

MAKE THE LINK
Kidneys, Diabetes & Heart

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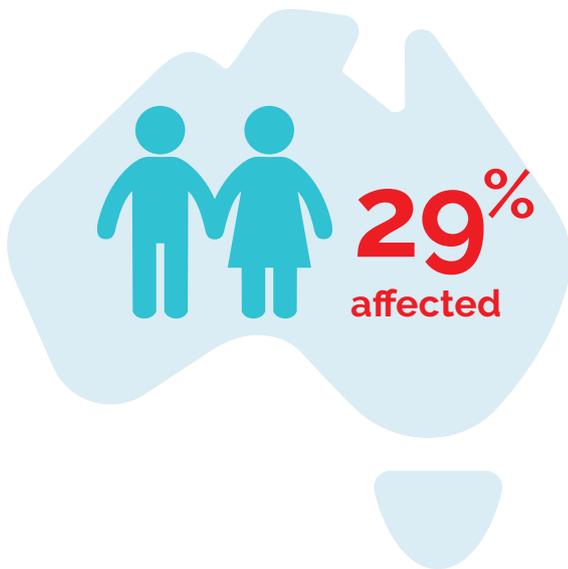
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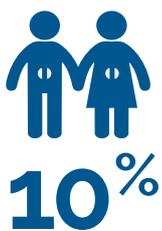
Executive summary



Chronic kidney disease, diabetes and cardiovascular disease together affect **29% of Australian adults** and frequently occur together.

Chronic kidney disease (CKD), diabetes and cardiovascular disease are each independently serious diseases, affecting millions of Australians. They each require careful management and place a large burden on the Australian health system, on individuals and on families.

Based on most recent estimates ^[1, 2]:



CKD affects 10% of the Australian adult population.

2.4 million

Based on Australia's current population age structure, this is equivalent to an estimated 2.4 million Australian adults affected by CKD in 2018, of whom an estimated 50% were aged over 65 years, and 30% over 75 years.



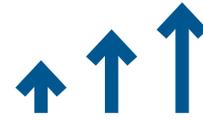
Fewer than 1 in 10 Australians with CKD are aware of their condition.

 **5.7%**

The prevalence of self-reported diabetes was 5.7% in 2017-2018, although true prevalence of diabetes (diagnosed and undiagnosed) is likely higher.

 **5.6%**

The prevalence of self-reported heart, stroke and vascular disease among Australian adults in 2017-2018 was 5.6%, with another 13% self-reporting a diagnosis of hypertension.



The prevalence of all three conditions increases steadily with increasing age.

CKD, diabetes and cardiovascular disease are inextricably linked, with **interrelated biological pathways** and **shared risk factors**.

29%

An estimated **29% of Australian adults have one or more of CKD, diabetes and/or cardiovascular disease**; of this number, approximately one quarter have at least two of these conditions.

+ age

The prevalence of comorbidity increases substantially with older age.

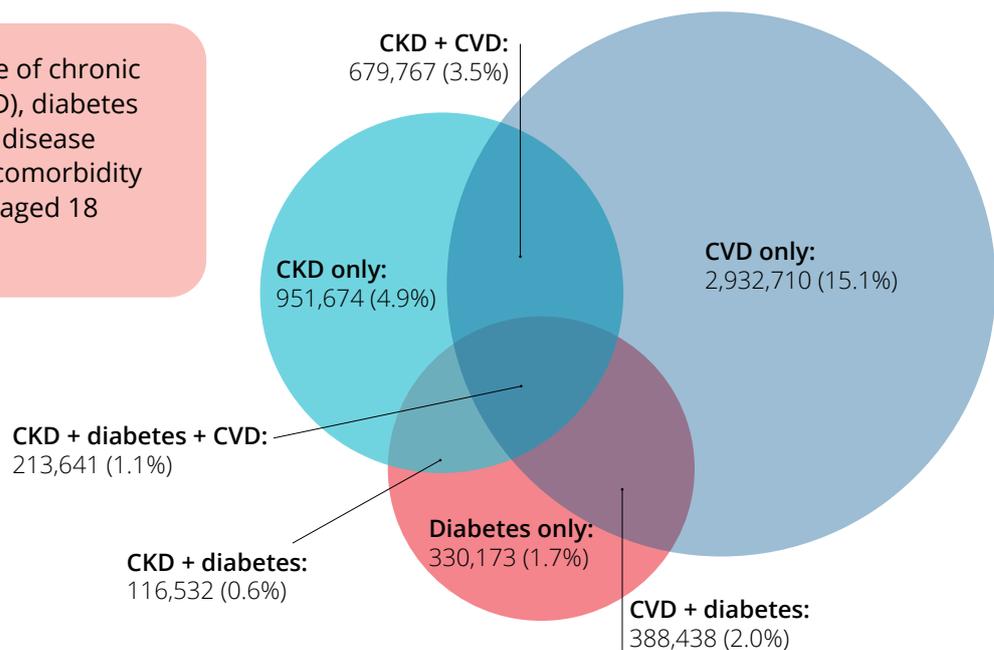
1.1%

Approximately 1.1% of Australian adults 18 years and older have all three conditions.

65+

For the population over 65 years, the proportion with all three conditions increases to 4.5% ^[1].

Figure i: Prevalence of chronic kidney disease (CKD), diabetes and cardiovascular disease (CVD) and rates of comorbidity among Australians aged 18 years and older.



Proportions are based on the 2011-12 Australian Health Survey, and have been applied to the 2018 Australian population to yield numerical estimates of burden of comorbidity (Source: AIHW analysis of unpublished data from the ABS Australian Health Survey, 2011-12 ^[1] and Australian Demographic Statistics – ABS 3101.0).

Lifestyle risk factors common to CKD, diabetes and cardiovascular disease include:



Physical inactivity



Poor nutrition



Smoking



Harmful use of alcohol

These in turn contribute to the development of biomedical risk factors including:



Overweight & obesity



High blood pressure



High blood cholesterol



Insulin resistance

In the event of the onset of diabetes or cardiovascular disease (including coronary heart disease, hypertensive disease, stroke, peripheral vascular disease, heart failure and cardiomyopathy), the likelihood of also subsequently developing comorbid CKD is significantly increased. The presence of comorbid CKD then greatly increases the burden of symptoms, rate of hospitalisations and risks of complications, cognitive decline, cardiovascular events and premature death.

The number of Australians at risk of comorbid CKD, diabetes and cardiovascular disease is increasing due to aging and risk factor trends

Population aging is not only increasing the number of Australians living with either CKD, diabetes or cardiovascular disease alone, but also the number of Australians living with two or more of these conditions. In addition, a steady reduction in cardiovascular mortality since the 1980's has meant that an increasing proportion of individuals are surviving their cardiovascular disease to subsequently develop CKD and/or diabetes.

CARDIOVASCULAR DISEASE DEATHS, BY SEX, 1981-2017

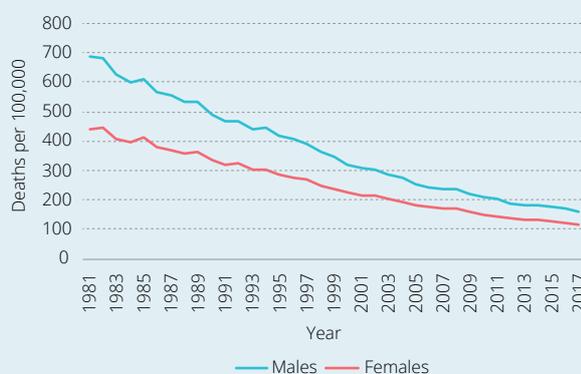


Figure ii: Trends in cardiovascular disease deaths, by sex, 1981-2017. Rates are age-standardised to the 2001 Australian population (Source: AIHW analysis of the National Mortality Database [3])

While there has been significant progress with respect to certain risk factors for CKD, diabetes and cardiovascular disease – specifically, reduction in smoking rates and a decline in alcohol consumption above recommended levels – the **continued rise in the proportion of the population who are overweight and obese and the high prevalence of insufficient physical activity and inadequate nutrition** are also contributing to greater multimorbidity in the Australian population [4]. More than two-thirds of Australian adults are now overweight or obese, and rates of obesity in children and young adults are rising [4].

PREVALENCE OF OVERWEIGHT AND OBESITY, BY SEX, 1995-2017/18

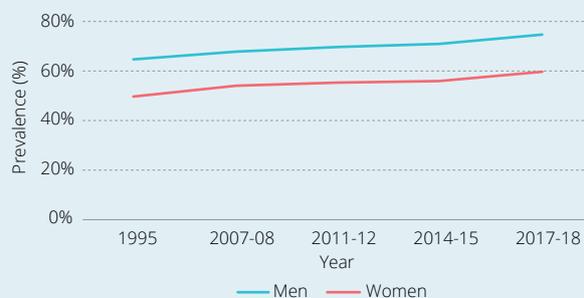
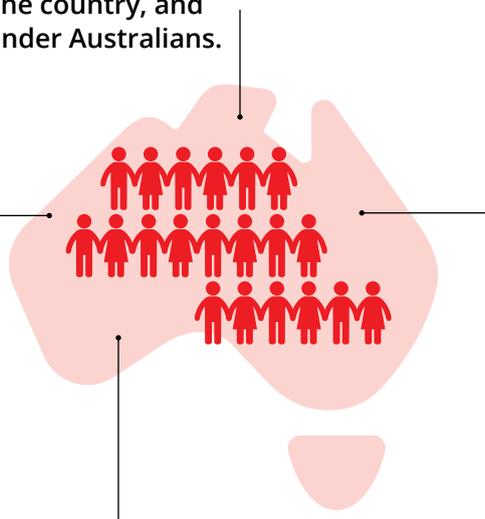


Figure iii: The proportion of Australian men and women aged over 18 years who were overweight or obese, 1995 to 2017-2018. (Source: 2017-28 ABS National Health Survey [4])

The burden of comorbid disease is unequally distributed across the Australian population

CKD, diabetes and cardiovascular disease are most prevalent among the most disadvantaged Australians, those living in remote parts of the country, and Aboriginal and Torres Strait Islander Australians.

Australian adults in the lowest socioeconomic group are more than twice as likely to have 2 or more comorbid diagnoses of CKD, diabetes or cardiovascular disease compared to adults in the highest socioeconomic group [1]. People living in outer regional and remote areas were twice as likely to have all three of CKD, diabetes and cardiovascular disease compared to people living in major cities in 2011-12 [1].



The comorbidity burden is similarly unevenly distributed across the population, disproportionately affecting those facing the greatest challenges with respect to health care access.

Rates of death in association with CKD, diabetes and/or cardiovascular disease also increase with greater geographical remoteness and greater socio-economic disadvantage. This reflects a higher burden of risk factors, poor access to health care and social services, and higher rates of socioeconomic disadvantage in remote populations. Shortages in the rural and remote health workforce, including general practitioners, nurses and nurse practitioners, mental health clinicians, regional nephrologists and other specialist doctors, contribute to these poorer outcomes.

Aboriginal and Torres Strait Islander Australians experience a higher burden of comorbid CKD, diabetes and cardiovascular disease



Over one-third of Aboriginal and Torres Strait Islander Australians have one or more of CKD, diabetes or cardiovascular disease and these diseases appear at a younger age, co-occur more frequently, progress faster, and are associated with more complications than in non-Indigenous Australians. By age 65, over half of Aboriginal and Torres Strait Islander Australians have CKD, diabetes, and/or cardiovascular disease, and usually more than one of these conditions.

56% 

Amongst Aboriginal and Torres Strait Islander adults with diabetes, 56% have comorbid CKD (compared to 32% of non-Indigenous Australians). **Among Aboriginal and Torres Strait Islander adults with cardiovascular disease, 32% have comorbid CKD** (compared to 21% of non-Indigenous Australians) ^[5]. A large proportion of hospitalisations for diabetes and cardiovascular disease in Aboriginal and Torres Strait Islander people involve comorbid CKD. In Aboriginal and Torres Strait Islander people aged over 25, CKD was an additional diagnosis in 30% of non-dialysis hospitalisations for diabetes and 42% of non-dialysis hospitalisations for cardiovascular disease (compared to 18% of non-Indigenous Australians) in 2013-14 ^[5].

6% 

CKD, diabetes and cardiovascular disease are also more commonly listed together on death certificates for Aboriginal and Torres Strait Islander Australians. **Six percent of all Aboriginal and Torres Strait Islander deaths listed all three conditions**, compared to less than 2% of non-Indigenous deaths.

The onset of comorbid CKD is associated with significantly worse prognosis and quality of life



Comorbidity results in greater health care utilisation, more hospitalisations and longer stays, and increased need for support from family and carers.

Individuals with comorbid CKD, diabetes and/or cardiovascular disease experience greater disease severity, significantly worse quality of life, and poorer prognosis than individuals with any one condition in isolation.

CKD independently increases the risk of developing hypertension and other cardiovascular diseases, including heart attack, angina, coronary artery disease, stroke and heart failure ^[6, 7]. Only a relatively small proportion of those with CKD will progress to kidney failure requiring dialysis or kidney transplant; a far greater proportion will die prematurely, largely due to cardiovascular complications^[7]. In people with existing cardiovascular disease, the presence of CKD increases the risks of death and hospitalisation ^[8]. **Cardiovascular mortality is approximately 60% higher in people with CKD compared to those without CKD** ^[9, 10]. Risks of non-fatal heart attack and stroke also steadily increase as kidney function declines and the quantity of albumin in the urine (indicating kidney damage) increases ^[11-13].

Anaemia is common in CKD [14], causing the heart to work harder to maintain oxygen levels and increasing risk of heart failure and death. Anaemia is also associated with reduced quality of life, increased prevalence of depressive symptoms, higher rates of hospital admissions and cognitive impairment in people with CKD [15-20]. Other important complications of CKD that impact on quality of life include mineral bone disease, which may cause bone pain and increased bone fragility, and metabolic acidosis, leading to further bone loss and muscle wasting [14].

Bone pain, frailty, fatigue, poor sleep quality, hypertension, fluid retention, peripheral neuropathy, itch and side-effects from medications are increasingly prevalent as kidney function declines.

This symptom burden is associated with depression, a greater overall burden of illness, and poorer life satisfaction [14, 21, 22].

The presence of any one of CKD, diabetes or cardiovascular disease increases the likelihood of having depression and is associated with reduced quality of life.



Depression is highly prevalent in persons with diabetes and cardiovascular disease, and is associated with poor outcomes, including elevated risk of developing CKD [23-25].

The onset of CKD causes worsening of depressive symptoms and further reductions in quality of life, exacerbating the psychosocial burden of diabetes and cardiovascular disease while compounding the physical symptom burden [26, 27].

The impact of an individual's disease on family and friends, feeling unwell, low mood, insufficient home care and other life stressors are other key factors that increase the likelihood of low self-reported quality of life in CKD [28].

As CKD advances to kidney failure, symptoms and comorbidity increase while physical function declines, contributing to an increased prevalence of depression and reduced quality of life [29-31].

Depression affects 25-50% of dialysis patients [32-36] and is strongly associated with increased rates of hospitalisation, cardiovascular events, cardiovascular disease deaths and all-cause mortality [31, 35, 37-40].

Caring for someone with KF has a major impact on relationships and disrupts roles within the family [41]. Depression has been found to extend to the spouses of dialysis recipients [42].

Rates of kidney failure (KF) due to diabetes have been increasing

Among non-Indigenous Australians with type 2 diabetes, the incidence of KF increased by 2.2% per annum from 2002-2013 [43]. This trend is driven by an **increasing incidence of treated KF in the younger type 2 diabetes population**, possibly reflecting earlier age of diabetes onset and/or a more aggressive disease phenotype [44]. At the same time, increasing incidence of treated KF in the diabetes population 80 years and over likely reflects an increasing willingness to actively treat KF in older persons with diabetes, combined with a reduction in cardiovascular mortality in this population.

→ **Diabetic kidney disease was the underlying cause of KF in 38% of patients commencing treatment (dialysis or kidney transplant) in 2018**, followed by glomerulonephritis (16%) and hypertension (13%) [45]. **Diabetes was the primary cause of kidney disease in 88% of Aboriginal and Torres Strait Islander Australians commencing treatment for KF between 2016 and 2018.**

For over a decade, diabetic kidney disease has accounted for a greater proportion of new dialysis and kidney transplant patients than any other single cause.

In absolute terms, the number of patients commencing KRT with a primary diagnosis of diabetic kidney disease doubled between 2004 and 2018 (591 versus 1176) [45].

→ **For those who are receiving dialysis or living with a kidney transplant, the presence of comorbid diabetes and/or cardiovascular disease significantly increases mortality risk.** Among dialysis patients in 2018, presence of type 2 diabetes increased the death rate by 33%, whereas the presence of coronary disease increased the death rate by 98%. For kidney transplant recipients, the presence of type 2 diabetes increased the death rate by 147%, whereas coronary disease increases the death rate by 277% (ANZDATA, unpublished data).

INCIDENCE OF TREATED KF BY PRIMARY KIDNEY DISEASE, 1997-2018

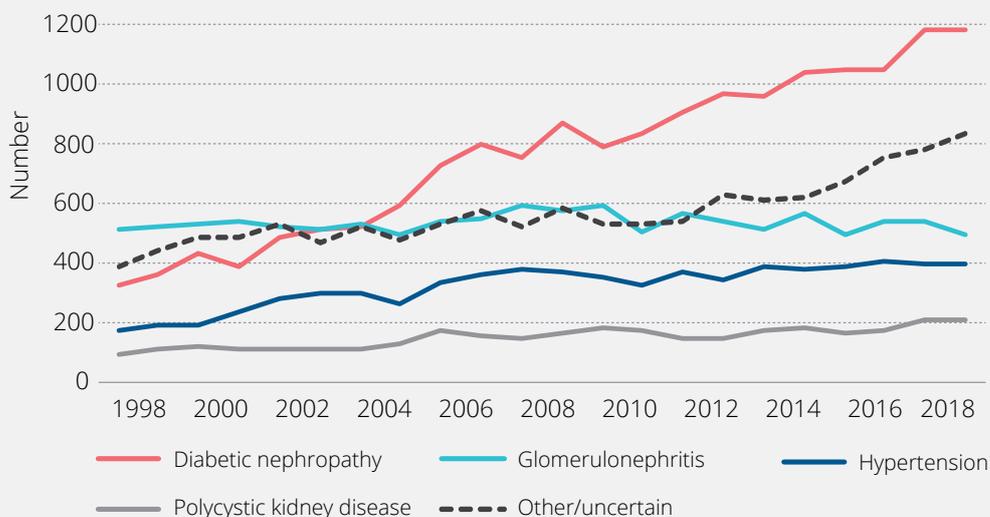


Figure iv: Crude incidence of treated kidney failure (KF) by primary kidney disease for all patients commencing kidney replacement therapy (all modalities) between 1997 and 2017 (Source: ANZDATA 2018 Annual Report).

Comorbid CKD increases the costs associated with diabetes and cardiovascular disease

The presence of comorbid CKD in diabetes and cardiovascular disease increases costs to the health system through:

- ↑ Increased rates of hospitalisation
- ↑ Increased length of hospitalisation
- ↑ Increased complexity of medical management
- ↑ Increased rates of adverse events and complications, and increased risk of onset of KF requiring kidney replacement therapy (KRT).



Based on AIHW analysis of 2012-2013 data from the National Hospital Morbidity database, an additional diagnosis of **CKD increased average length of hospital stay by 4 days for people with a diagnosis of cardiovascular disease, and by 2 days for people with a diagnosis of diabetes** (excluding hospitalisations for dialysis) ^[46].

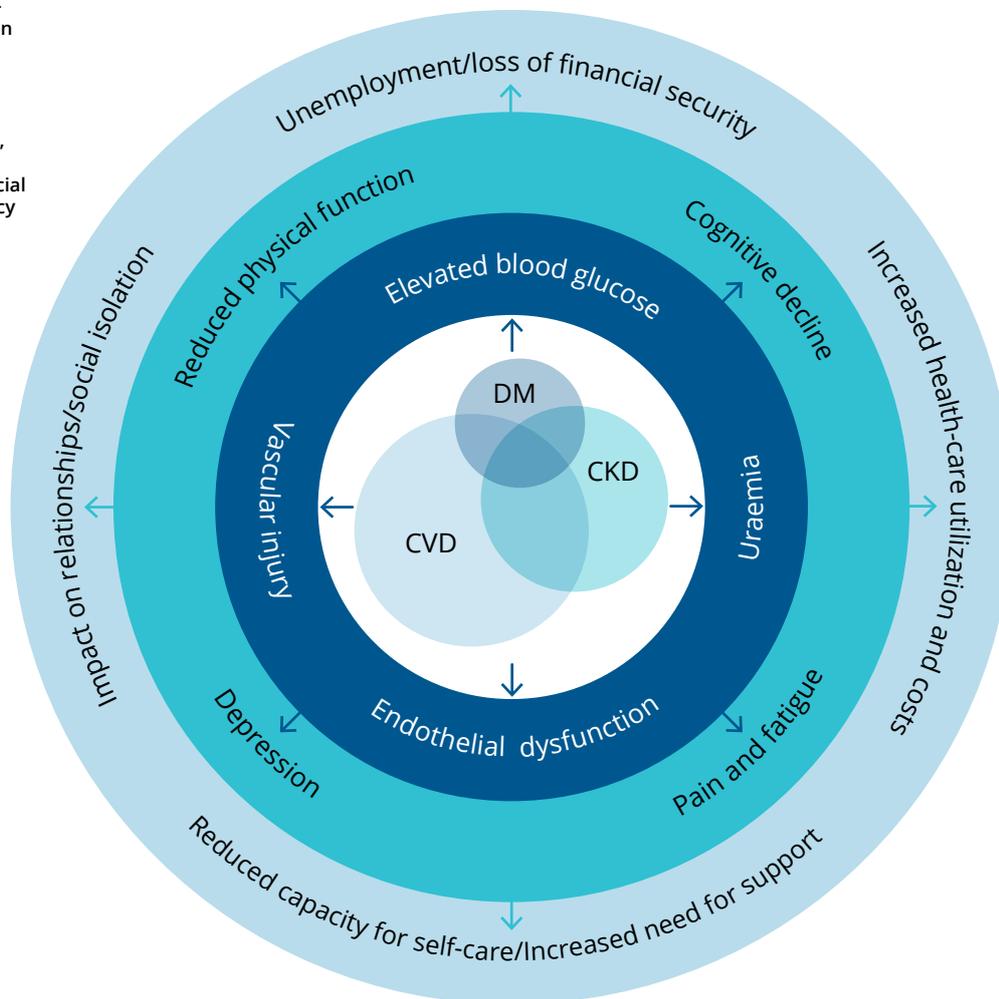
A bottom-up comparative costing analysis of Australians with and without CKD indicated that the presence of Stage 1 or 2 CKD increased direct per person health care costs in people with diabetes by 17% on average, compared to costs of diabetes alone. **The presence of Stage 3-5 CKD (excluding dialysis and transplant recipients) increased direct per person health care costs in people with diabetes by 57%** on average, compared to the cost of diabetes alone ^[47].

Dialysis or kidney transplantation vastly increases per person direct health care costs. **The annual cost to provide dialysis and transplantation to the 25,652 patients receiving KRT at 1 December 2018 exceeds \$1 billion** ^[45, 48]. Much of these costs relate to dialysis. Dialysis currently accounts for 13% of all hospitalisations Australia-wide, and 34% of all hospitalisations of Aboriginal and Torres Strait Islander Australians ^[49, 50]. Since 2009, admissions for dialysis have increased by 3.9% on average each year ^[51]. The cumulative cost of treating all current and new cases of KF with dialysis or kidney transplantation from 2009 to 2020 has been estimated to be between \$11.3 billion and \$12.3 billion ^[52].

The onset of CKD also increases out-of-pocket costs to patients and their families. An Australian study of **patients receiving care for CKD stage 3-5 found that patients faced out of pocket costs of over \$900 per quarter** on average and over half of households reported economic hardship as a result of the out-of-pocket costs of CKD ^[53]. With more advanced CKD, capacity to work may also be impacted, further exacerbating financial hardship. Given that CKD disproportionately affects the most disadvantaged Australians, these out-of-pocket costs to patients and their household result in financial catastrophe in many cases.

Multimorbidity has important implications for healthy brain aging

Figure v: A Ripple Effect - Schematic representation of the relationship between chronic kidney disease (CKD), diabetes, cardiovascular disease (CVD) and mental health, and knock-on effects on social functioning, financial security, care dependency and hospitalisations.



For patients with CKD, diabetes or cardiovascular disease, the presence of hyperglycaemia, accumulation of uraemic toxins, hypertension, hypercholesterolaemia, and chronic inflammation in turn cause pain, fatigue, depression, reduced in quality of life, and structural brain changes that may eventually lead to cognitive impairment. These associations are bi-directional: as underlying disease progresses, the psychosocial and somatic symptom burden grows, resulting in increasingly poor health outcomes.

CKD, diabetes and cardiovascular disease each have a strong association with presence of cognitive impairment ^[54]. Prospective studies of older adults have reported that moderate to severe reduction in kidney function is associated with worse cognitive performance and a higher risk of cognitive decline, and that **a faster rate of kidney function decline is associated with global cognitive decline and incident dementia** ^[55-58]. **Decline in cognitive function intensifies the challenges faced by the patient with respect to self-care, adherence to medical regimen, and maintenance of employment** ^[58, 59]. Low cognitive score has also been linked with an increased risk of death in elderly persons ^[60].

In the context of an aging population with an increasing burden of multimorbidity, prevention and management strategies **need to prioritise long-term cognitive outcomes of Australians with CKD, diabetes and/or cardiovascular disease.**

Patient-centred treatment approaches are needed that consider both physical and mental health

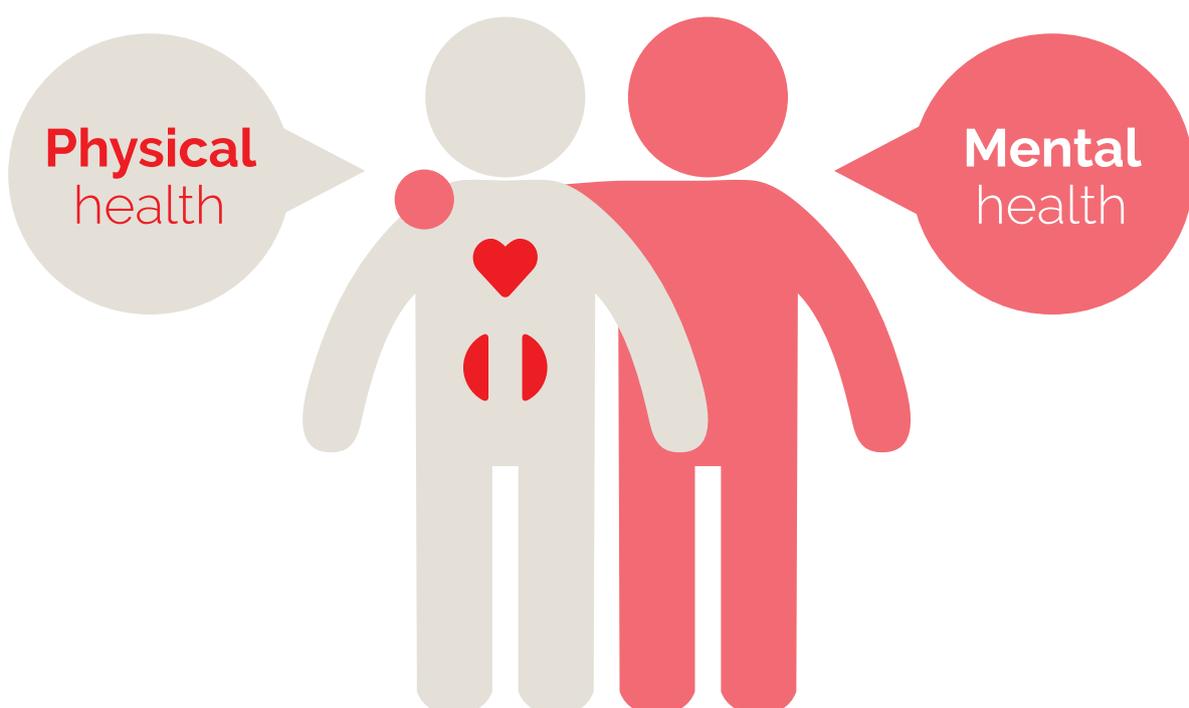
The growing emphasis on patient-centred care has increased appreciation of the importance of mental health to overall wellbeing and clinical outcomes in CKD, diabetes and cardiovascular disease. Much more work is to be done, however, to establish models of care that account for depression and quality of life as critical determinants of cardiometabolic outcomes and offer appropriate psychosocial support alongside medical treatment for persons with CKD, diabetes and cardiovascular disease ^[61, 62].

It is critical that health systems consider the inter-relationships between CKD, diabetes and cardiovascular disease and respond with integrated prevention strategies, clinical care pathways and broader support systems that take into account both:

- I. The physical symptom burden and medical risks associated with multiple comorbidities, AND
- II. The psychosocial impact of disease and the burden on families and carers.

This requires a **wholistic treatment approach that takes into account clinical, psychological and social factors** ^[63]. Such an approach would include:

- I. Treatment of medical risk factors for poor quality of life: anaemia, sleep apnoea, obesity, hypertension, hyperlipidaemia, elevated blood glucose, and albuminuria
- II. Pharmacological treatment of depression
- III. Non-pharmacological treatment of depression (such as cognitive behaviour therapy)
- IV. Provision of support services which address reduced capacity for self-care, social isolation, and financial stressors, and ameliorate the impact of socioeconomic factors (unemployment, low income, and low educational level).



A long-term, coordinated approach to the prevention of CKD, diabetes and cardiovascular disease is needed

Preventing and controlling the shared risk factors for CKD, diabetes and cardiovascular disease has the potential to generate large gains in health and wellbeing for the Australian population by reducing illness, hospitalisations and premature death, and by preventing unnecessary loss of quality of life ^[64-66].

Responding to the current and potential future burden of CKD, diabetes and cardiovascular disease in the Australian population will require a coordinated approach that consolidates the gains made to date with respect to risk factor reduction and addresses the social determinants of health.

All Australians should have equitable access to best practice care, should share equally in risk reduction, and should have equal expectations of their health outcomes regardless of their place of residence, ethnicity or socio-economic status.

Key goals include:

- > Reducing the prevalence of risk factors for the onset of kidney damage, insulin resistance, hypertension, atherosclerosis and dyslipidaemia, including overweight and obesity, poor diet, insufficient physical activity, risky alcohol consumption, and tobacco smoking.
- > Improving access to primary health care and preventive therapies for Aboriginal and Torres Strait Islander Australians and Australians who are socioeconomically disadvantaged or reside in remote areas.
- > Early detection of markers of CKD, diabetes and cardiovascular disease through targeted population screening.
- > Careful management of disease from its earliest stages to prevent complications and adverse events, including access to new therapies.
- > Provision of adequate psychosocial support to enable people to manage their own disease as effectively as possible, to prevent adverse mental health outcomes, and to support healthy cognitive aging.

Objectives of this report

In the context of a multimorbid, aging population, a comprehensive review of the inter-relationships between chronic kidney disease, diabetes and cardiovascular disease in the Australian population and the implications for the health system is needed.

The objectives of this Evidence Review are to:

- I. Synthesise current information on the burden of CKD in association with diabetes and cardiovascular disease in the Australian population.
- II. Describe health outcomes for people with co-existing CKD, diabetes and cardiovascular disease.
- III. Describe the impact of CKD, diabetes and cardiovascular disease on health service utilisation and costs.

While numerous publications over the past decade have reported on the burden of CKD, diabetes and cardiovascular disease in the Australian population, key statistics are distributed over multiple publications, making it difficult to grasp the bigger picture of how CKD interacts with diabetes and cardiovascular disease in terms of disease prevalence, morbidity and mortality. The majority of available information considers CKD, diabetes and cardiovascular disease largely in isolation of one another, when we know these diseases to be inter-related and frequently co-occurring.

What this Evidence Review adds to the existing literature is:

- ✓ A central summary of the current key statistics and information regarding CKD, diabetes and cardiovascular disease in Australia.
 - ✓ A detailed discussion of how comorbid CKD, diabetes, and cardiovascular disease interact and influence each other.
 - ✓ A more holistic view of the health burden associated with comorbid CKD, diabetes, and cardiovascular disease in Australia.
- ✓ Details on the current evidence concerning the impact of CKD, diabetes, cardiovascular disease and their comorbidity on mental health (Chapter 5). Given the increasing health burden related to dementia in Australia ^[67], the implications of comorbid CKD, diabetes and cardiovascular disease for cognitive aging are of critical importance.

1

Background

Key messages:

Chronic kidney disease, even in its early stages, affects every organ system in the body, and over time causes complications that greatly impact health and wellbeing.

Although onset is usually gradual and without symptoms, each advancing stage of chronic kidney disease is associated with increasing risks of cardiovascular mortality, progression to kidney failure, and death.

For persons with existing diabetes and/or cardiovascular disease, developing chronic kidney disease causes a reduction in quality of life, on top of increased risks of complications, hospitalisations and death.

In the context of a multimorbid aging population, a comprehensive review of the inter-relationships between chronic kidney disease, diabetes and cardiovascular disease in the Australian population and the implications for the health system is needed.

1.1 DEFINITION AND DIAGNOSIS OF CHRONIC KIDNEY DISEASE

What is Chronic Kidney Disease?

Chronic kidney disease (CKD) refers to all kidney conditions involving kidney damage and/or irreversible loss of kidney function exceeding that which would occur as a consequence of normal aging. When functioning normally, the kidneys remove water-soluble wastes and foreign substances from the blood and play a vital role in maintaining blood pressure and electrolyte balance. With progressive functional loss, this balance is disturbed. The resulting build-up of waste products causes symptoms including:

- Sleep disturbances
- Gastrointestinal symptoms (decreased appetite, nausea and vomiting)
- Itch and cramps
- Tingling of fingers and toes
- Shortness of breath
- Peripheral oedema (swelling)
- Fatigue and weakness
- Cognitive impairment/difficulty concentrating
- Urinary changes (little or no urine or foamy dark urine)
- Skin colour change.

Clinically, findings include fluid overload, hypertension, hyperlipidaemia, malnutrition, acidosis, bone disease, anaemia and insulin resistance. Collectively, these symptoms and clinical findings are known as uraemia ^[14, 68].

Diagnosis of CKD is made by establishing evidence of either:

- i. A chronic reduction in kidney function, defined as an estimated or measured glomerular filtration rate (GFR) < 60 mL/min/1.73m², persisting for at least 3 months; and/or
- ii. Kidney damage, defined as the presence of albuminuria, haematuria (after excluding urological causes), structural or pathological abnormalities, persisting for at least 3 months, regardless of underlying cause ^[14].

CKD is defined as having five stages of severity, ranging from Stage 1 (mildest) to Stage 5/kidney failure (KF). Each increasing stage of CKD is associated with increasing risks of all-cause mortality, cardiovascular mortality and progression to KF (see Table 1) ^[69].

Chronic kidney disease affects every organ system in the body and damage accumulates over time

Even in its early stages, CKD affects every organ system in the body. Cumulative organ damage over time causes complications that greatly impact overall health and wellbeing. Changes in kidney haemodynamics, increased blood pressure and other risk factors that increase risk of cardiovascular disease are already evident in the early stages of CKD ^[70]. However, onset of CKD and its complications is usually gradual, hence CKD may be without symptoms until advanced stages of disease ^[68]. If CKD is detected early, effective management may slow or even halt the progression to KF, and can also reduce the damage to other organ systems ^[70]. Given that up to 90% of kidney function may be lost before symptoms are present, screening of at-risk individuals is therefore critical to primary and secondary prevention of CKD and its complications ^[71].

In the late stages of CKD, kidney function is severely reduced, requiring symptom control and intensive intervention in preparation for kidney failure (KF). Once KF is reached, death will occur unless kidney replacement therapy (KRT) – dialysis or kidney transplantation – is undertaken. Alternatively, non-KRT medical management of KF is an option that involves ongoing active therapy to minimise the symptoms of kidney failure. Patients who choose a pathway without dialysis or transplantation often live with a large symptom burden and increasing frailty, ultimately requiring end-of-life care.

More information on the definition of CKD is given in Appendix A. Detailed guidance on the diagnosis and management of CKD for General Practitioners is provided in the Australian CKD Management in Primary Care handbook ^[71].

Table 1: Classification of CKD stages according to international guidelines ^[69, 72]

CKD Stage	Description	GFR (mL/min/1.73m ²)	Symptoms
Stage 1	Evidence of kidney damage (e.g. albuminuria) with normal or high kidney function	≥90	No symptoms**
Stage 2	Evidence of kidney damage (e.g. albuminuria) with mildly decreased* kidney function	60-89	Symptoms unlikely
Stage 3a	Mild to moderately decreased kidney function, with or without evidence of kidney damage	45-59	Symptoms unlikely
Stage 3b	Moderately to severely decreased kidney function, with or without evidence of kidney damage	30-44	Symptoms unlikely
Stage 4	Severely decreased kidney function, with or without evidence of kidney damage	15-29	Symptoms more likely
Stage 5	Kidney failure.	<15 or on dialysis	Symptoms highly likely

* Relative to young adult level of GFR.

** Symptoms can appear earlier in some causes of CKD such as polycystic kidney disease or immune conditions

Chronic kidney disease significantly increases risks of cardiovascular events and premature death

Different patients will experience different trajectories of CKD progression. A key outcome of the epidemiological research into CKD over the past two decades has been the recognition that premature death, typically from cardiovascular causes, is a far more likely outcome of CKD than progression to KF. People with an eGFR <60 mL/min/1.73m² are up to ten-times more likely to die prematurely than to require KRT, and risk of death rises exponentially with worsening kidney function ^[73, 74].

Onset of chronic kidney disease causes a reduction in quality of life

Anaemia is common in CKD, with increasing prevalence as kidney function declines. The kidney is the main source of erythropoietin, the hormone which stimulates red blood cell production and maintains haemoglobin homeostasis. Low levels of erythropoietin, uraemia, and malabsorption of dietary iron all contribute to the presence of anaemia in CKD ^[14]. Anaemia causes the heart to work harder to maintain oxygen levels. This can result in the heart becoming enlarged, which can lead to heart failure and increase the risk of death. Anaemia is also associated with reduced quality of life, increased prevalence of depressive symptoms, higher rates of hospital admissions and cognitive impairment in people with CKD ^[15-20].

Other important complications of CKD that impact on quality of life include mineral bone disease, which may cause bone pain and increased bone fragility, and metabolic acidosis, leading to further bone loss and muscle wasting ^[14]. Bone pain, frailty poor sleep quality, hypertension, fluid retention, peripheral neuropathy, itch and side-effects from medication are increasingly prevalent as kidney function declines. This symptom burden is associated with depression, a greater overall burden of illness, and poorer life satisfaction ^[14, 21, 22]. The impact of an individual's disease on family and friends, feeling unwell, low mood, insufficient home care and other life stressors are other key factors that increase the likelihood of low self-reported quality of life in CKD ^[28]. People with CKD are also at increased risk of cognitive impairment (see section 5.1) ^[59].

1.2 THE INTER-RELATIONSHIPS BETWEEN CHRONIC KIDNEY DISEASE, DIABETES AND CARDIOVASCULAR DISEASE

Chronic kidney disease, diabetes and cardiovascular disease are linked by common risk factors and interrelated causal mechanisms

CKD, diabetes and cardiovascular disease are each independently serious diseases, associated with increased morbidity and mortality and affecting millions of Australians. They each require careful management and place a large burden on the Australian health system, on individuals and on families.

CKD, diabetes and cardiovascular disease are inextricably linked. They have interrelated causal mechanisms, share common risk factors, and are frequently co-occurring – especially in older individuals. Behavioural risk factors common to CKD, diabetes and cardiovascular disease include physical inactivity, poor nutrition, smoking and harmful use of alcohol. These behavioural factors contribute to the development of biomedical risk factors including overweight and obesity, high blood pressure, high blood cholesterol and insulin resistance. In the event of the onset of diabetes or cardiovascular disease (including coronary heart disease, hypertensive disease, stroke, peripheral vascular disease, heart failure and cardiomyopathy), the likelihood of also subsequently developing comorbid CKD is significantly increased. The presence of comorbid CKD then greatly increases morbidity – complications, symptom burden, cognitive changes, cardiovascular events, rate of hospitalisations – and risk of death.

An elevated symptom burden and increased risks of morbidity and mortality mean that individuals with comorbid CKD, diabetes and/or cardiovascular disease therefore experience greater disease severity, significantly worse quality of life, and poorer prognosis than individuals with only one condition in isolation. The increased health and psychosocial burden associated with comorbidity is also likely to result in greater health care utilisation, more hospitalisations and longer stays, and increased need for support from family and carers.

The Australian Fact series, published by the Australian Institute of Health and Welfare in 2015, was the first attempt to systematically describe the disease burden associated with comorbid CKD, diabetes and cardiovascular disease in Australia. These reports described an increasing burden of comorbidity with advancing age, especially for Aboriginal and Torres Strait Islander Australians ^[1, 5, 46, 75, 76]. The present report draws on the findings of the Australian Facts series, with figures updated according to the most recent available data wherever possible.

Diabetes and cardiovascular disease are leading risk factors for chronic kidney disease

It is estimated that one in three Australians are at risk of developing CKD on the basis of existing risk factors ^[2]. The main risk factors for CKD in the Australian population are:

- Diabetes
- High blood pressure (hypertension)
- Cardiovascular disease (CVD) - heart attack, heart failure and vascular disease
- Obesity
- Tobacco smoking
- Other lifestyle factors (sedentary lifestyle, alcohol excess, high salt and sugar diets)
- Being of Aboriginal and Torres Strait Islander origin
- Family history of kidney failure
- History of acute kidney injury
- Age (60 years or older).

Diabetes and persistent high blood pressure are well-established causal risk factors for CKD. Untreated hypertension may cause damage to the blood vessels of the kidneys, eventually resulting in reduced blood flow and decreased kidney function^[14]. High blood glucose levels in diabetes can also cause damage to the blood vessels of the kidneys, leading to diabetic kidney disease (nephropathy)^[77, 78].

Diabetes and hypertension are the leading causes of CKD in all high-income countries^[14]. Limitations of existing population datasets available in Australian mean that it is not possible to report incidence or prevalence of CKD by cause for the entire Australian population. However, we do have information from ANZDATA on the distribution of primary kidney disease among persons commencing KRT (Figure 1 and Figure 2).

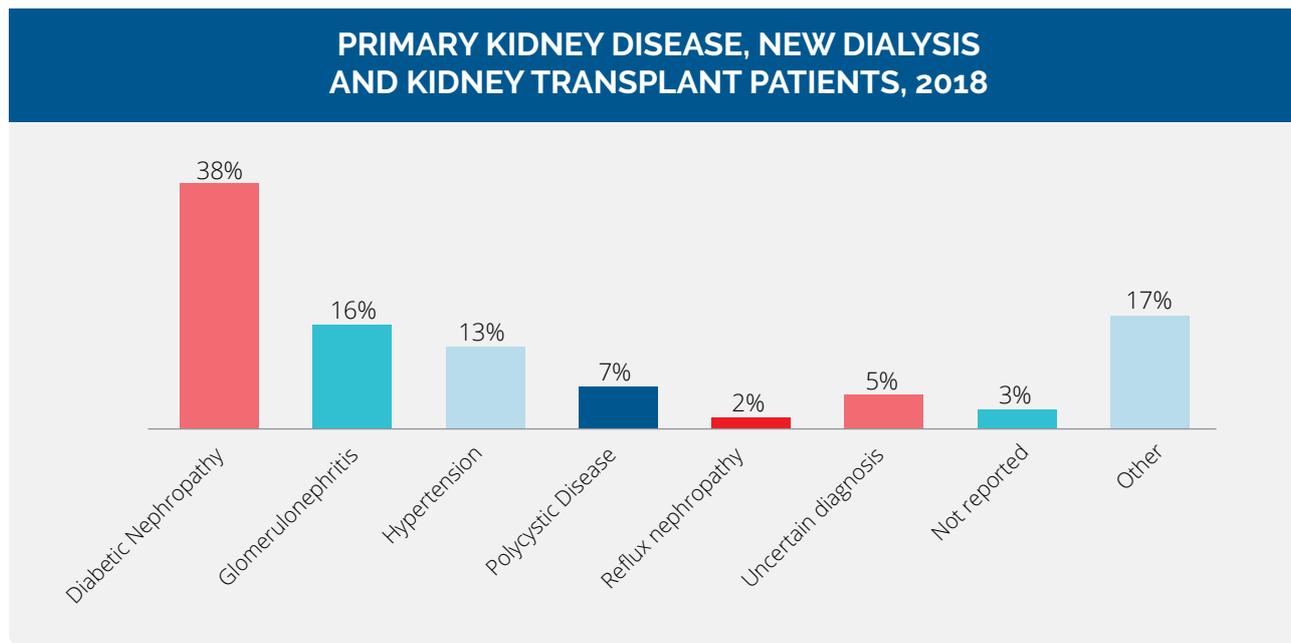


Figure 1: Distribution of primary kidney disease in new dialysis and kidney transplant patients, 2018 (Source: ANZDATA 2018 Annual Report).

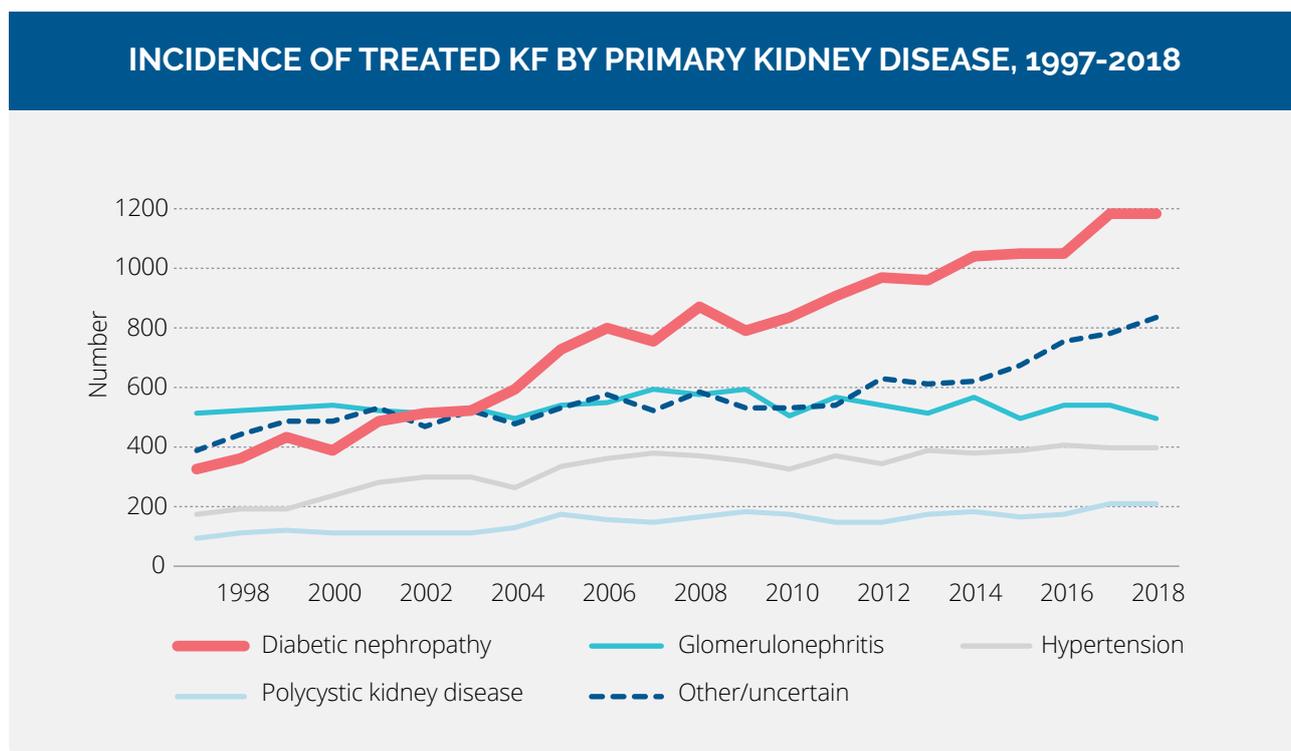


Figure 2: Crude incidence of treated KF by primary kidney disease for all patients commencing KRT (all modalities) between 1997 and 2017 (Source: ANZDATA 2018 Annual Report).

Diabetic nephropathy accounted for 38% of new KRT patients in 2018, followed by glomerulonephritis (16%) and hypertension (13%) [45]. For over a decade, diabetic nephropathy has accounted for a greater proportion of new KRT patients than any other single cause (see Figure 2), which is consistent with international trends. In absolute terms, the number of patients commencing KRT with a primary diagnosis of diabetic nephropathy doubled between 2004 and 2018 (591 versus 1176) [45].

Diabetic kidney disease accounts for more new dialysis and kidney transplant patients than any other single cause in all age groups except those younger than 35 years of age. Incidence of treated KF with a primary diagnosis of diabetic nephropathy is highest in the 65-74-year age group and declines after 75 years. By comparison, the incidence of KF due to hypertension increases progressively with age (Figure 3).

The proportion of treated KF due to diabetes in Australia is lower than the rate observed in the United States, Canada, and New Zealand, but higher than the rates observed in the United Kingdom, Scandinavia and several other Western European countries (Figure 4) [79].

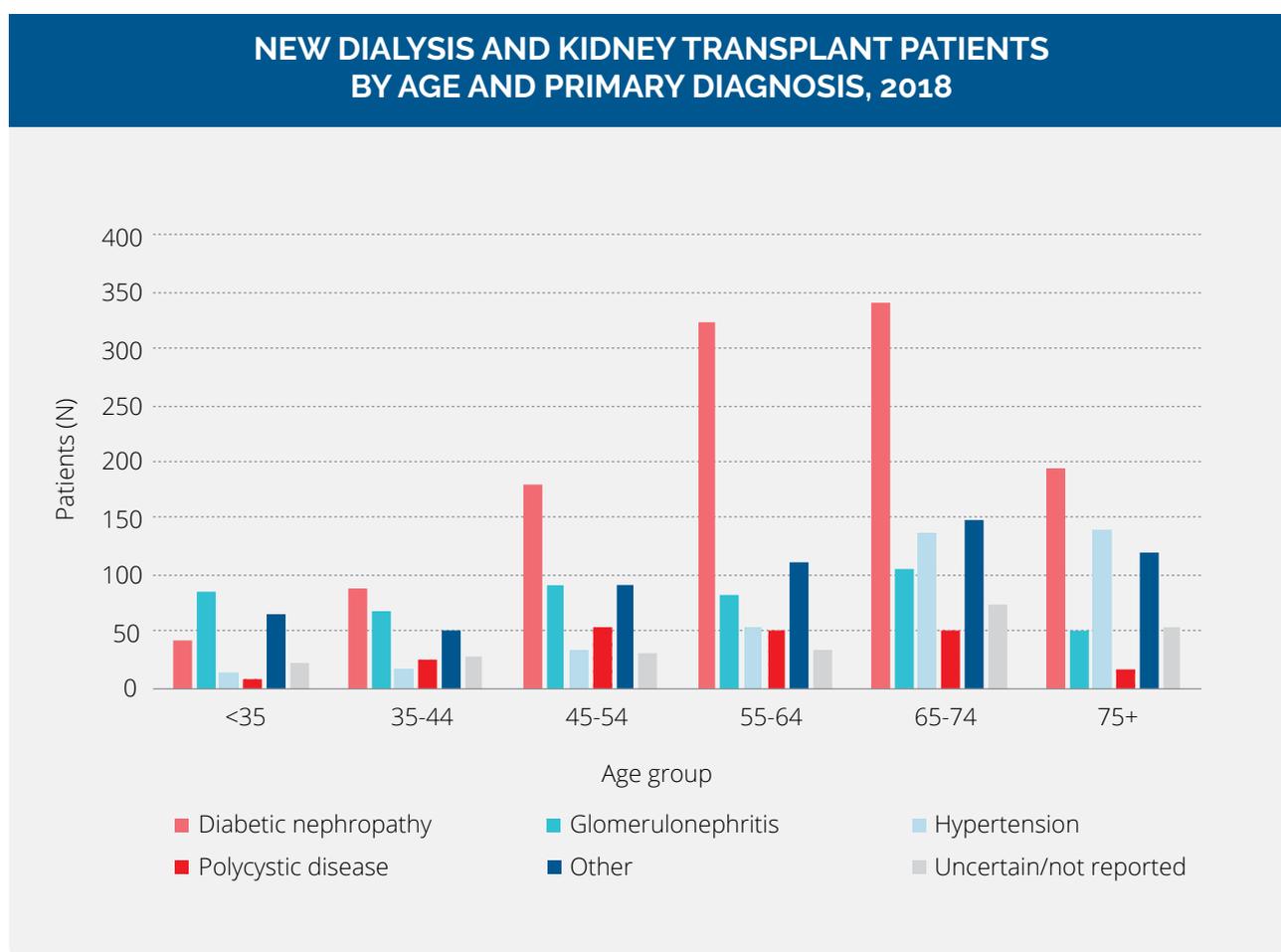


Figure 3: Incidence of KRT in 2018, by age group and primary kidney disease (Source: unpublished ANZDATA data)

PERCENTAGE OF NEW DIALYSIS AND KIDNEY TRANSPLANT PATIENTS WITH DIABETES AS PRIMARY CAUSE OF KF

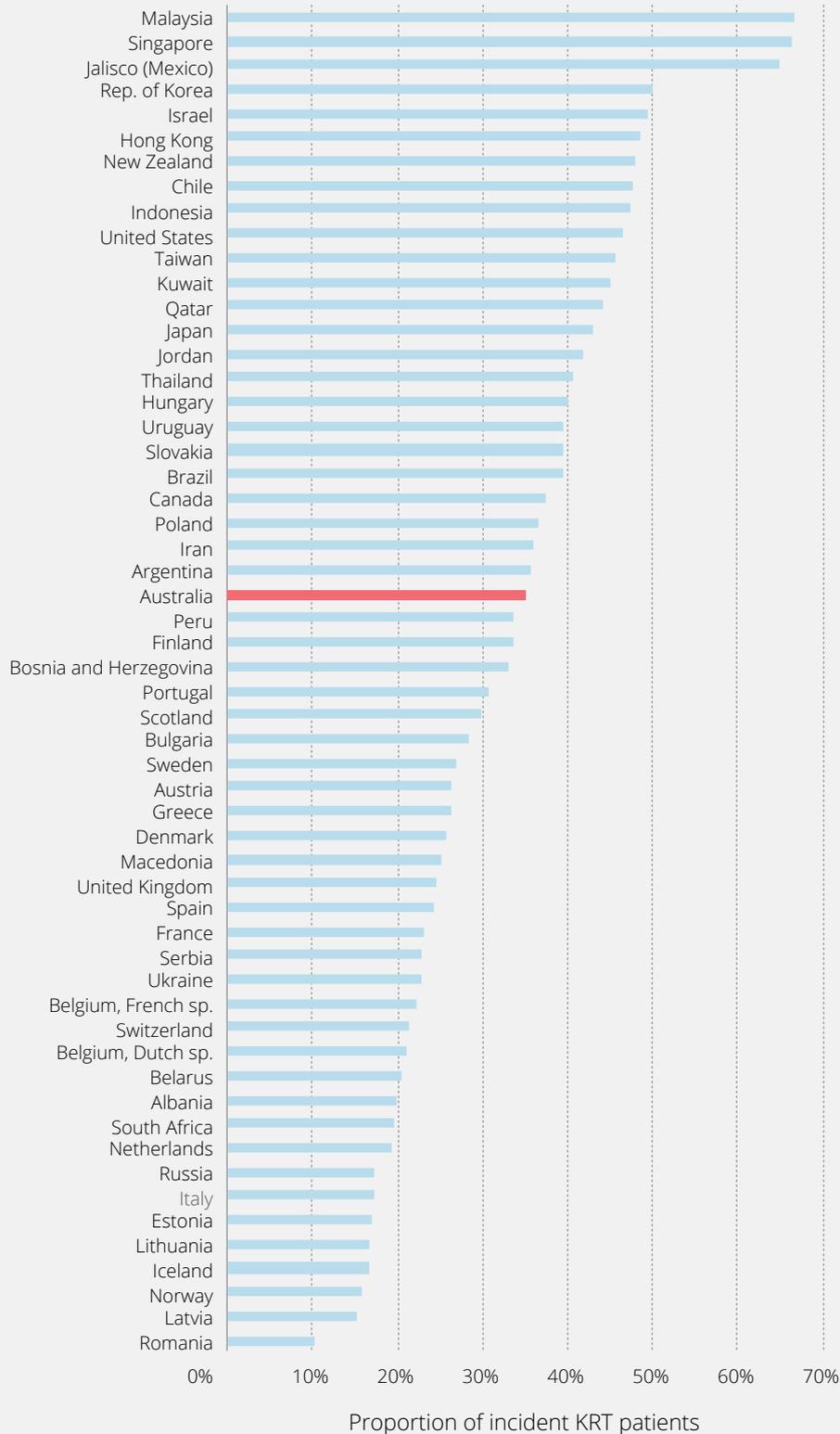


Figure 4: Percentage of new dialysis and kidney transplant patients with diabetes as the primary cause of KF, 2016 (Source: United States Renal Data System 2018 Annual Report. Chapter 11: International comparisons ⁽⁷⁹⁾)

Chronic kidney disease increases morbidity and mortality in persons with diabetes and cardiovascular disease

CKD independently increases the risk of incident hypertension and other cardiovascular diseases, including heart attack, angina, coronary artery disease, stroke and heart failure [6, 7]. In people with existing cardiovascular disease, the presence of CKD increases the risks of death and hospitalisation [8]. Only a relatively small proportion of those with CKD will progress to KF requiring treatment; a far greater proportion will die prematurely, largely due to cardiovascular complications [7]. Cardiovascular mortality is approximately 60% higher in people with CKD compared to those without CKD [9, 10]. Risks of non-fatal heart attack and stroke also steadily increase as kidney function declines and the quantity of albumin in the urine (indicating kidney damage) increases [11-13].

