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Suboptimal monitoring and management in patients with unrecorded stage 3 chronic kidney disease in real-world settings: Insights from REVEAL-CKD

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Abstract

Background: Clinical practice guidelines for patients with chronic kidney disease (CKD) recommend regular monitoring and management of kidney function and CKD risk factors. However, the majority of patients with stage 3 CKD lack a diagnosis code, and data on the implementation of these recommendations in the real world are limited.

Aim: To assess the implementation of guideline-directed monitoring and management practices in the real world in patients with stage 3 CKD without a recorded diagnosis code.

Methods: REVEAL-CKD (NCT04847531) is a multinational, observational study of patients with stage 3 CKD. Eligible patients had ≥2 consecutive estimated glomerular filtration rate (eGFR) measurements indicative of stage 3 CKD recorded >90 and ≤730 days apart, lacked an International Classification of Diseases 9/10 diagnosis code corresponding to CKD any time before and up to 6 months after the second eGFR measurement. Testing of key measures of care quality were assessed.

Results: The study included 435,971 patients from 9 countries. In all countries, the prevalence of urinary albumin–creatinine ratio and albuminuria testing was low. Angiotensin-converting enzyme inhibitor, angiotensin receptor blocker and statin prescriptions were highly variable, and sodium–glucose cotransporter-2 inhibitor prescriptions remained below 21%. Blood pressure measurements were recorded in 20.2%–89.9% of patients.

For affiliations refer to page 8.

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Conclusions: Overall, a large proportion of patients with evidence of stage 3 CKD did not receive recommended, guideline-directed monitoring and management. The variability in standard of care among countries demonstrates a clear opportunity to improve monitoring and management of these patients, most likely improving long-term outcomes.

KEYWORDS
chronic kidney disease, clinical guidelines, management, monitoring, real-world

1 | INTRODUCTION

An estimated 11% of the global population had chronic kidney disease (CKD) in 2017.[1] Owing to an aging population and increasing prevalence of risk factors for CKD such as type 2 diabetes (T2D), cardiovascular disease and hypertension, this percentage will likely rise.[2,3]

CKD is progressive and can lead to end-stage kidney disease, necessitating dialysis or kidney transplantation. Further, patients with CKD are at increased risk of cardiovascular complications and death.[4,5] Early diagnosis, monitoring and appropriate management of CKD and its risk factors and complications are crucial to slow CKD progression and reduce disease burden. As such, evidence-based clinical practice guidelines recommend regular monitoring of kidney function in patients with CKD (by measuring both estimated glomerular filtration rate [eGFR] and urinary albumin–creatinine ratio [UACR]).[6,7]

For most patients with CKD, treatment should include an angiotensin-converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB) together with a sodium–glucose cotransporter-2 inhibitor (SGLT-2i). Appropriate monitoring and management of CKD risk factors (T2D, cardiovascular disease and hypertension by monitoring blood pressure [BP]) and potential complications associated with CKD or its treatment (acute kidney injury, acidosis, anaemia, metabolic bone disease and hyperkalaemia) is also recommended.[6,8] This includes monitoring of bicarbonate, potassium, calcium and phosphate in serum. Data on the implementation of monitoring and management guidelines in real-world settings are scarce.

REVEAL-CKD (NCT04847531) is a multinational, observational study designed to assess the prevalence of unrecorded stage 3 CKD in patients with laboratory evidence of the condition, and to gather insights on the monitoring and management of these patients.[9] Although patients with stage 3 CKD tend to be asymptomatic, treatments at this stage are more effective at improving patient outcomes compared with stages 4 and 5.[10] Previously published results from REVEAL-CKD have identified a high prevalence of unrecorded stage 3 CKD in multiple countries.[11] In addition, an analysis of patients from the USA found that, after a CKD diagnosis was recorded, there were improvements in CKD management and monitoring practices and a significant attenuation of eGFR decline.[12] The aim of the study was to evaluate the quality of care of patients with CKD in different countries. Here, we assessed the differences in implementing guideline-directed monitoring and management practices, as well as prescribing recommended medications, in patients with stage 3 CKD from different countries who lack a recorded diagnosis code.

