospitalised with COVID-19, National Health Service data from across England provide extensive and robust information on outcomes. 47,780 individuals (mean age 65, 55% men) hospitalised with COVID-19 and discharged alive by 31 August 2020, were exactly matched on personal (age, sex, ethnicity, region, and deprivation) and clinical characteristics (including a variety of relevant co-morbidities) to controls from a pool of about 50 million people from 10 years of electronic health records (EHRs). The outcomes of interest were rates of hospital readmission for COVID-19 survivors and any admission for controls; all-cause mortality; and diagnoses of respiratory, cardiovascular, metabolic, kidney, and liver diseases until 30 September 2020 and the way in which rate ratios varied by age, sex, and ethnicity. Over a mean follow-up of 140 days, 29.4% (n=14,060) of COVID-19 hospitalised survivors were readmitted and 12.3% (n=5,875) died after discharge, with these events occurring at rates 3.5 and 7.8 times greater, respectively, than in the matched control group. Rates of respiratory disease, diabetes, and cardiovascular disease were also significantly higher in COVID-19 survivors than controls. Rates of all outcomes after discharge were greater among COVID-19 survivors aged ≥70 or more than in those <70years. However, rate ratios were higher among individuals <70 than for those aged ≥70 years. Thus, the increase in risk was not confined to the elderly. It was also not uniform across ethnicities[9].

Cerner Real-World Data is a US-wide de-identified data set of more than 60 million unique adult EHRs[10]. Based on this resource, a retrospective matched cohort design was used to study the impact and the nature of long COVID[11]. Case-patients (n=353,164) were adults, aged ≥18 years, within a subset of facilities that use Cerner EHRs who received a diagnosis of COVID-19 or a positive SARS-CoV-2 test result at inpatient, emergency department, or outpatient settings. Control patients (matched 5:1; n=1,640,776) were COVID-19-free during the observation period. All study patients had at least one encounter in their EHR during the year preceding and the year after the index encounter. Patients were followed for 30–365 days after the index encounter until the first occurrence at least one of 26 clinical conditions previously attributed to post-COVID illness or until October 31, 2021, whichever occurred first. The researchers concluded that 20% of COVID-19 survivors aged 18–64 years and 25% of survivors aged ≥65 years experienced a newly incident condition that could be attributable to previous COVID-19[11]. The risks were higher among survivors aged ≥65 years than among controls for all 26 incident conditions, with a range of relative risks (RRs) from 1.2 (substance-related disorder) to 2.2 (acute pulmonary embolism). For survivors 18 to 64 years, RRs were higher than among controls for 22 incident conditions: 1.1 (anxiety) to 2.1 (acute pulmonary embolism). Respiratory symptoms and musculoskeletal pain were the most common conditions in both age groups, with the highest RRs involving the respiratory system, including acute pulmonary embolism: RR = 2.2 (≥65 years) and 2.1 (18–64 years). Younger survivors were at higher risk than those ≥65 years for heart rhythm disturbances and musculoskeletal pain, consistent with other observations that long COVID is not just a disorder of older age[12]. However, risk of 10 incident conditions was statistically significantly higher among older survivors than among those aged 18–64 years, namely kidney failure, thromboembolic events, cerebrovascular disease (eg, stroke), type 2 diabetes, muscle disorders, neurologic conditions, mood disorders, anxiety, other mental conditions, and substance-related disorders[11].

Wong-Chew et al conducted a longitudinal study on the prevalence of, and risk factors for, the long-term health consequences of COVID-19 in patients discharged from the Temporary COVID-19 Hospital in Mexico City between September 2020 and January 2021. Self-reported symptom data was collected by telephone from 4670 participants and showed that neurologic, dermatologic, and mood-disorder symptom clusters persisted in >30% of patients at 90 days post-discharge. Although most symptoms decreased in frequency between day 30 and 90, alopecia (hair loss) and the dermatologic symptom cluster increased. Women were more prone than men to develop long-term symptoms; invasive mechanical ventilation increased the frequency of symptoms at 30 days post-discharge[13].

