MEDICINEINSIGHT

Clinical review, testing and management of renally cleared medicines among MedicineInsight patients with chronic kidney disease in 2018–2019

Australian Government Department of Health

November 2020

Independent, not-for-profit and evidence-based, NPS MedicineWise enables better decisions about medicines, medical tests and other health technologies.

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Suggested citation

NPS MedicineWise. MedicineInsight report: Clinical review, testing and management of renally cleared medicines among MedicineInsight patients with chronic kidney disease in 2018–2019. Sydney: NPS MedicineWise, 2020.

Acknowledgments

We are grateful to the patients, general practitioners and general practices who allow the use of de-identified information for MedicineInsight.

Contents

EXECUTIVE SUMMARY

The Australian Government Department of Health (DoH) requested information about monitoring and management of people with chronic kidney disease (CKD), using data from the MedicineInsight program. This report aims to describe the sociodemographic characteristics and common comorbidities of people with CKD, the appropriateness of monitoring of patients with early stage (1–3) CKD in accordance with Kidney Australia guidelines, and potentially inappropriate prescribing of selected renally cleared medicines for patients with stage 3 and stage 4 CKD. These data will be used to inform the Chronic Disease Policy Section and the Quality Use of Medicines Branch of the Department of Health and the Australian Institute of Health and Welfare (AIHW) about the state of CKD management in general practice. The information may also be used in the development of general practitioner educational interventions on management of CKD by NPS MedicineWise.

Key findings

CKD documentation

- Among the 1,680,457 patients eligible for the study, 24,954 patients (1.5%) had a record of CKD, based on the MedicineInsight condition flag. The prevalence of CKD was estimated at 1.9% when using pathology results alone.
- 32,744 patients were identified as having CKD from pathology results recorded in 2017 (baseline) – 3,105 with stage 1–2 CKD and 29,639 with stage 3–5 CKD.
- Patients identified as having CKD from pathology results who also had a CKD (any stage) condition flag were as follows:
    - 31.0% (10,149 patients) of the 32,744 patients with CKD (any stage);
    - 11.7% (362 patients) of the 3,105 patients with stage 1–2 CKD; and
    - 33.0% (9,787 patients) of the 29,639 patients with stage 3–5 CKD.

Sociodemographic characteristics of patients with CKD

- Among patients with CKD (any stage), just over half were females (52.0%) and two thirds (66.0%) were aged ≥ 75 years.
- Similarly, more than half of patients with stage 3–5 CKD were females (54.0%) and 70.3% were aged ≥ 75 years.
- In contrast, the majority of patients with stage 1–2 CKD were males (67.5%) and about a third (32.7%) were in the 65–74-years age group.
- The proportion of men with CKD (any stage) and stage 3–5 CKD increased with age and the majority were aged ≥ 75 years. For stage 1–2 CKD, there were more men in the 65–74-years age group (35.1%) than the other age groups.
- Among women, almost three quarters of those with any stage CKD (70.4%) and stage 3–5 CKD (73.3%) were aged ≥ 75 years while 53.4% of those with stage 1–2 CKD were aged ≥ 65 years.
- A greater proportion of patients with stage 1–2 CKD (5.7%) were Aboriginal and Torres Strait Islander than those with stage 3–5 CKD (1.6%).

- A greater proportion of patients with stage 1–2 CKD (12.9%) were current smokers than those with stage 3–5 CKD (4.5%).
- A greater proportion of patients with stage 3–5 CKD (87.2%) were concession card holders than those with stage 1–2 CKD (70.4%).

Comorbidities of patients with CKD

- Among patients with any stage CKD, the most prevalent comorbid conditions were hypertension (80.9%), anaemia (50.0%), cardiovascular disease (42.4%) and diabetes (41.4%).
- The majority of the patients with stage 1–2 CKD had hypertension (79.4%) and diabetes (77.2%), while cardiovascular disease was recorded in 31.0% and anaemia in 28.2%.
- The majority of the patients with stage 3–5 CKD had hypertension (81.1%), while anaemia was recorded in 52.3%, cardiovascular disease in 43.6% and diabetes in 37.6%.
- Patients with stage 3–5 CKD were more likely to have cardiovascular disease, anaemia, atrial fibrillation and heart failure than those with stage 1–2 CKD.
- Patients with stage 1–2 CKD were twice as likely to have a record of diabetes than those with stage 3–5 CKD which might reflect the definition we used to identify patients with stage 1–2 CKD (only albuminuria). As patients with diabetes are more likely to be regularly tested for albuminuria as part of the diabetes annual Cycle of Care while those without diabetes are not, our definition would have selectively picked up more patients with diabetes.

Monitoring patients with CKD

- The proportion of patients with any stage CKD who had complete monitoring of the selected tests and observations (ie, at least one record of each of the included assessments: Urine albumin to creatinine ratio (urine ACR), estimated glomerular filtration rate (eGFR), blood pressure (BP) measurement, total cholesterol, HbA_{1c} [if diabetic] and haemoglobin) during the 2-year study period was 44.7%; 68.1% for those with co-existing diabetes and 28.1% for those without diabetes.
- Patients with stage 1–2 CKD had a higher rate of complete monitoring of the selected tests and observations than those with stage 3–5 CKD (80.5% vs 40.9%), irrespective of diabetes status. This may reflect the low urine ACR recording among patients with stage 3–5 CKD compared to those with stage 1–2 CKD during 2018–19. This also possibly relates to most of the patients with stage 1–2 CKD in this study having diabetes and being more likely to be monitored for albuminuria regularly as part of the annual diabetes Cycle of Care.
- The rate of complete monitoring of the selected tests and observations was greater among patients with co-existing diabetes than those with no diabetes for both stage 1–2 CKD (83.3% vs 70.7%) and stage 3–5 CKD (64.9% vs 26.5%). This reflects regular monitoring of lipids, BP, eGFR, urine ACR and HbA_{1c} through the annual diabetes Cycle of Care.
- Patients with any stage CKD and co-existing diabetes were more likely than those without diabetes to have at least two records for each of the individual tests or observations during the study: eGFR (92.0% vs 87.3%), blood pressure measurement (90.0% vs 85.3%), total cholesterol (70.8% vs 48.2%) and urine ACR (53.9% vs 18.1%).

- Urine ACR appears to have been the least recorded test among patients with any stage CKD with 66.6% of the patients without diabetes and 25.0% of those with diabetes having no record during the study period.
- Among patients eligible for the yellow clinical action plan (stage 1–2 with albuminuria and stage 3a without albuminuria) at baseline (in 2017), patients with diabetes were more likely than those without diabetes to have optimal monitoring (at least two records) for each of the individual tests or observations during the 2-year study period: eGFR (92.0% vs 86.1%), blood pressure measurement (91.4% vs 86.6%), total cholesterol (75.2% vs 50.5%) and urine ACR (56.2% vs 15.2%).
- Among patients eligible for the orange clinical action plan (stage 3a with albuminuria and stage 3b with or without albuminuria) at baseline (in 2017), patients with diabetes were more likely than those without diabetes to have optimal monitoring (at least four records) for each of the individual tests or observations during the 2-year study period: eGFR (77.0% vs 67.9%), blood pressure measurement (79.5% vs 72.9%), haemoglobin (65.0% vs 60.7%), total cholesterol (36.4% vs 19.9%) and urine ACR (21.5% vs 8.2%).
- Monitoring for albuminuria (urine ACR) during 2018–19 appears to have been less than optimal among patients who were eligible for both the yellow and orange action plans, irrespective of diabetes status.
- The above results suggest that one way to improve monitoring of patients with CKD in general practice may be to provide incentives similar to the diabetes Cycle of Care.

Prescribing of renally cleared medicines for patients with CKD

- A small proportion of patients with CKD (any stage) were prescribed the combination of an angiotensin-converting enzyme (ACE) inhibitor/sartan, a diuretic and a nonsteroidal anti-inflammatory drug (NSAID) – also known as the ‘triple whammy’ – in 2019 (1.5%) and at least once on the same day during the study (0.4%).
- Among patients with any stage CKD, 3,201 patients (9.8%) were prescribed apixaban, 1,813 patients (5.5%) rivaroxaban and 571 patients (1.7%) dabigatran. Apixaban has the lowest fraction of renal excretion (27%) and was the most prescribed direct-acting oral anticoagulant.
- Among all patients with stage 3 CKD, 12.2% were prescribed pregabalin and the dose was potentially inappropriate for 81 (2.5%) of these patients.
- Among patients with stage 3b CKD, 4.8% of were prescribed sitagliptin and the dose was potentially inappropriate for 185 (43.7%) of these patients.
- Among patients with stage 3 CKD who also had atrial fibrillation, 13.7% were prescribed rivaroxaban and the dose was potentially inappropriate in 72 patients (17.7%). Similarly, 7.0% of patients with stage 3 CKD and atrial fibrillation were prescribed dabigatran and the dose was potentially inappropriate for 56 (12.5%) of these patients.
- Among patients with stage 4 CKD, 558 patients (19.5%) were prescribed rosuvastatin, 346 patients (12.1%) pregabalin, 121 patients (4.2%) sitagliptin and 61 patients (2.1%) duloxetine.
- Potentially inappropriate prescribing was apparent for 60.3% (73 patients) of the patients with stage 4 CKD who were prescribed sitagliptin; similarly, for duloxetine (42.6%; 26 patients) and rosuvastatin (38.9%; 217 patients).

- Potentially inappropriate prescribing was observed for 3.3% (26 patients) of the 779 patients with stage 4 CKD and atrial fibrillation who were prescribed rivaroxaban; and similarly, for dabigatran (0.8%; 6 patients). Both these medicines are contraindicated for these patients
- Among the 7,707 patients with CKD (any stage) and atrial fibrillation, 2,438 patients (31.6%) had at least one prescription for apixaban of whom 27 patients (1.1% of 2,438) were prescribed a potentially inappropriate dose on their first prescription during the study.
- Note that because of the time difference between the assessment of kidney function (2017) and the prescribing of medicines (2018–19), the estimates for potentially inappropriate prescribing described above may have been underestimated (see section 2.5 and section 7.2 for further detail).

1. BACKGROUND

1.1. Chronic kidney disease

Definition and CKD stages

Chronic kidney disease (CKD) is defined as:

- an estimated or measured glomerular filtration rate (GFR) < 60 mL/min/1.73 m^2 that is present for three or more months with or without evidence of kidney damage, or
- evidence of kidney damage with or without decreased GFR that is present for more than three months (albuminuria, haematuria, and structural or pathological abnormalities).

CKD is classified into 5 stages according to kidney function (Table 1).

TABLE 1: CLASSIFICATION OF THE STAGES OF CKD

Kidney function stage	GFR (mL/min/1.73 m^2)	Albuminuria (urine ACR, mg/mmol: males ≥ 2.5; females ≥ 3.5)
1	≥ 90	+ albuminuria
2	60–89	+ albuminuria
3a	45–59	± albuminuria
3b	30–44	± albuminuria
4	15–29	± albuminuria
5	< 15 or on dialysis	± albuminuria

ACR, albumin-to-creatinine ratio; CKD, chronic kidney disease; GFR, glomerular filtration rate.

Epidemiology

Chronic kidney disease is a major public health problem in Australia and costs the health system an estimated 5.1 billion dollars per year.[1] An estimated 10% of Australian adults aged 18 years and over had CKD in 2011–12 with the majority (97%) having early signs of the disease (stages 1–3).[2] Approximately 1 in 10 Australian deaths in 2018 were attributed to CKD, either as an underlying or associated cause of death.[2] Data from Australia indicate that older people, Aboriginal or Torres Strait Islanders and people living in remote and socioeconomically disadvantaged areas are at an increased risk of CKD.

The documented risk factors for CKD include:[1]

- diabetes
- hypertension
- cardiovascular disease
- family history of kidney failure
- obesity (body mass index ≥ 30 kg/m^2)
- smoking
- age (60 years or older)
- ethnicity (Aboriginal or Torres Strait Islander origin)
- history of acute kidney injury

Comorbidities

People with CKD often have other comorbid conditions that contribute to the CKD, are complications arising from CKD, or both. Some of the most common conditions in people with CKD include hypertension, diabetes and cardiovascular disease. CKD is one of the most important risk factors for cardiovascular disease and vice versa. Diabetes is a significant risk factor for CKD with up to 40% of CKD being caused by type 2 diabetes. It is estimated that 1 in 2 Australian adults who visit a general practice with type 2 diabetes have CKD.[3] Hypertension is both a risk factor and complication of CKD with uncontrolled hypertension a risk for progression of kidney disease.

Monitoring patients with CKD

Guidelines for management of CKD recommend regular monitoring and review of people identified as having CKD. Kidney Health Australia's CKD management in general practice guidelines provide clinical action plans on the basis of eGFR and albuminuria.[1] These guidelines include colour coded clinical action plans (red, orange and yellow) that outline management goals. Recommended monitoring and frequency of monitoring vary according to the stage of CKD. For patients with less severe CKD, monitoring can be undertaken on a yearly basis but, as severity increases, monitoring is recommended more frequently, every 3–6 months (Table 2).

During scoping, the issue of whether people with early stage CKD are being monitored adequately in order to prevent further progression of the condition was felt to be of particular importance. For this study, we limited assessment of monitoring frequency to patients within the yellow and orange clinical action plans.

Monitoring was assessed based on tests and observations as reported in the paper by Khanam et al,[4] and included blood pressure monitoring, urine albumin-to-creatinine ratio (ACR), eGFR, lipids and glycated haemoglobin (HbA_{1c}) (indicated in bold type in the 'Recommended assessments' column of Table 2).

TABLE 2: MONITORING FREQUENCY AND ASSESSMENTS FOR THE YELLOW AND ORANGE ACTION PLANS IN PEOPLE WITH CKD

Clinical action plan	Patient group	Recommended assessments	Frequency of review
Yellow	• Stage 1 or 2 CKD with microalbuminuria (urine ACR of 2.5–25 mg/mmol for males or 3.5–35 mg/mmol for females) • Stage 3a CKD with normoalbuminuria (urine ACR < 2.5 mg/mmol for males and < 3.5 mg/mmol for females)	• Blood pressure • Weight • Smoking status • Urine albumin-to-creatinine ratio (ACR) • Estimated glomerular filtration rate (eGFR) • Urea, creatinine & electrolytes • Fasting lipids • HbA_{1c} if diabetic	Every 12 months
Orange	• Stage 3a CKD with microalbuminuria • Stage 3b CKD with normal or microalbuminuria	As per yellow PLUS: • Full blood count (FBC) • Calcium and phosphate • Parathyroid hormone	Every 3–6 months

Potentially inappropriate prescribing of renally cleared medicines

For patients with CKD, avoidance of nephrotoxic medicines and adjustment of medicine doses to levels appropriate for kidney function are important to ensure safe and effective therapy. Renally cleared medicines[a] can accumulate as a result of slower elimination in impaired kidney function and can cause adverse effects. Commonly prescribed medicines that should be adjusted in people with CKD include medicines for diabetes, the direct acting oral anticoagulants (DOACs), analgesics, antihypertensives, antidepressants, bisphosphonates and pregabalin.[1,5] Appendix 1 shows a list of renally cleared medicines that may require renal function monitoring.[6]

The combination of angiotensin-converting enzyme (ACE) inhibitors (or angiotensin receptor blockers [ARBs]), diuretics and non-steroidal anti-inflammatory drugs (NSAIDs) or cyclooxygenase-2 (COX-2) inhibitors (the 'triple whammy') is not advised in patients with CKD as these medicines can impair or worsen kidney function or cause acute kidney injury.[1]

Data from Australia suggest potentially inappropriate prescribing of renally cleared medicines outside the recommended guidelines. A study of older Australians with renal impairment indicated that a quarter were potentially inappropriately prescribed at least one renally cleared medicine.[7] Of these, 4 in 5 appeared to have been prescribed a higher than recommended dose and 1 in 5 prescribed a contraindicated medicine. Doody and colleagues demonstrated that, in patients aged ≥ 40 years with poor renal function, at the time of their admission to hospital 32% were on a medicine that required renal adjustment or was potentially nephrotoxic, 16% were on a contraindicated medicine and 21% were taking inappropriate doses.[8]

[a] Or medicines which have an active metabolite that is renally cleared (eg, morphine)

Recent evidence and rationale for the study

Recent evidence using MedicineInsight data from January 2013 to June 2016 suggests that there may be some practice gaps in the monitoring and management of people with CKD. Data from these publications indicate that:

- a record of CKD diagnosis is recorded in general practice clinical information software (CIS) for only a fifth of patients who have laboratory results consistent with stage 3 CKD (Khanam et al 2019)[4]
- among patients with stage 3 CKD, just under half of those with diabetes and 86% of those without diabetes do not appear to have been monitored in accordance with guidelines[4]
- 2.6% of patients with stage 3–5 CKD appear to have been inappropriately prescribed the combination of a diuretic, ACE inhibitor/sartan and NSAID ('triple whammy')[9]
- approximately 35% of patients with CKD of any severity were prescribed a potentially inappropriate medicine within 90 days of the pathology tests which were used to identify them as having CKD.[10]

Since the above data were collected, Kidney Health Australia has released two updated editions of the guidelines for management of CKD in general practice. However, the recommendations from each edition have been largely unchanged.

