

# Medication prescribing quality in Australian primary care patients with chronic kidney disease

**Woldesellassie Bezabhe** (✉ [Woldesellassie.bezabhe@utas.edu.au](mailto:Woldesellassie.bezabhe@utas.edu.au))

University of Tasmania Faculty of Health <https://orcid.org/0000-0002-3028-6949>

**Alex Kitsos**

University of Tasmania, Wicking Dementia Research and Education Centre

**Timothy Saunder**

University of Tasmania, Wicking Dementia Research and Education Centre

**Gregory M. Peterson**

Division of Pharmacy, School of Medicine, University of Tasmania, Private Bag 26, Hobart, Tasmania, 7001

**Luke R. Bereznicki**

Division of Pharmacy, School of Medicine, University of Tasmania, Private Bag 26, Hobart, Tasmania, 7001

**Matthew Jose**

University of Tasmania Menzies Institute for Medical Research

**Barbara Wimmer**

Division of Pharmacy, School of Medicine, University of Tasmania, Private Bag 26, Hobart, Tasmania, 7001

**Jan Radford**

Launceston Clinical School, University of Tasmania

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## Research article

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# Abstract

**Background:** Drugs are commonly used in patients with chronic kidney disease (CKD) to treat an underlying cause, or its numerous complications and comorbidities. The objective of this study was to examine the quality of prescribing in patients with CKD in Australian general practice from February 01, 2016 and June 01, 2016, using validated indicators.

**Methods:** We evaluated Australian general practice data obtained from the NPS MedicineWise MedicineInsight dataset for patients with CKD and aged 18 years or older. We used 16 internationally validated prescribing quality indicators focused on medication need, choice and safety in patients with CKD, and we compared results for patients using clinical and sociodemographic factors.

**Results:** Among 44,259 patients with evidence of CKD stages 3-5, 13,263 (30%) had documentation of a diagnosis of diabetes. Less than half of all patients (40.8%) with CKD stages 3-5 and aged 50 to 65 years were prescribed a statin. The use of an angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) was higher in patients with concomitant diabetes (64.1%) compared with those without diabetes (51.5%;  $P < 0.001$ ), yet only 69.9% of the patients with diabetes and microalbuminuria were receiving an ACEI or ARB. There were 7,426 patients (16.8%) with CKD stages 3-5 potentially receiving non-steroidal anti-inflammatory drugs (NSAIDs), including 14.3% of those patients with an estimated glomerular filtration rate (eGFR) below 30 mL/min/1.73 m<sup>2</sup>. Potentially inappropriate medication use was more common in CKD patients living in relatively disadvantaged socioeconomic areas, as well as in regional and remote areas.

**Conclusions:** We identified areas for possible improvement in the prescribing of preventive medications, as well as deprescribing of potentially nephrotoxic medication, in patients with CKD stages 3-5. Australian programs working to improve quality use of medication need to focus on improving the appropriate prescribing of recommended preventive medications in patients with CKD, such as an ACEI/ARB and statin, and deprescribing of NSAIDs in patients with concurrent ACEI/ARB therapy.

**Keywords:** chronic kidney disease, drug therapy, quality indicators, inappropriate prescribing, general practice, quality use of medicine, primary care

## Background

An estimated 1.7 million Australian adults aged 18 years or older had indicators of chronic kidney disease (CKD) based on the 2011–12 Australian Health Survey. Of these, 604,000 patients had a moderate to a severe loss of kidney function (CKD stages 3–5). Only 1 in 10 of those who showed biomedical signs of CKD were also self-reported that they had CKD (1). Cardiovascular disease is a risk factor for progression of CKD and vice versa. Approximately a quarter of Australian general practice patients with CKD stages 3–5 had a recorded diagnosis of cardiovascular disease (2). CKD can progress to end-stage kidney disease (ESKD), and diabetes and hypertension are the two most common cause of ESKD. In 2016, 2,800 new cases of ESKD were reported in Australia (3).

General practitioners (GPs) manage the majority of patients with CKD in Australia. Kidney Health Australia's 'CKD management in general practice' guideline recommends, depending on the stage of CKD, adequate treatment of hypertension, albuminuria, anaemia, and mineral and bone disorders, and the use of statins (4). The third and the latest edition of this guideline was published in 2015 and is available in hard and electronic copies. The electronic copy is free to download and contains interactive hyperlinks. The Kidney Health Australia through Kidney Check Australia Taskforce (KCAT) also provides accredited education for GPs. These education sessions facilitate the translation of recommendations made in this guideline (4).

GPs are expected to meet guideline recommendations by prescribing blood pressure lowering medication, such as angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) and lipid lowering medications like statins (4). These medications lower cardiovascular risk and slow progression of CKD (5, 6). On the other hand, GPs are also expected to avoid prescribing medications that potentially damage kidney function (6). These include the combined use of an ACEI and ARB and long-term use of non-steroidal anti-inflammatory drugs (NSAIDs). The combined use of an ACEI and ARB can significantly decrease proteinuria compared with monotherapy. However, their combined use is not recommended as it may cause severe adverse drug reactions and is associated with poor renal outcomes (5). A recent population-based study found that new NSAID use compared with non-use was associated with a higher risk of developing acute renal injury (AKI) and hyperkalaemia (7).

