Prevention of the spread of respiratory viruses such as SARS-CoV-2 can also prevent cardiovascular deaths

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CARDIOVASCULAR CONDITIONS are responsible for more deaths than any other cause in Australia, so prevention is a critical objective in both primary care and public health practice. The very well–established reversible risk factors for cardiac disease include smoking, lack of exercise, poorly controlled diabetes, high blood pressure and high cholesterol (Table 1). Experience and data from the COVID-19 pandemic now suggest we could add to the list of modifiable risk factors for cardiovascular death: respiratory pathogens.

Data showing respiratory viruses as risk factors for cardiovascular events

Recent data have shown that SARS-CoV-2 infection is a specific risk factor for a subsequent cardiovascular event, including death.[1] This includes the convalescent phase after infection,[2] meaning that SARS-CoV-2 infection itself is also a risk factor for cardiovascular death. SARS-CoV-2 infection (and, far less commonly, mRNA vaccines) can also cause myocarditis[3] and multisystem inflammation syndrome. The likely mechanism by which the SARS-CoV-2 virus enters the myocardium is by binding to the angiotensin converting enzyme receptors, with the damage to cells being multifactorial, including via cytokine storm and coagulopathy.[4,5]

The relationship between cardiovascular events and deaths is fairly constant. Clearly, not all people who have a major cardiovascular event will die, but a percentage will. The finding that SARS-CoV-2 infection is a risk factor for cardiovascular events means that COVID-19 prevention measures will probably also prevent cardiovascular deaths.

There is evidence that other viruses, such as influenza, are also associated with cardiovascular deaths.[6] The respiratory syncytial virus (RSV) is associated with cardiovascular complications in people both with and without pre-existing conditions. If hospitalised for RSV, one in five adults can expect a cardiac complication such as congestive heart failure or myocardial infarction.[7]

Influenza vaccination has been previously associated with reductions in cardiovascular deaths in both observational studies and multiple randomised controlled trials (RCTs).[8] While these findings have been reported cautiously in the past, given that multiple respiratory viruses are now being associated with increased cardiovascular deaths, level 1 evidence showing that influenza vaccination reduces cardiovascular deaths should not be disregarded.

The experience of countries with low COVID-19 rates in 2020–21

In countries severely affected by the COVID-19 pandemic, the 'excess death rate' has been even higher than the number of COVID-19-related deaths,[9] with cardiovascular deaths being a major contributor towards excess deaths.[10] 'Excess cardiac deaths' during a COVID-19 wave could be contributed to by both undiagnosed/post-COVID-19 cases and possibly suboptimal acute care if the health system was not coping with the excess caseload.

Australia was one of only a handful of countries/regions that recorded negative excess deaths in the years 2020–21 (ie fewer deaths than expected), along with New Zealand, Iceland, Singapore and Taiwan.[9] Although Australia had a low COVID-19 case rate for most of 2020 and 2021, life was not 'normal'. There were impositions of lockdowns and other public health restrictions along with further voluntary avoidance of exposure to crowded venues. The specific death category most reduced in Australia in 2020–21 was respiratory deaths in general. However, there were also fewer

cardiovascular deaths than expected in winter during 2020 and 2021.[11–13]

Seasonality of cardiovascular deaths

It was well established (before COVID-19) that there is a strong seasonality to respiratory and cardiovascular deaths.[14,15] In cool and temperate climates, this meant that cardiovascular deaths peaked in winter. The seasonality of cardiovascular disease is not as strong in equatorial climates.[14,15] Ockham's razor suggests that perhaps this pattern is not as mysterious as we once considered it to be. If non-COVID-19 respiratory viruses, such as influenza, also lead to increased cardiovascular deaths, then it would explain the concurrent winter peaks of overall deaths, as well as respiratory and cardiovascular deaths.[14]

Levels of evidence

The highest standard evidence in medicine is usually a systematic review of RCTs. With respect to the link between respiratory viruses and cardiovascular deaths, we only have this level of evidence for the influenza vaccine lowering cardiovascular deaths.[8] As soon as RCTs of COVID-19 vaccines showed reduced risk of death as a result of COVID-19, emergency measures dictated an immediate attempt at universal vaccination rather than performing further RCTs to see whether COVID-19 vaccines also prevented cardiovascular deaths. Cohort studies have shown reduced cardiovascular complications in patients vaccinated against COVID-19 when compared with those who are unvaccinated,[16] including those with pre-existing cardiac disease.[17] Box 1 summarises the evidence that associates respiratory viruses with cardiovascular deaths, some of which is temporal association but paints a strong picture when considered in total.

