RESEARCH ARTICLE

Glucose-lowering treatment pathways of individuals with chronic kidney disease and type 2 diabetes according to the Kidney Disease: Improving Global Outcomes 2012 risk classification

Carol Pollock[1] | Juan Jose Garcia Sanchez[2] | Juan-Jesus Carrero[3] | Supriya Kumar[4] |
Roberto Pecoits-Filho[5,6] | Carolyn S. P. Lam[7,8] | Hungta Chen[9] | Eiichiro Kanda[10] |
Mitja Lainscak[11] | David C. Wheeler[12]

[1]Royal North Shore Hospital, Kolling Institute, University of Sydney, St Leonards, New South Wales, Australia

[2]Global Market Access and Pricing, BioPharmaceuticals Medical, AstraZeneca, Cambridge, UK

[3]Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden

[4]Real World Data Science, BioPharmaceuticals Medical, AstraZeneca, Gaithersburg, Maryland, USA

[5]School of Medicine, Pontifical Catholic University of Parana, Curitiba, Brazil

[6]Arbor Research Collaborative for Health, Ann Arbor, Michigan, USA

[7]Department of Cardiology, National Heart Centre Singapore, Singapore City, Singapore

[8]Duke-NUS Medical School, Singapore City, Singapore

[9]Medical and Payer Evidence Statistics, BioPharmaceuticals Medical, AstraZeneca, Gaithersburg, Maryland, USA

[10]Kawasaki Medical School, Kurashiki, Japan

[11]Division of Cardiology, General Hospital Murska Sobota, and Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia

[12]Department of Renal Medicine, University College London, London, UK

Correspondence
David C. Wheeler, Department of Renal Medicine, University College London, London, NW3 2PF, UK.
Email: d.wheeler@ucl.ac.uk

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Abstract

Aims: To describe treatment pathways for key glucose-lowering therapies in individuals with chronic kidney disease (CKD) and type 2 diabetes (T2D) using retrospective data from DISCOVER CKD (NCT04034992).

Methods: Data were extracted from the UK Clinical Practice Research Datalink (CPRD) linked to Hospital Episode Statistics data (2008–2020) and the US integrated Limited Claims and Electronic Health Records Database (LCED; 2012–2019). Eligible individuals were aged ≥18 years with CKD, identified by two consecutive estimated glomerular filtration rate (eGFR) measures (15–<75 mL/min/1.73 m^2; 90–730 days apart; index date was the second measurement) and T2D. Chronological treatment pathways for glucose-lowering therapies prescribed on or after CKD index to end of follow-up were computed. Median time and proportion of overall follow-up time on treatment were described for

each therapy by database and by eGFR and urinary albumin-to-creatinine ratio (UACR) categories.

Results: Of 36,951 and 4339 eligible individuals in the CPRD and LCED, respectively, median baseline eGFR was 67.8 and 64.9 mL/min/1.73 m^2; 64.2 and 63.9% received metformin prior to index; and median (interquartile range) time on metformin during follow-up was 917 (390–1671) and 454 (192–850) days (accounting for ~75% of follow-up time in both databases). The frequency of combination treatment increased over time. There were trends towards decreased metformin prescriptions with decreasing eGFR and increasing UACR within each eGFR category.

Conclusions: Individuals with CKD and T2D had many combinations of therapies and substantial follow-up time on therapy. These results highlight opportunities for improved CKD management.

KEYWORDS

database, diabetes mellitus, type 2, electronic health records, glomerular filtration rate, metformin, renal insufficiency, chronic, retrospective studies

1 | INTRODUCTION

Type 2 diabetes (T2D) is a leading cause of chronic kidney disease (CKD) worldwide and a frequent co-morbidity in individuals with CKD of non-diabetic aetiologies.[1,2] Individuals with CKD are at increased risk of adverse cardiovascular and renal outcomes, and mortality,[3,4] and the risk of these outcomes is further increased in those individuals with CKD and T2D.[4–6] The combination of CKD and T2D is also associated with reduced health-related quality of life and significant healthcare resource utilisation and costs.[7,8]

Optimal management of individuals with CKD and T2D is multifaceted, aiming to attain glycaemic control as well as reduce the risks of CKD progression and cardiovascular disease/mortality.[9] Renin–angiotensin–aldosterone system inhibitors are the mainstay of treatment to delay or prevent CKD progression[10]; however, more recent data from randomised trials and observational studies have suggested benefits of sodium–glucose co-transporter-2 inhibitors (SGLT2i) and finerenone (a non-steroidal mineralocorticoid receptor antagonist) in improving a range of kidney and cardiovascular outcomes in individuals with CKD.[11,12] In addition, glucagon-like peptide-1 (GLP-1) receptor antagonists have been reported to improve kidney outcomes compared with placebo, mainly driven by a reduction in albuminuria.[13,14]

Current guideline recommendations for the treatment of individuals with CKD and T2D differ. The Kidney Disease: Improving Global Outcomes (KDIGO) group recommends metformin and SGLT2i as first-line therapy

What's new?