1.3 MULTIMORBIDITY AND AGING: IMPLICATIONS FOR HEALTH SYSTEMS

Population aging and risk factor trends are increasing the number of Australians at risk of comorbid CKD, diabetes and cardiovascular disease

Comorbidity of CKD, diabetes and cardiovascular disease is more common with advancing age. Population aging, therefore, entails not only an increase in the number of Australians living with either CKD, diabetes or cardiovascular disease, but also an increase in the number of Australians living with two or more of these conditions.

In addition, a steady reduction in cardiovascular mortality since the 1980's has meant that an increasing proportion of individuals are surviving their cardiovascular disease to subsequently develop CKD and/or diabetes (discussed further in Section 2.5). The continued rise in the proportion of the population who are overweight and obese and the high prevalence of depressive disorders are also contributing to greater multimorbidity in the Australian population [4].

At the same time, there have been positive developments with regards to the risk profile of the Australian population, including a continued decline in smoking rates and a reduction in risky levels of alcohol consumption [4]. More significantly, the recent identification of effective drugs for prevention of KF and cardiovascular events in diabetic nephropathy has potentially significant implications for the burden of comorbid disease associated with diabetes (see Section 7.1) [80].

The burden of comorbid disease is unequally distributed across the Australian population

CKD, diabetes and cardiovascular disease are most prevalent among the most disadvantaged Australians, those living in remote parts of the country, and Aboriginal and Torres Strait Islander Australians. The burden of comorbid disease is similarly unevenly distributed across the population, disproportionately affecting those with the greatest challenges with respect to health care access. Based on 2011-12 data, Australian adults in the lowest socioeconomic group are more than twice as likely to have 2 or more comorbid diagnoses of CKD, diabetes or cardiovascular disease, compared to adults in the highest socioeconomic group [1]. People living in outer regional and remote areas were twice as likely to have all three of CKD, diabetes and cardiovascular disease compared to people living in major cities in 2011-12 (see Section 2.4) [1].

Rates of death in association with CKD, diabetes and/or cardiovascular disease also increase with greater geographical remoteness and greater socio-economic disadvantage. This reflects a higher burden of risk factors, poor access to health care and social services, inequities in the distribution of the health workforce, and higher rates of socioeconomic disadvantage in remote populations. It is also a reflection of the higher proportion of residents of remote communities that are Aboriginal and Torres Strait Islander in origin and the high prevalence of disease in Aboriginal and Torres Strait Islander communities.

Over one-third of Aboriginal and Torres Strait Islander Australians have one or more of CKD, diabetes or cardiovascular disease and these diseases appear at a younger age, co-occur more frequently, progress faster, and are associated with more complications than in non-Indigenous Australians. By middle age, most Aboriginal and Torres Strait Islander Australians have CKD, diabetes, and/or cardiovascular disease, and usually more than one of these conditions. Chapter 4 describes the burden, causes and outcomes of comorbid disease in Aboriginal and Torres Strait Islander Australians.

Multimorbidity has important implications for cognitive aging

For patients with CKD, diabetes or cardiovascular disease, the presence of hyperglycaemia, accumulation of uraemic toxins, hypertension, hypercholesterolaemia, and chronic inflammation in turn cause pain, fatigue, depression, reduced in quality of life, and structural brain changes that eventually lead to cognitive decline (see Chapter 5).

CKD, diabetes and cardiovascular disease all have a strong association with presence of cognitive impairment^[54]. Decline in cognitive function intensifies the challenges faced by the patient with respect to self-care, adherence to medical regimen, and maintenance of employment^[58, 59]. Low cognitive score has also been linked with an increased risk of death in elderly persons^[60].

Although there have been important developments in the treatment of cardiovascular disease and diabetes in recent years and the prevalence of certain cardiometabolic risk factors is declining, the fact that lifespans are increasing and an increasing proportion of those with diabetes and cardiovascular are surviving into advanced age means that the burden of comorbid CKD, diabetes and cardiovascular disease will remain high, and this burden will disproportionately affect those of older age. In this context, prevention and management strategies need to prioritise long-term cognitive outcomes of Australians with CKD, diabetes and/or cardiovascular disease.

A long-term, coordinated approach to the prevention of CKD, diabetes and cardiovascular disease is needed

Responding to the current and potential future burden of CKD, diabetes and cardiovascular disease in the Australian population will require a coordinated approach that consolidates the gains made to date with respect to risk factor reduction and addresses the social determinants of health. All Australians should have equitable access to best practice care, should share equally in risk reduction, and should have equal expectations of their health outcomes regardless of their place of residence, ethnicity or socio-economic status.

Preventing and controlling the shared risk factors for CKD, diabetes and cardiovascular disease has the potential to generate large gains in health and wellbeing for the Australian population by reducing illness, hospitalisations and premature death, and by preventing unnecessary loss of quality of life^[64-66]. It is critical that health systems consider the inter-relationships between CKD, diabetes and cardiovascular disease and respond with integrated prevention strategies, clinical care pathways and broader support systems that consider:

- I. The physical symptom burden and medical risks associated with multiple comorbidities, AND
- II. The psychosocial impact of disease and the burden on families and carers.

2

Chronic kidney disease, diabetes and cardiovascular disease in the Australian population: disease burden and trends

2.1 CHRONIC KIDNEY DISEASE

Key messages:

CKD affects approximately 10% of the Australian adult population over 18 years, 30% of the population over 65 years, and 42% of the population over 75 years.

The total number of Australians being treated with dialysis or transplantation for kidney failure increased by 44% between 2008 and 2018.

Based on Australia's current population age structure, this is equivalent to an estimated 2.4 million Australian adults affected by CKD in 2018, of whom an estimated 50% were aged over 65 years, and 30% over 75 years.

The growth of the population receiving dialysis or transplantation is attributable to population growth and aging, the growing burden of diabetes, improved survival among persons with cardiovascular disease, and improved dialysis outcomes.

It is estimated that fewer than 1 in 10 Australians with CKD are aware of their condition. ^[2]

CKD was a contributing factor in 11% of deaths in Australia in 2017.

Chronic kidney disease affects 1 in 10 Australian adults

CKD (all stages) currently affects approximately 10% of the Australian adult population and was listed as an underlying or associated cause in 11% of deaths in Australia in 2017 ^[2, 49]. The two main national surveys to have estimated the prevalence of CKD in Australia are the 1999-2000 AusDiab survey, and the 2011-2013 National Health Measures Survey ^[81, 82]. Direct comparison of the results of these two surveys has shown that CKD prevalence rates between 1999-2000 and 2011-2012 remained stable within each age category ^[83]. This is consistent with observations from the United Kingdom, United States and Norway, showing stable CKD prevalence over a similar period from the late 1990s to late 2000s ^[84-86].

However, the underlying Australian population has grown aged substantially since 1999, which has meant that the absolute number of people affected by CKD has increased. Compared to approximately 1 million adults affected by CKD in 1999-2000, this number would have increased to approximately 2.38 million by 2018 (95% confidence interval 1.78 million to 2.95 million) based on population growth and aging alone – assuming that age-specific CKD prevalence rates have continued to remain stable^[49, 87].

CKD affects an estimated 5% of Australians aged 18-44, 6% of those aged 45-54, and 8% of those aged 55-64^[49]. For Australians 65-74 years, CKD prevalence increases to 21% (25.5% in men and 12.2% in women); for those 75 years and older, CKD prevalence is as high as 42% (43.3% in men and 41.7% in women)^[49]. Based on Australia's population age structure in 2018, approximately 50% of Australian adults with CKD are aged over 65 years^[49, 87]. Overall, CKD is slightly more prevalent in men than in women (10.3% versus 9.5%) and (see Figure 5).

Although awareness of CKD has improved in recent years, particularly with automated eGFR reporting by pathology labs and proactive awareness campaigns^[88], it is estimated that fewer than 1 in 10 Australians with CKD are aware of their condition^[2].

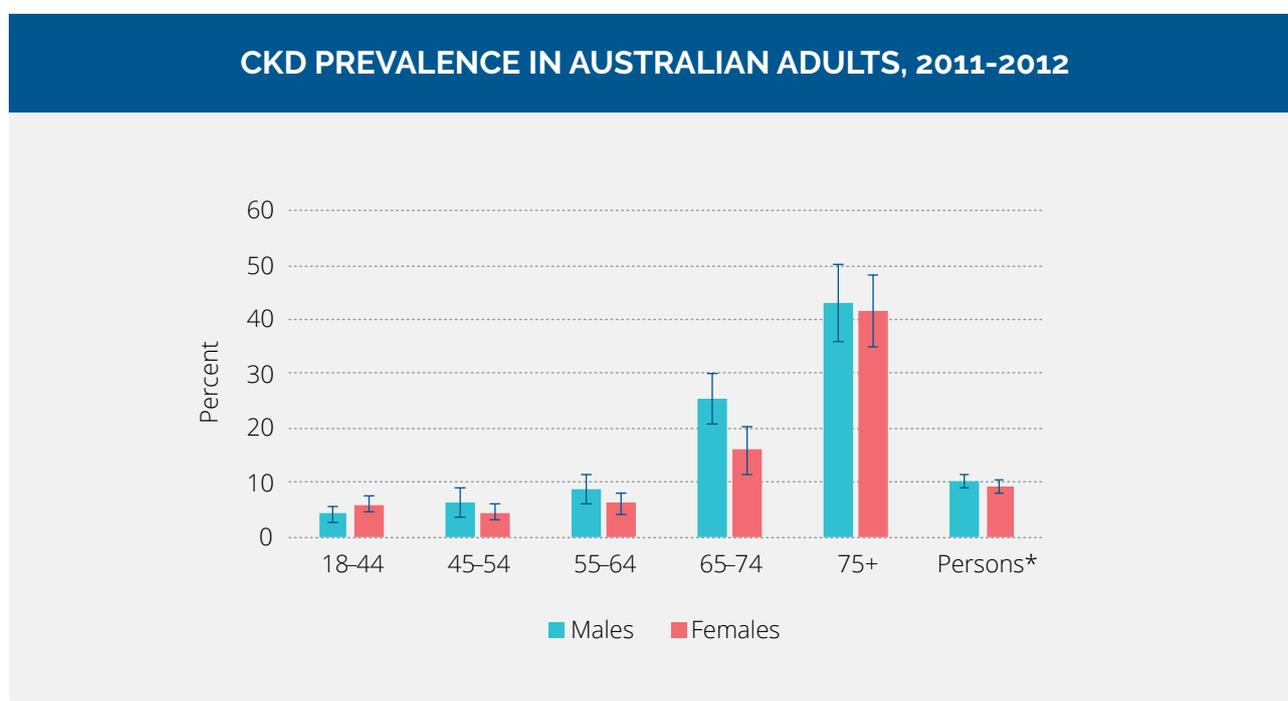


Figure 5: Prevalence of CKD in Australians aged 18 years and over, by age and sex, 2011-12 (Source: AIHW analysis of ABS Microdata: Australian Health Survey). *Data age-standardised to the 2001 Australian population.

The incidence of kidney failure in Australia (treated or untreated) is estimated to be approximately 21 per 100,000 population, with over 60% of cases occurring in persons 70 years and older^[89]. The vast majority (~90%) of people under 60 years of age with KF will receive treatment with dialysis or transplantation, whereas the majority of people over 75 years will die with kidney failure, without having received KRT^[89].

The overall incidence of new dialysis and kidney transplant patients in Australia increased steady among both males and females until 2006, after which the age-standardised incidence remained relatively steady (see Figure 6). A total of 3093 persons commenced dialysis or transplantation in 2018 – 1979 males and 1114 females^[45]. This number is slightly lower than previous projections made by AIHW of the incidence of new dialysis and kidney transplant cases in Australia to the year 2020, which predicted the total number of new patients to reach 3690 by 2018, and 4062 by 2020^[90].

INCIDENCE OF NEW DIALYSIS AND KIDNEY TRANSPLANT PATIENTS, 1989-2016

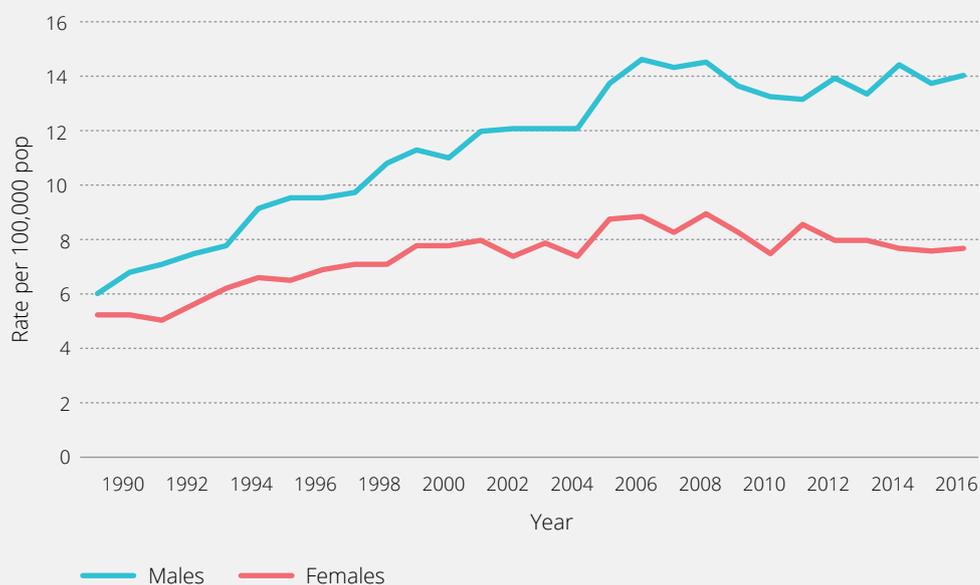


Figure 6: Incidence of new dialysis and kidney transplant patients in Australia; incidence is age-standardised to the 2001 Australian population. (source: AIHW analysis of ANZDATA).

The difference between actual and projected incidence of treated KF in the Australian population is largely due to shifting incidence trends in the population 75 years and older over the past two decades. Reductions in cardiovascular mortality and an increasing willingness to treat older patients with haemodialysis produced a steady increase in new KF patients aged 75 years and older between 1998 and 2008. Since 2008, however, the absolute number of patients aged 75+ commencing KRT has remained relatively steady. In contrast, the number of patients aged 65-74 commencing KRT has continued to grow, increasing by nearly 40% from 2008 to 2018 (621 new patients in 2008 versus 859 in 2018). The number of new KRT patients aged 25-64 increased by 20% over the same interval ^[45].

Figure 7 shows the crude number of new KRT patients in Australia over the period from 1998 to 2018, by age group. Figure 9 shows the population-adjusted rate of newly treated KF per 100,000 population within each age group.

In 1999, 1749 new KRT patients commenced treatment, compared to 3093 new patients in 2018 – an increase of 77% over this interval ^[45]. This increase is smaller than the estimated growth of the underlying CKD population over the same period (>140%). This disparity most likely relates to the aging of the CKD population. Whereas the estimated number of adults aged 45-54 and 65-74 with CKD increased by 45% and 52% respectively from 1999 to 2018, the estimated number with CKD aged 75 years and older increased by 127%. Previous analyses have established that, whereas 90% of KF cases in people less than 60 years are treated with KRT, treatment rates decline steeply from age 65 onwards ^[89]. After age 75, the majority of KF is not treated with KRT ⁵.

CRUDE INCIDENCE, KF



Figure 7: Crude incidence of new dialysis and kidney transplant patients in Australia, by age group, 1998-2018 (Source: ANZDATA Annual Report 2019)

CRUDE PREVALENCE, KF



Figure 8: Crude prevalence of dialysis and kidney transplant patients in Australia, by age group, 1998-2018 (Source: ANZDATA Annual Report 2019)

POPULATION-ADJUSTED INCIDENCE, KF



Figure 9: Population-adjusted incidence of new dialysis and kidney transplant patients in Australia, by age group, 1998-2018 (Source: ANZDATA Annual Report 2019 and Australian Demographic Statistics - ABS 3101.0)

POPULATION-ADJUSTED PREVALENCE, KF



Figure 10: Population-adjusted prevalence of dialysis and kidney transplant patients by age group, 1998-2018 (Source: ANZDATA Annual Report 2019 and Australian Demographic Statistics - ABS 3101.0)

A total of 25,652 Australians were receiving dialysis or living with a kidney transplant in 2018, a 44% increase compared to 2008. Of this number, 40% were aged over 65 years. Figure 10 shows trends in KRT prevalence by age group from 1998 to 2018, over which period population-adjusted prevalence increased nearly three-fold in the 75 and over age group, and by 80% in the 65-74 year age group, reflecting a combination of incidence trends and improved dialysis survival ^[45].

Fifty-two percent of the prevalent KRT population were receiving some form of dialysis (n=13,399) and 48% were alive with a functioning transplant in 2018 (n=12,253) ^[45]. Fifty-two percent of dialysis patients in 2018 were aged over 65 years (n=6956); in contrast, 72% of those alive with a functioning transplant were aged less than 65 years (see Figure 11).

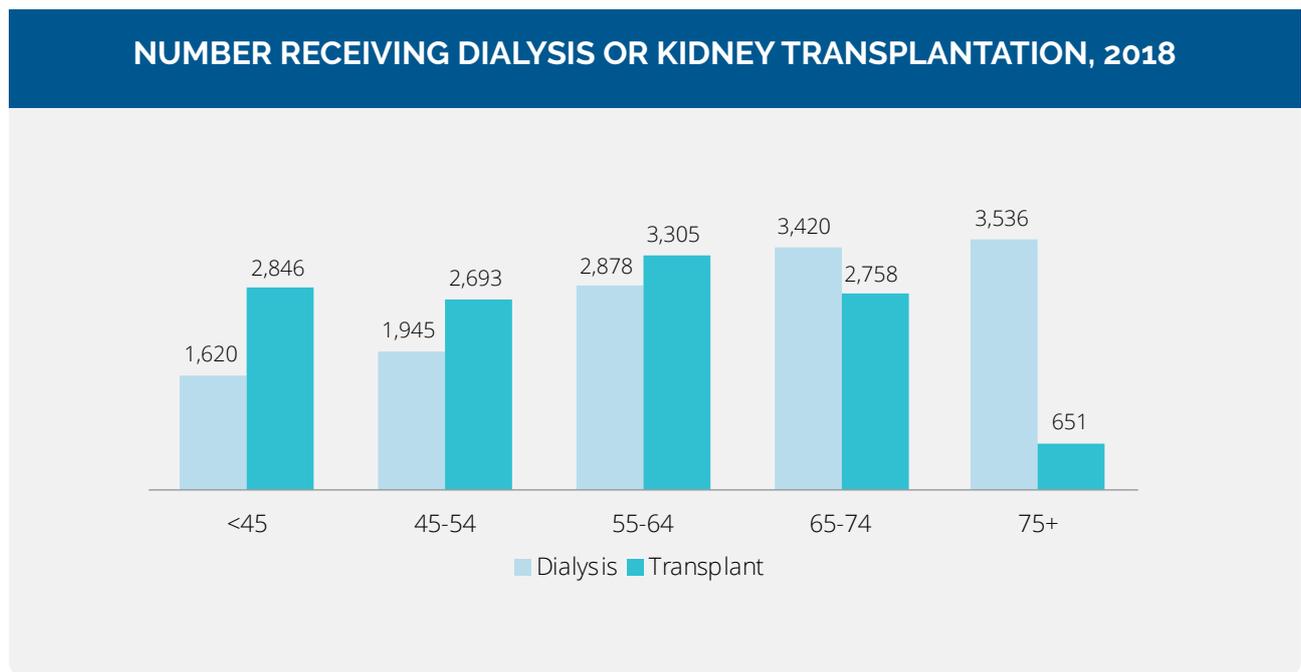


Figure 11: Number of patients receiving dialysis or with a functioning kidney transplant in Australia in 2018, by age group and modality (Source: ANZDATA Annual Report 2019).

Survival while receiving dialysis has improved over the past decade but is still much lower than for the general population. The mortality rate in the Australian dialysis population in 2017 was 14.4 deaths per 100 patient-years; by comparison, the rate of mortality among transplant recipients was 1.9 deaths per 100 patient-years ^[91]. The median survival while receiving dialysis during the period 2008 to 2017 for a patient aged between 45 and 64 at commencement of dialysis was 6.4 years. For patients aged 65-74 years at dialysis commencement, median survival was 4.7 years. For patients aged 75-84 and 85+ years respectively, median survival was 3.5 and 2.2 years ^[91]. Patients with comorbid cardiovascular disease and/or diabetes have lower median survival while receiving dialysis at any age ^[91].

2.2 DIABETES

Key messages:

The prevalence of self-reported diabetes among Australian adults was 5.7% in 2017-2018 (~1.3 million individuals); 86% of self-reported diabetes was type 2 diabetes.

Diabetes prevalence is higher in men than women at all ages.

Based on snapshot surveys of the Australian population, diabetes prevalence has increased nearly 4-fold since 1989-90, primarily driven by increasing prevalence of type 2 diabetes in the population over 65 years.

A substantial proportion of population have diabetes but are unaware that they have the condition; self-reported rates therefore underestimate the true prevalence of diabetes in the Australian population.

Diabetes was a contributing factor in 11% of deaths in Australia in 2017.

Diabetes mellitus (referred to in this report as diabetes) is a chronic disease marked by high levels of glucose in the blood. It is caused either by the inability to produce insulin, by the body being unable to use insulin effectively, or both. There are three main types of diabetes: type 1 diabetes, type 2 diabetes, and gestational diabetes. In this report, diabetes refers to any of the three main types of diabetes. For a more detailed explanation of how diabetes has been defined in this report, see Appendix A.

The prevalence of self-reported diabetes among Australian adults was 5.7% in 2017-2018 ^[92]. Prevalent diabetes in this context refers to persons who have been told by their doctor or nurse that they have diabetes, irrespective of diabetes type. Diabetes prevalence was higher in men than women at all ages, with an overall age-standardised rate of 6.5% for men and 4.8% for women ^[92].

PREVALENCE OF SELF-REPORTED DIABETES, 2017-2018

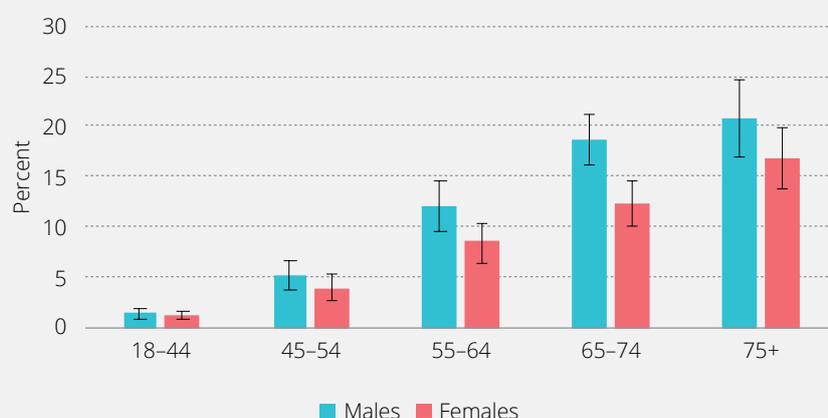


Figure 12: Prevalence of self-reported diabetes, among adults 18 years and older, by age and sex, 2017-2018. (Source : AIHW analysis of the ABS National Health Survey ^[92])

There were 1.3 million Australians with diabetes registered with the National Diabetes Services Scheme (NDSS) as at 30 September 2019 ^[93]. The NDSS was established in 1987 by the Australian government to provide testing strips, syringes and needles at subsidized prices to people with diabetes in Australia. Approximately 80-90% of all people in Australia with diagnosed diabetes are listed on this register ^[94]. Of the 1.3 million people with diabetes currently registered, 87% (1.15 million) had type 2 diabetes, 9% (121,076) had type 1 diabetes, 3% (41,176) had gestational diabetes and <1% had other/unknown diabetes type. Sixty-five percent (860,646) were aged 60 years or older ^[93].

Evidence from the NDSS and from the National Health Survey (ABS) indicate that the prevalence of diagnosed diabetes has been increasing in the Australian population since the start of data collection ^[1, 95]. According to AIHW analysis of National Health Survey data, self-reported diabetes prevalence in Australian adults increased from 1.5% in 1989-90, to 4.1% in 2007-2008, to 5.7% in 2017-2018 (rates standardised to the 2001 Australian population) ^[1, 92].

Growth in diabetes prevalence is being driven by increasing rates of type 2 diabetes, whereas the incidence of type 1 diabetes has remained steady for the past two decades ^[92]. Much of the growth in diabetes prevalence has also occurred in the population over 65. From 2001 to 2017-2018, the rate of self-reported diabetes increased by 23% (from 12.5% to 15.5%) in adults 65-74 years, and by 67% (from 11.2% to 18.7%) in adults 75 years and over ^[4]. Unfortunately, accurate data on prevalence trends based on measured rates (as opposed to self-reported rates) of diabetes are not available for the Australian population.

In addition to known diagnoses of diabetes, survey data collected in 1999-2000 and 2011-2012 suggest that there is also a substantial proportion of population with biomedical signs of diabetes who are unaware of/do not report that they have the condition ^[1]. The baseline AusDiab Study, conducted from 1999-2000 reported a prevalence of known diabetes in the population over 25 years of 3.7% ^[96]. In addition, screening for impaired fasting glucose and impaired glucose tolerance identified a further 3.7% of the population with previously unknown diabetes. The fact that the AusDiab survey screened all participants using an oral glucose tolerance test – the ‘gold standard’ for diagnosing diabetes – make these data regarding undiagnosed diabetes prevalence particularly reliable.

Results of the 2011-2012 National Health Measures Survey indicated that, for every 4 adults with diagnosed diabetes, there was 1 with undiagnosed diabetes ^[1]. These results were based on participant screening using a fasting plasma glucose test and a measure of glycated haemoglobin (HbA1c) - an oral glucose tolerance test was not administered as part of the National Health Measures Survey, hence this survey would not have detected as much unknown diabetes in the population as the previous AusDiab survey. As there have been no further population-representative biomedical surveys of the Australian population conducted since 2011-2012, more recent data on the prevalence of undiagnosed diabetes in the Australian population are unavailable. Even with improved diabetes awareness since 1999, it is likely that the 6% prevalence figure based on self-reported diabetes status is an underestimate of true diabetes prevalence.

Similar to CKD, diabetes was listed as an underlying or associated cause in 11% of deaths in Australia in 2017 ^[92]. Hospitalisations for diabetes have increased, predominantly for type 2 diabetes. This is attributed to increasing prevalence combined with unfavourable risk factor trends, such as increases in overweight and obesity, physical inactivity and dietary factors. Rates of death in association with diabetes, however, have remained steady for the past three decades ^[92].

2.3 CARDIOVASCULAR DISEASE

Key messages:

The prevalence of self-reported heart, stroke and vascular disease (excluding hypertension) among Australians adults in 2017-2018 was 5.6%. The prevalence of self-reported hypertension was 13%.

There have been significant declines in cardiovascular morbidity and mortality since the 1980s. Cardiovascular mortality rates halved between 1981 and 2000 and halved again between 2001 and 2017.

As the risk of death from cardiovascular events declines, the size of the population at risk of developing comorbid CKD increases.

The term cardiovascular disease refers to multiple conditions affecting the heart and blood vessels. In this report, a broad definition of cardiovascular disease is used that includes hypertensive diseases, heart disease, cerebrovascular disease, vascular disease and other diseases of the circulatory system. For a detailed definition, see Appendix A.

The most common types of cardiovascular disease in Australia are coronary heart disease, stroke and heart failure ^[1]. The principal underlying cause of cardiovascular disease is atherosclerosis – a process whereby deposits of fat, cholesterol and other substances build up on the inner lining of arteries to form plaque, which causes the artery walls to lose elasticity. This process is gradual and often begins early in life, progressing with age. Atherosclerosis is most serious when it leads to reduced or blocked blood supply to the heart (causing angina or heart attack) or to the brain (causing stroke). Major risk factors for atherosclerosis are overweight and obesity, tobacco smoking, high blood pressure, high blood cholesterol, insufficient physical activity, poor nutrition and diabetes.

Based on AIHW analysis of data from the 2017-2018 ABS National Health Survey, the prevalence of self-reported cardiovascular disease, excluding hypertensive diseases, among Australian adults in 2017-2018 was 5.6% (1.2 million people) ^[3]. In addition, approximately 1 in 8 Australian adults self-reported having hypertension (13% or 2.6 million people) ^[4].

The prevalence of heart, stroke and vascular disease increases steadily from age 45 onwards (see Figure 13). Self-reported prevalence is similar between men and women until age 65, at which point the rate reported by men increases to more than double that reported for women ^[3]. The proportion of Australians with self-reported hypertension increases steadily from age 35 onwards, and prevalence is similar for men and women. By age 75, over 40% of Australian's self-report having hypertension, although – being self-reported data – this is likely to be an underestimate of true prevalence ^[4]. The 1999-2000 baseline AusDiab survey found that 55% of Australian adults over 65 years had hypertension, and that a large proportion of this hypertension was unrecognised and untreated ^[97].

CARDIOVASCULAR DISEASE PREVALENCE, 2017-2018

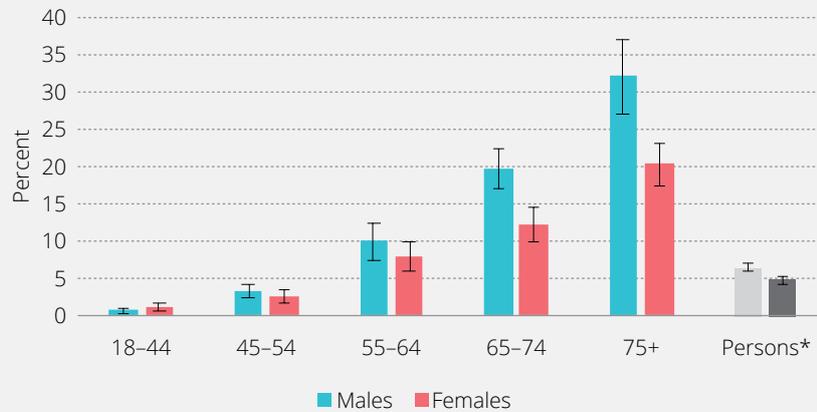


Figure 13: Prevalence of self-reported heart, stroke and vascular disease (excluding hypertension) among Australian adults 18 years and over, 2017-2018. (Source: AIHW analysis of ABS 2017-2018 National Health Survey data ^[3]) *Data age-standardised to the 2001 Australian population

Substantial progress has been made in recent decades in improving cardiovascular health, with significant declines in cardiovascular morbidity and mortality attributed to improved diagnosis and treatment, as well as improvements in risk factors such as reduced rates of smoking and hypertension ^[98-101]. The rate of acute coronary events declined by 40% between 2007 and 2016 for both men and women ^[3], largely attributable to improvements in medical and surgical treatment and increasing use of antithrombotic, antihypertensive and blood pressure lowering drugs ^[1]. The rate of stroke events fell by 24% between 2001 and 2013, and has remained stable since ^[3]. Cardiovascular mortality rates halved between 1981 and 2000, and then halved again between 2001 and 2017 ^[3].

CARDIOVASCULAR DISEASE DEATHS, BY SEX, 1981-2017

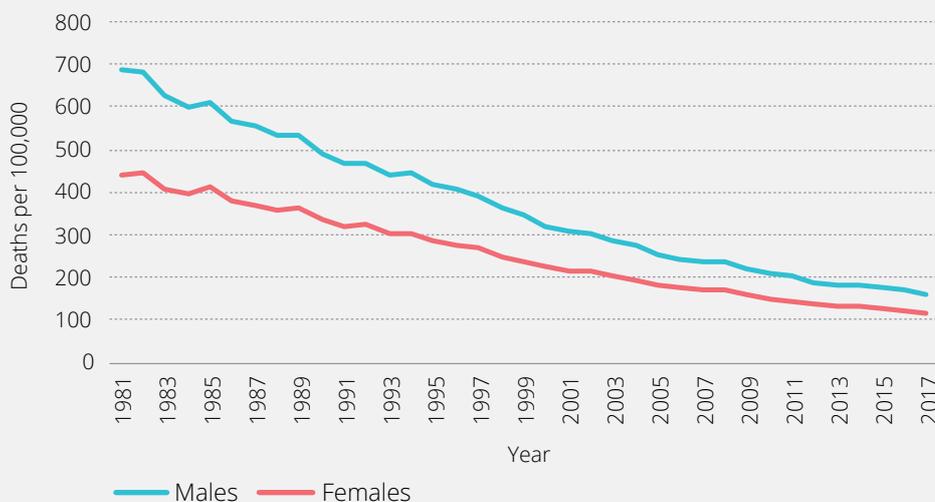


Figure 14: Trends in cardiovascular disease deaths, by sex, 1981-2017. Rates are age-standardised to the 2001 Australian population (Source: AIHW analysis of the National Mortality Database ^[3])

The steady fall in the cardiovascular death rate, while profoundly positive, has been one of the key factors driving the growth in KF prevalence in the Australian population. Those with cardiovascular disease are more likely to survive to older age, which means that they have more time to develop complications including CKD and KF. Thus, as the risk of death from cardiovascular events declines for the Australian population, the size of the population at risk of developing CKD and KF increases. For younger people with cardiovascular disease, this means an increased lifetime risk of progressing to KF. For older people with cardiovascular disease, the onset of CKD – even if this does not progress to KF in their lifetime – means an increase in symptom burden, increased hospitalisations, reduced quality of life, and increased risk of cognitive decline (see section 5.1).

Better management of cardiovascular risk in the KF population has also led to improved survival while receiving dialysis, resulting in further expansion of the prevalent dialysis population.

2.4 GEOGRAPHIC AND SOCIOECONOMIC DISPARITIES IN DISEASE BURDEN AND OUTCOMES

Key messages:

The most disadvantaged Australians experience a disproportionate burden of CKD, diabetes and cardiovascular disease and a higher rate of comorbidity of these conditions.

Disadvantaged Australians also experience higher rates of death in association with CKD, diabetes and/or cardiovascular disease.

Higher rates of comorbidity and higher rates of death in association with CKD, diabetes and cardiovascular disease are observed in remote and very remote Australia, reflecting the higher proportion of Aboriginal and Torres Strait Islander Australians living in these areas and the high disease prevalence experienced in these communities.

The burden of disease associated with CKD, diabetes and cardiovascular disease disproportionately affects the most disadvantaged Australians

The most disadvantaged Australians have the highest burden of CKD. For men in the lowest socioeconomic group, rates of CKD are approximately double those of the highest socio-economic group (prevalence of 14.2% versus 7.9%); for women, rates of CKD are approximately 60% higher in the lowest versus highest socioeconomic group (prevalence of 13.1% versus 8.9%)^[49].

Self-reported diabetes prevalence is approximately twice as high in the lowest socio-economic group in Australia compared to the highest socio-economic group (prevalence of 8.4% versus 3.9%)^[92]. For women this disparity is even greater, with a three-fold difference in diabetes prevalence comparing the lowest versus highest socioeconomic groups (7.7% versus 2.5%)^[92].

Self-reported prevalence of heart, stroke and vascular disease was also higher in the lowest socio-economic group in Australia (6.4%) versus the highest socioeconomic group (4.1%)

People in the lowest socioeconomic group in Australia also have higher rates of comorbid CKD, diabetes and cardiovascular disease. Based on 2011-12 data, 11.2% of Australian adults in the lowest socioeconomic group had 2 or more comorbid diagnoses of CKD, diabetes or cardiovascular disease, compared to 4.1% of adults in the highest socioeconomic group ^[1].

Socio-economic disadvantage is also associated with significantly worse outcomes of CKD, diabetes, and cardiovascular disease. The rate of death in 2017 with diabetes as an underlying or associated cause was 80 per 100,000 in the lowest socioeconomic group, compared to 33 per 100,000 in the highest socioeconomic group ^[92]. The rate of death with CKD as an underlying or associated cause was 70% higher in the most disadvantaged compared to the most advantaged Australians (72 versus 42 deaths per 100,000 population) ^[49]. Among females, the rate of CKD deaths was 85% higher; among males it was 58% higher (see Figure 15). The death rate from cardiovascular disease as the underlying cause in 2015-2017 was 46% higher in the most disadvantaged Australians compared to the most advantaged (164 versus 112 deaths per 100,000 population) ^[3].

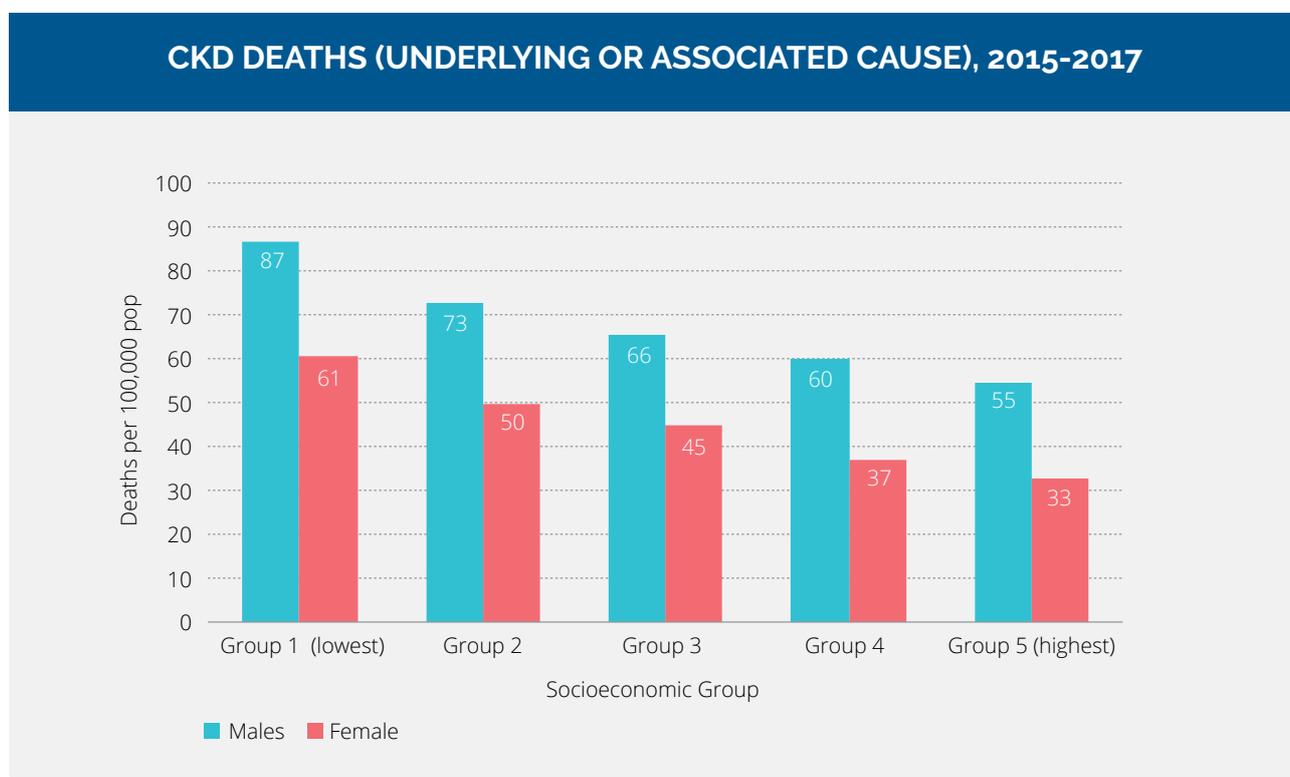


Figure 15: CKD death rates (underlying or associated cause), by socioeconomic status and sex, 2015-2017 (Source: AIHW analysis of the National Mortality Database ^[3])

The burden of CKD, diabetes and cardiovascular disease increases with greater geographical remoteness

Rates of comorbidity and death in association with CKD, diabetes and/or cardiovascular disease increase with greater geographical remoteness. People living in outer regional and remote areas were twice as likely to have all three of CKD, diabetes and cardiovascular disease compared to people living in major cities in 2011-12 ^[1]. Diabetes death and hospitalisation rates in remote and very remote areas are double the rates observed in major cities (101 deaths per 100,000 population compared to 51 per 100,000 in major cities in 2017) ^[92]. Similarly, the rate of death with CKD as an underlying or associated cause was twice as high in remote and very remote areas in 2017 compared to major cities (101 versus 54 deaths per 100,000 population) ^[49]. The cardiovascular death rate (underlying cause) in remote and very remote areas was 37% higher than in major cities in 2017 (185 versus 135 deaths per 100,000 population) ^[3].

Elevated mortality in association with CKD, diabetes and cardiovascular disease in remote areas of Australia partly reflect the higher proportion of Aboriginal and Torres Strait Islander Australians living in these areas and the high prevalence of disease in these communities. Other factors include poor accessibility of health care and social services and higher rates of socioeconomic disadvantage in remote populations ^[102]. It has previously been observed that geographical areas with higher cardiovascular death rates generally have lower socioeconomic scores ^[103].

Health workforce challenges in rural and remote Australia also contribute to poorer outcomes of CKD, diabetes and cardiovascular disease for Australians living in these regions. Shortages of general practitioners, nurses, nurse practitioners and other primary health care practitioners reduce the capacity for primary prevention, early detection and risk factor management ^[104]. Shortages of specialist clinicians increase the barriers to timely and effective treatment of disease.

2.5 RISK FACTOR TRENDS

Key messages:

The proportion of Australians who are current smokers has declined across all age groups, those who smoke are smoking fewer cigarettes per week, and there has been a large decline in uptake of smoking among young people.

Based on self-reported data, 16-18% of Australian adults regularly consume alcohol above the recommended level. However, the rate of risky alcohol consumption has declined since 2004-5, driven by declining consumption among men. There has also been a decline in alcohol consumption among young people.

Despite overall improvements in smoking rates and alcohol consumption, people living in remote areas are still more likely to be daily smokers and drink above recommended levels. Socioeconomically disadvantaged Australians also are still more likely to smoke.

Few Australians meet guidelines for physical activity, particularly young adults. Living in an area of socioeconomic disadvantage is strongly associated with insufficient or no exercise.

The rate of obesity among Australian adults has increased over the past decade, from 19% in 1995 to 31% in 2017-18. More than two-thirds of Australian adults are now overweight or obese – 75% of men and 60% of women.

95% of Australians do not meet guidelines for fruit and vegetable consumption.

Rates of overweight and obesity among young adults have also significantly increased: 46% of 18-24-year-olds are now overweight or obese.

Fewer Australians are smoking, and more young people have never smoked

Tobacco smoking is directly linked with a wide range of chronic health conditions and increases the risk of cardiovascular disease, diabetes, and CKD. Smoking damages the blood vessels, increases the risk of plaques and clots, and reduces blood oxygen levels, thereby increasing the risk of heart disease, stroke and other cardiovascular diseases. Smoking has also been linked with onset of type 2 diabetes^[105, 106] and CKD^[107]. Analysis of the relationship between smoking and kidney damage in the baseline AusDiab population found smoking was associated with presence of proteinuria, independent of hypertension or abnormal glucose metabolism^[107]. Risk of kidney function decline increases with greater lifetime exposure to smoking^[107].

While tobacco smoking remains one of the largest preventable causes of death and disease in Australia, the proportion of Australians who are current smokers has declined substantially across all age groups over the past two decades, and those who smoke are smoking fewer cigarettes per week^[108, 109]. According to information collected by the 2017-2018 National Health Survey, 13.8% of Australian adults self-reported being daily smokers, while a further 1.4% reported smoking less than daily^[4]. The 2016 National Drug Household Survey reported a slightly lower rate of daily smoking (12.2%) but a higher rate of less-than-daily smoking (2.7%)^[109]. By comparison, the self-reported rate of daily smoking in 1989-90 was 25.6%^[76]. Current daily smoking rates in Australia are among the lowest for Organisation for Economic Cooperation and Development (OECD) countries, but are still above the rates reported for Norway (12%), Canada (12%), the United States (10.5%), Sweden (10.4%), and Iceland (8.6%)^[110].

From 1989 to 2018, the daily smoking rate in Australia fell by 40% for men and 53% for women (see Figure 16). The decline in the smoking rate is largely attributable to the suite of tobacco control measures implemented over the past 3 decades, including stronger smoke-free laws, price increases, plain packaging, graphic health warning labels, media campaigns and support for smokers to quit^[111]. Primarily, this decline has been driven by people never taking up smoking, more so than smokers quitting^[109]. The ex-smoking rate has fluctuated over the past 3 decades, whereas the proportion of people who have never smoked has significantly increased: 55.7% of adults in 2017-2018 reported they had never smoked^[4]. In particular, there has been a large decline in the uptake of smoking among younger adults: in 2017-2018, more than two thirds of men aged 18-24 years (69.6%) and four in five women (81.5%) report they have never smoked^[4].

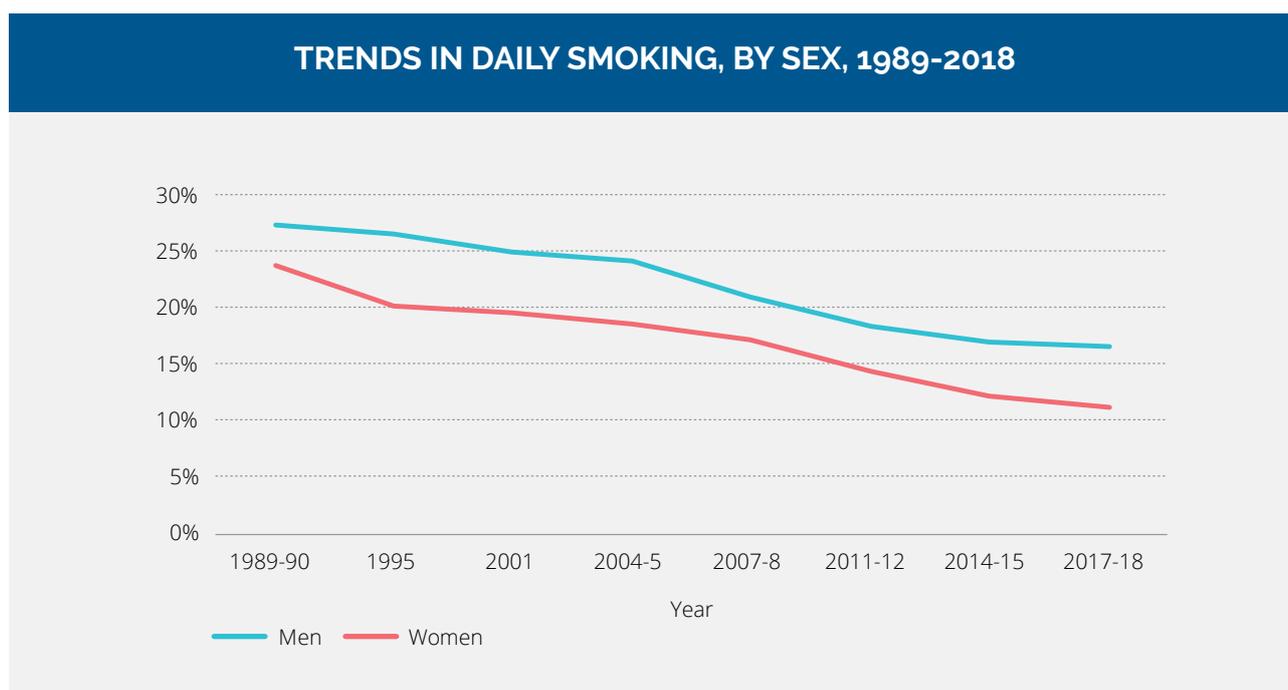


Figure 16: Proportion of the population 18 years and older who are current daily smokers, 1989-90 to 2017-2018 (Source: AIHW analysis of ABS data and ABS National Health Survey 2017-2018^[4, 76]).

Despite overall improvements in smoking rates in Australia, wide socioeconomic and geographic disparities persist. Rates of smoking in areas of greatest disadvantage are three-times higher compared to the least disadvantaged areas (21.7% versus 6.8% in 2017-2018) [4]. Data from the National Drug Household Survey show rates of daily smoking are also higher in remote and very remote areas compared to major cities (20.7% versus 10.6%), among unemployed versus employed people (22.8% versus 12.5%), and among Aboriginal and Torres Strait Islander Australians (27.4%) [109]. These disparities in smoking rates contribute to subsequent disparities in the prevalence of cardiovascular disease, diabetes and CKD by socioeconomic status observed for the Australian population [1].

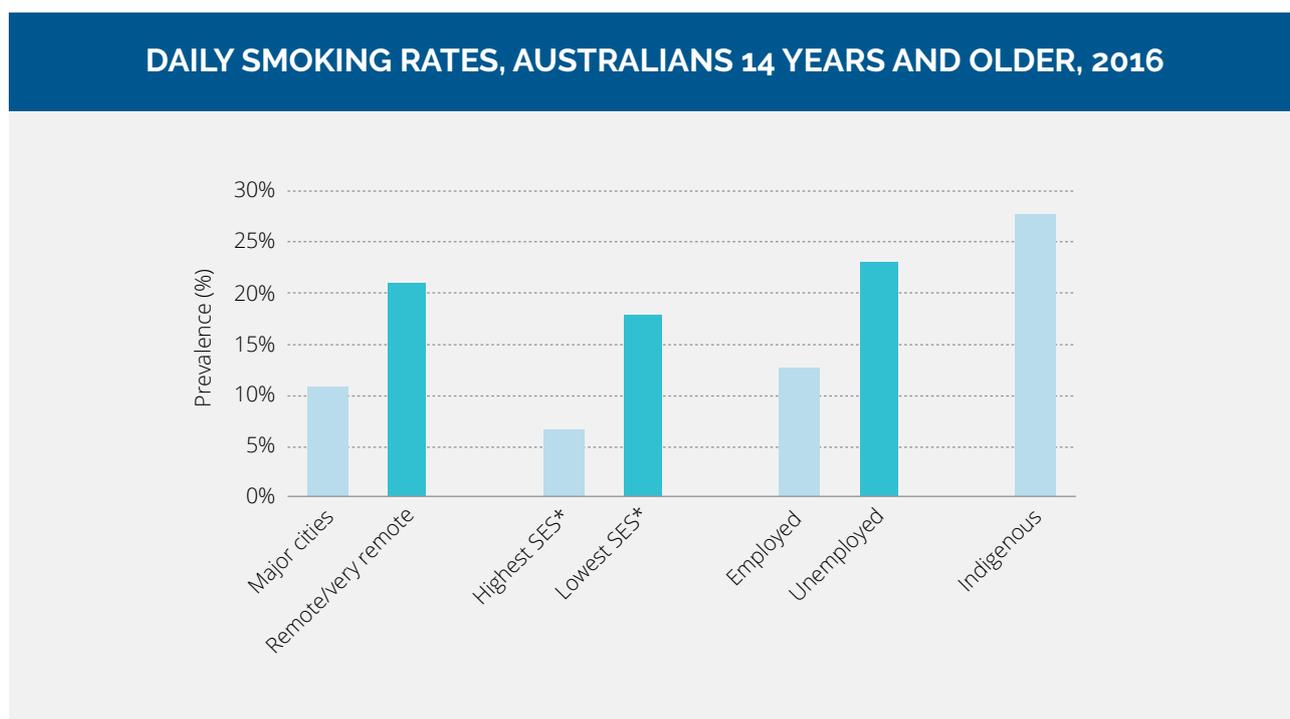


Figure 17: Prevalence of daily smoking among Australians 14 years and older in 2016, by selected socio-economic characteristics. *SES: socioeconomic status by area of residence (source: AIHW National Drug Strategy Household Survey 2016: Detailed findings [109])

Alcohol consumption has declined among men

Regular alcohol consumption at high levels can contribute to the development of chronic diseases including liver disease, some cancers, oral health problems and cardiovascular disease [112, 113]. In 2016, of all deaths attributed to alcohol consumption worldwide, 28.7% were due to injury, 21.3% to digestive diseases, 19% to cardiovascular diseases, 12.9% to infectious diseases, and 12.6% due to cancer [112]. Alcohol consumption can also play a part in excess energy intake, contributing to excess body weight and associated disease risks.