A Meta-analysis of Both Community Cases and the Hospitalised

Wulf Hanson and colleagues sought to estimate the international prevalence of long COVID in 2020 and 2021, the severity of symptoms, and likely patterns of recovery[14]. Consistent with WHO[15,16], they defined long COVID as “newly onset or persisting symptoms three months after an acute episode of COVID-19 which impact daily functioning and were not preexisting symptoms before SARS-CoV-2 infection”[14]. They selected three major symptom clusters – explicitly included in the WHO clinical case definition – based on frequency and the ability to quantify their relative severity using descriptions and disability weights from the Global Burden of Disease study[17]. The three symptom clusters were: i) fatigue with bodily pains and/or symptoms of depression or anxiety; ii) cognitive problems such as forgetfulness or difficulty in concentrating, commonly referred to as “brain fog”; and iii) continuing respiratory problems with shortness of breath and persistent cough, referred to, respectively, as fatigue, cognitive, and respiratory clusters. These clusters are a subset of

all manifestations of long COVID; the WHO definition goes on "…also others and generally have an impact on everyday functioning"[16]. They analysed ten cohort studies in ten countries for the occurrence of these three symptom clusters of long COVID. They pooled data from: i) the ten contributing studies; ii) two large medical record databases in the US; and iii) findings from 44 published studies. They considered separately the occurrence and recovery among hospitalised patients and those with milder infections.

They based their Bayesian meta-regression analysis on detailed information for 1,906 people with community infections and 10,526 hospitalised patients from the ten cohorts, three of which included children. They added published data on 37,262 community infections and 9,540 hospitalised patients and ICD-coded medical record data on 1.3 million. They estimated that, of 3.9 billion (95% uncertainty interval=3.8–4.1) infections with SARS-CoV-2 in 2020-21, 3.7% or 144.7 million (54.7–312.6) people developed long COVID to the end of 2021. Of these, 130 million (42.1—301.0) had experienced mild to moderate infections in the community, 11.5 million had been hospitalised, and 3.0 million had needed ICU care. Their estimate of the global number of infections is much higher than reported as diagnosed cases because, as they note, with just a little hand waving, "excess deaths, infection-to-death ratios, and seroprevalence surveys suggest that many more cases must have occurred". They estimated that 6.2% (2.4–13.3) of symptomatic SARS-CoV-2 infections who survived the acute episode developed long COVID. Their estimates for those admitted to ICU, hospitalised, and not-hospitalised were 43.1%, 27.5% and 5.7% respectively. The median duration of long COVID was estimated at 4.0 months (inter-quartile range (IQR)=3.8–4.2) for community infections and 8.8 months (IQR=8.1–9.8) for those hospitalised.

The global prevalence of long COVID (63.2% female) in 2020-2021 was 5.1 million (2.3–8.7) cases among more severe, hospitalised patients and 31.4 million (10.2–73.5) cases among those who had had milder infections. The fatigue, respiratory, and cognitive clusters occurred in 51.0%, 60.4%, and 35.4%; in 38.4%, two or all three of the clusters overlapped. The risk of long COVID at 3 months follow-up was 2.7% in children, 4.8% in adult males, and 9.9% in adult females. The peak of long COVID cases occurred in those aged 20-29 years[14]. Wulf Hanson and colleagues concluded that the average level of disability among long COVID cases (the ratio of overall long COVID severity-weighted prevalence to prevalence) was 0.231, equivalent to the Global Burden of Disease disability weights for severe neck pain, Crohn's disease, or the long-term consequences of moderately severe traumatic brain injury[17].

These findings – given their geographic coverage – are the most comprehensive overview of long COVID published to date. However, they have to be regarded as a lower bound of the burden of these long-term consequences of acute infection with SARS-CoV-2. The authors acknowledged several limitations to their study, three of which bear directly on the question of the extent of the burden. Firstly, they addressed 3 symptom clusters that are specifically named in the WHO definition but do not address other outcomes that are well characterised components of long COVID, including sleep disturbance, loss of senses of smell and taste, vision impairment, palpitations, and hair loss. Because we do not know the extent to which these and other symptoms overlap with the three clusters, it is not possible to say what their inclusion would do to the estimates of prevalence. Secondly, Wulf Hanson and colleagues do not have sufficient information on the contribution that asymptomatic infection makes to the subsequent burden of long COVID; this is likely to be low but not likely to be zero. For instance, in a study of almost 2 million patients based on private healthcare claims in the US, 19% of asymptomatic patients were still experiencing long