To explore any changes since the data used in the above studies were collected, the Department of Health requested that NPS MedicineWise provide an update of some of the findings in these studies to ascertain whether there has been an improvement in monitoring and management of people with CKD in the intervening period. The Department requested information on the sociodemographic characteristics and common comorbidities in people with CKD, the appropriateness of monitoring and review of patients with early stage (1–3) CKD and potentially inappropriate prescribing of selected renally cleared medicines in patients with stage 3–5 CKD.

Please note that people with stage 1 or 2 kidney disease are only considered to have CKD if they have albuminuria, haematuria, and/or a structural or pathological abnormality. Microscopic haematuria is likely to be investigated using a dipstick test within general practice and these results may not be recorded, or easily identified, in the clinical information system (CIS). Therefore, for this study, and consistent with other studies, only albuminuria was used to identify patients with stage 1–2 CKD.

1.2. MedicineInsight program

MedicineInsight is a leading large-scale primary care data set of longitudinal de-identified electronic health records (EHR) in Australia. MedicineInsight was initially established by NPS MedicineWise in 2011, with core funding from the Australian Government Department of Health, to collect general practice data to support quality improvement in Australian primary care and post-market surveillance of medicines. The monthly collation of collected data can be analysed for the purposes of improving patient care, quality improvement and evaluation, performing population health analysis, research and developing health policy.

MedicineInsight utilises third-party data extraction tools which extract, de-identify, encrypt and securely transmit whole-of-practice data from the clinical information systems of over 700 general practices.

Patient level data are de-identified ‘at source’ meaning patients’ personal identifiers such as name, date of birth and address are not extracted by the tool (although year of birth and postcode are extracted, enabling the calculation of age and Socio-Economic Indexes for Areas [SEIFA]). The data held in the MedicineInsight database are non-identifiable. However, each patient has a unique identifying number which allows all the records (clinical, prescription, referral etc) held in the database to be linked to the associated patient identifying number. The process of collecting patient data achieves a data collection that meets the definition of non-identified data in the NHMRC National Statement on Ethical Conduct in Human Research. [chapter 3.2, p.27].

Further information is available online: https://www.nps.org.au/medicine-insight

Representativeness

As of 1 July 2019, there were 5074 active GPs participating in the MedicineInsight program – this represents 14% of the national GP workforce. MedicineInsight has national coverage across all states and territories and remoteness areas. Practices in South Australia are underrepresented and practices in Tasmania are overrepresented, but otherwise the distribution of MedicineInsight practices in each state is similar to the distribution of all practices in each state or territory. Compared to MBS data, patients in MedicineInsight are representative of the Australian patient population in terms of age and gender. Of the patients in the MedicineInsight cohort, 2.4% had been identified as Aboriginal or Torres Strait Islander people, similar to the 2.9% rate reported in MBS statistics for total GP non-referred attendances. Further information about MedicineInsight is available elsewhere[11] and online: https://www.nps.org.au/medicine-insight.

1.3. Ethics approval for MedicineInsight

In December 2017, NPS MedicineWise was granted ethics approval for the standard operations and uses of the MedicineInsight database by NPS MedicineWise. This program approval was given by the Royal Australian College of General Practitioners (RACGP) National Research and Evaluation Ethics Committee (NREEC 17-017).

The use of MedicineInsight data for the purposes of this report was approved on July 20, 2020 by the independent Data Governance Committee (2020–019).

2. AIMS AND METHODS

2.1. Aims

The aims of this study are to:

- describe the sociodemographic characteristics and common comorbidities in people with CKD (identified by pathology results)
- describe monitoring and review of patients with stage 1–3 CKD in Australian general practice in comparison to the recommendations of Kidney Health Australia
- investigate whether a selection of commonly used renally cleared medicines are being prescribed at the appropriate dose in people with stage 3 or stage 4 CKD.

These analyses will be used to inform the Chronic Disease Policy Section and the Quality Use of Medicines Branch of the Department of Health and the Australian Institute of Health and Welfare about the state of CKD management in general practice. It may also be used in the development of GP educational interventions on management of CKD by NPS MedicineWise.

2.2. Research questions

The specific research questions are presented in Table 3.

TABLE 3: LIST OF STUDY OBJECTIVES AND RESEARCH QUESTIONS

Objectives	Questions*
1. Explore the documentation of CKD diagnoses in the CIS	a. What number and proportion of patients had a record of CKD (any stage) from their earliest record up to the end of the baseline period (31 December 2017), according to the MedicineInsight CKD flags**?
	b. What number and proportion of patients identified by pathology results† during 2017, the baseline period, as having CKD had a record of CKD according to the MedicineInsight CKD flags?
	c. What number and proportion of patients identified by pathology results during 2017 as having stage 1–2 CKD‡ had a record of CKD according to the MedicineInsight CKD flags (any)?
	d. What number and proportion of patients identified by pathology results during 2017 as having stage 3–5 CKD§ had a record of CKD according to the MedicineInsight CKD flags (any)?
2. Explore the sociodemographic characteristics of patients identified by pathology results as having CKD	a. What are the sociodemographic characteristics (age, Aboriginal and Torres Strait Islander status, socioeconomic status, remoteness and smoking status) of patients identified as having CKD, overall and stratified by sex?
	b. What are the sociodemographic characteristics (age, Aboriginal and Torres Strait Islander status, socioeconomic status, remoteness and smoking status) of patients identified as having stage 1–2 CKD, overall and stratified by sex?
	c. What are the sociodemographic characteristics (age, Aboriginal and Torres Strait Islander status, socioeconomic status, remoteness and smoking status) of patients identified as having stage 3–5 CKD, overall and stratified by sex?

Objectives	Questions*
3. Explore the common comorbidities of patients identified by pathology results as having CKD	a. What number and proportion of patients identified as having CKD (any) had a record of: • diabetes • cardiovascular disease • atrial fibrillation • hypertension • anaemia?
	b. What number and proportion of patients identified as having stage 1–2 CKD had a record of: • diabetes • cardiovascular disease • atrial fibrillation • hypertension • anaemia?
	c. What number and proportion of patients identified as having stage 3–5 CKD had a record of: • diabetes • cardiovascular disease • atrial fibrillation • hypertension • anaemia?
4.Explore the extent to which patients identified by pathology results as having CKD are monitored and reviewed is accordance with guidelines?	a. What number and proportion of patients identified as having CKD (any) had records of at least one of each of the following observations or tests over the study period, stratified by diabetes status: • ACR • eGFR • BP measurement • total cholesterol (proxy for lipids) • HbA_{1c}?
	b. What number and proportion of patients identified as having CKD (any) had records of at least one of each of the observations or tests listed in 4a above **PLUS** haemoglobin over the study period, stratified by diabetes status?
	c. What number and proportion of patients identified as having CKD (any) had 0, 1 or 2+ records of the following individual observations and tests over the study period, stratified by diabetes status: • ACR • eGFR • BP measurement • Total cholesterol • HbA_{1c} • Haemoglobin (proxy for FBC)?

Objectives	Questions*
	d. What number and proportion of patients identified as having CKD who met the yellow action plan criteria (stage 1–2 with albuminuria and stage 3a without albuminuria) had 0, 1 or 2+ records of the following individual observations or tests over the study period, stratified by diabetes status: • ACR • eGFR • BP measurement • Total cholesterol • HbA_{1c} • Haemoglobin (proxy for FBC)?
	e. What number and proportion of patients identified as having CKD who met the orange action plan criteria (stage 3a with albuminuria and stage 3b with or without albuminuria) had 0, 1, 2, 3 or 4+ records of the following individual observations or tests over the study period, stratified by diabetes status: • ACR • eGFR • BP measurement • total cholesterol • HbA_{1c} • Haemoglobin (proxy for FBC)?
5. Explore potentially inappropriate prescribing among patients identified by pathology results as having stage 1–5 CKD	a. What number and proportion of patients identified as having CKD (any) were prescribed all of the following medicines (triple whammy) during 2019: • a diuretic • an ACE inhibitor or a sartan • an NSAID? b. What number and proportion of patients identified as having CKD (any) were prescribed all of the following medicines (triple whammy) on the SAME day at least once during the study period: • a diuretic • an ACE inhibitor or a sartan • an NSAID?
6. Explore potentially inappropriate prescribing among patients identified by pathology results as having stage 3 CKD	a. What number and proportion of patients identified as having stage 3 CKD were prescribed one of the following renally cleared medicines at least once during the study period: • sitagliptin (alone or as part of an FDC) • rivaroxaban • pregabalin?
	b. What number and proportion of patients identified as having stage 3 CKD had their first issued prescription of the following medicines higher than the recommended dose, during the study period: • sitagliptin (more than 50 mg daily) • rivaroxaban (more than 15 mg daily) • pregabalin (more than 300 mg daily)?

Objectives	Questions*
7. Explore potentially inappropriate prescribing among patients identified by pathology results as having stage 4 CKD	a. What number and proportion of patients identified as having stage 4 CKD were prescribed one of the following renally cleared medicines at least once during the study period: • sitagliptin (alone or as part of an FDC) • rosuvastatin • rivaroxaban • duloxetine • pregabalin?
	b. What number and proportion of patients identified as having stage 4 CKD had their first issued prescription of the following medicines higher than the recommended dose, during the study period: • sitagliptin (more than 25 mg daily) • rosuvastatin (more than 10 mg daily) • rivaroxaban (contraindicated) • duloxetine (more than 30 mg daily) • pregabalin (more than 150 mg daily)?
8. Explore potentially inappropriate prescribing of apixaban among patients identified by pathology results as having CKD	a. What number and proportion of patients identified as having CKD were prescribed apixaban and their first issued prescription of apixaban was higher than the recommended dose, during the study period?
9. Explore prescribing of direct acting oral anticoagulants (DOAC) among patients identified by pathology results as having CKD	a. What number and proportion of patients identified as having CKD (any) were prescribed any of the following renally cleared medicines at least once during the study period: • apixaban • dabigatran • rivaroxaban?
	b. What number and proportion of patients identified as having stage 3 CKD were prescribed any of the following renally cleared medicines at least once during the study period: • apixaban • dabigatran • rivaroxaban?
	c. What number and proportion of patients identified as having stage 4 CKD were prescribed any of the following renally cleared medicines at least once during the study period: • apixaban • dabigatran • rivaroxaban?

ACE, Angiotensin-converting enzyme; ACR, albumin-to-creatinine ratio; BP, blood pressure; CKD, chronic kidney disease; CIS. Clinical information system; eGFR, estimated glomerular filtration rate; FBC, full blood count; FDC, fixed dose combination; HbA_{1c}, glycated haemoglobin; NSAID, nonsteroidal anti-inflammatory drug.

* CKD definitions are based on pathology results recorded during 2017 except where explicitly stated.

** MedicineInsight CKD flags are based on information recorded in one of the three diagnosis fields – diagnosis, reason for encounter and reason for prescription – in the patient's earliest record up to 31 December 2017.

† Pathology result definition of CKD (any) is two or more eGFR values < 60 mL/min/1.73 m^2, OR two or more urine ACR values ≥ 3.5 mg/mmol for females or ≥ 2.5 mg/mmol for males, at least 90 days apart.

‡ Pathology result definition of stage 1–2 CKD is two or more eGFR values ≥ 60 mL/min/1.73 m^2, AND albuminuria, at least 90 days apart.

§ Pathology result definition of stage 3–5 CKD is two or more eGFR values < 60 mL/min/1.73 m^2, WITH or WITHOUT albuminuria, at least 90 days apart.

2.3. Study design and period

This was a descriptive analysis, using Australian general practice data from MedicineInsight for 2 years from 1 January 2018 to 31 December 2019, inclusive, unless otherwise specified. CKD was identified using pathology results recorded from 1 January to 31 December 2017, the baseline period. Historical records outside of the study period were included when identifying patient demographics, and when assessing the presence of specified comorbidities.

2.4. Study cohort

General practice sites

De-identified patient data were obtained from 403 Australian general practice sites which met the standard data quality criteria in the MedicineInsight June 2020 download. A general practice site is used to describe one or more practices that share the same general practice database, either because they are operating within a common administrative system (eg, the same corporate entity) or in the same geographical area.

These standard data quality criteria were applied:

- the site had been established for at least 2 years, and
- had no significant interruptions of longer than 2 months in the 2 years prior to their practice data, and
- met the minimum threshold of clinical activity of at least 50 patients in the last two years.

Patient population

The general study population were patients who met the following inclusion criteria:

- visited a practice site that contributes data to MedicineInsight and meets specific MedicineInsight data quality requirements
- had valid information for age and sex
- were aged 18 years or older as at 1 July 2018
- had at least three clinical encounters during the study period – 1 January 2018 to 31 December 2019.

2.5. Definitions

Clinical encounters

A clinical encounter, or any professional exchange between a patient and a healthcare professional, was defined as all encounters at the practice site with a GP or a nurse that were: a) not identified as administrator entries nor encounters that have been transferred/imported from another practice and b) were not identified by predefined ‘administration-type’ terms found in the ‘reason for encounter’ field such as ‘administrative reasons’, ‘forms’, and ‘recall’.

Chronic kidney disease and albuminuria

Evidence from previous studies shows that CKD is often not documented as a diagnosis in the fields available to MedicineInsight.[4] Therefore, for this analysis, CKD was defined on the basis of pathology results (Table 4) recorded during 1 January to 31 December 2017, baseline.

Frequency and type of monitoring is dependent upon both stage of CKD and the presence or absence of albuminuria. A number of decisions were made when defining CKD for this study.

- Previous studies undertaken using MedicineInsight data from 2013 to 2016 identified small numbers of stage 1 CKD patients. Castelino et al found that only 27 patients had stage 1 CKD among the 28,729 patients who had CKD and were prescribed at least one of the medications of interest.[10] To preserve patient privacy, while providing as much information as possible, stage 1 and 2 CKD patients were reported as a single group.
- People with stage 1 or 2 kidney disease are only considered to have CKD if they also have albuminuria, haematuria, and/or a structural or pathological abnormality. As haematuria is likely investigated using a dipstick test in the GP surgery and the results not recorded or easily identified in the clinical information software (CIS), for this study and consistent with other studies, only albuminuria was investigated.
- Microalbuminuria and macroalbuminuria were combined into a single category of albuminuria given the greater interest in early CKD management and given any patient with macroalbuminuria, regardless of stage, is treated according to the red action plan.

TABLE 4: DEFINITIONS OF CKD STAGES AND ALBUMINURIA

Condition	Definition
Stages 1 and 2 CKD	Patients were defined as having stage 1 or stage 2 CKD if they had two or more eGFR values ≥ 60 mL/min/1.73 m^2, at least 90 days apart, and also had albuminuria (see definition below)
Stage 3a CKD	Patients were defined as having stage 3a CKD if they had two or more eGFR values 45–59 mL/min/1.73 m^2, but at least 90 days apart
Stage 3b CKD	Patients were defined as having stage 3b CKD if they had two or more eGFR values 30–44 mL/min/1.73 m^2, at least 90 days apart.
Stage 4 or 5 CKD*	Patients were defined as having stage 4 or 5 CKD if they had two or more eGFR values ≤ 29 mL/min/1.73 m^2, at least 90 days apart.
Albuminuria	Patients were defined as having albuminuria if they had two or more ACR values ≥ 3.5 mg/mmol for females or ≥ 2.5 mg/mmol for males, at least 90 days apart.
Normoalbuminuria	Patients who did not meet the criteria for albuminuria

*For the analysis of renally cleared medicines, we separately identified CKD Stage 5 (eGFR 0 to 14 mL/min/1.73 m^2, at least 90 days apart) differentiating it from Stage 4 (15 to 29 mL/min/1.73 m^2).

We also used the CKD condition flag currently included in MedicineInsight to determine the extent to which CKD is documented in the diagnosis, reason for encounter or reason for prescription fields in the CIS. Patients with a CKD flag are those who had CKD recorded in one of the three diagnosis fields at any time from their earliest record up to 31 December 2017 (ie, 'ever').

Monitoring

The definitions for the tests and observations used for CKD monitoring are shown in Table 5. Patients were considered to have complete monitoring if they had at least one record of all the selected tests and observations during the study period, January 2018 to December 2019. Complete monitoring included glycated haemoglobin (HbA_{1c}) for patients with co-existing diabetes but was not assessed for patients without diabetes.