Evidence on the association between alcohol consumption and CKD is mixed, with some studies reporting a link between heavy alcohol consumption and onset of CKD, and others reporting that alcohol consumption at any level is not detrimental to kidney function [114, 115]. Analysis of the impact of alcohol consumption on incidence of CKD in Australian adults found that more than two standard drinks per day on average was associated with increased risk of developing albuminuria, but lower risk of reduced kidney function [115]. Drinking patterns may be relevant, with a study from Japan showing that frequent low levels of alcohol consumption were not associated with kidney damage, whereas high levels of alcohol consumption on days when drinking – even if less frequent – was associated with increased risk of developing proteinuria [116].

The 2009 National Health and Medical Research Council (NHMRC) guidelines for reducing health risks associated with alcohol consumption state that, for health men and women, drinking no more than 2 standard drinks on any day reduces the lifetime risk of harm from alcohol-related disease or injury ^[117]. On any single occasion of drinking, drinking no more than four standard drinks is recommended to reduce the risk of alcohol-related injury.

Based on self-reported data from the 2017-2018 National Health survey, 16.1% of Australian adults consumed more than two standard drinks per day on average ^[4]. The 2016 National Drug Strategy Household Survey found a slightly higher proportion (18%) of Australians consumed more than two standard drinks per day on average ^[109]. After adjusting for changes in the age structure of the population over time, both surveys showed an overall decline in the rate of lifetime risky alcohol consumption since 2004-5 (see Figure 18). This decline in excess alcohol consumption has been largely driven by men: while, men are still more than twice as likely to exceed the lifetime guideline for alcohol consumption than women, the proportion of men consuming more than 2 standard drinks per day on average has fallen by 26% since 2004-2005 ^[4].

Rates of alcohol consumption among young people have also been declining. The proportion of young people aged 12-17 abstaining from drinking increased from 54% in 2004 to 82% in 2016, while the age at which people first tried alcohol has been increasing ^[109]. Since 2010, the proportion of 18-24-year-olds drinking at risky levels (more than 2 standards drinks per day) has declined (from 31% in 2010 to 18.5% in 2019). In addition, the proportion of young people drinking quantities of alcohol on a single occasion that exceed single occasion risk guidelines (more than 4 standard drinks) has also declined ^[109].

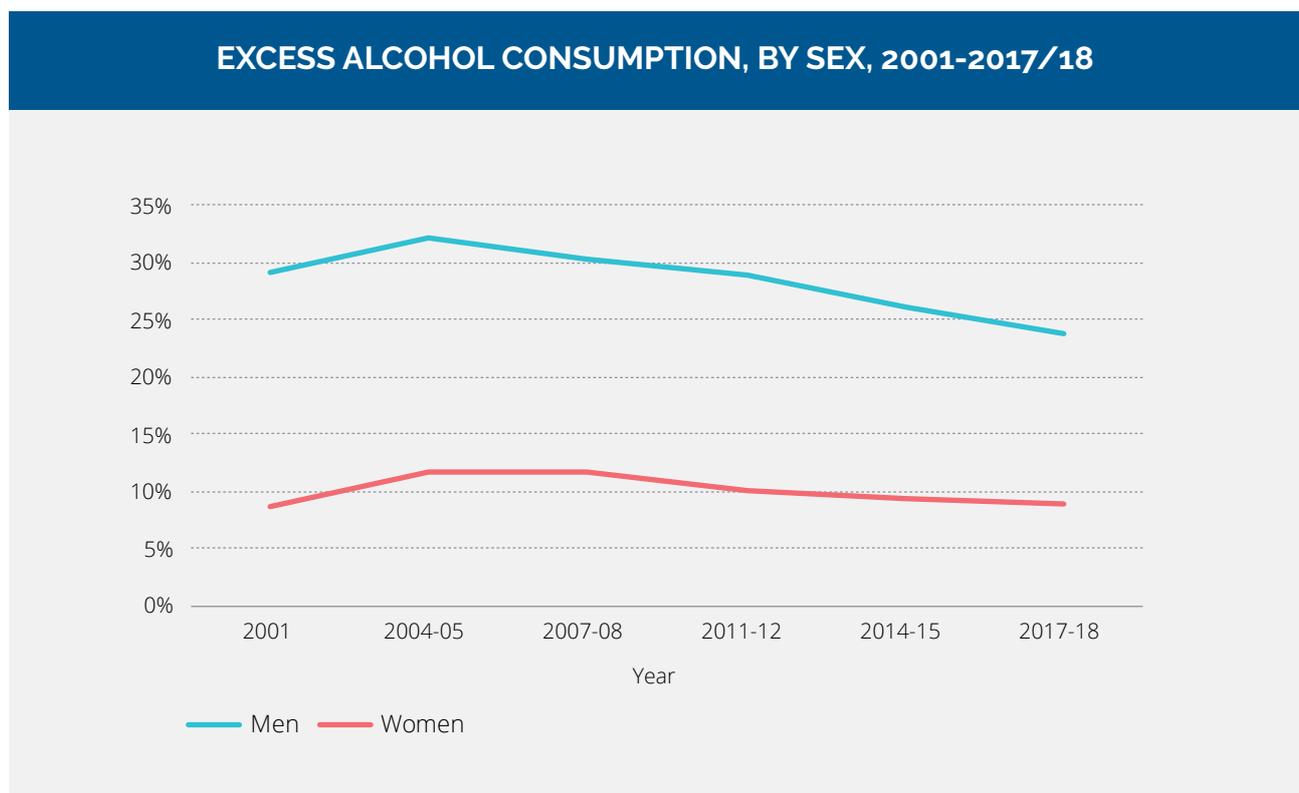


Figure 18: Excess alcohol consumption* among Australians 18 years and older, by survey year (Source: AIHW analysis of ABS data and ABS National Health Survey 2017-2018 ^[4, 76]).

*Excess alcohol consumption defined as more than 2 standard drinks per day.

Despite reductions in alcohol consumption in males and young people, significant geographical disparities persist in rates of excess alcohol consumption ^[108, 109]. Based on 2017-2018 National Health Survey data, Australians living in remote and very remote areas were 1.6 times as likely to exceed the lifetime risk guideline for alcohol consumption compared to Australians living in major cities (23.5% versus 14.6%). People living in remote and very remote areas were also more likely than people in major cities to drink alcohol in quantities that put them at risk of alcohol related harm from a single occasion of drinking (37% versus 24% in 2016) ^[109]. The opposite relationship, however, is observed between alcohol consumption and socioeconomic status for the Australian adult population. Australian adults living in the most advantaged areas are approximately 1.3 times as likely to exceed alcohol consumption guidelines compared to those living in the most disadvantaged areas (18% versus 14%) ^[4].

Few Australians meet the guidelines for physical activity

Being physically active improves mental and musculoskeletal health and reduces other risk factors such as overweight and obesity, high blood pressure and high blood cholesterol. Regardless of a person's weight, insufficient physical activity increases the risk of cardiovascular disease, type 2 diabetes and osteoporosis ^[118-120], and has been linked with higher prevalence of CKD ^[121, 122]. An analysis of the association between physical activity and CKD in Australian adults found that adults who were inactive (0 minutes of exercise per week) were significantly more likely to have markers of kidney damage compared to adults who met physical activity guidelines ^[121].

Australia's Physical Activity and Sedentary Behaviour Guidelines (2014) recommend at least 60 minutes of moderate to vigorous physical activity per day for young persons aged 15-17 years, plus muscle strengthening activities at least 3 days per week. For adults 18-64 years, 150-300 minutes of moderate intensity physical activity or 75-150 minutes of vigorous physical activity, or a combination, are recommended per week. Muscle strengthening activities are also recommended for 18-64-year-olds at least twice per week. For adults aged 65 years and over, at least 30 minutes of physical activity on most, preferably all, days is recommended ^[123].

The ABS National Health Survey asks respondents to report the intensity, duration and number of sessions spent on physical activity in the week preceding the survey, including exercise for fitness, recreation or sport, walking for transport, and – for the first time in 2017-18 – workplace physical activity ^[4]. Survey results for 2017-18 showed 10.3% of Australians aged 15-17 participated in 60 minutes of exercise per day and 15.3% did muscle strengthening exercise on 3 or more days in the past week. Only 1.9% of 15-17 years, however, met the guidelines for both physical activity and muscle strengthening activities (Figure 19^[4]).

Including workplace activity, 65.5% of Australians aged 18-64 engaged in sufficient physical activity in the week preceding the 2017-18 National Health Survey. However, more than two-thirds (69.6%) of Australians 18-64 years did not conduct any strength or toning activities. Overall, only 17% of 18-64-year-olds met the guidelines for both physical activity and muscle strengthening activities (including workplace activities) ^[4]. In addition, 43.7% of 18-64-year-olds described their working day as mostly sitting ^[4].

Just over a quarter (26.1%) of Australians aged 65+ engaged in 30 minutes or more of exercise on 5 or more days in the week preceding the 2017-18 National Health Survey, in line with guidelines ^[4].

Data limitations and changing recommendations mean that it is not possible to accurately describe trends in physical activity for the Australian population over time. What data are available suggest there has been very little change since 1989-90 in the overall proportion of Australian adults who are either inactive or insufficiently active ^[76].

PROPORTION OF AUSTRALIANS MEETING PHYSICAL ACTIVITY GUIDELINES

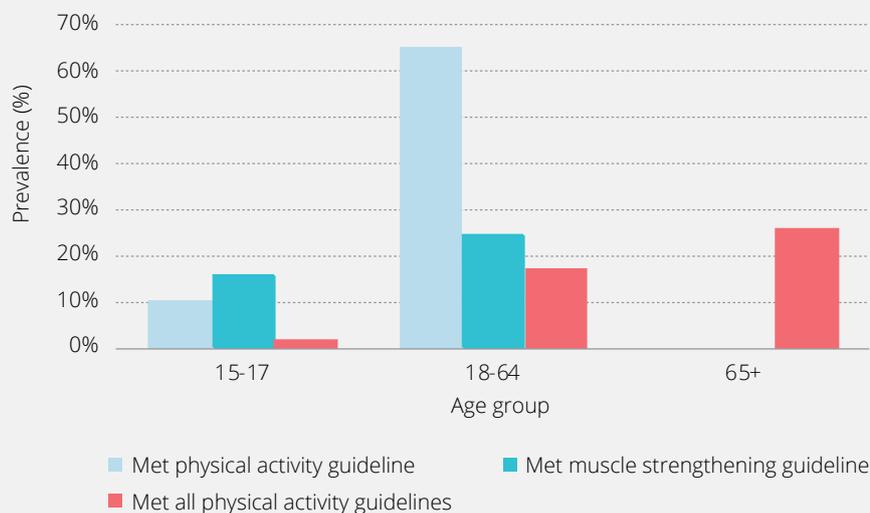


Figure 19: Proportion of Australians meeting physical activity guidelines in 2017-2018 according to self-reported exercise history. For 18-64-year age group, physical activity includes workplace activity. For the 65+ age group, there are not separate guidelines for physical activity and muscle strengthening exercise. (Source: 2017-2018 ABS National Health Survey ^[4])

In 2017-2018, Australian adults living in areas of most disadvantage were more likely to engage in no exercise than Australians living in the most advantaged areas (28.5% versus 10.4%) and were less likely to meet physical activity guidelines compared to counterparts living in the most advantaged areas (10.2% versus 21.5%). Australian adults living in outer regional and remote Australia were also less likely to meet guidelines for physical activity compared to Australians living in major cities (12.2% versus 16.2%) ^[4].

PROPORTION REPORTING NO EXERCISE, BY AREA OF RESIDENCE

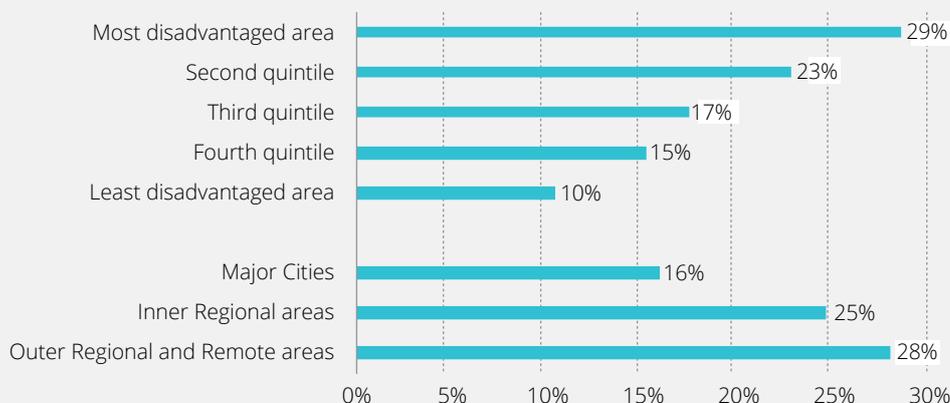


Figure 20: Proportion of Australian adults aged 18 years and older reporting no exercise in the week preceding the 2017-2018 National Health Survey, by index of relative socio-economic disadvantage and remoteness classification (Source: 2017-18 ABS National Health Survey ^[4]).

Very few Australians have adequate fruit and vegetable intake

Australian Dietary Guidelines, developed by the National Health and Medical Research Council in 2013, recommend eating a variety of food to provide our bodies with the energy, protein, essential fats, vitamins and minerals to live and function properly. Poor nutrition is linked with coronary heart disease, stroke, hypertension, atherosclerosis, obesity, some forms of cancer, type 2 diabetes, osteoporosis, dental caries, gall bladder disease, dementia and nutritional anaemias ^[124].

In line with the Australian Dietary Guidelines, the National Health Survey asks participants about their adherence to the recommendation that adults eat 2 serves of fruit and 5-6 serves of vegetables per day ^[4]. In 2017-18, more than 1 in 2 (51.3%) Australian adults did not meet the guidelines for recommended daily serves of fruit, and 92.5% did not meet the guidelines for recommended daily serves of vegetables ^[4]. These proportions have changed very little over time ^[108]. Only 5.4% of adults met the guidelines for both fruit and vegetable consumption, with older people meet the guidelines more over than younger people (8.3% of 65-74 year-olds compared to 3.6% of 18-24 year-olds) ^[4].

More than two thirds of Australians are now overweight or obese

Overweight and obesity, defined as a body mass index (BMI) 25-29.9 kg/m² and ≥30 kg/m² respectively, are leading risk factors for ill-health in Australia. Being overweight or obese significantly increases the risks of cardiovascular disease, high blood pressure, high blood cholesterol, type 2 diabetes, sleep apnoea, musculoskeletal conditions and some cancers ^[125]. As the amount of excess weight an individual carries increases, so does the risk of developing these conditions. Being overweight or obese can also make it more difficult to control or manage chronic diseases ^[108].

Weight loss can reduce the risk of many of these conditions ^[125]. As in much of the rest of the world, however, rates of overweight and obesity in the Australian population continue to rise (see Figure 21) ^[4]. Australia now ranks 8th among OECD countries for prevalence of overweight and obesity in the population 15 years and older ^[126].

Based on data from the 2017-2018 National Health Survey, more than two thirds (67%) of Australian adults are now overweight or obese, up from 56% in 1995 ^[4]. This rise has primarily been driven by an increase the prevalence of obesity among Australian adults, from 19% in 1995 to 31% in 2017-18. The proportion of the adult population who are overweight has remained steady (see Figure 22) ^[4].

A greater proportion of Australian men aged 18 years and older are overweight or obese than women (74.5% versus 59.7% in 2017-2018), and prevalence of overweight and obesity increase with age ^[4]. By age 65-74, 73.3% of Australians are overweight or obese (34% overweight, 38.7% obese). For men aged 65-74, the prevalence of overweight or obesity in 2017-2018 was 83.3%, for women it was 38.7% ^[4].

It is therefore particularly concerning that, in the most recent two National Health Surveys, the largest increase in rates of overweight and obesity was in the 18-24 year age group, among whom the rate increased from 39% in 2014-15 to 46% in 2017-18 ^[4]. Rates of obesity in children aged 5-17 years have also been increasing. Compared to obesity prevalence of 4.9% in children in 1995, the rate in 2014-15 was 7.4%, and increased further to 8.1% in 2017-2018 ^[4]. Growing rates of overweight and obesity at younger ages have important implications for the future burden of overweight and obesity-associated diseases in the Australian population.

Rates of overweight and obesity increase with greater remoteness and socioeconomic disadvantage. In 2017-18, 71.8% of Australians living in areas of greatest disadvantage were overweight or obese, compared to 62.6% of those in the least disadvantaged areas. Similarly, 72.2% of Australians living in outer regional and remote parts of Australia were overweight or obese, compared to 65.0% of persons living in major cities ^[4].

PREVALENCE OF OVERWEIGHT AND OBESITY, BY SEX, 1995-2017/18

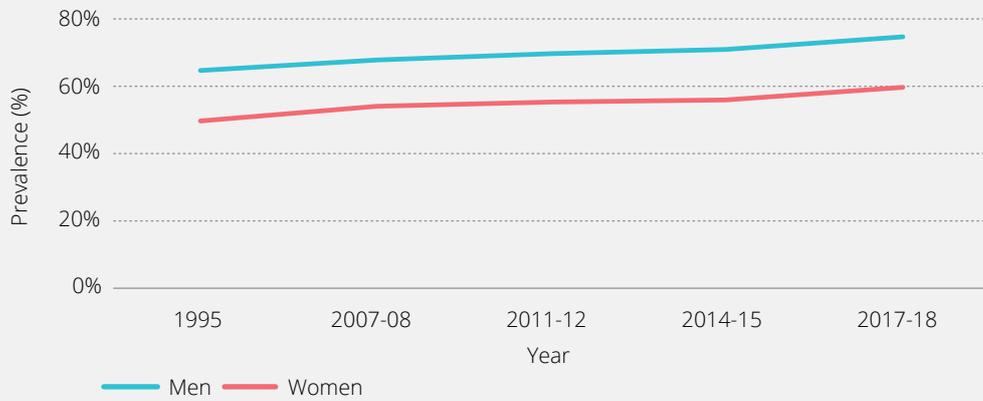


Figure 21: The proportion of Australian men and women aged over 18 years who were overweight or obese, 1995 to 2017-2018. (Source: 2017-28 ABS National Health Survey ⁽⁴⁾)

PREVALENCE OF OVERWEIGHT AND OBESITY, 2007/8-2017/18

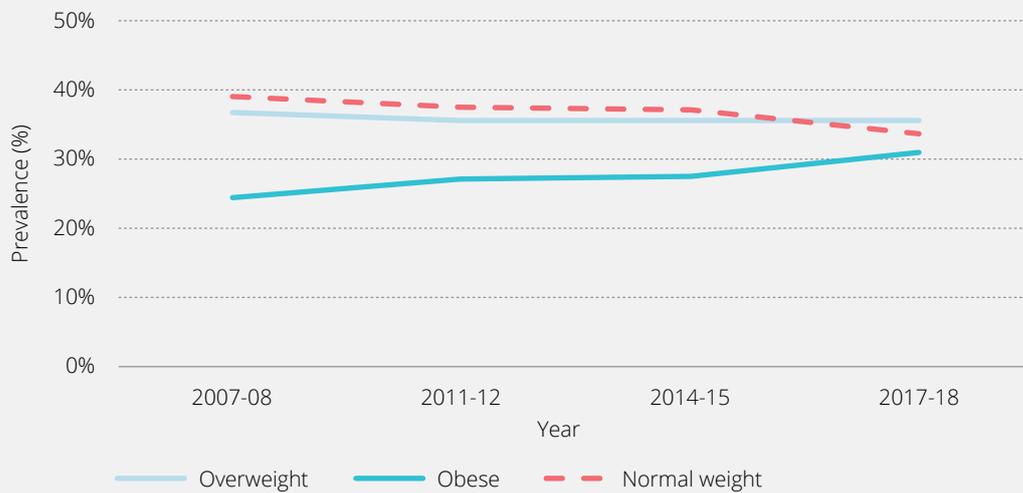


Figure 22: The proportion of Australian adults aged 18 years or over who were overweight or obese, 2007-08 to 2017-2018. (Source: 2017-28 ABS National Health Survey ⁽⁴⁾)

3

Interrelationships between chronic kidney disease, diabetes and cardiovascular disease in the Australian population

3.1 PREVALENCE

Key messages:

Approximately 29% of Australian adults have one or more of CKD, diabetes or cardiovascular disease. Adults with diabetes have the highest rate of comorbidity, with 68% having comorbid CKD and/or cardiovascular disease.

32% of adults with diabetes have comorbid CKD; 21% of adults with cardiovascular disease have comorbid CKD.

The prevalence of comorbidity increases with age: 74% of adults with CKD aged 65 years and older had comorbid diabetes or cardiovascular disease; 81% of adults with diabetes aged 65 years and older had comorbid CKD or cardiovascular disease; 44% of adults with cardiovascular disease 65 years and older had comorbid CKD or diabetes.

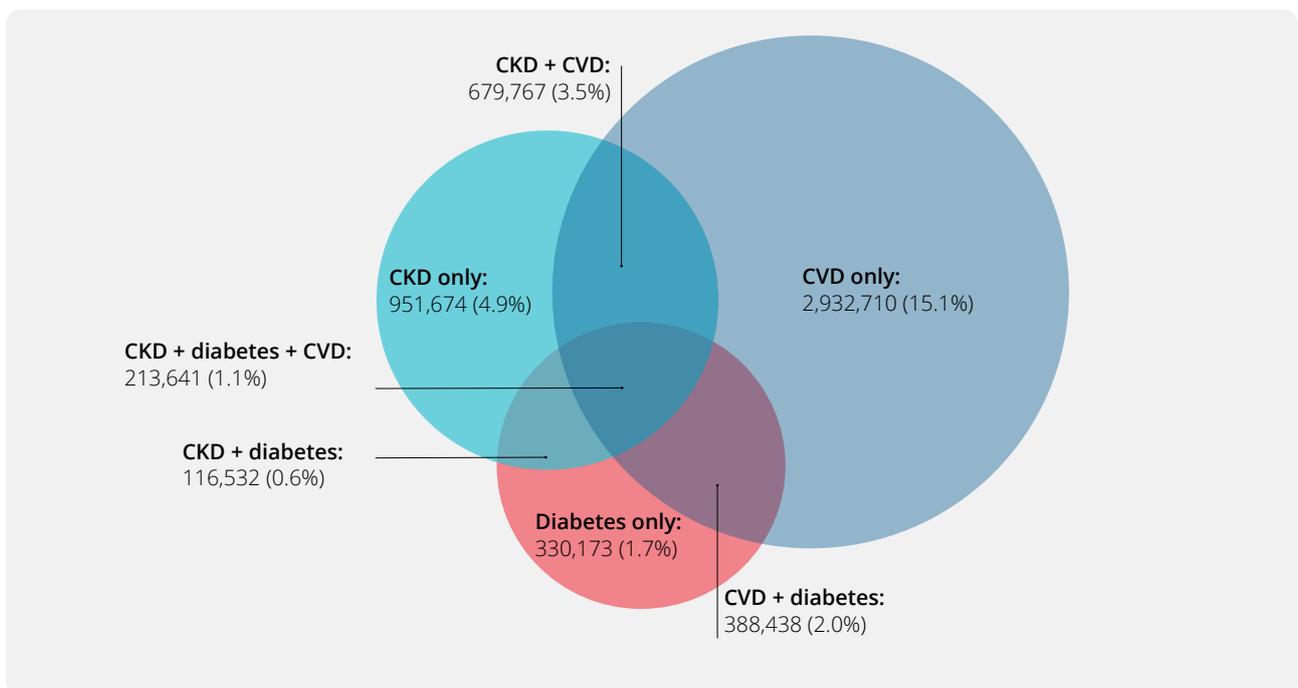


Figure 23: Prevalence of CKD, diabetes and cardiovascular disease and rates of comorbidity among Australians aged 18 years and older. Proportions are based on the 2011-12 Australian Health Survey, and have been applied to the 2018 Australian population to yield numerical estimates of burden of comorbidity (Source: AIHW analysis of unpublished data from the ABS Australian Health Survey, 2011-12^[1] and Australian Demographic Statistics – ABS 3101.0).

Based on a 2014 AIHW analysis of data from the ABS 'Australian Health Survey, 2011-2012' approximately 29% of Australian adults have one or more of CKD, diabetes or cardiovascular disease, where cardiovascular disease is defined as self-reported hypertensive disease, coronary heart disease, heart failure, cerebrovascular disease, vascular disease, or other heart disease or other diseases of the circulatory system ^[1].

Figure 24 and Figure 23 show the estimated prevalence and rates of comorbidity for CKD, diabetes and cardiovascular disease. Adults with diabetes had the highest proportion with comorbid disease at 68%, followed by CKD at 51% and cardiovascular disease at 30% ^[1]. Among adults with diabetes, approximately 32% had comorbid CKD, or an estimated 330,173 individuals based on 2018 population data. Among adults with cardiovascular disease, approximately 21% (893,408) had comorbid CKD. An estimated 5.2% of the total Australian adult population had CKD in combination with either diabetes or cardiovascular disease – equivalent to over 1 million individuals based on 2018 population data. Approximately 1.1% (213,641) of Australian adults had all three conditions. For the population over 65 years, the proportion with all three conditions increased to 4.5% ^[1].

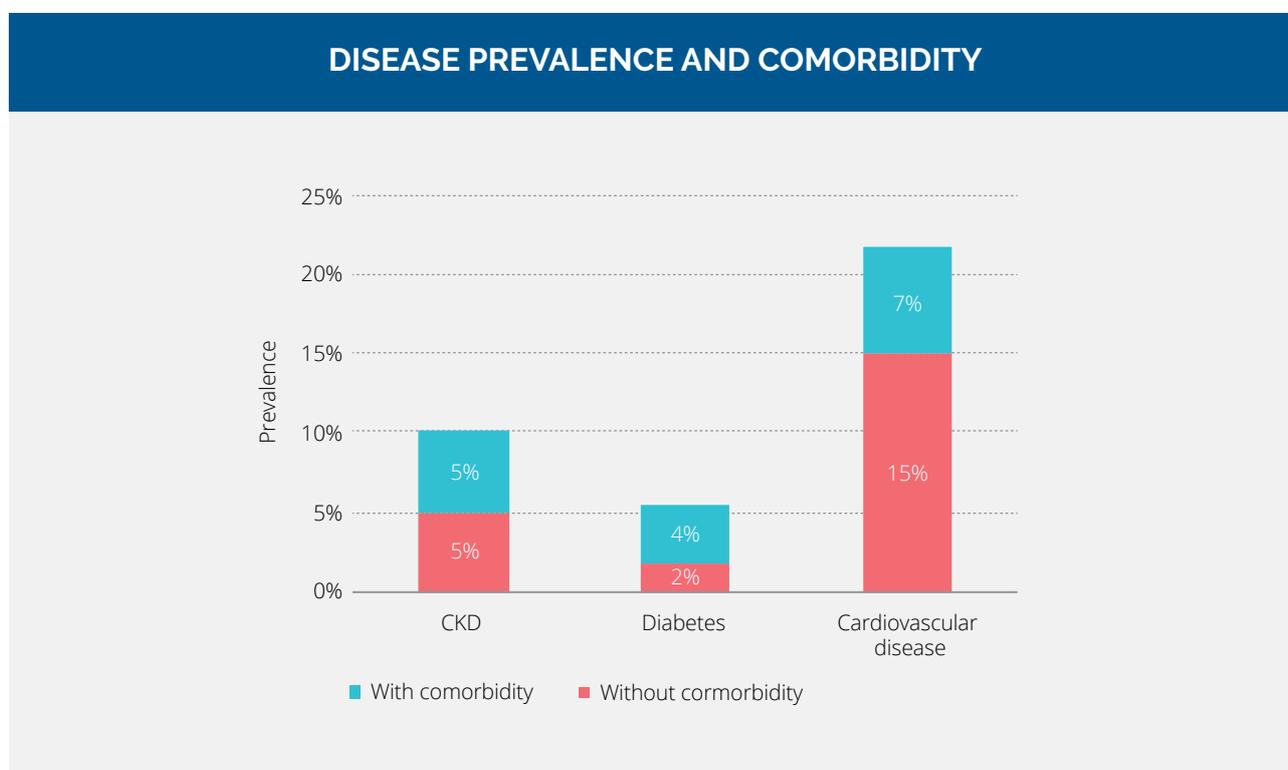


Figure 24: Prevalence of CKD, diabetes and cardiovascular disease in Australia, showing the proportion with 1 or more of comorbid CKD, diabetes and/or cardiovascular disease (Source: AIHW analysis of unpublished data from the ABS Australian Health Survey, 2011-12 ^[1])

Figure 25 shows how prevalence of comorbidity increases with age. The proportion of adults with CKD who had comorbid diabetes and/or cardiovascular disease was 10% in the 18-44 year age group, 50% in the 45-64 year age group, and 74% in the 65 years and older age group ^[1]. The proportion of adults with diabetes who had comorbid CKD and/or diabetes was 34% in the 18-44-year age group, 63% in the 45-64-year age group, and 81% in the 65 years and over age group. The prevalence of comorbidity in cardiovascular disease also increased with age, tripling between the ages of 18-44 and 65 (from 12% to 44%) ^[1].

The authors of the original AIHW analysis note, however, that rates of comorbidities among older Australians may be even higher than reported. The data used to derive these estimates are from a survey of the non-institutionalised Australian population, and therefore do not capture rates of comorbidity amongst older Australians living in residential care facilities ^[1].

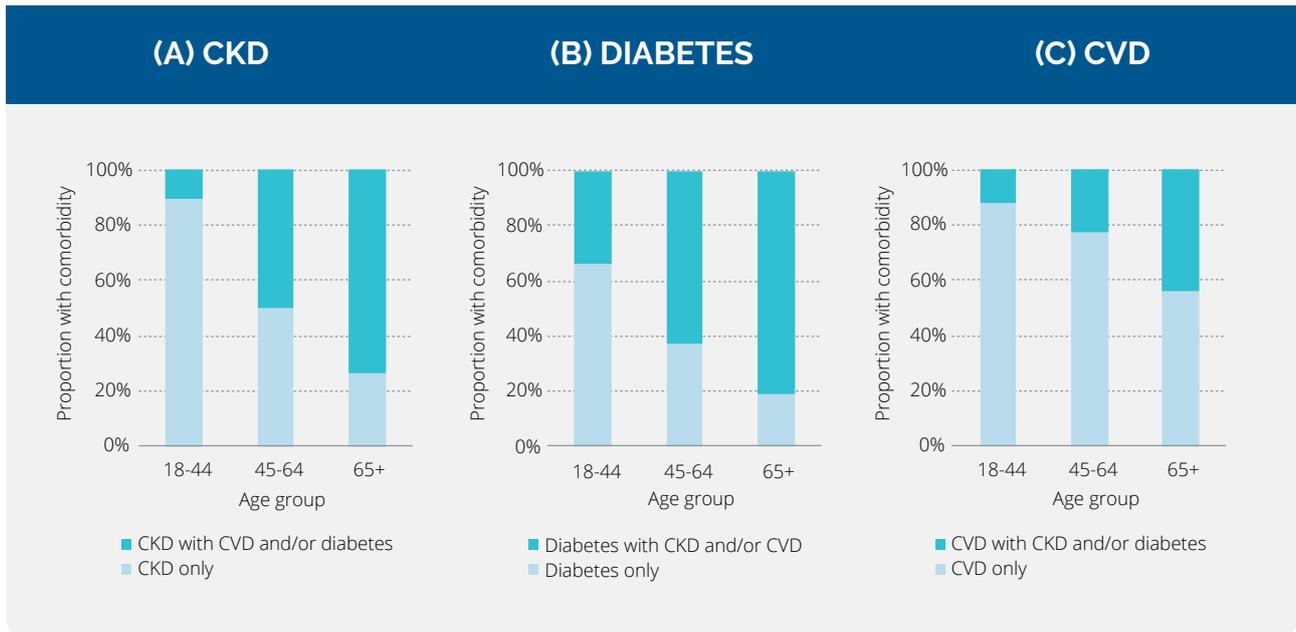


Figure 25: Comorbidity in adults 18 years and older with CKD, diabetes and cardiovascular disease, by age, 2011-12. Cardiovascular disease prevalence is based on the self-reported data of people who participated in the measured part of the Australia Health Survey; diabetes prevalence is based on HbA1c and self-reported data, and CKD prevalence is based on eGFR and ACR test results. (Source: AIHW analysis of unpublished data from the ABS 'Australian Health Survey 2011-12 (National Health Measures Survey Component))

3.2 HOSPITALISATION

Key messages:

Approximately 2 million non-dialysis hospitalisations each year are associated with CKD, diabetes or cardiovascular disease; 22% had two or more of these conditions present.

Of patients receiving regular in-hospital dialysis in 2016-2017, diabetes was the underlying cause of KF in approximately 40% of cases. Thus, 5% of all hospitalisations in Australia in 2016-2017 were for haemodialysis to treat diabetes related KF.

Of the 1.17 million non-dialysis hospitalisations involving diabetes in 2016-2017, CKD was present as the principal or an additional diagnosis in approximately 18% of cases.

Of the 1.19 million non-dialysis hospitalisations involving cardiovascular disease in 2016-2017, CKD was present as the principal or an additional diagnosis in approximately 15% of cases.

Regular dialysis is the most common reason for hospitalisation in Australia, accounting for 13% of all hospitalisations in 2016-2017 (1.4 million hospitalisations).

The majority (~80%) of non-dialysis hospitalisations involving CKD occurred in combination with a diagnosis of diabetes and/or cardiovascular disease.

1 in 3 hospitalisations involve diabetes, cardiovascular disease and/or CKD (including dialysis)

Defining hospitalisations

Hospitalisations data contained in this report are taken from the Australian Institute of Health and Welfare (AIHW) National Hospital Morbidity Database (NHMD), which records information on patients admitted to hospital for essentially all hospitals in Australia. Hospitalisations are routinely reported to the NHMD in accordance with the requirements of the Admitted Patient Care Minimum Data Set (APC NMDS). Reporting occurs at the end of a person's admitted episode of care and is based on the clinical documentation for that hospitalisation.

A 'hospitalisation' refers to an episode of admitted care. This can be a total hospital stay (from admission to discharge/transfer/death) or a portion of a hospital stay beginning or ending in a change of type of care (e.g. from acute care to rehabilitation). The same person may have multiple hospitalisations, therefore the numbers presented below reflect episodes of admitted care, not the number of individuals admitted to hospital.

There are two separate hospital admission types recorded in the NHMD:

- **Principal diagnosis:** the diagnosis established after study to be chiefly responsible for occasioning the patient's hospitalisation
- **Additional diagnosis:** a condition or complaint that either coexists with the principal diagnosis or arises during the hospitalisation. An additional diagnosis is reported if the condition affects patient management.

Combined, CKD, diabetes and cardiovascular disease were associated with approximately 2 million non-dialysis hospitalisations in 2016-2017, or nearly 20% of all hospitalisations nationwide [3, 49, 92]. In addition, a total of 1.4 million hospitalisations were recorded for regular dialysis, accounting for a further 13% of all hospitalisations [49]. Regular dialysis is the most common reason for hospitalisation in Australia [46]. In the 10 years from 2006-7 to 2016-17, the number of hospitalisations for regular dialysis in Australia increased by 53% (an increase of approximately 50,000 hospitalisations per year), while the age-standardised rate increased by 21% [49].

Dialysis hospitalisations count the number of dialysis episodes rather than the number of people who receive dialysis. Patients receiving facility-based haemodialysis (as opposed to home haemodialysis or peritoneal dialysis) attend three sessions per week on average, equivalent to 156 hospitalisation per person per year. Given that diabetic nephropathy was the underlying cause of KF in 40% of persons receiving facility-based haemodialysis in 2017, the treatment of diabetes-related KF accounted for over 5% of all hospitalisations in Australia.

Non-dialysis hospitalisations with CKD listed as the principal or as an additional diagnosis accounted for 3.2% of hospitalisations in Australia in 2016-2017. CKD is far more commonly listed as an associated rather than as a principal diagnosis in hospital admissions – 309,327 hospitalisations listed CKD as an additional diagnosis in 2016-2017 versus 47,887 hospitalisations for CKD as the principal diagnosis [49]. Figure 26 shows the relative number of CKD hospitalisations by diagnosis type.

Type 2 Diabetes was recorded in 1,037,873 hospitalisations in 2016-2017. Of this number, type 2 diabetes was recorded as the principal diagnosis in 3% of cases (n=31,688) and as an additional diagnosis in 97% (n=1,006,205) [92]. Type 1 diabetes was recorded as the principal or additional diagnosis in 63,077 hospitalisations, and gestational and other or unspecified diabetes in a further 70,649 hospitalisations. Altogether, there were 1,169,124 hospitalisations for diabetes in 2016-2017 (50,150 with diabetes as the principal diagnosis), or 10.6% of all hospitalisations [92].

There were 1.19 million hospitalisations in 2016-2017 where cardiovascular disease was recorded as the principal or an additional diagnosis – 10.8% of all hospitalisations [3]. Coronary heart disease accounted for 28% of hospitalisations where cardiovascular disease was the principal diagnosis, followed by heart failure and cardiomyopathy (12%) and stroke (11%) [3].

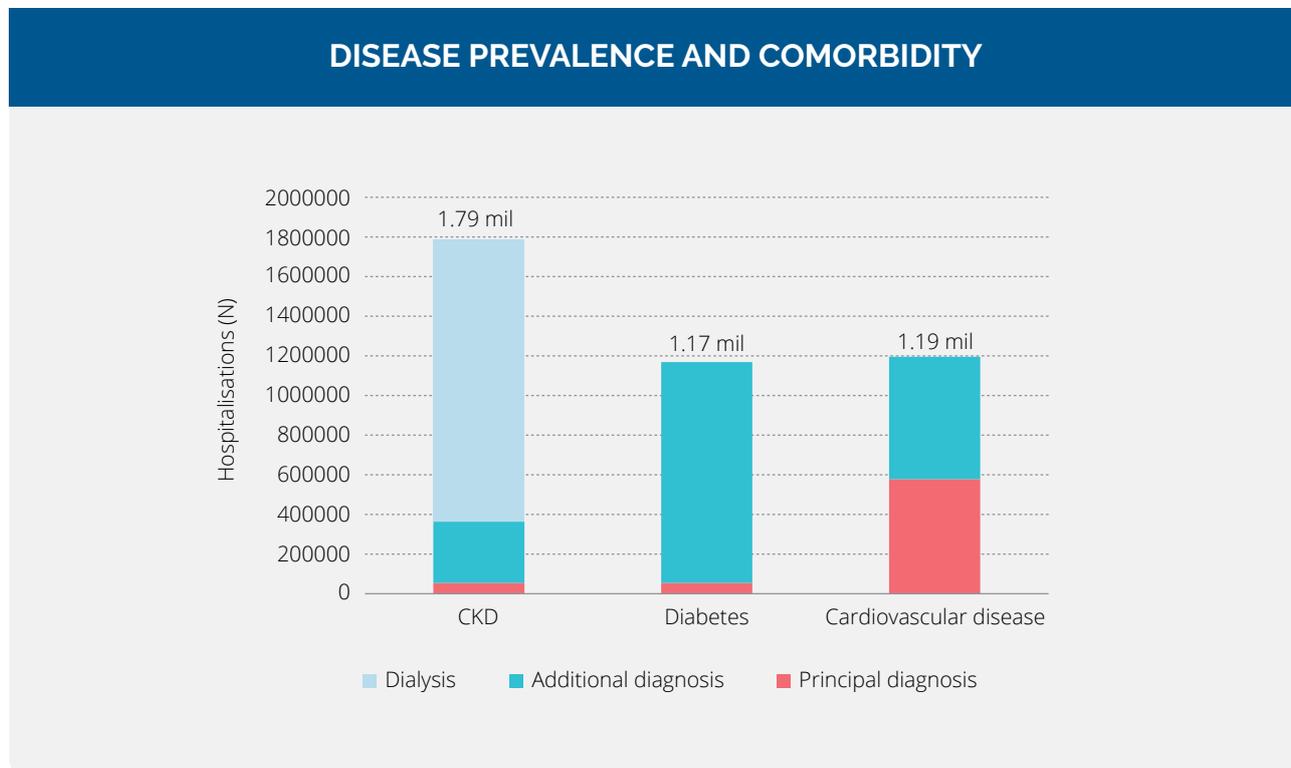


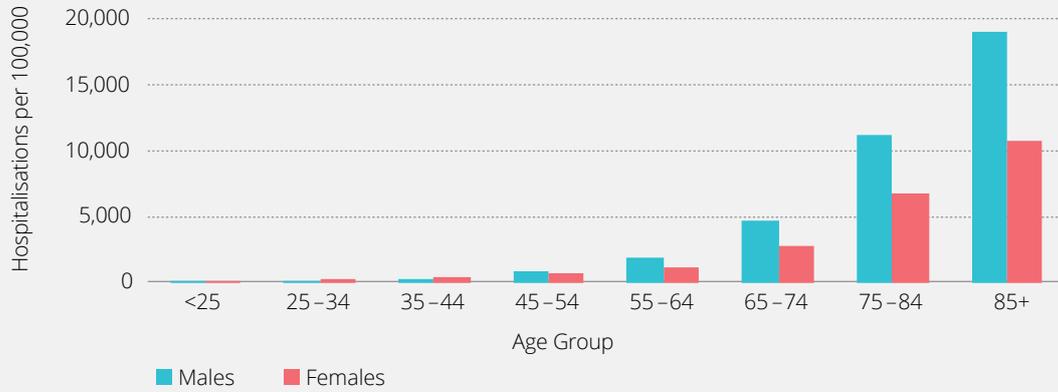
Figure 26: Number of hospitalisations in 2016-2017 by hospital diagnosis type (AIHW analysis of the National Hospital Morbidity database) [3, 49, 92].

The vast majority of hospitalisations for CKD, diabetes and cardiovascular disease in 2016-2017 occurred in people aged over 55 years [3]. Under 45 years of age, hospitalisations for CKD or type 2 diabetes are more frequent among women than men [3, 49, 92]. Over 55 years of age, however, hospitalisations for type 2 diabetes, CKD and cardiovascular disease are significantly more frequent in men (Figure 27). Overall, men are 1.3 times more likely to be hospitalised for CKD, 1.4 times more likely to be hospitalised for type 2 diabetes, and 1.4 times more likely to be hospitalised for cardiovascular disease.

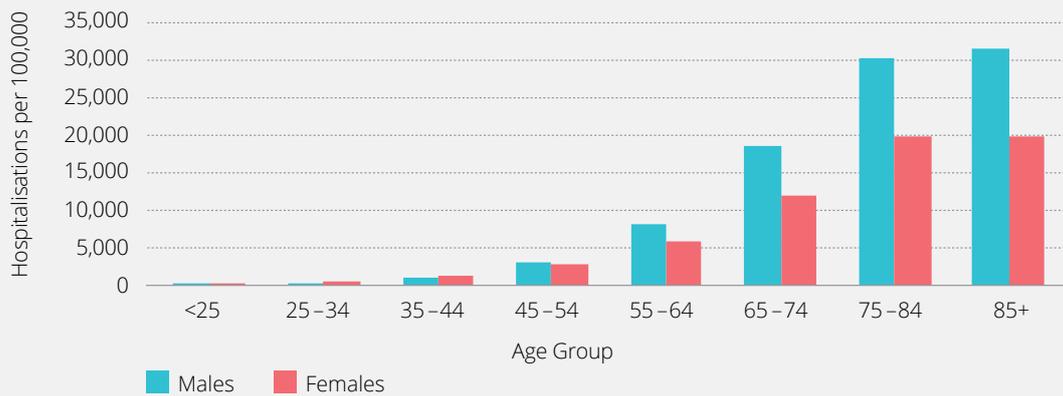
A previous analysis by the Australian Institute of Health and Welfare has examined the extent of comorbidity in 2012-2013 among adults 25 years and older hospitalised with a diagnosis of CKD, diabetes and/or cardiovascular disease [46]. Based on this analysis, 22% of all non-dialysis hospitalisations recording CKD, diabetes and/or cardiovascular disease as the principal or additional diagnosis had two or more of these diseases present; all three diseases were present in 6% of hospitalisations [46]. The most frequent combination of diseases recorded was diabetes and cardiovascular disease, followed by all three diseases – CKD, diabetes and cardiovascular disease (see Figure 28).

The proportion of hospitalisations involving comorbid diagnoses increases with age, especially for hospitalisations involving CKD. Of hospitalisations with a diagnosis of CKD in 2012-13, 48% of those occurring in persons 65-74 years listed comorbid diagnoses of both cardiovascular disease and diabetes (see Figure 30). Fewer than 15% of non-dialysis hospitalisations for CKD in over 65 year-olds were for a diagnosis of CKD alone – the vast majority involved a comorbid diagnosis of diabetes and/or cardiovascular disease [46].

**(A) CKD HOSPITALISATIONS EXCL. DIALYSIS
(PRINCIPAL AND/OR ADDITIONAL DIAGNOSIS)**



**(B) TYPE 2 DIABETES HOSPITALISATIONS
(PRINCIPAL AND/OR ADDITIONAL DIAGNOSIS)**



**(C) CARDIOVASCULAR DISEASE HOSPITALISATIONS
(PRINCIPAL DIAGNOSIS)**

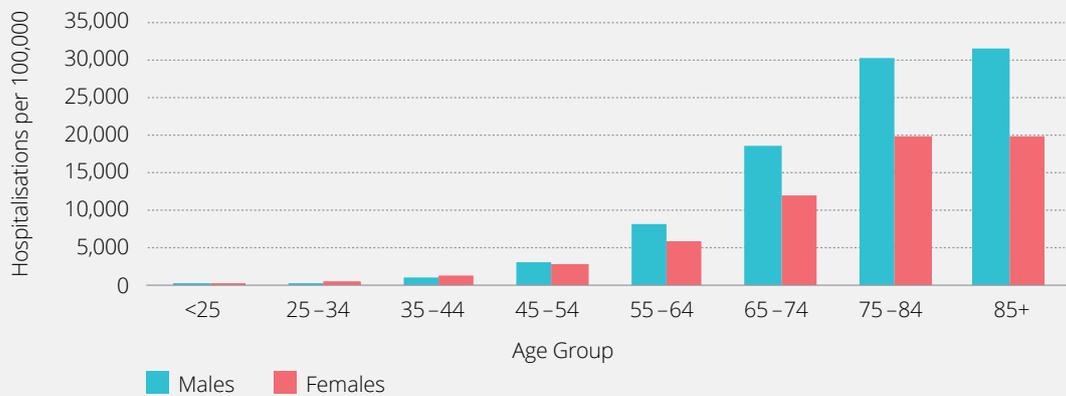


Figure 27: Hospitalisations for (A) CKD (excluding dialysis hospitalisations, principal and/or additional diagnosis), (B) type 2 diabetes (principal and/or additional diagnosis), and (C) cardiovascular disease (principal diagnosis), by age and sex, 2016-2017 (Source: AIHW analysis of the National Hospital Morbidity Database) ^[3, 49, 92].

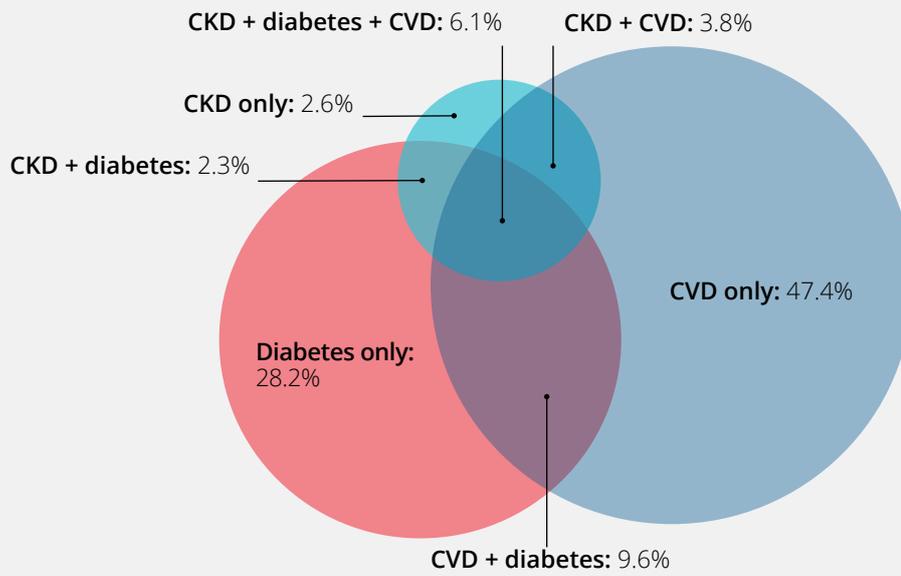


Figure 28: Hospitalisations (excluding dialysis) among persons aged 25 years and older with a diagnosis of CKD, diabetes or cardiovascular disease, and the proportion with overlapping diagnoses. Percentages reflect the proportion in each comorbidity category for all hospitalisations with a diagnosis of one or more of CKD, diabetes and cardiovascular disease (source: AIHW National Hospital Morbidity Database ^[46])

HOSPITALISATION RATES FOR PERSONS WITH A COMBINATION OF CKD / DIABETES / CVD

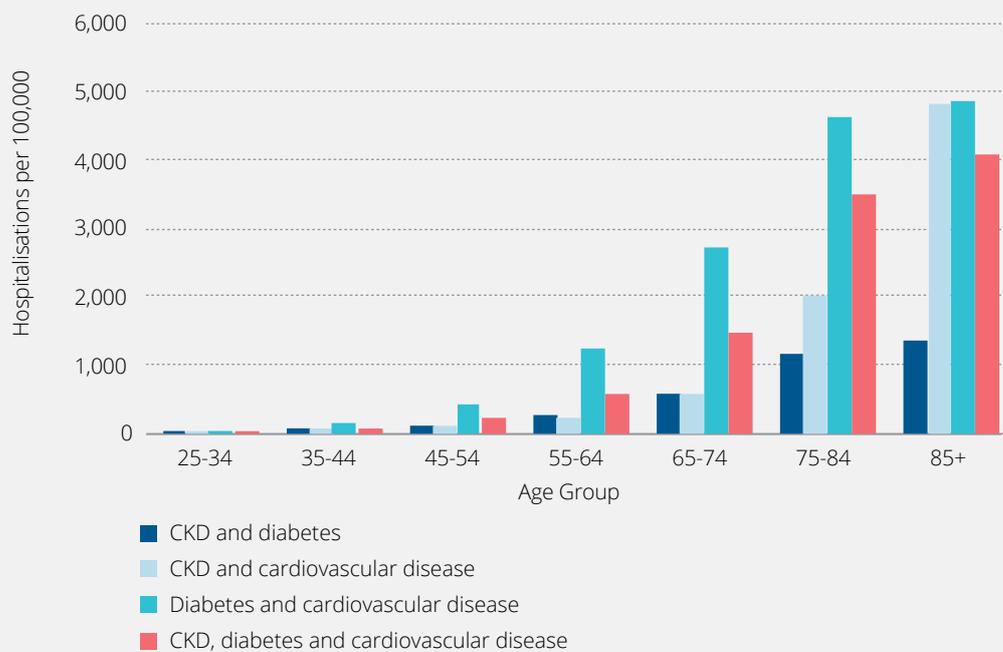
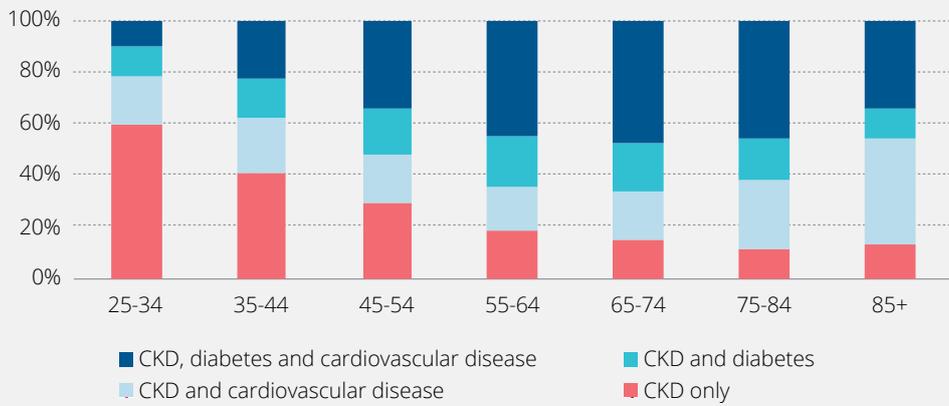
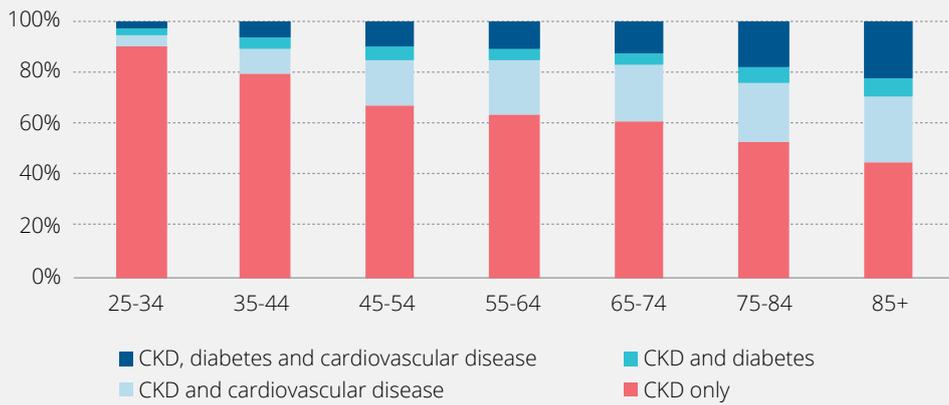


Figure 29: Hospitalisation rates for persons with 2 or more diagnoses of CKD, diabetes and/or cardiovascular disease, 2012-2013

(A) CKD HOSPITALISATIONS



(B) DIABETES HOSPITALISATIONS



(C) CARDIOVASCULAR HOSPITALISATIONS

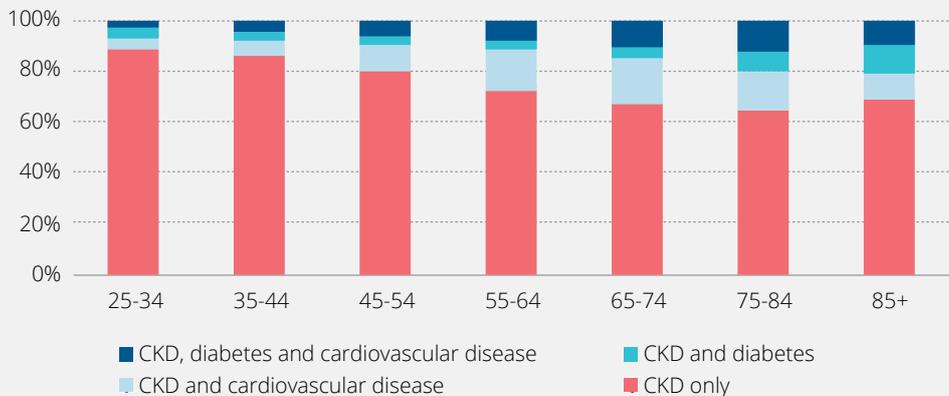


Figure 30: Hospitalisations among adults aged 25 years and older with one or more diagnoses of CKD, diabetes or cardiovascular disease, by age, 2012-13 (Source: AIHW National Hospital Morbidity Database ⁽⁴⁶⁾)

3.3 MORTALITY

Key messages:

Of deaths with diabetes listed as the underlying cause in 2011, 27% had CKD listed as an associated cause of death.