COVID symptoms 30 days post-infection[18]. Also, Doykov et al reported abnormal inflammatory responses 40 days post-infection in a group designated asymptomatic/low symptomatic[19]; Cirulli et al found that, even among those with very mild and initially asymptomatic infection, 21.3% had complications that persisted for at least 30 days[20]; and Helms described imaging evidence of two asymptomatic patients each with a small acute ischaemic stroke[21]. Thirdly and most crucially, the known severe outcomes of acute COVID-19[9,22] – including those involving heart[23,24], lung[25], brain[26], kidney[27,28], pancreatic beta cells[29], and erectile dysfunction[30] – are not included as components of long COVID as discussed here. These are the most important of the long COVID outcomes.

Finally, although it is clear that the burden of the three identified symptom clusters does decline over time, there is not complete recovery for 15% of these individuals even after 12 months[14].

Reinfection with SARS-CoV-2 and Long COVID

Using national data from the US Department of Veterans Affairs, Al-Aly and colleagues established a COVID-19-related cohort that included: a non-infected control group (n = 5,396,855); people who had experienced one SARS-CoV-2 infection (n = 257,427) and those with a history of two or more infections (n = 38,926, including 36,417 with two infections, 2,263 with three, and 246 people with four or more)[31]. Those experiencing reinfection exhibited an increased risk of all-cause mortality (hazard ratio [HR]=2.1; 95% confidence interval [CI]: 2.0-2.3) and hospitalisation (HR=3.0; 2.8-3.1) – and they were at increased risk of at least one long-term symptom or pathologic outcome of SARS-CoV-2 infection (HR=1.8; 1.8-1.9), including disorders of the respiratory (HR=2.5; 2.3-2.7) and cardiovascular (HR=2.4; 2.2-2.5) systems; coagulation and haematologic disorders (HR=2.2; 2.1-2.4); fatigue (HR=2.4; 2.2-2.6); gastrointestinal (HR=1.7; 1.6-1.8) and renal disorders (HR=1.7; 1.5-2.5); mental-health disorders (HR=2.0; 1.9-2.0); diabetes (HR=1.6; 1.5-1.8); and musculoskeletal (HR=1.3; 1.2-1.4) and neurologic disorders (HR=1.4; 1.3-1.5). There was a dose-response pattern with risks of adverse health outcomes increasing as the number of infections increased. Compared to the non-infected control group, those who had had one infection had an increased risk of at least one long COVID symptom or pathology (HR=1.4). The risk was higher among people who had had two infections (HR=2.1) and highest among those who had had three or more infections (HR=3.0). These higher risks following reinfections were seen among the unvaccinated, those who had had one dose, and those who had had two or more doses prior to the second infection.

In summary, these findings are based on very large numbers and show a dose-response relationship between number of reinfections and the risk of deleterious outcomes, patterns that are essentially independent of vaccination status.

Impact of Vaccination and Variants

The UK Health Security Agency summarised what was known about the relationship between vaccination and long COVID up to early 2022[32]. Seven studies examined whether vaccination before infection reduced the symptoms or incidence of long COVID, seven examined whether vaccination in people already experiencing long COVID reduced or cleared symptoms, and one study examined both. Six of the eight studies of vaccination before SARS-C0V-2 infection suggested that vaccinated (1 or 2 doses) individuals were less likely to develop symptoms of long COVID following infection, in the short (4 weeks post infection), medium (12 to 20 weeks), and long term (6 months). All eight studies were of

individuals who had had COVID-19; thus, the extent to which vaccination reduced the incidence of COVID-19 itself cannot not be measured[32]. Accordingly, these studies underestimate the total population effectiveness of vaccines in the prevention of long COVID (if you did not get COVID-19, you cannot get long COVID). Two studies measured individual long COVID symptoms and found that fully vaccinated individuals were less likely than the unvaccinated to have the following symptoms in the medium or long term: fatigue, headache, weakness in arms and legs, persistent muscle pain, hair loss, dizziness, shortness of breath, anosmia, interstitial lung disease, myalgia, and other pain[32].