2 | MATERIALS AND METHODS

2.1 | Study design

The study design for REVEAL-CKD has been published in detail elsewhere,[9] and is briefly summarized below.

Data were extracted from relevant secondary databases in the countries of interest between 2015 and 2020 with the exceptions of data from Australia (2015–2022) and Canada (2015–2021; Table S1). Patients (aged 18 years or older) were included in this study if they had at least two consecutive eGFR measurements that fell within the range indicative of stage 3 CKD (30–60 mL/min/1.73 m^2 inclusive) that were recorded >90 and ≤730 days apart (per Kidney Disease: Improving Global Outcomes [KDIGO] guideline recommendations), taken on or after 1 January 2015, and lacked an International Classification of Diseases (ICD) 9/10 diagnosis code corresponding to CKD (any stage) any time before and up to 6 months after the second qualifying eGFR measurement (index date). Patients included in this analysis were required to have ≥12 months of continuous presence in the database post-index and were followed to the database end date (unique to each database) or loss owing to death or disenrolment (Figure S1). Full inclusion and exclusion criteria are shown in Table S2.

eGFR was calculated using the CKD Epidemiology Collaboration equation, using serum creatinine values,

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sex and age.[13] Race modifiers were not used in the calculation of eGFR, in line with current practice among both physicians[14,15] and expert guidance.[16] The ICD coding system varied based on what was available in each database. The full list of ICD-9/10 codes used to determine recorded cases can be found in Table S3. Patient clinical and demographic characteristics at index are presented descriptively.

Patients were followed from 6 months post-index date (analysis start date). The quality of patient monitoring and management was assessed descriptively, based on the number of patients with recorded tests for key measures of care quality during analysis timeframes defined in Table S4. The proportions of patients with recorded tests were calculated based on the total number of qualifying patients included in each country's database, unless stated otherwise. Measurements were made in line with clinical practice protocols for each country.

3 | RESULTS

3.1 | Patient characteristics

Patient characteristics at index from 10 databases across nine countries (Australia, Canada, England, France, Germany, Italy, Japan, Spain and the USA [two databases]) are shown in Table 1. The median age at index ranged from 71 to 80 years, the percentage of males was 36%–52% and the median eGFR at index was 47–54 mL/min/1.73 m^2. The most common recorded comorbidities were hypertension (range 30.3%–85.7%), T2D (17.3%–44.9%), established cardiovascular disease (6.5%–34.2%) and heart failure (3.3%–31.2%). The prevalence of unrecorded CKD ranged from 56.9% to 95.5% (Table S5).

3.2 | Monitoring of kidney function and complications

This analysis included a total of 435,971 (range 959–129,819) patients. The prevalence of UACR testing within 18 months of analysis start date varied substantially among databases, with all countries recording less than 34% of patients (range 1.3%–33.4%; Figure 1, Table S6). In the majority of countries, testing for albuminuria within 18 months of analysis start date was less than 5%. The exception was Australia, where 17.7% of patients had recorded albuminuria results (Table S6). Serum albumin testing was also highly variable among countries (range 1.4%–72.0%). In comparison, measuring of serum creatinine levels was consistently high (range 57.7%–89.4%). Monitoring for acidosis by measuring serum bicarbonate and CKD metabolic bone disease by measuring serum calcium and phosphate was highly variable among databases (bicarbonate range 0.2%–70.4%; calcium range 26.4%–74.9%; phosphate range 9.0%–28.0%). Monitoring patients with CKD and heart failure, and for anaemia by measuring serum potassium and haemoglobin, respectively, was more than 40% across all countries, with some variation (potassium range 41.6%–80.9%; haemoglobin range 52.7%–87.1%; Table S6).

3.3 | Use of medication

The percentage of patients being prescribed an ACEi and/or ARB within 12 months of analysis start date ranged from 12.1% (Australia) to 69.7% (Spain; Figure 1, Table S6). In the subgroup of patients receiving an ACEi and/or ARB prescription, the monitoring of serum creatinine levels within 7–30 days was less than 40% (range 9.5%–39.7%).