Of deaths with cardiovascular disease listed as the underlying cause in 2011, 11.4% had CKD listed as an associated cause of death. Of deaths with hypertension listed as the underlying cause, 28% had CKD listed as an associated cause of death.

Of deaths with CKD listed as the underlying cause in 2011, 19% had heart failure and cardiomyopathy listed as associated causes, and 27% had coronary heart disease listed as an associated cause.

Cardiovascular disease was the underlying cause of 27% of all deaths in Australia in 2017 (n=43,477), and was an underlying or associated cause of 53% of all deaths (n=84,874)^[3]. Diabetes and CKD also have a substantial impact on mortality in Australia but are more commonly reported as associated causes of death than as the underlying cause. CKD and diabetes also tend to be under-reported as contributing causes of death^[75]. For example, a data linkage study conducted in 2011 found that 12% of persons who died while receiving KRT between 2003 and 2007 did not have CKD listed as cause of death^[127].

Diabetes was an underlying or associated cause of 10.6% of all deaths in Australian in 2017 (n=17,020)^[92]. Of these deaths, 5% were due to type 1 diabetes, 56% to type 2 diabetes, and the remaining 39% to unspecified diabetes type^[92]. CKD was an underlying or associated cause of 10.9% of all deaths in Australia in 2017 (n=17,502)^[49].

The complex overlapping causal relationships between CKD, diabetes and cardiovascular disease mean that these diseases are frequently listed in combination with each other on death certificates (see Table 2). Based on 2011 data, where cardiovascular disease was listed as the underlying cause of death, CKD was listed as an associated cause of death in 11.4% of cases. Where diabetes was the underlying cause of death, CKD was listed as an associated cause of death in 26.8% of cases^[75]. Where CKD was listed as an underlying cause of death, the most common associated causes death were heart failure/cardiomyopathy, coronary heart disease, hypertensive disease or other cardiovascular disease^[75].

In 2011, CKD, diabetes and cardiovascular disease together were the underlying cause of 36% of all deaths in Australia. Overall, 61% of all deaths had at least one of these diseases listed as an underlying or associated cause of death^[75]. At least 2 of CKD, diabetes or cardiovascular disease were found on 14% of all death records, and approximately 2% of deaths had all three diseases listed as contributing causes of death^[75].

Figure 31 shows, for deaths listing CKD, diabetes or cardiovascular disease as an underlying or associated cause in 2011, the proportions listing 2 or more of these conditions.

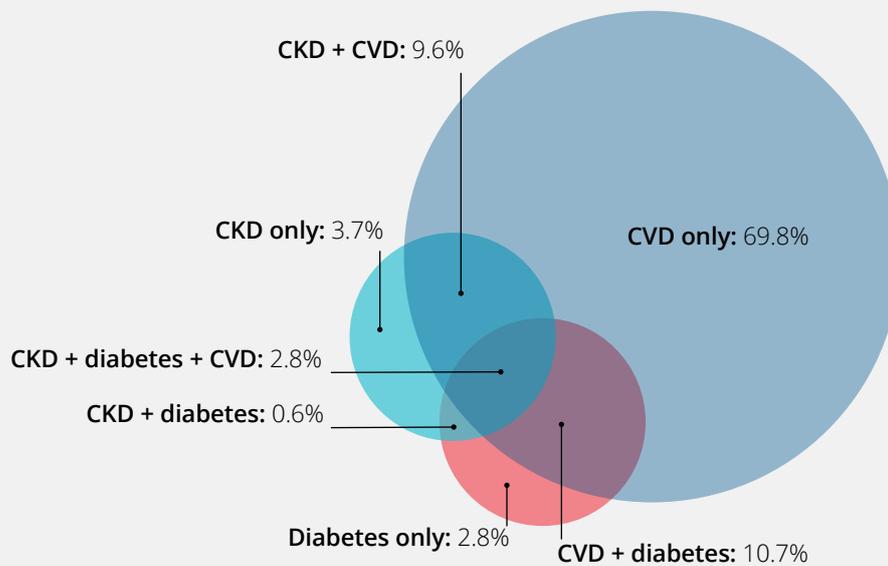


Figure 31: Deaths with CKD, diabetes or cardiovascular disease listed as any cause of death (underlying or associated) in 2011. Percentages reflect the proportion of deaths listing one or more of CKD, diabetes and cardiovascular disease within each comorbidity category (source: AIHW National Mortality Database ^[75]).

Table 2: Most common associated causes of death where cardiovascular disease, diabetes or CKD are the underlying cause of death, 2011 ^[75].

Underlying cause of death	Most common associated causes of death (percent of deaths)				
Cardiovascular disease*	Dementia and Alzheimer disease (13.1%)	CKD (11.4%)	Diabetes (10.0%)	Influenza and pneumonia (8.5%)	Chronic obstructive pulmonary disease (COPD) (8.0%)
Diabetes	CHD (64.0%)	Hypertensive disease (34.8%)	Other CVD (29.0%)	CKD (26.8%)	Cerebrovascular disease (22.6%)
Chronic Kidney disease (CKD)	Heart failure and cardiomyopathy (29.1%)	Other CVD (27.8%)	CHD (26.5%)	Hypertensive disease (19.8%)	Acute kidney failure unspecified (17.5%)

*Includes deaths with an underlying cause of coronary heart disease, cerebrovascular disease, heart failure and cardiomyopathy, peripheral vascular disease and hypertensive disease.

3.4 KIDNEY FAILURE

Key messages:

52% of people starting treatment for KF in 2018 had comorbid diabetes, and 34% had known or suspected coronary artery disease.

The presence of comorbidity significantly increases the risk of mortality on KRT.

The dialysis death rate is nearly doubled when comorbid coronary artery disease is present and is increased by 33% when comorbid diabetes is present.

Presence of diabetes increases the rate of death in transplant recipients by 147%, whereas coronary artery disease increases the death rate by 227%.

Incidence of KF in Australians with diabetes

A recent data linkage study examined trends over time in the incidence of KF among registrants of Australia's National Diabetes Services Scheme (NDSS) ^[43]. Of 1,375,877 NDSS registrants between 2002 and 2013, 9,977 commenced treatment for KF over this interval, representing an overall incidence of treated KF in Australians with diabetes of 10 per 10,000 person years.

Among non-Indigenous Australians with type 2 diabetes, the incidence of KF increased by 2.2% per annum over this interval ^[43]. This increase in KF incidence was driven by trends in the diabetes population under 50 years and over 80 years. Increasing incidence of treated KF in the younger type 2 diabetes population possibly reflects earlier age of diabetes onset and/or a more aggressive disease phenotype ^[44]. Increasing incidence of treated KF in the diabetes population 80 years and over likely reflects an increasing willingness to actively treat KF in older persons with diabetes, combined with a reduction in cardiovascular mortality in this population.

Incidence of treated KF among Australians with type 1 diabetes was stable between 2002 and 2013 ^[43].

Prevalence of comorbid diabetes and cardiovascular disease in treated KF

In 2018, 52% of people starting treatment for KF had comorbid diabetes, and 34% had known or suspected coronary artery disease (see Figure 32) ^[45]. The prevalence of comorbid diabetes at KRT entry has been increasing steadily for the past 2 decades (see Figure 33). In contrast, the prevalence of comorbid coronary artery disease, cerebrovascular disease and peripheral vascular disease at KRT have declined since 2011, consistent with wider trends population trends ^[1].

Figure 34 shows the variation in prevalence of co-morbidities at KRT entry by state and territory. Most notable is the high rate of comorbid diabetes among patients commencing KRT in the Northern Territory in 2018 (75%), which is a reflection of the high proportion of Aboriginal and Torres Strait Islander KF patients with diabetic nephropathy as the primary kidney disease ^[45].

PREVALENCE OF CO-MORBIDITIES (KNOWN OR SUSPECTED) AT KRT ENTRY, 2018

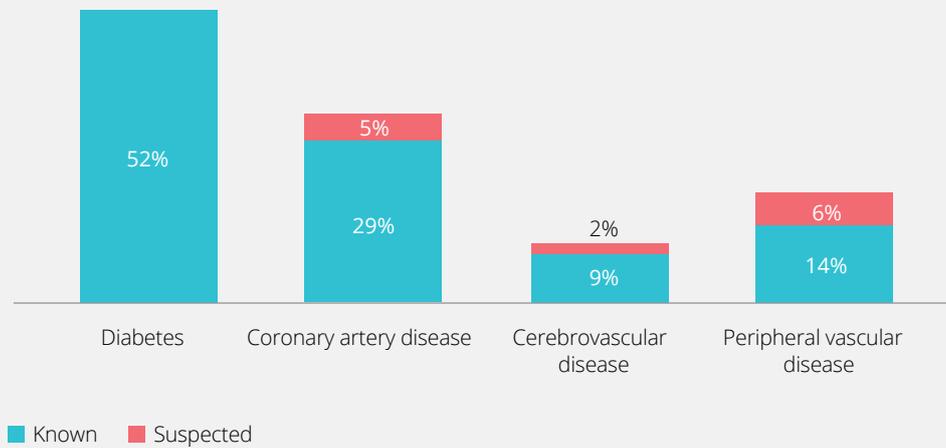


Figure 32: Prevalence of co-morbidities (known or suspected) at KRT entry, 2018 (Source: ANZDATA ^[45])

PREVALENCE OF CO-MORBIDITIES AT KRT ENTRY, NEW PATIENTS 1997-2018

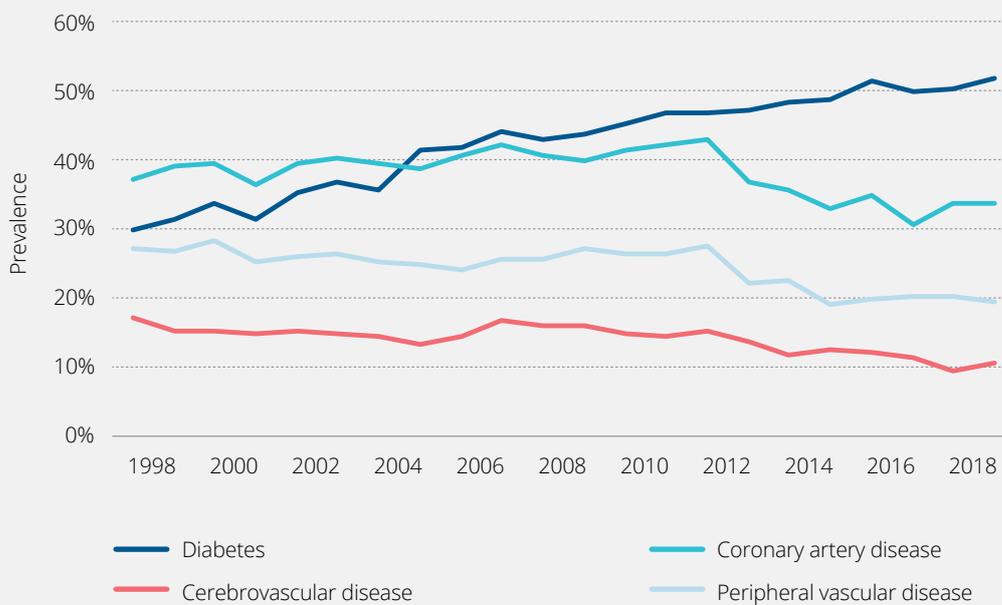


Figure 33: Temporal trends in prevalence of co-morbidities (known or suspected) at KRT entry, 1997-2018 (Source: ANZDATA ^[45])

PREVALENCE OF CO-MORBIDITIES (KNOWN OR SUSPECTED) AT KRT ENTRY, BY STATE/TERRITORY IN 2018

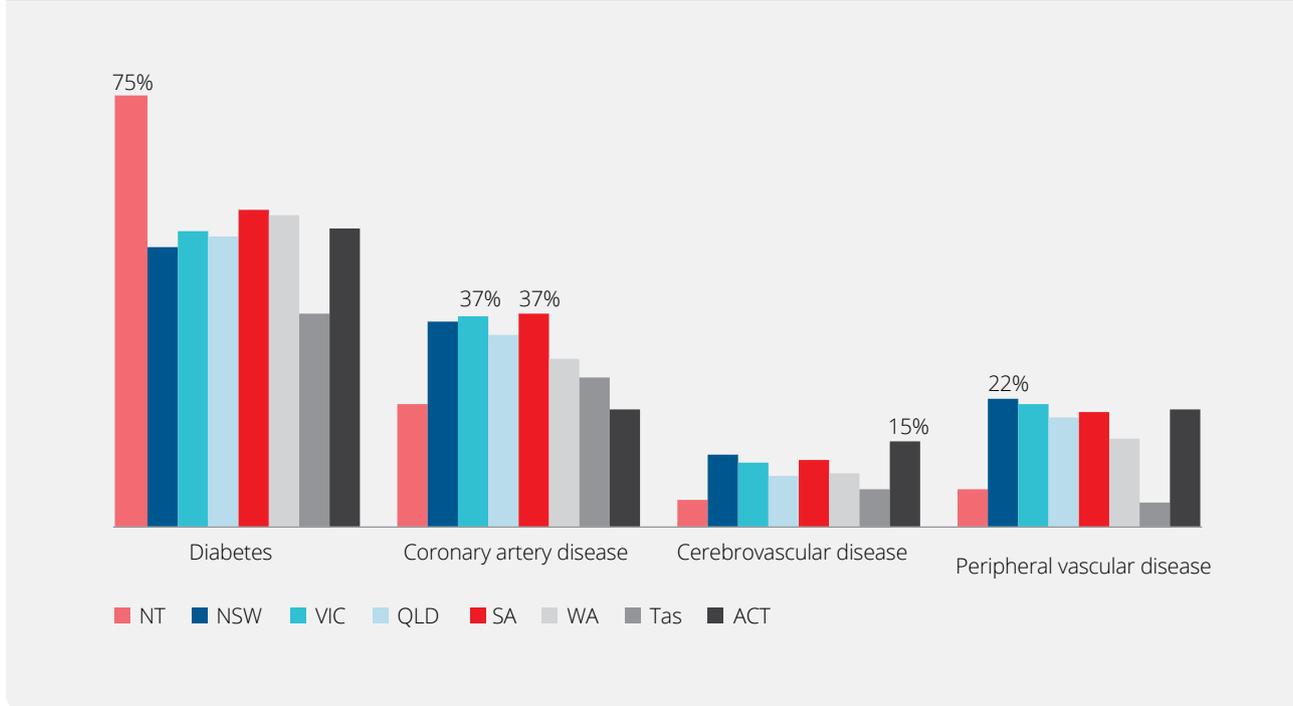


Figure 34: Prevalence of co-morbidities (known or suspected) at KRT entry, by state/territory in 2018.

Comorbid diabetes and cardiovascular disease are associated with poorer KF outcomes

Approximately half of incident KF cases in Australia receive treatment with dialysis or transplantation. More than 90% of KF cases in persons younger than 60 years are treated with Kidney Replacement Therapy (KRT), with rates of treatment declining sharply with age over 60 years ^[89]. Between 2003 and 2007, less than half of incident KF in persons aged 75 years and older was treated with KRT ^[89]. The burden of comorbid medical conditions and overall quality of life are factors which influence whether patients will be referred for KRT ^[17,18,19]. In a US study of KF patients aged 80 years and older, those not offered dialysis were more likely to be referred late, be socially isolated, have diabetes and have greater functional impairment ^[14]. The combination of older age and comorbid diabetes therefore increase the likelihood that an individual will die prematurely of their KF (or related comorbidities).

For those who receive treatment for KF, the presence of comorbid diabetes and/or cardiovascular disease significantly increases mortality, regardless of treatment modality. Figure 35 shows the rate of death for KRT patients with comorbid diabetes versus without, and for patients with comorbid coronary disease versus without. Among dialysis patients, presence of type 2 diabetes was associated with a 33% increase in death rate, whereas presence of coronary disease increased the death rate by 98%. Similarly, for kidney transplant patients, presence of type 2 diabetes increases the death rate by 147%, whereas coronary disease increases the death rate by 277%.

Multiple comorbidities in older KRT patients further reduce expected survival Figure 36.

DEATH RATE PER 100 PATIENT YEARS, 2018

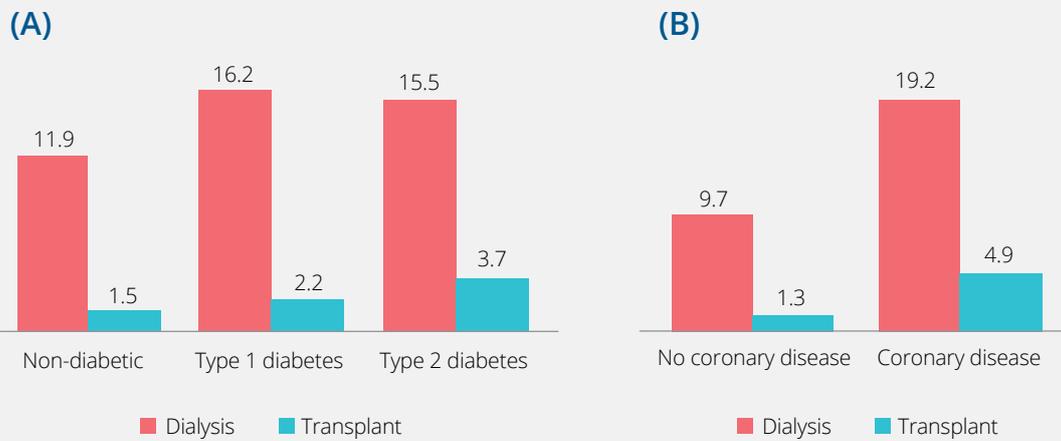


Figure 35: Death rate per 100 patient years among KRT patients in 2018, by treatment modality and (A) diabetes status and (B) coronary disease status (ANZDATA, unpublished data).

MEDIAN SURVIVAL ON DIALYSIS BY AGE AND COMORBIDITY STATUS, 2008-2017

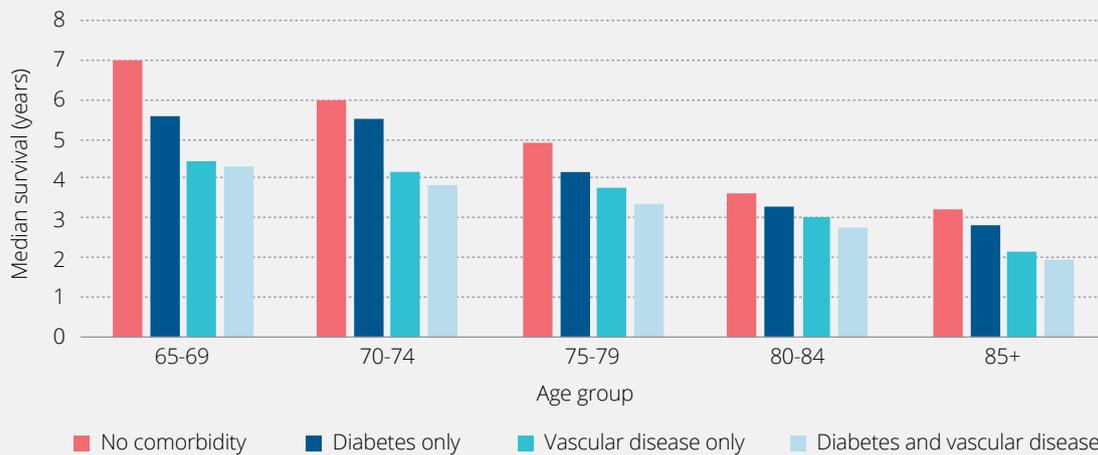


Figure 36: Median survival while receiving dialysis by age and comorbidity status, 2008-2017 (source: 42nd Annual ANZDATA report ^[45])

4

CKD, diabetes and cardiovascular disease in Aboriginal and Torres Strait Islander Australians

Key messages:

Over one-third of Aboriginal and Torres Strait Islander Australians have one or more of CKD, diabetes or cardiovascular disease. These diseases appear at a younger age, co-occur more frequently, progress faster, and are associated with more complications than in non-Indigenous Australians.

By middle age, most Aboriginal and Torres Strait Islander Australians have CKD, diabetes, and/or cardiovascular disease, and usually more than one of these conditions.

High rates of CKD, diabetes and cardiovascular disease among Aboriginal and Torres Strait Islander Australians are attributable to complex interactions between social, behavioural, psychological, epigenetic, economic and environmental factors, acting across the life course.

Among Aboriginal and Torres Strait Islander adults with diabetes, 56% have comorbid CKD (compared to 32% of non-Indigenous Australians). Among Aboriginal and Torres Strait Islander adults with cardiovascular disease, 32% have comorbid CKD (compared to 21% of non-Indigenous Australians).

Diabetes was the primary cause of kidney disease in 88% of Aboriginal and Torres Strait Islander Australians commencing treatment for ESKD between 2016 and 2018.

Aboriginal and Torres Strait Islander people made up 17% of Australians receiving dialysis 2018, despite comprising only 3% of the resident Australian population. More than one third of all hospitalisations of Aboriginal and Torres Strait Islander Australians are for regular dialysis.

Aboriginal and Torres Strait Islanders are more likely to be hospitalised for comorbid CKD, diabetes and cardiovascular disease than non-Indigenous Australians. A large proportion of diabetes and cardiovascular hospitalisations involve comorbid CKD (30% of diabetes hospitalisations and 42% of cardiovascular disease hospitalisations).

CKD, diabetes and cardiovascular disease are more commonly listed together on death certificates for Aboriginal and Torres Strait Islander people than for non-Indigenous Australians.

4.1 THE BURDEN OF CKD, DIABETES AND CARDIOVASCULAR DISEASE IN ABORIGINAL AND TORRES STRAIT ISLANDER AUSTRALIANS

Aboriginal and Torres Strait Islander Australians experience higher a prevalence of CKD, diabetes and cardiovascular disease than non-Indigenous Australians

Aboriginal and Torres Strait Islander Australians experience significantly higher rates of CKD, diabetes and cardiovascular disease than the non-Indigenous population, with the scale of this disparity increasing with greater geographical remoteness. Approximately 35% of the total Aboriginal and Torres Strait Islander population have one or more of CKD, diabetes or cardiovascular disease ^[1, 5]. Sixty-four percent of the total burden of disease among Aboriginal and Torres Strait Islander Australians is due to chronic diseases ^[50], and these diseases tend to appear at a younger age, progress faster, co-occur more frequently with other chronic diseases and cause more premature death in Aboriginal and Torres Strait Islander Australians compared to non-Indigenous Australians ^[128]. By middle age, most Aboriginal and Torres Strait Islander Australians have CKD, diabetes or cardiovascular disease, and most ultimately have multiple conditions.

Aboriginal and Torres Strait Islanders adults are approximately twice as likely as non-Indigenous Australian adults to have any stage of CKD (22% compared to 10%) and are 3.6 times more likely than non-Indigenous Australians to have diabetes (18% versus 5%) ^[129]. These disparities are greatest for the 25-54 year age group (see Figure 37) ^[129].

Aboriginal and Torres Strait Islander adults also have higher rates of cardiovascular disease compared to non-Indigenous Australians (26.5% versus 20.7%) ^[5]. This disparity is greatest for the 18-34 age group: Aboriginal and Torres Strait Islander Australians aged 18-34 are 2.5 times more likely to have CVD compared to non-Indigenous Australians (8.6% versus 3.9%) ^[5]. In addition, Aboriginal and Torres Strait Islander Australians continue to have a high occurrence of rheumatic heart disease, a condition that is caused by delayed complications of acute rheumatic fever as a result of infection by Group A streptococcus bacteria ^[128]. Rarely reported in the non-Indigenous population, there were over 2000 cases of rheumatic heart disease registered between 2010 and 2013 in Aboriginal and Torres Strait Islander Australians living in Queensland, the Northern Territory or Western Australia ^[5].

Aboriginal and Torres Strait Islander Australians experience higher rates of comorbid CKD, diabetes and cardiovascular disease compared to non-Indigenous Australians

In addition to a higher prevalence of CKD, diabetes and cardiovascular disease compared to the non-Indigenous population, Aboriginal and Torres Strait Islander Australians are more likely to experience complications of these conditions and to have higher rates of comorbid disease ^[5]. Of the 35% of Aboriginal and Torres Strait Islander adults with CKD, diabetes or cardiovascular, approximately 38% have more than one of these conditions and approximately 11% have all three. For Aboriginal and Torres Strait Islander Australians over 65 years, the proportion with one or more of CKD, diabetes and/or cardiovascular disease exceeds 50%, of which approximately 19% have all three conditions ^[5].

Among Aboriginal and Torres Strait Islander adults with diabetes, approximately 56% have comorbid CKD, compared to 32% of non-Indigenous adults with diabetes. Among adults with cardiovascular disease, approximately 32% have comorbid CKD, compared to 21% of non-Indigenous adults with diabetes ^[5]. Approximately 10% of the adult Aboriginal and Torres Strait Islander population overall have CKD in combination with either diabetes or cardiovascular disease, compared to 5% of the total Australian adult population ^[1, 5]. Approximately 4% of Aboriginal and Torres Strait Islander Australians have all three conditions, compared to 1% of the non-Indigenous population ^[1, 5].

PREVALENCE OF CKD, DIABETES AND CARDIOVASCULAR DISEASE BY INDIGENOUS STATUS, 2011-2013

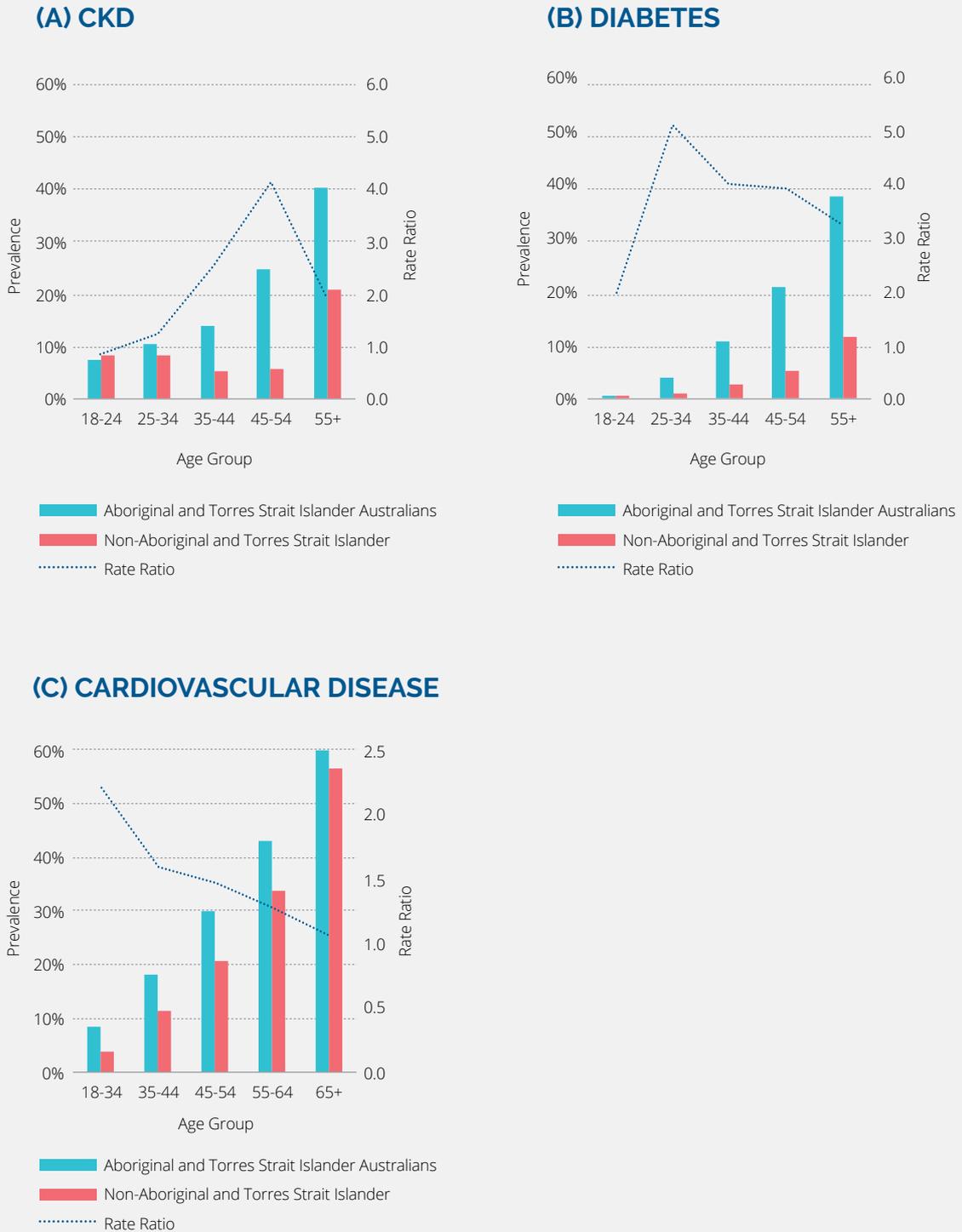


Figure 37: Prevalence of (A) CKD, (B) diabetes and (C) cardiovascular disease, by Aboriginal and Torres Strait Islander status and age group in 2011-2013. The rate ratio is the ratio of prevalence in the Aboriginal and Torres Strait Islander population to the prevalence in the non-Indigenous population within each age strata (Source of CKD and diabetes data: AIHW 2017. Aboriginal and Torres Strait Islander health performance framework 2017: supplementary online tables. Cat. No. WEB 170. Canberra: AIHW; source of CVD data: AIHW 2015. Cardiovascular disease, diabetes and chronic kidney disease – Australian facts: Aboriginal and Torres Strait Islander people. Canberra, 2014).

Social determinants of health account for much of the disparity in disease burden

The high rates of CKD, diabetes and cardiovascular disease among Aboriginal and Torres Strait Islander Australians are attributable to complex interactions between medical, social, behavioural, psychological, epigenetic, economic and environmental factors. These include younger age of onset of underlying disease, poor glycaemic control, problems with access to medical care, insufficient support for diabetes self-care, socioeconomic factors and psychological stressors [130, 131].

These factors have a cumulative impact on health outcomes across the life-course, beginning in utero. For Aboriginal and Torres Strait Islander people living in remote and outer regional parts of Australia, there are the additional issues of food security and the complexities of delivering health services to geographically isolated areas.

An estimated 39% of the gap in health outcomes between Aboriginal and Torres Strait Islander Australians and non-Indigenous Australians can be explained by social determinants [50]. Figure 38 shows the relationship between selected social and psychological determinants of health and the prevalence of self-reported CKD among Aboriginal and Torres Strait Islander adults [50]. For each of the indicators shown, greater disadvantage and higher stress levels are linked with higher prevalence of self-reported CKD.

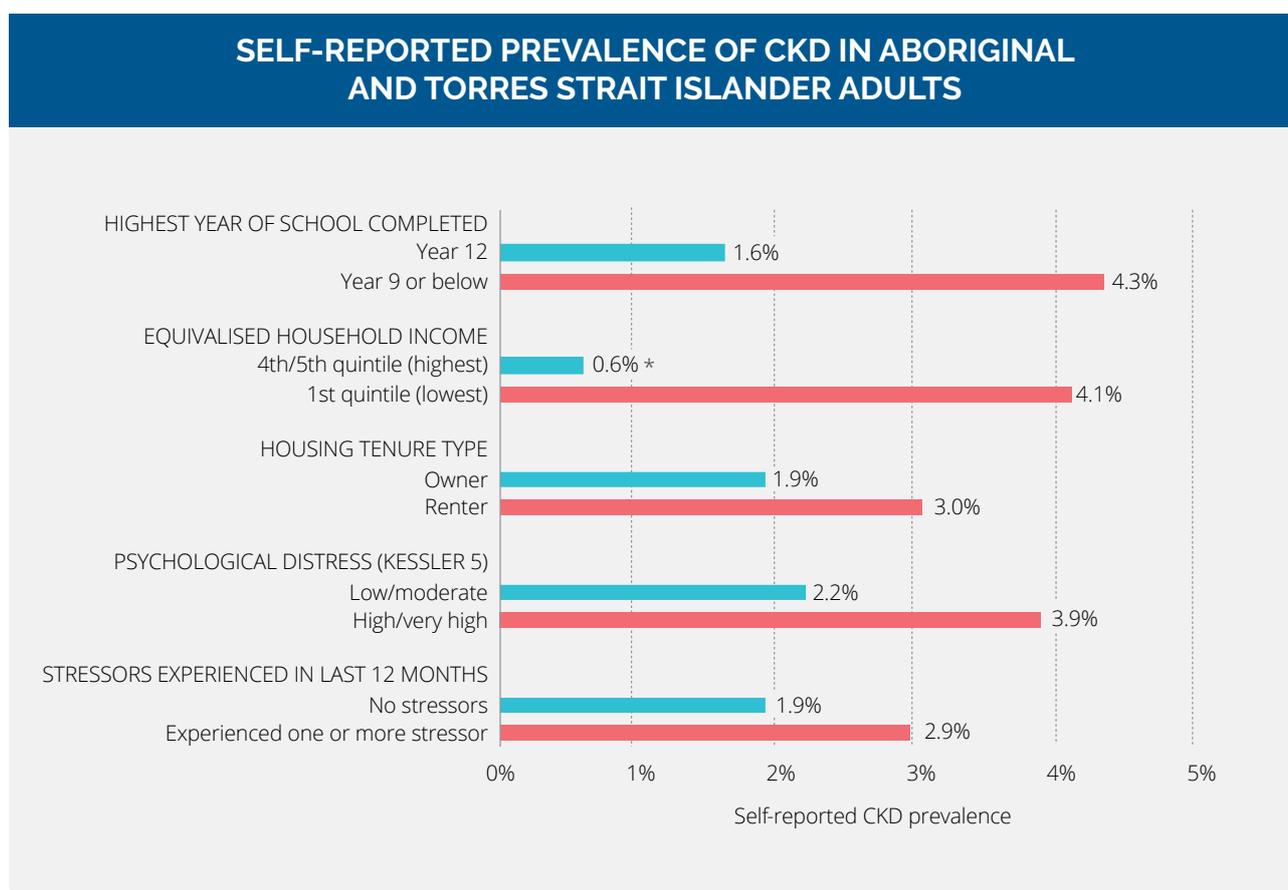


Figure 38: Self-reported prevalence of CKD among Aboriginal and Torres Strait Islander Australians 18 years and older, by selected social determinants of health, 2012-13 (Source: AIHW and ABS analysis of Australian Aboriginal and Torres Strait Islander Health Survey 2012-13 [50]). *Estimate has a relative standard error between 25% and 50% and should be used with caution.

Aboriginal and Torres Strait Islander Australians experience higher rates of all major risk factors CKD, diabetes and cardiovascular disease

Higher rates of lifestyle-related risk factors for CKD, diabetes and cardiovascular disease – in particular higher rates of current smoking (42% versus 16%), insufficient physical activity (60% versus 49% for the 45-54 age group), risky alcohol consumption (51.9% versus 45.3%), and inadequate fruit and vegetable consumption – are an extension of the social, economic and environmental circumstances in which many Aboriginal and Torres Strait Islander Australians live^[5, 50]. Tobacco smoking is a particularly critical modifiable risk factor for the Aboriginal and Torres Strait Islander population, estimated to be responsible for one-third of the total cardiovascular disease burden in Aboriginal and Torres Strait Islander Australians^[132]. In addition, smoking while pregnant (45.8% of Aboriginal and Torres Strait Islander pregnant women versus 11.9% of non-Indigenous pregnant women) is a leading preventable risk factor for adverse birth outcomes, including low birth weight^[50]. The incidence of low birthweight for live-born singleton babies born to Aboriginal and Torres Strait Islander mothers in 2014 was 10.5%, compared to 4.6% for non-Indigenous mothers^[50]. Low birth weight has been linked to subsequent increased risk of CKD in later life^[133].

Lifestyle-related risk factors contribute in turn to high rates of overweight and obesity, high blood pressure, high cholesterol and impaired fasting glucose in the Aboriginal and Torres Strait Islander population. Aboriginal and Torres Strait Islander adults are 1.6 times more likely to be obese, 1.2 times more likely to have high blood pressure, and 1.8 times more likely to have impaired fasting glucose than non-Indigenous people^[5]. These disparities tend to be greatest in younger age groups: in particular, the prevalence of impaired fasting glucose was nearly 4 times higher among 18 to 44 year old Aboriginal and Torres Strait Islander Australians (4.2% versus 1.1%) compared to non-Indigenous people (see Figure 39)^[5].

Lastly, evidence suggests there is a link between childhood trauma and methylation changes in genes regulating stress response, which may increase subsequent risk of developing obesity, diabetes, cardiovascular disease and psychiatric disorders^[134]. These epigenetic modifications are a molecular response to the surrounding environment, which preserve the health of the individual in the short term by upregulating and downregulating genes as necessary for survival (i.e. a 'fight or flight response'). However, when the stressors encountered are chronic, the overactivation of the stress response system in the long term has negative consequences on health and well-being for the individual and across generations.

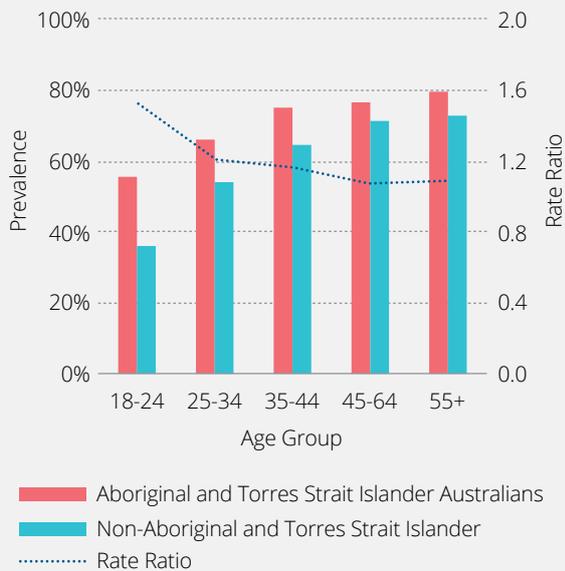
Psychological distress and depression increase the disease burden associated with CKD, diabetes and cardiovascular disease

Aboriginal and Torres Strait Islander Australians experience higher levels of psychological distress, including depression, and are at much higher risk of exposure to stressful life events than non-Indigenous Australians^[135-137]. Thirty percent of Aboriginal and Torres Strait Islander adults report high levels of psychological distress, compared to 11% of non-Indigenous adults^[50].

As discussed in detail in Section 5.1, the presence of depression increases the risk of new onset diabetes and cardiovascular disease. Depression is also a risk marker for worse outcomes of both conditions, including greater likelihood of developing CKD. This is particularly relevant to Aboriginal and Torres Strait Islander Australians, for whom psychological distress and depression are among the consequences of the intergenerational trauma, cumulative stress, disadvantage, marginalisation, oppression, forced separation from family and land and overwhelming sense of loss that are the result of colonisation^[135]. Depressive symptoms in Aboriginal and Torres Strait Islander Australians are also linked to experiences of interpersonal racism^[138]. Numerous studies have demonstrated strong associations between self-reported racism and presence of chronic disease among minority populations of high-income countries^[139-141].

PREVALENCE OF BIOMEDICAL RISK FACTORS FOR CKD, DIABETES AND CARDIOVASCULAR DISEASE

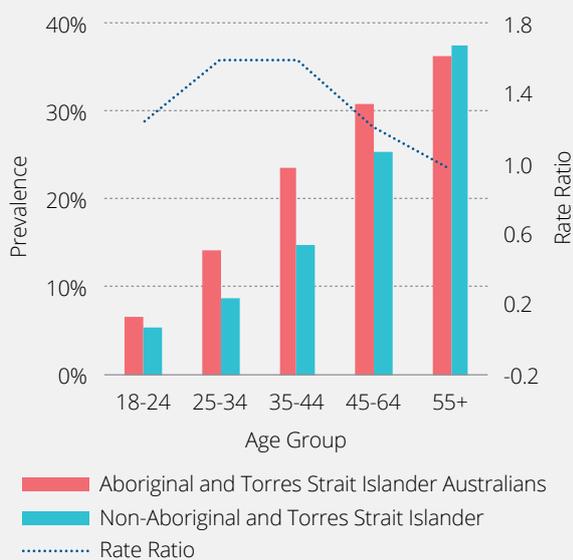
(A) OVERWEIGHT AND OBESITY



(B) DYSLIPIDAEMIA



(C) HIGH BLOOD PRESSURE



(D) IMPAIRED FASTING GLUCOSE



Figure 39: Prevalence of biomedical risk factors for CKD, diabetes and cardiovascular disease: (A) overweight and obesity, (B) dyslipidaemia, (C) high blood pressure, (D) impaired fasting glucose. Data are for the years 2011-13, stratified by age and Aboriginal and Torres Strait Islander status (Source: AIHW 2015. Cardiovascular disease, diabetes and chronic kidney disease – Australian facts: Aboriginal and Torres Strait Islander people. Canberra: AIHW [5])

A survey of Aboriginal men living in urban and remote settings in Central Australia found 4% had possible major depressive disorder, while 40% of the cohort had evidence of depressive symptoms ^[135]. Similarly, a study of the prevalence of depressive disorders among older Aboriginal and Torres Strait Islander Australians living in remote communities in the Kimberley observed a prevalence of depressive disorder of approximately 4% for men and 10% for women, the majority of which was classified as major depression^[142]. In the latter study, depression was found to be more common in persons with CKD, diabetes or heart problems: those with heart problems were 3 times more likely to have depression than those in good cardiovascular health ^[142]. Heart disease has also been linked with high rates of late life depression in Aboriginal Australians ^[143].

Depression has also been found to be more prevalent in Aboriginal people with type 2 diabetes living in metropolitan areas compared to non-Indigenous type 2 diabetes patients, and this depression is more likely to be major and far more likely to be untreated ^[144]. Factors correlated with depression in Aboriginal persons with diabetes include educational attainment, smoking, body mass index, fasting plasma glucose and alcohol use ^[144]. High rates of late life depression are also observed in Aboriginal Australians (18.1%).

Based on our understanding of the bidirectional association between depression and cardiometabolic health in non-Indigenous populations, it is probable that depression is a factor in the high rates of CKD, diabetes and cardiovascular disease observed in the Aboriginal and Torres Strait Islander population, although studies directly linking depression with cardiometabolic disease biomarkers in Aboriginal and Torres Strait Islander persons are not yet available.

Conversely, high rates of CKD, diabetes and cardiovascular disease among Aboriginal and Torres Strait Islander Australians are contributing factors in the high burden of psychological distress experienced by this population.

Aboriginal and Torres Strait Islander Australians living in remote areas experience a disproportionately high burden of disease combined with limited access to primary health care

Aboriginal and Torres Strait Islander adults living in remote areas are more than twice as likely as those living in non-remote areas to have signs of CKD, are twice as likely to have diabetes, and are 1.4 times more likely to have cardiovascular disease ^[5]. Compared to non-Indigenous Australians living in remote areas, Aboriginal and Torres Strait Islanders living in remote areas are approximately 5 times as likely to have CKD, nearly 6 times as likely to have diabetes, and 1.4 times as likely to have cardiovascular disease ^[5].

Remoteness is also associated with a higher risk of microvascular complications of diabetes. Compared Aboriginal and Torres Strait Islander Australians with diabetes who live in urban areas, those living in remote areas have a more adverse risk profile with respect to waist-to-hip ratio, HDL-cholesterol, urine albumin-to-creatinine ratio and C-reactive protein ^[131].

The high burden of CKD, diabetes and cardiovascular disease among Aboriginal and Torres Strait Islander Australians living in remote parts of Australia is often met with poor access to primary health care. For many Aboriginal and Torres Strait Islander people living in remote areas, access to primary health care is limited, and high rates of preventable hospitalisations are observed where there is very limited access to primary health-care ^[145].

PREVALENCE OF CKD, DIABETES AND CARDIOVASCULAR DISEASE BY REMOTENESS

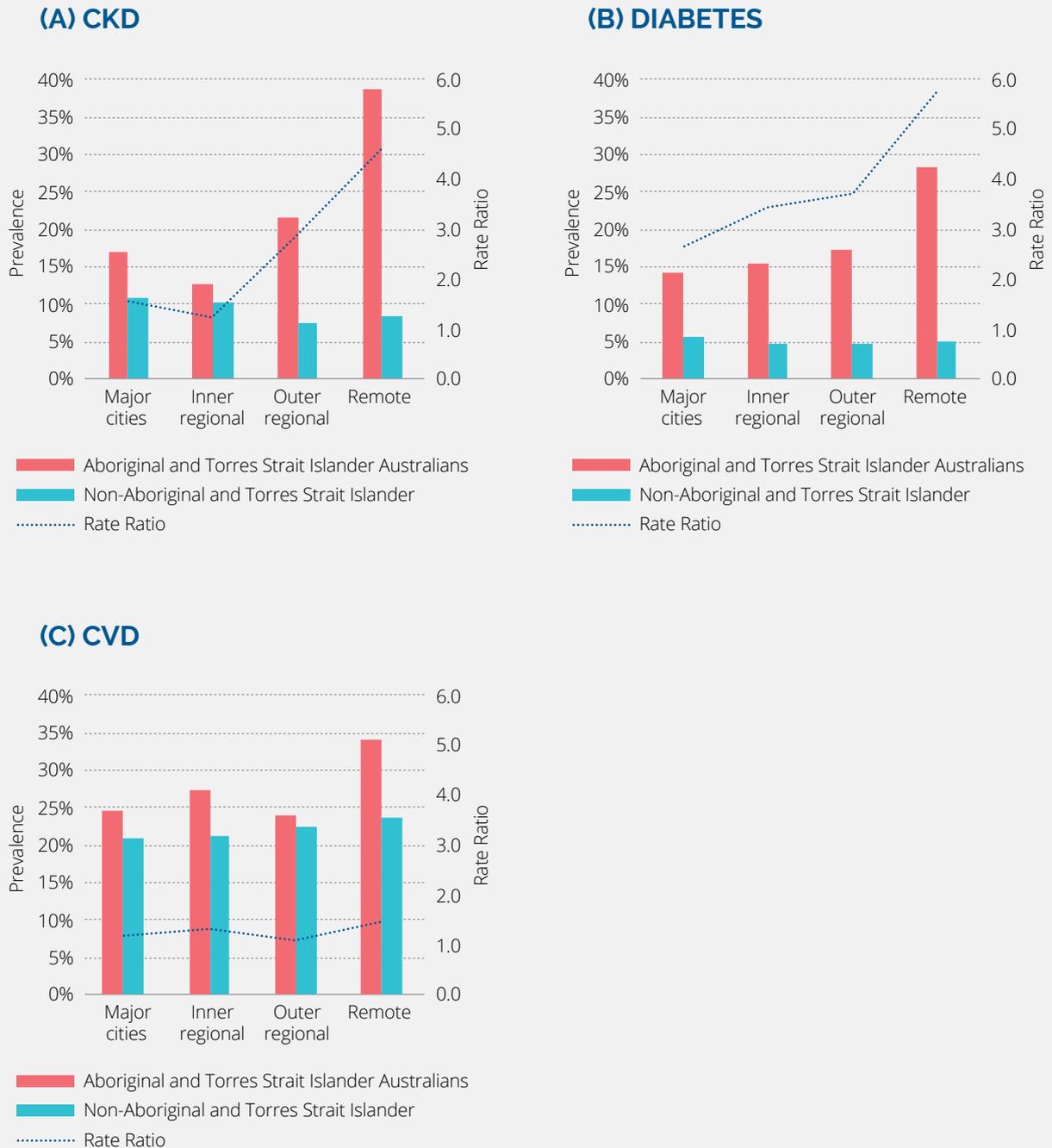


Figure 40: Prevalence of (A) CKD, (B) diabetes and (C) cardiovascular disease, by Aboriginal and Torres Strait Islander status and remoteness in 2011-2013. The rate ratio is the ratio of prevalence in the Aboriginal and Torres Strait Islander population to the prevalence in the non-Indigenous population within each geographical area (Source: AIHW 2017. Aboriginal and Torres Strait Islander health performance framework 2017: supplementary online tables. Cat. No. WEB 170. Canberra: AIHW; and AIHW 2015. Cardiovascular disease, diabetes and chronic kidney disease – Australian facts: Aboriginal and Torres Strait Islander people. Canberra, 2014).

4.2 DISPARITIES IN OUTCOMES OF CKD, DIABETES AND CARDIOVASCULAR DISEASE

4.2.1 Kidney failure

Incidence of kidney failure is far higher among Aboriginal and Torres Strait Islander Australians and occurs at younger ages

At 31 December, 2018, there were 2232 Aboriginal and/or Torres Strait Islander Australians receiving dialysis or living with a kidney transplant ^[45]. Aboriginal and Torres Strait Islander Australians therefore constituted 8.7% of the 25,652 people receiving KRT and 16.9% of the 13,399 people receiving dialysis in 2018, despite making up only 3.3% of the resident Australian population ^[146]. After taking into account differences in age structure between the Aboriginal and Torres Strait Islander and non-Indigenous populations, incidence of treated KF is 7 times higher in Aboriginal and Torres Strait Islander Australians compared to non-Indigenous Australians ^[49]. For Aboriginal and Torres Strait Islander women, incidence of treated KF is more than 11 times higher ^[49].

Onset of KF also occurs at younger ages in the Aboriginal and Torres Strait Islander population compared to the non-Indigenous population. The median age at KRT commencement was 11 years lower among Aboriginal and Torres Strait Islander compared to non-Indigenous Australians in 2018, a disparity which has remained unchanged for the past 20 years (see Figure 41).

The greatest disparity in the incidence of treated KF is in the 45-54 year age group, among whom the incidence of treated KF is more than 11 times higher in Aboriginal and Torres Strait Islander compared to non-Indigenous Australians (Figure 42). For Aboriginal and Torres Strait Islander women, incidence of treated KF among those aged 45-54 is more than 16 times higher compared to non-Indigenous women aged 45-64 years ^[50].

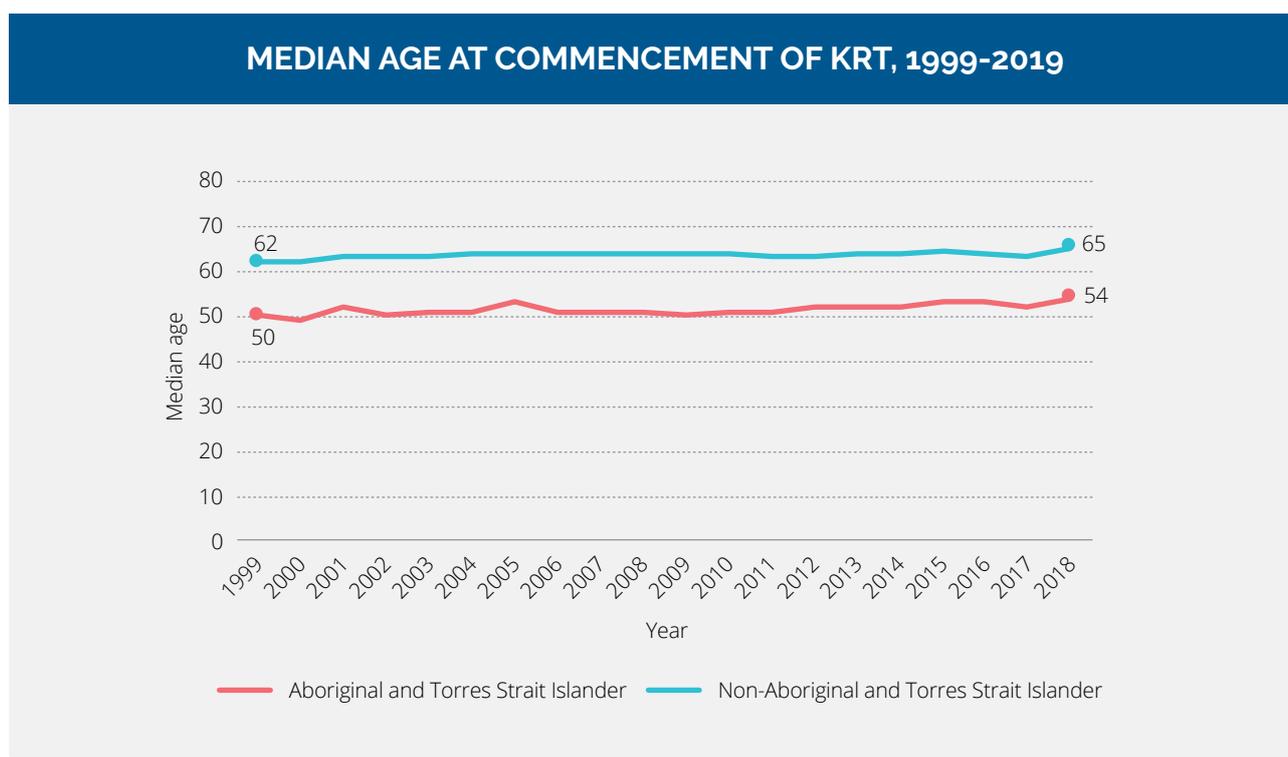


Figure 41: Median age at commencement of KRT by Aboriginal and Torres Strait Islander status, 1999-2019 (Source: unpublished ANZDATA data)

INCIDENCE OF TREATED KF, 2012-2014

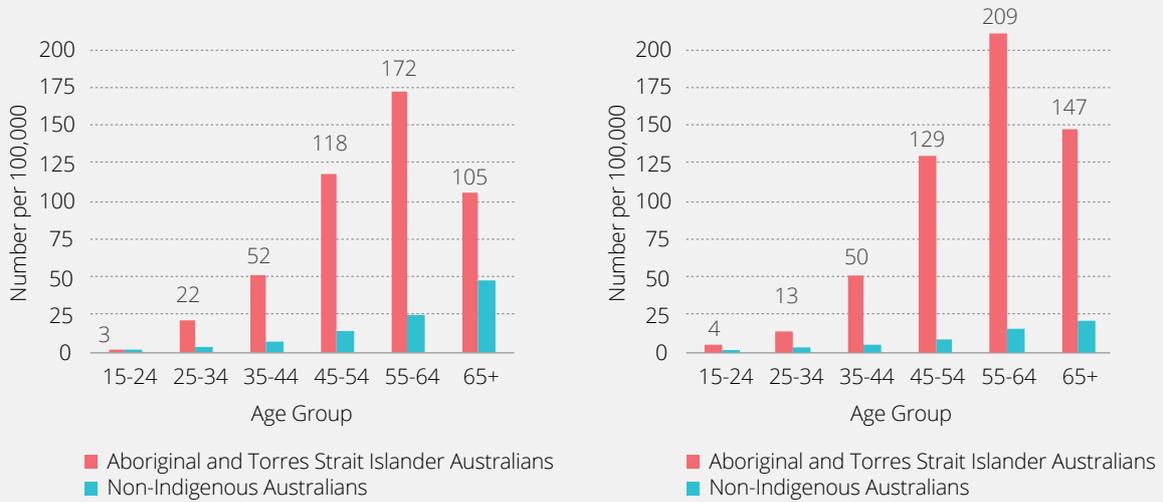


Figure 42: Incidence of treated KF, by age group and Aboriginal and Torres Strait Islander status, 2012-2014 (source: AIHW analysis of ANZDATA data^[50])

High rates of kidney failure among Aboriginal and Torres Strait Islander Australians are due primarily to diabetes

The number of Aboriginal and Torres Strait Islander Australians commencing KRT increased by 79% between 2001 to 2016 (from 174 to 311)^[45]. The majority of these newly treated cases of KF in Aboriginal and Torres Strait Islander Australians were attributable to diabetes (Figure 43). Diabetic nephropathy was recorded as the primary kidney disease of 88% of Aboriginal and Torres Strait Islander Australians commencing KRT between 2016 and 2018, compared to 34% of non-Indigenous Australians (source: unpublished ANZDATA data).