Three of four studies examining the effect of vaccination among people already experiencing long COVID found that more individuals reported an improvement in symptoms after vaccination, either immediately or over several weeks. There were, however, some cases in all these studies who reported that their symptoms worsened after vaccination[32].

Three studies of unvaccinated people with long COVID compared individuals who were subsequently vaccinated with those who remained unvaccinated. These studies suggested that people with long COVID were less likely to report long COVID symptoms shortly after vaccination and over longer periods, than people with long COVID who remained unvaccinated[32].

In three of the five studies reporting on symptom changes following vaccination of people with long COVID, a higher proportion of individuals with long COVID reported unchanged symptoms following vaccination (up to 70%) than people whose symptoms improved or worsened[32].

All studies were observational, so the results may be from differences other than vaccination, and there was large heterogeneity between studies in the definition of long COVID[32].

A separate UK study included COVID-19 Infection Survey participants aged 18-69 years who tested positive for SARS-CoV-2 between 26 April 2020 and 30 November 2021[33]. People who were double-vaccinated ≥14 days before infection were 1:1 propensity-score matched, based on socio-demographic characteristics and time from infection to follow-up for long COVID and compared to those who were unvaccinated at time of infection. Long COVID symptoms were reported by 294 double-vaccinated participants (prevalence 9.5%) compared with 452 unvaccinated participants (14.6%) among 3,090 double-vaccinated participants (mean age 49 years; 54% female; 92% white; median follow-up time from infection 96 days) and matched controls. This represents an adjusted odds ratio of 0.59 (0.50-0.69). There was no evidence of heterogeneity by vaccine type (adenovirus vector versus mRNA).

Data from the UK suggest that, among those who are double vaccinated, there was a lower risk of long COVID following Omicron BA.1 than following Delta. Among the double-vaccinated, the prevalence of self-reported long COVID four to eight weeks after a first infection compatible with the Delta variant was 15.9% compared with 8.7% for infections compatible with the Omicron BA.1 variant. Further, even though there was no difference in first infections among the triple-vaccinated between Delta and Omicron BA.1 or Omicron BA.2, the likelihood of long COVID symptoms four to eight weeks after a first COVID-19 infection among adults who were triple-vaccinated when infected was higher after an infection compatible with Omicron BA.2 (9.3%) than Omicron BA.1 (7.8%)[34].

Although from a much smaller study, data from Japan are also consistent with the conclusion that long COVID symptoms are less common following Omicron infection than infection with other strains[35].

Evidence of substantially reduced risk of progression to severe clinical outcomes following infection with the Omicron variant relative to time-matched Delta infections within a large, integrated healthcare system in southern California (adjusted HRs for any hospital admission, symptomatic hospital admission, intensive-care-unit admission, mechanical ventilation, and death were 0.59 (95% CI: 0.51-0.69), 0.59 (0.51-0.68), 0.50 (0.29-0.87), 0.36 (0.18-0.72), and 0.21 (0.10-0.44) respectively) are also consistent with the evidence for a lower impact of Omicron on long COVID[36].

The nature of long COVID may be influenced by the specific infecting variant and by vaccination. One study in the UK provided us with the picture of the trajectory of long COVID that emerges following infection before vaccination. The presence of long COVID symptoms at least 12 weeks after infection was observed in 28,356 participants, aged 18-69 years (55.6% women and 88.7% white), in the Office for National Statistics COVID-19 Infection Survey who had received at least one dose of an adenovirus vector or mRNA COVID-19 vaccine after testing positive for SARS-CoV-2 infection. Follow-up was 3 February to 5 September 2021; median follow-up was 141 days from first vaccination (all participants) and 67 days from second vaccination (83.8%). 6729 participants (23.7%) reported long COVID symptoms of any severity at least once during follow-up. A first vaccine dose was associated with an initial 12.8% decrease (95% CI= -18.6% to -6.6%, $p<0.001$) in the odds of long COVID, with no clear direction for the subsequent trajectory of symptoms. A second vaccine dose was associated with an initial 8.8% decrease (95% CI= -14.1% to -3.1%, $p=0.003$) in the odds of long COVID, with a subsequent decrease of 0.8% per week (-1.2% to -0.4% per week, $p<0.001$). The associations between vaccination and long COVID did not differ by: sociodemographic characteristics; health status; hospital admission for acute COVID-19; vaccine type (adenovirus vector or mRNA); or time between SARS-CoV-2 infection and vaccination. The authors concluded that the likelihood of long COVID symptoms decreased after vaccination and probably further improved after a second dose, at least over the median follow-up of 67 days[37].