The percentage of patients prescribed statins within 12 months of analysis start date was also highly variable (range 9.2%–52.5%). Treatment with SGLT-2is in patients with stage 3 CKD and T2D any time during analysis was low (range 0.1%–20.6%; Figure 1, Table S6).

3.4 | Monitoring and management of BP

The percentage of patients with recorded BP measurements within the first 6 months of analysis start date ranged from 18.6% in Germany to 77.8% in Spain. This variability among countries was also observed when assessing BP monitoring any time during analysis, which ranged from 20.2% in Germany to 89.9% in Australia. More than half of the databases recorded at least 70% of patients with BP monitoring any time during analysis (Figure 1, Table S6).

3.5 | Monitoring and management in patients with stage 3a and stage 3b CKD

In general, the percentage of patients with recorded UACR and serum creatinine testing, statin and ACEi/ARB prescriptions, and BP measurements were similar among patients with stage 3a and stage 3b CKD (Figure S2). In France the percentage of patients with recorded BP measurements was higher in patients with stage 3a CKD than in those with stage 3b CKD, and in Japan the percentage of patients prescribed ACEi/ARB was lower in patients with stage 3a CKD than in those with stage 3b CKD.

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TABLE 1 Patient characteristics at index.

Country	Australia	Canada	England	France	Germany	Italy	Japan	Spain	USA	
Database	Pen CS	CPCSSN	CPRD	THIN Cegedim	Disease Analyzer	LPD	Japan RWD	BIG-PAC	LCED	TriNetX
	N = 1002	*N* = 42,226	*N* = 84,237	*N* = 19,120	*N* = 22,557	*N* = 50,547	*N* = 83,693	*N* = 27,035	*N* = 13,845	*N* = 161,254
≥12 months post-index[a], *n* (%)	959 (95.7)	42,226 (100.0)	74,470 (88.4)	17,373 (90.9)	13,382 (59.3)	49,395 (97.7)	69,745 (83.3)	26,868 (99.4)	11,734 (84.8)	129,819 (80.5)
Age, y, median (IQR)	77 (71–83)	77 (70–84)	76 (69–83)	80 (72–86)	79 (72–84)	80 (74–85)	76 (69–83)	78 (68–86)	74 (64–82)	71 (64–79)
Age groups, y										
<45	6 (0.6)	349 (0.8)	744 (0.9)	58 (0.3)	46 (0.2)	95 (0.2)	652 (0.8)	310 (1.1)	109 (0.8)	2426 (1.5)
45–64	102 (10.2)	5488 (13.0)	11,593 (13.8)	1551 (8.1)	1957 (8.7)	2724 (5.4)	12,260 (14.6)	4992 (18.5)	3754 (27.1)	38,302 (23.8)
65–74	274 (27.3)	11,919 (28.2)	23,575 (28.0)	4421 (23.1)	5088 (22.6)	10,976 (21.7)	23,696 (28.3)	6360 (23.5)	3415 (24.7)	57,891 (35.9)
≥75	620 (61.9)	24,470 (58.0)	48,325 (57.4)	13,090 (68.5)	15,466 (68.6)	36,752 (72.7)	47,085 (56.3)	15,373 (56.9)	6 567 (47.4)	62,635 (38.8)
Male, *n* (%)	429 (42.8)	17,847 (42.3)	40,498 (48.1)	8599 (45.0)	9173 (40.7)	19,820 (39.2)	43,658 (52.2)	13,607 (50.3)	5438 (39.3)	57,989 (36.0)
eGFR, mL/min/1.73 m^2, median (IQR)	52 (46–56)	51 (44–56)	54 (50–58)	52 (46–56)	52 (45–56)	51 (44–55)	53 (47–56)	47 (39–53)	53 (47–57)	53 (47–57)
CKD stage, *n* (%)										
CKD stage 3a	805 (80.3)	31,469 (74.5)	74,365 (88.3)	14,661 (76.7)	16,871 (74.8)	36,460 (72.1)	66,955 (80.0)	15,335 (56.7)	11,348 (82.0)	131,385 (81.5)
CKD stage 3b	197 (19.7)	10,757 (25.5)	9872 (11.7)	4459 (23.3)	5686 (25.2)	14,087 (27.9)	16,738 (20.0)	11,700 (43.3)	2497 (18.0)	29,869 (18.5)
UACR available, *n* (%)	109 (10.9)	22,135 (52.4)	12,809 (15.2)	424 (2.2)	NA[b]	4 (< 0.1)[c]	3851 (4.6)	3909 (14.5)	474 (3.4)	2455 (1.5)
HDL, mmol/L, median (IQR)	1.3 (1.1–1.6)	1.4 (1.2–1.7)	1.4 (1.1–1.7)	1.37 (1.11–1.65)	1.34 (1.11–1.63)	1.32 (1.11–1.59)	1.40 (1.16–1.71)	1.4 (1.0–1.8)	1.24 (1.03–1.53)	1.24 (1.03–1.55)
Missing, *n*	214	5071	26,448	6172	6904	13,379	33,243	2448	5673	88,031
LDL, mmol/L, median (IQR)	2.3 (1.7–3.1)	2.7 (2.0–3.5)	2.6 (1.9–3.4)	2.89 (2.24–3.61)	2.87 (2.20–3.70)	2.74 (2.12–3.39)	2.77 (2.22–3.34)	3.1 (1.9–4.3)	2.46 (1.89–3.13)	2.43 (1.87–3.13)
Missing, *n*	223	5369	37,807	6331	6026	14,915	31,643	2448	4988	78,408
Comorbidities, *n* (%)										
Hypertension	304 (30.3)	29,359 (69.5)	53,631 (63.7)	11,737 (61.4)	10,969 (48.6)	38,849 (76.9)	47,311 (56.5)	17,601 (65.1)	11,863 (85.7)	123,002 (76.3)
Type 2 diabetes	184 (18.4)	11,255 (26.7)[d]	17,989 (21.4)	3311 (17.3)	5145 (22.8)	15,785 (31.2)[e]	15,655 (18.7)	12,134 (44.9)	4667 (33.7)	49,299 (30.6)