For Aboriginal and Torres Strait Islander men, the proportion of newly treated KF attributable to diabetes between 2016 and 2018 was 92%, reaching 98% for men aged over 65 years (Figure 44). Seventy-five percent of Aboriginal and Torres Strait Islander women commencing RRT had diabetic nephropathy recorded as their primary kidney disease. The second and third leading causes of KF for Aboriginal and Torres Strait Islander women commencing KRT between 2016 and 2018 were glomerulonephritis (11%) followed by hypertension (6%) (source: unpublished ANZDATA data).

PEOPLE COMMENCING KRT WITH KIDNEY DISEASE CAUSED BY DIABETES



Figure 43: Percentage of people commencing KRT between 2016 and 2018 with diabetes recorded as their primary kidney disease, by age group and Aboriginal and Torres Strait Islander status (Source: unpublished ANZDATA data).

ABORIGINAL AND TORRES STRAIT ISLANDER PEOPLE COMMENCING KRT WITH KIDNEY DISEASE CAUSED BY DIABETES

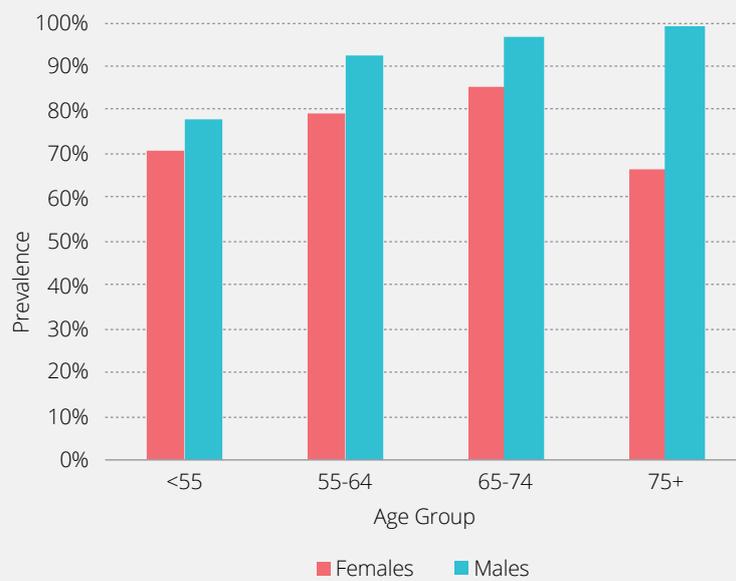


Figure 44: Percentage of Aboriginal and Torres Strait Islander Australians commencing KRT between 2016-2018 with diabetes recorded as their primary kidney disease, by sex (Source: unpublished ANZDATA data).

Disparities in kidney failure prevalence increase dramatically with greater remoteness

The burden of KF among Aboriginal and Torres Strait Islander Australians is significantly greater in remote areas. For Aboriginal and Torres Strait Islander Australians living in remote and very remote areas, prevalence of treated KF is over 3 times higher than for Aboriginal and Torres Strait Islander Australians living major cities [5]. The gap between Aboriginal and Torres Strait Islander and non-Indigenous Australians with respect to the prevalence of treated KF also widens dramatically with increasing remoteness [5]. Aboriginal and Torres Strait Islander Australians living in remote and very remote areas are approximately 13 times more likely to be receiving treatment for KF compared to non-Indigenous residents (see Figure 45).

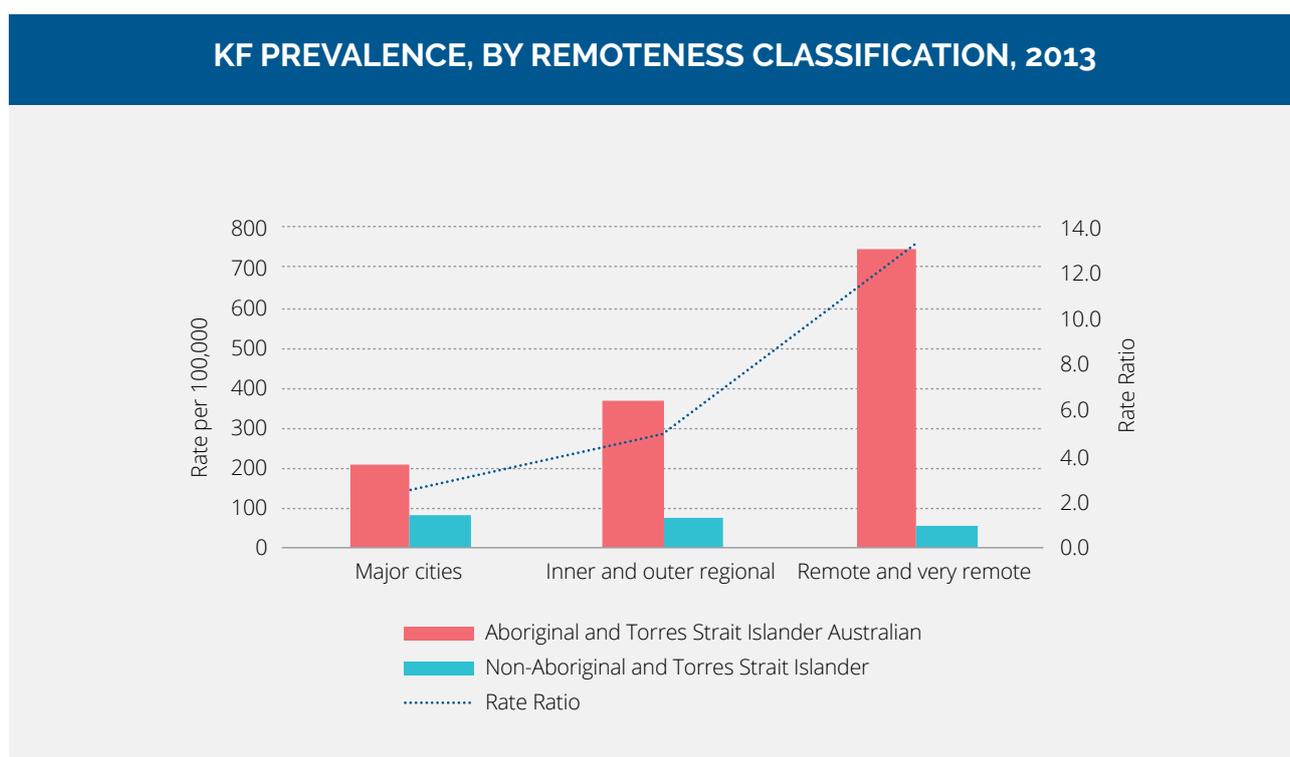


Figure 45: Age-standardised prevalence of treated KF by Aboriginal and Torres Strait Islander status and remoteness, 2013 (Source: AHIW 2015. Cardiovascular disease, diabetes and chronic kidney disease – Australian facts: Aboriginal and Torres Strait Islander people. Canberra, 2014 [5]).

The size of the Aboriginal and Torres Strait Islander population receiving treatment for kidney failure is growing

Prevalence of treated KF has been increasing more rapidly in the Aboriginal and Torres Strait Islander population over the past two decades compared to the non-Indigenous population (see Figure 46). The number of Aboriginal and Torres Strait Islander Australians receiving KRT increased 3-fold between 2006 and 2018, from 763 to 2232 [45]. Over the same interval, KRT numbers in the non-Indigenous population approximately doubled, from 11,651 to 23,420 [45]. Much of this growth in KRT prevalence occurred in the Northern Territory, Queensland and Western Australia (see Figure 47). Of the 2232 Aboriginal and Torres Strait Islander Australians receiving KRT at the end of 2018, 78% were receiving treatment in either the Northern Territory, Queensland or Western Australia [45].

The growth of the Aboriginal and Torres Strait Islander population receiving treatment for KF is being driven by reduced cardiovascular mortality, increasing incidence of KF – especially due to diabetic nephropathy – the provision of dialysis service in more remote areas, and improved survival while receiving dialysis^[147]. Consistent with trends in the non-Indigenous population, age-standardised deaths from cardiovascular disease as the underlying cause declined among Aboriginal and Torres from 386.5 per 100,000 population in 2001 to 165 per 100,000 population in 2015^[50]. While this is a positive development, the reduction in competing risk means that more individuals will survive for longer and go on to develop KF requiring treatment.

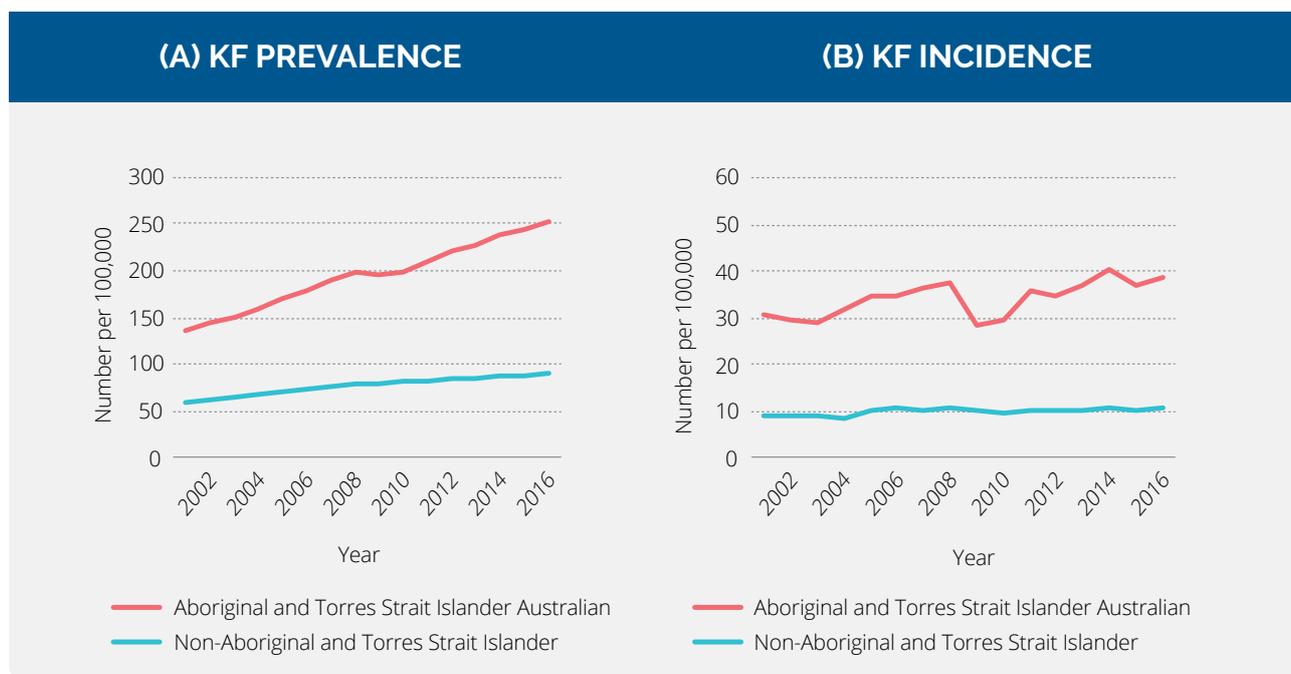


Figure 46: Trends in (A) prevalence and (B) incidence of KF in the Aboriginal and Torres Strait Islander and non-Indigenous Australian population, from 2001 to 2016. Numbers are crude prevalence rates based on the estimated Aboriginal and Torres Strait Islander and non-Indigenous population in each calendar year (source: ANZDATA 42nd Annual Report 2019; ABS Australian Historical Population Statistics 2016 cat. No. 3105.0.65.001; ABS Estimates and Projections, Aboriginal and Torres Strait Islander Australians, 2006-2031 cat. No. 3238.0)

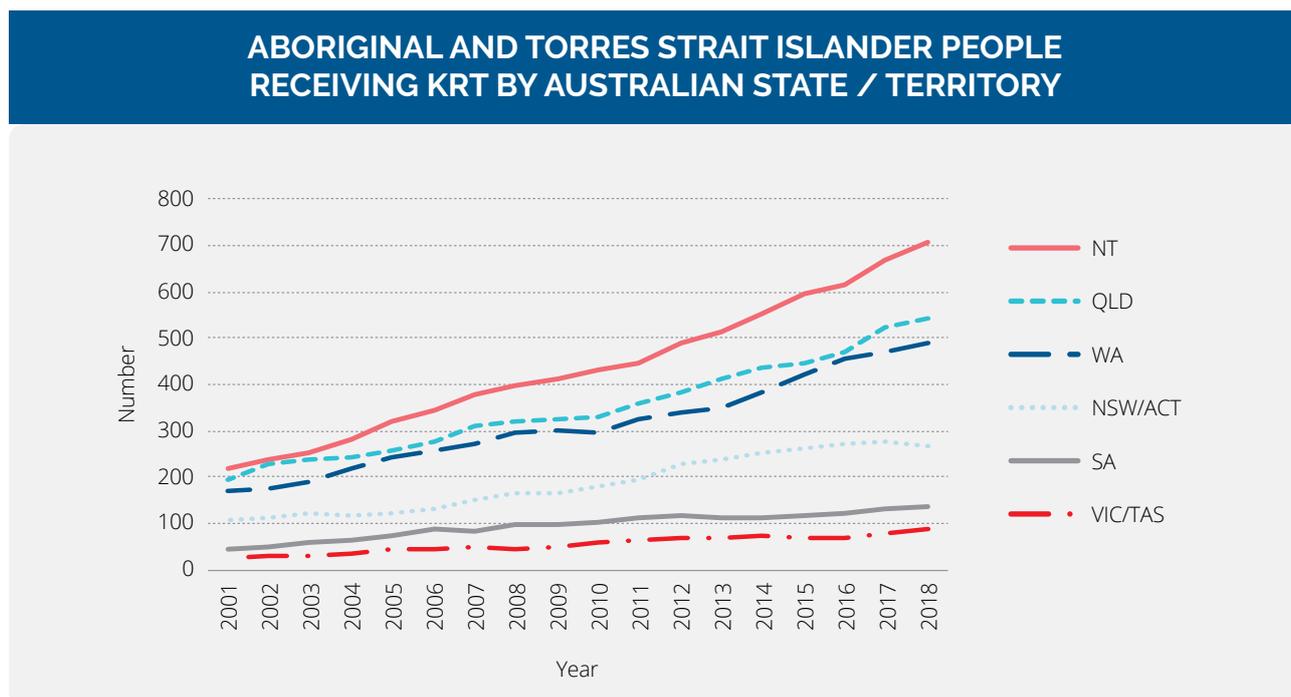


Figure 47: Number of Aboriginal and Torres Strait Islander Australians receiving KRT at 31 December of each year, by state/territory (Source: ANZDATA 42nd Annual Report 2019).

Aboriginal and Torres Strait Islander people with kidney failure are less likely to be wait-listed for transplantation

Aboriginal and Torres Strait Islander Australians with KF are far less likely to be waitlisted for and receive a transplant than non-Indigenous Australians [148]. In 2018, 87% of Aboriginal and Torres Strait Islander KRT recipients were being treated with dialysis while only 13% were alive with a functioning transplant; by comparison, 51% of non-Indigenous KRT recipients were being treated with dialysis in 2018 and 49% were alive with a functioning transplant [45]. Growth of the Aboriginal and Torres Strait Islander KF population has predominantly resulted in the expansion of the number of Aboriginal and Torres Strait Islander people who are dialysis dependent (Figure 48).

The principal barrier to transplantation for Aboriginal and Torres Strait Islander Australians is access to the kidney transplantation waiting list in the first year of KRT [148]. An Aboriginal or Torres Strait Islander KF patient aged 30 years or younger living in a major city has less than half the likelihood of being wait-listed for a kidney transplant in the first year of KRT compared to a non-Indigenous patient with similar characteristics [148]. The likelihood of wait-listing for transplantation falls with older age and greater remoteness: Aboriginal and Torres Strait Islander KF patients aged 60 years and older living in remote areas have approximately 10% the chance of a non-Indigenous patient of being waitlisted for transplantation in the first year of KRT [148]. The reasons for this are logistical and cultural. Living further from major centres presents challenges for pre-transplant assessment, while patients from remote areas may spend their first year of dialysis focused on the challenges of relocation and adjusting to treatment [148]. Greater remoteness is also related to wider cultural differences, greater communication challenges, and greater divergence in concepts of health [149].

Late referral, being female, obesity, presence of comorbid conditions, smoking and primary kidney disease are also factors associated with reduced likelihood of being waitlisted for kidney transplantation among Aboriginal and Torres Strait Islander KF patients [148]. Aboriginal and Torres Strait Islander KF patients with comorbid diabetes are the least likely to be wait-listed for transplantation. Given that diabetic nephropathy was the primary kidney disease in 88% of Aboriginal and Torres Strait Islander Australians commencing KRT between 2016 and 2018, this has significant implications for access to kidney transplantation for Aboriginal and Torres Strait Islander KF patients.

The 2019 Transplantation Society of Australia and New Zealand (TSANZ) Performance Report “Improving Access to and Outcomes of Kidney Transplantation for Aboriginal and Torres Strait Islander People In Australia” provides a detailed analysis of the reasons for this disparity in access to transplantation and recommendations for action [150].

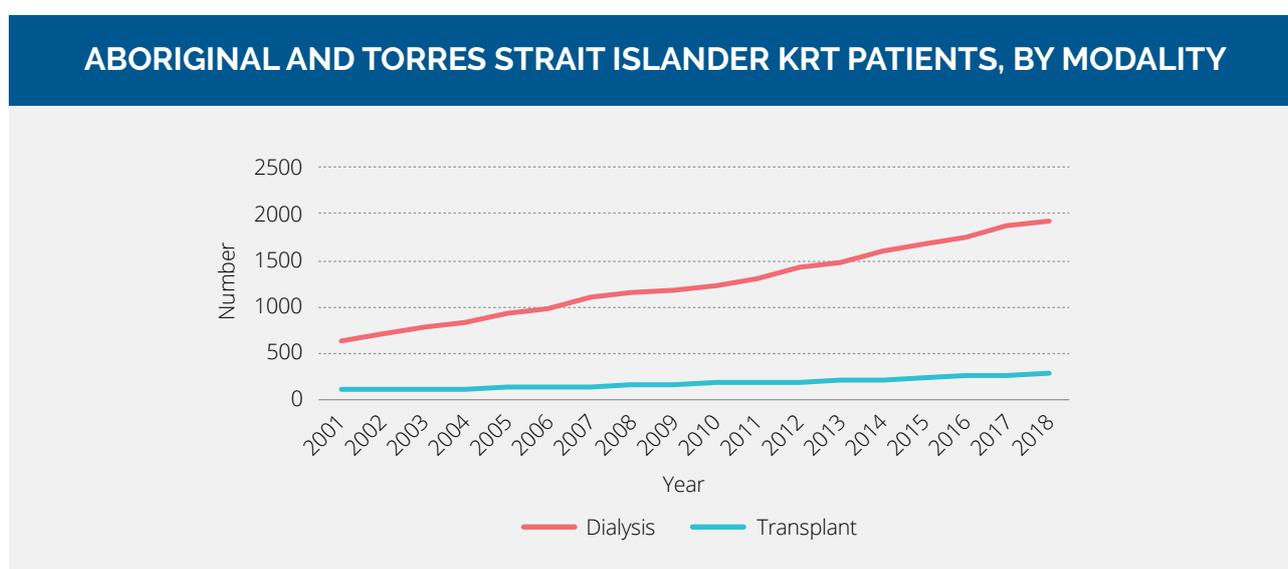
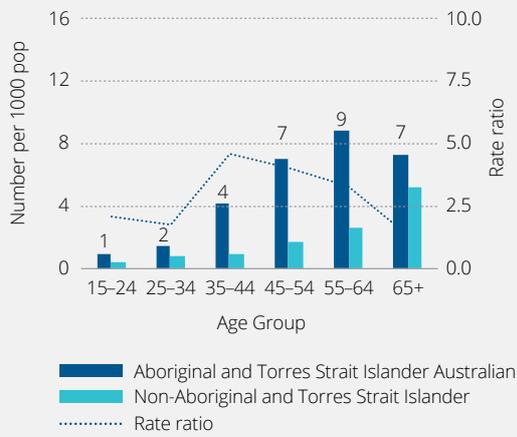
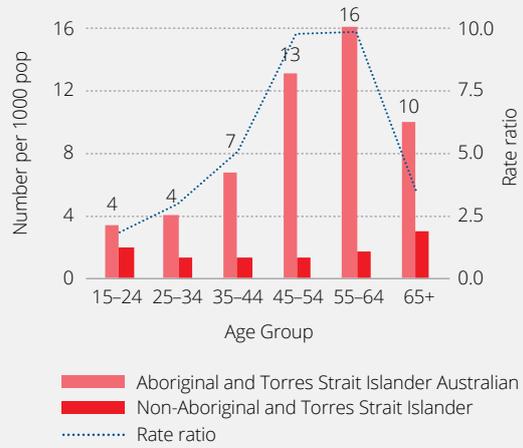


Figure 48: Prevalent number of Aboriginal and Torres Strait Islander KRT patients by treatment modality, 2001-2018 (source: ANZDATA 42nd Annual Report 2019).

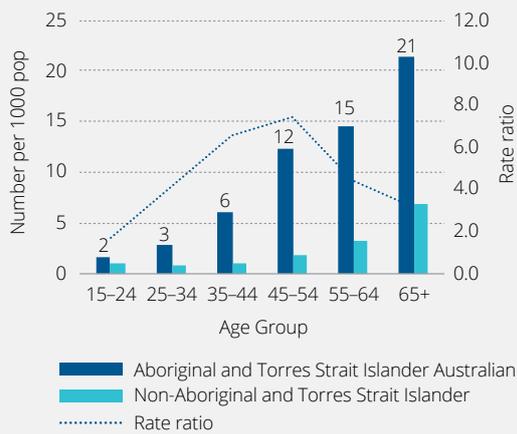
(A) CKD HOSPITALISATIONS: MALES



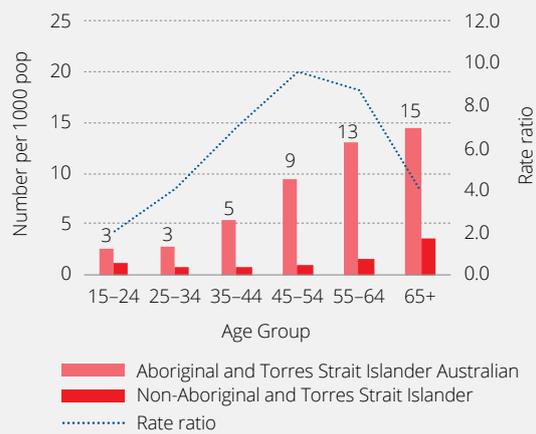
(B) CKD HOSPITALISATIONS: FEMALES



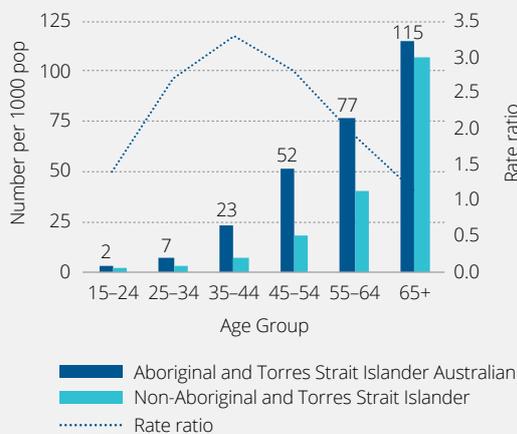
(C) DIABETES HOSPITALISATIONS: MALES



(D) DIABETES HOSPITALISATIONS: FEMALES



(E) CVD HOSPITALISATION: MALES



(F) CVD HOSPITALISATIONS: FEMALES

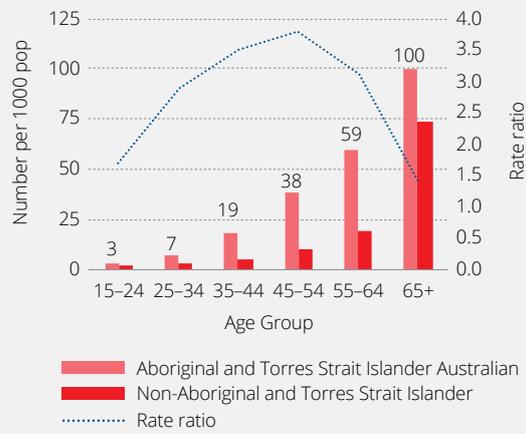


Figure 49: Age-specific hospitalisation rates (per 1000 population) for a principal diagnosis of CKD (A, B), diabetes (C,D) and cardiovascular disease (E,F), by age, sex and Aboriginal and Torres Strait Islander status, July 2013 to June 2015. Source: AIHW analysis of National Hospital Morbidity Database [50].

4.2.2 Hospitalisation

Aboriginal and Torres Strait Islander Australians are more likely to be hospitalised for CKD, diabetes or cardiovascular disease and hospitalisation rates increase with greater remoteness

Rates of hospitalisation for CKD, diabetes and cardiovascular disease are all significantly higher among Aboriginal and Torres Strait Islander Australians compared to the non-Indigenous population. These disparities are widest for adults in the 35-64-year age group (see Figure 49).

The gap between Aboriginal and Torres Strait Islander and non-Indigenous Australians with respect to CKD, diabetes and cardiovascular hospitalisations also widens with greater remoteness (see Table 3). Non-dialysis hospitalisations for CKD as the principal or additional diagnosis were 2.7 times higher for Aboriginal and Torres Strait Islander Australians living in major cities than for non-Indigenous people in 2013-2014; for Aboriginal and Torres Strait Islander people living in remote and very remote areas, non-dialysis hospitalisations for CKD were 13 times higher than for non-Indigenous people ^[5].

Age-standardised hospitalisation rates for type 2 diabetes as the principal or additional diagnosis, were 2.2 times higher among Aboriginal and Torres Strait Islander people living in remote areas compared to Aboriginal and Torres Strait Islander people living in major cities in 2013-14 ^[5]. Compared to the non-Indigenous population living in remote areas, the age-standardised rate of hospitalisation for type 2 diabetes was more than 8 times higher among Aboriginal and Torres Strait Islander people ^[5].

Table 3: Hospitalisation rate ratios for Aboriginal and Torres Strait Islander Australians compared to non-Indigenous Australians, by reason for hospitalisation and remoteness category, 2013-2014 [5]

Reason for hospitalisation	Rate ratio*		
	Major city	Inner and Outer regional	Remote/very remote
Dialysis	6.32	11.54	75.13
Non-dialysis CKD (principal or additional diagnosis)	2.72	4.15	13.38
Type 2 diabetes (principal or additional diagnosis)	3.22	3.60	8.41
Cardiovascular disease (principal diagnosis)	1.41	1.67	2.13

* hospitalisation rate for Aboriginal and Torres Strait Islander Australians divided by the rate for non-Indigenous Australians

Diabetes and cardiovascular hospitalisations among Aboriginal and Torres Strait Islander Australians frequently involve CKD

A large proportion of hospitalisations for diabetes and cardiovascular disease in Aboriginal and Torres Strait Islander people involve comorbid CKD. Of hospitalisations for diabetes among Aboriginal and Torres Strait Islander Australians aged 25 years and older in 2013-2014, 30% recorded an additional diagnosis of CKD (excluding dialysis hospitalisations). The corresponding proportion in non-Indigenous Australians

was 18%^[5]. Of hospitalisations for cardiovascular disease among Aboriginal and Torres Strait Islander Australians aged 25 years and older in 2013-14, 42% recorded an additional diagnosis of CKD (excluding dialysis), compared to 18% of non-Indigenous Australians ^[5].

Of non-dialysis hospitalisations of Aboriginal and Torres Strait Islander Australians aged 25 years and older in 2013-2014 where CKD, diabetes or cardiovascular disease were listed as a principal or additional diagnosis, 18% recorded all three diseases (see Figure 50). By comparison, only 7% of non-Indigenous hospitalisations for CKD, diabetes or cardiovascular disease listed all three diseases ^[5].

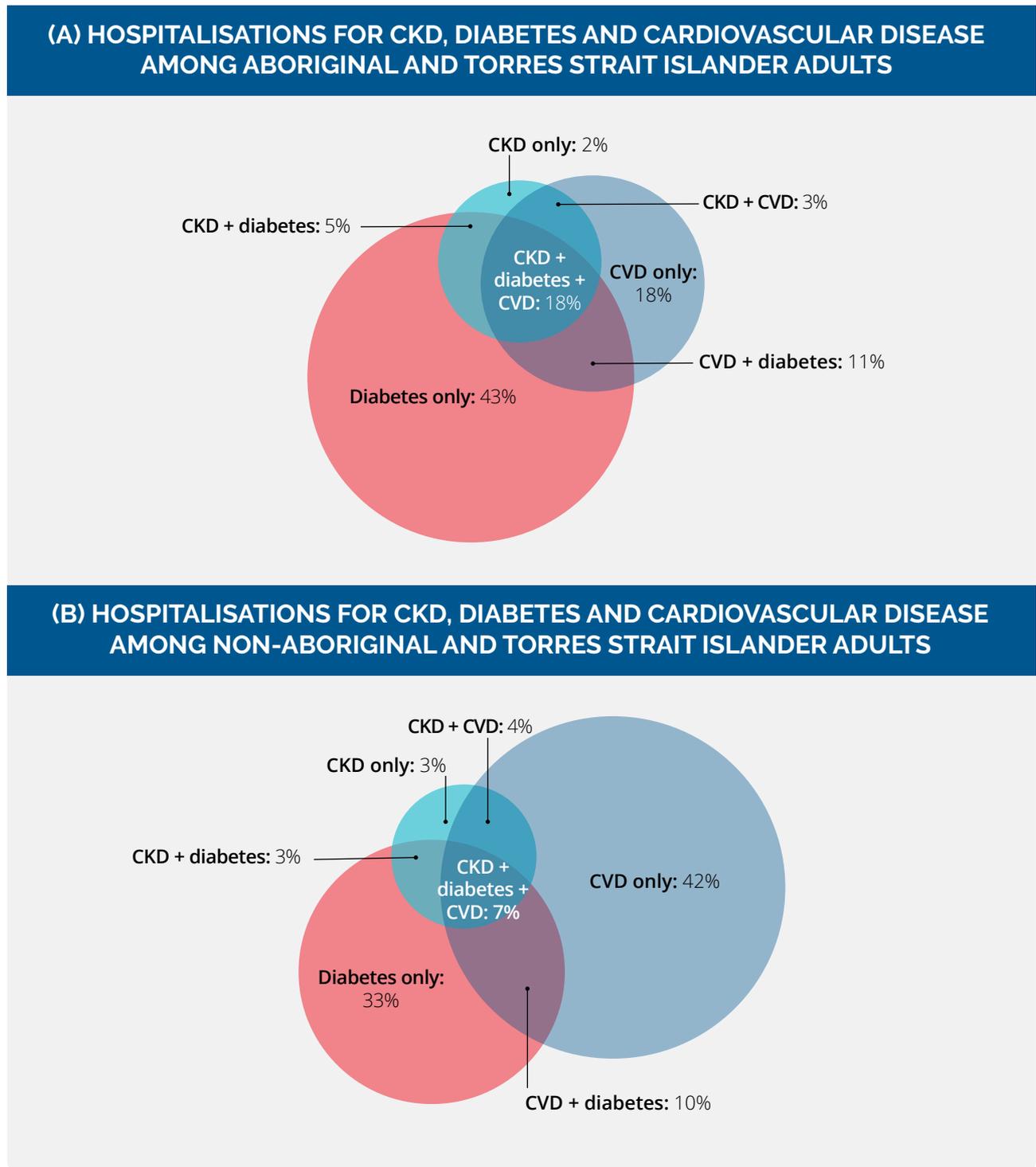


Figure 50: Hospitalisations (excluding regular dialysis) for (A) Aboriginal and Torres Strait Islander adults aged 25 years and older and (B) non-Aboriginal and Torres Strait Islander adults aged 25 years and older with a diagnosis of one or more of CKD, diabetes and cardiovascular disease, 2013-2014 (Source: and AIHW 2015. Cardiovascular disease, diabetes and chronic kidney disease – Australian facts: Aboriginal and Torres Strait Islander people. Canberra, 2014^[5]).

More than one third of all hospitalisations of Aboriginal and Torres Strait Islander Australians are for regular dialysis

Reflecting the disproportionately high rate of KF in the Aboriginal and Torres Strait Islander population and ongoing disparities in access to kidney transplantation, regular dialysis hospitalisations in 2016-17 were 6.3 times more frequent among Aboriginal and Torres Strait Islander compared to non-Indigenous Australians (crude rate of 31,494 versus 4,953 per 100,000 population) ^[49]. After adjusting for the differences in age structure between the Aboriginal and Torres Strait Islander and non-Indigenous population, Aboriginal and Torres Strait Islander Australians are 12 times more likely to be hospitalised for dialysis than non-Indigenous Australians ^[49].

Regular dialysis hospitalisations accounted for 34% of all hospitalisations of Aboriginal and Torres Strait Islander people in 2017, compared to 6.7% of all hospitalisations of non-Indigenous Australians ^[49, 50]. Again, rates of hospitalisation for dialysis among Aboriginal and Torres Strait Islander Australians increase with greater remoteness. The age-standardised hospitalisation rate for dialysis was 2.6 times higher for Aboriginal and Torres Strait Islander people living in remote areas compared to those living in major cities in 2013-2014 ^[5].

DIALYSIS HOSPITALISATION RATES BY ABORIGINAL AND TORRES STRAIT ISLANDER STATUS, AGE AND SEX

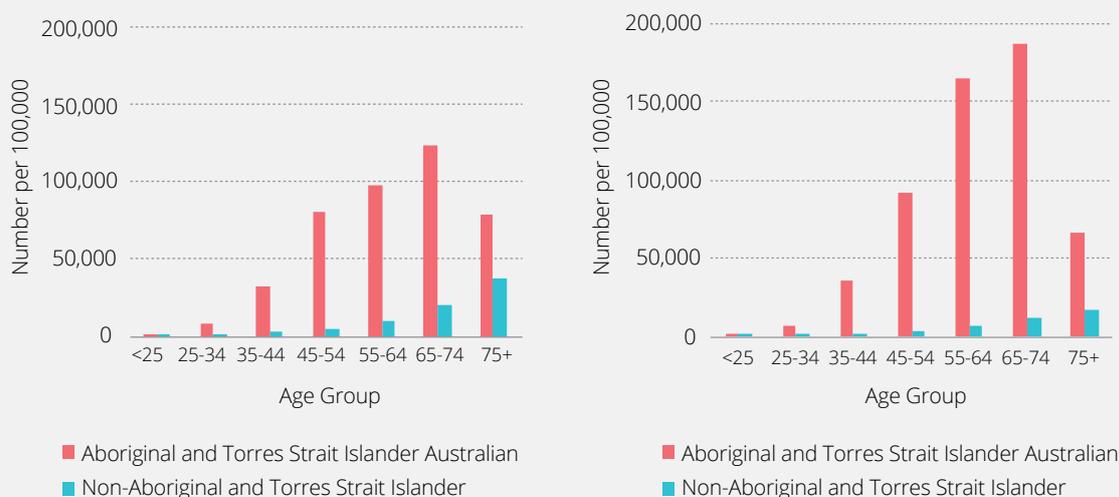


Figure 51: Dialysis hospitalisation rates (principal diagnosis) per 100,00 population, by Aboriginal and Torres Strait Islander status, age and sex, 2013-2014 Source: AIHW analysis of National Hospital Morbidity Database ^[50].

4.2.3 Mortality

Aboriginal and Torres Strait Islander Australians are more likely to die from CKD, diabetes or cardiovascular disease than non-Indigenous Australians

Cardiovascular disease is the leading cause of death in the Aboriginal and Torres Strait Islander population, and was the underlying cause of approximately a quarter of all deaths in Aboriginal and Torres Strait Islander people between 2011 and 2015 ^[50]. Premature deaths from cardiovascular causes are the biggest contributor to the mortality gap between Aboriginal and Torres Strait Islander and non-Indigenous Australians, accounting for approximately a quarter of this disparity ^[128]. In 2016-17, the age-standardised cardiovascular death rate was 1.8 times higher in Aboriginal and Torres Strait Islander Australians compared to the non-Indigenous population (262 versus 143 deaths per 100,000 population) ^[3]. For Aboriginal and Torres Strait Islander Australians aged 35-44 years, the cardiovascular death rate was approximately 8 times higher compared to the non-Indigenous population ^[5].

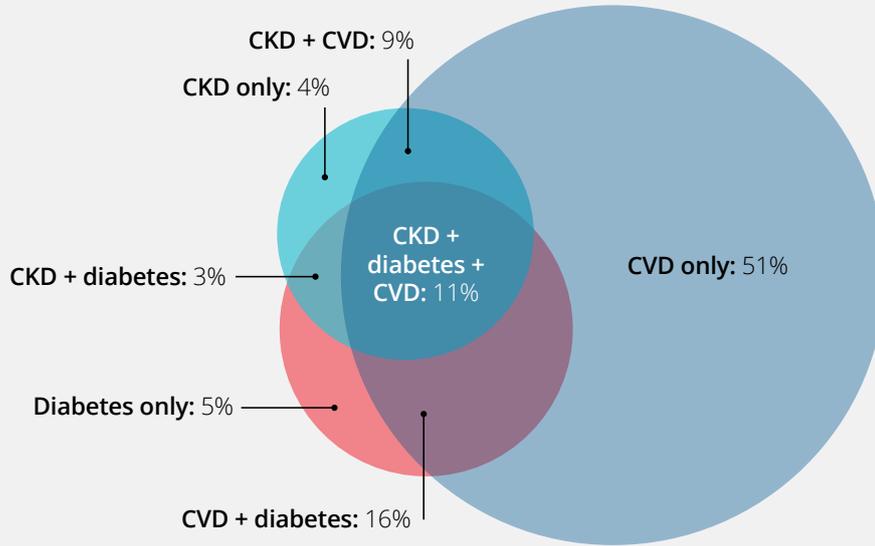
In 2017, Aboriginal and Torres Strait Islander Australians were 3.7 times more likely to have diabetes listed as an underlying or associated cause of death compared to non-Indigenous Australians (age-standardised rate of 201 versus 54 deaths per 100,000 population), and 3.6 times more likely to have CKD listed as an underlying or associated cause of death (age-standardised rate of 197 versus 54 deaths per 100,000 population) ^[49, 92]. Diabetes was the underlying cause of 8% of all deaths in the Aboriginal and Torres Strait Islander population between 2011 and 2015, and an underlying or associated cause in 20% of deaths in Aboriginal and Torres Strait Islander Australians ^[50]. CKD was the underlying cause of 2% of all deaths in the Aboriginal and Torres Strait Islander population between 2011 and 2015, but was an underlying or associated cause in 17% of deaths ^[50]. Disparities in mortality attributable to diabetes and CKD in Aboriginal and Torres Strait Islander compared to non-Indigenous Australians are greatest in the population under 65 years of age ^[5].

CKD, diabetes and cardiovascular disease are frequently listed together on death certificates for Aboriginal and Torres Strait Islander Australians

CKD, diabetes and cardiovascular disease are more commonly listed together on death certificates for Aboriginal and Torres Strait Islander Australians (see Figure 52). In 2010-2012, 23% of all deaths of Aboriginal and Torres Strait Islander people reported any 2 of these diseases as an underlying or associated cause, compared with 14% of non-Indigenous deaths ^[5]. Six percent of all Aboriginal and Torres Strait Islander deaths had all three conditions listed, compared to less than 2% of non-Indigenous deaths.

Of Aboriginal and Torres Strait Islander deaths in 2010-12 where diabetes was an underlying or associated cause, 38% listed CKD as a contributing cause of death. By comparison, 20% of diabetes-related deaths in the non-Indigenous population listed CKD as a contributing cause ^[5]. Of Aboriginal and Torres Strait Islander deaths where cardiovascular disease was an underlying or associated cause, 25% listed CKD as a contributing cause, compared to 14% of cardiovascular deaths among non-Indigenous Australians listing CKD as a contributing cause.

(A) DEATHS WITH CKD, DIABETES OR CARDIOVASCULAR DISEASE AS ASSOCIATED OR UNDERLYING CAUSE - ABORIGINAL AND TORRES STRAIT ISLANDER AUSTRALIANS



(B) DEATHS WITH CKD, DIABETES OR CARDIOVASCULAR DISEASE AS ASSOCIATED OR UNDERLYING CAUSE – NON-ABORIGINAL AND TORRES STRAIT ISLANDER AUSTRALIANS

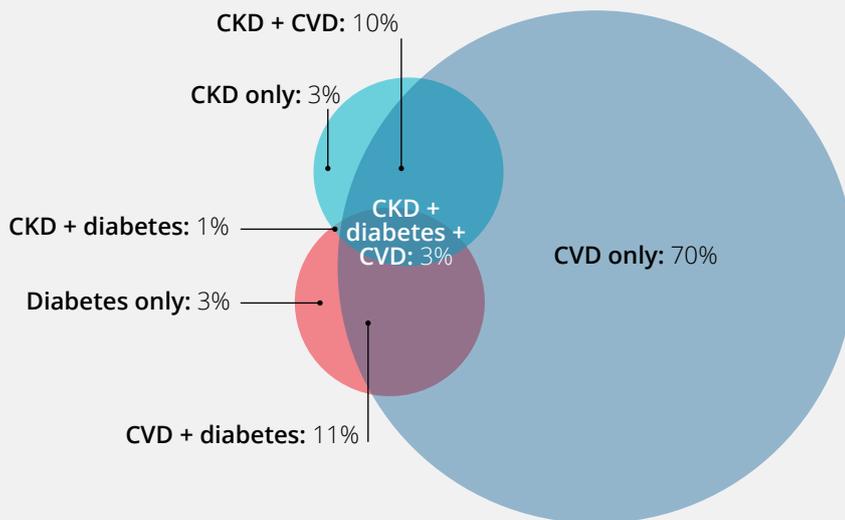


Figure 52: Deaths of (A) Aboriginal and Torres Strait Islander Australians and (B) non-Aboriginal and Torres Strait Islander Australians with CKD, diabetes or cardiovascular disease as the underlying or associated cause, 2010-2012 (Source: and AIHW 2015. Cardiovascular disease, diabetes and chronic kidney disease – Australian facts: Aboriginal and Torres Strait Islander people. Canberra, 2014 ^[5]).

Improvements in cardiovascular mortality

There has been significant improvement in cardiovascular death rates for both the Aboriginal and Torres Strait Islander and non-Indigenous Australian population since 1998, as well as a reduction in the cardiovascular mortality gap between Aboriginal and Torres Strait Islander and non-Indigenous Australians, particularly for females^[5]. The reduction in deaths from chronic disease extends to Aboriginal and Torres Strait Islander Australians living in outer regional, remote and very remote areas^[151].

This shift is largely attributable to improvements in chronic disease diagnosis, monitoring and treatment, and to reductions in rates of smoking and high blood pressure^[98, 101]. Health surveys conducted ten years apart in one high-risk remote Aboriginal community in the Top End of the Northern Territory also observed a decline in low birthweight, improvements in nutrition among youth, better overall health among young adult males (including a significant decline in systolic blood pressure), improved high density lipoprotein (HDL) cholesterol levels and stable or lower levels of albuminuria^[151]. Rates of diabetes, however, had increased, particularly in women and those aged older than 45 years, which is likely to reflect improved survival of middle-aged and older adults with risk factors for diabetes^[151].

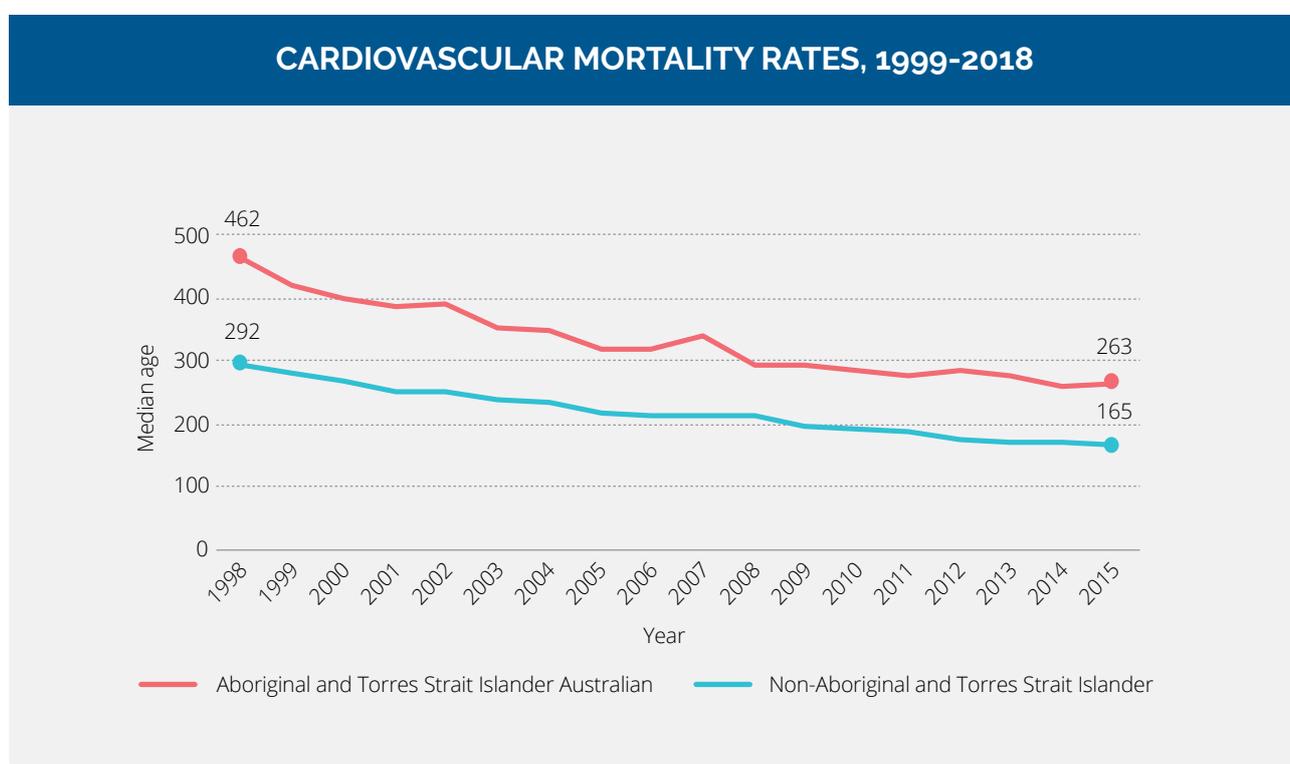


Figure 53: Age-standardised mortality rates from cardiovascular causes (100-199), by Aboriginal and Torres Strait Islander status. Data are for NSW, Queensland, WA, SA and NT only, which are considered to have adequate levels of Aboriginal and Torres Strait Islander identification in mortality data. Data for these jurisdictions over-represent Aboriginal and Torres Strait Islander populations in less urbanised and more remote locations. Rates are age-standardised to the 2001 Australian population. (Source: AIHW 2017. Aboriginal and Torres Strait Islander health performance framework 2017: supplementary online tables. Cat. No. IHW 194. Measure 1.23: Leading causes of mortality^[50]).

4.2.4 Cognitive aging in Aboriginal and Torres Strait Islander Australians

As discussed in Section 5.1, CKD, diabetes and cardiovascular disease all have a strong association with prevalence of cognitive impairment, with this association being mediated by a common set of pathophysiological mechanisms ^[54]. Higher prevalence of CKD, diabetes and cardiovascular disease may therefore also contribute to higher rates of cognitive impairment and dementia among Aboriginal and Torres Strait Islander Australians.

Higher prevalence and earlier onset of cognitive impairment and dementia have been observed in Aboriginal and Torres Strait Islander Australians compared to the non-Indigenous population ^[152, 153]. A study of the prevalence of dementia among Aboriginal adults living in the Kimberley found dementia affected 12.4% of adults aged 45 years and older, while cognitive impairment (not dementia) was observed in 8% ^[154]. Prevalence of dementia increased to 26.8% in those aged over 65 years, and prevalence of cognitive impairment (not dementia) increased to 13.4% ^[154]. Similarly, a study of Aboriginal and Torres Strait Islander adults aged 60 and over living in urban and regional areas observed a prevalence of dementia of 21% ^[155]. By comparison, the estimated prevalence of dementia in the general Australian population aged 45 years and older in 2018 was approximately 3-4% ^[156].

A recent study of risk factors for dementia in Aboriginal and Torres Strait Islander Australians aged 60 years and older living in urban and regional communities in New South Wales found that socioeconomic disadvantage and trauma in childhood, unskilled work, stroke and head injury were associated with presence of dementia ^[152]. Cardiometabolic diseases, including diabetes, hypercholesterolaemia, hypertension and heart disease, were not significantly associated with a dementia diagnosis in this study, however it is possible that the very high prevalence of these conditions precluded the observation of an association ^[152]. Duration of cardiometabolic disease was also not considered. The association between CKD and dementia was not assessed.

More research is needed into the implications of CKD, diabetes, cardiovascular disease and their comorbidity for cognitive aging in Aboriginal and Torres Strait Islander Australians.

4.3 HEALTH SYSTEM CHALLENGES

Addressing the social determinants of health

Underlying social inequalities adversely affect the health of Aboriginal and Torres Strait Islander people across the life course, impacting early childhood development, educational outcomes, employment, income, housing, nutrition, community safety, use of alcohol and other drugs, and numerous other determinants of health ^[5]. These inequalities affect families, communities and the environments in which Aboriginal and Torres Strait Islander people live. They also influence how people interact with the health system and are the necessary framework for understanding and responding to lifestyle risk factors for chronic disease (smoking, physical inactivity, poor nutrition etc).

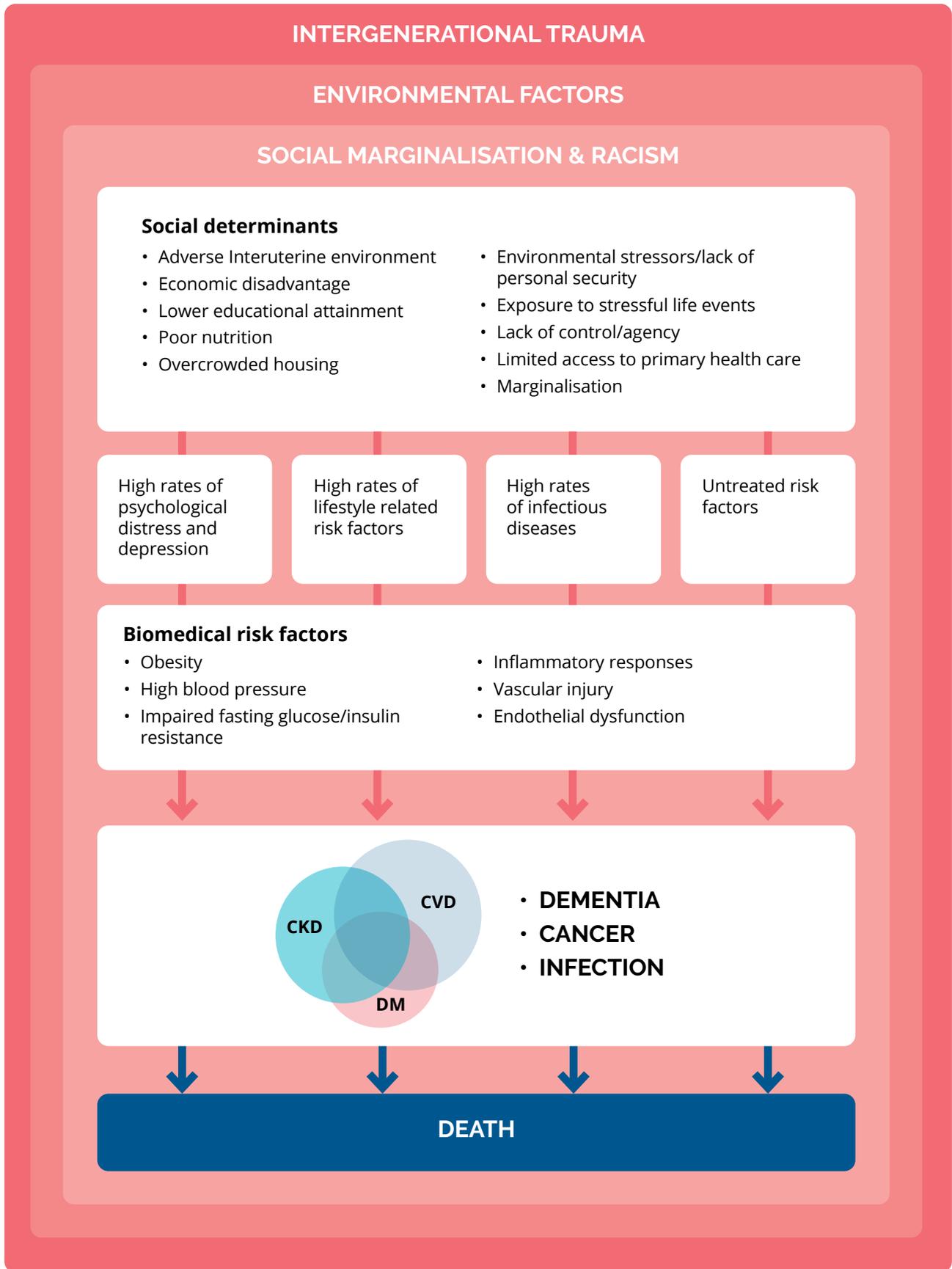


Figure 54: Social determinants of health and pathways to CKD, diabetes and cardiovascular disease in Aboriginal and Torres Strait Islander Australians.