Awareness of CKD in primary care remains low compared with other chronic diseases such as diabetes. This leads to low use of guideline-recommended preventive medication and the continuing practice of prescribing potentially nephrotoxic medication across the globe. Several studies evaluated prescribing quality in primary care patients with CKD. For instance, a study in Canada reported that only 26.8% of patients with CKD but no diabetes were prescribed an ACEI or ARB compared with 76.3% of those with CKD and diabetes (8). A study in the United States found that of total 627 patients with CKD and an indication for an ACEI or ARB, only 402 patients were prescribed these medications (9). A study conducted in the Netherlands reported that adequate CKD progression monitoring and blood pressure control were achieved only in 42% and 43% of general practice patients, respectively (10).

However, there are no studies that have examined how well the Kidney Health Australia's 'CKD management in general practice' guideline recommendations are implemented in practice in Australian patients with CKD. Our objective was, therefore, to evaluate the quality of prescribing in a large sample of patients with CKD using a set of internationally published primary care quality indicators (11).

## Methods

We analysed retrospective data obtained from the NPS MedicineWise MedicinesInsight dataset. The data were de-identified and extracted from the electronic health records (EHRs) of general practices and include demographics, encounters, diagnoses, prescriptions, observations and pathology tests. NPS MedicineWise MedicinesInsight is the largest geographically representative primary care dataset in Australia. As of October 2018, NPS MedicineWise MedicinesInsight had recruited 671 general practices across Australia. A total of 2,974,031 patients had at least three clinical encounters in the previous two years. Details about this dataset can be found elsewhere (2, 12–14). We used MedicinesInsight data from January 01, 2013 to June 01, 2016 collected from 329 general practices.

In this study, we included patients with evidence of CKD based on having two renal function tests that were performed at least three months apart with: (1) estimated glomerular filtration rate (eGFR) values  $<60$  mL/min/1.73 m<sup>2</sup> and/or (2) albumin-to-creatinine ratio (ACR) values  $\geq 3.5$  mg/mmol for females or  $\geq 2.5$  mg/mmol for males. The renal function tests were performed between January 01, 2013 and June 01, 2015. The CKD epidemiology collaboration equation (CKD-EPI) was used to calculate eGFR. This definition of CKD is congruent with that recommended for the diagnosis of CKD in Australian general practice (4). Regular patients (defined by the Royal Australian College of General Practitioners as those with three or more encounters in the previous two years) were included if at the time of data extraction (July 2016) they were aged at least 18 years. Patients were excluded if they did not have at least one follow-up GP visit between June 02, 2015 and June 01, 2016, in addition to patients who died during that period.

Variables such as age, gender, socio-economic status (based on the Index of Relative Socio-economic Advantage and Disadvantage, one of the socio-economic indexes for areas (SEIFA)) (15), rurality, continuity of care (CoC), documentation of a diagnosis of CKD and serum electrolyte levels (e.g., calcium, and phosphate) were examined. SEIFA

quintile is an index developed by Australian Bureau of Statistics (ABS) and ranks areas in Australia from 1 (most disadvantaged area) to 5 (most advantaged area). Rurality was assigned according to the postcode of the patient's residence and classified as major cities, regional, and remote Australia. CoC was calculated for each included patient after the time of laboratory evidence of CKD, over the remainder of the data collection period, using the Herfindahl-Hirschman Index, which has been shown to be highly correlated with other common measures of CoC (16). Its value range from 0 to 1 and cut off points for low and high CoC were  $<0.75$  and  $\geq 0.75$ , respectively. Low CoC in general practice, measured with this index, has also been associated with a higher risk of mortality (17, 18).

Documentation of a diagnosis of CKD was extracted from condition codes and manual searches conducted on 'free-text' or narrative information in the past medical history, reason for encounter and reason for prescription data fields. Baseline comorbidities, including cardiovascular disease (myocardial infarction, heart failure, coronary artery bypass graft, transient ischaemic attack and stroke), hypertension and diabetes, were examined. The comorbidities were based on 'condition flags' provided by MedicineInsight, using an algorithm that analyses coded and free-text patient information. The prescribed medications that were examined included: diuretics (anatomical therapeutic chemical (ATC) code: C03), beta-blockers (C07), calcium channel blockers (C08), ACEIs (C09A), ARBs (C09C), other agents acting on renin-angiotensin system (RAS) (C09), other antihypertensives (C02), statins (C10AA or combinations as in C10BA and C10BX), phosphate binders (A12AA04, A12AA12, V03AE and A02AB01), erythropoiesis-stimulating agents (ESAs) (B03XA), non-steroidal anti-inflammatory drugs (NSAIDs) (M01A, M01BA and B01AC), metformin (A10BA02 or in combination as A10BD) and digoxin (C01AA05).

The recorded data, including prescriptions and laboratory tests during the last four months of follow-up (between February 01, 2016 and June 01, 2016), were used to assess the quality of pharmacotherapy based on 12 prescribing quality indicators (PQIs), developed and validated by Smits et al. (11) in the Netherlands. Four of the original 16 indicators were deemed to be of limited relevance in this study as they focus on medications such as phosphate binders and ESAs that are not commonly initiated and managed by Australian GPs (generally prescribed by renal physicians). The first three indicators looked at the treatment of hypertension, including in those with albuminuria and diabetes. Indicator four and five assessed the percentage of patients with CKD and albuminuria receiving treatment with an ACEI or ARB. The remaining items were focused on assessing the appropriate prescribing of medications, such as statins, NSAIDs, RAS blockers, vitamin D, metformin, digoxin and diuretics.

Simultaneous prescribing of RAS blockers was defined as at least two of the ATC codes C09A, C09B, C09C, C09D, C09X or combination (as in C10BX) within the last four months of the follow-up (between February 01, 2016 and June 01, 2016). Simultaneous use of NSAID, RAS blocker and diuretic was defined as at least one prescription for each of the three class of medications during the follow-up period. Specific details of the definitions of the prescribing quality indicators can be found elsewhere (11). It was acknowledged that we were not capable of capturing the use of over-the-counter NSAIDs and vitamin D. We could also not capture whether NSAIDs were prescribed as a regular medication or for 'as needed' use.