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TABLE 1 (Continued)

Country	Australia	Canada	England	France	Germany	Italy	Japan	Spain	USA	
Database	Pen CS	CPCSSN	CPRD	THIN Cegedim	Disease Analyzer	LPD	Japan RWD	BIG-PAC	LCED	TriNetX
Established CVD[f]	107 (10.7)	5125 (12.1)	21,680 (25.7)	1368 (7.2)	1467 (6.5)	5153 (10.2)[g]	23,248 (27.8)	9258 (34.2)	3337 (24.1)	26,666 (16.5)
Heart failure	33 (3.3)	4122 (9.8)	9416 (11.2)	922 (4.8)	3318 (14.7)	4248 (8.4)	26,077 (31.2)	5921 (21.9)	2523 (18.2)	22,422 (13.9)
Medication use, *n* (%)										
ACE inhibitor	22 (2.2)	14,436 (34.1)	27,246 (32.3)	4363 (22.8)	8023 (35.6)	19,141 (37.9)	4027 (4.8)	6941 (25.7)	5058 (36.5)	33,532 (20.8)
ARB	62 (6.2)	10,536 (24.9)	14,032 (16.7)	6181 (32.3)	8855 (39.3)	19,770 (39.1)	18,959 (22.7)	11,218 (41.5)	3605 (26.0)	22,656 (14.0)
SGLT2 inhibitor	9 (0.9)	3150 (7.4)	563 (0.7)	0 (0.0)	0 (0.0)	287 (0.6)	1082 (1.3)	353 (1.3)	11 (0.1)	1171 (0.7)
GLD (any)	50 (5.0)	11,419 (27.0)	13,668 (16.2)	3300 (17.3)	6742 (29.9)	13,108 (25.9)	11,303 (13.5)	12,160 (45.0)	5012 (36.2)	29,690 (18.4)
Anti-platelets	29 (2.9)	11,023 (26.1)	22,532 (26.7)	5636 (29.5)	5451 (24.2)	23,245 (46.0)	16,690 (19.9)	6607 (24.4)	1274 (9.2)	8256 (5.1)
Loop diuretic	45 (4.5)	5593 (13.2)	15,055 (17.9)	2747 (14.4)	8564 (38.0)	15,719 (31.1)	10,346 (12.4)	5353 (19.8)	2720 (19.6)	21,136 (13.1)
Anti-coagulants	31 (3.1)	8573 (20.3)	13,562 (16.1)	2885 (15.1)	6838 (30.3)	12,214 (24.2)	12,886 (15.4)	3994 (14.8)	3434 (24.8)	28,521 (17.7)