- Treatment of chronic kidney disease (CKD) and type 2 diabetes (T2D) aims to achieve glycaemic control and reduce the risks of CKD progression and cardiovascular disease/mortality.
- This analysis assessed recent trends in treatment of CKD and T2D using real-world UK and US data.
- Individuals with CKD and T2D had a high therapy burden, including use of combination therapies and substantial follow-up time on therapy.
- These findings highlight opportunities for improved management of this high-risk population; future studies are warranted to assess the impact of new therapies and updated clinical practice guidelines on treatment patterns.

for all individuals with CKD and T2D who have an eGFR ≥30 mL/min/1.73 m^2.[9] Additional agents, including GLP-1 receptor agonists, are recommended as required to achieve glycaemic control, with consideration of individual factors and preference.[9] The American Diabetes Association (ADA) also advocates for initial use of metformin in individuals with CKD and T2D, with the addition of SGLT2i recommended for those with eGFR ≥25 mL/min/1.73 m^2 or urinary albumin-to-creatinine ratio (UACR) ≥300 mg/g for cardiovascular risk reduction. In individuals who are

at increased risk of cardiovascular events or CKD progression, or who are unable to use an SGLT2i, a non-steroidal mineralocorticoid receptor antagonist (finerenone) is recommended; GLP-1 receptor antagonists may also be considered for cardiovascular and potentially CKD risk reduction.[15]

Assessments of real-world treatment patterns in individuals with CKD and T2D are important to inform knowledge of disease burden and to ascertain whether optimal disease management strategies are being implemented in clinical practice. DISCOVER CKD (clinicaltrials.gov identifier: NCT04034992) is a hybrid, multinational, observational cohort study of individuals with CKD.[16] The study aims to provide contemporary real-world insights to inform clinical practice and improve understanding of the epidemiology, and clinical and economic burden of CKD.[16–18] The aim of this analysis was to describe the treatment pathways for key glucose-lowering therapies in individuals with CKD and T2D, using data from two databases within the DISCOVER CKD retrospective cohort.

2 | METHODS

2.1 | Study population

This analysis used a subset of data from the DISCOVER CKD retrospective cohort.[16] Data were extracted from the UK Clinical Practice Research Datalink (CPRD; [Information Sharing and Analysis Centre protocol number: 19_226A4] primary care data)[19] linked to Hospital Episode Statistics data between 2008 and 2020, and the US integrated Limited Claims and Electronic Health Records Database (LCED; primary and secondary care data) between 2012 and 2019.

Adults (aged ≥18 years) with non–dialysis-dependent CKD, identified by two consecutive eGFR measures of 15–<75 mL/min/1.73 m^2 recorded ≥90 days apart (maximum 730 days) on or after January 2008 (UK) or January 2012 (US), were eligible for inclusion. Eligible individuals were required to have ≥1 UACR measurement within 1 year before or any time up to 5 years after the index date (date of second eGFR measurement) and were categorised by the UACR measure closest to index. Individuals were also required to have T2D at index, identified by either a diagnostic code and/or a prescription for a glucose-lowering therapy (including, but not limited to, SGLT2i, dipeptidyl peptidase 4 inhibitors [DPP4i], insulin and metformin). Exclusion criteria included death within 30 days of index (where available in the data source), history of type 1 diabetes, or a history of kidney transplant or renal replacement therapy at index.

The analysis protocol followed the principles of the Declaration of Helsinki. Data were collected in compliance with the Health Insurance Portability and Accountability Act, the Data Protection Act, independent review board and ethics committees and participating data custodian's policies as appropriate. No individual's identifiable information was shared outside of the protective firewalls of participating data custodians without prior informed consent; within the firewalls, only approved persons had access to anonymised individual-level data.

2.2 | Analysis variables, outcomes and analysis

The observation period for this analysis spanned the individuals' full registration period until the first occurrence of either death, loss to follow-up, database end or end of data collection. Baseline characteristics assessed included demographics and laboratory parameters determined using the most recent measurement within 12 months before index. Co-morbidities, determined any time before index, were also assessed.

Sankey plots were used to visualise chronological treatment pathways for key glucose-lowering therapies (SGLT2i, DPP4i, insulin, metformin, and other glucose-lowering therapies [including sulfonylureas, thiazolidinediones, alpha-glucosidase inhibitors and GLP-1 receptor agonists]) prescribed on or after CKD index to end of follow-up in the UK CPRD and US LCED. Treatments that were initiated prior to CKD but that overlapped with the CKD index date were also included. Treatments with a duration of ≤6 days were excluded from analyses, and days from partially overlapping treatment durations were brought forward and added to the subsequent prescription. Median time and proportion of overall follow-up time on treatment were described for each key glucose-lowering therapy by database and per KDIGO category (according to eGFR and UACR) and included any time receiving treatment (even if not continuous). This was a descriptive analysis and no hypotheses were tested. Categorical data are presented as numbers and percentages; mean (standard deviation) values and median (interquartile range [IQR]) values are reported, as appropriate.

3 | RESULTS

3.1 | Attrition

Among all eligible individuals, 347,216 of 425,246 (81.7%) in the CPRD and 181,604 of 224,100 (81.0%) in the LCED had two measurements of eGFR 15–<75 mL/min/1.73 m^2

(Figure 1). Among those individuals with two eGFR measurements, 102,133 of 347,216 (29.4%) and 9041 of 181,604 (4.5%) individuals in the CPRD and LCED, respectively, met the UACR inclusion criteria. After applying additional inclusion criteria, including the presence of T2D at index, 36,951 and 4339 individuals in the CPRD and LCED, respectively were included in the present analysis. An overview of excluded individuals without T2D at index is given in Supplementary Table 1.