TABLE 5: DEFINITIONS OF TESTS AND OBSERVATIONS USED FOR CKD MONITORING

Observation or test	Definition
Urine albumin-to-creatinine ratio (ACR)	A record of a urine ACR result in the atomised pathology table
Estimate glomerular filtration rate (eGFR)	A record of eGFR result in the atomised pathology table
Total cholesterol (proxy for lipids)	A record of a total cholesterol result in the atomised pathology table
Glycated haemoglobin (HbA_{1c}) (if diabetic)	A record of a HbA_{1c} result in the atomised pathology table
Haemoglobin (proxy for full blood count)	A record of a haemoglobin result in the atomised pathology table
Blood pressure measurement	A record of a blood pressure reading in the observations table

Comorbid conditions

The comorbidities that were included in this study are cardiovascular disease (CVD), diabetes (type 1 or type 2), hypertension, atrial fibrillation and anaemia.

MedicineInsight 'condition flags' were used to identify patients with all conditions, except anaemia. The flags identify patients using an algorithm that looks at relevant coded (Docle, Pyefinch) or free text entry in one of the three diagnosis fields – diagnosis, reason for encounter or reason for prescription – recorded at any time from the patient's earliest record up to the end of the study, 31 December 2019 (ie, ever). The terms that were used in the definition of each of the condition flags are shown in Table 6.

While anaemia in patients with CKD can be multifactorial in origin, it is mostly related to deficiency in erythropoietin production.[12] For this study, because the limitations of the data do not allow us to clearly identify the different forms of anaemia, we did not attempt to differentiate between the different forms of anaemia. Thus, we used the World Health Organization's (WHO) thresholds for anaemia[13] but not the thresholds specified for patients with CKD.[12] Patients with anaemia were identified using coded or free text entries in one of the three diagnosis fields and/or according to the WHO serum haemoglobin criteria (Table 6).

TABLE 6: CLINICAL DEFINITIONS USED TO IDENTIFY COMMON COMORBIDITIES AMONG MEDICINEINSIGHT PATIENTS WITH CKD

Comorbid condition	Definition
CVD (excluding AF)	Relevant terms included: atherosclerosis, coronary heart disease (including myocardial infarction and angina), peripheral vascular disease, stroke and transient ischaemic attack.
Heart failure	Relevant terms included: Includes: acute cardiac failure, biventricular heart failure, cardiac failure, CCF, chronic heart failure, congestive cardiac failure, congestive heart failure, cor pulmonale, diastolic cardiac dysfunction, diastolic heart failure, heart failure, HFmrEF, HFpEF, HFrEF, High output cardiac failure, high output heart failure, hypertensive heart failure, left heart failure, left ventricular failure, LHF (left heart failure), LVF (left ventricular failure), pulmonary oedema, RHF (right heart failure), right heart failure, right ventricular failure, RVF (right ventricular failure), systolic cardiac dysfunction, systolic heart failure, ventricular diastolic dysfunction
Diabetes (type 1 or type 2)	Relevant terms included: diabetes, diabetes (controlled or cortisone induced or unstable), diabetes mellitus, diabetes mellitus (IDDM or type I or type 1NIDDM or type ii or type 2 or type 3c), IDDM, insulin dependent diabetes mellitus, juvenile onset diabetes, latent autoimmune diabetes of adults, NIDDM, non insulin dependent diabetes mellitus, pancreatogenic, diabetes, T2DM, t11 or tii
Hypertension	Relevant terms included:(blood pressure or bp) and (labile or review or unstable), HBP, high blood pressure, HT, hypertension, hypertension (controlled or diastolic or essential or isolated systolic or labile or life style management or malignant or pregnancy or primary or renal or renovascular or review or unstable), PIH, pregnancy induced hypertension or severe refractory hypertension, free text terms in one of the three diagnosis field only such as 'BP medicine'.
Atrial fibrillation	Relevant terms included: AF, A FIB, atrial f, atrial fibrillation, atrial fibrillation (isolated episode or paroxysmal or ablation or non-valvular or valvular), fibrillation or rapid atrial fibrillation
DVT*	Relevant terms included: deep vein thrombosis, DVT
Anaemia	Relevant terms included: anaemia/anemia or anaemic/anemic. The WHO thresholds for anaemia: - females with a haemoglobin ≥ 120 g/L and males with a haemoglobin ≥ 130 g/L were categorised as not being anaemic - females with a haemoglobin ≤ 119 g/L and males with a haemoglobin ≤ 129 g/L were categorised as being anaemic - as only patients aged 18 years or older were included there was no need to use the WHO anaemia thresholds for children - due to the complexities in determining whether a patient was pregnant at the time of haemoglobin testing using data collected from clinical software, no attempt was made to use the WHO thresholds for pregnant patients

* The direct acting oral anticoagulants (DOACs) can also be used to manage people with a history of deep vein thrombosis (DVT). As the dose schedules for the prevention of subsequent events, differ from those used to manage atrial fibrillation, patients with a history of DVT will be excluded from the analyses of renally cleared medicines.

Renally cleared medicines of interest

Patients were defined as having had a renally cleared medicine that should be used cautiously in patients with stage 3 or 4 CKD if they had at least one record of an issued prescription of these medicines during the study period (January 2018 to December 2019). Potentially inappropriate prescribing was defined as the use of a contraindicated medication or inappropriately high dose according to the renal function in patients with CKD.

The list of the included medicines is provided in Table 7. Lithium, digoxin or other medicines with a narrow therapeutic index were not included in this study as these medicines are routinely monitored and adjusted according to therapeutic effect. The medicines included were chosen with reference to the 2019 Veterans' MATES program,[5] Kidney Health Australia guidelines[1] and a recent publication by Castelino and colleagues.[10]

Information on dose strength was restricted to the first issued prescription of these medicines in the study period (2018–19) given that patients with CKD were identified 12 months (1 January to 31 December 2017) prior to the study period. Due to the time lag in identification of CKD and assessment of the dose for the selected medicines, there is potential for this study to underestimate the potentially inappropriate prescribing rates.

Castelino and colleagues showed good agreement in determining the appropriateness of medicines between the Cockcroft-Gault equation or eGFR, with approximately 97% of the medications classified as appropriate by eGFR also considered appropriate by the Cockcroft-Gault equation.[10] Therefore, we used eGFR to determine appropriateness of dose.[a]

The following decisions were made.

- Metformin was not included because it was one of the medicines where Castelino and colleagues observed higher disagreement in determining appropriateness of doses between eGFR or by Cockcroft-Gault.
- The analysis on potentially inappropriate doses of the selected medicines only assessed patients with stage 4 CKD, rather than stages 4 and 5, given the greater interest in earlier rather than end-stage CKD management, and to avoid the added complexity of having two different thresholds for some medicines.

[a] We acknowledge that for people at both extremes of body size, creatinine clearance may be a better option for determining dosage or the eGFR should be adjusted to the individual's body surface area (BSA).

TABLE 7: COMMON RENALLY CLEARED MEDICINES REQUIRING DOSE ADJUSTMENT IN PEOPLE WITH STAGE 3 OR HIGHER CKD

Active ingredient (indication)	ATC code	Reduced dose according to Australian Medicines Handbook
Sitagliptin (diabetes)	A10BH01 (alone) A10BD07 (with metformin) A10BD24 (with ertuglifozin)	50 mg daily if eGFR 30–45 mL/min/1.73 m^2 (stage 3b) 25 mg daily if eGFR < 30 mL/min/1.73 m^2 (stage 4)
Rosuvastatin (lipids)	C10AA07 C10BA06	Maximum of 10 mg daily if eGFR < 30 mL/min/1.73 m^2 (stage 4)
Rivaroxaban (DOAC)	B01AF01	AF patients only: 15 mg daily if eGFR 30–49 mL/min/1.73 m^2 (stage 3) Contraindicated if eGFR < 30 mL/min/1.73 m^2 (stage 4) DVT/PE patients will be excluded
Dabigatran	B01AE07	AF patients only: 110 mg twice daily if eGFR 30–59 mL/min/1.73 m^2 (stage 3) or if patient is aged ≥ 75 years. Contraindicated if eGFR < 30 mL/min/1.73 m^2 (stage 4) DVT/PE patients will be excluded
Apixaban	B01AF02	AF patients only: 5 mg twice daily unless they meet two of the following: • Weight < 60 kg • Age > 80 years • Serum creatinine > 133 micromol/L in which case 2.5 mg twice daily. DVT/PE patients will be excluded
Pregabalin (pain)	N03AX16	Maximum of 300 mg daily if eGFR 30–60 mL/min/1.73 m2 (stage 3) Maximum 150 mg daily if eGFR 15–30 mL/min/1.73 m2 (stage 4)
Duloxetine (depression)	N06AX21	30 mg daily if eGFR < 30 mL/min/1.73 m^2 (stage 4)
triple whammy	C09A plus M01A plus C03 C09B plus M01A plus C03 C09C plus M01A plus C03 C09D plus M01A plus C03 C09BA plus M01A C09DA plus M01A	Combination use of an ACE inhibitor/sartan, a diuretic and an NSAID (including a COX-2 selective NSAID)

ACE, Angiotensin-converting enzyme; AF, atrial fibrillation; ATC, anatomical therapeutic chemical; eGFR, estimated glomerular filtration rate; DOAC, direct acting oral anticoagulants; DVT, deep vein thrombosis; NSAID, nonsteroidal anti-inflammatory drug; PE, pulmonary embolism.

Sociodemographic characteristics

Sociodemographic characteristics included in the study are defined in Table 8.

TABLE 8: SOCIODEMOGRAPHIC DEFINITIONS

Characteristic	Definition
Age	Age was calculated at 1 July 2018 based on the patient's date of birth (defined as 1 July in the patient's year of birth) and presented as 10-year age groups. Valid age was defined as 18–112 years.
Gender	As recorded in the clinical information system (CIS) (male or female)
Aboriginal and Torres Strait Islander status	As recorded in the CIS
State in Australia	State was assigned based on each patient's postcode of residence. If patient postcode was missing, the practice postcode was used as a proxy.
Rurality/Remoteness	Rurality was assigned based on a mapping of each patient's postcode of residence using the Australian Bureau of Statistics (ABS) mapping of postcode 2016 to the Australian Statistical Geography Standard (ASGS) Remoteness Areas 2016 data[14]
Socioeconomic status (SEIFA)	SEIFA was assigned based on a mapping of each patient's postcode of residence using the Australian Bureau of Statistics (ABS) mapping of postcode 2016 to the Index of Relative Socioeconomic Advantage and Disadvantage (IRSAD).[15]
Smoking status	Smoking status was based on each patient's current smoking status recorded in the CIS (Current smoker, ex-smoker, non-smoker, unknown)
Concession card status	A patient was considered to be a concession card holder if they were recorded as having any concession card (eg, Pensioner or Health Care Card), or had a limited or full Department of Veteran Affairs (DVA) card

2.6. Data analysis and reporting

Analysis of the data was conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA). Measures included are descriptive statistics, frequencies, proportions and odds ratios as appropriate. To indicate the reliability of the estimates of prevalence and proportion, 95% confidence intervals (CI) were included as needed. Non-overlap of 95% CIs (adjusted for clustering by practice site) determined if there were significant differences between CKD stages or other groups when appropriate.

If a particular result was only reported in 1–4 patients, this result has been reported as < 5 in order to preserve the privacy of individuals (with the exception of missing variables).

3. CKD DOCUMENTATION

- Among the 1,680,457 patients eligible for the study, 24,954 patients (1.5%) had a record of CKD based on the MedicineInsight condition flag.
- The prevalence of CKD was estimated at 1.9% when using pathology results.
- 32,744 patients were identified as having CKD from the pathology results in 2017 – 3,105 with stage 1–2 CKD and 29,639 with stage 3–5 CKD.
- Patients identified as having CKD from pathology results who had a CKD (any stage) condition flag were as follows:
    - 31.0% (10,149 patients) of the 32,744 patients with CKD (any stage);
    - 11.7% (362 patients) of the 3,105 patients with stage 1–2 CKD; and
    - 33.0% (9,787 patients) of the 29,639 patients with stage 3–5 CKD.

3.1. Study questions

- What number and proportion of patients had a record of CKD (any stage) from their earliest record up to the end of the baseline period (31 December 2017), according to the MedicineInsight CKD flags?
- What number and proportion of patients identified by pathology results during 2017, the baseline period, as having CKD had a record of CKD according to the MedicineInsight CKD flags?
- What number and proportion of patients identified by pathology results during 2017 as having stage 1–2 CKD had a record of CKD according to the MedicineInsight CKD flags (any)?
- What number and proportion of patients identified by pathology results during 2017 as having stage 3–5 CKD had a record of CKD according to the MedicineInsight CKD flags (any)?

3.2. CKD identified by MedicineInsight flags and pathology results

Of the 1,680,457 eligible patients, 24,954 patients (1.5%) had a record of CKD based on the MedicineInsight condition flag (Table 9). There were 32,744 patients identified as having CKD from the pathology results in 2017 – 3,105 with stage 1–2 CKD and 29,639 with stage 3–5 CKD. Almost 1 in 3 patients (31.0%) identified as having CKD from the pathology results had a record of CKD according to the condition flag; only 362 patients (11.7%) of those identified as having stage 1–2 CKD had CKD (any stage) based on the condition flag; and 9,787 patients (33.0%) of those identified as having stage 3–5 CKD had CKD (any stage) based on the condition flag (Table 9).

The 14,805 patients who had CKD based on the condition flag but did not have evidence of CKD according to the pathology results recorded in 2017 might be patients who did not have records for eGFR or urine ACR results during 2017. These patients might have had their tests done elsewhere (eg, at a non-MedicineInsight practice, hospital or specialist setting) during 2017 or test results may have been recorded in fields not accessible to MedicineInsight, thus the data are not available.

The prevalence of CKD was estimated at 1.9% when using pathology results, compared with 1.5% using the CKD condition flag. This represents an absolute reduction in estimated prevalence of 0.4%, or a relative reduction of 21.1%. Our findings are consistent with previous reports that show that CKD is often not documented in the diagnosis fields available to MedicineInsight.[4,9,16] Bezabhe et al also found that only a quarter of patients with evidence of stage 3–5 CKD had a documentation of the

diagnosis,[9] while Khanam and colleagues found that 20% of the patients with laboratory evidence of stage 3 CKD had a diagnosis documented.[4]

Please note that the definition used to identify patients with stage 1–2 CKD (based on albuminuria only) may have selectively restricted this CKD group largely to patients with diabetes as they are likely to be tested regularly for albuminuria as part of the diabetes annual Cycle of Care,[17] thus these data should be interpreted with caution.

TABLE 9: PATIENTS IDENTIFIED AS HAVING CKD USING PATHOLOGY RESULTS WHO ALSO HAVE A CKD FLAG

CKD stage	Denominator number of patients	Patients who also had a CKD flag*	
	Number	Number	% (95% CI)
Baseline study population	1,680,457	24,954	1.5 (1.3–1.7)
Baseline patients with no evidence of CKD on pathology results in 2017	1,647,713	14,805	0.9 (0.8–1.0)
Any stage CKD (from pathology results in 2017)	32,744	10,149	31.0 (28.6–33.4)
Stage 1–2 CKD (with albuminuria) (from pathology results in 2017)	3,105	362	11.7 (9.0–14.4)
Stage 3–5 CKD (± albuminuria) (from pathology results in 2017)	29,639	9,787	33.0 (30.5–35.6)

* Patients with a CKD flag are those who had CKD recorded in one of the three diagnosis fields at any time from their earliest record up to 31 December 2017.

It is important to note that the estimates of CKD prevalence in this study are lower than the 10% reported by the AIHW. This figure was obtained from the 2011–12 ABS National Health Survey (NHS) which relied on a single blood test to estimate the prevalence of kidney disease using eGFR and/or urine ACR. However, diagnosis of CKD requires evidence of impaired kidney function over a period of three months because there can be transient declines in eGFR or transient increases in urine ACR. The lower prevalence of CKD observed in this study is because we used a stricter definition of CKD (two abnormal results recorded at least 90 days apart) than that used in the ABS NHS.