Note: Unless otherwise stated, percentages represent the proportion of patients in a specific group (e.g. age) or with a specific variable (e.g. medical history).

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; CKD, chronic kidney disease; CPCSSN, Canadian Primary Care Sentinel Surveillance Network; CPRD, Clinical Practice Research Datalink; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; GLD, glucose-lowering drug; HDL, high-density lipoprotein; ICD, International Classification of Diseases; IQR, interquartile range; LCED, Explorys Linked Claims and Electronic Medical Records Data; LDL, low-density lipoprotein; LPD, Longitudinal Patient Data; NA, not available; RWD, Real-World Data; SGLT2, sodium–glucose cotransporter-2; THIN, The Health Improvement Network; UACR, urinary albumin–creatinine ratio; y, years.

[a]Patients were followed from 6 months post-index date (analysis start date).

[b]UACR testing data not available in the German Disease Analyzer database.

[c]Direct measurements of UACR were not available in the IQVIA Longitudinal Patient Database in Italy, however, UACR was calculated as urine albumin (mg/dL) divided by urine creatinine (g/dL) if patients had records for both of these variables on the same day.

[d]Owing to a lack of granularity in ICD codes in the CPCSSN, it was not possible to determine type of diabetes (type 1 or type 2) for Canada.

[e]Owing to a lack of granularity for ICD-9 diagnostic codes in the database used, type of diabetes could not be determined in patients from Italy.

[f]Established CVD includes patients with a history of myocardial infarction, unstable angina, stroke, transient ischaemic attack, coronary artery bypass graft and percutaneous coronary intervention, identified using ICD-9/10 codes.

[g]Owing to a lack of granularity for ICD-9 diagnostic codes in the database used, established CVD does not include coronary artery bypass graft and percutaneous coronary intervention in patients from Italy.

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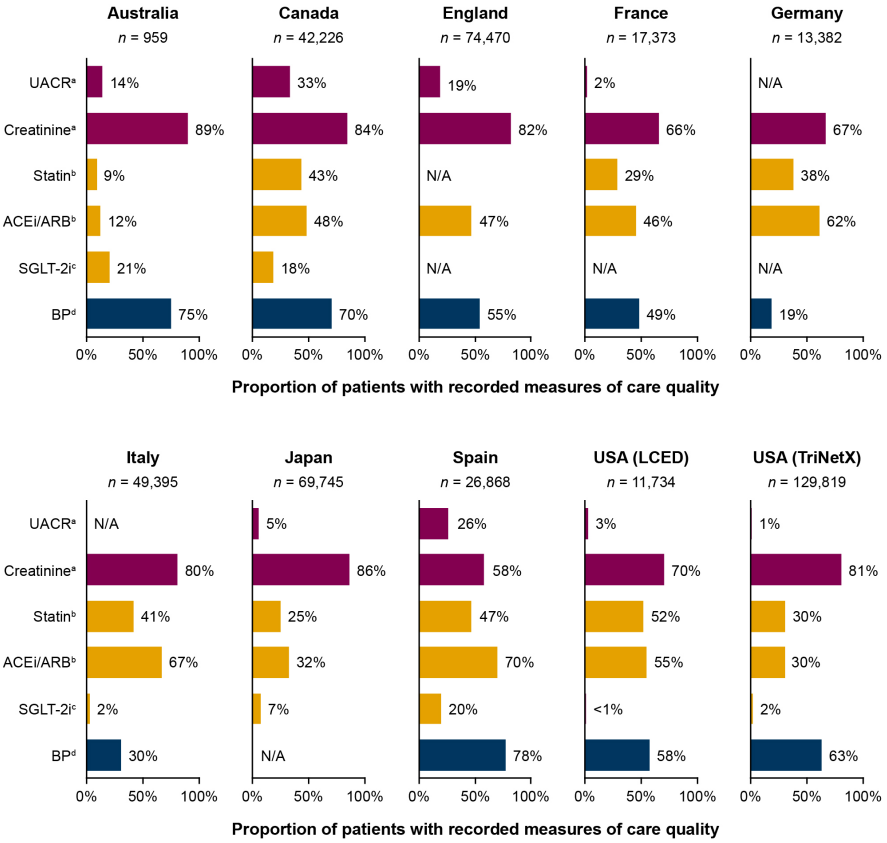