3.2 | Baseline characteristics

Overall, 43.0% and 49.5% of individuals in the CPRD and LCED, respectively, were female, with median (IQR) ages of 68 (62–75) and 64 (59–73) years in the CPRD and LCED, respectively (Table 1). Median (IQR) body mass index was 30.4 (27.0–34.6) and 32.0 (28.3–37.4) kg/m^2 in the CPRD and LCED, respectively. Individuals in the CPRD had a notably lower prevalence of hypertension (63.9% vs. 89.7%), heart failure (5.9% vs. 9.7%) and stroke (5.6% vs. 16.8%) compared with individuals in the LCED. Retinopathy was more frequent in individuals in the CPRD compared with the LCED (25.1% vs. 11.4%). Individuals in

the CPRD and LCED had similar median baseline eGFR (67.8 and 64.9 mL/min/1.73 m^2, respectively), UACR (10.6 and 9.0 mg/g, respectively) and glycated haemoglobin (52 mmol/mol [6.9%] and 50 mmol/mol [6.7%], respectively). Metformin was prescribed to 64.2% and 63.9% of individuals in the CPRD and LCED, respectively, at baseline. Insulin, DDP4i and GLP-1 agonists were prescribed more frequently in the LCED (20.7%, 15.4%, 7.1%, respectively) than in the CPRD (12.0%, 8.7%, 3.4%, respectively), at baseline. Median (IQR) follow-up times were 1483 (734–2400) days in the CPRD and 1184 (692–1672) days in the LCED.

3.3 | T2D treatment pathways

In both the CPRD and LCED, metformin (either as a monotherapy or in combination with other glucose-lowering therapies) was the most frequently prescribed T2D treatment both prior to and after CKD index (Figure 2). In both databases, the proportion of individuals prescribed combination therapy regimens, as well as the number of different regimens, increased with progression from first-line therapy to subsequent therapies following CKD index.
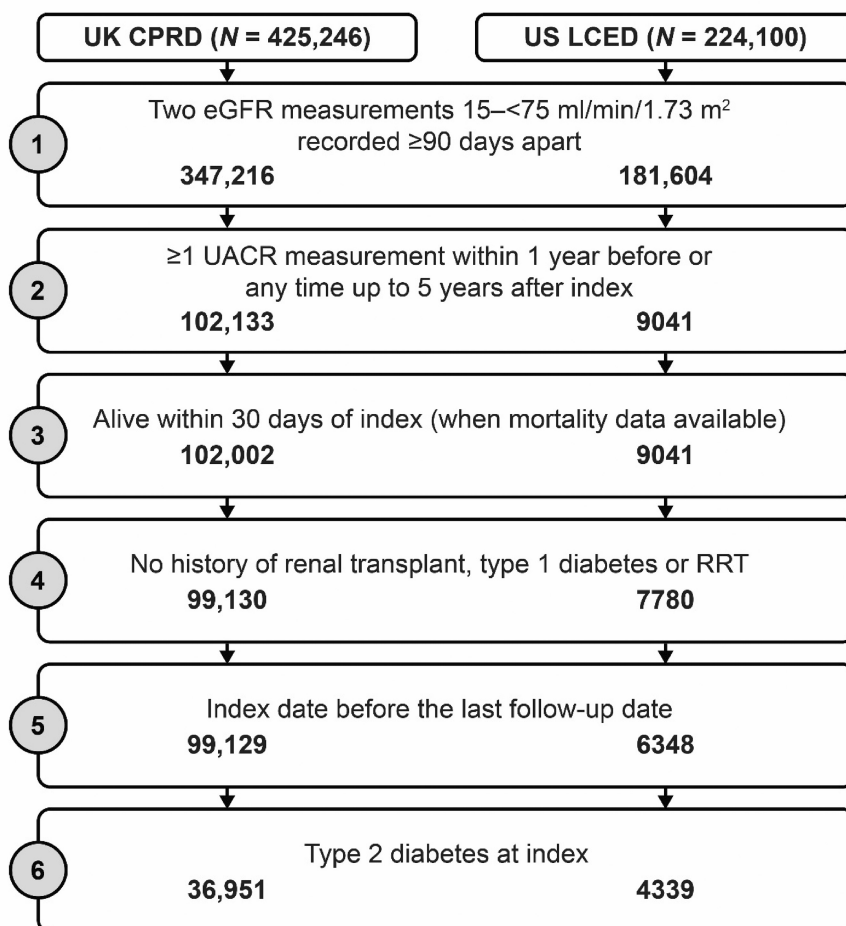

FIGURE 1 Attrition. CPRD, Clinical Practice Research Datalink; eGFR, estimated glomerular filtration rate; LCED, Limited Claims and Electronic Health Records Database; RRT, renal replacement therapy; UACR, urinary albumin-to-creatinine ratio.

TABLE 1 Baseline characteristics.

	UK CPRD $N = 36{,}951$	US LCED $N = 4339$
Demographic		
Age (years), median (IQR)	68 (62–75)	64 (59–73)
Female (%)	43.0	49.5
BMI (kg/m^2), median (IQR)[a]	30.4 (27.0–34.6)	32.0 (28.3–37.4)
eGFR (ml/min/1.73 m^2), median (IQR)	67.8 (60.9–71.8)	64.9 (56.2–70.5)
eGFR category, n (%)		
15–<30	319 (0.9)	75 (1.7)
30–<45	1479 (4.0)	328 (7.6)
45–<60	6664 (18.0)	1092 (25.2)
60–<75	28,489 (77.1)	2844 (65.5)
UACR (mg/g), median (IQR)[a]	10.6 (5.1–28.3)	9.0 (4.0–25.1)
UACR category, n (%)		
<30	27,601 (74.7)	3251 (74.9)
30–<300	7728 (20.9)	836 (19.3)
≥300	1622 (4.4)	252 (5.8)
Co-morbidities (%)		
Hypertension	63.9	89.7
Heart failure	5.9	9.7
Myocardial infarction	8.6	6.5
Stroke	5.6	16.8
Retinopathy	25.1	11.4
Laboratory parameters, median (IQR)		
HbA1c (mmol/mol)[a]	52 (45–62)	50 (44–59)
HbA1c (%)[a]	6.9 (6.3–7.8)	6.7 (6.2–7.5)
Medications (%)		
Metformin	64.2	63.9
Insulin	12.0	20.7
DPP4i	8.7	15.4
GLP-1 agonist	3.4	7.1
Median (IQR) follow-up time, days	1483 (734–2400)	1184 (692–1672)