All data analyses and management were conducted using the statistical and graphical computing language of R (19). Data were presented as numbers and proportions. Chi-square tests were used to determine differences in characteristics, including prescribed medications, in CKD patients with and without concomitant diabetes, and one-way ANOVA (analysis of variance) was used to compare continuous variables. A two-sided P value of less than 0.05 was considered to indicate statistical significance.

## Results

### *Baseline characteristics*

This study included 44,259 patients with evidence of CKD. Most patients (57.8%) had eGFR values between 45 and 59 mL/min/1.73 m<sup>2</sup>. More than half (54.6%) of the patients were females, and 70% were aged 70 years or older. The baseline characteristics of the study participants are shown in Table 1 and Table 2. Only a quarter of patients with evidence of CKD had documentation of the diagnosis, and documentation was less likely with increasing age (e.g. 51.3% for patients aged 30–39 years with evidence of CKD vs. 23.9% in those aged ≥80 years; P<0.001).

Approximately 80% and 30% of the patients also had hypertension and diabetes, respectively. Hypertension and cardiovascular disease were more common in patients with diabetes than in those patients without diabetes.

#### *Treatment of hypertension and albuminuria*

Of the 39,716 patients whose blood pressure was monitored and recorded between June 02, 2015 and June 01, 2016, one-third were found to have elevated systolic blood pressure (>140 mmHg) at last measurement. Antihypertensive medication prescribing was significantly higher in CKD patients with diabetes compared with those without diabetes (82.1% vs. 70.6%, P<0.001). We also noted that a higher proportion of patients with diabetes were prescribed guideline-recommended medications compared with patients with no diabetes. Specifically, 64.1% of CKD patients with diabetes were prescribed an ACEI/ARB compared with 51.5% of those without diabetes (P<0.001) (Table 2). The prescribing of an ACEI/ARB occurred in 69.9% of patients aged between 18 and 80 years with CKD stages 3–5 with microalbuminuria and diabetes, and in 62.3% of patients aged 18 and 80 years with CKD stages 3–5 and macroalbuminuria (Table 3). The proportion of patients who were prescribed an ACEI/ARB were significantly lower in patients with CKD stages 4/5 compared with patients with CKD stage 3. Among 13,551 patients with CKD stage 3b, over half of them were receiving an ACEI/ARB while only a quarter of the 701 patients with CKD stage 5 were prescribed an ACEI/ARB.

#### *Prescription of statins*

We examined the prescribing of statins in CKD patients with diabetes and in those aged between 50 and 65 years, as guidelines recommend statin use in both of these groups (20). Over 60% of CKD patients with diabetes were prescribed a statin compared with less than 40% without diabetes (P<0.001) (Table 2). The percentage of statin prescribing was 40.8% in patients with CKD aged between 50 and 65 years. Prescribing of statins in this age group was more common in patients with a SEIFA score ≤3 than ≥4 (45.3% vs. 38.9%, P<0.001) and in patients with a documented CKD diagnosis (45.1% vs. 38.9%) (Table 3).

#### *Medication safety*

Overall, the prescribing of NSAIDs between February 01, 2016 and June 01, 2016 occurred in 16.8% of the patients. The percentage of potentially inappropriate prescribing of a NSAID in combination with a RAS blocker and a diuretic was 2.6% overall and 3.0% in those patients whose CKD diagnosis was documented. It was slightly higher in patients with SEIFA score ≤3 than ≥4 (3.2% vs. 2.4%, P<0.001) and in CKD patients living in regional and remote areas than in patients living in major cities (2.8% vs. 2.5%; P = 0.032).

Of those patients with CKD stages 3–5 and a prescription of RAS blockers between February 01, 2016 and June 01, 2016, 7.6% were prescribed at least two RAS blockers simultaneously. This was more likely in stages 3–5 CKD patients with SEIFA score ≤3 than ≥4 (8.3% vs. 7.3%; P = 0.005) and in stages 3–5 CKD patients living in major cities than those living in regional and remote areas (8.0% vs. 7.0%; P = 0.002) (Table 3). In addition, more patients (6.0%) with diabetes were prescribed multiple RAS blockers compared with patients without diabetes (3.4%; P<0.001) (Table 2).

There were 5,130 patients with diabetes who were prescribed metformin. The rate of potentially inappropriate prescribing of metformin was 14.1% in patients with an eGFR <30 mL/min/1.73 m<sup>2</sup>. This was slightly greater in patients

living in regional and remote Australia (16.8%) than those living in major cities (12.3%;  $P = 0.005$ ) and in patients whose CKD diagnosis was not documented (16.3% vs. 12.5%;  $P = 0.018$ ) (Table 3).

## Discussion

This is the largest study that has evaluated the quality of medication prescribing in patients with CKD in Australian general practice using internationally validated indicators (11). The results of this study indicated possible gaps in the treatment of hypertension and albuminuria in patients with CKD, which are likely to have negative implications for the prevention of CKD progression and development of cardiovascular complications.

Despite guideline recommendations (4), less than 70% of Australian adult patients with CKD stages 3–5 with diabetes and microalbuminuria were receiving an ACEI or ARB. The prescribing percentage was even lower (62.3%) in those patients with macroalbuminuria. Studies from different provinces of Canada (8, 21, 22) in CKD reported rates of 74% to 80% for ACEI or ARB prescribing, while the Netherlands study found prescribing in 78% and 82% of non-diabetes and diabetes patients, respectively (11). Similar to our study, the percentages of prescribing of an ACEI or ARB reported by studies in Canada and the Netherlands (8, 11, 21, 22) were higher in CKD patients with diabetes compared to those without diabetes.