FIGURE 1 Global monitoring of kidney function, treatments, BP and glycaemic control among patients with stage 3 CKD who lacked a recorded CKD diagnosis, by country and database. Patients were followed from 6 months post-index date (analysis start date). Red bars represent monitoring of kidney function monitoring, yellow bars represent the use of medication and blue bars represent monitoring of blood pressure. [a]Within 18 months; [b]Within 12 months; [c]In patients with type 2 diabetes (Italian data include type 1, type 2 and unspecified diabetes owing to a lack of granularity in ICD-9 codes) during analysis, SGLT-2i use was only assessed in patients with type 2 diabetes because this was the only indication during the study period; [d]Within 6 months. ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; BP, blood pressure; ICD, International Classification of Diseases; LCED, Explorys Linked Claims and Electronic Medical Records Data; N/A, not available; SGLT-2i, sodium–glucose cotransporter-2 inhibitor; UACR, urinary albumin–creatinine ratio.

4 | DISCUSSION

REVEAL-CKD is a large, multinational, observational study that uses data extracted from contemporary, country-specific databases to assess the prevalence of unrecorded CKD and subsequent monitoring and management practices. Our results show that there is considerable variability among countries in achieving metrics of quality of CKD care and that, for most patients with stage 3 CKD, testing for albuminuria and prescription of disease-modifying therapy remains suboptimal. While some countries in this analysis performed better than others, all countries should continue to commit to making improvements, particularly during the earlier stages of the course of this disease. Taken together, these findings highlight the need to implement innovative approaches to improve the diagnosis and management of CKD.

The KDIGO guidelines highlight best management practices for patients with CKD to improve patient outcomes and identify the development of complications at an early stage. Both eGFR and UACR measurements are needed to identify all patients at risk of CKD. Testing of UACR is critical for monitoring kidney damage and assessing risk of kidney failure and cardiovascular disease, with implications for whether a patient's current management program could benefit from changes. Strategies such as quick resolution consultations to improve management and extensive CKD training and research activity programs may lead to better monitoring and management.[17,18] In addition, management recommendations for conditions such as T2D, hypertension and heart failure frequently overlap with those for CKD, such as UACR testing and treatment with guideline-recommended medication. Despite this, UACR testing in the present study

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was typically low, with half of the reporting databases having ≤5% of patients with a UACR record, similar to previously published data.[19] These low rates within the first 18 months of analysis start date contrast with the relatively higher rates of serum creatinine monitoring in all countries. A standardized approach whereby serum creatinine testing and UACR testing are performed at the same time as part of routine practice could help to improve rates of UACR testing and in turn improve the early identification of patients with CKD.

In patients with and without T2D, SGLT-2is have been shown to reduce fatal and non-fatal renal and cardiovascular events.[20,21] Treatment of patients with CKD without T2D with an SGLT-2i was first approved in 2021. However, given that the REVEAL-CKD study collected data predominantly from a time period when SGLT-2is were indicated to treat CKD only in patients with T2D (2015–2020; Table S1), we looked at the rate of prescribing of SGLT-2is in this patient population.