Abbreviations: BMI, body mass index; CPRD, Clinical Practice Research Datalink; DPP4i, dipeptidyl peptidase 4 inhibitor; eGFR, estimated glomerular filtration rate; GLP-1, glucagon-like peptide-1; HbA1c, glycated haemoglobin; IQR, interquartile range; LCED, Limited Claims and Electronic Health Records Database; UACR, urinary albumin-to-creatinine ratio.

[a]Proportion of missing data (%) for BMI, UACR, and HbA1c was 14.6, 30.0, and 4.0, respectively, in the UK CPRD, and 45.4, 34.5, and 23.1, respectively, in the US LCED.

3.4 | Time on treatment for key glucose-lowering therapies

Time on treatment varied substantially between the different therapies assessed (Table 2; Supplementary Table 2).

In both the CPRD and LCED, individuals spent the longest time on metformin compared with other therapies. In the CPRD, the median (IQR) time on metformin during follow-up (for prescriptions dispensed before and after CKD index) was 917 (390–1671) days, accounting for a median of 75% of total follow-up time. In the LCED, the median (IQR) time on metformin was 456 (193–850) days, accounting for a median of 76% of total follow-up time. The least time was spent on SGLT2i (CPRD: 361 [125–732] days, 26% of follow-up time; LCED: 292 [141–541] days, 42% of follow-up time).

3.5 | Time on treatment for key glucose-lowering therapies according to eGFR and UACR levels

Time on therapy and percentage of follow-up time on therapy stratified by baseline KDIGO category are shown in Figures 3 and 4, Supplementary Figures 1 and 2, and Supplementary Tables 3 and 4. Numbers of individuals by KDIGO category and database are shown in Supplementary Table 5. There was a trend towards decreased median time on metformin with decreasing eGFR and increasing UACR within each eGFR category; in the CPRD, median time on therapy decreased from 964.0 days in individuals with eGFR 60–<75 mL/min/1.73 m^2 and UACR 0–<30 mg/g to 80.5 days in those with eGFR 15–<30 mL/min/1.73 m^2 and UACR ≥300 mg/g. In the LCED, the corresponding decrease was from 496.0 to 23.0 days (Figure 3). The proportion of follow-up time accounted for by metformin prescriptions also declined as eGFR decreased and UACR increased (CPRD: from 76% in individuals with eGFR 60–<75 mL/min/1.73 m^2 and UACR 0–<30 mg/g to 14% in those with eGFR 15–<30 mL/min/1.73 m^2 and UACR ≥300 mg/g; LCED: from 79% in individuals with eGFR 60–<75 mL/min/1.73 m^2 and UACR 0–<30 mg/g to 2% in those with eGFR 15–<30 mL/min/1.73 m^2 and UACR ≥300 mg/g) (Figure 4). No notable trends were seen with other glucose-lowering therapies, including SGLT2i; however, there was a slight trend towards lower median time on other glucose-lowering therapies with increasing UACR in the CPRD (Supplementary Figure 1).

Numbers of individuals decreased as eGFR increased regardless of therapy, database or UACR category (Supplementary Table 5). SGLT2i use was especially low among those with eGFR 15–<30 or 30–<45 mL/min/1.73 m^2.