The prescribing of an ACEI or ARB in patients with CKD with albuminuria was slightly lower (5–10%) in Australian general practice compared to other developed nations (8, 21–23). Furthermore, the proportion of patients prescribed at least two RAS blockers concurrently was 7.6%, which is double the proportion (3.7%) reported by the Netherlands study (11) using the same indicator. Studies in the United Kingdom and Canada also reported lower percentages of ACEI and ARB co-prescribing, ranging from 0.7% to 4% (22–24).

Statins are relatively well-tolerated medications and are beneficial in lowering the risk of developing cardiovascular events in patients with CKD (20, 24). Notwithstanding the Australian Pharmaceutical Benefits Scheme restrictions on the prescribing of statins, the current Kidney Disease: Improving Global Outcomes (KDIGO) and Kidney Health Australia guidelines (4, 20) recommend statin or statin/ezetimibe treatment in adults aged 50 years and over with  $eGFR < 60$  mL/min/1.73 m<sup>2</sup> but not treated with chronic dialysis or kidney transplantation. In this study, we found that only 46.1% and 40.8% of all patients and patients aged 50 to 65 years, respectively, were receiving statins. A similar study by Smits et al. (11) in the Netherlands reported a higher (74%) rate of statin prescribing in patients with CKD stages 3–5 aged 50 to 65 years. Statin prescribing rates reported in this study were also lower compared with previous studies in the United States (64%) (9) and Canada (64%) (21). The AusHeart study (25) reported that 54% of patients with CKD were receiving lipid-lowering medications in Australian primary care.

NSAIDs should be avoided in patients with advanced CKD ( $eGFR < 30$  mL/min/1.73 m<sup>2</sup>) per practice guidelines (4, 24). They are potentially nephrotoxic medications, which can cause acute kidney injury (AKI) and worsen the progression of CKD (24, 26). In our study, potentially inappropriate prescribing of NSAIDs occurred in 14.3% of these patients. The longitudinal North West Adelaide Health Study in South Australia reported a similar percentage (15.9%) of prescribing of NSAIDs in patients with CKD (27). The Netherlands study (11), which developed the PQIs that we used, reported a lower rate (3%) of NSAID prescribing in patients with  $eGFR < 30$  mL/min/1.73 m<sup>2</sup>. A study in Canada reported that almost 10% of patients were prescribed NSAIDs despite patients' high risk for renal and cardiovascular complications (28). Another study in the UK on patients with moderate to severe CKD reported 5.7% NSAID use (29). Given that some NSAIDs are also available over the counter, their use is likely to be higher than the estimates reported here using general practice prescription data.

In addition, concurrent use of NSAIDs with other potentially nephrotoxic medications, such as RAS blockers, increases the risk of developing AKI and the progression of CKD (24, 30). In this study, we found that 2.6% of all patients aged 18 to 80 years with CKD were potentially receiving triple therapy (“triple whammy”): a diuretic and an ACEI or ARB plus an NSAID. Smits *et al.* (11) reported a rate of 4.6% for triple therapy in patients with CKD aged 18 to 80 years from the Netherlands. Patients who were diagnosable with CKD based on laboratory evidence, regardless of whether formally diagnosed and recorded as having CKD by their GP, were included in this study. It is interesting to note that only approximately a quarter of patients had a documented diagnosis of CKD. Details of variation in documenting diagnosable CKD in Australian general practice can be found elsewhere (31). The poor documentation of CKD may indicate a lack of awareness and recognition in diagnosing and managing CKD in Australian general practice. By contrast, the low rate of CKD documentation may also be because of GPs’ caution to avoid unnecessary labelling of older patients with normally declining kidney function with age as having CKD (32). Previous studies in Australian general practice reported even lower levels (8.9% to 18%) of CKD diagnosis documentation (25, 33). A significantly lower rate of ACEI or ARB prescribing in patients with macro-albuminuria with documented CKD as compared to those without documented CKD is unexpected. This may indicate that GPs prescribe an ACEI or ARB to prevent CKD progression while still cautious not to label their patients as having CKD.

Of those patients with CKD and their blood pressure was monitored in the year 2016, more than one-third had uncontrolled blood pressure (systolic blood pressure above 140 mmHg). This may be due to finding it difficult to control hypertension in this group of patients or a lack of awareness of the need to control hypertension within this target for patients with CKD. Treatment guidelines recommend controlling blood pressure  $\leq 140/90$  mmHg to prevent CKD progression and cardiovascular complications (4, 34).

This study also suggests that CKD patients’ SEIFA and rurality may, to some extent, influence the quality of prescribing. Potentially inappropriate medication use, such as simultaneous prescribing of two RAS blockers, prescribing of NSAIDs for CKD patients with eGFR  $<30$  mL/min per  $1.73$  m<sup>2</sup> and triple therapy, were more common in CKD patients living in disadvantaged socioeconomic areas. Similarly, potentially inappropriate prescribing of NSAIDs, metformin and digoxin were more common in CKD patients living in regional and remote areas. In contrast, appropriate prescribing of statins in CKD patients aged 50 to 65 years was higher in patients living in disadvantaged socioeconomic areas, and inappropriate co-prescribing of two RAS blockers was higher in patients living in major cities. A study in France (35) reported that inappropriate prescribing was low in older people living in municipalities with high socioeconomic status and was high in those with low socioeconomic status. A similar study in Ireland (36) also found that inappropriate prescribing was more prevalent in relatively deprived patients aged over 70 years.