A much smaller study focused specifically on how neurologic symptoms evolved among long COVID patients who had not been hospitalised 6–9 months after their initial neurologic evaluation. Of 52 patients who completed the study (27 SARS-CoV-2pos; 25 SARS-CoV-2neg) a median 14.8 months after symptom onset, the mean age=42.8 years, 73% were female, and 77% were vaccinated. Overall, there was no significant change in the frequency of most neurologic symptoms between first and follow-up evaluations, including “brain fog” (81 vs 71%); numbness/tingling (69 vs 65%); headache (67 vs 54%); dizziness (50 vs 54%); blurred vision (34 vs 44%); tinnitus (33 vs 42%); and fatigue (87 vs 81%). However, loss of taste and smell decreased (63 vs 27%; 58 vs 21%, both $p < 0.001$). Conversely, heart rate and blood pressure variation (35 vs 56%, $p = 0.01$) and gastrointestinal symptoms (27 vs 48%, $p = 0.04$) increased at follow-up. Vaccination had no impact on cognitive function or fatigue[38].

Lessons Not Learned and the Collapse of Public-Health Measures

One of the absolutely critical things about long COVID is that we should not underestimate it. It is now clear from multiple large studies that:

- it is a set of syndromes;

- it affects multiple organs and systems;
- it resolves in some but seems to remain persistent in others;
- it can be markedly debilitating;
- its risk is reduced by vaccination
- its pathology is poorly understood;
- we are just beginning to find ways to predict risk and monitor its course;
- perhaps most crucially: because reinfection is common with the Omicron variant, reinfection may become a feature of the pandemic for at least the next 12 to 36 months and the risk of long COVID rises in a dose-response way with each episode.

This will result in an increasing long-term burden on individuals, whanau, communities, and the healthcare system.

The influential Italian newspaper – *Corriere della Sera* – reported daily death tolls from influenza during the 1918-19 influenza pandemic until civil authorities asserted that it was stirring up anxiety among people and forced it to stop this coverage[39]. As Spinney notes, people could see the exodus of dead bodies from their neighbourhoods so the silence was even more anxiety provoking[1]. The pandemic and the silence conspired to confuse people further about the efficacy of public-health measures and compliance dropped off even further. People drifted back to church and race meetings – and left masks at home. Public-health infrastructure collapsed[1,39,40].

With COVID, it seems increasingly that vaccines (not available a hundred years ago) are almost all that stands between us – including in Aotearoa New Zealand – and this Italian-style collapse. We would remain stronger and healthier – and there would be less strain on healthcare systems and less worry about the prolonged burden of long COVID – if we increased vaccination coverage (including with the fourth dose) and we universally adopted and continued with Japanese-style regular mask use and physical distancing.

*Prof John D. Potter, Research Centre for Hauora and Health, Massey University, Wellington. Email: j.d.potter@massey.ac.nz. Phone: 021-230-5181

References

1. Spinney L. Pale Rider: The Spanish Flu of 1918 and How It Changed the World. London: Vintage; 2017.
2. Rice GW. Japan and New Zealand in the 1918 Influenza Pandemic: comparative perspectives on official responses and crisis management. In: Phillips H, killingray D, eds. The Spanish Influenza Pandemic of 1918-19: New perspectives. London and New York: Routledge; 2003: 73-85.
3. Bootsma MC, Ferguson NM. The effect of public health measures on the 1918 influenza pandemic in U.S. cities. *Proc Natl Acad Sci U S A* 2007; **104**(18): 7588-93.
4. Rice GW. Black November: "The 1918 Influenza Pandemic in New Zealand". Revised and Enlarged Second Edition ed. Christchurch: Canterbury University Press; 2005.
5. Rice GW. Black Flu 1918: The Story of New Zealand's Worst Public Health Disaster. Christchurch: Canterbury University Press; 2017.
6. Choutka J, Jansari V, Hornig M, Iwasaki A. Unexplained post-acute infection syndromes. *Nature Medicine* 2022; **28**(5): 911-23.
7. Vedel Sørensen AI, Spiliopoulos L, Bager P, et al. Post-acute symptoms, new onset diagnoses and health problems 6 to 12 months after SARS-CoV-2 infection: a nationwide questionnaire study in the adult Danish population. *medRxiv* 2022:

2022.02.27.22271328.
8. Whitaker M, Whitaker M, Elliott J, et al. Persistent symptoms following SARS-CoV-2 infection in a random community sample of 508,707 people. *medRxiv* 2021.
9. Ayoubkhani D, Khunti K, Nafilyan V, et al. Post-covid syndrome in individuals admitted to hospital with covid-19: retrospective cohort study. *BMJ* 2021; **372**: n693.
10. Ehwerhemuepha L, Carlson K, Moog R, et al. Cerner real-world data (CRWD) – A de-identified multicenter electronic health records database. *Data in Brief* 2022; **42**: 108120.
11. Bull-Otterson L, Baca S, Saydah S, et al. Post–COVID Conditions Among Adult COVID-19 Survivors Aged 18–64 and ≥65 Years — United States, March 2020–November 2021. *MMWR Morbidity and Mortality Weekly Report* 2022; **71**(21): 713-7.
12. Potter JD. Long COVID: a crucial reason for vax, mask, and distance. Public Health Expert. https://blogs.otago.ac.nz/pubhealthexpert/long-covid-a-crucial-reason-for-vax-mask-and-distance/#more-19237: University of Otago; 2022.
13. Wong-Chew RM, Rodriguez Cabrera EX, Rodriguez Valdez CA, et al. Symptom cluster analysis of long COVID-19 in patients discharged from the Temporary COVID-19 Hospital in Mexico City. *Ther Adv Infect Dis* 2022; **9**: 20499361211069264.
14. Wulf Hanson S, Abbafati C, Aerts JG, et al. A global systematic analysis of the occurrence, severity, and recovery pattern of long COVID in 2020 and 2021. *medRxiv* 2022: 2022.05.26.22275532.
15. Soriano JB, Murthy S, Marshall JC, Relan P, Diaz JV. A clinical case definition of post-COVID-19 condition by a Delphi consensus. *The Lancet Infectious Diseases* 2022; **22**(4): e102-7.
16. World Health Organization. A clinical case definition of post COVID-19 condition by a Delphi consensus. https://www.who.int/publications/i/item/WHO-2019-nCoV-Post_COVID-19_condition-Clinical_case_definition-2021.1: WHO, 2021.
17. Salomon JA, Haagsma JA, Davis A, et al. Disability weights for the Global Burden of Disease 2013 study. *Lancet Glob Health* 2015; **3**(11): e712-23.
18. FAIR Health. A Detailed Study of Patients with Long-Haul COVID: An Analysis of Private Healthcare Claims. https://bit.ly/3v8RSQv: FAIR Health, Inc., 2021.
19. Doykov I, Hallqvist J, Gilmour KC, Grandjean L, Mills K, Heywood WE. 'The long tail of Covid-19' – The detection of a prolonged inflammatory response after a SARS-CoV-2 infection in asymptomatic and mildly affected patients. *F1000Res* 2020; **9**: 1349.
20. Cirulli ET, Schiabor Barrett KM, Riffle S, et al. Long-term COVID-19 symptoms in a large unselected population. *medRxiv* 2020: 2020.10.07.20208702.
21. Helms J, Kremer S, Merdji H, et al. Neurologic Features in Severe SARS-CoV-2 Infection. *N Engl J Med* 2020; **382**(23): 2268-70.
22. Gupta A, Madhavan MV, Sehgal K, et al. Extrapulmonary manifestations of COVID-19. *Nat Med* 2020; **26**(7): 1017-32.
23. Xie Y, Xu E, Bowe B, Al-Aly Z. Long-term cardiovascular outcomes of COVID-19. *Nat Med* 2022; **28**(3): 583-90.
24. Long B, Brady WJ, Koyfman A, Gottlieb M. Cardiovascular complications in COVID-19. *Am J Emerg Med* 2020; **38**(7): 1504-7.
25. Kommoss FKF, Schwab C, Tavernar L, et al. The Pathology of Severe COVID-19-Related Lung Damage. *Dtsch Arztebl Int* 2020; **117**(29-30): 500-6.
26. Douaud G, Lee S, Alfaro-Almagro F, et al. SARS-CoV-2 is associated with changes in brain structure in UK Biobank. *Nature* 2022; **604**(7907): 697-707.
27. Bowe B, Xie Y, Xu E, Al-Aly Z. Kidney Outcomes in Long COVID. *J Am Soc Nephrol*