4 | DISCUSSION

This analysis assessed treatment pathways for common glucose-lowering therapies using real-world data from
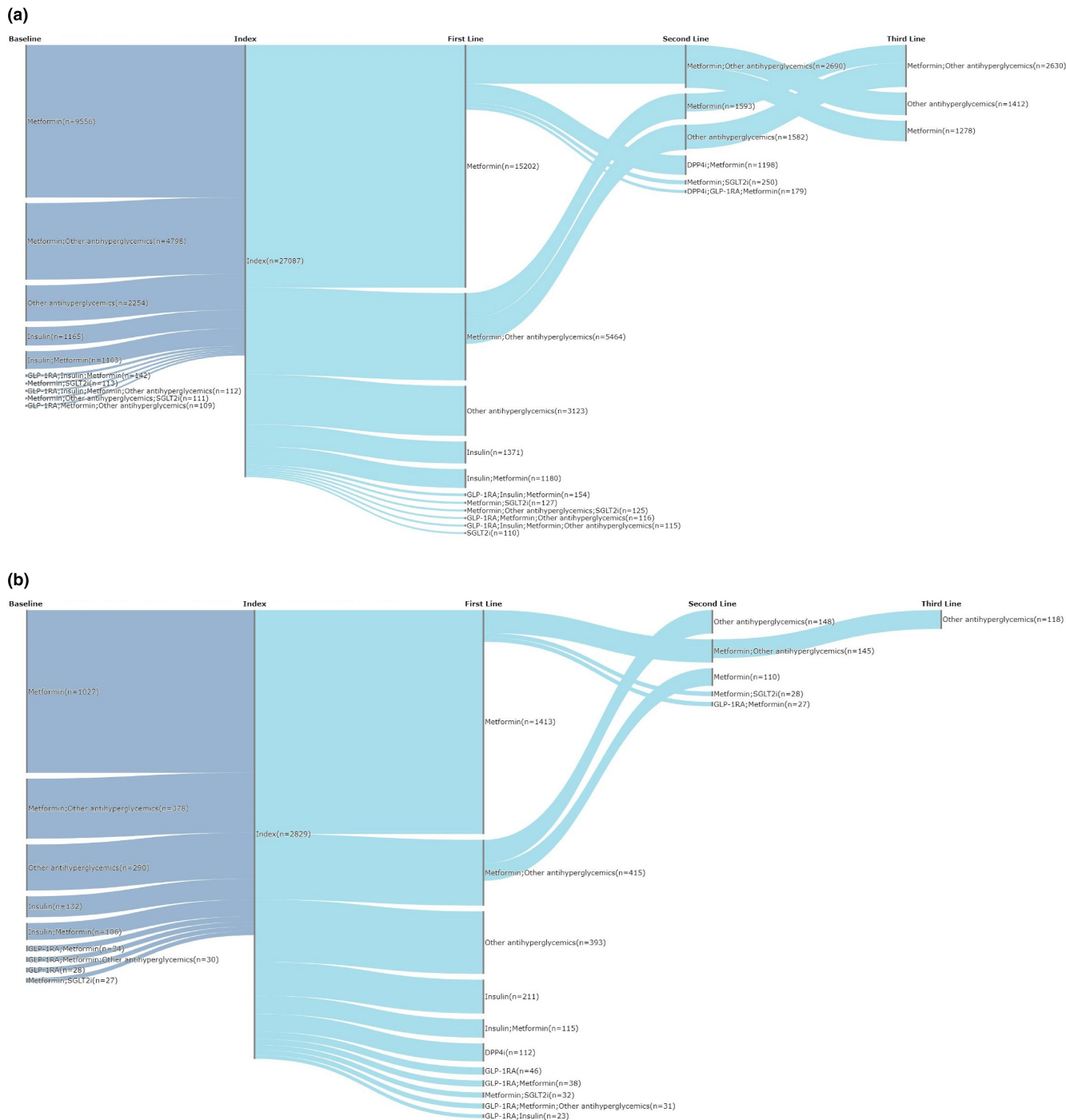
FIGURE 2 Treatment pathways for glucose-lowering therapies in (a) CPRD and (b) LCED. (a) Includes any treatment pathway with >1000 individuals, or > 50 individuals if the treatment pathway contains GLP-1RA or SGLT2i, in the CPRD. (b) Includes any treatment pathway with >100 individuals, or >30 individuals if the treatment pathway contains GLP-1RA or SGLT2i, in the LCED. Other anti-hyperglycaemics include sulfonylureas, thiazolidinediones, alpha-glucosidase inhibitors, and GLP-1RA. CPRD, Clinical Practice Research Datalink; DPP4i, dipeptidyl peptidase 4 inhibitor; GLP-1RA, glucagon-like peptide-1 receptor agonist; LCED, Limited Claims and Electronic Health Records Database; SGLT2i, sodium–glucose co-transporter-2 inhibitor.

individuals with CKD and T2D between 2008 and 2020 in the UK and between 2012 and 2019 in the US. Most individuals were receiving glucose-lowering therapy prior to CKD index, reflecting the significant proportion of individuals with T2D who subsequently develop CKD.[20]

Baseline levels of glycated haemoglobin in both databases were within range of the target level for adults with diabetes.[9] This may be a result of non-diabetic aetiologies of CKD, rigorous treatments (reflecting the wide use of combination regimens) or other unknown factors.

TABLE 2 Median time on therapy for key glucose-lowering therapies.

Database	Metformin		Insulin		SGLT2i	
	CPRD	**LCED**	**CPRD**	**LCED**	**CPRD**	**LCED**
Therapy prior to CKD index						
N	18,273	1926	3328	445	601	108
Therapy at any time during follow-up						
N	27,494	2727	7242	881	3395	345
Median (IQR) time on therapy (days)	917 (390–1671)	456 (193–850)	738 (278–1463)	394 (158–830)	361 (125–732)	292 (141–541)
Median (IQR) % follow-up time, days	75 (47–94)	76 (44–93)	63 (27–91)	59 (30–85)	26 (9–59)	42 (16–77)

Abbreviations: CKD, chronic kidney disease; CPRD, Clinical Practice Research Datalink; IQR, interquartile range; LCED, Limited Claims and Electronic Health Records Database; SGLT2i, sodium–glucose co-transporter-2 inhibitor.

Consistent with international treatment guideline recommendations (both current and at the time of data collection),[9,15,21,22] the most frequently prescribed therapy in the UK CPRD and US LCED (both prior to and after CKD index) was metformin, either as a monotherapy or in combination with other glucose-lowering therapies. The median time on metformin during follow-up, which included any time receiving treatment (even if not continuous), was twice as long for individuals in the CPRD than those in the LCED. This may be partially attributed to the longer follow-up of individuals in the CPRD (median time 1483 days) versus those in the LCED (median time 1184 days). Following the first therapy after CKD index, there was significant diversity in the choice of second therapies. This may reflect the variety of available treatment options and the need for treatment intensification as T2D progresses.[9,21–23]

Overall, individuals in the analytic cohort had a high therapy burden, reflected by the wide use of combination therapy regimens by many individuals and substantial follow-up time on therapy. This finding demonstrates the complexities associated with managing individuals with CKD and T2D, including the need to consider eGFR level and the potential for hypoglycaemia or other side effects.[2,9] Optimising treatment regimens, including the timely use of glucose-lowering therapies that confer cardiorenal protection independent of glycaemic control, may improve outcomes in these individuals and minimise medication burden.