Unlike a previous study by Khanam *et al* (37), using MedicinesInsight data, which found higher CoC led to better blood pressure control, in this study, there were no significant differences in prescribing quality between patients with higher and lower CoC (Table 3).

## Strengths And Limitations

This study had a large sample, and patient characteristics within the MedicinesInsight dataset were similar to the Australian population (2, 12, 14). There are several limitations. Medications prescribed solely by specialists, such as nephrologists and cardiologists, who are working in hospitals and speciality clinics were not recorded in NPS MedicineWise MedicinesInsight. For instance, phosphate binders and ESAs are not usually prescribed by GPs (generally prescribed by renal physicians) and thus our data were not complete on the use of these medications.

Adverse drug reactions are recorded in free text in ‘Allergies/Reactions Table’ in NPS MedicineWise MedicinesInsight dataset. This table is not an event-based table and does not necessarily record each occurrence of adverse drug

reaction. Free-text search for an adverse drug reaction from this table is of poor quality. We did not account for medication contraindications and adverse drug reactions that may have prevented GPs from prescribing a specific class of medication to patients.

NSAIDs are also available without a prescription, but we could only obtain data on prescribed NSAIDs. Simultaneous prescribing of at least two RAS blockers within the four months might not necessarily indicate concomitant inappropriate use. It might be an overlapping period of switching from one RAS blocker monotherapy to the other. We also did not look at the impact of medication use on patient outcomes.

GPs collected the data for clinical decision making, not for research purposes. The EHRs may not contain all sociodemographic and clinical characteristics. For instance, indigenous status was not recorded for 24.3% of the patients. There is a possibility that aspects of patients' medical history, prescriptions and laboratory tests were recorded in notes and not included in the research data, which used specified fields and not the body of free-text consultation notes.

In conclusion, we identified the potential for possible improvement in the prescribing of recommended preventive medications and deprescribing of nephrotoxic medication in patients with CKD in Australian primary care. Australian programs working to improve the quality use of medication need to focus on improving the prescribing practice of preventive medications, such as an ACEI or ARB and a statin, and deprescribing concurrent NSAIDs and RAS blockers in patients with CKD.

## List Of Abbreviations

ACEIs, angiotensin-converting enzyme inhibitors; ACR, albumin-to-creatinine ratio; AKI, acute kidney injury; ANOVA, analysis of variance; ARBs, angiotensin receptor blockers; ATC, anatomical therapeutic chemical; CKD, chronic kidney disease; CoC, continuity of care, EHRs, electronic health records; eGFR, estimated glomerular filtration rate; ESAs, erythropoiesis-stimulating agents; GPs, general practitioners; KDIGO, Kidney Disease: Improving Global Outcomes; NSAIDs, non-steroidal anti-inflammatory drugs; PQIs, prescribing quality indicators; RAS, renin-angiotensin system; SEIFA, socio-economic indexes for areas.

## Declarations

### *Ethics approval and consent to participate*

Ethics approval was obtained from the Tasmanian Health and Medical Human Research Ethics Committee (H0015651). De-identified data obtained from the MedicinesInsight for this study did not have any patient-specific information, such as date of birth, age and postcode. Patients were informed about the program through promotional material that was displayed with the waiting room of all participating practices. Patients choice to opt out from the program was respected, and robust and effective security controls safeguarded their safety.

### *Consent for publication*

Not applicable.

### *Availability of data and material*

The data we used for this study is stored only in Australia and can be obtained from MedicinesInsight.

### *Competing interests*

The authors declare that they have no competing interests.

### *Funding*

There was no funding for this study.

### *Authors' contributions*

WB, AK, GP, LB, MJ and JR conceived the study design. AK and TS analysed the data. WB wrote the first draft of the manuscript. All authors (WB, AK, TS, JR, LB, GP, MJ and BW) reviewed and provided feedback several times on the manuscript. All authors read and approved the final manuscript.

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## Tables

Table 1. Baseline characteristics of patients with CKD overall and by diabetes status