2021; **32**(11): 2851-62.
28. Hultstrom M, Lipcsey M, Wallin E, Larsson IM, Larsson A, Frithiof R. Severe acute kidney injury associated with progression of chronic kidney disease after critical COVID-19. *Crit Care* 2021; **25**(1): 37.
29. Sathish T, Kapoor N, Cao Y, Tapp RJ, Zimmet P. Proportion of newly diagnosed diabetes in COVID-19 patients: A systematic review and meta-analysis. *Diabetes Obes Metab* 2021; **23**(3): 870-4.
30. Kresch E, Achua J, Saltzman R, et al. COVID-19 Endothelial Dysfunction Can Cause Erectile Dysfunction: Histopathological, Immunohistochemical, and Ultrastructural Study of the Human Penis. *World J Mens Health* 2021; **39**(3): 466-9.
31. Al-Aly Z, Bowe B, Xie Y. Outcomes of SARS-CoV-2 Reinfection. *Research Square Preprint* 2022.
32. UK Health Security Agency. The effectiveness of vaccination against long COVID: A rapid evidence briefing. https://ukhsa.koha-ptfs.co.uk/cgi-bin/koha/opac-retrieve-file.pl?id=fe4f10cd3cd509fe045ad4f72ae0dfff: UK Health Security Agency, 2022.
33. Ayoubkhani D, Bosworth ML, King S, et al. Risk of Long Covid in people infected with SARS-CoV-2 after two doses of a COVID-19 vaccine: community-based, matched cohort study. *medRxiv* 2022: 2022.02.23.22271388.
34. Office for National Statistics. Self-reported long COVID after infection with the Omicron variant in the UK: 6 May 2022. https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/selfreportedlongcovidafterinfectionwiththeomicronvariant/6may2022/pdf: Office for National Statistics, 2022.
35. Morioka S, Tsuzuki S, Suzuki M, et al. Post COVID-19 condition of the Omicron variant of SARS-CoV-2. *medRxiv* 2022: 2022.05.12.22274990.
36. Lewnard JA, Hong VX, Patel MM, Kahn R, Lipsitch M, Tartof SY. Clinical outcomes associated with SARS-CoV-2 Omicron (B.1.1.529) variant and BA.1/BA.1.1 or BA.2 subvariant infection in southern California. *Nat Med* 2022.
37. Ayoubkhani D, Bermingham C, Pouwels KB, et al. Trajectory of long covid symptoms after covid-19 vaccination: community based cohort study. *BMJ* 2022; **377**: e069676.
38. Ali ST, Kang AK, Patel TR, et al. Evolution of neurologic symptoms in non-hospitalized COVID-19 “long haulers”. *Ann Clin Transl Neurol* 2022; **n/a**(n/a).
39. Tognotti E. Lessons from the history of quarantine, from plague to influenza A. *Emerg Infect Dis* 2013; **19**(2): 254-9.
40. Tognotti E. Scientific triumphalism and learning from facts: bacteriology and the “Spanish flu” challenge of 1918. *Soc Hist Med* 2003; **16**(1): 97-110.

Public Health Expert Briefing (ISSN 2816-1203)

Source URL:
https://www.phcc.org.nz/briefing/long-covid-century-old-lessons-we-still-have-not-learned