When individuals were stratified by eGFR and UACR levels according to the KDIGO 2012 classification, there were trends towards decreased metformin prescription with declining eGFR, as seen previously,[24] but no obvious changes in prescription of other therapies, such as insulin. These findings are in accordance with clinical guidelines that recommend against metformin prescription when eGFR declines to <30 mL/min/1.73 m^2, owing to concerns of increased risk of complications such as lactic acidosis.[9,15] By contrast, there are no restrictions on insulin use in individuals with renal impairment—doses can be uptitrated to achieve glycaemic goals[20,25]—and some individuals in the analytic cohort may have had late-stage T2D and required insulin due to beta-cell failure. However, it is important to note the disadvantages associated with insulin use in individuals with impaired renal function, including increased risk of hypoglycaemia, which is associated with morbidity and mortality.[26] Insulin use is also associated with significant burden in terms of administration, side effects and cost, and does not confer the documented benefits seen across various cardiovascular and kidney outcomes with some oral medications, such as SGLT2i, finerenone and GLP-1 receptor antagonists.[15,27–30]

Data from recent clinical studies have suggested potential benefits of SGLT2i on kidney outcomes in individuals with CKD,[11,12] and current ADA guidelines recommend the use of SGLT2i in those with eGFR ≥25 mL/min/1.73 m^2 or UACR ≥300 mg/g.[15] Our data did not reveal any notable trends in SGLT2i prescriptions according to UACR level, but this may reflect the infrequent prescription of SGLT2i in the analysis period and the timeframe of our dataset, most of which was prior to the completion of clinical trials evaluating SGLT2i in CKD and the recommendation for these agents as part of first-line therapy regimens in individuals with CKD and T2D.[15] Our findings, therefore, serve as a baseline from which the uptake of new therapies with demonstrated renoprotective and cardioprotective effects can be assessed in the next few years. Similarly, although recent KDIGO guidelines recommend the preferential use of GLP-1 receptor antagonists as additional drug therapy following first-line therapy, this was not evident in our findings. Notably, use of GLP-1 receptor antagonists was low and could not be assessed as a separate drug category; this is again likely attributable to the analysis period, where many individuals had initiated treatment prior to publication of the guidelines.
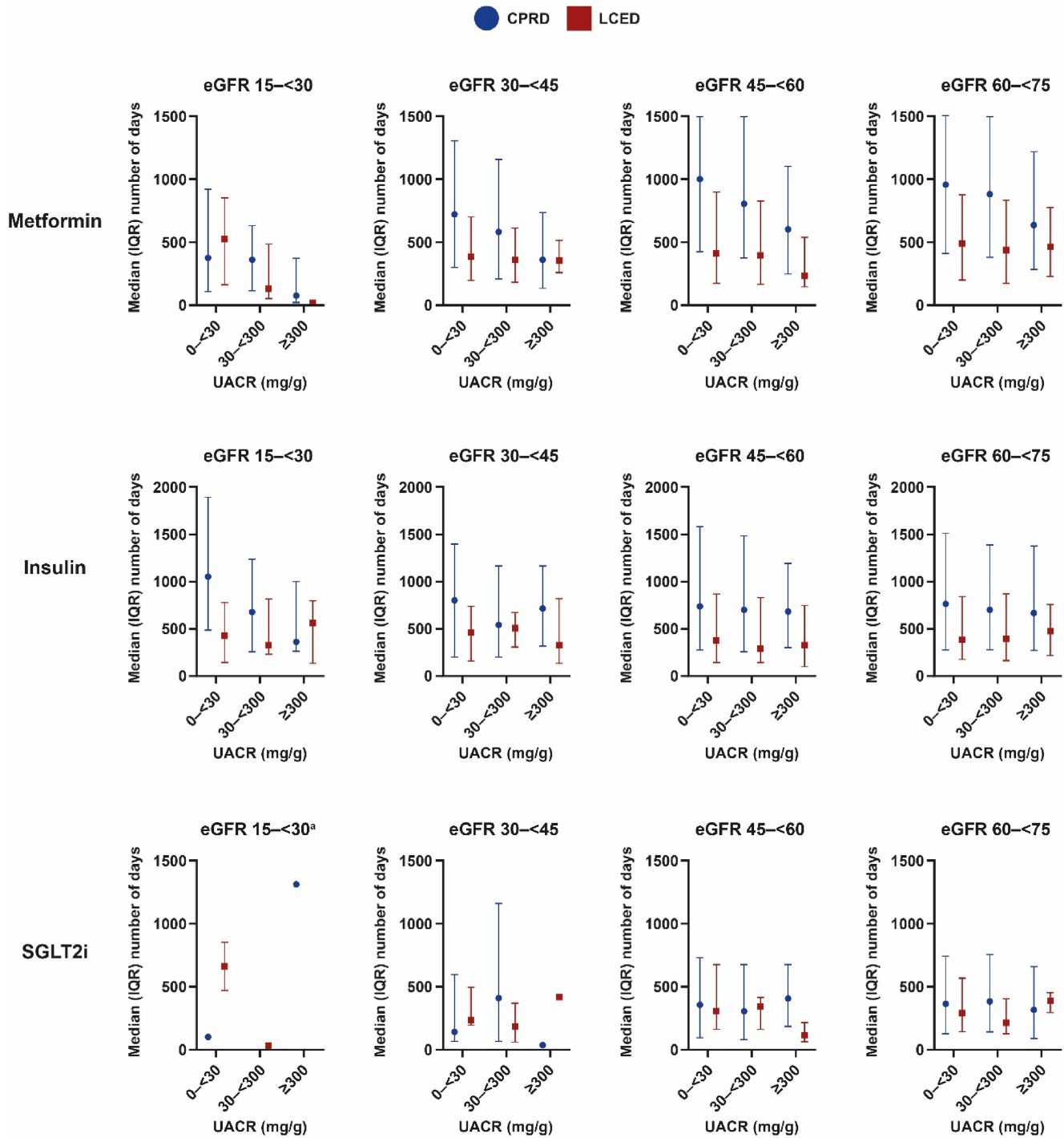
FIGURE 3 Median time on key glucose-lowering therapies, according to KDIGO category. [a]Data not available in this group for the UACR 30–<300 (CPRD) and ≥300 (LCED) mg/g categories. CPRD, Clinical Practice Research Datalink; eGFR, estimated glomerular filtration rate; IQR, interquartile range; KDIGO, Kidney Disease: Improving Global Outcomes; LCED, Limited Claims and Electronic Health Records Database; SGLT2i, sodium–glucose co-transporter-2 inhibitor; UACR, urinary albumin-to-creatinine ratio.