	Overall, n=44,259 n (%)	Diabetes		P Value
		No n=30,996 n (%)	Yes n=13,263 n (%)	
<b>Age groups (years)</b>				<0.836
<65	4,373 (9.9)	3,069 (9.9)	1,304 (9.8)	
>=65	39,886 (90.1)	27,927 (90.1)	11,959 (90.2)	
Female	24,165 (54.6)	17,620 (56.8)	6,545 (49.3)	<0.001
<b>CKD Stage</b>				<0.001
Stage 3a (45-59 mL/min/1.73 m <sup>2</sup> )	25,562 (57.8)	18,724 (60.4)	6,838 (51.6)	
Stage 3b (30-44 mL/min/1.73 m <sup>2</sup> )	13,551 (30.6)	9,093 (29.3)	4,458 (33.6)	
Stage 4 (15-29 mL/min/1.73 m <sup>2</sup> )	4,186 (9.5)	2,573 (8.3)	1,613 (12.2)	
Stage 5 (<15 mL/min/1.73 m <sup>2</sup> )	960 (2.2)	606 (2.0)	354 (2.7)	
<b>ACR (mg/mmol)</b>				
Normal <2.5 (male) <3.5 (female)	7,877 (17.8)	2,850 (14.4)	5,027 (20.5)	0.023
Microalbumin urea 2.5-25 (male) 3.5-35 (female)	4,707 (10.6)	1,689 (8.5)	3,018 (12.3)	
Macroalbuminuria >25 (male) >35 (female)	2,427 (5.5)	946 (4.8)	1,481 (6.0)	
Missing	29,248 (66.1)	14,289 (61.1)	14,959 (61.1)	
<b>Indigenous Status</b>				<0.001
Indigenous	436 (1.0)	212 (0.7)	224 (1.7)	
Non-Indigenous	33,067 (74.7)	23,020 (74.3)	10,047 (75.8)	
Missing	10,756 (24.3)	7,764 (25.0)	2,992 (22.6)	
<b>SEIFA quintile*</b>				
≤3	12,254 (27.8)	8,302 (26.9)	3,952 (30.0)	<0.001
≥4	31,754 (72.2)	22,559 (73.1)	9,225 (70.0)	
Missing	251 (0.6)	165 (0.5)	86 (0.6)	
<b>Rurality*</b>				
Major Cities of Australia	26,617 (60.4)	18,468 (59.9)	8,149 (61.8)	<0.001
Regional and Remote Australia	17,420 (39.6)	12,385 (40.1)	5,035 (38.2)	
Missing	222 (0.5)	143 (0.5)	79 (0.6)	
<b>Comorbidities</b>				
Hypertension	35,386 (80.0)	23,778 (76.7)	11,608 (87.5)	<0.001
Cardiovascular Disease	17,945 (40.5)	11,688 (37.7)	6,257 (47.2)	<0.001
Atrial fibrillation	7,038 (15.9)	4,893 (15.8)	2,145 (16.2)	0.315
Anxiety	5,658 (12.8)	4,124 (13.3)	1,534 (11.6)	<0.001
Bipolar disorder	505 (1.1)	365 (1.2)	140 (1.1)	0.290
Schizophrenia	363 (0.8)	227 (0.7)	136 (1.0)	0.002
<b>GP Continuity of Care</b>				<0.001
Low (<0.75)	17,421 (39.4)	11,917 (38.5)	5,504 (41.5)	
High (≥0.75)	26,833 (60.6)	19,075 (61.5)	7,758 (58.5)	
Missing	5 (0.0)	1 (0.0)	4 (0.0)	
<b>Documentation of CKD</b>				<0.001
	11,618 (26.3)	7,722 (24.9)	3,896 (29.4)	

ACR, albuminuria-to-creatinine ratio; CKD, chronic kidney disease; SEIFA, socioeconomic indexes for areas; GP, general practitioner. \*Excludes patients without a recorded postcode in the electronic health record.

Table 2. Proportion of patients with CKD receiving monitoring and medications by diabetes status

	Total n=44,259 n (%)	Diabetes		P Value
		No n=30,996 n (%)	Yes n=13,263 n (%)	
<b>Blood Pressure</b>				
Patients with BP Recorded	39,716 (89.7)	27,411 (88.4)	12,305 (92.8)	<0.001
Low Diastolic BP (<70 mmHg)	13,602 (34.2)	8,935 (32.6)	4,667 (37.9)	<0.001
High Systolic BP (>140 mmHg)	13,338 (33.6)	9,108 (33.2)	4,230 (34.4)	0.033
<b>Pathology</b>				
Patients with phosphate test recorded	23,133 (52.3)	16,060 (51.8)	7,073 (53.3)	0.004
Elevated phosphate level (>1.49 mmol/L)	1,322 (5.7)	872 (5.4)	450 (6.4)	0.005
Patients with calcium test recorded	22,818 (51.6)	16,096 (51.9)	6,722 (50.7)	0.017
Elevated calcium level (>2.54 mmol/L)	1,343 (5.9)	893 (5.5)	450 (6.7)	<0.001
Low calcium level (<2.10 mmol/L)	589 (2.6)	409 (2.5)	180 (2.7)	0.584
Patients with Hb test recorded	40,601 (91.7)	28,723 (92.7)	11,878 (89.6)	<0.001
Low Hb level (<7.5 mmol/L)	14,125 (34.8)	9,252 (32.2)	4,873 (41.0)	<0.001
<b>Medication</b>				
<b>Antihypertensives</b>				
All antihypertensives †	32,782 (74.1)	21,893 (70.6)	10,889 (82.1)	<0.001
Diuretic	9,539 (21.6)	5,956 (19.2)	3,583 (27.0)	<0.001
Beta Blocker	10,763 (24.3)	6,862 (22.1)	3,901 (29.4)	<0.001
Calcium Channel Blocker	9,551 (21.6)	6,232 (20.1)	3,319 (25.0)	<0.001
ACEI or ARB	24,485 (55.3)	15,978 (51.5)	8,507 (64.1)	<0.001
Multiple ACEI or ARB	1,859 (4.2)	1,066 (3.4)	793 (6.0)	<0.001
<b>Statin</b>	20,411 (46.1)	12,370 (39.9)	8,041 (60.6)	<0.001
<b>All phosphate binders</b>	244 (0.6)	155 (0.5)	89 (0.7)	0.031
Non-calcium-containing phosphate binders	67 (0.2)	41 (0.1)	26 (0.2)	0.148
Calcium-containing phosphate binders	182 (0.4)	119 (0.4)	63 (0.5)	0.197
<b>Vitamin D</b>	1,444 (3.3)	939 (3.0)	505 (3.8)	<0.001
<b>ESAs</b>	42 (0.1)	24 (0.1)	18 (0.1)	0.098
<b>NSAIDs</b>	7,426 (16.8)	4,862 (15.7)	2,564 (19.3)	<0.001
<b>Metformin</b>	5,189 (11.7)	59* (0.2)	5,130 (38.7)	<0.001
<b>Digoxin</b>	1,516 (3.4)	976 (3.1)	540 (4.1)	<0.001

BP, blood pressure; Hb, haemoglobin; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ESAs, erythropoiesis-stimulating agents; NSAIDs, non-steroidal anti-inflammatory drugs.