Rates of prescribing SGLT-2is were low across all countries, indicating that many patients who could benefit from an SGLT-2i may not be receiving optimal treatment. This may, for instance, be due to healthcare professionals having questions not clearly addressed in the guidelines, or concerns over the cost of SGLT-2is when considering the benefit to the patient. SGLT-2i prescriptions have increased over the years,[22] and will most likely continue to increase as a result of the new guidelines recommending that the first-line treatment for CKD should include an SGLT-2i together with an ACEi or ARB.[7]

In contrast, ACEis and ARBs have been recommended for the treatment of CKD for over a decade. Despite this, the rate of prescribing ACEis/ARBs did not exceed 70% in our study and the variability observed may reflect the indication of ARBs being limited to hypertension in some countries. Similarly, Pantalone et al. assessed the Cleveland Clinic Health System records and found that the percentage of patients with CKD who were prescribed ACEis or ARBs was 42.4% for those with T2D and 27.7% for those without T2D.[19] The authors noted that ACEis or ARBs were more likely to be prescribed to patients with both CKD and T2D compared with patients with CKD alone or T2D alone.[19] Indeed, a recent study found that use of ACEis/ARBs and/or SGLT-2is was higher in patients with both CKD and T2D (43%–73%) compared with those with CKD without T2D (18%–48%).[23] Underdiagnosis of CKD and a lack of knowledge about the benefits of ACEi/ARB and SGLT-2i treatment were suggested as potential reasons for treatment inertia in this population.[23]

Monitoring and managing BP in patients with CKD is recommended by multiple guidelines, including recently published guidelines from the European Society of Hypertension.[24,25] Despite these recommendations, the observed rate of BP recording in some countries in the present study was low. For example, only 19% of patients in Germany and 30% of patients in Italy had a BP record within the first 6 months of analysis start date. These results are surprising given that measuring BP is well ingrained in primary care around the world. It is possible that BP is being measured by physicians but not being diligently recorded in patients' notes, making it impossible to monitor for changes in BP. This finding indicates serious shortcomings in the recording of an important modifiable factor for CKD progression,[26] as well as poor awareness of the importance of BP measurement and recording.

One potential reason for a lack of adherence to KDIGO recommendations is their publication in English. For example, in Spain, multiple scientific societies have collaborated to produce and update a consensus document to establish the joint management and prevention of kidney disease, which was published in both Spanish and English, removing this potential language barrier.[27,28] Another potential reason for the low adherence to recommendations is the "awareness gap" observed with primary care physicians. The Disease Awareness Innovation Network pilot study for primary care physicians demonstrated that CKD identification training and networking with nephrologists improved awareness and increased testing and recognition of CKD in Italy.[29] Together, there are lessons to be learned from different healthcare systems and the initiatives being implemented by various countries to improve monitoring and management of CKD.

4.1 | Strengths and limitations

This study uses 10 large, contemporary, country-specific data sets to provide robust estimates of the extent of monitoring and management received by patients with unrecorded stage 3 CKD. The assessment of monitoring and management was in patients with stage 3 CKD lacking an ICD-9/10 diagnosis code. The databases used in this study may not be generalizable to other countries, which may have different diagnostic coding practices, screening policies and healthcare systems. The TriNetX and Explorys Linked Claims and Electronic Medical Records Data databases contained a high proportion of commercially insured patients, which may introduce bias, although the Explorys Linked Claims and Electronic Medical Records Data database aligns with USA National Health and Nutrition Examination Survey and, therefore, is representative of the US census. Databases may not be able to distinguish individual ACEi or ARB prescriptions when prescribed as part of combination therapies. Therefore, the rates of ACEi and/or ARB prescriptions may be underrepresented. Data availability was limited to whether

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a test result was recorded; data such as individual patient values, methods, dates or dosages were not available.