To the best of our knowledge, this is the first longitudinal analysis assessing treatment pathways in individuals with CKD and T2D. Additional strengths of the present analysis include the large cohort size, inclusion of data from both the UK and US, and the longitudinal assessment of treatment pathways. Limitations include those inherent to retrospective data, including the potential for coding errors in the source databases as the data were not collected for research purposes. Additionally, prescriptions were not fully captured and there was no way of verifying whether individuals were taking their prescribed medications. There was potential for underestimation of
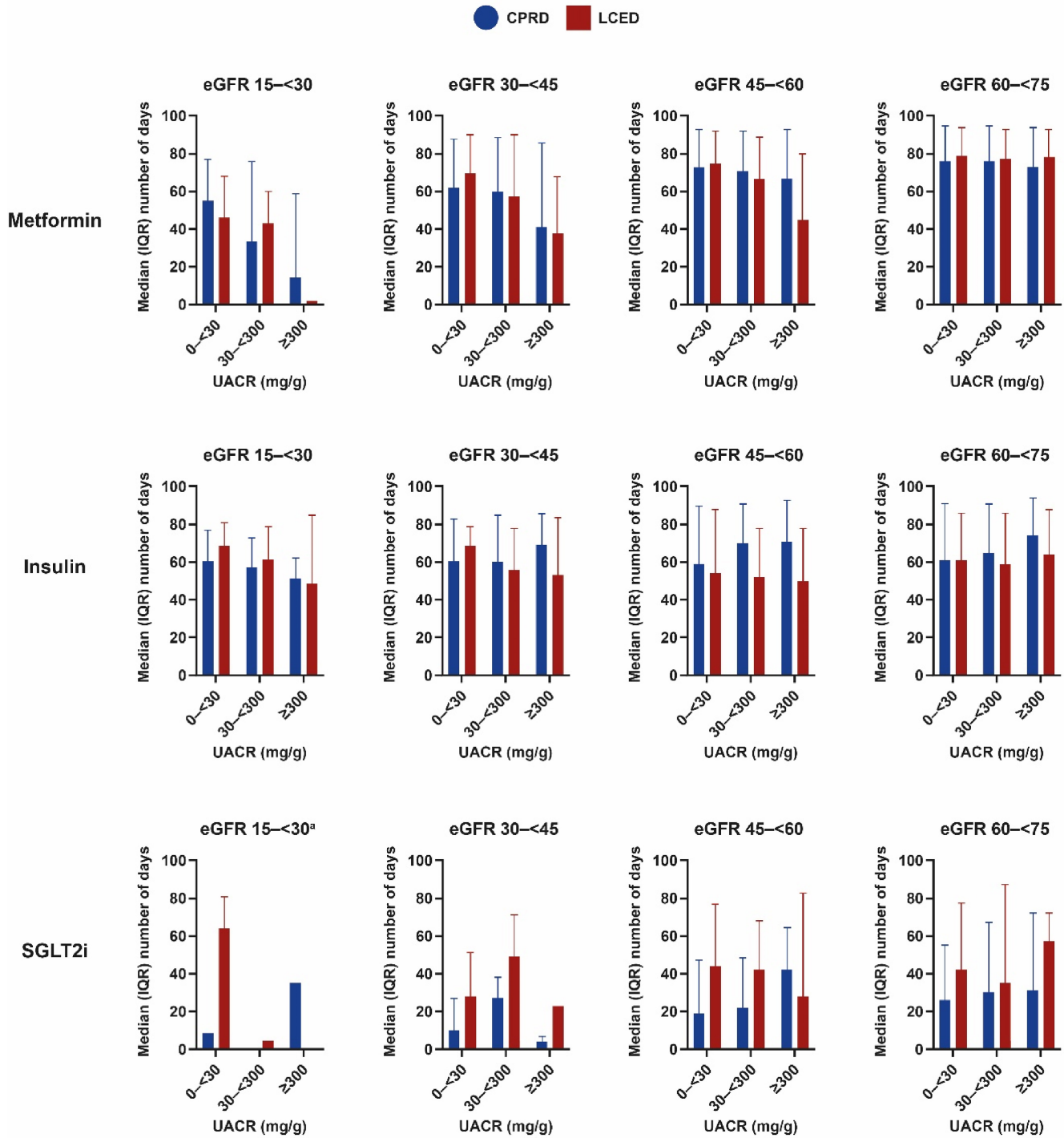
FIGURE 4 Percentage of follow-up time on therapy by KDIGO category. Data are median percentage (IQR). Percentages were calculated by dividing the total treated time on therapy in follow-up by the total follow-up time. [a]Data not available in this group for the UACR 30–<300 (CPRD) and ≥300 (LCED) mg/g categories. CPRD, Clinical Practice Research Datalink; eGFR, estimated glomerular filtration rate; IQR, interquartile range; KDIGO, Kidney Disease: Improving Global Outcomes; LCED, Limited Claims and Electronic Health Records Database; SGLT2i, sodium–glucose co-transporter-2 inhibitor; UACR, urinary albumin-to-creatinine ratio.