† Includes all antihypertensives with anatomical therapeutic chemical (ATC) code C02, C03, C07, C08, C09 or combinations (as in C10BX).

\*Patients with a prescription for metformin who did not have a recorded diagnosis of type 2 diabetes.

Table 3. Number and proportion of patients meeting prescribing quality indicators by rurality, SEIFA and CKD documentation [4].

Quality indicator			Numerator	Denominator	Percentage	P Value
<b>Treatment of hypertension</b>						
1. Percentage of patients aged 18 to 80 years with CKD stages 4-5 and hypertension who are prescribed antihypertensives unless undesirable because of low diastolic blood pressure	Overall*		1,029	1,288	79.9	
	Rurality	Major cities of Australia	532	672	79.2	0.565
		Regional and Remote Australia	490	609	80.5	
	SEIFA quintile	≤3	345	433	79.7	0.947
		≥4	677	848	79.8	
	CoC	High	375	459	81.7	0.228
		Low	654	829	78.9	
	CKD documented	No	380	485	78.4	0.284
		Yes	649	803	80.8	
	Systolic BP	> 140 mmHg	455	573	79.4	0.541
		≤ 140 mmHg	588	728	80.8	
	Age	<65 years	318	437	72.8	<0.001
		≥65 years	711	851	83.5	
	Sex	Female	450	561	80.2	0.800
		Male	579	727	79.6	
2. Percentage of patients aged 18 to 80 years with CKD stages 3-5 and macroalbuminuria treated with multiple antihypertensives who are prescribed a combination of an ACEI or ARB and a diuretic	Overall*		298	1,464	20.4	
	Rurality	Major cities of Australia	174	837	20.8	0.679
		Regional and Remote Australia	123	618	19.9	
	SEIFA quintile	≤3	94	496	19.0	0.315
		≥4	203	958	21.2	
	CoC	High	104	528	19.7	0.639
		Low	194	936	20.7	
	CKD documented	No	148	751	19.7	0.527
		Yes	150	713	21.0	
	Systolic BP	>140 mmHg	143	643	22.2	0.123
		≤ 140 mmHg	150	792	19.0	
	Age	<65 years	74	444	16.7	0.021
		≥65 years	224	1,020	22	
	Sex	Female	102	468	21.8	0.348
		Male	196	996	19.7	
3. Percentage of patients aged 18 to 80 years with CKD	Overall*		337	1,634	20.6	
	Rurality	Major cities of	190	956	19.9	0.270

stages 3-5, microalbuminuria and diabetes treated with multiple antihypertensives who are prescribed a combination of an ACEI or ARB and a diuretic		Australia				
		Regional and Remote Australia	147	664	22.1	
	SEIFA quintile	≤3	110	513	21.4	0.672
		≥4	227	1,106	20.5	
	CoC	High	144	641	22.5	0.140
		Low	193	993	19.4	
	CKD documented	No	216	1,075	20.1	0.462
		Yes	121	556	21.8	
	Systolic BP	>140 mmHg	119	563	21.1	0.667
		≤ 140 mmHg	213	1,053	20.2	
	Age	<65 years	40	228	17.5	0.215
		≥65 years	297	1,406	21.1	
	Sex	Female	149	655	22.7	0.083
		Male	188	979	19.2	
<b>Treatment of albuminuria</b>						
4. Percentage of patients aged 18 to 80 years with CKD stages 3-5 and macroalbuminuria who are prescribed an ACEI or ARB	Overall*		1,084	1,741	62.3	
	Rurality	Major cities of Australia	636	1,016	62.6	0.725
		Regional and Remote Australia	441	714	61.8	
	SEIFA quintile	≤3	353	573	61.6	0.705
		≥4	723	1,156	62.5	
	CoC	High	387	645	60.0	0.135
		Low	697	1,096	63.6	
	CKD documented	No	578	898	64.5	0.046
		Yes	506	845	60.0	
	Age	<65 years	331	590	56.1	<0.001
		≥65 years	753	1,151	65.4	
	Sex	Female	327	544	60.1	0.212
Male		757	1,197	63.2		
5. Percentage of patients aged 18 to 80 years with CKD stages 3-5, microalbuminuria and diabetes who are prescribed an ACEI or ARB	Overall*		1,252	1,790	69.9	
	Rurality	Major cities of Australia	738	1,064	69.4	0.516
		Regional and Remote Australia	502	709	70.8	
	SEIFA quintile	≤3	393	546	72.0	0.207
≥4		846	1,226	69.0		