4. SOCIODEMOGRAPHICS OF PATIENTS WITH CKD

- Among patients with CKD (any stage), just over half were females (52.0%) and two thirds (66.0%) were aged ≥ 75 years.
- Similarly, more than half of patients with stage 3–5 CKD were females (54.0%) and 70.3% were aged ≥ 75 years.
- In contrast, the majority of patients with stage 1–2, CKD were males (67.5%) and about a third (32.7%) were in the 65–74-years age group.
- The proportion of men with CKD (any stage) and stage 3–5 CKD increased with age and the majority were aged ≥ 75 years. For stage 1–2 CKD, there were more men in the 65–74-years age group (35.1%) than the other age groups.
- Among women, almost three quarters of those with any stage CKD (70.4%) and stage 3–5 CKD (73.3%) were aged ≥ 75 years while 53.4% of those with stage 1–2 CKD were aged ≥ 65 years.
- A greater proportion of patients with stage 1–2 CKD (5.7%) were Aboriginal and Torres Strait Islander than those with stage 3–5 CKD (1.6%).
- A greater proportion of patients with stage 1–2 CKD (12.9%) were current smokers than those with stage 3–5 CKD (4.5%).
- Similarly, in separate analyses for men and women, the proportion with stage 1–2 CKD who were current smokers was significantly greater than those with stage 3–5 CKD.
- A greater proportion of patients with stage 3–5 CKD (87.2%) were concession card holders than those with stage 1–2 CKD (70.4%).
- Likewise, the proportion of men or women with stage 3–5 CKD who had a concession card was significantly greater than among those with stage 1–2 CKD.
- There were no statistically significant differences between patients with stage 1–2 CKD and those with stage 3–5 CKD in relation to remoteness, state/territory and socioeconomic status.

4.1. Study questions

- What are the sociodemographic characteristics (age, Aboriginal and Torres Strait Islander status, SEIFA, remoteness and smoking status) of patients identified as having CKD, overall and stratified by sex?
- What are the sociodemographic characteristics (age, Aboriginal and Torres Strait Islander status, SEIFA, remoteness and smoking status) of patients identified as having stage 1–2 CKD, overall and stratified by sex?
- What are the sociodemographic characteristics (age, Aboriginal and Torres Strait Islander status, SEIFA, remoteness and smoking status) of patients identified as having stage 3–5 CKD, overall and stratified by sex?

4.2. Sociodemographic characteristics of patients with CKD

Characteristics of patients with CKD

Table 10 shows sociodemographic characteristics of patients with CKD (any stage), those with stage 1–2 and those with stage 3–5 CKD. Among patients with CKD (any stage), just over half were females (52.0%) and two thirds (66.0%) were aged ≥ 75 years. Similar findings were observed for patients with stage 3–5 CKD. Unlike CKD (any stage) and stage 3–5 CKD, the majority of patients with stage 1–2 CKD were males (67.5%) and the largest proportion (32.7%) were in the 65–74-years age group. The finding that the majority of patients with stage 1–2 CKD were men might relate to the large number of

patients with diabetes in this CKD group (77.2%) as diabetes is more prevalent among men than women.[18]

A greater proportion of patients with stage 1–2 CKD were current smokers (12.9% vs 4.5%) and Aboriginal and Torres Strait Islanders (5.7% vs 1.6%) compared to those with stage 3–5 CKD. A greater proportion of patients with stage 3–5 CKD were concession card holders (87.2% vs 70.4%) than those with stage 1–2 CKD. This may reflect the direct relationship between age and CKD severity with older patients more likely to have a concession card. There were no statistically significant differences observed between patients with stage 1–2 CKD and those with stage 3–5 CKD regarding remoteness, state/territory and socioeconomic status.

TABLE 10: SOCIODEMOGRAPHIC CHARACTERISTICS OF PATIENTS WITH CKD IDENTIFIED BY PATHOLOGY RESULTS IN MEDICINEINSIGHT

Characteristic	Any stage CKD (N = 32,744)		Stage 1–2 CKD (N = 3,105)		Stage 3–5 CKD (N = 29,639)	
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
Gender						
Female	17,012	52.0 (51.1, 52.8))	1,009	32.5 (30.8, 34.2)	16,003	54.0 (53.2, 54.8)
Male	15,732	48.0 (47.2, 48.9)	2,096	67.5 (65.8, 69.2)	13,636	46.0 (45.2, 46.8)
Age, mean (SD)	77.5 (11.3)		65.2 (13.2)		78.8 (10.2)	
Age, median (Q1–Q3)	79 (72–85)		67 (58–74)		80 (73–86)	
Age group (years)						
18–44	465	1.4 (1.2, 1.6)	231	7.4 (6.3, 8.6)	234	0.8 (0.7, 0.9)
45–54	841	2.6 (2.3, 2.8)	359	11.6 (10.1, 13.0)	482	1.6 (1.4, 1.8)
55–64	2,443	7.5 (7.0, 8.0)	730	23.5 (22.0, 25.1)	1,713	5.8 (5.3, 6.2)
65–74	7,373	22.5 (21.8, 23.3)	1,014	32.7 (31.0, 34.3)	6,359	21.5 (20.7, 22.3)
75+	21,622	66.0 (64.7, 67.4)	771	24.8 (22.9, 26.8)	20,851	70.3 (69.1, 71.6)
Remoteness						
Major city	17,310	52.9 (46.3, 59.4)	1,705	54.9 (48.0, 61.9)	15,605	52.7 (46.0, 59.3)
Inner regional	10,115	30.9 (25.1, 36.7)	796	25.7 (20.1, 31.2)	9,319	31.4 (25.5, 37.4)
Outer regional	4,831	14.8 (10.5, 19.0)	531	17.1 (11.7, 22.5)	4,300	14.5 (10.3, 18.8)
Remote or very remote	484	1.5 (0.7, 2.3)	71	2.3 (0.8, 3.8)	413	1.4 (0.6, 2.2)
Not recorded	<5		< 5		<5	
Indigenous status						
Aboriginal and/or Torres Strait Islander	664	2.0 (1.3, 2.7)	178	5.7 (2.5, 9.0)	486	1.6 (1.2, 2.1)
Other Australian	28,053	85.7 (82.5, 88.8)	2,647	85.2 (81.8, 88.7)	25,406	85.7 (82.4, 89.0)
Not known	4,027	12.3 (9.2, 15.4)	280	9.0 (7.0, 11.1)	3,747	12.6 (9.3, 16.0)
Current smoker						
Yes	1,666	5.3 (4.9, 5.8)	390	12.9 (11.6, 14.2)	1,276	4.5 (4.1, 4.9)
No	29,697	94.7 (94.2, 95.1)	2,641	87.1 (85.8, 88.4)	27,056	95.5 (95.1, 95.9)
Not recorded	1,381		74		1,307	
State/Territory						
ACT	484	1.5 (0.2, 2.8)	64	2.1 (0.2, 3.9)	420	1.4 (0.1, 2.7)
NSW	12,002	36.7 (30.3, 43.0)	1,082	34.8 (28.4, 41.3)	10,920	36.8 (30.4, 43.3)
NT	310	0.9 (0.2, 1.7)	72	2.3 (0.3, 4.3)	238	0.8 (0.1, 1.5)
QLD	4,186	12.8 (9.2, 16.3)	348	11.2 (6.8, 15.6)	3,838	12.9 (9.3, 16.6)
SA	1,212	3.7 (1.4, 6.0)	78	2.5 (0.8, 4.2)	1,134	3.8 (1.5, 6.2)
Tas	3,265	10.0 (5.8, 14.1)	328	10.6 (5.8, 15.3)	2,937	9.9 (5.8, 14.1)
Vic	8,583	26.2 (19.4, 33.0)	680	21.9 (15.7, 28.1)	7,903	26.7 (19.7, 33.6)

Characteristic	Any stage CKD (N = 32,744)		Stage 1–2 CKD (N = 3,105)		Stage 3–5 CKD (N = 29,639)	
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
WA	2,702	8.3 (4.9, 11.6)	453	14.6 (8.7, 20.5)	2,249	7.6 (4.5, 10.7)
Socioeconomic status (SEIFA)						
1 (most disadvantaged)	8,450	25.8 (21.0, 30.6)	773	24.9 (20.3, 29.6)	7,677	25.9 (21.0, 30.8)
2	6,563	20.0 (16.5, 23.6)	638	20.6 (16.8, 24.3)	5,925	20.0 (16.4, 23.6)
3	6,920	21.1 (17.4, 24.9)	682	22.0 (17.8, 26.2)	6,238	21.0 (17.3, 24.8)
4	4,783	14.6 (12.0, 17.2)	473	15.2 (12.4, 18.1)	4,310	14.5 (11.9, 17.2)
5 (most advantaged)	6,024	18.4 (14.4, 22.4)	537	17.3 (13.3, 21.3)	5,487	18.5 (14.4, 22.6)
Not recorded	<5		< 5		<5	
Concession card holder						
Yes	26,766	85.7 (84.3, 87.0)	1,995	70.4 (67.7, 73.2)	24,771	87.2 (85.9, 88.5)
No	4,477	14.3 (13.0, 15.7)	838	29.6 (26.8, 32.3)	3,639	12.8 (11.5, 14.1)
Not recorded	1,501		272		1,229	

CKD, chronic kidney disease; SD, standard deviation; SEIFA, socioeconomic index for areas; Q1, quartile 1 (25th percentile); Q3, quartile 3 (75th percentile).

NB: Practices were recruited to MedicineInsight using non-random sampling, and systematic sampling differences between regions cannot be ruled out. Tasmania is overrepresented whereas South Australia is underrepresented in MedicineInsight. Comparisons between regions should be interpreted with caution'

Characteristics of patients with CKD stratified by sex

In a separate analysis for men, the proportion with CKD (any stage) and stage 3–5 CKD increased with age and most were aged ≥ 75 years (Table 11). The largest proportion (35.1%) of men with stage 1–2 CKD was in the 65–74-years age group.

Among women, almost three quarters of those with any stage CKD (70.4%) and stage 3–5 CKD (73.3%) were aged ≥ 75 years while more than half of those with stage 1–2 CKD (53.4%) were aged ≥ 65 years (Table 12). A greater proportion of women with stage 1-2 CKD were Aboriginal and Torres Strait Islander compared to those with stage 3–5 CKD (8.4% vs 1.7%).

A greater proportion of women (14.2% vs 4.2%) and men (12.2% vs 4.9%) with stage 1–2 CKD were current smokers compared to those with stage 3–5 CKD (Tables 11 and 12). A greater proportion of women (88.3% vs 75.6%) and men (85.9% vs 67.9%) with stage 3–5 CKD were concession card holders than those with stage 1–2 CKD. No statistically significant differences were observed between men or women with stage 1–2 CKD and those with stage 3–5 CKD with regard to remoteness, state/territory and socioeconomic status.

TABLE 11: SOCIODEMOGRAPHIC CHARACTERISTICS OF MALE PATIENTS WITH CKD IDENTIFIED BY PATHOLOGY RESULTS IN MEDICINEINSIGHT

Characteristic	Any stage CKD (N = 15,732)		Stage 1–2 CKD (N = 2,096)		Stage 3–5 CKD (N = 13,636)	
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
Age, mean (SD)	76.2 (11.2)		65.8 (12.3)		77.8 (10.2)	
Age, median (Q1–Q3)	78 (70–84)		68 (59–74)		79 (72–85)	
Age group (years)						
18–44	240	1.5 (1.3, 1.8)	123	5.9 (4.7, 7.0)	117	0.9 (0.7, 1.0)
45–54	481	3.1 (2.7, 3.4)	225	10.7 (9.1, 12.3)	256	1.9 (1.6, 2.1)

Characteristic	Any stage CKD (N = 15,732)		Stage 1–2 CKD (N = 2,096)		Stage 3–5 CKD (N = 13,636)	
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
55–64	1,335	8.5 (7.8, 9.1)	501	23.9 (22.0, 25.8)	834	6.1 (5.5, 6.7)
65–74	4,036	25.7 (24.8, 26.6)	735	35.1 (33.1, 37.1)	3,301	24.2 (23.2, 25.2)
75+	9,640	61.3 (59.8, 62.8)	512	24.4 (22.4, 26.5)	9,128	66.9 (65.5, 68.4)
Remoteness						
Major city	8,091	51.4 (44.9, 58.0)	1,159	55.3 (48.4, 62.3)	6,932	50.8 (44.2, 57.5)
Inner Regional	4,981	31.7 (25.9, 37.5)	545	26.0 (20.4, 31.6)	4,436	32.5 (26.6, 38.5)
Outer Regional	2,395	15.2 (11.0, 19.4)	340	16.2 (11.1, 21.3)	2,055	15.1 (10.8, 19.3)
Remote or very remote	262	1.7 (0.7, 2.6)	51	2.4 (0.8, 4.1)	211	1.5 (0.7, 2.4)
Not recorded	< 5		< 5		< 5	
Indigenous status						
Aboriginal and/or Torres Strait Islander	305	1.9 (1.3, 2.6)	93	4.4 (1.6, 7.2)	212	1.6 (1.2, 2.0)
Other Australian	13,519	85.9 (82.8, 89.0)	1,804	86.1 (82.9, 89.3)	11,715	85.9 (82.6, 89.3)
Not known	1,908	12.1 (9.0, 15.2)	199	9.5 (7.4, 11.6)	1,709	12.5 (9.2, 15.9)
Current smoker						
Yes	892	5.9 (5.3, 6.4)	250	12.2 (10.7, 13.7)	642	4.9 (4.4, 5.4)
No	14,270	94.1 (93.6, 94.7)	1,798	87.8 (86.3, 89.3)	12,472	95.1 (94.6, 95.6)
Not recorded	570		48		522	
State/Territory						
ACT	235	1.5 (0.1, 2.9)	49	2.3 (0.3, 4.4)	186	1.4 (0.1, 2.6)
NSW	5,752	36.6 (30.3, 42.9)	756	36.1 (29.4, 42.7)	4,996	36.6 (30.2, 43.1)
NT	170	1.1 (0.2, 2.0)	46	2.2 (0.3, 4.1)	124	0.9 (0.2, 1.7)
QLD	2,064	13.1 (9.4, 16.8)	234	11.2 (6.9, 15.4)	1,830	13.4 (9.6, 17.2)
SA	579	3.7 (1.4, 5.9)	45	2.1 (0.5, 3.7)	534	3.9 (1.5, 6.3)
Tas	1,563	9.9 (5.7, 14.1)	206	9.8 (5.3, 14.4)	1,357	10.0 (5.7, 14.2)
Vic	3,988	25.3 (18.6, 32.1)	442	21.1 (14.9, 27.3)	3,546	26.0 (18.9, 33.1)
WA	1,381	8.8 (5.3, 12.3)	318	15.2 (9.0, 21.3)	1,063	7.8 (4.6, 11.0)
Socioeconomic status (SEIFA)						
1 (most disadvantaged)	4,131	26.3 (21.5, 31.0)	509	24.3 (19.6, 29.0)	3,622	26.6 (21.7, 31.5)
2	3,175	20.2 (16.7, 23.7)	434	20.7 (16.9, 24.6)	2,741	20.1 (16.5, 23.7)
3	3,372	21.4 (17.7, 25.2)	465	22.2 (18.1, 26.3)	2,907	21.3 (17.5, 25.1)
4	2,301	14.6 (12.0, 17.2)	309	14.7 (12.0, 17.5)	1,992	14.6 (11.9, 17.3)
5 (most advantaged)	2,750	17.5 (13.7, 21.3)	378	18.0 (13.7, 22.4)	2,372	17.4 (13.5, 21.3)
Not recorded	< 5		< 5		< 5	
Concession card holder						
Yes	12,419	83.6 (82.0, 85.1)	1,291	67.9 (64.8, 70.9)	11,128	85.9 (84.4, 87.3)
No	2,442	16.4 (14.9, 18.0)	611	32.1 (29.1, 35.2)	1,831	14.1 (12.7, 15.6)
Not recorded	871		194		677	

CKD, chronic kidney disease; SD, standard deviation; SEIFA, socioeconomic indexes for areas; Q1, quartile 1 (25th percentile); Q3, quartile 3 (75th percentile).