Implications for prevention of cardiovascular deaths

There is certainly further work to do on the prevention of cardiovascular deaths in the traditional sense. This includes obtaining better compliance with medications to reduce risk factors (eg statins for patients with high cholesterol levels), further discouraging smoking, encouraging and funding exercise in the community, rolling out cardiopulmonary resuscitation education and making public access defibrillators more available.

The post-COVID-19 environment should not be thought of as a binary option (that is, full societal lockdown or pre-pandemic business as usual). Full lockdown measures, while successful in hindsight during 2020 and 2021, are either no longer justified or palatable as ongoing public health measures. Lower-cost interventions may be retained, especially at times when circulating levels of respiratory illness are high. Such interventions could include mask use in indoor settings, hybrid working from home models, increased outdoor dining options and improved ventilation, among others (Box 2). Emphasising that this is

Box 1. Evidence linking respiratory viruses to cardiovascular deaths

- Influenza vaccination reduces subsequent cardiovascular mortality in multiple randomised controlled trials.[8]
- Patients with COVID-19 have higher rates of cardiovascular deaths in the subsequent months post recovery, even if only affected by a case of COVID-19 that does not require hospitalisation,[1,2] with vaccination offering some protection.[16,17]
- In Australia, we managed to substantially reduce cardiovascular deaths in 2020–21 at the same time as we supressed respiratory deaths.[11,12] The rate of cardiovascular deaths has returned to expected levels in early 2022.[13]
- In most countries within a temperate zone, cardiovascular deaths and respiratory deaths cycle in tandem between higher levels in winter and lower levels in summer, in concert with the rate of circulating respiratory viruses.[14,15]

Table 1. Established and emerging ways to reduce cardiovascular deaths

Established modifiable individual risk factors for cardiovascular deaths (traditional prevention)	Established interventions to reduce death rates from cardiovascular events (optimal early management)	Emerging public health interventions to potentially reduce cardiovascular deaths via suppression of respiratory viruses (novel prevention)
• Reduce cigarette smoking • Treat hypertension • Treat high low-density lipoprotein cholesterol • Control high blood glucose • Exercise according to minimum weekly guidelines	• Train the population in early response to sudden cardiac arrest, including basic life support • Ensure access to automated external defibrillators in as many public locations as possible • Maintain well-functioning ambulance services, emergency departments and coronary care units • Institute evidence-based early intervention treatments (eg streptokinase for acute thrombotic myocardial infarction)	• Vaccinate against influenza viruses • Vaccinate against COVID-19 viruses • Encourage a 'stay home when sick' mentality, especially for those who work indoors • Encourage/rollout better ventilation for crowded indoor venues, such as schools, hospitals, restaurants, movie theatres, etc • Encourage mask wearing in crowded venues (eg flights, public transport, large meetings) and when there are outbreaks of respiratory viruses in winter

Box 2. Measures to reduce spread of respiratory viruses that may also reduce subsequent cardiovascular death

- Stay home when sick with any respiratory illness[12] to prevent onward spread (including permanently moving some routine primary care consultations for acute illness from in person to telehealth).
- Encourage better ventilation of all buildings, including doctor consultation rooms.
- For large events, especially when eating and drinking is involved, move to outdoor, semi-outdoor (eg open windows, high-efficiency particulate absorbing filters) or hybrid settings.
- Use masks in crowded situations, such as public transport and large indoor meetings, especially during seasonal peaks of respiratory illness.
- Vaccinate against respiratory pathogens (and particularly COVID-19 and influenza viruses, which the Australian Technical Advisory Group on Immunisation has approved to be co-administered).

not only respiratory prevention but also cardiovascular prevention can assist with societal acceptance of a post-COVID-19 normal, as cardiovascular death may loom larger as a fear in the mindset of the general public when compared with respiratory viruses.

The decision on which settings to adopt for ongoing COVID-19 prevention has become somewhat political, with passionate advocates on either side of any specific policy. Mandates for mask wearing while at busy indoor venues is one example. There is certainly a moderate degree of evidence that masks prevent transmission of respiratory illnesses in general,[18] albeit that some randomised studies during the COVID-19 pandemic have found weak protection only.[19] The general exception from mask mandates allowed for indoor eating and drinking may weaken the efficacy of mask mandates, given that indoor eating and drinking is known to be a strong driver of COVID-19 transmission.[20]

Now that COVID-19 and influenza viruses are known to be cardiovascular risk factors, it is time to consider prevention of spread of respiratory pathogens as a means of prevention of cardiovascular disease. If prevention of cardiovascular death is better highlighted as an outcome associated with prevention of respiratory disease spread, the public may be more accepting of these measures in an ongoing sense.

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