The need for culturally appropriate, integrated approaches to prevention and improved access to primary care

The degree of comorbidity between CKD, diabetes and cardiovascular disease for Aboriginal and Torres Strait Islander people highlights the importance of integrated approaches to disease prevention. For example, interventions to improve cardiovascular outcomes alone do not necessarily reduce the risk of onset of diabetes and CKD. Conversely, diabetes-focused approaches may neglect opportunities to address risk factors for cardiovascular disease and CKD ^[157].

Given the earlier onset of CKD, diabetes, cardiovascular disease and KF in Aboriginal and Torres Strait Islander people, many require treatment interventions in early to mid-adult life, followed by many years of treatment ^[157]. Yet, despite the large burden of complex, multi-morbid chronic disease in the Aboriginal and Torres Strait Islander population, Medical Benefits Schedule claim rates for general practitioner visits were only 5% higher for Aboriginal and Torres Strait Islander people compared to non-Indigenous people in 2013-2014, whereas claim rates for specialist services were 39% lower. Total expenditure on pharmaceuticals per Aboriginal and Torres Strait Islander person was less than half the amount spent per non-Indigenous person ^[5].

A lack of locally available, culturally appropriate and affordable primary health services contributes to the burden of chronic disease, especially for Aboriginal and Torres Strait Islander people living in geographically isolated areas ^[145]. In addition to the distance required to travel to access services, health worker absenteeism has been identified as a major impediment to accessing care and receiving appropriate follow-up ^[157].

Understanding the links between mental health and CKD, diabetes and cardiovascular disease in Aboriginal and Torres Strait Islander people

For Aboriginal and Torres Strait Islander people, health and wellbeing are inextricably linked with the impacts of colonisation, intergenerational trauma, grief, loss and ongoing social marginalisation. Standard tools for assessing psychosocial wellbeing do not sufficiently account for these factors and tend to narrowly focus on objective social, economic and health indicators, with consideration given only to the “sick individual”. In contrast, Aboriginal and Torres Strait Islander concepts of health are more wholistic and take into account family and kinship, social networks, culture and connectedness to country ^[158].

Successful identification and management of depression may decrease the incidence of CKD, diabetes and cardiovascular events in Aboriginal and Torres Strait Islander people ^[142]. Culturally appropriate, community-based strategies for screening for depression in Aboriginal patients with diabetes are needed, as are culturally appropriate, validated psychosocial assessment tools ^[135, 159]. Advancements have been made in recent years, including the development and validation of the Kimberly Indigenous Cognitive Assessment of Depression (KICA-dep) scale and the adapted 9-item Patient Health Questionnaire (aPHQ-9) ^[135, 142, 160-162]. Validated screening tools would permit early detection of depressive symptoms during routine primary care visits. They would also enable much-needed research into the relationships between psychosocial distress, depression and biomarkers for the onset and progression of CKD, diabetes and cardiovascular disease ^[160].

Better social support for Aboriginal and Torres Strait Islander Australians receiving KRT

Separation from country entails significant health, psychosocial and economic consequences for individuals, their families, communities and the wider health and welfare system. At present, there is inadequate support for Aboriginal and Torres Strait Islander patients to assist and support the kidney pathway journey, including emotional and social support for the 78% of Aboriginal and Torres Strait Islander patients who have to relocate to access dialysis and transplant services ^[72].

Improving access to kidney transplantation

In June 2018, the Minister for Indigenous Health, the Hon Ken Wyatt MP, established an expert panel to provide a detailed analysis of the barriers faced by Aboriginal and Torres Strait Islander Australians in accessing and maintaining a kidney transplant. The resulting TSANZ Performance Report: Improving Access to and Outcomes of Kidney Transplantation for Aboriginal and Torres Strait Islander People in Australia makes 35 recommendations and nominates the following key priorities:

1. Establishing a resourced National Indigenous Kidney Transplantation Taskforce to drive policies and programs related to improving transplant access and outcomes (established in 2019)
2. Implement programs to improve access to wait listing, including piloting a patient navigator program and the establishment of multidisciplinary pre- and post-transplant clinics
3. Create a framework for post-transplant monitoring through enhanced data collection and reporting.

The National Strategic Action Plan for Kidney Disease, developed by Kidney Health Australia on behalf of the Australian Government Department of Health, commits to assisting in the implantation of the key priorities of the TSANZ Performance report ^[163].

5

Impact of chronic kidney disease, diabetes and cardiovascular disease on mental health and cognitive outcomes

5.1 INTER-RELATIONSHIPS BETWEEN CKD, DIABETES, CARDIOVASCULAR DISEASE, AND MENTAL HEALTH

Key messages:

Psychosocial factors – depression, quality of life, cognitive impairment – have complex and multidirectional associations with CKD, diabetes and cardiovascular disease.

The association between depression and cardiometabolic disease is partly explained by a higher burden of lifestyle-related risk factors, reduced capacity to adhere to treatment recommendations, and worse self-care. There is also evidence for a direct biological link between depression and the risk of new onset diabetes, cardiovascular disease and, subsequently, CKD.

High levels of depressive symptoms in persons with CKD are linked to reduced quality of life, poor treatment adherence, more rapid decline in kidney function, increased risk of progression to KF, higher rates of hospitalisation, higher rates of dialysis withdrawal, and increased mortality.

Depression is highly prevalent in persons with CKD, diabetes and cardiovascular disease. Depression is both a cause and a symptom of cardiometabolic disease and is a risk factor for the onset of CKD and progression to KF, dementia and death.

There is strong evidence of a relationship between depression and risk and severity of diabetes complications, including CKD.

The presence of CKD worsens the physical symptom burden and exacerbates the psychosocial burden associated diabetes and cardiovascular disease.

Quality of life scores decline with worsening kidney function. As CKD progresses, sleep disorders, pain, and anaemia become increasingly prevalent. Depression affects 20-25% of adults with CKD, and 25-50% of persons receiving dialysis.

CKD, diabetes and CVD also have a strong association with cognitive decline. Loss of cognitive function intensifies the challenges faced by the patient with respect to self-care, adherence to medical regimen, and recognition of critical clinical symptoms such as heart failure or hypoglycaemia.

Prevalence of cognitive impairment in haemodialysis patients is estimated at 30-60%, and is associated with longer hospitalisations, increased health care utilisation, and higher mortality.

Patient-centred treatment approaches that consider both physical and mental health in the context of an individual's social circumstances are key to optimising health outcomes.

The psychosocial burden of CKD extends beyond the individual, to their family and carers.

Prevention and disease management strategies need to prioritise the psychosocial wellbeing and long-term cognitive outcomes of Australians with CKD, diabetes, and cardiovascular disease.

CKD, diabetes and cardiovascular disease: complex relationships with depression, quality of life, and cognitive function

The presence of any one of CKD, diabetes or cardiovascular disease increases the likelihood of having depression and is associated with reduced in quality of life. Depression is highly prevalent in persons with diabetes and cardiovascular disease, and is associated with poor outcomes, including elevated risk of developing CKD [23-25]. The onset of CKD causes further reductions in quality of life, exacerbating the psychosocial burden of diabetes and cardiovascular disease while compounding the physical symptom burden [26, 27, 164]. Comorbid depression increases the risk of progression to KF, due in part to behavioural factors including lower adherence to treatment recommendations [165-168]. There is also some evidence for direct biological mechanisms linking depression with risk of KF [169-171].

Once an individual reaches KF, treatment places a new and significant burden on patients, and is frequently associated with additional stresses such as changes in family dynamics, social isolation, reduced employment and financial insecurity, which in turn further reduce quality of life and increase levels of anxiety and depression [172, 173]. Studies have reported that between 25-50% of dialysis patients have symptoms of depression and 45% have symptoms of anxiety [32]. The psychosocial burden of KF treatment is not limited to the patient, but also extends to their carers and family [174].

In addition, similar biological mechanisms to those involved in the onset and progression of CKD, diabetes and cardiovascular disease have been linked to the development of structural changes in the brain associated with cognitive impairment [54, 56]. CKD, diabetes and cardiovascular disease all have a strong association with presence of cognitive impairment [54], while faster GFR decline has been linked with global cognitive decline and increased risk of incident dementia [56]. Decline in cognitive function intensifies the challenges faced by the patient with respect to self-care, adherence to medical regimen, and maintenance of employment [58, 59]. Low cognitive score has also been linked with an increased risk of death in elderly persons both with and without CKD [60].

CKD, diabetes and cardiovascular disease therefore have a profound impact on mental health through multiple mechanisms. Depression is both a cause and a symptom of cardiometabolic disease and is a risk factor for the onset of CKD and for progression to KF. The onset and progression of CKD vastly increase the psychosocial burden experienced by patients with diabetes or cardiovascular disease. Without intervention, reduced quality of life and depression increase the likelihood of disease progression and the onset of new complications, leading to further reductions in quality of life, cognitive decline, and risk of major depression, which in turn increase the risk of progression to KF, dementia and death.

The growing emphasis on patient-centred care has increased appreciation of the importance of mental health to overall wellbeing and clinical outcomes in CKD, diabetes and cardiovascular disease. Much more work is to be done, however, to establish models of care that account for depression and quality of life as critical determinants of cardiometabolic outcomes and offer appropriate psychosocial support alongside medical treatment for persons with CKD, diabetes and cardiovascular disease [61, 62].

Depression is highly prevalent in people with diabetes

Depression in persons with diabetes is a complex phenomenon resulting from interactions between genetic, biological, psychosocial and socioeconomic factors [175]. Major depressive disorder is approximately twice as prevalent in individuals with type 2 diabetes than in the general population, while depressive symptoms are common [176, 177]. For example, a Canadian study found nearly half of their type 2 diabetes cohort suffered at least one episode of subthreshold depressive symptoms over a 5 year assessment period [178]. The association between diabetes and depression is also bidirectional: depression is associated with increased risk of incident type 2 diabetes [175, 179-182] and diabetes is a risk factor for onset of depression [175, 181, 183].

The association between depressive symptoms and new onset type 2 diabetes is explained in part, though not entirely, by lifestyle factors [182]. Depressed individuals are more likely to be physically inactive [184-189], more likely to have high caloric intake [186], less likely to adhere to weight loss recommendations [186, 190, 191], and more likely to be smokers [184-187, 189]. However, large longitudinal cohort studies have found that the association between depression and incident diabetes persists after adjustment for lifestyle factors and metabolic covariates (fasting insulin and glucose, lipids, blood pressure and adiposity) [186]. It is also possible that this residual association is partly due to confounding by low socioeconomic status, a causal link between antidepressant use and diabetes risk, or weight gain as a result of antidepressant use [186]. There is also growing evidence for a direct biological link between depression and type 2 diabetes [192].

Depression and type 2 diabetes share biological origins

Proposed mechanisms by which depression may be causally associated with diabetes include overactivation of innate immunity leading to a cytokine-mediated inflammatory response and dysregulation of the hypothalamic pituitary-adrenal (HPA) axis [192]. Both depression and type 2 diabetes are associated with increased C-reactive protein, TNF- α and proinflammatory cytokines [193-197]. Depression is also associated with increased activity of the HPA axis and the sympathetic nervous system [198], which results in increased release of cortisol, epinephrine and norepinephrine. Cortisol stimulates glucose production, increases lipolysis and circulating free fatty acids, decreases insulin secretion and decreases insulin sensitivity [198-200]. Epinephrine generates responses in glucose and fat metabolism similar to those of cortisol. Throughout the life-course, these pathways can lead to insulin resistance, cardiovascular disease, depression, increased risk of type 2 diabetes, increased risk of CKD, and increased mortality (see Figure 55).

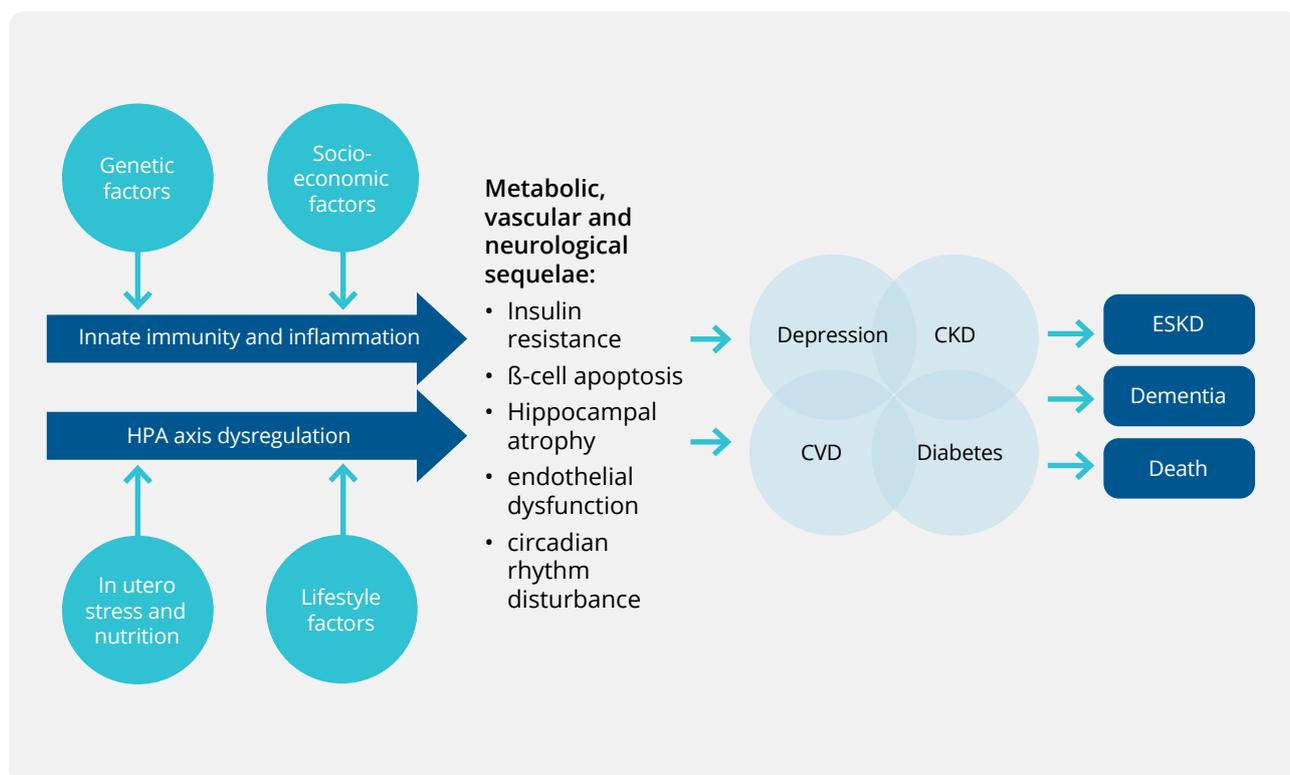


Figure 55: Summary of the proposed biological pathways contributing to the pathogenesis of depression and cardiometabolic disease. Adapted from Moulton et al. [192]

Presence of depression leads to worse outcomes in people with diabetes

Diabetes may also be a cause of new onset depression (see Figure 56). This may relate to the psychological stress associated with diabetes management and the impact of diabetic complications and co-morbidities on quality of life [182, 201, 202]. The presence of depression in individuals with diabetes is associated with reduced quality of life [203], increased symptom burden [204], worse glycaemic control [205], increased health care utilization [206], increased risk and severity of complications [23, 207], functional impairment [208], and increased risk of mortality [207]. There is a consistent documented relationship between depression and/or anxiety and the presence of hyperglycaemia and diabetes complications [23, 209]. Complications of diabetes for which depression is a risk factor include CKD, diabetic retinopathy, neuropathy, macrovascular complications and sexual dysfunction [23].

The relationship between depression and poor diabetes outcomes is mediated, to some extent, through depression's relationship to poorer self-care and treatment adherence [210]. A large volume of studies have shown that patients with depression are less likely to adhere to their diabetic medications and attend medical appointments, and that depression is associated with poorer ability for self-care [210-213]. Treatment of depression has been shown to improve glycaemic control [214-216], and screening for depression in individuals with diabetes, coupled with care pathways for responding to depression of increasing degrees of severity, is recommended [217, 218].

However, the association between depression in people with diabetes and increased risks of CKD is not entirely explained by diabetes self-care [169, 219]. A prospective study of 3886 primary care diabetic adults in the United States found that major depressive symptoms were associated with nearly two-times the risk of incident KF over a median of 9 years of follow-up [169]. This association was independent of demographics, socio-economic factors, lifestyle factors, anaemia, kidney function at baseline and was independent of adherence to diabetes self-care.

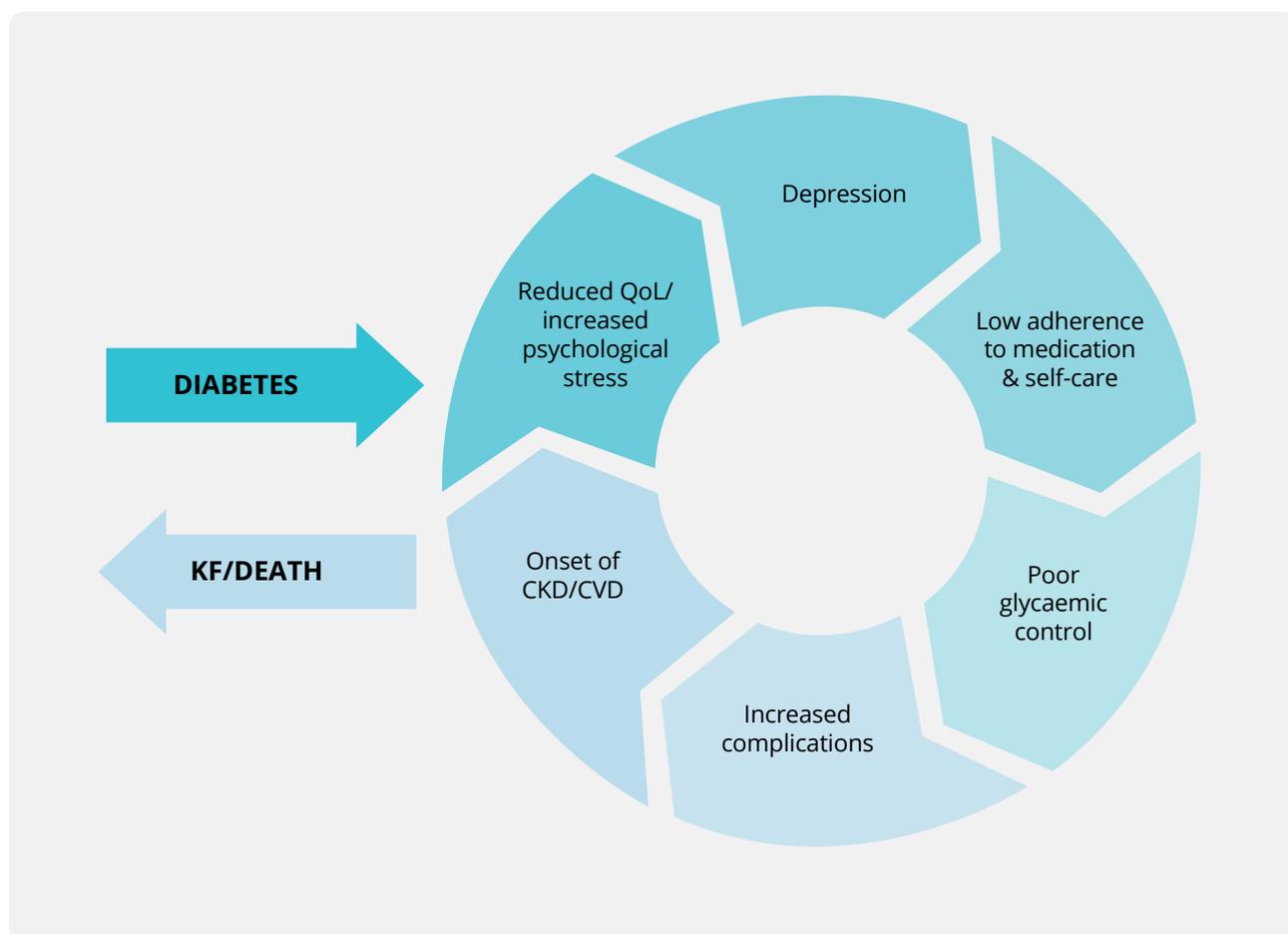


Figure 56: Schematic diagram of diabetes as a risk factor for depression, and depression as a risk factor for diabetes complications including onset of CKD and premature death.

Cardiovascular disease has a well-established bidirectional association with depression

The link between cardiovascular disease and depression has long been appreciated, with the observation first made over 50 years ago that symptoms of depression are apparent in 40-60% of patients following myocardial infarction [220, 221]. Depression following an acute coronary event is a natural reaction to a life-threatening event and is often viewed as an 'adjustment disorder with depressed mood' [222, 223]. In well-managed patients there should be a significant improvement in depressive symptoms over time [222]. Patients fulfilling the criteria of major depressive disorder, however, are at high risk of further cardiovascular events and of significant reduction in quality of life [224].

Major depression is found in approximately 15% of cardiovascular patients overall [225], in 15-20% of patients following coronary artery bypass surgery [226], and in upwards of 20% of chronic heart failure patients, with more severe functional impairment being associated with higher rates of depression [227]. Two years after receiving an implantable cardioverter defibrillator, over 25% of patients are depressed, and those who experience more shocks are the most likely to be depressed [228]. The presence of CKD may exacerbate depression in persons with cardiovascular disease. For example, an analysis of data from the Swedish Heart Failure Registry found that the presence of CKD in heart failure patients was associated with significantly worse patient-rated health [229].

As for diabetes, the association between cardiovascular disease and depression is bidirectional. Cardiovascular disease increases the risk of developing depression, while the presence of depression approximately doubles the risk of new onset cardiovascular disease [25, 225]. In a large case-control study, the four most important risk factors for acute coronary syndromes were lipid levels, smoking, psychosocial factors (predominantly depression) and diabetes [230]. Depression is a risk marker for poorer outcomes of existing cardiovascular disease, and has been shown to predict mortality after acute myocardial infarction [25, 231] and mortality among chronic heart failure patients [232-235].

Depression is understood to increase cardiovascular disease risk via many of the same biological mechanisms that increase diabetes risk (see Figure 55) [222]. These mechanisms include endothelial dysfunction [236], neurohormonal factors, genetic factors [237, 238], pro-inflammatory cytokines [239], alterations in the autonomic nervous system [240], and alterations in platelet receptors and function [241]. Biological mechanisms are likely to be reinforced by behavioural risk factors, in particular smoking, obesity, lack of physical activity, risky alcohol consumption, poor diet and poor medication adherence [222]. The loss of perceived health and vitality, functional capacity, independence, sexual relationships, employment and financial security associated with cardiovascular disease in turn lead to a worsening of depressive symptoms [222]. Numerous studies have linked depression with poor medication adherence in patients with cardiovascular disease [167, 242, 243]. These biological and behavioural risk factors linked with presence of depression, combined with poor disease self-management, in turn increase the risk of new onset CKD in people with cardiovascular disease.

The onset of CKD is associated with worsening of depressive symptoms in diabetes and cardiovascular disease

While comorbid depression in diabetes increases the risk of new onset CKD and progression to KF [169, 219], the onset of CKD may also lead to the development of depression or worsening of depressive symptoms in persons with diabetes and a reduction in quality of life. In a US-managed care diabetes cohort, physical and mental quality of life scores declined with worsening eGFR, and eGFR<30 ml/min/1.73m² was associated with a higher prevalence of depressive symptoms [244]. Similarly, a longitudinal Chinese study of type 2 diabetes patients found that presence of CKD was associated with a significant decline quality of life over time [245]. A cohort study from Canada reported that the presence of KF was associated with a greater reduction in quality of life in type 2 diabetes patients than myocardial infarction, amputation or stroke [246].

Reduced kidney function has also been linked with worse depressive symptoms and poorer quality of life scores in persons with cardiovascular disease [247]. In a Greek heart failure cohort, presence of CKD was associated with significantly worse health-related quality of life – more so than presence of diabetes, cancer or chronic respiratory failure [248]. In a US study of patients hospitalised with congestive heart failure, those with comorbid CKD were nearly 3 times as likely to have depressive symptoms compared to those without CKD [249]. Both depression and CKD were predictors of mortality in this study.

Depression affects approximately 20-25% of adults with CKD, a rate that is more than three times higher than the lifetime risk of depression in the general population (and higher than the rates of depression observed in populations with diabetes or CVD alone) [33, 250]. High levels of depressive symptoms in people with CKD have been linked to lower quality of life [251-253], lower treatment adherence [165], more rapid decline in kidney function [254], increased risk of progression to KF [254], higher rates of hospitalisation and dialysis withdrawal [255, 256] and increased mortality [255].

The onset of CKD is associated with reduction in quality of life

Clinical factors influencing quality of life in persons with CKD include sleep disorders, pain and anaemia. Poor sleep quality and pain are increasingly prevalent as kidney function declines, and are associated with depression, greater burden of illness, and poorer life satisfaction [21, 22, 257, 258]. Anaemia affects approximately half of people with pre-kidney failure [259], and is well established to be strongly associated with quality of life and the prevalence of depressive symptoms in persons with CKD [17-20]. From the patient's perspective, the impact of their disease on family and friends, feeling unwell, low mood, insufficient home care and other life stressors are other key factors that increase the likelihood of low self-reported quality of life [28].

Reduced quality of life is observed at all stages of CKD [34, 260-262]. Examination of Chinese biobank data found that self-rated health was significantly lower in middle-aged and elderly adults with CKD versus those without, and that this association persisted after adjustment for a wide range of comorbidities [263]. Similarly, the REGARDs study, a population-based cohort study of over 30,000 US adults aged over 45 years, concluded that lower levels of GFR were associated with an increased burden of physical limitations and reduced quality of life after adjusting for comorbid cardiovascular disease, diabetes, socio-economic status, and other individual-level characteristics [262]. The United States NHANES III study similarly found that physical limitations increase with declining kidney function [264]. In the NHANES III study, the ability to walk a quarter-mile and to lift 10 lb decreased significantly as GFR declined from 60 to 15 mL/min/1.73m² [264]. The presence of albuminuria in older, hypertensive adults has similarly been shown to be associated with impairments in functional performance (i.e. gait speed and Falls Efficacy Scale score) and in self-reported functional status [265].

Evidence for a link between CKD and the mental components of quality of life is less clear [262, 266-268]. Data from the baseline AusDiab study found that SF-36 Physical Functioning, Role Physical, General Health, Vitality and Role-Emotional scores were lower among participants with a GFR <60 mL/min/1.73m² compared to participants with GFR in the normal range [266]. However, no significant association was observed between GFR <60 mL/min/1.73m² and Mental Health or Social Functioning scores in persons over 50 years. Overall, the baseline AusDiab study indicated that, for persons under 50, the clinically relevant effects of reduced kidney function were impairment in Vitality, Mental Health and Social Functioning, whereas – for persons over 50 years – Physical Functioning and Role Physical were most impacted. The AusDiab study also found that impact of CKD on quality of life was greater for women than men and, whereas problems relating to Body Pain were more prominent in women, problems relating to Mental Health were more prominent in men [266]. Subsequent longitudinal analysis of the AusDiab cohort found that Physical Component scores, but not Mental Component scores, declined over 12 years of follow-up in persons with CKD at baseline [269]. Lower Physical Component Score was associated with increased all-cause mortality and increased cardiovascular mortality in persons with CKD [269].

5.2 CKD, DIABETES AND CARDIOVASCULAR DISEASE AS RISK FACTORS FOR COGNITIVE IMPAIRMENT

CKD, diabetes and cardiovascular disease are strongly associated with presence of cognitive impairment

Mild cognitive impairment is defined as cognitive decline greater than expected for an individual's age and education level, that does not notably interfere with activities of daily life. Estimates of the population burden of mild cognitive impairment range from between 3% and 19% of adults older than 65 being affected, of whom ~50% will progress to dementia within 5 years [270].

CKD, diabetes and cardiovascular disease all have a strong association with prevalence of cognitive impairment, and this association is mediated by a common set of pathophysiological mechanisms (see Figure 57) [54]. For individuals with CKD, diabetes or cardiovascular disease, the decline of cognitive function has a detrimental effect on the performance of complex self-care tasks such as handling of medication and recognition of critical clinical symptoms, for example those of heart failure or hypoglycaemia [271-273]. This results in increased risk of progression to KF and increased mortality risk, especially for older individuals.

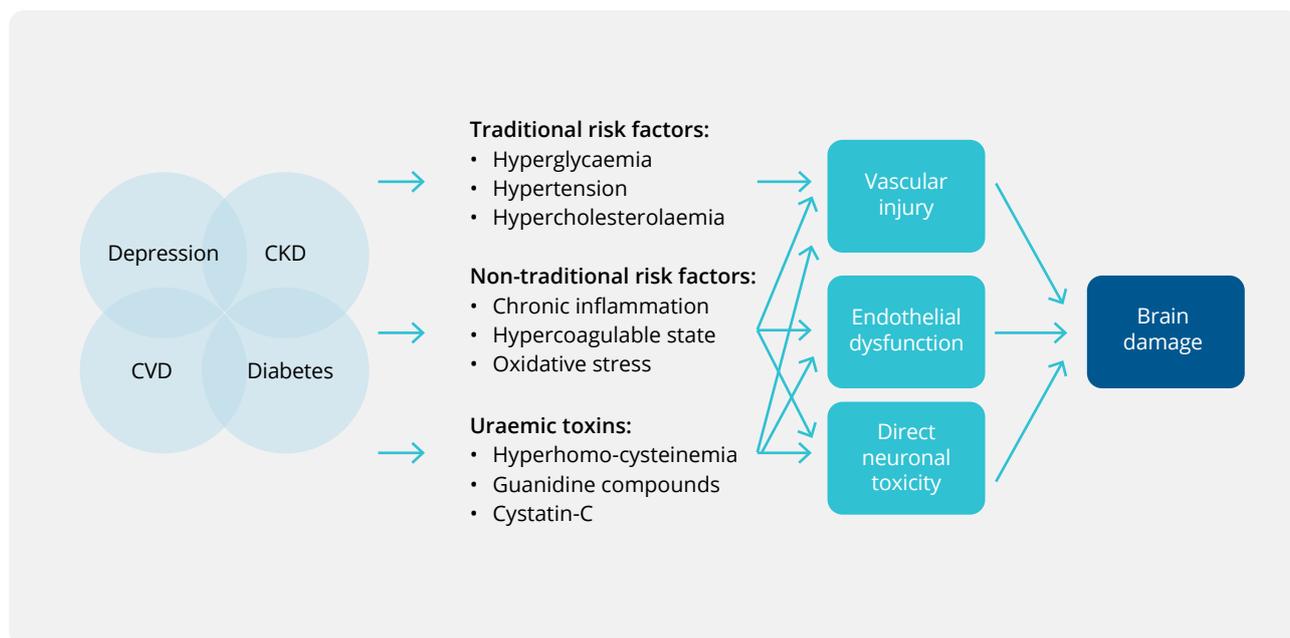


Figure 57: Schematic representation of the potential pathways leading from cardiometabolic disease to cognitive impairment and brain damage. Adapted from Bugnicourt et al [274].

Studies of middle-aged and older adults have linked presence of type 2 diabetes with risk of late-life cognitive decline, onset of Alzheimer's disease and all-cause dementia [275-279]. There is also increasing evidence linking type 2 diabetes with mild cognitive impairment at younger ages [280-282]. Longitudinal analysis of the AusDiab cohort found that having diabetes at baseline was associated with slower processing speed at 12 years of follow-up in both younger (25-59 years) and older (>60 years) age groups [282]. Neuroimaging research supports the idea that insulin resistance and high blood glucose levels are associated with progressive atrophy in regions of the brain affected by early Alzheimer's disease and loss of grey matter volume in the medial temporal lobe [283, 284]. These effects have also been demonstrated in pre-diabetic cohorts [285, 286]. More research is needed to establish whether optimal disease management

can stop or slow cognitive decline. One study has shown that strict glycaemic control reduced the loss of Gray matter in persons with type 2 diabetes aged 55-80 years, although cognitive outcomes were not improved over 40 months of follow-up [287].

Cognitive impairment in people with cardiovascular disease is linked to ischaemic and anoxic changes in the brain [288, 289] and is an independent risk factor for mortality [288]. In heart failure patients, structural brain changes are thought to be primarily the result of ischaemia from decreased blood flow to the brain [289]. Comorbid sleep apnoea, anaemia and pulmonary oedema may contribute to brain injury [288]. There is also increasing evidence for a role of inflammation, obesity and diabetes in this process [288-290]. There is evidence, however, that prevention can protect brain health: a recent French cohort study showed that greater adherence to the American Heart Association's metrics for optimal cardiovascular health was associated with lower risk of new onset dementia and lower rates of cognitive decline [291].

Numerous epidemiological studies have reported an association between CKD and increased risk of mild cognitive impairment [59]. A 2012 meta-analysis found that individuals with CKD were 65% more likely to have evidence of cognitive impairment and were 39% more likely to experience cognitive decline than individuals without CKD [59]. In community-based cohort studies, albuminuria has repeatedly been shown to be associated with lower cognitive function and with greater decline in cognitive function over time [57, 58, 292-294]. Higher urinary albumin levels are associated with poorer cognitive outcomes, suggestive of a causal relationship [57]. Longitudinal analysis of the AusDiab cohort found that presence of albuminuria was associated with worse memory function at 12 years of follow-up after adjustment for demographic, education, lifestyle and cardiovascular risk factors [292].

The evidence for a relationship between eGFR and cognitive function is less clear. Analysis of the AusDiab cohort did not find an association between eGFR < 60 ml/min/1.73m² and cognitive function at 12-year follow-up, despite the finding of a significant association between cognitive function and albuminuria [292]. Studies from the United States and the Netherlands have similarly observed significant associations between cognitive function and albuminuria but not eGFR [57, 293, 294].

A possible explanation for these findings relates to participation bias in cohort studies. People with low eGFR tend to be older on average than people with albuminuria. However, older people – especially those with cognitive impairment – are less likely to participate in community-based health studies or return for follow-up assessment. Hence, community-based cohorts may under-represent the population with reduced eGFR, and specifically the proportion of that population with cognitive impairment. This results in a biased cohort that is more 'cognitively healthy' than the surrounding population and that is under-powered to detect any effect of low eGFR on cognitive outcomes [292].

The NHANES III study addressed this issue by randomising half of their cohort to receive cognitive function tests. After addressing participation bias in this manner, this study found that moderate reduction in eGFR (eGFR 30-59 ml/min/1.73m²) was associated with poorer visual attention and learning/concentration [295]. The Chronic Renal Insufficiency Cohort Study - a large cohort limited to persons with CKD – also found that cognitive performance worsens with declining eGFR [296, 297]. Studies specifically designed to examine cognitive outcomes have repeatedly found that lower eGFR at baseline is associated with more rapid decline in cognitive function and increased risk of incident dementia [54, 298, 299]. Similarly, prospective studies limited to older adults have reported that low eGFR is associated with worse cognitive performance and a higher risk of cognitive decline, and that a faster rate of GFR decline is associated with global cognitive decline and incident dementia [55-58].

Presence of CKD may affect cognitive function through multiple mechanisms

The vascular hypothesis of cognitive impairment in CKD proposes that haemodynamic changes that are a cause and a consequence of CKD also cause cerebrovascular damage, leading to cognitive impairment and increasing the risk of subsequent dementia [274, 300]. An increase in the rate of silent brain infarcts, microbleeds and white matter lesions in individuals with CKD result in cumulative brain damage [274]. An estimated 50% of persons with advanced stages of CKD have silent brain infarcts [301], which have been linked with stroke, cognitive decline and incident dementia in CKD patients [302]. White matter lesions and microbleeds have been shown to be highly prevalent in haemodialysis patients [303, 304], which is consistent with the high prevalence of frontal lobe atrophy observed in long-term haemodialysis patients [305, 306].

Non-traditional risk factors for cerebrovascular damage – hyperhomocysteinaemia, hypercoagulable states, inflammation and oxidative stress – are also likely to have a role in the relationship between CKD and cognitive impairment by accelerating atherosclerosis and contributing to vascular endothelial dysfunction [307-309].

A second hypothesis draws a link between the accumulation of uraemic toxins as a result of CKD with cerebral endothelial dysfunction, brain injury and cognitive impairment [310]. Generalised endothelial dysfunction is a cause of both albuminuria and cerebral small-vessel disease, which increases blood-brain permeability and subsequent neuronal damage [311]. Progressive loss of kidney function may lead to further neuronal damage via accumulation of neurotoxins [311]. This is consistent with the epidemiological evidence, which suggests that in the earlier stages of kidney disease, associations between CKD and cognitive performance are largely attributable to generalized endothelial dysfunction, for which albuminuria is a marker [274, 311]. In later stages of CKD, as eGFR declines the build-up of uraemic toxins appears to have an independent effect on cognitive function [274].

Other important factors likely to be involved in the pathophysiology of cognitive decline in CKD include anaemia, interactions between multiple medications in CKD patients, and sleep disturbances leading to impaired concentration and fatigue [312, 313].

5.3 PSYCHOSOCIAL BURDEN OF KIDNEY FAILURE

Kidney failure is associated with high rates of depression and reduced quality of life

As CKD advances to KF, somatic symptoms and comorbidity increase, contributing to an increased prevalence of depression and progressive reduction in quality of life [29-31]. People with KF are also at high risk of experiencing a host of negative medical experiences, including cardiovascular events, cancer diagnoses, hospitalisations, and loss of physical function, all of which have the potential to significantly impact psychosocial wellbeing [314]. A large body of literature reports a high prevalence of depression and impaired quality of life in persons with KF, with persons receiving dialysis affected more than those who are alive with a functioning kidney transplant [63, 315-317].

Severe psychological distress is common amongst patients receiving dialysis [29, 251], with depression affecting 25-50% in this population, depending on the assessment method used [32-36]. Dialysis modality also matters, with haemodialysis patients reported to experience worse depressive symptoms than peritoneal dialysis patients [318]. The high prevalence of depression in dialysis patients is strongly associated with impaired quality of life, increased rates of hospitalisation, cardiovascular events, cardiovascular disease deaths and all-cause mortality [31, 35, 37-40]. Other than depression, symptoms of KF that have the greatest impact on quality of life for dialysis patients include pain (present in ~50% of dialysis patients) and erectile dysfunction (affecting the majority of men on chronic dialysis) [38, 319-322]. Additional stressors include physiological changes, self-image and self-esteem, unemployment, increased dependence and limitations

on physical activities [323]. Overarching these challenges is concern and uncertainty about the future [63].

Presence of depression in persons with KF is associated with lower medication and dietary adherence and with missed and abbreviated dialysis treatments [37, 324]. Factors which have been linked to more severe depressive symptoms in KF patients include female gender, lower educational attainment and divorced/widowed marital status [325]. This is consistent with the general literature on quality of life in chronic disease states [326]. Caring for a person with KF has a major impact on relationships with partners or primary carers and disrupts roles within the family [41]. Depression has been found to extend to the spouses of dialysis patients [42].

Dialysis patients experience high rates of cognitive impairment

Moderate to severe cognitive impairment is also highly prevalent in KF [327]. In haemodialysis patients, estimated rates of cognitive impairment range from 30-60% [296, 303, 328, 329], with impairment evident across multiple domains but affecting memory and cognitive function in particular [329]. Cognitive impairment in the dialysis population is associated with prolonged hospitalisation, increased demands on healthcare professionals, and elevated mortality rates [60, 329]. Survival analysis of a UK dialysis cohort found that 7-year survival among cognitively impaired patients was 49%, versus 83% in patients with no cognitive impairment. After adjusting for sociodemographic, clinical and psychological factors, risk of all-cause mortality was 2.5 higher in cognitive impaired dialysis patients [329].

5.4 IMPLICATIONS FOR PATIENTS, FAMILIES AND THE HEALTH SYSTEM

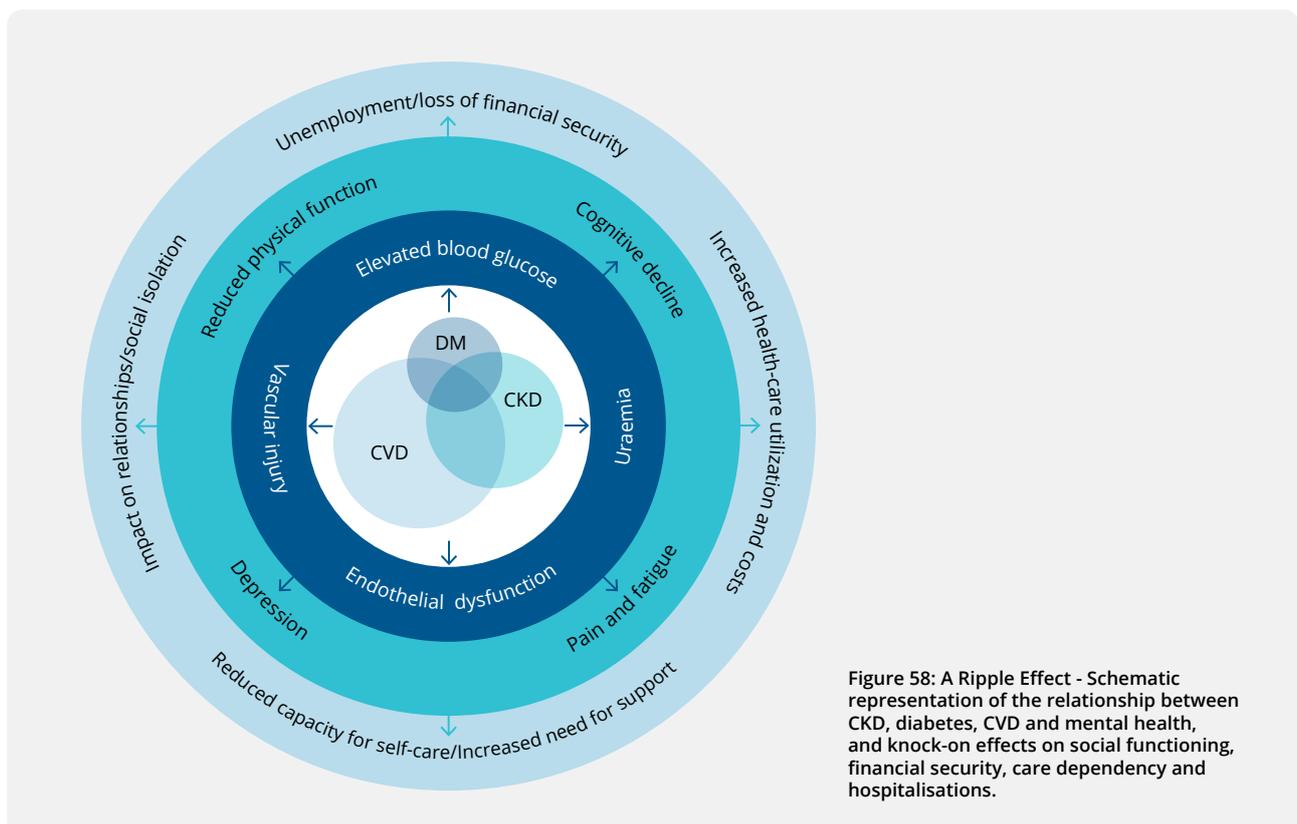


Figure 58: A Ripple Effect - Schematic representation of the relationship between CKD, diabetes, CVD and mental health, and knock-on effects on social functioning, financial security, care dependency and hospitalisations.

A ripple effect: impact of CKD, diabetes and cardiovascular disease on mental health, social functioning, financial security, care dependency and health care utilisation

Figure 58 offers a conceptual overview of the psychosocial burden attributable to CKD, diabetes and CVD. For patients with CKD, diabetes or cardiovascular disease, the presence of hyperglycaemia, accumulation of uraemic toxins, hypertension, hypercholesterolaemia, and chronic inflammation leading to vascular injury and endothelial dysfunction in turn cause pain, fatigue, depression, reduced in quality of life (especially functional performance), and structural brain changes that eventually lead to cognitive decline. These associations are bi-directional: as underlying disease progresses, the psychosocial and somatic symptom burden grows, resulting in increasingly poor health outcomes.

Depression, poor quality of life and cognitive decline also have broader implications for the health and well-being of patients and their families. Depressed and cognitively impaired persons have less capacity for self-care and may require significantly more support from family/carers, while simultaneously experiencing greater relationship strain and social isolation. Sexual dysfunction may be a factor placing strain on intimate relationships ^[321, 322]. Patients with poor quality of life, particularly as a consequence of reduced physical functioning, chronic pain or fatigue may be unable to work and therefore may experience a loss of financial security as a result. All these factors compound the original disease burden, lead to increased utilization of health care resources, and increase the risks of KF, dementia and death.

Patient-centred treatment approaches are needed that consider both physical and mental health

Improving health outcomes in CKD, diabetes and cardiovascular disease requires a wholistic approach that takes into account clinical, psychological and social factors, and offers appropriate psychological and social support alongside medical treatment ^[63]. Such an approach would include:

1. Treatment of medical risk factors for poor quality of life: anaemia, sleep apnoea, obesity, hypertension, hyperlipidaemia, elevated blood glucose, and albuminuria
2. Pharmacological treatment of depression (if indicated)
3. Non-pharmacological treatment of depression (such as cognitive behaviour therapy)
4. Provision of support services which address reduced capacity for self-care, social isolation, and financial stressors, and ameliorate the impact of socioeconomic factors (unemployment, low income, and low educational level).

Pharmacological Interventions to reduce depressive symptoms and anxiety may improve quality of life for both people with diabetes or cardiovascular disease and their carers ^[330-332]. There is also evidence that non-pharmacological interventions, such as mindfulness-based stress reduction or cognitive behaviour therapy (CBT), may be effective in the management of depression and medical risk in persons with diabetes or cardiovascular disease ^[170, 333, 334]. In a recent randomised trial, CBT plus lifestyle counselling was found to be effective in reducing depressive symptoms and treatment-related distress, while also improving self-care and medication adherence, in adults with type 2 diabetes and comorbid depression ^[334]. Similarly, a meta-analysis of trials conducted prior to 2015 concluded that CBT is effective in reducing depression in adults with diabetes and improves in glycaemic control in the short-medium term ^[335]. Studies have shown CBT to be more effective in cardiac patients when used in combination with anti-depressant medication ^[330] or exercise ^[336]. A randomised trial of CBT for depression and self-care in patients with heart failure found that CBT was effective in improving depression, anxiety, fatigue, social functioning and quality of life; however, heart failure self-care was not improved, with the authors noting the need for more research into the reasons underlying self-care deficits in different patient populations ⁵.

Evidence of the effectiveness of pharmacological treatment for the management of depression in persons with CKD or KF is limited and inconclusive [314, 338]. There is some evidence that CBT [339-341] or exercise therapy [342-344] in patients with KF may successfully improve depressive symptoms, although there is a need for further carefully designed trials of treatment strategies for management depression in this population [314]. Another area where more research is needed is in the development of more accurate depression screening tools for application in dialysis populations. Generic depression screening tools perform poorly in dialysis patients as the symptoms of depression and symptoms of KF overlap, for example fatigue, altered sleep and loss of appetite [314]. These overlapping symptoms may still, however, be predisposing factors for depression in KF patients, hence screening tools need to be sufficiently sophisticated to distinguish when intervention for depression management is indicated [314].

Depression has a negative effect on social functioning and is associated impairments in interpersonal behaviour such as social withdrawal, disengagement from important activities, avoidance and disruption of interpersonal relationships [345]. For patients with CKD, diabetes and cardiovascular disease, this can translate into missed medical appointments and non-adherence with treatment regimen [210]. A meta-analysis of depression and medication adherence in chronic disease found that depressed patients are 1.76 times more likely to be non-adherent to medication regimens [346]. In addition, depressed patients report greater levels of dissatisfaction with their providers [347], while on the other hand providers experience greater frustration and decreased empathy, with an overall deterioration of communication and continuity of care [348, 349].

In contrast, better social support, coping skills and life satisfaction are associated with higher quality of life and better health outcomes [267]. For example, a study of diabetes self-care activities in a cohort of Australians with CKD found that greater participation in self-management activities, particularly those focused on general diet, exercise and medication taking, were associated with higher health-related quality of life [350]. Telephone and other telehealth psychosocial support services have been proposed as a means of addressing the psychosocial challenges facing patients with chronic disease [351, 352] and demonstrate potential to:

- Enhance psychological health (reduced anxiety, depression, stress, burden, irritation and isolation)
- Support self-management
- Improve caregiving knowledge/skills/patient management
- Provide social work support to improve social and occupational functioning
- Improve coping/problem solving skills/goal attainment/decision-making
- Enhance communication with providers and continuity of care
- Save costs
- Improve physical health.

An Australian randomised controlled trial of a lifestyle-focused cardiovascular secondary prevention program delivered via text message (the TEXT ME trial) has demonstrated the potential benefits of this type of support. The TEXT ME intervention of four text messages per week for 6 months, providing education, motivation and support on diet, physical activity, general cardiac health and smoking, resulted in significant reductions in blood pressure, LDL cholesterol, BMI, smoking and depressive symptoms [353, 354].

Patient priorities and patient reported outcomes measures in CKD

For KF patients, quality of life is about living well on KRT, not just survival. Historically, however, clinical studies have tended to neglect outcomes valued by patients and focus instead on biochemical indicators and mortality ^[355].

A study of dialysis patients in Australia and Canada identified the following top ten outcomes valued by patients ^[355]:

1. Fatigue/energy
2. Survival
3. Ability to travel
4. Dialysis-free time
5. Impact on family
6. Ability to work
7. Sleep
8. Anxiety/stress
9. Decrease in blood pressure
10. Lack of appetite/taste.

The recent shift towards patient-centred outcomes as a priority of research and the embedding of patient-reported outcome measures into the assessment of clinical quality has begun to reorient thinking about health outcomes towards patient priorities.

Focus-groups conducted with Australian CKD patients identified eight priorities for CKD research ^[356]:

1. Prevention of kidney disease
2. Better access to and improvement in kidney transplantation
3. Reduction of symptoms of CKD and complications associated with treatment
4. New therapeutic technologies
5. Psychosocial aspects of living with CKD
6. Whole-body not organ-specialised care
7. Improvement in dialysis treatment
8. Improvement in caregiver support.

Better understanding and support around the psychosocial aspects of CKD, a holistic consideration of the entire person, and support for families are priorities for CKD patients ^[356]. More patient-centred research is also needed into the symptoms of CKD and the side-effects of KF treatment that most affect quality of life ^[356].

Lastly, it is important to consider that there have been important developments in the treatment of cardiovascular disease and diabetes in recent years and the prevalence of certain cardiometabolic risk factors (e.g. smoking) is declining. However, lifespans are increasing and an increasing proportion of those with diabetes and cardiovascular are surviving into advanced age. This means that the burden of comorbid CKD, diabetes and cardiovascular disease will remain high, and this burden will disproportionately affect those of older age. In this context, prevention and management strategies need to commence early and prioritise long-term mental health and cognitive outcomes of Australians with CKD, diabetes and/or cardiovascular disease ^[357].

6

Economic impact of chronic kidney disease in diabetes and cardiovascular disease

Key messages:

Health care costs increase with progressive severity of CKD. These include direct costs to the health system and costs incurred personally by the patient and their family.

More than \$1 billion is spent on the provision KRT annually, with the greatest proportion of these costs attributable to in-centre haemodialysis.

Comorbid CKD increases the costs associated with diabetes. For a person with diabetes, annual per person health care costs are increased by 17% with the onset of early stage CKD, and by 57% where moderate to severe CKD was present.

Out of pocket costs to patients and their families are substantial and increase the risk of financial catastrophe and falling into relative poverty.

Loss of productivity affecting both patients and caregivers contributes significantly to the indirect costs of CKD.

The onset of CKD is associated with significantly increased health care costs

At an individual level, the onset of CKD is associated with a significant increase in direct health care costs [47]. Direct health care costs may increase due to:

- Increased general practitioner visits
- Increase medical specialist visits
- Hospital emergency admissions
- Hospitalisations
- Medications and medically related consumables.

Costs associated with pre-kidney failure CKD, by age and diabetes status, have previously been calculated for the 2012 Australian population [47]. The estimated direct health care costs associated with a diagnosis of CKD in 2012 were \$2719 per person per year for Stage 1 and 2 CKD, \$3489 per person for Stage 3 CKD, and \$14,545 for Stage 4 and 5 CKD (excluding costs associated with KRT).

Estimated annual direct health care costs of CKD increased with age, from \$1557 per person aged 30-49 years, to \$5866 per person aged 70 years and older. Direct health care costs were also higher for people with comorbid diabetes (see Figure 59).

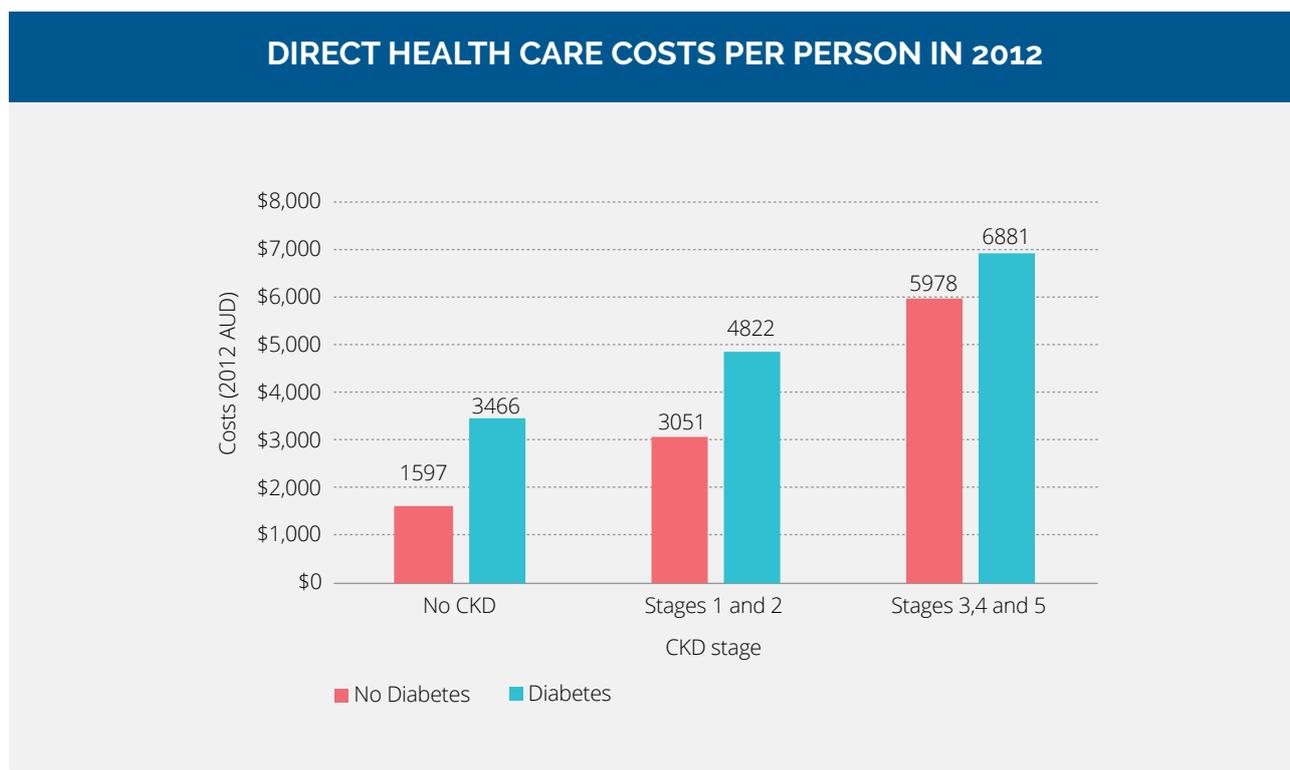


Figure 59: Estimated annual direct health care costs per person per year by CKD and diabetes status, in 2012 Australian dollars. Estimates are not adjusted for age, to reflect the higher costs associated with an older age distribution among persons with more advanced CKD (Source: Wyld 2015 [47])

The analysis by Wyld et al. reported additional health care costs attributable to CKD of \$4.1 billion per annum (2012 Australian dollars), based on 1.6 million adults affected by CKD in 2012. This additional cost is made up of \$2.5 billion in direct healthcare costs, \$0.7 billion in direct non-healthcare costs (costs incurred by patients and their family), and \$0.9 billion in government subsidies [47]. Inflating these cost estimates to 2018 Australian dollars gives \$4.6 billion per annum in total health care costs and \$2.8 billion per annum in direct health care costs. These estimates, however, do not consider population growth and aging since the data underlying this study were collected, hence the contemporary costs associated with pre-kidney failure CKD may be higher. The estimates also do not consider the costs of CKD in the institutionalised population – i.e. those living in nursing homes – for whom costs related to CKD may be higher.