NB: Practices were recruited to MedicineInsight using non-random sampling, and systematic sampling differences between regions cannot be ruled out. Tasmania is overrepresented whereas South Australia is underrepresented in MedicineInsight. Comparisons between regions should be interpreted with caution'

TABLE 12: SOCIODEMOGRAPHIC CHARACTERISTICS OF FEMALE PATIENTS WITH CKD IDENTIFIED BY PATHOLOGY RESULTS IN MEDICINEINSIGHT

Characteristic	Any stage CKD (N = 17,012)		Stage 1–2 CKD (N = 1,009)		Stage 3–5 CKD (N = 16,003)	
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
Age, mean (SD)	78.6 (11.2)		64.0 (14.8)		79.6 (10.2)	
Age, median (Q1–Q3)	80 (73–86)		66 (55–75)		81 (74–87)	
Age group (years)						
18–44	225	1.3 (1.1, 1.5)	108	10.7 (8.7, 12.7)	117	0.7 (0.6, 0.9)
45–54	360	2.1 (1.8, 2.4)	134	13.3 (11.0, 15.6)	226	1.4 (1.2, 1.6)
55–64	1,108	6.5 (6.0, 7.0)	229	22.7 (20.1, 25.3)	879	5.5 (5.0, 6.0)
65–74	3,337	19.6 (18.8, 20.5)	279	27.7 (24.9, 30.4)	3,058	19.1 (18.2, 20.0)
75+	11,982	70.4 (69.1, 71.8)	259	25.7 (22.5, 28.8)	11,723	73.3 (72.0, 74.5)
Remoteness/territory						
Major city	9,219	54.2 (47.5, 60.9)	546	54.2 (46.5, 61.8)	8,673	54.2 (47.4, 60.9)
Inner Regional	5,134	30.2 (24.3, 36.1)	251	24.9 (18.9, 30.9)	4,883	30.5 (24.6, 36.5)
Outer Regional	2,436	14.3 (10.0, 18.6)	191	18.9 (12.6, 25.3)	2,245	14.0 (9.7, 18.3)
Remote or Very Remote	222	1.3 (0.6, 2.1)	20	2.0 (0.6, 3.3)	202	1.3 (0.5, 2.0)
Not recorded	< 5		< 5			
Indigenous status						
Aboriginal and/or Torres Strait Islander	359	2.1 (1.4, 2.9)	85	8.4 (4.1, 12.7)	274	1.7 (1.2, 2.2)
Other Australian	14,534	85.4 (82.2, 88.7)	843	83.5 (79.0, 88.1)	13,691	85.6 (82.2, 88.9)
Not known	2,119	12.5 (9.2, 15.7)	81	8.0 (5.5, 10.6)	2,038	12.7 (9.4, 16.1)
Current smoker						
Yes	774	4.8 (4.3, 5.2)	140	14.2 (11.7, 16.8)	634	4.2 (3.8, 4.6)
No	15,427	95.2 (94.8, 95.7)	843	85.8 (83.2, 88.3)	14,584	95.8 (95.4, 96.2)
Not recorded	811		26		785	
State/Territory						
ACT	249	1.5 (0.2, 2.8)	15	1.5 (0.0, 3.2)	234	1.5 (0.2, 2.8)
NSW	6,250	36.7 (30.3, 43.1)	326	32.3 (25.6, 39.0)	5,924	37.0 (30.5, 43.5)
NT	140	0.8 (0.1, 1.5)	26	2.6 (0.3, 4.9)	114	0.7 (0.1, 1.3)
QLD	2,122	12.5 (9.0, 16.0)	114	11.3 (6.2, 16.4)	2,008	12.5 (9.0, 16.1)
SA	633	3.7 (1.4, 6.0)	33	3.3 (0.9, 5.7)	600	3.7 (1.4, 6.1)
Tas	1,702	10.0 (5.8, 14.2)	122	12.1 (6.6, 17.6)	1,580	9.9 (5.7, 14.0)
Vic	4,595	27.0 (20.2, 33.9)	238	23.6 (16.7, 30.5)	4,357	27.2 (20.2, 34.2)
WA	1,321	7.8 (4.5, 11.0)	135	13.4 (7.8, 19.0)	1,186	7.4 (4.3, 10.5)
SEIFA						
1 (most disadvantaged)	4,319	25.4 (20.5, 30.3)	264	26.2 (21.1, 31.3)	4,055	25.3 (20.4, 30.3)
2	3,388	19.9 (16.3, 23.6)	204	20.2 (15.7, 24.8)	3,184	19.9 (16.2, 23.6)
3	3,548	20.9 (17.1, 24.7)	217	21.5 (16.4, 26.6)	3,331	20.8 (17.0, 24.6)
4	2,482	14.6 (12.0, 17.2)	164	16.3 (12.8, 19.8)	2,318	14.5 (11.8, 17.1)
5 (most advantaged)	3,274	19.2 (15.0, 23.5)	159	15.8 (11.7, 19.8)	3,115	19.5 (15.1, 23.9)
Not recorded	< 5		< 5			
Concession card holder						
Yes	14,347	87.6 (86.3, 88.9)	704	75.6 (72.2, 79.1)	13,643	88.3 (87.0, 89.6)
No	2,035	12.4 (11.1, 13.7)	227	24.4 (20.9, 27.8)	1,808	11.7 (10.4, 13.0)
Not recorded	630		78		552	

CKD, chronic kidney disease; SD, standard deviation; SEIFA, socioeconomic index for areas; Q1, quartile 1 (25th percentile); Q3, quartile 3 (75th percentile).

NB: Practices were recruited to MedicineInsight using non-random sampling, and systematic sampling differences between regions cannot be ruled out. Tasmania is overrepresented whereas South Australia is underrepresented in MedicineInsight. Comparisons between regions should be interpreted with caution'

5. COMORBIDITIES OF PATIENTS WITH CKD

- Among patients with any stage CKD, the most prevalent comorbid conditions were hypertension (80.9%), anaemia (50.0%), cardiovascular disease (42.4%) and diabetes (type 1 or 2) (41.4%).
- The majority of the patients with stage 1–2 CKD had hypertension (79.4%) and diabetes (77.2%), while cardiovascular disease was recorded in 31.0% and anaemia in 28.2%.
- The majority of the patients with stage 3–5 CKD had hypertension (81.1%), while anaemia was recorded in 52.3%, cardiovascular disease in 43.6% and diabetes in 37.6%.
- Patients with stage 3–5 CKD were more likely to have cardiovascular disease, anaemia, atrial fibrillation and heart failure than those with stage 1–2 CKD.
- Patients with stage 1–2 CKD were twice as likely to have a record of diabetes than those with stage 3–5 CKD which might reflect the definition we used to identify patients with stage 1–2 CKD (only albuminuria). As patients with diabetes are more likely to be regularly tested for albuminuria as part of the diabetes annual Cycle of Care while those without diabetes are not, our definition would have selectively picked up more patients with diabetes.

5.1. Study questions

- What number and proportion of patients identified as having CKD (any), stage 1–2 CKD, and stage 3–5 CKD, had a record of: diabetes (type 1 or 2), cardiovascular disease, atrial fibrillation, hypertension and anaemia?

5.2. Patients with CKD and a record of specified comorbidities

Hypertension (80.9%) was the most commonly recorded comorbid condition among patients with CKD (any stage), followed by anaemia (50.0%), cardiovascular disease (42.4%) and diabetes (41.4%) (Table 13). Among patients with stage 1–2 CKD, the majority had hypertension (79.4%) and diabetes (77.2%), while cardiovascular disease was recorded in 31.0% and anaemia in 28.2%. Most patients with stage 3–5 CKD had hypertension (81.1%) and a large number had anaemia (52.3%), cardiovascular disease (43.6%) and diabetes (37.6%). Bezabhe and colleagues recently showed that 80.0% of patients with stage 3–5 CKD had hypertension, 30.0% diabetes and 15.9% had atrial fibrillation.[9]

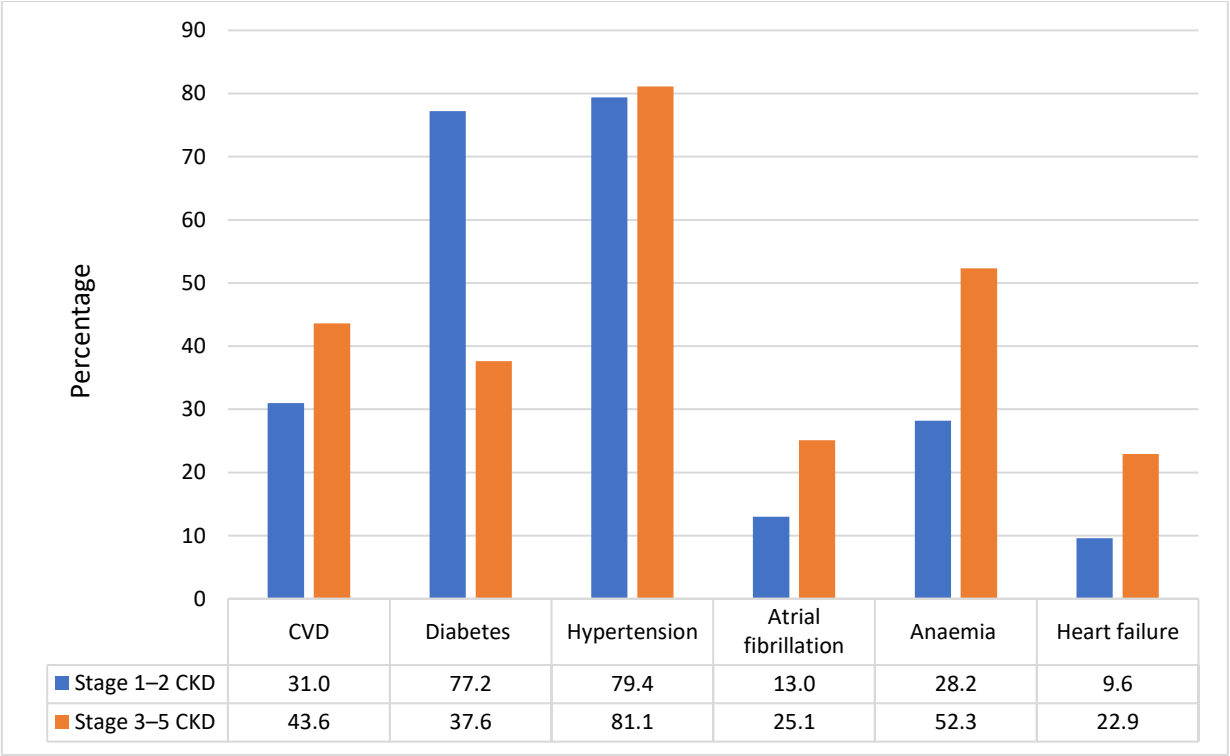
Patients with stage 3–5 CKD were more likely to have a record of anaemia, cardiovascular disease, atrial fibrillation and heart failure than those with stage 1–2 CKD (Table 13 and Figure 1). On the other hand, patients with stage 1–2 CKD in this study were more likely to have a record of diabetes (77.2% vs 37.6%) than those with stage 3–5 CKD. The greater likelihood of diabetes among patients with stage 1–2 CKD than those with stage 3–5 CKD might reflect the definition we used to identify patients with stage 1–2 CKD (only albuminuria) in this study. As the annual Cycle of Care for patients with diabetes includes testing for albuminuria at least once every year,[17] this implies that patients with diabetes are tested for albuminuria regularly while those without diabetes may not be. Our cohort of patients with stage 1–2 CKD possibly largely consists of patients with diabetes than the typical stage 1–2 CKD population.

TABLE 13: PREVALENCE OF COMMON COMORBIDITIES (EVER, EXCEPT ANAEMIA) IN PATIENTS WITH CKD IDENTIFIED BY PATHOLOGY RESULTS IN MEDICINEINSIGHT

Comorbid condition	Any stage CKD (N = 32,744)		Stage 1–2 CKD (N = 3,105)		Stage 3–5 CKD (N = 29,639)	
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
Hypertension	26,489	80.9 (80.0–81.8)	2,464	79.4 (77.7–81.0)	24,025	81.1 (80.2–81.9)
Anaemia (2018–19)	16,388	50.0 (49.2–50.9)	875	28.2 (26.4–30.0)	15,513	52.3 (51.5–53.2)
Cardiovascular disease	13,874	42.4 (41.3–43.4)	964	31.0 (29.3–32.8)	12,910	43.6 (42.5–44.7)
Diabetes (type 1 or 2)	13,545	41.4 (40.0–42.8)	2,396	77.2 (74.9–79.4)	11,149	37.6 (36.4–38.9)
Atrial fibrillation	7,839	23.9 (23.1–24.7)	404	13.0 (11.6–14.4)	7,435	25.1 (24.3–25.9)
Heart failure	7,093	21.7 (20.8–22.5)	297	9.6 (8.4–10.7)	6,796	22.9 (22.1–23.8)

CKD, chronic kidney disease.

FIGURE 1: PREVALENCE OF COMMON COMORBIDITIES IN PATIENTS WITH STAGES 1–2 AND 3–5 CKD



CKD, chronic kidney disease; CVD, cardiovascular disease.

6. MONITORING PATIENTS WITH CKD

- The proportion of patients with any stage CKD who had complete monitoring of the selected tests and observations (ie, at least one record of all the included assessments, urine ACR, eGFR, BP measurement, total cholesterol, HbA_{1c} [if diabetic, type 1 or 2] and haemoglobin) during the 2-year study period was 44.7%; 68.1% for those with co-existing diabetes and 28.1% for those without diabetes.
- Patients with stage 1–2 CKD had a higher rate of complete monitoring of the selected tests and observations than those with stage 3–5 CKD (80.5% vs 40.9%), irrespective of diabetes status. This may reflect the low urine ACR recording among patients with stage 3–5 CKD compared to those with stage 1–2 CKD. This also possibly relates to the fact that most of the patients with stage 1–2 CKD in this study have diabetes and are more likely to be monitored for albuminuria regularly as part of the annual diabetes Cycle of Care.
- The rate of complete monitoring of the selected tests and observations was greater among patients with co-existing diabetes than those with no diabetes for both stage 1–2 CKD (83.3% vs 70.7%) and stage 3–5 CKD (64.9% vs 26.5%). This reflects regular monitoring of lipids, BP, eGFR, urine ACR and HbA_{1c} through the annual diabetes Cycle of Care.
- Patients with any stage CKD and co-existing diabetes were more likely than those without diabetes to have at least two records for each of the individual tests or observations during the study – eGFR (92.0% vs 87.3%), blood pressure measurement (90.0% vs 85.3%), total cholesterol (70.8% vs 48.2%) and urine ACR (53.9% vs 18.1%).
- Urine ACR appears to have been the least recorded test among patients with any stage CKD as 66.6% of the patients without diabetes and 25.0% of those with diabetes had no record during the study period.
- Among patients eligible for the yellow clinical action plan at baseline (in 2017), patients with diabetes were more likely than those without diabetes to have optimal monitoring (at least two records) for each of the individual tests or observations during the 2-year study period – eGFR (92.0% vs 86.1%), blood pressure measurement (91.4% vs 86.6%), total cholesterol (75.2% vs 50.5%) and urine ACR (56.2% vs 15.2%).
- Among patients eligible for the orange clinical action plan at baseline (in 2017), patients with diabetes were more likely than those without diabetes to have optimal monitoring (at least four records) for each of the individual tests or observations during the 2-year study period – eGFR (77.0% vs 67.9%), blood pressure measurement (79.5% vs 72.9%), haemoglobin (65.0% vs 60.7%), total cholesterol (36.4% vs 19.9%) and urine ACR (21.5% vs 8.2%).
- Monitoring for albuminuria (urine ACR) during 2018–19 appears to have been less than optimal among patients who were eligible for both the yellow and orange action plans, irrespective of diabetes status.
- The above results suggest that one way to improve monitoring of patients with CKD in general practice may be to provide incentives similar to the diabetes Cycle of Care.

6.1. Study questions

- What number and proportion of patients identified as having CKD (any) had records of at least one of each of the following observations or tests over the study period, stratified by diabetes status: ACR, eGFR, BP measurement, total cholesterol (proxy for lipids) and HbA_{1c} (if diabetic)?
- What number and proportion of patients identified as having CKD (any) had records of at least one of each of the observations or tests listed above **PLUS** haemoglobin over the study period, stratified by diabetes status?
- What number and proportion of patients identified as having CKD (any) had 0, 1 or 2+ records of the following individual observations and tests over the study period, stratified by diabetes status: ACR, eGFR, BP measurement, total cholesterol, HbA_{1c}, haemoglobin (proxy for full blood count)?
- What number and proportion of patients identified as having CKD who met the yellow action plan criteria (stage 1–2 with albuminuria and stage 3a without albuminuria) had 0, 1 or 2+ records of

the following individual observations or tests over the study period, stratified by diabetes status: ACR, eGFR, BP measurement, total cholesterol, HbA_{1c}, haemoglobin (proxy for full blood count)?

- What number and proportion of patients identified as having CKD who met the orange action plan criteria (stage 3a with albuminuria and stage 3b with or without albuminuria) had 0, 1, 2, 3 or 4+ records of the following individual observations or tests over the study period, stratified by diabetes status: ACR, eGFR, BP measurement, total cholesterol, HbA_{1c}, haemoglobin (proxy for full blood count)?

6.2. Monitoring patients with CKD

All tests or observations

Kidney Health Australia recommends regular monitoring of patients with CKD to reduce progression and prevent complications such as cardiovascular disease.[1] Monitoring of patients with CKD appears to be less than optimal with only 44.7% of patients with any stage CKD having had complete monitoring of the selected tests and observations (ie, at least one record of each of the assessments, urine ACR, eGFR, BP measurement, total cholesterol, HbA_{1c} [if diabetic] and haemoglobin) during the 2-year study period, January 2018 to December 2019 (Table 14). Similar rates for complete monitoring of the selected tests and observations were observed with the exclusion of haemoglobin as one of the tests.

