

## PERSONAL VIEWPOINT

# Impact of COVID-19 on the worsening crisis of chronic kidney disease: the imperative to fund early detection is now

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**Abstract**

The number of Australians affected by kidney disease will increase as the impacts of COVID-19 infection on kidney health are realised. Chronic kidney disease (CKD) imposes significant health and economic burdens from dialysis costs, loss of employment, premature death and increased admissions to hospital. Screening for kidney disease must be integrated into post-COVID-19 care; however, currently there is no reimbursement for kidney health checks in primary care. Early detection can reduce the progression of CKD by as much as 50% and thus the imperative to fund the Kidney Health Check is now.

Kidney disease is a growing public health problem in Australia and globally and has traditionally been driven by an epidemic of diabetes and obesity. Worldwide, 850 million people are affected by chronic kidney disease (CKD).<sup>1</sup> Within Australia, over 1.7 million Australians are living with CKD and more than 90% of these individuals are completely unaware that they have the condition.<sup>2</sup> The inexorable rise of kidney disease has now received a further substantial boost from the COVID-19 pandemic, which has had a devastating impact. Worldwide, over 260 million confirmed cases of SARS-CoV-2 infection have been reported and deaths have eclipsed 5 million.<sup>3</sup> Despite the early and aggressive response to the pandemic by the state, territory and federal governments of Australia, more than 2000 deaths have been reported and over 220 000 cases confirmed.<sup>3</sup> The clinical spectrum of SARS-CoV-2 infection is varied and ranges from asymptomatic infection through to severe viral pneumonia with diffuse alveolar haemorrhage, respiratory failure and death.<sup>4</sup> The virus mediates disease through binding to the angiotensin-converting enzyme 2 (ACE2) receptor, after which the virus is internalised

and replicates.<sup>5</sup> While ACE2 is present in the lung, the receptor is also present in the kidney, and there is clear evidence that SARS-CoV-2 infection commonly leads to both acute kidney disease and CKD through both direct infection and systemic effects.<sup>5</sup>

Acute kidney injury (AKI) complicates COVID-19 infection in approximately 20% of cases, with over one-third (39%) of these requiring kidney replacement therapy.<sup>4</sup> AKI in the setting of COVID-19 is associated with poor outcomes and high mortality rates.<sup>6</sup> One retrospective study of nearly 10 000 patients showed that in-hospital death increased from 7% in those without AKI to 46% in those with AKI not receiving dialysis and to 79% in those with AKI requiring dialysis.<sup>7</sup> For those with AKI requiring treatment with dialysis, 31% remained on dialysis at discharge.<sup>7</sup> In contrast, for those with AKI not requiring dialysis, one-quarter did not achieve complete kidney function recovery. However, even with full biochemical recovery, AKI is a recognised risk factor for subsequent CKD, kidney failure and death.<sup>8</sup> Emerging data suggest that COVID-19-induced AKI is associated with a greater rate of kidney function loss after discharge.<sup>9</sup> In a retrospective cohort study of patients who experienced AKI in five US hospitals, the estimated glomerular filtration rate (eGFR) declined more rapidly by 11.3 mL/min/1.73 m<sup>2</sup>/year in patients

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with COVID-19-induced AKI compared with AKI not associated with COVID-19, an effect that persisted after adjusting for the severity of AKI.

Kidney disease has also recently been described in 'long COVID',<sup>10</sup> which refers to the presence of symptoms weeks to months after infection. Nine core features of long COVID have been described and include dyspnoea, fatigue/malaise, chest/throat pain, headache, abdominal symptoms, myalgia, other pain, cognitive symptoms and anxiety/depression.<sup>11</sup> Among 273 618 patients with confirmed COVID-19 infection, 57% had at least one feature of long COVID in the following 6 months, with 37% experiencing them 90–180 days post-acute infection.<sup>11</sup> Co-occurrence of features of long COVID were noted, as well as the relapsing nature of the features and delayed onset in some.<sup>11</sup> Furthermore, long-COVID features were seen across demographics, and while a higher incidence was noted in those with severe COVID-19 disease, features were also observed in more than half of non-hospitalised patients who had a relatively mild illness.<sup>11</sup> In a retrospective cohort study of kidney outcomes in long COVID involving 89 216 30-day COVID-19 survivors and 1 637 467 non-infected controls, survivors of COVID-19 exhibited higher risks of AKI (adjusted hazard ratio (HR) 1.94; 95% confidence interval (CI) 1.86–2.04), a 50% or greater loss of eGFR (HR 1.62; 95% CI 1.1.51–1.74), kidney failure (HR 2.96; 95% CI 2.49–3.51) and major adverse kidney events (HR 1.66; 95% CI 1.58–1.74).<sup>10</sup> The risk of excess eGFR decline in COVID-19 survivors was observed across the spectrum of severity of infection, being most marked in those admitted to intensive care ( $-7.69$  mL/min/ $1.73$  m<sup>2</sup>/year; 95% CI  $-8.27$  to  $-7.12$ ). Notably, however, even in individuals whose COVID-19 infection was mild enough not to warrant hospitalisation, which represented the majority of people infected with COVID-19, eGFR decline was greater ( $-3.26$  mL/min/ $1.73$  m<sup>2</sup>/year; 95% CI  $-3.58$  to  $-2.94$ ) than in non-infected controls.<sup>10</sup>