5 | CONCLUSIONS

This analysis of 10 large, secondary databases from 9 countries found that a large proportion of patients with evidence of stage 3 CKD did not receive recommended, guideline-directed monitoring and management. The results highlight large differences in the standard of care among countries and demonstrate clear opportunities to improve monitoring and management of these patients, particularly UACR testing and prescription of SGLT-2is. By raising awareness among both patients and healthcare professionals of CKD, the importance of these tests, and the link between CKD and associated conditions such as cardiovascular disease and T2D, patients may receive a higher quality of care. International sharing of best practices to stimulate training and CKD awareness could help to promote adherence to guidelines for CKD monitoring and management, most likely improving long-term patient outcomes and reducing the healthcare burden.

AUTHOR CONTRIBUTIONS

NT, CSA, SB, HC, KJ and PK conceived and designed the study. MA and HC performed data analysis. All authors critically reviewed the data and drafts of the manuscript during its development. All authors approved the final manuscript for submission.

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CONFLICT OF INTEREST STATEMENT

NT has received grants from AstraZeneca, Boehringer Ingelheim/Eli Lilly and Company, Janssen Pharmaceuticals, Otsuka Pharmaceutical Co, Ltd and Tricida, Inc, has received honoraria from AstraZeneca, Boehringer Ingelheim/Eli Lilly and Company, Janssen Pharmaceuticals, Otsuka Pharmaceutical Co, Ltd and Tricida, Inc, and holds stock options from Mesentech, Inc, Rénibus Therapeutics, Inc, pulse Data and Tricida, Inc. CSA was part of the contingent workforce of AstraZeneca at the time of the development of this work. MA is an employee of AstraZeneca. SB, HC and KJ are employees of AstraZeneca and hold stock options. AC has received consultancy or speaker fees from AstraZeneca, Boehringer Ingelheim, Eli Lilly and Company, Janssen, Merck Sharp and Dohme, Novo Nordisk and Sanofi. LDN has received fees for scientific consultation and/or lectures from Astellas Pharma Inc, AstraZeneca, Mundipharma

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GmbH and Vifor Pharma Group. NK has received honoraria and travel grants from AstraZeneca, Boehringer Ingelheim, Lilly, Mylan, Napp, Novo Nordisk and Sanofi. KSL is engaged as Chief Medical Advisor to PenCS and has received honoraria from AstraZeneca and Novartis for advisory and speaking engagements. RPF is an employee of Arbor Research Collaborative for Health, which receives global support for the ongoing Dialysis Outcomes and Practice Patterns Study Programs (provided without restriction on publications by a variety of funders; for details see https://www.dopps.org/AboutUs/Support.aspx) and has received research grants from Fresenius Medical Care; consulting fees from AstraZeneca, Akebia, Novo Nordisk and Fresenius; non-financial support from AstraZeneca, Bayer, Boehringer Ingelheim, Novo Nordisk and Akebia outside the submitted work. MCRC has received advisory board fees and honoraria from Alexion, AstraZeneca, Biotest, EMS and Pfizer. RS has received consultancy or speaker fees from AstraZeneca, Boehringer Ingelheim and Vifor Fresenius Medical Care Renal Pharma. MPS has received advisory board fees and honoraria from AstraZeneca, Bayer AG, Vifor Pharma Group and Boehringer Ingelheim/Eli Lilly and Company. PK has received speaker's bureau and advisory board fees from Abbott, AstraZeneca, Boehringer Ingelheim and Eli Lilly and Company and Novo Nordisk A/S; speaker's fees from Bayer AG and Boehringer Ingelheim; and honoraria from AstraZeneca and Eli Lilly and Company. TM and JBV have no conflicts of interest to disclose.

DATA AVAILABILITY STATEMENT

Data used in this study were obtained from a third party and may not be publicly available. Results from the UK were based on data from the Clinical Practice Research Datalink (CPRD) obtained under licence from the UK Medicines and Healthcare products Regulatory Agency (MHRA). The data were provided by patients and collected by the National Health Service (NHS) as part of their care and support. The interpretation and conclusions contained in this study are those of the authors alone. Copyright © (2020), re-used with the permission of NHS Digital. All rights reserved. Protocol reference: 20_000139. Other data underlying the findings described in this manuscript may be obtained in accordance with AstraZeneca's data sharing policy described at https://astrazenecagrouptrials.pharmacm.com/ST/Submission/Disclosure.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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