CKD patients who had diabetes were 2 times more likely to have at least one record of each of the assessed observations and tests during the study period than those without diabetes (68.1% vs 28.1%) (Table 14). Similar findings were observed in the analysis that excluded haemoglobin as one of the assessed tests. Khanam and colleagues also found that among patients with stage 3 CKD, those who had co-existing diabetes were more likely (54.9%) to have had at least one record of each of the assessments, including BP, urine ACR, eGFR and serum lipids over an 18-month period, than those without diabetes (14.1%).[4]

TABLE 14: PATIENTS WITH ANY STAGE CKD WITH AT LEAST ONE RECORD OF ALL OF THE INDIVIDUAL OBSERVATIONS OR TESTS BETWEEN JANUARY 2018 AND DECEMBER 2019

	All patients with any stage CKD (N = 32,744)		Patients with CKD and no diabetes (N = 19,199)		Patients with CKD and diabetes (N = 13,545)	
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
All tests and observations (including haemoglobin)	14,622	44.7 (42.9–46.4)	5,393	28.1 (26.2–29.9)	9,229	68.1 (66.4–69.8)
All tests and observations (excluding haemoglobin)	14,984	45.8 (44.0–47.6)	5,450	28.4 (26.5–30.3)	9,534	70.4 (68.6–72.2)

'All tests and observations' denotes having all assessments, urine albumin-to-creatinine ratio, estimated glomerular filtration rate, total cholesterol, blood pressure measurement, glycated haemoglobin (HbA_{1c}; if diabetic), and haemoglobin, recorded at least once during the study. For patients with no diabetes, HbA_{1c} is NOT required, thus was not included in the 'All tests and observations'.

Similarly, patients with stage 1–2 CKD and with stage 3–5 CKD who also had diabetes were better monitored, compared with patients without diabetes (Table 15 and Table 16), which reflects regular monitoring of lipids, BP, eGFR, urine ACR and HbA_{1c} through the annual diabetes Cycle of Care.[17] Our findings show a significantly higher rate of complete monitoring of the selected tests and observations in patients with stage 1–2 CKD than those with stage 3–5 CKD, irrespective of diabetes status (Tables 15 and 16). These findings may reflect the low rates of urine ACR test (one of the

included tests) among patients with stage 3–5 CKD and possibly relates to the majority of the patients with stage 1–2 CKD in this study having diabetes and more likely to be monitored for albuminuria regularly as part of the annual diabetes Cycle of Care.[17] Most patients (89.2%) with stage 1–2 CKD, in this study, had at least one record of urine ACR whereas only 46.5% of those with stage 3–5 CKD had urine ACR recorded during 2018–19. Data for patients with stage 1–2 CKD in this study should be interpreted with caution given that this might be a relatively sicker sub-population than the typical stage 1–2 CKD population. It is also possible that the low rate of complete monitoring in patients with stage 3–5 CKD is because some of these patients who have severe disease are being monitored by specialists or in hospital settings and these data are not available in MedicineInsight.

TABLE 15: PATIENTS WITH STAGE 1–2 CKD WITH AT LEAST ONE RECORD OF ALL OF THE INDIVIDUAL OBSERVATIONS OR TESTS BETWEEN JANUARY 2018 AND DECEMBER 2019

	All patients with stage 1–2 CKD (N = 3,105)		Patients with stage 1–2 CKD and no diabetes (N = 709)		Patients with stage 1–2 CKD and diabetes (N = 2,396)	
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
All tests and observations (including haemoglobin)	2,498	80.5 (78.6–82.3)	501	70.7 (67.1–74.2)	1,997	83.3 (81.3–85.4)
All tests and observations (excluding haemoglobin)	2,616	84.3 (82.6–85.9)	510	71.9 (68.4–75.5)	2,106	87.9 (86.2–89.6)

'All tests and observations' denotes having all assessments, urine albumin-to-creatinine ratio, estimated glomerular filtration rate, total cholesterol, blood pressure measurement, glycated haemoglobin (HbA_{1c}; if diabetic), and haemoglobin, recorded at least once during the study. For patients with no diabetes, HbA_{1c} is NOT required, thus was not included in the 'All tests and observations'.

TABLE 16: PATIENTS WITH STAGE 3–5 CKD WITH AT LEAST ONE RECORD OF ALL OF THE INDIVIDUAL OBSERVATIONS OR TESTS BETWEEN JANUARY 2018 AND DECEMBER 2019

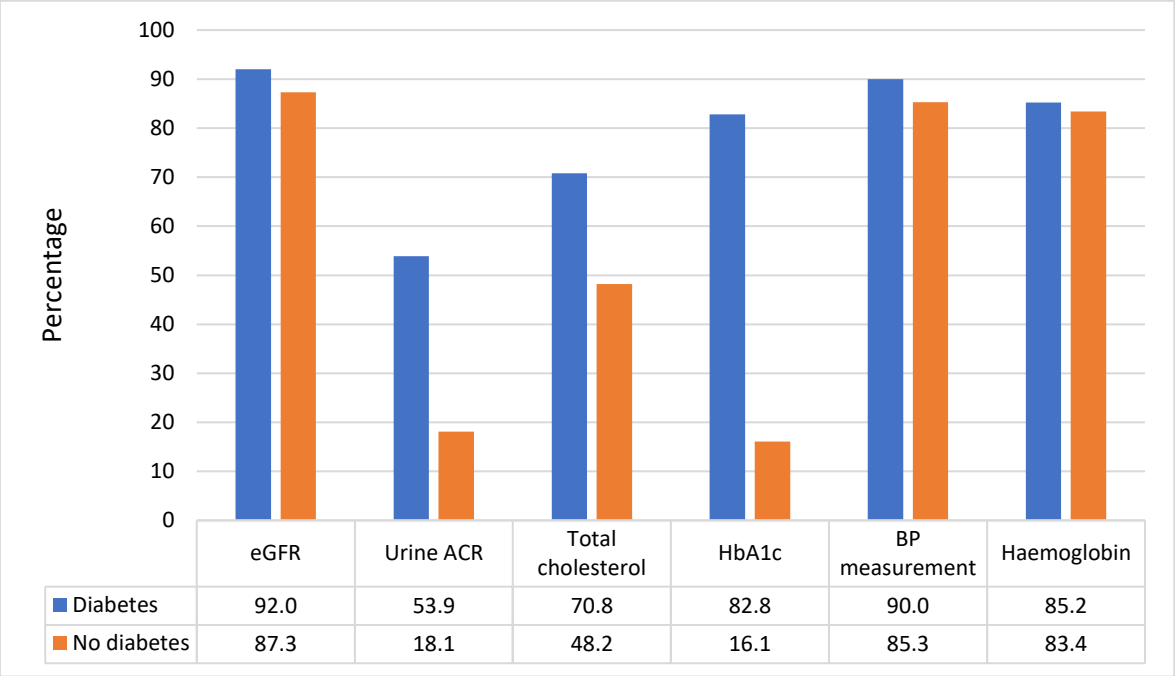
	All patients with stage 3–5 CKD (N = 29,639)		Patients with stage 3–5 CKD and no diabetes (N = 18,490)		Patients with stage 3–5 CKD and diabetes (N = 11,149)	
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
All tests and observations (including haemoglobin)	12,124	40.9 (39.3–42.5)	4,892	26.5 (24.7–28.2)	7,232	64.9 (63.1–66.6)
All tests and observations (excluding haemoglobin)	12,368	41.7 (40.1–43.4)	4,940	26.7 (24.9–28.5)	7,428	66.6 (64.8–68.5)

'All tests and observations' denotes having all assessments, urine albumin-to-creatinine ratio, estimated glomerular filtration rate, total cholesterol, blood pressure measurement, glycated haemoglobin (HbA_{1c}; if diabetic), and haemoglobin, recorded at least once during the study. For patients with no diabetes, HbA_{1c} is NOT required, thus was not included in the 'All tests and observations'.

Individual tests or observations

Among patients with any stage CKD, patients with a record of diabetes were more likely to have at least two records for each of the individual tests and observations compared to those without diabetes, except for haemoglobin where there were no statistically significant differences (Figure 2 and Table 17). In contrast, patients without diabetes were more likely to have no record of each of the individual tests or observations during the study (Table 17). Consistent with data from previous studies,[4] monitoring of patients with any stage CKD for albuminuria appears to have been less than optimal as 25.0% of the patients with co-existing diabetes and 66.6% of those without diabetes had no record of urine ACR test during the study period.

FIGURE 2: PATIENTS WITH ANY STAGE CKD WHO HAD AT LEAST TWO RECORDS OF THE INDIVIDUAL ASSESSMENTS DURING THE 2-YEAR STUDY, STRATIFIED BY DIABETES STATUS



	eGFR	Urine ACR	Total cholesterol	HbA1c	BP measurement	Haemoglobin
Diabetes	92.0	53.9	70.8	82.8	90.0	85.2
No diabetes	87.3	18.1	48.2	16.1	85.3	83.4

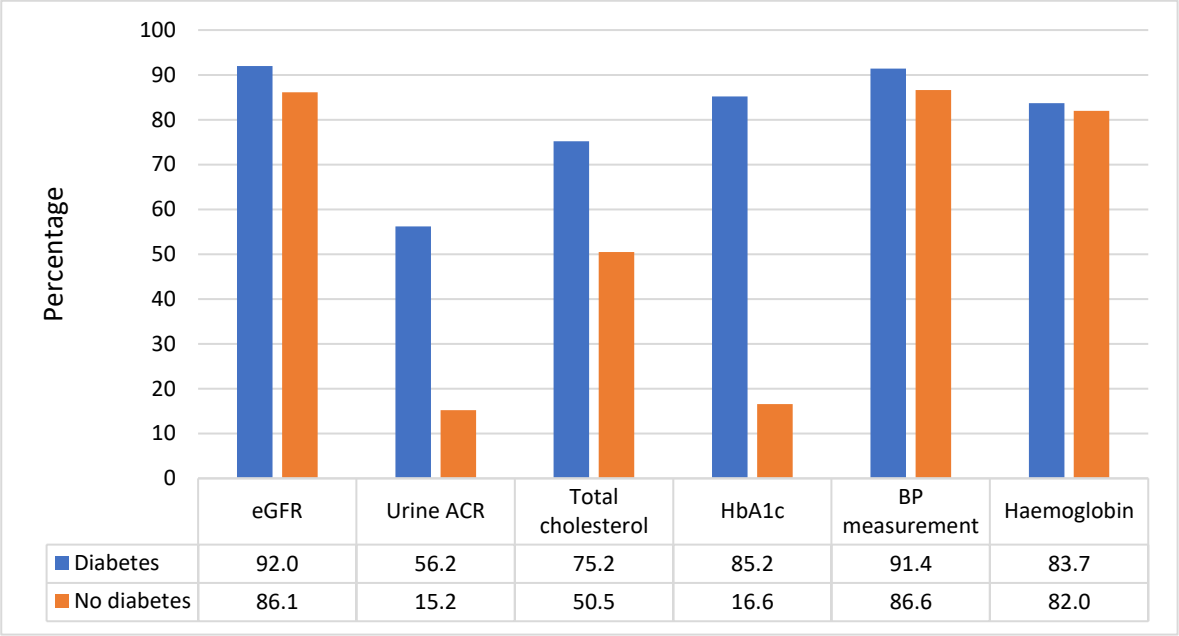
ACR, albumin-to-creatinine ratio; BP, blood pressure; eGFR, estimated glomerular filtration rate; HbA_{1c}, glycated haemoglobin

Patients with CKD who meet the yellow action plan criteria (stage 1–2 with albuminuria and stage 3a without albuminuria) are recommended to be monitored annually.[1] Among patients eligible for the yellow clinical action plan at baseline (in 2017), patients with diabetes were more likely than those without diabetes to have at least two records for each of the individual tests or observations during the 2-year study period (2018 to 2019) (Figure 3 and Table 18). The proportion of patients with and those without diabetes who had at least two records for haemoglobin was similar. Findings of our 2-year study indicate that majority of patients (ranging from 75.2% for total cholesterol to 92.0% for eGFR) who met the yellow action plan criteria and had diabetes had optimal monitoring (at least two records) for each of the individual tests or observations, with the exception of urine ACR, where only 56.2% of the patients were monitored optimally. Among patients who were eligible for the yellow action plan and did not have diabetes, the majority had optimal monitoring for blood pressure measurement (86.6%), eGFR (86.1%) and haemoglobin (82.0%).

As documented by Khanam and colleagues,[4] monitoring for albuminuria appears to have been less than optimal in this study as 21.6% of the patients with diabetes and 69.7% of those without diabetes had no record of urine ACR during the study period (Table 18).

Of note, although our study includes a cohort of patients who are regular attenders, it is possible that some patients may have had tests or observations done elsewhere (eg, at a non-MedicineInsight practice, hospital or specialist setting). Some test results (eg, urine dipstick) may be recorded in fields not accessible to researchers. These data are therefore not available in MedicineInsight.

FIGURE 3: PATIENTS WITH CKD ELIGIBLE FOR THE YELLOW ACTION PLAN WHO HAD AT LEAST TWO RECORDS OF THE INDIVIDUAL ASSESSMENTS DURING THE 2-YEAR STUDY, STRATIFIED BY DIABETES STATUS



	eGFR	Urine ACR	Total cholesterol	HbA1c	BP measurement	Haemoglobin
Diabetes	92.0	56.2	75.2	85.2	91.4	83.7
No diabetes	86.1	15.2	50.5	16.6	86.6	82.0

ACR, albumin-to-creatinine ratio; BP, blood pressure; eGFR, estimated glomerular filtration rate; HbA_{1c}, glycated haemoglobin. Note that HbA_{1c} is recommended for people with diabetes.

TABLE 17: PATIENTS WITH ANY STAGE CKD WHO HAD NIL, ONE AND TWO OR MORE RECORDS OF THE INDIVIDUAL OBSERVATIONS OR TESTS BETWEEN JANUARY 2018 AND DECEMBER 2019

Test/observation	Patients with no record				Patients with 1 record				Patients with 2+ records			
	No diabetes		Diabetes		No diabetes		Diabetes		No diabetes		Diabetes	
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
eGFR	794	4.1 (3.8–4.5)	395	2.9 (2.5–3.3)	1,645	8.6 (8.1–9.1)	692	5.1 (4.6–5.6)	16,760	87.3 (86.6–88.0)	12,458	92.0 (91.2–92.8)
Urine ACR	12,789	66.6 (64.6–68.7)	3,391	25.0 (23.3–26.8)	2,935	15.3 (14.4–16.1)	2,856	21.1 (20.1–22.1)	3,475	18.1 (16.7–19.5)	7,298	53.9 (51.7–56.1)
Total cholesterol	5,508	28.7 (26.6–30.8)	1,757	13.0 (11.8–14.2)	4,431	23.1 (21.9–24.3)	2,196	16.2 (15.0–17.4)	9,260	48.2 (45.4–51.1)	9,592	70.8 (68.6–73.0)
HbA_{1c}	12,102	63.0 (60.9–65.1)	988	7.3 (6.6–7.9)	4,013	20.9 (19.8–22.0)	1,348	10.0 (9.3–10.6)	3,084	16.1 (14.6–17.5)	11,209	82.8 (81.7–83.8)
BP measurement	1,550	8.1 (7.3–8.9)	702	5.2 (4.6–5.8)	1,272	6.6 (6.1–7.2)	650	4.8 (4.3–5.3)	16,377	85.3 (84.1–86.5)	12,193	90.0 (89.1–90.9)
Haemoglobin	1,047	5.5 (5.0–5.9)	787	5.8 (5.1–6.5)	2,131	11.1 (10.5–11.7)	1,221	9.0 (8.3–9.7)	16,021	83.4 (82.6–84.3)	11,537	85.2 (83.9–86.4)

ACR, albumin-to-creatinine ratio; BP, blood pressure; eGFR, estimated glomerular filtration rate; HbA_{1c}, glycated haemoglobin.

Note that the groups of patients with 0, 1 or 2+ records are mutually exclusive for each test/observation.