As of early December 2021, over 40 million COVID-19 vaccines have been administered in Australia and 89% of people aged 16 years and over are double vaccinated.<sup>12</sup> While the real-world effectiveness of the COVID-19 vaccines has been realised, it is clear that immunity does wane, which together with the emergence of the Omicron variant has prompted the Australian Technical Advisory Group on Immunisation to recommend a third dose to anyone in Australia aged 18 years and over who has completed their primary course of vaccination at least 6 months earlier.<sup>12</sup> Prior to the emergence of the Omicron variant, breakthrough infections were noted to be relatively uncommon, and while 46% were asymptomatic, 26% had severe or critical illness and another 20% had moderate disease.<sup>13</sup>

Some have proposed that the risk of vaccine-breakthrough SARS-CoV-2 infections and associated morbidity and mortality align with the risk factors for severe disease originally described – obesity, diabetes, cardiovascular disease, insulin resistance, CKD and liver disease<sup>14</sup> – all common chronic diseases among Australians.

Collectively, these findings have major clinical implications for the screening and management of kidney disease in Australia. As we emerge from lockdowns and live with COVID-19, the number of Australians requiring post-COVID-19 care will be staggering and should necessarily include assessment of, and provision of, care for acute and CKD. The cornerstone of kidney disease prevention is screening and early detection with the implementation of management to mitigate progressive disease. The combination of a blood test to assess eGFR, urinalysis to determine the presence of albuminuria and blood pressure measurement constitute the 'kidney health check'.<sup>15</sup> It is recommended that these tests are performed in those at risk of kidney disease, which includes those with diabetes, hypertension, cardiovascular disease, obesity, smoking history, an episode of AKI or a family history of kidney failure, and that screening should start at age 60 years in those with any of these risk factors or at age 30 years if of Aboriginal and/or Torres Strait Islander ancestry. On top of this, the evidence also suggests that people who have experienced COVID-19 infection, regardless of severity, are also at risk of kidney disease. We suggest that a history of COVID-19 infection should therefore be added to the list of risk factors for kidney disease.

A key question is are we as a nation prepared for the influx of people with kidney failure to provide the care that they need? Inadequate infrastructure, strain on existing dialysis units, insufficient numbers of trained healthcare professionals and inadequate healthcare planning are obvious roadblocks, not to mention soaring healthcare costs to deliver these therapies. Three-quarters of those receiving dialysis therapy do so through a hospital or satellite centre, which are distributed throughout the country dictated in part by population. Thus, access to these centres can be challenging, particularly for those living in regional, rural and remote Australia. The cost of haemodialysis is in the order of \$85 000/year/person, increasing to at least \$120 000/year/person for remote services.<sup>16</sup> Prior to the pandemic, the Australian healthcare system was struggling to meet the health needs of the burgeoning kidney disease population and that pressure is going to become even more acute in the aftermath of the COVID-19 pandemic.

In addition to lifestyle modification and optimal control of hypertension, dyslipidaemia and diabetes mellitus, prevention of COVID-19 infection through vaccination,

mask-wearing and physical distancing has emerged as another important strategy for preventing kidney disease. The potent effect of new pharmacotherapies (sodium-glucose cotransporter-2 inhibitors) in slowing the progression of kidney disease<sup>17</sup> together with a new kidney disease risk factor, COVID-19 infection, frame the case for an urgent need for federal funding of kidney health checks in at-risk Australians. At present there is no reimbursement for kidney health checks in primary care, such that kidney disease goes largely undetected. Over 90% of Australians with kidney disease are completely unaware that they have this condition<sup>18</sup> and the situation is only likely to worsen as the number of people with kidney disease spikes in the setting of

COVID-19 infection and healthcare systems continue to be overwhelmed by the care needs of those affected by the pandemic. The current rebate for screening for other chronic disease is <\$100.<sup>19</sup> Given early detection can reduce the progression of CKD by as much as 50%,<sup>20</sup> we call on the Federal government to decisively and definitively address the incoming tsunami of kidney disease, exacerbated by the COVID-19 pandemic, through incentivised kidney disease screening and detection programmes targeting at-risk Australians during primary health encounters. This will substantially mitigate the excessive morbidity, mortality and healthcare costs associated with undetected kidney disease that is allowed to progress unchecked.

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