The commencement of KRT vastly increases per person direct health care costs. There were 25,652 patients receiving KRT in Australia at 31 December 2018 (13,399 dialysis patients and 12,253 kidney transplant patients) [45]; the annual cost of the provision of dialysis and transplantation to this population exceeds \$1 billion [358]. Much of these costs relate to dialysis. Of the 11 million admissions to hospitals in 2016-17, dialysis for KF was the most common single reason for care (over 1.4 million admissions). Dialysis currently accounts for 13% of all hospitalisations in Australia [49]. Since 2009, admissions for dialysis have increased by 3.9% on average each year [51]. The cumulative cost of treating all current and new cases of KF from 2009 to 2020 has been estimated to be between approximately \$11.3 billion and \$12.3 billion [52].

Comorbid CKD increases the costs associated with diabetes and cardiovascular disease

The presence of comorbid CKD in diabetes and cardiovascular disease increases costs to the health system through increased rates of hospitalisation, increased length of hospitalisation, increased complexity of medical management, increased rates of adverse events and complications, and increased risk of onset of KF requiring KRT.

Based on AIHW analysis of 2012-2013 data from the National Hospital Morbidity database, an additional diagnosis of CKD increased average length of hospital stay by 4 days for people with a diagnosis of cardiovascular disease, and by 2 days for people with a diagnosis of diabetes (excluding hospitalisations for dialysis) ^[46]. Another way in which CKD increases the costs associated with cardiovascular disease is by increasing the complication rate in cardiac procedures. An Australian study comparing rates of hospitalisation and associated direct costs following percutaneous coronary intervention in patients with and without CKD found that presence of Stage 4-5 CKD significantly increased health care costs ^[359].

The analysis by Wyld et al. indicated that the presence of Stage 1 or 2 CKD increased direct per person health care costs in people with diabetes by 17%, compared to costs of diabetes alone (direct per person health care costs in 2012 of \$3677 versus \$3132, adjusted for age and sex). The presence of Stage 3-5 CKD (excluding dialysis and transplant recipients) increased direct per person health care costs in people with diabetes by 57%, compared to the cost of diabetes alone (direct per person health care costs in 2012 of \$4915 versus \$3132, adjusted for age and sex) ^[47]. Costs of government subsidies were increased, from \$1855 per person per year in persons with diabetes but without CKD, to \$2576 per person per year in people with diabetes and Stage 3-5 CKD ^[47].

The finding of a significant increase in the health care costs associated with diabetes with the onset and progression of CKD is supported by international evidence ^[360, 361]. A study of members of a large health care maintenance organisation from the United States found that the costs incurred by patients with type 2 diabetes and comorbid CKD increased substantially as CKD progressed ^[360]. Increasing costs among patients with progressive CKD were driven by inpatient costs, and may relate to an increase in cardiovascular events with declining kidney function ^[360]. A similar study from the United States reported that inpatient visits among persons with type 2 diabetes increased significantly with each advancing stage of CKD and were linked with large differences in medical-related expenses ^[361].

Onset of CKD increases out-of-pocket costs to patients and their families

The personal financial impact of CKD can relate to:

- Treatment and medication associated costs
- Transport for treatment and specialist appointment costs
- Impact of the disease on capacity to work
- The need for ongoing care from a family member, further impacting on family income
- Difficulty accessing carers support payments.

For those requiring KRT, additional costs may also include:

- The need to relocate to be closer to a hospital or dialysis centre
- The need for supported accommodation
- The purchase of special food ^[47].

Due to these out-of-pocket costs to patients and their families, more advanced CKD is associated with increased odds of falling into relative poverty ^[362]. In an analysis of the impact of moderate to severe CKD on household income over time across 14 countries, over half of CKD patients ended up in relative poverty ^[362]. Notably, those patients who received a kidney transplant had half the risk of falling into poverty compared to those who commenced dialysis.

An Australian study of patients receiving care for CKD stage 3-5 found that patients faced out of pocket costs of over \$900 per quarter on average, which exceeded 10% of household costs in over 70% of cases. Over half of households reported economic hardship as a result of the out-of-pocket costs of CKD ^[53]. Consequences for people with low financial resources included going without meals, being unable to heat their homes, missing medical appointments or failing to fill prescriptions because they were short of money^[53]. Given that CKD disproportionately affects the most disadvantaged Australians, these out-of-pocket costs to patients and their household result in financial catastrophe in many cases.

Onset of CKD is linked to reduced employment and increased reliance on government subsidies

In addition to a significant increase in direct health care costs for governments and out-of-pocket costs for individuals and families, the onset of CKD is also associated with reduced employment opportunities and a significant increase in government subsidies ^[47]. The analysis of Wyld et al. found that, for Australians with pre-kidney failure CKD, government subsidies (pensions, allowances and unemployment benefits) increased with a diagnosis of CKD from \$1 196 per person per year for those without CKD to \$4029 per person per year for those with Stages 4 and 5 CKD ^[47].

Loss of productivity affecting both patients and caregivers contributes significantly to the indirect costs of CKD ^[363]. A study examining the social cost of CKD in Italy found that the employment rate of the working age population with CKD was significantly lower than that of the age-matched general population (39% versus 64%). More than half of patients with stage 4 and 5 CKD were found to need the presence of a caregiver to attend specialist visits, and more than one in three needed domestic help ^[363]. The combined loss of productivity for patients and caregivers was a significant contributor to the total social cost of CKD.

7

Reducing the burden of comorbid disease and improving outcomes

7.1 RECENT ADVANCES IN CKD PREVENTION

Until recently, the only approved treatment for the prevention of CKD progression in type 2 diabetes was renin-angiotensin system blockade. Several recent randomised controlled trials and registry studies have reported the efficacy of a new agent - sodium-glucose cotransporter-2 (SGLT2) inhibitors - in reducing the risk of heart failure and CKD progression in type 2 diabetes.

SGLT2 inhibitors improve glycaemic control by promoting urinary glucose and sodium excretion and inhibiting reabsorption of filtered glucose by the kidney, thereby moderately lowering glycated haemoglobin levels and influencing intra-renal haemodynamics, leading to reductions in systolic blood pressure and albuminuria^[364, 365]. The effect of SGLT2 inhibition on glycaemic diminishes as kidney function declines; however, the effect on cardiovascular events persists even at lower levels of kidney function, with benefits observed so far down to eGFR 30 mL/min/1.73m²^[364].

Three large cardiovascular trials previously reported promising impacts of SGLT2 inhibition on kidney outcomes^[366-368]. The recent publication of several trials specifically designed to determine the effect of SGLT2 inhibition on kidney outcomes in patients with diabetic nephropathy has focused interest on the possibility of SGLT2 inhibition as a major therapeutic advance of reducing progression of CKD in people with type 2 diabetes^[80, 364, 369].

Overall, these trials suggest SGLT2 inhibition in patients with diabetic nephropathy reduces risks of admission to hospital for heart failure, risk of major cardiovascular events, risk of KF, risk of acute kidney injury, and risk of death due to kidney disease^[80, 364, 369]. SGLT2 inhibition is also associated with significant reduction in urinary albumin to creatinine ratio [80, 369]. Reno-protective effects of SGLT2 inhibition have been demonstrated across a range of baseline kidney function down to an eGFR of 30 ml/min/1.73m²^[80, 364, 369]. However, it remains unclear whether these benefits extend to patients with an eGFR of <30 ml/min/1.73m².

SGLT2 inhibitors are increasingly being used in clinical practice, and are recommended by American and European guidelines as second-line treatment after metformin in type 2 diabetes patients with prior atherosclerotic cardiovascular disease, heart failure or CKD^[364]. Safety data are generally favourable, although with some uncommon but notable side effects, including mycotic genital infections, volume depletion, euglycaemic diabetic ketoacidosis and possibly amputations^[364].

In Australia, Metformin remains the first-line pharmacotherapy in type 2 diabetes at this time, due to lower cost, high tolerability and established safety profile, with SGLT2 inhibitors recommended where metformin monotherapy has failed.

A recent study reported that the effects of SGLT2 inhibitors on progression of CKD may be consistent between people with and without type 2 diabetes ^[377]. Further data is awaited from ongoing clinical trials evaluating the use of SGLT2 inhibitors in people with CKD and/or CVD without diabetes. The expansion of potential therapeutic options for CKD is a further incentive to focus on early detection of CKD - especially in people with diabetes and cardiovascular disease.

7.2 THE NEED FOR AN INTEGRATED PUBLIC HEALTH APPROACH TO CKD, DIABETES AND CARDIOVASCULAR DISEASE

Meaningful progress towards addressing the burden of disease attributable to CKD, diabetes, cardiovascular disease and their comorbidity in Australia requires a coordinated, public health approach to disease prevention and treatment that is simultaneously working towards:

- Reducing the prevalence of risk factors for the onset of kidney damage, insulin resistance, hypertension, atherosclerosis and dyslipidaemia, including overweight and obesity, poor diet, insufficient physical activity, risky alcohol consumption, and tobacco smoking
- Improving access to primary health care and preventive therapies for Aboriginal and Torres Strait Islander Australians and Australians who are socioeconomically disadvantaged or reside in remote areas
- Early detection of markers of CKD, diabetes and cardiovascular disease through targeted population screening
- Careful management of disease from its earliest stages to prevent complications and adverse events
- Provision of adequate psychosocial support to enable people to manage their own disease as effectively as possible, to prevent adverse mental health outcomes, and to support healthy cognitive aging.

Progress has been made over the past 10-15 years with respect to early detection of CKD following the introduction of automatic eGFR reporting by laboratories ^[88]. In 2005, the Australasian Creatinine Consensus Working Group recommended that all Australasian laboratories automatically report the eGFR each time a serum creatinine was ordered in a healthy adult ^[370, 371]. The implementation of this recommendation was accompanied by a health provider and consumer education strategy led by Kidney Health Australia (the KHA Primary Care Education Program) ^[88].

Since the introduction of eGFR reporting, there is evidence of improved CKD detection, particularly among patient subgroups most at risk of under-detection on the basis of serum creatinine results alone (e.g. older patients, women, Aboriginal and Torres Strait Islander Australians). An audit of kidney services in Queensland found a 40% increase in referral rates and a greater number of appropriate referrals in the 12 months following the implementation of eGFR reporting and the accompanying education program^[372]. Nearly 10 years later, an analysis of ANZDATA registry data showed that this change in practice was associated with a significant reduction in the proportion of patients who were being referred late for commencement of KRT ^[373].

There have also been important achievements in risk factor reduction for the Australian population in recent years. Young people are more likely to have never smoked than ten years ago, smoking rates continue to decline overall and alcohol consumption has reduced among men ^[4]. More work is to be done to extend these risk factor reductions to all sectors of the population. Risk factors for CKD, diabetes and cardiovascular disease that continue to increase in prevalence include overweight and obesity, inadequate consumption of fruit and vegetables, and insufficient exercise ^[4].

Despite the high burden of multimorbid chronic disease in the Aboriginal and Torres Strait Islander population, expenditure on pharmaceuticals per Aboriginal and Torres Strait Islander person is lower than for non-Indigenous Australians, and access to primary health care is often limited for those living in remote parts of the country, where the burden of CKD, diabetes and cardiovascular disease is highest [5, 145]. These factors contribute to the poor glycaemic control observed among Aboriginal and Torres Strait Islander Australians [130, 131]. There is a need to understand and address prescribing gaps, especially where these affect population groups at high risk of CKD, diabetes and CKD and related adverse outcomes. As long as these issues persist, the full potential benefits of new drugs such as SGLT2 inhibitors will not be realised in the populations that stand to gain the most from these therapies.

7.3 THE NATIONAL STRATEGIC ACTION PLAN FOR KIDNEY DISEASE

In early 2020, the National Strategic Action Plan for Kidney Disease (The Action Plan), developed by Kidney Health Australia on behalf of the Australian Government Department of Health, was released.^[163] The Action Plan articulates a national vision for preventing kidney disease and improving the lives of those affected by kidney disease, underpinned by the effective use of research, evidence and data. The Action Plan aligns with the 2017 National Strategic Framework for Chronic Conditions [7], with its emphasis on prevention, efficient, effective and appropriate care and support and targeting priority populations.

The Action Plan identifies three priority areas:

Priority One: Prevention, detection and education

- 1.1 Develop a nationally coordinated approach to increase the effectiveness of the prevention of chronic conditions in Australia
- 1.2 Increase early detection and management to slow the progression of kidney disease and empower people to self-manage their conditions
- 1.3 Raise community and healthcare professional awareness and understanding of CKD and other chronic conditions to support prevention and early detection targeted at priority groups

Priority Two: Optimal care and support

- 2.1 Deliver high quality, equitable kidney care across Australia
- 2.2 Reduce the financial impact of kidney disease on patients, carers and families and the health system
- 2.3 Improve support for people affected by CKD
- 2.4 Reduce the disproportionate burden of kidney disease on Aboriginal and Torres Strait Islander Communities

Priority Three: Research and Data

- 3.1 Establish a well-funded collaborative kidney research program to increase strategic research investment, foster cross-collaboration and translate cutting edge research into real world outcomes
- 3.2 Use data, evidence and research to drive improvements in kidney disease prevention, treatment and outcomes.

The successful implementation of these strategic priorities over the long term will have a significant impact on the burden and outcomes of comorbid CKD, diabetes and cardiovascular disease in the Australian population.

References

1. *Cardiovascular disease, diabetes and chronic kidney disease: Australian facts: prevalence and incidence.* 2014, Australian Institute of Health and Welfare: Canberra.
2. *Australian Health Survey: Biomedical Results for Chronic Diseases, 2011-12.* 2013, Australian Bureau of Statistics: Canberra.
3. AIHW, *Cardiovascular disease: Web report (CVD 83).* 2019, Australian Institute of Health and Welfare: Canberra.
4. ABS, *4364.0.55.001 - National Health Survey: Australia 2017-18.* 2018, Australian Bureau of Statistics: Canberra.
5. *Cardiovascular disease, diabetes and chronic kidney disease: Australian facts: Aboriginal and Torres Strait Islander people.* 2014, Australian Institute of Health and Welfare: Canberra.
6. Hajhosseiny, R., K. Khavandi, and D.J. Goldsmith, *Cardiovascular disease in chronic kidney disease: untying the Gordian knot.* *Int J Clin Pract*, 2013. **67**(1): p. 14-31.
7. Keith, D.S., et al., *Longitudinal follow-up and outcomes among a population with chronic kidney disease in a large managed care organization.* *Arch Intern Med*, 2004. **164**(6): p. 659-63.
8. Go, A.S., et al., *Hemoglobin level, chronic kidney disease, and the risks of death and hospitalization in adults with chronic heart failure: the Anemia in Chronic Heart Failure: Outcomes and Resource Utilization (ANCHOR) Study.* *Circulation*, 2006. **113**(23): p. 2713-23.
9. Di Angelantonio, E., et al., *Renal function and risk of coronary heart disease in general populations: new prospective study and systematic review.* *PLoS Med*, 2007. **4**(9): p. e270.
10. Perkovic, V., et al., *The relationship between proteinuria and coronary risk: a systematic review and meta-analysis.* *PLoS Med*, 2008. **5**(10): p. e207.
11. Chronic Kidney Disease Prognosis, C., et al., *Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis.* *Lancet*, 2010. **375**(9731): p. 2073-81.
12. Gansevoort, R.T., et al., *Lower estimated GFR and higher albuminuria are associated with adverse kidney outcomes. A collaborative meta-analysis of general and high-risk population cohorts.* *Kidney Int*, 2011. **80**(1): p. 93-104.
13. Masson, P., et al., *Chronic kidney disease and the risk of stroke: a systematic review and meta-analysis.* *Nephrol Dial Transplant*, 2015. **30**(7): p. 1162-9.
14. Webster, A.C., et al., *Chronic Kidney Disease.* *Lancet*, 2017. **389**(10075): p. 1238-1252.
15. Lefebvre, P., et al., *Relationship between hemoglobin level and quality of life in anemic patients with chronic kidney disease receiving epoetin alfa.* *Curr Med Res Opin*, 2006. **22**(10): p. 1929-37.
16. Locatelli, F., et al., *Anaemia in haemodialysis patients of five European countries: association with morbidity and mortality in the Dialysis Outcomes and Practice Patterns Study (DOPPS).* *Nephrol Dial Transplant*, 2004. **19**(1): p. 121-32.
17. Perlman, R.L., et al., *Quality of life in chronic kidney disease (CKD): a cross-sectional analysis in the Renal Research Institute-CKD study.* *Am J Kidney Dis*, 2005. **45**(4): p. 658-66.
18. de Goeij, M.C., et al., *Haemoglobin levels and health-related quality of life in young and elderly patients on specialized predialysis care.* *Nephrol Dial Transplant*, 2014. **29**(7): p. 1391-8.
19. Johansen, K.L., et al., *Systematic review and meta-analysis of exercise tolerance and physical functioning in dialysis patients treated with erythropoiesis-stimulating agents.* *Am J Kidney Dis*, 2010. **55**(3): p. 535-48.
20. Gandra, S.R., et al., *Impact of erythropoiesis-stimulating agents on energy and physical function in nondialysis CKD patients with anemia: a systematic review.* *Am J Kidney Dis*, 2010. **55**(3): p. 519-34.
21. Kurella, M., et al., *Self-assessed sleep quality in chronic kidney disease.* *Int Urol Nephrol*, 2005. **37**(1): p. 159-65.
22. Cohen, S.D., et al., *Pain, sleep disturbance, and quality of life in patients with chronic kidney disease.* *Clin J Am Soc Nephrol*, 2007. **2**(5): p. 919-25.
23. de Groot, M., et al., *Association of depression and diabetes complications: a meta-analysis.* *Psychosom Med*, 2001. **63**(4): p. 619-30.
24. Lichtman, J.H., et al., *Depression and coronary heart disease: recommendations for screening, referral, and treatment: a science advisory from the American Heart Association Prevention Committee of the Council on Cardiovascular Nursing, Council on Clinical Cardiology, Council on Epidemiology and Prevention, and Interdisciplinary Council on Quality of Care and Outcomes Research: endorsed by the American Psychiatric Association.* *Circulation*, 2008. **118**(17): p. 1768-75.
25. Nicholson, A., H. Kuper, and H. Hemingway, *Depression as an aetiologic and prognostic factor in coronary heart disease: a meta-analysis of 6362 events among 146 538 participants in 54 observational studies.* *Eur Heart J*, 2006. **27**(23): p. 2763-74.
26. Zalai, D., L. Szeifert, and M. Novak, *Psychological distress and depression in patients with chronic kidney disease.* *Semin Dial*, 2012. **25**(4): p. 428-38.

27. Abdel-Kader, K., M.L. Unruh, and S.D. Weisbord, *Symptom burden, depression, and quality of life in chronic and end-stage kidney disease*. Clin J Am Soc Nephrol, 2009. **4**(6): p. 1057-64.
28. Zimbudzi, E., et al., *Patient reported barriers are associated with low physical and mental well-being in patients with co-morbid diabetes and chronic kidney disease*. Health Qual Life Outcomes, 2018. **16**(1): p. 215.
29. Tong, A., et al., *Patients' experiences and perspectives of living with CKD*. Am J Kidney Dis, 2009. **53**(4): p. 689-700.
30. Zimbudzi, E., et al., *Predictors of Health-Related Quality of Life in Patients with Co-Morbid Diabetes and Chronic Kidney Disease*. PLoS One, 2016. **11**(12): p. e0168491.
31. Boulware, L.E., et al., *Temporal relation among depression symptoms, cardiovascular disease events, and mortality in end-stage renal disease: contribution of reverse causality*. Clin J Am Soc Nephrol, 2006. **1**(3): p. 496-504.
32. Yoong, R.K., et al., *Prevalence and determinants of anxiety and depression in end stage renal disease (ESRD). A comparison between ESRD patients with and without coexisting diabetes mellitus*. J Psychosom Res, 2017. **94**: p. 68-72.
33. Palmer, S., et al., *Prevalence of depression in chronic kidney disease: systematic review and meta-analysis of observational studies*. Kidney Int, 2013. **84**(1): p. 179-91.
34. Kimmel, P.L. and R.A. Peterson, *Depression in end-stage renal disease patients treated with hemodialysis: tools, correlates, outcomes, and needs*. Semin Dial, 2005. **18**(2): p. 91-7.
35. Hedayati, S.S., et al., *Death or hospitalization of patients on chronic hemodialysis is associated with a physician-based diagnosis of depression*. Kidney Int, 2008. **74**(7): p. 930-6.
36. Shirazian, S., et al., *Depression in Chronic Kidney Disease and End-Stage Renal Disease: Similarities and Differences in Diagnosis, Epidemiology, and Management*. Kidney Int Rep, 2017. **2**(1): p. 94-107.
37. Weisbord, S.D., et al., *Associations of depressive symptoms and pain with dialysis adherence, health resource utilization, and mortality in patients receiving chronic hemodialysis*. Clin J Am Soc Nephrol, 2014. **9**(9): p. 1594-602.
38. Davison, S.N. and G.S. Jhangri, *Impact of pain and symptom burden on the health-related quality of life of hemodialysis patients*. J Pain Symptom Manage, 2010. **39**(3): p. 477-85.
39. Lopes, A.A., et al., *Depression as a predictor of mortality and hospitalization among hemodialysis patients in the United States and Europe*. Kidney Int, 2002. **62**(1): p. 199-207.
40. Farrokhi, F., et al., *Association between depression and mortality in patients receiving long-term dialysis: a systematic review and meta-analysis*. Am J Kidney Dis, 2014. **63**(4): p. 623-35.
41. Low, J., et al., *The impact of end-stage kidney disease (ESKD) on close persons: a literature review*. NDT Plus, 2008. **1**(2): p. 67-79.
42. Daneker, B., et al., *Depression and marital dissatisfaction in patients with end-stage renal disease and in their spouses*. Am J Kidney Dis, 2001. **38**(4): p. 839-46.
43. Koye, D.N., et al., *Trends in Incidence of ESKD in People With Type 1 and Type 2 Diabetes in Australia, 2002-2013*. Am J Kidney Dis, 2019. **73**(3): p. 300-308.
44. Lascar, N., et al., *Type 2 diabetes in adolescents and young adults*. Lancet Diabetes Endocrinol, 2018. **6**(1): p. 69-80.
45. *The 42nd Annual ANZDATA Report. Australia and New Zealand Dialysis and Transplant Registry*. 2019, ANZDATA Registry: Adelaide, Australia.
46. *Cardiovascular disease, diabetes and chronic kidney disease: Australian facts: Morbidity - Hospital care*. 2014, Australian Institute of Health and Welfare: Canberra.
47. Wyld, M.L., et al., *Cost to government and society of chronic kidney disease stage 1-5: a national cohort study*. Intern Med J, 2015. **45**(7): p. 741-7.
48. Cass, A., et al., *The economic impact of end-stage kidney disease in Australia: Projections to 2020*. 2010, Kidney Health Australia, Melbourne, Australia.
49. AIHW, *Chronic Kidney Disease: Web report (CDK 16)*. 2019, Australian Institute of Health and Welfare: Canberra.
50. AIHW, *Aboriginal and Torres Strait Islander Health Performance Framework (HPF) report 2017: Web report (IHW 194)*. 2017, Australian Institute of Health and Welfare: Canberra.
51. *Admitted patient care 2014-15: Australian hospital statistics. Health services series no. 68. Cat. no. HSE 172*. 2016, Australian Institute of Health and Welfare: Canberra.52. *Projections of the incidence of treated end-stage kidney disease in Australia, 2010-2020. Cat. No. PHE 150*. 2011, Australian Institute of Health and Welfare: Canberra.
53. Essue, B.M., et al., *How are patients managing with the costs of care for chronic kidney disease in Australia? A cross-sectional study*. BMC Nephrol, 2013. **14**: p. 5.
54. Kurella Tamura, M., et al., *Kidney function and cognitive impairment in US adults: the Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study*. Am J Kidney Dis, 2008. **52**(2): p. 227-34.
55. Darsie, B., et al., *Kidney function and cognitive health in older adults: the Cardiovascular Health Study*. Am J Epidemiol, 2014. **180**(1): p. 68-75.
56. Helmer, C., et al., *Chronic kidney disease, cognitive decline, and incident dementia: the 3C Study*. Neurology, 2011. **77**(23): p. 2043-51.
57. Joosten, H., et al., *Association of cognitive function with albuminuria and eGFR in the general population*. Clin J Am Soc Nephrol, 2011. **6**(6): p. 1400-9.
58. Martens, R.J., et al., *Estimated GFR, Albuminuria, and Cognitive Performance: The Maastricht Study*. Am J Kidney Dis, 2017. **69**(2): p. 179-191.
59. Etgen, T., et al., *Chronic kidney disease and cognitive impairment: a systematic review and meta-analysis*. Am J Nephrol, 2012. **35**(5): p. 474-82.
60. Raphael, K.L., et al., *Cognitive function and the risk of death in chronic kidney disease*. Am J Nephrol, 2012. **35**(1): p. 49-57.
61. Ducharlet, K., et al., *Patient-reported outcome measures and their utility in the management of patients with advanced chronic kidney disease*. Nephrology (Carlton), 2018.
62. Jones, D.J.W., *Why Is a Psychologist Interested in the Kidneys?* Am J Kidney Dis, 2018. **71**(2): p. A10-A11.
63. White, C. and H. McDonnell, *Psychosocial distress in patients with end-stage kidney disease*. J Ren Care, 2014. **40**(1): p. 74-81.
64. Drawz, P.E. and M.E. Rosenberg, *Slowing progression of chronic kidney disease*. Kidney Int Suppl (2011), 2013. **3**(4): p. 372-376.
65. Kataoka, Y., et al., *Multiple risk factor intervention and progression of coronary atherosclerosis in patients with type 2 diabetes mellitus*. Eur J Prev Cardiol, 2013. **20**(2): p. 209-17.

66. Levey, A.S. and J. Coresh, *Chronic kidney disease*. Lancet, 2012. **379**(9811): p. 165-80.
67. AIHW, *Australian Burden of Disease Study: impact and causes of illness and death in Australia 2015. Australian Burden of Disease series no. 19. Cat. no. BOD 22*. 2019, Australian Institute of Health and Welfare: Canberra.
68. Meyer, T.W. and T.H. Hostetter, *Uremia*. N Engl J Med, 2007. **357**(13): p. 1316-25.
69. *Chapter 1: Definition and classification of CKD*. Kidney Int Suppl (2011), 2013. **3**(1): p. 19-62.
70. Johnson, D.W., *Evidence-based guide to slowing the progression of early renal insufficiency*. Intern Med J, 2004. **34**(1-2): p. 50-7.
71. Kidney Health Australia, *Chronic Kidney Disease (CKD) Management in Primary Care (4th edition)*. 2020, Melbourne. 90.
72. *Evidence Document: A compendium to the National Strategic Action Plan for Kidney Disease*. 2019, Kidney Health Australia.
73. Tonelli, M., et al., *Chronic kidney disease and mortality risk: a systematic review*. J Am Soc Nephrol, 2006. **17**(7): p. 2034-47.
74. Thompson, S., et al., *Cause of Death in Patients with Reduced Kidney Function*. J Am Soc Nephrol, 2015. **26**(10): p. 2504-11.
75. *Cardiovascular disease, diabetes and chronic kidney disease: Australian facts: Mortality*. 2014, Australian Institute of Health and Welfare: Canberra.
76. *Cardiovascular disease, diabetes and chronic kidney disease: Australian facts: risk factors*. 2014, Australian Institute of Health and Welfare: Canberra.
77. Chase, H.P., et al., *Glucose control and the renal and retinal complications of insulin-dependent diabetes*. JAMA, 1989. **261**(8): p. 1155-60.
78. Cohen, A.J., et al., *Glomerulopathy in spontaneously diabetic rat. Impact of glycemic control*. Diabetes, 1987. **36**(8): p. 944-51.
79. *United States Renal Data System. Chapter 11: International Comparisons; 2018 USRDS Annual Data Report: Epidemiology of kidney disease in the United States*. 2018, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases: Bethesda, MD.
80. Perkovic, V., et al., *Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy*. N Engl J Med, 2019. **380**(24): p. 2295-2306.
81. ABS, *Australian Health Survey: Biomedical Results for Chronic Diseases, 2011-12. Cat no. 4364.0.55.005*. 2013, Australian Bureau of Statistics: Canberra.
82. Dunstan, D.W., et al., *The Australian Diabetes, Obesity and Lifestyle Study (AusDiab)--methods and response rates*. Diabetes Res Clin Pract, 2002. **57**(2): p. 119-29.
83. AIHW, *Chronic kidney disease prevalence among Australian adults over time. Cardiovascular, diabetes and chronic kidney disease series no. 6. Cat no. CDK 6*. 2018, Australian Institute of Health and Welfare: Canberra.
84. Hallan, S.I., et al., *Long-term trends in the prevalence of chronic kidney disease and the influence of cardiovascular risk factors in Norway*. Kidney Int, 2016. **90**(3): p. 665-73.
85. Aitken, G.R., et al., *Change in prevalence of chronic kidney disease in England over time: comparison of nationally representative cross-sectional surveys from 2003 to 2010*. BMJ Open, 2014. **4**(9): p. e005480.
86. Murphy, D., et al., *Trends in Prevalence of Chronic Kidney Disease in the United States*. Ann Intern Med, 2016. **165**(7): p. 473-481.
87. ABS, *3101.0 Australian Demographic Statistics, March 2019. Table 59. Estimated Resident Population By Single Year of Age*. 2019, Australian Bureau of Statistics: Canberra.
88. Ludlow, M., S. Jesudason, and D.W. Johnson, *Automatic reporting of estimated glomerular filtration rate in Australia turns 13: re-examining the impact*. Med J Aust, 2018. **209**(6): p. 244-245.
89. Sparke, C., et al., *Estimating the total incidence of kidney failure in Australia including individuals who are not treated by dialysis or transplantation*. Am J Kidney Dis, 2013. **61**(3): p. 413-9.
90. *Australian Institute of Health and Welfare 2014. Projections of the prevalence of treated end-stage kidney disease in Australia 2012-2020. Cat no. PHE 176*. AIHW: Canberra.
91. *The 41st Annual ANZDATA Report. Australia and New Zealand Dialysis and Transplant Registry*. 2018, ANZDATA Registry: Adelaide, Australia.
92. AIHW, *Diabetes: Web report (CVD 82)*. 2019, Australian Institute of Health and Welfare: Canberra.
93. *NDSS, All Types of Diabetes: Statistical snapshot at 30 September 2019*. 2019, National Diabetes Services Scheme, Diabetes Australia: Melbourne.
94. AIHW, *Diabetes prevalence in Australia: an assessment of national data sources*. 2009, Australian Institute of Health and Welfare: Canberra.
95. *NDSS. Diabetes data snapshots*. 2019 [cited 2019 November]; Available from: <https://www.ndss.com.au/about-the-ndss/diabetes-facts-and-figures/diabetes-data-snapshots/>.
96. Dunstan, D.W., et al., *The rising prevalence of diabetes and impaired glucose tolerance: the Australian Diabetes, Obesity and Lifestyle Study*. Diabetes Care, 2002. **25**(5): p. 829-34.
97. Briganti, E.M., et al., *Untreated hypertension among Australian adults: the 1999-2000 Australian Diabetes, Obesity and Lifestyle Study (AusDiab)*. Med J Aust, 2003. **179**(3): p. 135-9.
98. Taylor, R., A. Dobson, and M. Mirzaei, *Contribution of changes in risk factors to the decline of coronary heart disease mortality in Australia over three decades*. Eur J Cardiovasc Prev Rehabil, 2006. **13**(5): p. 760-8.
99. AIHW, *Impact of falling cardiovascular disease death rates: deaths delayed and years of life extended. Bulletin no. 70. Cat. no. AUS 113*. 2009, Australian Institute of Health and Welfare: Canberra.
100. Briffa, T., et al., *Long term survival after evidence based treatment of acute myocardial infarction and revascularisation: follow-up of population based Perth MONICA cohort, 1984-2005*. BMJ, 2009. **338**: p. b36.
101. Ford, E.S. and S. Capewell, *Proportion of the decline in cardiovascular mortality disease due to prevention versus treatment: public health versus clinical care*. Annu Rev Public Health, 2011. **32**: p. 5-22.
102. AIHW, *Australia's health 2014. Australia's health series no. 14. Cat no. AUS 178*. 2014, Australian Institute of Health and Welfare: Canberra.
103. Waters, A.M. and L. Moon, *Socioeconomic inequalities in cardiovascular disease in Australia: current picture and trends since the 1990s. Bulletin no.37 Cat. no. AUS 74*. . 2006, Australian Institute of Health and Welfare: Canberra.

104. Briffa, T.G., et al., *An integrated and coordinated approach to preventing recurrent coronary heart disease events in Australia*. Med J Aust, 2009. **190**(12): p. 683-6.
105. Xie, X.T., et al., *Impact of cigarette smoking in type 2 diabetes development*. Acta Pharmacol Sin, 2009. **30**(6): p. 784-7.
106. Willi, C., et al., *Active smoking and the risk of type 2 diabetes: a systematic review and meta-analysis*. JAMA, 2007. **298**(22): p. 2654-64.
107. Briganti, E.M., et al., *Smoking is associated with renal impairment and proteinuria in the normal population: the AusDiab kidney study*. Australian Diabetes, Obesity and Lifestyle Study. Am J Kidney Dis, 2002. **40**(4): p. 704-12.
108. AIHW, *Risk factors to health: Web report*. 2017, Australian Institute of Health and Welfare: Canberra.
109. AIHW, *National Drug Household Survey 2016: detailed findings*. Cat. no. PHE 214. 2017, Australian Institute of Health and Welfare: Canberra.
110. OECD, *OECD Data: Daily smokers*. 2018, Organisation for Economic Cooperation and Development: Paris.
111. Wakefield, M.A., et al., *Time series analysis of the impact of tobacco control policies on smoking prevalence among Australian adults, 2001-2011*. Bull World Health Organ, 2014. **92**(6): p. 413-22.
112. WHO, *Global status report on alcohol and health 2018*. 2018, World Health Organization: Geneva.
113. Corrao, G., et al., *Alcohol and coronary heart disease: a meta-analysis*. Addiction, 2000. **95**(10): p. 1505-23.
114. Kusek, J.W., *Is it time to tip your glass to prevent CKD?* Kidney Int, 2015. **87**(5): p. 877-9.
115. White, S.L., et al., *Alcohol consumption and 5-year onset of chronic kidney disease: the AusDiab study*. Nephrol Dial Transplant, 2009. **24**(8): p. 2464-72.
116. Uehara, S., et al., *Relationship Between Alcohol Drinking Pattern and Risk of Proteinuria: The Kansai Healthcare Study*. J Epidemiol, 2016. **26**(9): p. 464-70.
117. NHMRC, *Australian guidelines to reduce health risks from drinking alcohol*. 2009, National Health and Medical Research Council: Canberra.
118. Nocon, M., et al., *Association of physical activity with all-cause and cardiovascular mortality: a systematic review and meta-analysis*. Eur J Cardiovasc Prev Rehabil, 2008. **15**(3): p. 239-46.
119. Wannamethee, S.G., et al., *Lifestyle and 15-year survival free of heart attack, stroke, and diabetes in middle-aged British men*. Arch Intern Med, 1998. **158**(22): p. 2433-40.
120. Helmrich, S.P., et al., *Physical activity and reduced occurrence of non-insulin-dependent diabetes mellitus*. N Engl J Med, 1991. **325**(3): p. 147-52.
121. White, S.L., et al., *Physical inactivity and chronic kidney disease in Australian adults: the AusDiab study*. Nutr Metab Cardiovasc Dis, 2011. **21**(2): p. 104-12.
122. Hallan, S., et al., *Obesity, smoking, and physical inactivity as risk factors for CKD: are men more vulnerable?* Am J Kidney Dis, 2006. **47**(3): p. 396-405.
123. *Australia's Physical Activity and Sedentary Behaviour Guidelines and the Australian 24-hour Movement Guidelines*. 2019, Australian Government Department of Health: Canberra.
124. NHMRC, *Australian Dietary Guidelines*. 2013, National Health and Medical Research Council: Canberra.
125. NHMRC, *Clinical practice guidelines for the management of overweight and obesity in adults, adolescents and children in Australia*. 2013, National Health and Medical Research Council: Melbourne.
126. OECD, *OECD Data: Overweight or obese population*. 2018, Organisation for Economic Cooperation and Development: Paris.
127. AIHW, *End-stage kidney disease in Australia: Total incidence, 2003-2007*. Cat. no. PHE 143. 2011, Australians Institute of Health and Welfare: Canberra.
128. *The health and welfare of Australia's Aboriginal and Torres Strait Islander peoples 2015*. Cat. no. IHW 147 2015, Australian Institute of Health and Welfare: Canberra.
129. *Aboriginal and Torres Strait Islander health performance framework 2017: supplementary online tables*. Cat. no. WEB 170. 2017, Australian Institute of Health and Welfare: Canberra.
130. Maple-Brown, L., et al., *Complications of diabetes in urban Indigenous Australians: the DRUID study*. Diabetes Res Clin Pract, 2008. **80**(3): p. 455-62.
131. Maple-Brown, L.J., et al., *Cardiovascular disease risk profile and microvascular complications of diabetes: comparison of Indigenous cohorts with diabetes in Australia and Canada*. Cardiovasc Diabetol, 2012. **11**: p. 30.
132. Vos, T., et al., *The burden of disease and injury in Aboriginal and Torres Strait Islander peoples 2003*. 2007, School of Public Health, University of Queensland: Brisbane.
133. White, S.L., et al., *Is low birth weight an antecedent of CKD in later life? A systematic review of observational studies*. Am J Kidney Dis, 2009. **54**(2): p. 248-61.
134. Brockie, T.N., M. Heinzlmann, and J. Gill, *A Framework to Examine the Role of Epigenetics in Health Disparities among Native Americans*. Nurs Res Pract, 2013. **2013**: p. 410395.
135. Brown, A., et al., *Men, hearts and minds: developing and piloting culturally specific psychometric tools assessing psychosocial stress and depression in central Australian Aboriginal men*. Social Psychiatry & Psychiatric Epidemiology, 2016. **51**(2): p. 211-23.
136. K, K., et al., *Living on the edge: social and emotional wellbeing and risk and protective factors for serious psychological distress among Aboriginal and Torres Strait Islander People (Discussion Paper No. 10)*. Cooperative Research Centre for Aboriginal Health, Darwin. 2009.
137. Marmot, M., *Social determinants of health inequalities*. Lancet, 2005. **365**(9464): p. 1099-104.
138. Paradies, Y.C. and J. Cunningham, *The DRUID study: exploring mediating pathways between racism and depressive symptoms among indigenous Australians*. Social Psychiatry & Psychiatric Epidemiology, 2012. **47**(2): p. 165-73.
139. Paradies, Y., *A systematic review of empirical research on self-reported racism and health*. Int J Epidemiol, 2006. **35**(4): p. 888-901.
140. Williams, D.R. and S.A. Mohammed, *Discrimination and racial disparities in health: evidence and needed research*. J Behav Med, 2009. **32**(1): p. 20-47.
141. Pascoe, E.A. and L. Smart Richman, *Perceived discrimination and health: a meta-analytic review*. Psychol Bull, 2009. **135**(4): p. 531-54.
142. Almeida, O.P., et al., *The Kimberley assessment of depression of older Indigenous Australians: prevalence of depressive disorders, risk factors and validation of the KICA-dep scale*. PLoS ONE [Electronic Resource], 2014. **9**(4): p. e94983.

143. Shen, Y.T., et al., *Depression, Suicidal Behaviour, and Mental Disorders in Older Aboriginal Australians*. Int J Environ Res Public Health, 2018. **15**(3).
144. Davis, T.M., et al., *Prevalence of depression and its associations with cardio-metabolic control in Aboriginal and Anglo-Celt patients with type 2 diabetes: the Fremantle Diabetes Study Phase II*. Diabetes Research & Clinical Practice, 2015. **107**(3): p. 384-91.
145. *Spatial variation in Aboriginal and Torres Strait Islander people's access to primary health care*. Cat. no. IHW 155 2015, Australian Institute of Health and Welfare: Canberra.
146. ABS, *Estimates of Aboriginal and Torres Strait Islander Australians, June 2016*. Cat. no. 3228.0.55.001. 2018, Australian Bureau of Statistics: Canberra.
147. Lawton, P.D., et al., *Survival of Indigenous Australians receiving renal replacement therapy: closing the gap?* Med J Aust, 2015. **202**(4): p. 200-4.
148. Khanal, N., et al., *Disparity of access to kidney transplantation by Indigenous and non-Indigenous Australians*. Med J Aust, 2018. **209**(6): p. 261-266.
149. Cass, A., et al., *Renal transplantation for Indigenous Australians: identifying the barriers to equitable access*. Ethn Health, 2003. **8**(2): p. 111-9.
150. *Improving Access to and Outcomes of Kidney Transplantation for Aboriginal and Torres Strait Islander People in Australia: Performance Report*. 2019, The Transplantation Society of Australia and New Zealand: Adelaide.
151. Wang, Z., et al., *Trends in health status and chronic disease risk factors over 10-14 years in a remote Australian community: a matched pair study*. Aust N Z J Public Health, 2014. **38**(1): p. 73-7.
152. Radford, K., et al., *Factors Associated with the High Prevalence of Dementia in Older Aboriginal Australians*. J Alzheimers Dis, 2019. **70**(s1): p. S75-S85.
153. Li, S.Q., et al., *Dementia prevalence and incidence among the Indigenous and non-Indigenous populations of the Northern Territory*. Med J Aust, 2014. **200**(8): p. 465-9.
154. Smith, K., et al., *High prevalence of dementia and cognitive impairment in Indigenous Australians*. Neurology, 2008. **71**(19): p. 1470-3.
155. Radford, K., et al., *Prevalence of dementia in urban and regional Aboriginal Australians*. Alzheimers Dement, 2015. **11**(3): p. 271-9.
156. AIHW. *Dementia overview*. 2019 [cited 2019 18 November]; Available from: <https://www.aihw.gov.au/reports-data/health-conditions-disability-deaths/dementia/overview>.
157. Hoy, W.E., et al., *Chronic disease profiles in remote Aboriginal settings and implications for health services planning*. Aust N Z J Public Health, 2010. **34**(1): p. 11-8.
158. Le Grande, M., et al., *Social and emotional wellbeing assessment instruments for use with Indigenous Australians: A critical review*. Social Science & Medicine, 2017. **187**: p. 164-173.
159. Brown, A., et al., *Exploring the expression of depression and distress in aboriginal men in central Australia: a qualitative study*. BMC Psychiatry, 2012. **12**: p. 97.
160. Hackett, M.L., et al., *Getting it Right: study protocol to determine the diagnostic accuracy of a culturally-specific measure to screen for depression in Aboriginal and/or Torres Strait Islander people*. BMJ Open, 2016. **6**(12): p. e015009.
161. Esler, D., et al., *The validity of a depression screening tool modified for use with Aboriginal and Torres Strait Islander people*. Aust N Z J Public Health, 2008. **32**(4): p. 317-21.
162. Kroenke, K., R.L. Spitzer, and J.B. Williams, *The PHQ-9: validity of a brief depression severity measure*. J Gen Intern Med, 2001. **16**(9): p. 606-13.
163. *National Strategic Action Plan for Kidney Disease*. 2019, Kidney Health Australia: Adelaide.
164. Yapa, H.E., et al., *The Relationship Between Chronic Kidney Disease, Symptoms and Health-Related Quality of Life: A Systematic Review*. J Ren Care, 2020. **46**(2): p. 74-84.
165. Sensky, T., C. Leger, and S. Gilmour, *Psychosocial and cognitive factors associated with adherence to dietary and fluid restriction regimens by people on chronic haemodialysis*. Psychother Psychosom, 1996. **65**(1): p. 36-42.
166. DiMatteo, M.R., H.S. Lepper, and T.W. Croghan, *Depression is a risk factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence*. Arch Intern Med, 2000. **160**(14): p. 2101-7.
167. Gehi, A., et al., *Depression and medication adherence in outpatients with coronary heart disease: findings from the Heart and Soul Study*. Arch Intern Med, 2005. **165**(21): p. 2508-13.
168. Eze-Nliam, C.M., et al., *The association of depression with adherence to antihypertensive medications: a systematic review*. J Hypertens, 2010. **28**(9): p. 1785-95.
169. Yu, M.K., et al., *Associations between depressive symptoms and incident ESRD in a diabetic cohort*. Clin J Am Soc Nephrol, 2014. **9**(5): p. 920-8.
170. Pascoe, M.C., et al., *Psychosocial Interventions for Depressive and Anxiety Symptoms in Individuals with Chronic Kidney Disease: Systematic Review and Meta-Analysis*. Front Psychol, 2017. **8**: p. 992.
171. Shirazian, S., *Depression in patients undergoing hemodialysis: time to treat*. Kidney Int, 2019. **96**(6): p. 1264-1266.
172. Untas, A., et al., *The associations of social support and other psychosocial factors with mortality and quality of life in the dialysis outcomes and practice patterns study*. Clin J Am Soc Nephrol, 2011. **6**(1): p. 142-52.
173. Theofilou, P., *Quality of life in patients undergoing hemodialysis or peritoneal dialysis treatment*. J Clin Med Res, 2011. **3**(3): p. 132-8.
174. Gilbertson, E.L., et al., *Burden of Care and Quality of Life Among Caregivers for Adults Receiving Maintenance Dialysis: A Systematic Review*. Am J Kidney Dis, 2019. **73**(3): p. 332-343.
175. Talbot, F. and A. Nouwen, *A review of the relationship between depression and diabetes in adults: is there a link?* Diabetes Care, 2000. **23**(10): p. 1556-62.
176. Anderson, R.J., et al., *The prevalence of comorbid depression in adults with diabetes: a meta-analysis*. Diabetes Care, 2001. **24**(6): p. 1069-78.
177. Ali, S., et al., *The prevalence of co-morbid depression in adults with Type 2 diabetes: a systematic review and meta-analysis*. Diabet Med, 2006. **23**(11): p. 1165-73.
178. Schmitz, N., et al., *Recurrent subthreshold depression in type 2 diabetes: an important risk factor for poor health outcomes*. Diabetes Care, 2014. **37**(4): p. 970-8.
179. Knol, M.J., et al., *Depression as a risk factor for the onset of type 2 diabetes mellitus. A meta-analysis*. Diabetologia, 2006. **49**(5): p. 837-45.

180. Cosgrove, M.P., L.A. Sargeant, and S.J. Griffin, *Does depression increase the risk of developing type 2 diabetes?* *Occup Med (Lond)*, 2008. **58**(1): p. 7-14.
181. Mezuk, B., et al., *Depression, neighborhood deprivation and risk of type 2 diabetes.* *Health Place*, 2013. **23**: p. 63-9.
182. Golden, S.H., et al., *Examining a bidirectional association between depressive symptoms and diabetes.* *JAMA*, 2008. **299**(23): p. 2751-9.
183. Nouwen, A., et al., *Type 2 diabetes mellitus as a risk factor for the onset of depression: a systematic review and meta-analysis.* *Diabetologia*, 2010. **53**(12): p. 2480-6.
184. Carnethon, M.R., et al., *Symptoms of depression as a risk factor for incident diabetes: findings from the National Health and Nutrition Examination Epidemiologic Follow-up Study, 1971-1992.* *Am J Epidemiol*, 2003. **158**(5): p. 416-23.
185. Arroyo, C., et al., *Depressive symptoms and risk of type 2 diabetes in women.* *Diabetes Care*, 2004. **27**(1): p. 129-33.
186. Golden, S.H., et al., *Depressive symptoms and the risk of type 2 diabetes: the Atherosclerosis Risk in Communities study.* *Diabetes Care*, 2004. **27**(2): p. 429-35.
187. Carnethon, M.R., et al., *Longitudinal association between depressive symptoms and incident type 2 diabetes mellitus in older adults: the cardiovascular health study.* *Arch Intern Med*, 2007. **167**(8): p. 802-7.
188. Everson-Rose, S.A., et al., *Depressive symptoms, insulin resistance, and risk of diabetes in women at midlife.* *Diabetes Care*, 2004. **27**(12): p. 2856-62.
189. Engum, A., *The role of depression and anxiety in onset of diabetes in a large population-based study.* *J Psychosom Res*, 2007. **62**(1): p. 31-8.
190. Golden, S.H., et al., *Depression and type 2 diabetes mellitus: the multiethnic study of atherosclerosis.* *Psychosom Med*, 2007. **69**(6): p. 529-36.
191. Marcus, M.D., et al., *Lifetime prevalence of major depression and its effect on treatment outcome in obese type II diabetic patients.* *Diabetes Care*, 1992. **15**(2): p. 253-5.
192. Moulton, C.D., J.C. Pickup, and K. Ismail, *The link between depression and diabetes: the search for shared mechanisms.* *Lancet Diabetes Endocrinol*, 2015. **3**(6): p. 461-471.
193. Dentino, A.N., et al., *Association of interleukin-6 and other biologic variables with depression in older people living in the community.* *J Am Geriatr Soc*, 1999. **47**(1): p. 6-11.
194. Kiecolt-Glaser, J.K. and R. Glaser, *Depression and immune function: central pathways to morbidity and mortality.* *J Psychosom Res*, 2002. **53**(4): p. 873-6.
195. Maes, M., et al., *Increased serum IL-6 and IL-1 receptor antagonist concentrations in major depression and treatment resistant depression.* *Cytokine*, 1997. **9**(11): p. 853-8.
196. Pradhan, A.D., et al., *C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus.* *JAMA*, 2001. **286**(3): p. 327-34.
197. Schmidt, M.I., et al., *Markers of inflammation and prediction of diabetes mellitus in adults (Atherosclerosis Risk in Communities study): a cohort study.* *Lancet*, 1999. **353**(9165): p. 1649-52.
198. Bjorntorp, P., *Do stress reactions cause abdominal obesity and comorbidities?* *Obes Rev*, 2001. **2**(2): p. 73-86.
199. Ramasubbu, R., *Insulin resistance: a metabolic link between depressive disorder and atherosclerotic vascular diseases.* *Med Hypotheses*, 2002. **59**(5): p. 537-51.
200. Weber-Hamann, B., et al., *Hypercortisolemic depression is associated with increased intra-abdominal fat.* *Psychosom Med*, 2002. **64**(2): p. 274-7.
201. Maraldi, C., et al., *Diabetes mellitus, glycemic control, and incident depressive symptoms among 70- to 79-year-old persons: the health, aging, and body composition study.* *Arch Intern Med*, 2007. **167**(11): p. 1137-44.
202. Lustman, P.J., et al., *Depression in adults with diabetes.* *Diabetes Care*, 1992. **15**(11): p. 1631-9.
203. Wexler, D.J., et al., *Correlates of health-related quality of life in type 2 diabetes.* *Diabetologia*, 2006. **49**(7): p. 1489-97.
204. Ludman, E.J., et al., *Depression and diabetes symptom burden.* *Gen Hosp Psychiatry*, 2004. **26**(6): p. 430-6.
205. Lustman, P.J., et al., *Depression and poor glycemic control: a meta-analytic review of the literature.* *Diabetes Care*, 2000. **23**(7): p. 934-42.
206. Egede, L.E., D. Zheng, and K. Simpson, *Comorbid depression is associated with increased health care use and expenditures in individuals with diabetes.* *Diabetes Care*, 2002. **25**(3): p. 464-70.
207. Black, S.A., K.S. Markides, and L.A. Ray, *Depression predicts increased incidence of adverse health outcomes in older Mexican Americans with type 2 diabetes.* *Diabetes Care*, 2003. **26**(10): p. 2822-8.
208. Von Korff, M., et al., *Work disability among individuals with diabetes.* *Diabetes Care*, 2005. **28**(6): p. 1326-32.
209. Anderson, R.J., et al., *Anxiety and poor glycemic control: a meta-analytic review of the literature.* *Int J Psychiatry Med*, 2002. **32**(3): p. 235-47.
210. Gonzalez, J.S., et al., *Depression and diabetes treatment nonadherence: a meta-analysis.* *Diabetes Care*, 2008. **31**(12): p. 2398-403.
211. Mann, D.M., et al., *Predictors of adherence to diabetes medications: the role of disease and medication beliefs.* *J Behav Med*, 2009. **32**(3): p. 278-84.
212. Chao, J., et al., *The mediating role of health beliefs in the relationship between depressive symptoms and medication adherence in persons with diabetes.* *Res Social Adm Pharm*, 2005. **1**(4): p. 508-25.
213. Kalsekar, I.D., et al., *Depression in patients with type 2 diabetes: impact on adherence to oral hypoglycemic agents.* *Ann Pharmacother*, 2006. **40**(4): p. 605-11.
214. Lustman, P.J., et al., *Fluoxetine for depression in diabetes: a randomized double-blind placebo-controlled trial.* *Diabetes Care*, 2000. **23**(5): p. 618-23.
215. Lustman, P.J., et al., *Effects of nortriptyline on depression and glycemic control in diabetes: results of a double-blind, placebo-controlled trial.* *Psychosom Med*, 1997. **59**(3): p. 241-50.
216. Lustman, P.J., et al., *Cognitive behavior therapy for depression in type 2 diabetes mellitus. A randomized, controlled trial.* *Ann Intern Med*, 1998. **129**(8): p. 613-21.
217. van der Feltz-Cornelis, C.M., et al., *Effect of interventions for major depressive disorder and significant depressive symptoms in patients with diabetes mellitus: a systematic review and meta-analysis.* *Gen Hosp Psychiatry*, 2010. **32**(4): p. 380-95.
218. Holt, R.I. and C.M. van der Feltz-Cornelis, *Key concepts in screening for depression in people with diabetes.* *J Affect Disord*, 2012. **142 Suppl**: p. S72-9.