TABLE 18: PATIENTS WITH STAGE 1–2 WITH ALBUMINURIA AND STAGE 3A WITHOUT ALBUMINURIA CKD (YELLOW ACTION PLAN) WHO HAD NIL, ONE AND TWO OR MORE RECORDS OF THE INDIVIDUAL OBSERVATIONS OR TESTS BETWEEN JANUARY 2018 AND DECEMBER 2019

Test/observation	Patients with no record				Patients with 1 record				Patients with 2+ records			
	No diabetes		Diabetes		No diabetes		Diabetes		No diabetes		Diabetes	
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
eGFR	509	4.3 (3.9–4.8)	207	2.7 (2.2–3.2)	1,119	9.6 (8.9–10.2)	412	5.3 (4.7–6.0)	10,076	86.1 (85.2–86.9)	7,110	92.0 (91.1–92.9)
Urine ACR	8,157	69.7 (67.6–71.8)	1,669	21.6 (19.9–23.3)	1,767	15.1 (14.1–16.1)	1,719	22.2 (21.0–23.5)	1,780	15.2 (13.8–16.6)	4,341	56.2 (53.8–58.5)
Total cholesterol	2,969	25.4 (23.4–27.3)	763	9.9 (8.8–10.9)	2,822	24.1 (22.8–25.4)	1,151	14.9 (13.6–16.2)	5,913	50.5 (47.7–53.3)	5,815	75.2 (73.2–77.2)
HbA_{1c}	7,271	62.1 (59.9–64.3)	440	5.7 (5.0–6.4)	2,485	21.2 (20.0–22.4)	705	9.1 (8.3–9.9)	1,948	16.6 (15.1–18.1)	6,584	85.2 (84.0–86.4)
BP measurement	817	7.0 (6.2–7.8)	332	4.3 (3.6–5.0)	752	6.4 (5.8–7.0)	331	4.3 (3.8–4.8)	10,135	86.6 (85.4–87.8)	7,066	91.4 (90.5–92.3)
Haemoglobin	663	5.7 (5.1–6.2)	484	6.3 (5.3–7.2)	1,448	12.4 (11.6–13.1)	776	10.0 (9.2–10.9)	9,593	82.0 (81.0–83.0)	6,469	83.7 (82.1–85.2)

ACR, albumin-to-creatinine ratio; BP, blood pressure; eGFR, estimated glomerular filtration rate; HbA_{1c}, glycated haemoglobin.

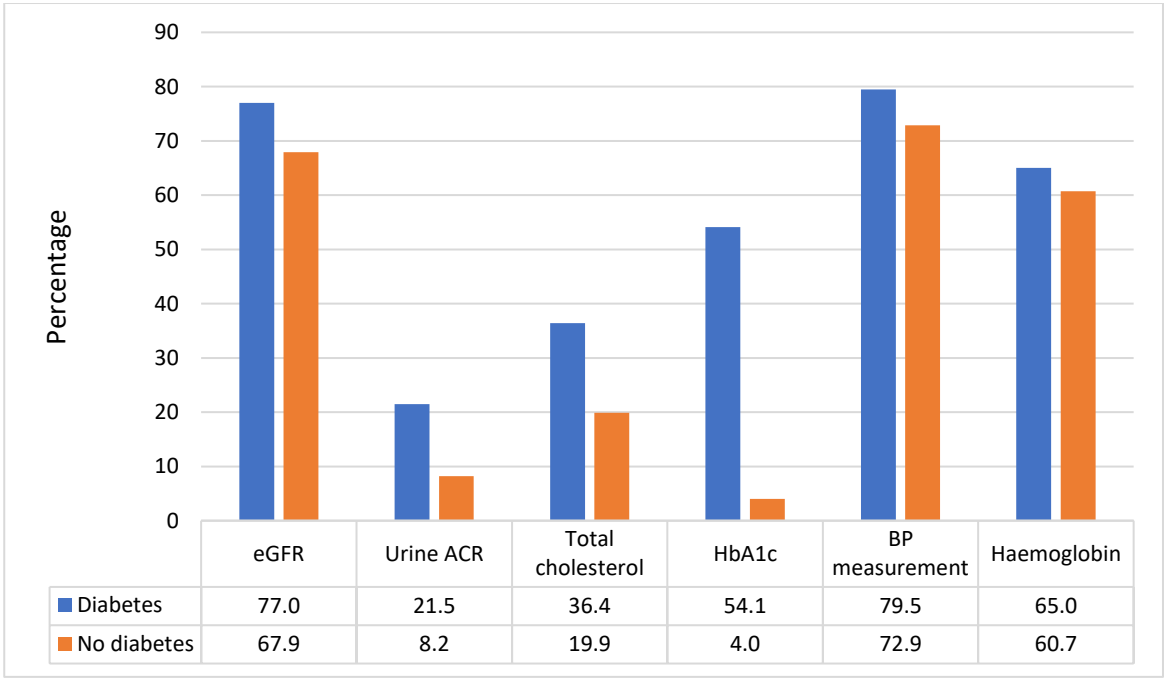
Note that the groups of patients with 0, 1 or 2+ records are mutually exclusive for each test/observation.

Kidney Health Australia recommends that patients with CKD who meet the orange clinical action plan criteria (stage 3a with albuminuria and stage 3b with or without albuminuria) should be monitored on a 3–6-month basis.[1] Ideally, for a 2-year follow-up period (January 2018 to December 2019), at least four records for each of the individual tests or observations would be considered optimal monitoring for a patient who was eligible for the orange action plan at baseline (in 2017).

Among patients eligible for the orange action plan, those with diabetes were more likely than patients without diabetes to have optimal monitoring (at least four records) for each of the individual tests or observations (Figure 4 and Table 19). Among patients who met the orange action plan criteria and had diabetes, the majority had optimal monitoring for blood pressure measurement (79.5%), eGFR (77.0%) and haemoglobin (65.0%). Similarly, most patients who met the orange action plan criteria and did not have diabetes had optimal monitoring for blood pressure measurement (72.9%), eGFR (67.9%) and haemoglobin (60.7%).

Cognisant that some patients may have had tests or observations done at a non-MedicineInsight practice, it is noteworthy that in this cohort of regular attenders, just over half (54.1%) of the patients eligible for the orange action plan who had diabetes had optimal monitoring for HbA_{1c} in the 2-year study. Tests that were monitored sub-optimally in patients who met the orange action plan criteria, irrespective of diabetes status, were urine ACR and total cholesterol. The low rate of monitoring for total cholesterol may be as a result of the CKD guideline that suggests that once patients are placed on statin therapy, ongoing monitoring of lipid levels may not be required.[19]

FIGURE 4: PATIENTS WITH CKD ELIGIBLE FOR THE ORANGE ACTION PLAN WHO HAD AT LEAST FOUR RECORDS OF THE INDIVIDUAL ASSESSMENTS DURING THE 2-YEAR STUDY, STRATIFIED BY DIABETES STATUS



	eGFR	Urine ACR	Total cholesterol	HbA1c	BP measurement	Haemoglobin
Diabetes	77.0	21.5	36.4	54.1	79.5	65.0
No diabetes	67.9	8.2	19.9	4.0	72.9	60.7

ACR, albumin-to-creatinine ratio; BP, blood pressure; eGFR, estimated glomerular filtration rate; HbA_{1c}, glycated haemoglobin. Note that HbA_{1c} is recommended for people with diabetes.

TABLE 19: PATIENTS WITH STAGE 3A WITH ALBUMINURIA AND STAGE 3B WITH OR WITHOUT ALBUMINURIA CKD (ORANGE ACTION PLAN) WHO HAVE 0, 1, 2, 3 OR 4+ RECORDS OF THE INDIVIDUAL OBSERVATIONS OR TESTS BETWEEN JANUARY 2018 AND DECEMBER 2019

Test/ observation	Patients with no record				Patients with 1 record				Patients with 2 records				Patients with 3 records				Patients with 4+ records			
	No diabetes		Diabetes		No diabetes		Diabetes		No diabetes		Diabetes		No diabetes		Diabetes		No diabetes		Diabetes	
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
eGFR	215	3.8 (3.3–4.4)	135	3.2 (2.6–3.8)	394	7.1 (6.3–7.8)	206	4.9 (4.1–5.6)	543	9.7 (9.0–10.5)	244	5.8 (5.0–6.5)	639	11.4 (10.6–12.3)	388	9.2 (8.2–10.1)	3,796	67.9 (66.4–69.5)	3,263	77.0 (75.2–78.8)
Urine ACR	3,447	61.7 (59.2–64.2)	1,104	26.1 (23.8–28.3)	915	16.4 (15.2–17.6)	852	20.1 (18.6–21.6)	501	9.0 (8.0–10.0)	778	18.4 (17.1–19.6)	266	4.8 (4.1–5.4)	591	14.0 (12.7–15.2)	458	8.2 (7.1–9.3)	911	21.5 (19.5–23.5)
Total cholesterol	1,790	32.0 (29.5–34.5)	617	14.6 (12.9–16.2)	1,229	22.0 (20.5–23.5)	744	17.6 (15.9–19.2)	972	17.4 (16.2–18.6)	730	17.2 (15.8–18.7)	484	8.7 (7.8–9.5)	605	14.3 (13.1–15.5)	1,112	19.9 (16.7–23.1)	1,540	36.4 (32.7–40.0)
HbA_{1c}	3,537	63.3 (60.8–65.8)	348	8.2 (7.3–9.2)	1,183	21.2 (19.7–22.7)	440	10.4 (9.2–11.5)	446	8.0 (7.0–9.0)	532	12.6 (11.4–13.8)	196	3.5 (2.9–4.1)	623	14.7 (13.6–15.8)	225	4.0 (3.2–4.9)	2,293	54.1 (51.9–56.4)
BP measurement	504	9.0 (7.9–10.1)	250	5.9 (5.0–6.8)	355	6.4 (5.6–7.1)	211	5.0 (4.2–5.8)	328	5.9 (5.1–6.6)	199	4.7 (4.0–5.4)	326	5.8 (5.2–6.5)	208	4.9 (4.2–5.7)	4,074	72.9 (71.0–74.8)	3,368	79.5 (77.8–81.2)
Haemoglobin	289	5.2 (4.5–5.8)	234	5.5 (4.7–6.3)	538	9.6 (8.8–10.5)	344	8.1 (7.2–9.1)	662	11.8 (11.1–12.6)	408	9.6 (8.6–10.6)	708	12.7 (11.8–13.5)	498	11.8 (10.8–12.7)	3,390	60.7 (59.1–62.3)	2,752	65.0 (63.0–66.9)

ACR, albumin-to-creatinine ratio; BP, blood pressure; eGFR, estimated glomerular filtration rate; HbA_{1c}, glycated haemoglobin.

Note that the groups of patients with 0, 1, 2, 3 or 4+ records are mutually exclusive for each test/observation.

Consistent with previous studies using primary care data,[4] our findings suggest that there is room for improvement in monitoring of patients with early stage (1–3) CKD, particularly, in patients with no co-existing diabetes. According to national guidelines,[1] monitoring of albuminuria was less than optimal in patients with CKD but was significantly lower among those without diabetes. The better monitoring of CKD in patients with diabetes may be a benefit from the diabetes annual Cycle of Care in which patients with diabetes are monitored annually for kidney function and other risk factors, thus undertaking regular tests including eGFR and urine ACR.[17] Encouraging system changes, such as general practice incentive funding policies for CKD care as per the diabetes Practice Incentive Program, could help improve the delivery of care for CKD. Implementation of the National Strategic Action Plan for Kidney Disease which has a focus on early CKD detection and management and the establishment of standardised care pathways may also assist.

7. PRESCRIBING OF RENALLY CLEARED MEDICINES FOR PATIENTS WITH CKD

- A small proportion of patients with CKD (any stage) were prescribed the combination of an ACE inhibitor/sartan, a diuretic and an NSAID ('triple whammy') in 2019 (1.5%) and at least once on the same day during the study (0.4%).
- Among patients with any stage CKD, 3,201 patients (9.8%) were prescribed apixaban, 1,813 patients (5.5%) rivaroxaban and 571 patients (1.7%) dabigatran.
- Among all patients with stage 3 CKD, 12.2% were prescribed pregabalin and it was potentially inappropriate for 81 (2.5%) of these patients.
- Among patients with stage 3b CKD, 4.8% of were prescribed sitagliptin and it was potentially inappropriate for 185 (43.7%) of these patients.
- Among patients with stage 3 CKD who also had atrial fibrillation, 13.7% were prescribed rivaroxaban and the dose was potentially inappropriate in 72 patients (17.7%). Similarly, 7.0% of patients with stage 3 CKD and atrial fibrillation were prescribed dabigatran and it was potentially inappropriate for 56 (12.5%) of these patients.
- Among patients with stage 4 CKD, 558 patients (19.5%) were prescribed rosuvastatin, 346 patients (12.1%) pregabalin, 121 patients (4.2%) sitagliptin and 61 patients (2.1%) duloxetine.
- Potentially inappropriate prescribing was apparent for 60.3% (73 patients) of the patients with stage 4 CKD who were prescribed sitagliptin; similarly, for duloxetine (42.6%; 26 patients) and rosuvastatin (38.9%; 217 patients).
- Potentially inappropriate prescribing was observed for 3.3% (26 patients) of the 779 patients with stage 4 CKD and atrial fibrillation who were prescribed rivaroxaban; and similarly, for dabigatran (0.8%; 6 patients). Both these medicines are contraindicated for these patients
- Among the 7,707 patients with CKD (any stage) and atrial fibrillation, 2,438 patients (31.6%) had at least one prescription for apixaban of whom 27 patients (1.1% of 2,438) were prescribed a potentially inappropriate dose on their first prescription during the study.

7.1. Study questions

- What number and proportion of patients identified as having CKD (any) were prescribed all of the following medicines (triple whammy) during 2019: a diuretic, an ACE inhibitor or a sartan and an NSAID?
- What number and proportion of patients identified as having CKD (any) were prescribed all of the following medicines (triple whammy) on the SAME day at least once during the study period: a diuretic, an ACE inhibitor or a sartan and an NSAID?
- What number and proportion of patients identified as having stage 3 CKD were prescribed one of the following renally cleared medicines at least once during the study period: sitagliptin (alone or as part of a fixed dose combination), rivaroxaban or pregabalin?
- What number and proportion of patients identified as having stage 3 CKD had their first issued prescription of the following medicines higher than the recommended dose, during the study period:
  - sitagliptin (more than 50 mg daily)
  - rivaroxaban (more than 15 mg daily)
  - pregabalin (more than 300 mg daily)?
- What number and proportion of patients identified as having stage 4 CKD were prescribed one of the following renally cleared medicines at least once during the study period: sitagliptin (alone or as part of a fixed dose combination), rosuvastatin, rivaroxaban, duloxetine and pregabalin?

- What number and proportion of patients identified as having stage 4 CKD had their first issued prescription of the following medicines at higher than the recommended dose, during the study period:
  - sitagliptin (more than 25 mg daily)
  - rosuvastatin (more than 10 mg daily)
  - rivaroxaban (contraindicated)
  - duloxetine (more than 30 mg daily)
  - pregabalin (more than 150 mg daily)?
- What number and proportion of patients identified as having CKD were prescribed apixaban and had their first issued prescription of apixaban higher than the recommended dose, during the study period?
- What number and proportion of patients identified as having CKD (any) were prescribed any of the following renally cleared medicines at least once during the study period: apixaban, dabigatran, rivaroxaban?
- What number and proportion of patients identified as having stage 3 CKD were prescribed any of the following renally cleared medicines at least once during the study period: apixaban, dabigatran, rivaroxaban?
- What number and proportion of patients identified as having stage 4 CKD were prescribed any of the following renally cleared medicines at least once during the study period: apixaban, dabigatran, rivaroxaban?

7.2. Prescribing of renally cleared medicines and potentially inappropriate prescribing

Prescribing of the triple whammy among patients with CKD

The Kidney Health Australia guidelines for management of CKD advise against use of the combination of an ACE inhibitor/sartan, a diuretic and an NSAID ('triple whammy') among patients with CKD.[1] Our findings indicate that a small proportion of patients with CKD were prescribed the triple whammy in 2019 (1.5%) and at least once on the same day during the study (0.4%) (Table 20).

Though the difference was not statistically significant, the results indicate that patients with stage 1–2 CKD were more likely to be prescribed the triple whammy in 2019 (2.0% vs 1.4%) and on the same day during the study period (0.6% vs 0.4%) compared to those with stage 3–5 CKD. Findings from a previous study show that 2.6% of the patients with stage 3–5 CKD had potentially inappropriate prescribing of the triple whammy during a 4-month follow-up period.[9]

Note that estimates for potentially inappropriate prescribing of the triple whammy may have been underestimated because we do not have access to data relating to over-the-counter NSAIDs.