	CoC	High	502	705	71.2	0.348
		Low	750	1,085	69.1	
	CKD documented	No	841	1,179	71.3	0.075
		Yes	411	611	67.3	
	Age	<65 years	176	259	68	0.450
		≥65 years	1,076	1,531	70.3	
	Sex	Female	496	711	69.8	0.891
		Male	759	1,079	70.1	
<b>Prescription of statins</b>						
6. Percentage of patients aged 50 to 65 years with CKD stages 3-5 who are prescribed a statin	Overall*		1,508	3,693	40.8	
	Rurality	Major cities of Australia	823	2,023	40.7	0.898
		Regional and Remote Australia	669	1,636	40.9	
	SEIFA quintile	≤3	488	1,077	45.3	<0.001
		≥4	1,004	2,581	38.9	
	CoC	High	542	1,292	42.0	0.311
		Low	966	2,401	40.2	
	CKD documented	No	991	2,547	38.9	<0.001
		Yes	517	1,146	45.1	
	Sex	Female	714	1,814	39.4	0.073
Male		794	1,879	42.3		
<b>Treatment of MBD</b>						
7. Percentage of patients aged 18 to 80 years with CKD stages 3-5 and with an elevated phosphate level who are prescribed a phosphate binder			54	815	6.6	
8. Percentage of patients aged 18 to 80 years with CKD stages 3-5 treated with phosphate binders and with an elevated calcium level who are prescribed a non-calcium-containing phosphate binder			5	7	71.4	
9. Percentage of patients aged 18 to 80 years with CKD stages 3-5 treated with phosphate binders and with a low calcium level who are prescribed a calcium-containing phosphate binder			6	12	50.0	
<b>Medication safety</b>						
10. Percentage of patients 18 years or older with CKD stages 3-5 and a prescription of RAS blockers who are prescribed at least two RAS blockers simultaneously	Overall*		1,859	24,485	7.6	
	Rurality	Major cities of Australia	1,175	14,639	8.0	0.002
		Regional and Remote Australia	678	9,732	7.0	
	SEIFA quintile	≤3	587	7,037	8.3	0.005
		≥4	1,264	17,317	7.3	
	CoC	High	727	9,756	7.5	0.499
		Low	1,132	14,729	7.7	

	CKD documented	No	1,339	18,073	7.4	0.069
		Yes	520	6,412	8.1	
	Age	<65 years	182	2,076	8.8	0.035
		≥65 years	1,677	22,409	7.5	
	Sex	Female	1,007	13,466	7.5	0.455
		Male	852	11,019	7.7	
11. Percentage of patients 18 years or older with CKD stages 3-5 and elevated calcium levels who are prescribed active vitamin D			67	1,343	5.0	
12. Percentage of patients 18 years or older with CKD stages 3-5 and Hb ≥7.5 who are prescribed ESA			0	26,476	0.0	
13. Percentage of patients 18 years or older with eGFR<30ml/min/1.73 m <sup>2</sup> who are prescribed a NSAID	Overall*		735	5,146	14.3	
	Rurality	Major cities of Australia	421	3,054	13.8	0.201
		Regional and Remote Australia	312	2,072	15.1	
	SEIFA quintile	≤3	238	1,496	15.9	0.033
		≥4	494	3,627	13.6	
	CoC	High	119	829	14.4	0.810
		Low	159	1,138	14.0	
	CKD documented	No	136	835	16.3	0.018
		Yes	142	1,132	12.5	
	Age	<65 years	68	724	9.4	<0.001
		≥65 years	667	4,422	15.1	
Sex	Female	360	2,648	13.6	0.147	
	Male	375	2,498	15.0		
14. Percentage of patients 18 years or older with eGFR<30 ml/min/1.73 m <sup>2</sup> and diabetes who are prescribed metformin	Overall*		278	1,967	14.1	
	Rurality	Major cities of Australia	149	1,208	12.3	0.005
		Regional and Remote Australia	126	749	16.8	
	SEIFA quintile	≤3	80	608	13.2	0.444
		≥4	195	1,349	14.4	
	CoC	High	119	829	14.4	0.810
		Low	159	1,138	14.0	
	CKD documented	No	136	835	16.3	0.018
		Yes	142	1,132	12.5	
	Age	<65 years	32	244	13.1	0.625
		≥65 years	246	1,723	14.3	
Sex	Female	127	957	13.3	0.285	
	Male	151	1,010	15		
15. Percentage of patients 18 years or	Overall*		995	26,434	3.8	

older with eGFR<50 ml/min/1.73 m <sup>2</sup> who are prescribed digoxin>0.125 mg/day	Rurality	Major cities of Australia	558	16,020	3.5	0.002
		Regional and Remote Australia	433	10,282	4.2	
	SEIFA quintile	≤3	293	7,394	4.0	0.295
		≥4	697	18,893	3.7	
	CoC	High	366	10,623	3.4	0.025
		Low	629	15,807	4.0	
	CKD documented	No	696	17,547	4.0	0.015
		Yes	299	8,887	3.4	
	Age	<65 years	25	2,252	1.1	<0.001
		≥65 years	970	24,182	4.0	
	Sex	Female	596	14,411	4.1	<0.001
		Male	399	12,023	3.3	
	16. Percentage of patients 18 years or older with CKD stages 3-5 and who are prescribed with a combination of NSAID, RAS blocker and diuretic	Overall*		1,160	44,259	2.6
Rurality		Major cities of Australia	663	26,617	2.5	0.032
		Regional and Remote Australia	492	17,420	2.8	
SEIFA quintile		≤3	397	12,254	3.2	<0.001
		≥4	757	31,758	2.4	
CoC		High	452	17,421	2.6	0.777
		Low	708	26,833	2.6	
CKD documented		No	809	32,641	2.5	0.002
		Yes	351	11,618	3.0	
Age		<65 years	86	4373	2.0	0.004
		≥65 years	1,074	39,886	2.7	
Sex		Female	640	24,165	2.6	0.691
		Male	520	20,094	2.6	
<p>BP, blood pressure; CKD, chronic kidney disease; MBD, mineral and bone density; CoC, continuity of care; SEIFA, socioeconomic indexes for areas; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; RAS, renin-angiotensin system; eGFR, estimated glomerular filtration rate; ESAs, erythropoiesis-stimulating agents; NSAIDs, non-steroidal anti-inflammatory drugs. *</p> <p>'Patient SEIFA', 'Patient Rurality', Patient CoC' and 'CKD documented' for the indicator does not add up to 'Overall' due to missing data.</p>						

## Supplementary Files

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