219. Yu, M.K., W. Katon, and B.A. Young, *Diabetes self-care, major depression, and chronic kidney disease in an outpatient diabetic population*. *Nephron Clin Pract*, 2013. **124**(1-2): p. 106-12.
220. Wynn, A., *Unwarranted emotional distress in men with ischaemic heart disease (IHD)*. *Med J Aust*, 1967. **2**(19): p. 847-51.
221. Cay, E.L., et al., *Psychological status during recovery from an acute heart attack*. *J Psychosom Res*, 1972. **16**(6): p. 425-35.
222. Hare, D.L., et al., *Depression and cardiovascular disease: a clinical review*. *Eur Heart J*, 2014. **35**(21): p. 1365-72.
223. Maercker, A., F. Einsle, and V. Kollner, *Adjustment disorders as stress response syndromes: a new diagnostic concept and its exploration in a medical sample*. *Psychopathology*, 2007. **40**(3): p. 135-46.
224. Thombs, B.D., et al., *Depression screening and patient outcomes in cardiovascular care: a systematic review*. *JAMA*, 2008. **300**(18): p. 2161-71.
225. Colquhoun, D.M., et al., *Screening, referral and treatment for depression in patients with coronary heart disease*. *Med J Aust*, 2013. **198**(9): p. 483-4.
226. Tully, P.J. and R.A. Baker, *Depression, anxiety, and cardiac morbidity outcomes after coronary artery bypass surgery: a contemporary and practical review*. *J Geriatr Cardiol*, 2012. **9**(2): p. 197-208.
227. Rutledge, T., et al., *Depression in heart failure a meta-analytic review of prevalence, intervention effects, and associations with clinical outcomes*. *J Am Coll Cardiol*, 2006. **48**(8): p. 1527-37.
228. Suzuki, T., et al., *Prevalence and persistence of depression in patients with implantable cardioverter defibrillator: a 2-year longitudinal study*. *Pacing Clin Electrophysiol*, 2010. **33**(12): p. 1455-61.
229. Lawson, C.A., et al., *Comorbidity health pathways in heart failure patients: A sequences-of-regressions analysis using cross-sectional data from 10,575 patients in the Swedish Heart Failure Registry*. *PLoS Med*, 2018. **15**(3): p. e1002540.
230. Yusuf, S., et al., *Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study*. *Lancet*, 2004. **364**(9438): p. 937-52.
231. Meijer, A., et al., *Prognostic association of depression following myocardial infarction with mortality and cardiovascular events: a meta-analysis of 25 years of research*. *Gen Hosp Psychiatry*, 2011. **33**(3): p. 203-16.
232. Jiang, W., et al., *Relationship of depression to increased risk of mortality and rehospitalization in patients with congestive heart failure*. *Arch Intern Med*, 2001. **161**(15): p. 1849-56.
233. Sherwood, A., et al., *Relationship of depression to death or hospitalization in patients with heart failure*. *Arch Intern Med*, 2007. **167**(4): p. 367-73.
234. Frasure-Smith, N., et al., *Elevated depression symptoms predict long-term cardiovascular mortality in patients with atrial fibrillation and heart failure*. *Circulation*, 2009. **120**(2): p. 134-40, 3p following 140.
235. Jani, B.D., et al., *Comorbid Depression and Heart Failure: A Community Cohort Study*. *PLoS One*, 2016. **11**(6): p. e0158570.
236. van Dooren, F.E., et al., *Associations of low grade inflammation and endothelial dysfunction with depression - The Maastricht Study*. *Brain Behav Immun*, 2016. **56**: p. 390-6.
237. Parissis, J.T., et al., *Depression in coronary artery disease: novel pathophysiologic mechanisms and therapeutic implications*. *Int J Cardiol*, 2007. **116**(2): p. 153-60.
238. de Jonge, P., et al., *Psychophysiological biomarkers explaining the association between depression and prognosis in coronary artery patients: a critical review of the literature*. *Neurosci Biobehav Rev*, 2010. **35**(1): p. 84-90.
239. Brouwers, C., et al., *Positive affect dimensions and their association with inflammatory biomarkers in patients with chronic heart failure*. *Biol Psychol*, 2013. **92**(2): p. 220-6.
240. de Jonge, P., D. Mangano, and M.A. Whooley, *Differential association of cognitive and somatic depressive symptoms with heart rate variability in patients with stable coronary heart disease: findings from the Heart and Soul Study*. *Psychosom Med*, 2007. **69**(8): p. 735-9.
241. Ziegelstein, R.C., et al., *Depression and coronary artery disease: is there a platelet link?* *Mayo Clin Proc*, 2007. **82**(11): p. 1366-8.
242. Carney, R.M., et al., *Adherence to a prophylactic medication regimen in patients with symptomatic versus asymptomatic ischemic heart disease*. *Behav Med*, 1998. **24**(1): p. 35-9.
243. Ziegelstein, R.C., et al., *Patients with depression are less likely to follow recommendations to reduce cardiac risk during recovery from a myocardial infarction*. *Arch Intern Med*, 2000. **160**(12): p. 1818-23.
244. Campbell, K.H., et al., *Association between estimated GFR, health-related quality of life, and depression among older adults with diabetes: the Diabetes and Aging Study*. *Am J Kidney Dis*, 2013. **62**(3): p. 541-8.
245. Wan, E.Y., et al., *Main predictors in health-related quality of life in Chinese patients with type 2 diabetes mellitus*. *Qual Life Res*, 2016. **25**(11): p. 2957-2965.
246. O'Reilly, D.J., et al., *Estimation of the impact of diabetes-related complications on health utilities for patients with type 2 diabetes in Ontario, Canada*. *Qual Life Res*, 2011. **20**(6): p. 939-43.
247. Guo, X., et al., *Depression and quality of life in relation to decreased glomerular filtration rate among adults with hypertension in rural northeast China*. *Kidney Blood Press Res*, 2015. **40**(1): p. 31-40.
248. Fotos, N.V., et al., *Health-related quality of life of patients with severe heart failure. A cross-sectional multicentre study*. *Scand J Caring Sci*, 2013. **27**(3): p. 686-94.
249. Hedayati, S.S., et al., *The association between depression and chronic kidney disease and mortality among patients hospitalized with congestive heart failure*. *Am J Kidney Dis*, 2004. **44**(2): p. 207-15.
250. Avramovic, M. and V. Stefanovic, *Health-related quality of life in different stages of renal failure*. *Artif Organs*, 2012. **36**(7): p. 581-9.
251. Watnick, S., et al., *The prevalence and treatment of depression among patients starting dialysis*. *Am J Kidney Dis*, 2003. **41**(1): p. 105-10.
252. Lopes, G.B., et al., *Depression as a potential explanation for gender differences in health-related quality of life among patients on maintenance hemodialysis*. *Nephron Clin Pract*, 2010. **115**(1): p. c35-40.
253. Lee, Y.J., et al., *Association of depression and anxiety with reduced quality of life in patients with predialysis chronic kidney disease*. *Int J Clin Pract*, 2013. **67**(4): p. 363-8.
254. Tsai, Y.C., et al., *Association of symptoms of depression with progression of CKD*. *Am J Kidney Dis*, 2012. **60**(1): p. 54-61.

255. Hedayati, S.S., et al., *Association between major depressive episodes in patients with chronic kidney disease and initiation of dialysis, hospitalization, or death*. JAMA, 2010. **303**(19): p. 1946-53.
256. Lacson, E., Jr., et al., *Depressive symptoms associate with high mortality risk and dialysis withdrawal in incident hemodialysis patients*. Nephrol Dial Transplant, 2012. **27**(7): p. 2921-8.
257. Almutary, H., A. Bonner, and C. Douglas, *Symptom burden in chronic kidney disease: a review of recent literature*. J Ren Care, 2013. **39**(3): p. 140-50.
258. Rhee, E.P., et al., *Prevalence and Persistence of Uremic Symptoms in Incident Dialysis Patients*. Kidney360, 2020. **1**(2): p. 86-92.
259. Hsu, C.Y., C.E. McCulloch, and G.C. Curhan, *Epidemiology of anemia associated with chronic renal insufficiency among adults in the United States: results from the Third National Health and Nutrition Examination Survey*. J Am Soc Nephrol, 2002. **13**(2): p. 504-10.
260. Kimmel, P.L. and S.S. Patel, *Quality of life in patients with chronic kidney disease: focus on end-stage renal disease treated with hemodialysis*. Semin Nephrol, 2006. **26**(1): p. 68-79.
261. Gorodetskaya, I., et al., *Health-related quality of life and estimates of utility in chronic kidney disease*. Kidney Int, 2005. **68**(6): p. 2801-8.
262. McClellan, W.M., et al., *Physical and psychological burden of chronic kidney disease among older adults*. Am J Nephrol, 2010. **31**(4): p. 309-17.
263. Song, X., et al., *Association between multiple comorbidities and self-rated health status in middle-aged and elderly Chinese: the China Kadoorie Biobank study*. BMC Public Health, 2018. **18**(1): p. 744.
264. National Kidney, F., *K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification*. Am J Kidney Dis, 2002. **39**(2 Suppl 1): p. S1-266.
265. Wolfgram, D.F., et al., *Association of Albuminuria and Estimated Glomerular Filtration Rate with Functional Performance Measures in Older Adults with Chronic Kidney Disease*. Am J Nephrol, 2017. **45**(2): p. 172-179.
266. Chow, F.Y., et al., *Health-related quality of life in Australian adults with renal insufficiency: a population-based study*. Am J Kidney Dis, 2003. **41**(3): p. 596-604.
267. Porter, A., et al., *Quality of life and psychosocial factors in African Americans with hypertensive chronic kidney disease*. Transl Res, 2012. **159**(1): p. 4-11.
268. Porter, A.C., et al., *Predictors and Outcomes of Health-Related Quality of Life in Adults with CKD*. Clin J Am Soc Nephrol, 2016. **11**(7): p. 1154-62.
269. Wyld, M.L.R., et al., *The impact of progressive chronic kidney disease on health-related quality-of-life: a 12-year community cohort study*. Qual Life Res, 2019. **28**(8): p. 2081-2090.
270. Gauthier, S., et al., *Mild cognitive impairment*. Lancet, 2006. **367**(9518): p. 1262-70.
271. Cameron, J., et al., *Does cognitive impairment predict poor self-care in patients with heart failure?* Eur J Heart Fail, 2010. **12**(5): p. 508-15.
272. Alosco, M.L., et al., *Cognitive impairment is independently associated with reduced instrumental activities of daily living in persons with heart failure*. J Cardiovasc Nurs, 2012. **27**(1): p. 44-50.
273. Lee, C.S., et al., *Blunted responses to heart failure symptoms in adults with mild cognitive dysfunction*. J Cardiovasc Nurs, 2013. **28**(6): p. 534-40.
274. Bugnicourt, J.M., et al., *Cognitive disorders and dementia in CKD: the neglected kidney-brain axis*. J Am Soc Nephrol, 2013. **24**(3): p. 353-63.
275. Whitmer, R.A., et al., *Midlife cardiovascular risk factors and risk of dementia in late life*. Neurology, 2005. **64**(2): p. 277-81.
276. Lu, F.P., K.P. Lin, and H.K. Kuo, *Diabetes and the risk of multi-system aging phenotypes: a systematic review and meta-analysis*. PLoS One, 2009. **4**(1): p. e4144.
277. Crane, P.K., et al., *Glucose levels and risk of dementia*. N Engl J Med, 2013. **369**(6): p. 540-8.
278. Yaffe, K., et al., *Diabetes, glucose control, and 9-year cognitive decline among older adults without dementia*. Arch Neurol, 2012. **69**(9): p. 1170-5.
279. Palta, P., et al., *Diabetes and Cognitive Decline in Older Adults: The Ginkgo Evaluation of Memory Study*. J Gerontol A Biol Sci Med Sci, 2017. **73**(1): p. 123-130.
280. Winkler, A., et al., *Association of diabetes mellitus and mild cognitive impairment in middle-aged men and women*. J Alzheimers Dis, 2014. **42**(4): p. 1269-77.
281. Nooyens, A.C., et al., *Type 2 diabetes and cognitive decline in middle-aged men and women: the Doetinchem Cohort Study*. Diabetes Care, 2010. **33**(9): p. 1964-9.
282. Anstey, K.J., et al., *Association of cognitive function with glucose tolerance and trajectories of glucose tolerance over 12 years in the AusDiab study*. Alzheimers Res Ther, 2015. **7**(1): p. 48.
283. Willette, A.A., et al., *Insulin resistance, brain atrophy, and cognitive performance in late middle-aged adults*. Diabetes Care, 2013. **36**(2): p. 443-9.
284. Cherbuin, N., P. Sachdev, and K.J. Anstey, *Higher normal fasting plasma glucose is associated with hippocampal atrophy: The PATH Study*. Neurology, 2012. **79**(10): p. 1019-26.
285. Kerti, L., et al., *Higher glucose levels associated with lower memory and reduced hippocampal microstructure*. Neurology, 2013. **81**(20): p. 1746-52.
286. Mortby, M.E., et al., *High "normal" blood glucose is associated with decreased brain volume and cognitive performance in the 60s: the PATH through life study*. PLoS One, 2013. **8**(9): p. e73697.
287. Launer, L.J., et al., *Effects of intensive glucose lowering on brain structure and function in people with type 2 diabetes (ACCORD MIND): a randomised open-label substudy*. Lancet Neurol, 2011. **10**(11): p. 969-77.
288. Pan, A., et al., *Visual assessment of brain magnetic resonance imaging detects injury to cognitive regulatory sites in patients with heart failure*. J Card Fail, 2013. **19**(2): p. 94-100.
289. Woo, M.A., et al., *Regional hippocampal damage in heart failure*. Eur J Heart Fail, 2015. **17**(5): p. 494-500.
290. Almeida, O.P. and L. Flicker, *The mind of a failing heart: a systematic review of the association between congestive heart failure and cognitive functioning*. Intern Med J, 2001. **31**(5): p. 290-5.
291. Samieri, C., et al., *Association of Cardiovascular Health Level in Older Age With Cognitive Decline and Incident Dementia*. JAMA, 2018. **320**(7): p. 657-664.
292. Sacre, J.W., et al., *Associations of Chronic Kidney Disease Markers with Cognitive Function: A 12-Year Follow-Up Study*. J Alzheimers Dis, 2018.

293. Jassal, S.K., D. Kritz-Silverstein, and E. Barrett-Connor, *A prospective study of albuminuria and cognitive function in older adults: the Rancho Bernardo study*. *Am J Epidemiol*, 2010. **171**(3): p. 277-86.
294. Kurella Tamura, M., et al., *Albuminuria, kidney function, and the incidence of cognitive impairment among adults in the United States*. *Am J Kidney Dis*, 2011. **58**(5): p. 756-63.
295. Hailpern, S.M., et al., *Moderate chronic kidney disease and cognitive function in adults 20 to 59 years of age: Third National Health and Nutrition Examination Survey (NHANES III)*. *J Am Soc Nephrol*, 2007. **18**(7): p. 2205-13.
296. Kurella, M., et al., *Cognitive impairment in chronic kidney disease*. *J Am Geriatr Soc*, 2004. **52**(11): p. 1863-9.
297. Yaffe, K., et al., *Chronic kidney disease and cognitive function in older adults: findings from the chronic renal insufficiency cohort cognitive study*. *J Am Geriatr Soc*, 2010. **58**(2): p. 338-45.
298. Etgen, T., et al., *Chronic kidney disease is associated with incident cognitive impairment in the elderly: the INVADE study*. *Nephrol Dial Transplant*, 2009. **24**(10): p. 3144-50.
299. Seliger, S.L., et al., *Moderate renal impairment and risk of dementia among older adults: the Cardiovascular Health Cognition Study*. *J Am Soc Nephrol*, 2004. **15**(7): p. 1904-11.
300. Mogi, M. and M. Horiuchi, *Clinical Interaction between Brain and Kidney in Small Vessel Disease*. *Cardiol Res Pract*, 2011. **2011**: p. 306189.
301. Vermeer, S.E., et al., *Silent brain infarcts and the risk of dementia and cognitive decline*. *N Engl J Med*, 2003. **348**(13): p. 1215-22.
302. Vermeer, S.E., W.T. Longstreth, Jr., and P.J. Koudstaal, *Silent brain infarcts: a systematic review*. *Lancet Neurol*, 2007. **6**(7): p. 611-9.
303. Fazekas, G., et al., *Brain MRI findings and cognitive impairment in patients undergoing chronic hemodialysis treatment*. *J Neurol Sci*, 1995. **134**(1-2): p. 83-8.
304. Yokoyama, S., et al., *High incidence of microbleeds in hemodialysis patients detected by T2*-weighted gradient-echo magnetic resonance imaging*. *Neurol Med Chir (Tokyo)*, 2005. **45**(11): p. 556-60; discussion 560.
305. Kamata, T., et al., *Morphologic abnormalities in the brain of chronically hemodialyzed patients without cerebrovascular disease*. *Am J Nephrol*, 2000. **20**(1): p. 27-31.
306. Savazzi, G.M., F. Cusmano, and S. Musini, *Cerebral imaging changes in patients with chronic renal failure treated conservatively or in hemodialysis*. *Nephron*, 2001. **89**(1): p. 31-6.
307. Romero, J.R., et al., *Carotid artery atherosclerosis, MRI indices of brain ischemia, aging, and cognitive impairment: the Framingham study*. *Stroke*, 2009. **40**(5): p. 1590-6.
308. Vidal, J.S., et al., *Coronary artery calcium, brain function and structure: the AGES-Reykjavik Study*. *Stroke*, 2010. **41**(5): p. 891-7.
309. Breteler, M.M., *Vascular risk factors for Alzheimer's disease: an epidemiologic perspective*. *Neurobiol Aging*, 2000. **21**(2): p. 153-60.
310. Stinghen, A.E. and R. Pecoits-Filho, *Vascular damage in kidney disease: beyond hypertension*. *Int J Hypertens*, 2011. **2011**: p. 232683.
311. Knopman, D.S., *Invited commentary: Albuminuria and microvascular disease of the brain—a shared pathophysiology*. *Am J Epidemiol*, 2010. **171**(3): p. 287-9; author reply 290-1.
312. Stivelman, J.C., *Benefits of anaemia treatment on cognitive function*. *Nephrol Dial Transplant*, 2000. **15 Suppl 3**: p. 29-35.
313. Iliescu, E.A., et al., *Quality of sleep and health-related quality of life in haemodialysis patients*. *Nephrol Dial Transplant*, 2003. **18**(1): p. 126-32.
314. Hackett, M.L. and M.J. Jardine, *We Need to Talk about Depression and Dialysis: but What Questions Should We Ask, and Does Anyone Know the Answers?* *Clin J Am Soc Nephrol*, 2017. **12**(2): p. 222-224.
315. Akman, B., et al., *Depression levels before and after renal transplantation*. *Transplant Proc*, 2004. **36**(1): p. 111-3.
316. Cukor, D., et al., *Depression and anxiety in urban hemodialysis patients*. *Clin J Am Soc Nephrol*, 2007. **2**(3): p. 484-90.
317. Szeifert, L., et al., *Symptoms of depression in kidney transplant recipients: a cross-sectional study*. *Am J Kidney Dis*, 2010. **55**(1): p. 132-40.
318. Ginieri-Coccosis, M., et al., *Quality of life, mental health and health beliefs in haemodialysis and peritoneal dialysis patients: investigating differences in early and later years of current treatment*. *BMC Nephrol*, 2008. **9**: p. 14.
319. Davison, S.N. and G.S. Jhangri, *The impact of chronic pain on depression, sleep, and the desire to withdraw from dialysis in hemodialysis patients*. *J Pain Symptom Manage*, 2005. **30**(5): p. 465-73.
320. Davison, S.N., *Pain in hemodialysis patients: prevalence, cause, severity, and management*. *Am J Kidney Dis*, 2003. **42**(6): p. 1239-47.
321. Carreon, M., et al., *Clinical correlates and treatment of bone/joint pain and difficulty with sexual arousal in patients on maintenance hemodialysis*. *Hemodial Int*, 2008. **12**(2): p. 268-74.
322. Rosas, S.E., et al., *Prevalence and determinants of erectile dysfunction in hemodialysis patients*. *Kidney Int*, 2001. **59**(6): p. 2259-66.
323. Griva, K., et al., *Illness and treatment cognitions and health related quality of life in end stage renal disease*. *Br J Health Psychol*, 2009. **14**(Pt 1): p. 17-34.
324. Kutner, N.G., et al., *Psychosocial predictors of non-compliance in haemodialysis and peritoneal dialysis patients*. *Nephrol Dial Transplant*, 2002. **17**(1): p. 93-9.
325. Theofilou, P., *Depression and anxiety in patients with chronic renal failure: the effect of sociodemographic characteristics*. *Int J Nephrol*, 2011. **2011**: p. 514070.
326. Sprangers, M.A., et al., *Which chronic conditions are associated with better or poorer quality of life?* *J Clin Epidemiol*, 2000. **53**(9): p. 895-907.
327. Murray, A.M., et al., *Cognitive impairment in hemodialysis patients is common*. *Neurology*, 2006. **67**(2): p. 216-23.
328. Sehgal, A.R., et al., *Prevalence, recognition, and implications of mental impairment among hemodialysis patients*. *Am J Kidney Dis*, 1997. **30**(1): p. 41-9.
329. Griva, K., et al., *Cognitive impairment and 7-year mortality in dialysis patients*. *Am J Kidney Dis*, 2010. **56**(4): p. 693-703.
330. Berkman, L.F., et al., *Effects of treating depression and low perceived social support on clinical events after myocardial infarction: the Enhancing Recovery in Coronary Heart Disease Patients (ENRICH) Randomized Trial*. *JAMA*, 2003. **289**(23): p. 3106-16.

331. Glassman, A.H., et al., *Sertraline treatment of major depression in patients with acute MI or unstable angina*. JAMA, 2002. **288**(6): p. 701-9.
332. Lesperance, F. and N. Frasure-Smith, *Sertraline for treatment of depression in acute coronary syndromes*. JAMA, 2002. **288**(19): p. 2403; author reply 2403-4.
333. Dickens, C., et al., *Characteristics of psychological interventions that improve depression in people with coronary heart disease: a systematic review and meta-regression*. Psychosom Med, 2013. **75**(2): p. 211-21.
334. Cummings, D.M., et al., *Randomized Trial of a Tailored Cognitive Behavioral Intervention in Type 2 Diabetes With Comorbid Depressive and/or Regimen-Related Distress Symptoms: 12-Month Outcomes From COMRADE*. Diabetes Care, 2019. **42**(5): p. 841-848.
335. Uchendu, C. and H. Blake, *Effectiveness of cognitive-behavioural therapy on glycaemic control and psychological outcomes in adults with diabetes mellitus: a systematic review and meta-analysis of randomized controlled trials*. Diabet Med, 2017. **34**(3): p. 328-339.
336. Gary, R.A., et al., *Combined exercise and cognitive behavioral therapy improves outcomes in patients with heart failure*. J Psychosom Res, 2010. **69**(2): p. 119-31.
337. Freedland, K.E., et al., *Cognitive Behavior Therapy for Depression and Self-Care in Heart Failure Patients: A Randomized Clinical Trial*. JAMA Intern Med, 2015. **175**(11): p. 1773-82.
338. Palmer, S.C., et al., *Antidepressants for treating depression in adults with end-stage kidney disease treated with dialysis*. Cochrane Database Syst Rev, 2016(5): p. CD004541.
339. Cukor, D., et al., *Psychosocial intervention improves depression, quality of life, and fluid adherence in hemodialysis*. J Am Soc Nephrol, 2014. **25**(1): p. 196-206.
340. Duarte, P.S., et al., *Cognitive-behavioral group therapy is an effective treatment for major depression in hemodialysis patients*. Kidney Int, 2009. **76**(4): p. 414-21.
341. Chen, H.Y., et al., *Cognitive-behavioral therapy for sleep disturbance in patients undergoing peritoneal dialysis: a pilot randomized controlled trial*. Am J Kidney Dis, 2008. **52**(2): p. 314-23.
342. Greenwood, S.A., et al., *Evaluation of a pragmatic exercise rehabilitation programme in chronic kidney disease*. Nephrol Dial Transplant, 2012. **27 Suppl 3**: p. iii126-34.
343. Ouzouni, S., et al., *Effects of intradialytic exercise training on health-related quality of life indices in haemodialysis patients*. Clin Rehabil, 2009. **23**(1): p. 53-63.
344. Kouidi, E., et al., *Depression, heart rate variability, and exercise training in dialysis patients*. Eur J Cardiovasc Prev Rehabil, 2010. **17**(2): p. 160-7.
345. Wells, K.B., et al., *The functioning and well-being of depressed patients. Results from the Medical Outcomes Study*. JAMA, 1989. **262**(7): p. 914-9.
346. Grenard, J.L., et al., *Depression and medication adherence in the treatment of chronic diseases in the United States: a meta-analysis*. J Gen Intern Med, 2011. **26**(10): p. 1175-82.
347. Desai, R.A., E.A. Stefanovics, and R.A. Rosenheck, *The role of psychiatric diagnosis in satisfaction with primary care: data from the department of veterans affairs*. Med Care, 2005. **43**(12): p. 1208-16.
348. Hamilton, W., A. Round, and D. Sharp, *Patient, hospital, and general practitioner characteristics associated with non-attendance: a cohort study*. Br J Gen Pract, 2002. **52**(477): p. 317-9.
349. Pesata, V., G. Pallija, and A.A. Webb, *A descriptive study of missed appointments: families' perceptions of barriers to care*. J Pediatr Health Care, 1999. **13**(4): p. 178-82.
350. Zimbudzi, E., et al., *Self-management in patients with diabetes and chronic kidney disease is associated with incremental benefit in HRQOL*. J Diabetes Complications, 2017. **31**(2): p. 427-432.
351. Chi, N.C. and G. Demiris, *A systematic review of telehealth tools and interventions to support family caregivers*. J Telemed Telecare, 2015. **21**(1): p. 37-44.
352. Blakeman, T., et al., *Effect of information and telephone-guided access to community support for people with chronic kidney disease: randomised controlled trial*. PLoS One, 2014. **9**(10): p. e109135.
353. Shariful Islam, S.M., et al., *Effect of text messaging on depression in patients with coronary heart disease: a substudy analysis from the TEXT ME randomised controlled trial*. BMJ Open, 2019. **9**(2): p. e022637.
354. Chow, C.K., et al., *Effect of Lifestyle-Focused Text Messaging on Risk Factor Modification in Patients With Coronary Heart Disease: A Randomized Clinical Trial*. JAMA, 2015. **314**(12): p. 1255-63.
355. Urquhart-Secord, R., et al., *Patient and Caregiver Priorities for Outcomes in Hemodialysis: An International Nominal Group Technique Study*. Am J Kidney Dis, 2016. **68**(3): p. 444-54.
356. Tong, A., et al., *Patients' priorities for health research: focus group study of patients with chronic kidney disease*. Nephrol Dial Transplant, 2008. **23**(10): p. 3206-14.
357. Walker, K.A., et al., *Association of Midlife to Late-Life Blood Pressure Patterns With Incident Dementia*. JAMA, 2019. **322**(6): p. 535-545.
358. Cass, A., *The Economic Impact of End Stage Kidney Disease in Australia: projects to 2020* 2010.
359. Ariyaratne, T.V., et al., *Cardiovascular readmissions and excess costs following percutaneous coronary intervention in patients with chronic kidney disease: data from a large multi-centre Australian registry*. Int J Cardiol, 2013. **168**(3): p. 2783-90.
360. Vupputuri, S., et al., *The economic burden of progressive chronic kidney disease among patients with type 2 diabetes*. J Diabetes Complications, 2014. **28**(1): p. 10-6.
361. McQueen, R.B., et al., *Economic burden of comorbid chronic kidney disease and diabetes*. J Med Econ, 2017. **20**(6): p. 585-591.
362. Morton, R.L., et al., *Impact of CKD on Household Income*. Kidney Int Rep, 2018. **3**(3): p. 610-618.
363. Turchetti, G., et al., *The social cost of chronic kidney disease in Italy*. Eur J Health Econ, 2017. **18**(7): p. 847-858.
364. Neuen, B.L., et al., *Sodium-glucose cotransporter inhibitors in type 2 diabetes: thinking beyond glucose lowering*. CMAJ, 2019. **191**(41): p. E1128-E1135.
365. Liu, J.J., T. Lee, and R.A. DeFronzo, *Why Do SGLT2 inhibitors inhibit only 30-50% of renal glucose reabsorption in humans?* Diabetes, 2012. **61**(9): p. 2199-204.
366. Zinman, B., et al., *Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes*. N Engl J Med, 2015. **373**(22): p. 2117-28.
367. Neal, B., et al., *Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes*. N Engl J Med, 2017. **377**(7): p. 644-657.

368. Wiviott, S.D., I. Raz, and M.S. Sabatine, *Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes. Reply*. N Engl J Med, 2019. **380**(19): p. 1881-1882.
369. Pollock, C., et al., *Albuminuria-lowering effect of dapagliflozin alone and in combination with saxagliptin and effect of dapagliflozin and saxagliptin on glycaemic control in patients with type 2 diabetes and chronic kidney disease (DELIGHT): a randomised, double-blind, placebo-controlled trial*. Lancet Diabetes Endocrinol, 2019. **7**(6): p. 429-441.
370. Mathew, T.H. and G. Australasian Creatinine Consensus Working, *Chronic kidney disease and automatic reporting of estimated glomerular filtration rate: a position statement*. Med J Aust, 2005. **183**(3): p. 138-41.
371. Mathew, T.H., et al., *Chronic kidney disease and automatic reporting of estimated glomerular filtration rate: revised recommendations*. Med J Aust, 2007. **187**(8): p. 459-63.
372. Noble, E., et al., *The impact of automated eGFR reporting and education on nephrology service referrals*. Nephrol Dial Transplant, 2008. **23**(12): p. 3845-50.
373. Foote, C., et al., *Impact of estimated GFR reporting on late referral rates and practice patterns for end-stage kidney disease patients: a multilevel logistic regression analysis using the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA)*. Am J Kidney Dis, 2014. **64**(3): p. 359-66.
374. Levey, A.S., C. Becker, and L.A. Inker, *Glomerular filtration rate and albuminuria for detection and staging of acute and chronic kidney disease in adults: a systematic review*. JAMA, 2015. **313**(8): p. 837-46.
375. Levey, A.S., et al., *National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification*. Ann Intern Med, 2003. **139**(2): p. 137-47.
376. *Chronic Kidney Disease (CKD) Management in Primary Care (4th edition)*. 2020: Kidney Health Australia, Melbourne.
377. Heerspink H.J.L., et al., DAPA-CKD Trial Committees and Investigators. *Dapagliflozin in Patients with Chronic Kidney Disease*. N Engl J Med. 2020. **383**(15):1436-1446

List of abbreviations

ABS	Australian Bureau of Statistics
ACR	Albumin-to-creatinine ratio
AIHW	Australian Institute of Health and Welfare
ANZDATA	Australia and New Zealand Dialysis and Transplant Registry
AusDiab	Australia Diabetes, Obesity and Lifestyle Study
BMI	Body mass index
CKD	Chronic kidney disease
CVD	Cardiovascular disease
DM	Diabetes mellitus
ESKD	End-stage kidney disease
eGFR	Estimated glomerular filtration rate
GFR	Glomerular filtration rate
KHA	Kidney Health Australia
KF	Kidney failure
KRT	Kidney replacement therapy
NDSS	National Diabetes Services Scheme
NHMRC	National Health and Medical Research Council
SES	Socioeconomic status
SGLT2	Sodium-glucose cotransporter-2
TSANZ	The Transplantation Society of Australia and New Zealand

A

Appendix A: Definitions

Diagnosis and definition of Chronic Kidney Disease (CKD)

Diagnosis of CKD is made by establishing evidence of a chronic reduction in kidney function and/or structural kidney damage, persisting for at least 3 months, regardless of underlying cause^[14]. The best measure of kidney function is glomerular filtration rate (GFR) – the total amount of fluid filtered through all functioning nephrons per unit of time^[374]. The gold-standard method of GFR measurement is by timed clearance of an exogenous compound cleared solely by kidney filtration, although in clinical practice GFR is usually estimated from the clearance of the endogenous filtration marker creatinine, a natural product of muscle metabolism. GFR can be estimated from urinary creatinine clearance or from serum creatinine concentration, which rises as kidney function deteriorates and the body's ability to clear waste products is reduced.

Of the various markers of structural kidney damage that exist, albuminuria is most commonly used for diagnosis of CKD. Normally a person excretes about 80mg of total protein per day in the urine, consisting of filtered plasma proteins including albumin, immunoglobulin, and secreted proteins. Elevation in either total protein or the amount of albumin being excreted is a sign of kidney damage. Kidney damage may therefore be diagnosed by the presence of one or more of:

- Albuminuria (protein in the urine)
- Haematuria (blood in the urine) after exclusion of urological causes
- Structural abnormalities (e.g. on kidney imaging tests)
- Pathological abnormalities (e.g. kidney biopsy)
- Abnormal kidney function.

Current international guidelines define CKD as GFR of less than 60 mL/min/1.73m² (representing a loss of approximately half the normal young adult functional capacity of the kidney) and/or evidence of kidney damage, persisting for at least three months. The definition and classification of CKD has evolved over time, with the first consensus definition of CKD published by the Kidney Disease Outcomes Quality Initiative (K/DOQI) of the National Kidney Foundation of the United States in 2002^[375]. This definition has subsequently been refined by an international kidney disease guideline working group (KDIGO), taking into account the epidemiological evidence that has been generated over the past two decades^[69].

The KDIGO CKD Work Group Clinical Practice Guidelines define five stages of CKD, ranging from Stage 1 (mildest) to Stage 5/kidney failure (KF). Each increasing stage of CKD is associated with increasing risks of all-cause mortality, cardiovascular mortality and progression to KF (see Table 1). Detailed guidance on the diagnosis and management of CKD for General Practitioners is provided in the Kidney Health Australia CKD Management in Primary Care handbook^[376].

Table A1: Classification of CKD according to KDIGO Guidelines, and corresponding risk of all-cause mortality^[69]

GFR category	Description	GFR range (mL/min/1.73m ²)	Risk of all-cause mortality by albuminuria category		
			ACR <30 mg/g	30-300 mg/g	>300 mg/g
G1	Normal or high	≥90	Low [†]	Increased Risk	High Risk
G2	Mildly decreased*	60-89	Low [†]	Increased Risk	High Risk
G3a	Mild to moderately decreased	45-59	Increased Risk	High Risk	Very High Risk
G3b	Moderately to severely decreased	30-44	Increased/High Risk	High Risk	Very High Risk
G4	Severely decreased	15-29	Very High Risk	Very High Risk	Very High Risk
G5	Kidney failure	<15	Very High Risk	Very High Risk	Very High Risk

* Relative to young adult level of GFR.

† In the absence of evidence of kidney damage, neither GFR category G1 or G2 fulfil the criteria for CKD.

The International Statistical Classification of Diseases and Related Health Conditions, 10th Revision (ICD-10), codes used to define diagnosis groups for CKD in this report are:

Group of CKD	ICD-10 2016 codes
Diabetic nephropathy	E10.2, E11.2, E13.2, E14.2
Hypertensive kidney disease	I12, I13, I15.0, I15.1
Glomerular diseases	N00-N07, N08
Kidney tubule-interstitial diseases	N11, N12, N14, N15, N16
Chronic kidney failure	N18
Unspecified kidney failure	N19
Other disorders of kidney and ureter	N25-N28, N391, N392, E85.1, D59.3, B52.0
Congenital malformations	Q60-Q63
Complications related to dialysis and kidney transplant	T82.4, T86.1
Preparatory care for dialysis	Z49.0
Haemodialysis	Z49.1
Peritoneal dialysis	Z49.2
Kidney transplant and dialysis status	Z94.0, Z99.2

Definition of diabetes used in this report

Diabetes mellitus (referred to in this report as diabetes) is a chronic disease marked by high levels of glucose in the blood. It is caused either by the inability to produce insulin, by the body being unable to use insulin effectively, or both. There are 3 main types of diabetes:

1. Type 1 diabetes – an autoimmune disease that usually has onset in childhood or early adulthood, but can be diagnosed at any age
2. Type 2 diabetes – largely preventable, usually associated with lifestyle factors and with onset later in life
3. Gestational diabetes – when higher than normal blood glucose levels are diagnosed during pregnancy.

In this report, diabetes refers to any of the three main types of diabetes listed above, as well as diabetes of other or undefined type. Corresponding ICD-10 codes are as follows:

Type of diabetes	ICD-10 2016 codes
Type 1 diabetes	E10, O24.0
Type 2 diabetes	E11, O24.1
Other and unspecified diabetes	E13-E14, O24.2, O24.3
Gestational diabetes	O24.4, O24.9

Definition of cardiovascular disease used in this report

Different Australian data sources use slightly different inclusion criteria to define cardiovascular disease. For the purposes of this report, the broadly inclusive definition of cardiovascular disease used by the AIHW in their 2014-2015 Australian Fact Series is used [99]. The definition that was used for the 2011-2012 Australian Health Survey (see Appendix B) is as follows:

Condition	Condition status*
Hypertensive diseases	1
Ischaemic heart diseases (coronary heart disease)	1, 2 and 3
Other heart diseases	1, 2 and 3
Tachycardia	1
Cerebrovascular diseases	1, 2 and 3
Oedema	1
Diseases of arteries arterioles and capillaries	1
Diseases of veins, lymphatic vessels etc	1
Other diseases of circulatory system	1
Symptoms/signs involving circulatory system	1

* Condition status is defined based on the following criteria:

1. Ever told has condition, still current and long term
2. Ever told has condition, still current but not long term
3. Ever told has condition, not current.

ICD-10 codes used to define diagnosis groups for cardiovascular disease were as follows:

Cardiovascular disease type	ICD-10 2016 codes
Cardiovascular disease	I00-I99
Coronary heart disease	I20-I25
Acute myocardial infarction	I21
Angina	I20
Cerebrovascular disease	I60-I69
Stroke	I60-I64
Transient ischaemic attack (TIA)	G45
Heart failure and cardiomyopathy	I50, I25.5, I42.0, I42.5-I42.9, I43
Heart failure	I50
Peripheral vascular disease	I70-I74
Congenital heart disease	Q20-Q28

B

Appendix B: Data sources

2017-18 National Health Survey (NHS)

The 2017-18 National Health Survey (NHS) is the most recent in a series of Australia-wide surveys conducted by the Australian Bureau of Statistics. The survey was designed to collect a range of information about the health of Australians, including:

- Prevalence of long-term health conditions
- Health risk factors such as smoking, overweight and obesity, alcohol consumption and physical activity, and
- Demographic and socioeconomic characteristics.

The survey was conducted throughout Australia from July 2017 to June 2018. Previous surveys were conducted in 1989-90, 1995, 2001, 2004-05, 2007-08, 2011-12 and 2014-15.

The 2017-18 NHS was conducted from a sample of approximately 21,300 people in 16,400 private dwellings across Australia. Dwellings were selected at random using a multistage area sample of private dwellings, with a 76.1% response rate.

Trained ABS interviewers conducted personal interviews with selected residents in sampled dwellings. One adult (aged 18 years and over) in each dwelling was selected and interviewed about their own health characteristics as well as information about the household (for example, income of other household members). An adult, nominated by the household, was interviewed about one child in the household. Some children aged 15-17 years may have been personally interviewed with parental consent.

Urban and rural areas in all states and territories were included, while Very Remote areas of Australia and discrete Aboriginal and Torres Strait Islander communities were excluded. These exclusions

are unlikely to affect national estimates and will only have a minor effect on aggregate estimates produced for individual states and territories, excepting the Northern Territory where the population living in Very Remote areas accounts for around 20.3% of persons.

Non-private dwellings such as hotels, motels, hospitals, nursing homes and short-stay caravan parks were excluded from the survey. This may affect estimates of the number of people with some long-term health conditions (for example, conditions which may require periods of hospitalisation or long-term care).

The following groups were excluded from the survey:

- Certain diplomatic personnel of overseas governments, customarily excluded from the Census and estimated resident population
- Persons whose usual place of residence was outside Australia
- Members of non-Australian Defence forces (and their dependents) stationed in Australia; and
- Visitors to private dwellings.

2011-12 Australian Health Survey (AHS)

The Australian Bureau of Statistics (ABS) 2011-12 Australian Health Survey (AHS) combined the existing National Health Survey for 2011-12 with two additional components: A National Nutrition and Physical Activity Survey and a National Health Measures Survey (NHMS). All people selected in the AHS were selected in either the National Health Survey or the National Nutrition and Physical Activity Survey. However, there was a core set of data items common to both surveys; therefore, information for these data items is available for all persons in the AHS (approximately 32,000). This core set

of data items included household information, demographics, self-assessed health status and self-assessed body mass. All people aged 5 and over were then invited to participate in the voluntary NHMS.

The NHMS collected voluntary samples from around 11,200 Australian adults and children across urban, remote and very remote locations (very remote was only sampled in the Indigenous component of the survey). Voluntary urine samples were collected from respondents aged 5 and over, and voluntary blood samples from respondents aged 12 and over. The survey focuses on test results from these samples for chronic diseases, including diabetes, CVD, CKD and liver function. Results also include measures of exposure to tobacco smoke, and risk of anaemia.

The ABS 2011–12 AHS covered approximately 25,000 private dwellings across Australia. Urban and rural areas in all states and territories were included, while Very remote areas of Australia and discrete Aboriginal and Torres Strait Islander communities (and the remainder of the Collection Districts in which these communities were located) were excluded. These exclusions are unlikely to affect national estimates but will impact on prevalence estimates by remoteness. The aggregation of Remote areas with Outer regional areas and the exclusion of Very remote areas mean that the influence of remoteness on disease prevalence could not be fully assessed in this report.

Non-private dwellings such as institutional care facilities (including hospitals and aged care facilities), hotels, motels and short-stay caravan parks were excluded from the survey. The following groups were also excluded: certain diplomatic personnel of overseas governments, customarily excluded from the Census and estimated resident population; persons whose usual place of residence was outside Australia; members of non-Australian Defence forces (and their dependants) stationed in Australia; and visitors to private dwellings.

The AHS collected self-reported data on whether a respondent had 1 or more long-term health conditions; that is, conditions that had lasted, or were expected to last, 6 months or more. It should be noted that the AHS may underestimate the number of people with these conditions for the reasons given below:

1. People living in institutional care facilities, such as hospitals and aged care facilities, were not included in the survey. This excludes a sector of the population where high levels of cardiovascular disease, diabetes and chronic kidney disease are expected to occur.
2. Some respondents may not have known or been able to accurately report their health status, while others may have over-reported their condition.

Using data from the AHS to examine differences in disease prevalence by remoteness does not present a complete picture because the AHS excludes those living in *Very remote* areas. Further aggregation of *Outer regional* with *Remote* areas may mask important differences in remote areas, given the population in *Outer regional* areas is much larger than in *Remote* areas.

AusDiab Study

The AusDiab (Australian Diabetes, Obesity and Lifestyle Study) baseline study was conducted from 1999 to 2000, providing national estimates of the prevalence of diabetes, obesity, hypertension and CKD in Australia (<https://www.baker.edu.au/ausdiab/>). The second phase of AusDiab, completed in December 2005, was a five-year follow-up of the people who participated in the baseline survey. A twelve-year follow-up was completed in 2012, with the results released in August 2013.

AusDiab consisted of field surveys involving biomedical testing and questionnaires. A team of researchers went to each of 42 randomly selected testing sites across the six states and the Northern Territory of Australia, testing 11,247 individuals in the baseline study (1999–2000). Six and a half thousand of the baseline participants came back to attend the five-year follow-up survey, and self-reported health information was obtained for an additional 2000 participants who could not attend the survey site.

Non-institutionalised adults aged ≥ 25 years were eligible to participate in AusDiab. Biomedical examination included an oral glucose tolerance test (OGTT), fasting blood measurements (blood glucose, blood lipids and HbA1c), blood pressure measurements, serum creatinine, spot urine measurements (albumin and creatinine) and standard anthropometric tests. Questionnaires

captured demographic characteristics, medical and family history, lifestyle-related factors and health-related behaviours.

Further information about the AusDiab survey methods and findings can be found at <https://www.baker.edu.au/impact/ausdiab/resources>

ANZDATA

The Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) collects information to monitor dialysis and transplant treatments from all renal units in Australia and New Zealand on all patients receiving kidney replacement therapy where the intention to treat is long-term. Cases of acute kidney injury are excluded. The registry is coordinated within the Queen Elizabeth Hospital in Adelaide and compiles data on incidence and prevalence of treated-KF, complications, comorbidities and patient deaths. All relevant hospitals and related dialysis units participate. While patients have the option of opting out of having part or all their data recorded, this rarely happens. The interpretation and reporting of these data are the responsibility of the author and in no way should be seen as an official policy or interpretation of ANZDATA.

Further information about ANZDATA can be found in the ANZDATA 42nd Annual Report 2019 (<https://www.anzdata.org.au/report/anzdata-42nd-annual-report-2019/>).

AIHW Cardiovascular disease, diabetes and chronic kidney disease – Australian Facts Series

In 2014, the National Centre for Monitoring Vascular Diseases at the Australian Institute for Health and Welfare (AIHW) released a series of reports examining cardiovascular diseases, diabetes and CKD and their interrelationships (*Cardiovascular Disease, Diabetes and Chronic Kidney Disease – Australian Facts*). Reports in the series include:

- *Cardiovascular disease, diabetes and chronic kidney disease – Australian Facts: mortality*
- *Cardiovascular disease, diabetes and chronic kidney disease – Australian Facts: prevalence and incidence*
- *Cardiovascular disease, diabetes and chronic kidney disease – Australian Facts: morbidity*
- *Cardiovascular disease, diabetes and chronic kidney disease – Australian Facts: risk factors*

- *Cardiovascular disease, diabetes and chronic kidney disease – Australian Facts: Indigenous Australians.*

These reports present up-to-date statistics as of 2014, trend data, and variation across population groups, by age group, sex, geographical location, socioeconomic status and Aboriginal and Torres Strait Islander status.

Data sources: mortality

Mortality data up to 2011 were obtained from the Registries of Births, Deaths and Marriages, the Coroners and the National Coroners Information System and coded by the Australian Bureau of Statistics (ABS). These data are maintained at the Australian Institute of Health and Welfare (AIHW) in the National Mortality Database.

Since 2007, ABS has put in place a mortality data revision process that supplies up to 3 levels of data releases: preliminary, revised and final. This analysis is based on the final versions for the years prior to 2010, the revised version for 2010 and the preliminary version for 2011, these being the most recent available data at time of production.

The data quality statements underpinning the Australian Institute of Health and Welfare (AIHW) National Mortality Database can be found in the ABS quality declaration summary for *Causes of death, Australia, 2012* (ABS cat. no. 3303.0) and the quality declaration summary for *Deaths, Australia, 2011* (ABS cat. no. 3302.0)

Data sources: prevalence and incidence

ANZDATA
See above.

2011-12 Australian Health Survey (AHS)
See above.

National Health Survey (NHS)
The report *Cardiovascular disease, diabetes and chronic kidney disease – Australian Facts: prevalence and incidence* presents findings from the 1989-90, 1995, 2001, 2004-5, 2007-8 and 2011-12 NHS.

National (insulin-treated) Diabetes Register
The NDR is maintained by the AIHW under contract with the Department of Health. The NDR is derived from two primary data sources: the NDSS and the APEG.

The NDSS, which was established in 1987 and is administered by Diabetes Australia, is an initiative of the Australian Government to subsidise the supply of diabetes-related products—such as pens and needles to administer insulin, blood glucose test strips and insulin pump consumables—to people who are registered with the scheme.

The APEG is a professional body that represents health professionals involved in the management and research of children and adolescents with disorders of the endocrine system, including diabetes. The APEG maintains clinic-based state and territory diabetes registers, with paediatricians, physicians, paediatric endocrinologists, endocrinologists, diabetes educators and nurses reporting incident cases to these registers.

The NDR is a database of people living in Australia with insulin-treated diabetes. It was established in 1999 to monitor the incidence and prevalence of insulin-treated diabetes in Australia. The NDR aims to record all new cases of people who use insulin to treat their diabetes, and includes people with type 1, type 2, gestational and other forms of diabetes. As people with type 1 diabetes require insulin for survival, almost all new cases of type 1 diabetes should be covered by the NDR. Only a proportion of type 2 and gestational diabetes cases require insulin treatment; those that do not require insulin treatment are not within the scope of the NDR.

National Perinatal Data Collection

The National Perinatal Data Collection is a national data set maintained by the National Perinatal Statistics Unit, one of the collaborating units of the AIHW and part of the University of New South Wales. The National Perinatal Statistics Unit contains selected information relating to births that are reported to the perinatal data collection in each Australian state and territory. The National Perinatal Data Collection includes demographic, diagnostic, procedural and duration-of-stay information for both mothers and babies. Selected information is compiled annually into this collection by the National Perinatal Statistics Unit. For the 2009–2011 period, Victoria did not supply data and Tasmania only incomplete data.

Data sources: morbidity

ANZDATA

See above.

National Hospital Morbidity Database

The NHMD is a compilation of episode-level records from admitted patient morbidity data collection systems in Australian hospitals. The database contains data relating to admitted patients in almost all hospitals in Australia.

The counting unit for the NHMD is the separation. A separation is an episode of care for an admitted patient, which can be a total hospital stay (from admission to discharge, transfer or death) or a portion of a hospital stay beginning or ending in a change of type of care (for example, from acute care to rehabilitation).

Data on diagnoses are recorded uniformly using the International statistical classification of diseases and related health problems, 10th revision, Australian modification (ICD-10-AM, 8th edition) (NCCC 2012). Information on procedures was recorded using the Australian Classification of Health Interventions.

Hospitalisation data are sourced from the AIHW National Hospital Morbidity Database (NHMD), which is a compilation of episode-level records from admitted patient morbidity data collection systems in Australian hospitals. Data were mostly for the financial year 2012–13. Some trend information was also included from 1993–94 to 2012–13. The data in this report were extracted from the AIHW NHMD in June 2014 and small changes may have occurred since this time.

The NHMD is based on the Admitted Patient Care National Minimum Data Set (APC NMDS). It records information on admitted patient care (hospitalisations) in essentially all hospitals in Australia, and includes demographic, administrative and length-of-stay data, as well as data on the diagnoses of the patients, the procedures they underwent in hospital and external causes of injury and poisoning.

The scope of the APC NMDS is episodes of care for admitted patients in all public and private acute and psychiatric hospitals, freestanding day hospital facilities and alcohol and drug treatment centres in Australia. Hospitals operated by the Australian Defence Force, corrections authorities and in Australia's offshore territories are not in scope but some are included.

Reporting to the NHMD occurs at the end of a person's admitted episode of care (separation or hospitalisation) and is based on the clinical documentation for that hospitalisation. Hospitalisations (separations) are reported to the NHMD in accordance with the requirements of the APC NMDS. The APC NMDS requires the principal diagnosis and any additional diagnoses to be reported according to the most recent edition of the International Statistical Classification of Diseases and Health Related Problems, 10th Revision, Australian Modification (ICD-10-AM) and associated Australian Coding Standards.

Data sources: risk factors

2011-12 Australian Health Survey (AHS)

See above.

National Health Survey (NHS)

The report *Cardiovascular disease, diabetes and chronic kidney disease – Australian Facts: prevalence and incidence* presents findings from the 1989-90, 1995, 2001, 2004-5, 2007-8 and 2011-12 NHS.

Data sources: Indigenous Australians

ABS 2012-13 Australian Aboriginal and Torres Strait Islander Health Survey (AATSIHS) and the 2011-12 Australian Health Survey (AHS)

The ABS 2012-13 AATSIHS was used for estimates of Indigenous disease and risk factor prevalence. The ABS 2011-12 AHS was used for non-Indigenous estimates.

ABS 2012-13 Australian Aboriginal and Torres Strait Islander Health Survey (AATSIHS)

The 2012-13 AATSIHS, which forms part of the broader 2011-13 Australian Health Survey, collected information from an additional sample of around 12,900 people from 8,300 households. The AATSIHS includes the NATSIHS, the National Aboriginal and Torres Strait Islander Nutrition and Physical Activity Survey and the NATSIHMS.

All Aboriginal and Torres Strait Islander people selected in the AATSIHS responded to either the NATSIHS or the National Aboriginal and Torres Strait Islander Nutrition and Physical Activity Survey. However, there was a core set of data items common to both surveys; therefore, information for these data items is available for all persons in the AATSIHS (approximately 12,900 persons). This core

set of data items included household information, demographics, self-assessed health status and self-assessed body mass. All Aboriginal and Torres Strait Islander people aged 18 and over were then invited to participate in the voluntary NATSIHMS.

That the AATSIHS may underestimate the number of people with CVD, diabetes, CKD and their comorbidities as people living in institutional care facilities such as hospitals and aged care facilities were not included in the survey. This excludes a section of the population where high levels of chronic diseases are expected to occur. Some respondents may not have known or been able to accurately report their health status, while other may have overreported their condition.

AIHW National Hospital Morbidity Database

The Indigenous status data in the NHMD for all states and territories are considered of sufficient quality for statistical reporting from 2010-11 onwards. In 2011-12, for instance, an estimated 88% of Indigenous patients were correctly identified in public hospitals. Indigenous identification varied by remoteness, ranging from 77% in Major cities to 99% in Very remote areas. Records where Indigenous status was not stated are excluded from analyses that compare Indigenous and non-Indigenous hospitalisation rates.

Improvements in Indigenous identification in hospitals permit CVD trend analysis from 2004-05 to 2013-14 for most hospitals, except for those in the Australian Capital Territory, Tasmania and the private hospital in the Northern Territory. Note that no trend analysis was undertaken for diabetes and CKD hospitalisations, because of changes in hospital coding practices.

AIHW National Mortality Database

The ABS has assessed the quality of Indigenous identification in death registration data by state and territory in the Census Data Enhancement Indigenous Mortality Quality Study. Indigenous identification in South Australia, Western Australia and the Northern Territory has been of sufficient quality to include in mortality analyses from 1991 onwards, with Queensland and New South Wales included from 1998 onwards.

ANZDATA

See above.

About Kidney Health Australia

Kidney Health Australia has a clear purpose. We want to achieve good kidney health for all Australians.

As the peak body for kidney disease in Australia, we bring together the many voices within the kidney community, advocating on their behalf for health initiatives that will improve their quality of life. We strive to create a healthier community through increased awareness and detection of kidney disease and connect kidney patients to vital resources and services to help them manage their condition and improve their quality of life.

For over 50 years, we have worked with the clinical and research community to support treatment and research improvements and innovations to foster a future without kidney disease.

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