metformin prescription in cases where individuals were taking fixed-dose drug combinations (e.g. dapagliflozin and metformin), and time-on-treatment analyses assessed single therapies only, whereas individuals might have been receiving combination therapies. Additionally, it is likely

that the duration of treatment and proportion of individuals on metformin were significantly underestimated in the LCED. Owing to its low cost and lack of reimbursement incentive, many individuals obtain metformin without health insurance coverage in the US, meaning that not all

prescriptions will have been documented. Moreover, low prescription numbers for some therapies, including GLP-1 receptor agonists, meant that these therapies could not be analysed separately.

A considerable proportion of the initial study population did not have an available UACR measurement recorded. Use of this as a selection criterion therefore restricted the size of the final study population and may have biased selection of individuals towards those with severe CKD who are likely to receive more frequent monitoring than lower-risk individuals. To mitigate against the extensive exclusion of individuals without UACR measurements at baseline, we included those with ≥1 UACR measurement within 1 year before or any time up to 5 years after the index date; however, this may have led to immortal time bias in our results.

Notably, not all individuals had a diagnostic code for CKD; therefore, eGFR measures were used to infer the presence of CKD. Similarly, prescription data were sometimes used to infer the presence of T2D. In addition, doses and dose changes of glucose-lowering therapies were not assessed as part of the analysis and the reasons for therapy changes were unknown. The CPRD comprises primary care data only, while the US LCED comprises data from both primary and secondary care settings. Baseline characteristics and treatment needs are therefore likely to vary between the two databases, precluding any direct comparisons in this descriptive analysis, although future investigations into the variations that exist between the datasets might be of interest. Finally, the findings of this analysis of data from the UK and US are not necessarily generalisable to other countries.

5 | CONCLUSIONS

In this analysis of contemporary real-world data from the UK and US, individuals with CKD and T2D had a high therapy burden, including the use of combination therapy regimens and substantial follow-up time on therapy. There were trends towards decreased metformin prescriptions with decreasing eGFR and with increasing UACR. These findings highlight opportunities for improved management of this high-risk population with future studies warranted to assess the impact of new therapies and updated clinical practice guidelines on treatment patterns in this setting.

AUTHOR CONTRIBUTIONS
Study design: Juan Jose Garcia Sanchez, Supriya Kumar, Hungta Chen. Data collection: Supriya Kumar. Data analysis: Supriya Kumar. Data interpretation: All authors. Drafting and reviewing the manuscript: All authors.

CONFLICT OF INTEREST STATEMENT
Juan Jose Garcia Sanchez, Supriya Kumar and Hungta Chen are employees of, and hold or may hold stock in, AstraZeneca. Juan-Jesus Carrero reports institutional grants from Astellas, AstraZeneca and Vifor Pharma; speaker fees from AstraZeneca, Abbott and Nutricia; and consultancy for AstraZeneca and Bayer. Roberto Pecoits-Filho 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/About Us/Support.aspx). He also reports research grants from Fresenius Medical Care, non-financial support from Akebia, AstraZeneca, Bayer, Boehringer, Novo Nordisk and FibroGen; as well as personal fees from Travere Therapeutics and consulting fees from George Clinical, outside the submitted work. Carolyn S.P. Lam is supported by a Clinician Scientist Award from the National Medical Research Council of Singapore; has received research support from AstraZeneca, Bayer, Boston Scientific, Medtronic, Roche Diagnostics and Vifor Pharma; has served as a consultant or on the advisory board/steering committee/executive committee for Abbott Diagnostics, Amgen, Applied Therapeutics, AstraZeneca, Bayer, Biofourmis, Boehringer Ingelheim, Boston Scientific, Corvia Medical, Cytokinetics, Darma Inc., Eko.ai Pte Ltd., Jana Care, Janssen Research & Development LLC, Medtronic, Menarini Group, Merck, MyoKardia, Novartis, Novo Nordisk, Radcliffe Group Ltd., Roche Diagnostics, Sanofi, Stealth BioTherapeutics, The Corpus, Vifor Pharma and WebMD Global LLC; and serves as co-founder and non-executive director of Us2.ai Pte Ltd. Eiichiro Kanda is a consultant for AstraZeneca. Mitja Lainscak is supported by the Slovenian Research Agency; has received research support from Roche Diagnostics; has served as a consultant or on the advisory board/steering committee for AstraZeneca, Boehringer Ingelheim, Novartis and Vifor Pharma; and has received personal fees from

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DATA AVAILABILITY STATEMENT

ORCID

David C. Wheeler https://orcid.org/0000-0003-0745-3478

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SUPPORTING INFORMATION

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