TABLE 20: PATIENTS WITH CKD WHO HAVE THE TRIPLE WHAMMY (COMBINATION OF AN ACE INHIBITOR/SARTAN, A DIURETIC AND AN NSAID [INCLUDING A COX-2 SELECTIVE NSAID]) RECORDED IN 2019 AND ON THE SAME DAY DURING THE STUDY PERIOD

Period	Any stage CKD (N = 32,744)		Stage 1–2 CKD (N = 3,105)		Stage 3–5 CKD (N = 29,639)	
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
Triple whammy recorded in 2019	484	1.5 (1.3–1.7)	62	2.0 (1.5–2.5)	422	1.4 (1.3–1.6)
Triple whammy recorded on the same day during the study period	134	0.4 (0.3–0.5)	18	0.6 (0.3–0.9)	116	0.4 (0.3–0.5)

ACE, Angiotensin-converting enzyme; CKD, chronic kidney disease; NSAID, nonsteroidal anti-inflammatory drug.
Triple whammy denotes combination of an ACE inhibitor/sartan, a diuretic and an NSAID (including a COX-2 selective NSAID).

Prescribing of direct-acting oral anticoagulants in patients with CKD

Among patients with any stage CKD, 3,201 patients (9.8%) were prescribed apixaban, 1,813 patients (5.5%) rivaroxaban and 571 patients (1.7%) dabigatran (Table 21). A similar order of frequency was observed for these direct-acting oral anticoagulants among patients with stage 3 and stage 4 CKD. Apixaban has the lowest fraction of renal excretion (27%)[20] and was the most prescribed direct-acting oral anticoagulant.

Patients with stage 3 CKD were more likely than those with stage 4 CKD to have at least one prescription for apixaban (10.8% vs 7.0%), rivaroxaban (6.2% vs 1.2%) and dabigatran (2.0% vs 0.3%), during the study period.

Dabigatran is contraindicated for patients with eGFR less than 30 mL/min/1.73 m^2 (stage 4–5 CKD), however, our results suggest that a small proportion of patients (0.3%) with stage 4 CKD were prescribed this medicine. Note that at the time of this study rivaroxaban was contraindicated for patients with stage 4 CKD for the treatment of atrial fibrillation but was not contraindicated for deep vein thrombosis (or venous thromboembolism) treatment.

TABLE 21: PATIENTS WITH CKD WHO WERE PRESCRIBED ONE OF THE DIRECT-ACTING ORAL ANTICOAGULANTS AT LEAST ONCE DURING THE STUDY PERIOD

DOAC medicine	Any stage CKD (N = 32,744)		Stage 3 CKD (N = 26,151)		Stage 4 CKD (N = 2,864)	
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
Apixaban	3,201	9.8 (9.3–10.3)	2,836	10.8 (10.3–11.4)	201	7.0 (6.1–8.0)
Rivaroxaban*	1,813	5.5 (5.2–5.9)	1,632	6.2 (5.8–6.7)	33	1.2 (0.8–1.5)
Dabigatran**	571	1.7 (1.6–1.9)	516	2.0 (1.7–2.2)	9	0.3 (0.1–0.5)
Any of the above	5,305	16.2 (15.5–16.9)	4,726	18.1 (17.3–18.8)	233	8.1 (7.1–9.1)

*Contraindicated for patients with stage 4 CKD in atrial fibrillation but not deep vein thrombosis treatment. **Contraindicated for patients with stage 4 CKD. CKD, chronic kidney disease; DOAC, direct acting oral anticoagulant.

Potentially inappropriate prescribing among patients with stage 3 CKD

Among the 8,866 patients with stage 3b CKD, 423 patients (4.8%) were prescribed sitagliptin at least once during the study, of whom 185 patients (43.7% of 423) were prescribed a higher than recommended dose on their first prescription in the study (Table 22).

Of the 2,981 patients with stage 3 CKD (eGFR=30–49 mL/min/1.73 m^2) who also had atrial fibrillation (but no DVT/PE), 407 patients (13.7%) were prescribed rivaroxaban at least once during the study period, of whom 17.7% (72 patients) had a potentially inappropriate high dose on their first prescription recorded during the study.

Among the 6,400 patients with stage 3 CKD and atrial fibrillation (but no DVT/PE), 449 patients (7.0%) were prescribed dabigatran, of whom 12.5% (56 patients) had a potentially inappropriate high dose on their first prescription in the study.

A total of 3,182 patients (12.2%) with stage 3 CKD were prescribed pregabalin at least once during the study period and 2.5% (81 patients) of them had their first prescription in the study potentially inappropriately prescribed.

Our findings indicate that some patients with stage 3 CKD were prescribed a potentially inappropriate high dose of the selected medicines, sitagliptin, rivaroxaban, dabigatran and pregabalin. Castelino and colleagues also found that sitagliptin and rivaroxaban were some of the medicines that appeared to be commonly prescribed at an inappropriately high dose in patients with CKD.[10] Of note, our findings may be an underestimate of the potentially inappropriate prescribing rates because of the time difference between the assessment of kidney function (2017) and the prescribing of medicines (2018–19). To minimise this, we assessed only the first prescription recorded during the study (2018–19) for inappropriate prescribing. Our findings, thus, indicate minimum estimates for potentially inappropriate prescribing of the selected medicines in this population.

TABLE 22: PATIENTS WITH STAGE 3 CKD WHO WERE PRESCRIBED ONE OF THE SELECTED MEDICINES AT LEAST ONCE AND THEIR FIRST ISSUED PRESCRIPTION WAS A HIGHER THAN RECOMMENDED DOSE FOR THEIR RENAL FUNCTION, DURING THE STUDY PERIOD

Medicine	Additional selection criterion	Denominator number of patients (N)	Patients prescribed at least once during 2018–19		Patients whose first script was a higher than recommended dose	
			n	% (95% CI)	n	% of patients prescribed selected medicine
Sitagliptin	CKD stage 3b	8,866	423	4.8 (4.2–5.3)	185	43.7
Rivaroxaban	Patient has AF, but no DVT/PE; eGFR=30-49	2,981	407	13.7 (12.3–15.0)	72	17.7
Dabigatran	Patient has AF, but no DVT/PE	6,400	449	7.0 (6.2–7.8)	56	12.5
Pregabalin	Nil	26,151	3,182	12.2 (11.6–12.7)	81	2.5

AF, atrial fibrillation; CKD, chronic kidney disease; DVT, deep vein thrombosis; eGFR, estimated glomerular filtration rate; PE, pulmonary embolism.

Potentially inappropriate prescribing among patients with stage 4 CKD

Among the 2,864 patients with stage 4 CKD, 121 patients (4.2%) were prescribed sitagliptin at least once during the study, of whom 73 patients (60.3% of 121) had a potentially inappropriate high dose on their first prescription recorded during the study (Table 23).

Duloxetine was prescribed for 61 patients (2.1%) with stage 4 CKD and 42.6% (26 patients) of them had a potentially inappropriate dose on their first prescription in the study.

A total of 558 patients (19.5%) with stage 4 CKD were prescribed rosuvastatin at least once during the study, of whom 38.9% (217 patients) had a potentially inappropriate high dose on their first prescription recorded during the study.

Potentially inappropriate prescribing was apparent for 3.3% (26 patients) of the 779 patients with stage 4 CKD and atrial fibrillation (but no DVT/PE) who were prescribed rivaroxaban; similarly, for dabigatran (0.8%; 6 patients). Both these medicines are contraindicated for these patients.

A total of 346 patients (12.1%) with stage 4 CKD were prescribed pregabalin at least once during the study period but very few had a potentially inappropriate dose on their first prescription in the study.

Consistent with other Australian studies,[7,8,10] our findings suggest some level of potentially inappropriate prescribing in patients with stage 4 CKD, particularly, sitagliptin, duloxetine and rosuvastatin, and indicate that there is scope for improvement. As mentioned above, it is possible that we underestimated the potentially inappropriate prescribing rates as we did not account for CKD progression over time and only assessed the first prescription recorded during the study to determine inappropriate prescribing.

TABLE 23: PATIENTS WITH STAGE 4 CKD WHO WERE PRESCRIBED ONE OF THE SELECTED MEDICINES AT LEAST ONCE AND THEIR FIRST ISSUED PRESCRIPTION WAS A HIGHER THAN RECOMMENDED DOSE FOR THEIR RENAL FUNCTION, DURING THE STUDY PERIOD

Medicine	Additional selection criterion	Denominator number of patients (N)	Patients prescribed at least once during 2018–19		Patients whose first script was contraindicated or higher than recommended dose	
			n	% (95% CI)	n	% of patients prescribed selected medicine
Sitagliptin	Nil	2,864	121	4.2 (3.4–5.0)	73	60.3
Duloxetine	Nil	2,864	61	2.1 (1.6–2.7)	26	42.6
Rosuvastatin	Nil	2,864	558	19.5 (17.9–21.1)	217	38.9
Rivaroxaban*	Patient has AF, but no DVT/PE	779	26	3.3 (2.1–4.6)	26	3.3
Dabigatran**	Patient has AF, but no DVT/PE	779	6	0.8 (0.2–1.4)	6	0.8
Pregabalin	Nil	2,864	346	12.1 (11.0–13.2)	< 5	-

* Contraindicated for patients with stage 4 CKD in atrial fibrillation. ** Contraindicated for patients with stage 4 CKD. AF, atrial fibrillation; CKD, chronic kidney disease; DVT, deep vein thrombosis; PE, pulmonary embolism.

Potentially inappropriate prescribing of apixaban for patients with CKD

Among the 7,707 patients with CKD (any stage) who had atrial fibrillation (but no DVT/PE), 2,438 patients (31.6%) had at least one prescription for apixaban, of whom 27 patients (1.1% of 2,438) were prescribed a potentially inappropriate dose on their first prescription during the study (Table 24).

TABLE 24: PATIENTS WITH ANY STAGE CKD WHO WERE PRESCRIBED APIXABAN AT LEAST ONCE AND THEIR FIRST ISSUED PRESCRIPTION WAS A HIGHER THAN RECOMMENDED DOSE FOR THEIR RENAL FUNCTION, DURING THE STUDY PERIOD

Medicine	Additional selection criterion	Denominator number of patients (N)	Patients prescribed at least once during 2018–19		Patients whose first script was a higher than recommended dose	
			n	% (95% CI)	n	% of patients prescribed apixaban
Apixaban	Patient has AF, but no DVT/PE	7,707	2,438	31.6 (30.3–33.0)	27	1.1

Note: where records for serum creatinine and for maximum weight in 2017 were incomplete, they were assumed to be low risk values, therefore the "higher than recommended" result may be an underestimate. AF, atrial fibrillation; CKD, chronic kidney disease; DVT, deep vein thrombosis; PE, pulmonary embolism.

GUIDE TO INTERPRETING THE DATA

When interpreting the information presented in this report, readers should note the following caveats and/or assumptions related to the MedicineInsight data.

- MedicineInsight data are dependent on the accuracy and completeness of data recorded in, and available for extraction from, the general practice clinical systems.
- Identification of conditions is dependent on GPs recording these items in their clinical software systems. Conditions may be underreported in MedicineInsight data depending on GPs' recording practices.
- Calculation of the relative proportion of different indications assumes that non-recording of conditions occurs at random.
- Medicines prescribed or tests requested at non-MedicineInsight practices or by specialists will not routinely be available to MedicineInsight and may lead to an underestimate of the true history of prescribing and monitoring/reviews.
- We identified CKD from pathology results recorded during 2017 and may not have picked up patients who had abnormal eGFR or urine ACR results in the earlier years. Given that the focus of our study was not to determine prevalence of CKD but rather to assess monitoring and potentially inappropriate prescribing in patients with CKD, this should not affect our findings. Moreover, as most CKD patients would be monitored for eGFR and/or albuminuria at least once annually, it is likely that the number of patients with CKD not picked up was small.
- As patients with severe CKD such as end stage renal failure might be monitored by specialists or in hospital settings, and these data are not always available in MedicineInsight, there may be some underestimation of monitoring rates in patients with stage 3–5 CKD.
- To determine CKD stages, if a patient had only two eGFRs that were 90+ days apart, and one was very low and the other moderately low, they were grouped as moderate. For example, if the first eGFR was 25 mL/min/1.73 m^2, and the second was 35 mL/min/1.73 m^2, they were grouped as Stage 3b (not Stage 4).
- As CKD severity progresses over time and we only assessed the first prescription recorded during the study for inappropriate prescribing, it is possible that we underestimated the rates of potentially inappropriate prescribing.
- For drug dosing in people at both extremes of body size, it is advised to calculate an eGFR that is adjusted to the individual's body surface area (BSA), but we were not able to make this adjustment in this study.
- Because we cannot clearly identify the different forms of anaemia to assess CKD-specific anaemia from the data, we did not differentiate between the different forms of anaemia. Thus, we used the WHO thresholds for anaemia instead of using the CKD-specific thresholds, which might have overestimated the prevalence estimates for anaemia in patients with CKD.
- Identification of risk factor information is dependent on whether this information has been recorded in fields from which data can be extracted and analysed.
- Due to confidentiality issues, we do not have access to progress notes, which may contain further information on symptoms, family history, reasons for encounters, diagnoses and test results.

- Patients are free to visit multiple other practices. We do not have data on patients from non-MedicineInsight clinics. Currently we cannot identify patients who have attended multiple MedicineInsight practices.
- Practices were recruited to MedicineInsight using non-random sampling, and systematic sampling differences between regions cannot be ruled out. Tasmania is overrepresented whereas South Australia is underrepresented in MedicineInsight. Comparisons between regions should be interpreted with caution.

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APPENDIX 1: RENALLY CLEARED MEDICINES

Table A1. Medicines that may accumulate and require renal function monitoring[a]

Blood	Cardiovascular	Analgesics
dabigatran	ACE-inhibitors	codeine
enoxaparin	angiotensin receptor blockers	morphine
rivaroxaban	atenolol	hydromorphone
Endocrine	bisoprolol	oxycodone
glibenclamide	digoxin	tramadol
gliptins (saxagliptin, sitagliptin, vildagliptin)	fenofibrate	
glimepiride	Psychotropic	Genitourinary
metformin	acamprosate	solifenacin
Neurological	amisulpride	sildenafil
baclofen	benzodiazepines	tadalafil
gabapentin	bupropion	tolterodine
galantamine	desvenlafaxine	vardenafil
levetiracetam	duloxetine	Musculoskeletal
memantine	lithium	allopurinol
methysergide	reboxetine	bisphosphonates
paliperidone	venlafaxine	colchicine
pramipexole	Gastrointestinal	strontium ranelate
pregabalin	H2-antagonists	teriparatide
topiramate		
varenicline		

Adapted from veteran's MATES[6]

[a] List does not include antibiotic, antifungal or antiviral medicines, or those medicines predominately used in hospital settings

APPENDIX 2: BASELINE POPULATION

Table A2: Sociodemographic characteristics of the baseline study population (N = 1,680,457)

Characteristic	Baseline study population (N = 1,680,457)	
	n	% (95% CI)
Gender		
Female	969,797	57.7 (57.1–58.3)
Male	710,660	42.3 (41.7–42.9)
Age group (years)		
18–44	727,192	43.3 (41.3–45.3)
45–54	272,050	16.2 (15.9–16.5)
55–64	266,206	15.8 (15.4–16.3)
65–74	229,809	13.7 (12.9–14.5)
75+	185,200	11.0 (10.1–11.9)
Remoteness (missing n=205)		
Major city	1,014,982	60.4 (54.2–66.6)
Inner Regional	424,450	25.3 (20.1–30.4)
Outer Regional	213,821	12.7 (9.5–15.9)
Remote or very remote	26,999	1.6 (0.8–2.5)
Indigenous status		
Aboriginal and/or Torres Strait Islander	40,763	2.4 (2.0–2.9)
Other Australian	1,356,547	80.7 (78.1–83.4)
Not known	283,147	16.8 (14.1–19.6)
Current smoker (missing n=179,715)		
Yes	231,301	15.4 (14.1–16.7)
No	1,269,441	84.6 (83.3–85.9)
State/Territory		
ACT	41,358	2.5 (0.7–4.2)
NSW	574,489	34.2 (28.6–39.8)
NT	30,499	1.8 (0.6–3.1)
QLD	272,793	16.2 (12.0–20.4)
SA	45,277	2.7 (1.1–4.2)
Tas	122,658	7.3 (4.0–10.6)
Vic	428,693	25.5 (18.4–32.6)
WA	164,690	9.8 (6.3–13.3)
SEIFA (missing n=205)		
1 (most disadvantaged)	318,929	19.0 (15.7–22.3)
2	305,734	18.2 (15.3–21.1)
3	369,342	22.0 (18.8–25.1)
4	315,546	18.8 (16.2–21.4)
5 (most advantaged)	370,701	22.1 (18.2–26.0)
Concession card holder (missing n=318,647)		
Yes	581,324	42.7 (39.9–45.5)
No	780,486	57.3 (54.5–60.1)

SEIFA, socioeconomic index for areas. NB: Practices were recruited to MedicineInsight using non-random sampling, and systematic sampling differences between regions cannot be ruled out. Tasmania is overrepresented whereas South Australia is underrepresented in MedicineInsight. Comparisons between regions should be interpreted with caution'