Original Research

Prevalence of Chronic Kidney Disease in Type 2 Diabetes: The Canadian REgistry of Chronic Kidney Disease in Diabetes Outcomes (CREDO) Study

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ABSTRACT

Purpose: Chronic kidney disease (CKD) in patients with type 2 diabetes (T2D) is associated with an elevated risk of end-stage kidney disease, cardiovascular disease (CVD), and death. As the breadth of treatment options for CKD in patients with T2D (CKD in T2D) continues to expand, an analysis of the current use of therapies and cardiovascular and kidney outcomes is necessary. The objectives of the study were to assess the prevalence of CKD in T2D among a contemporary cohort of patients, to describe patient characteristics and treatment patterns, and to examine health care practitioner rationale for initiating therapies.

Methods: The study was a retrospective, observational study (module A) with a prospective component (module B). For module A, sociodemographic data, medical history, prescription information, and laboratory investigations for patients seen by an endocrinologist in 2019 were retrieved from the LMC Diabetes Registry. Module B included a subset of patients for health care practitioner surveys to understand rationale for administering angiotensin-converting enzyme inhibitors (ACEis) or angiotensin receptor blockers (ARBs), steroidal mineralocorticoid receptor antagonists (MRAs), sodium-glucose cotransporter 2 inhibitors (SGLT2is), and glucagon-like peptide 1 receptor agonists (GLP-1RAs). Descriptive analyses were conducted.

Findings: The study included 14,873 patients (59% male). Mean patient age was 67 years, mean body mass index was 31 kg/m^2, and mean glycosylated hemoglobin was 7.6%. Mean diabetes duration was 16 years. The prevalence of CKD in patients with T2D was 47.9%. Common comorbidities were hypertension (76%), dyslipidemia (71%), and obesity (51%). CVD was reported in 22%. The proportion of kidney medications and emerging therapies varied, with 76% of patients using an ACEi or ARB, 48% using an SGLT2i, 30% using a GLP-1RA, and 3% using a steroidal MRA. In module B, physicians identified that ACEis/ARBs, SGLT2is, GLP-1RAs, or steroidal MRAs were administered to primarily treat CKD in 33%, 12%, 0%, and 4% of the patients (n = 500), respectively.

Implications: These findings improved our understanding of the current landscape and treatment patterns of CKD inT2D and highlighted the importance of considering treatments that will provide a comprehensive strategy for cardiovascular and kidney risk protection. Despite the high prevalence of CKD and comorbidities reported in a large, Canadian T2D specialist population, ACEis/ARBs, SGLT2is, and GLP-1RAs were underused, especially considering recent clinical trial reports. The relative use of steroidal MRAs was expectedly low. With an immense burden of CKD progression and among patients with T2D, the use of treatments that provide a comprehensive strategy for kidney protection will transform the landscape of CKD in T2D. ClinicalTrials.gov identifier: NCT04445181. (*Clin Ther.* 2021;43:1558–1572.) © 2021 The Authors. Published by Elsevier Inc.

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INTRODUCTION

Diabetes remains the predominant risk factor for the development of chronic kidney disease (CKD) and is the leading cause of end-stage kidney disease (ESKD) worldwide.[1–3] CKD is also associated with an increased risk of cardiovascular events, hospitalization for heart failure, and premature death.[4–7] CKD progression contributes to high health care costs and significant morbidity, especially among patients with ESKD requiring kidney replacement therapy. Consequently, the use of effective therapy when managing patients with multiple medical conditions aimed at glycemic control, kidney protection, and cardiovascular risk reduction is critical to reduce the burden and significant incremental health care costs of CKD in patients with type 2 diabetes (CKD in T2D).

Clinical practice guideline recommendations for CKD in T2D have, for many years, encouraged the use of angiotensin-converting enzyme inhibitors (ACEis) or angiotensin receptor blockers (ARBs).[8–10] Antagonism of the renin-angiotensin-aldosterone system with either an ACEi or ARB to reduce kidney disease events in people with albuminuria, hypertension, and T2D has been well established.[11–14] Recently, metformin and sodium-glucose cotransporter 2 inhibitor (SGLT2i) therapies were also included in the 2020 Kidney Disease: Improving Global Outcomes Diabetes Management in CKD Guideline recommendations for patients with T2D and CKD and an estimated glomerular filtration rate (eGFR) $\geq$30 mL/min/1.73m^2.[8] After a prolonged hiatus since the landmark trials for ACEi/ARB use were published 20 years ago,[11,14] as well as some unsuccessful trials,[15,16] there are finally a few promising potential therapies available or on the horizon for the management of CKD in T2D, including SGLT2is, glucagon-like peptide-1 receptor agonists (GLP-1RAs), and the nonsteroidal mineralocorticoid receptor antagonist (MRA), finerenone.

Recent clinical trials have shown promising results that support the use of GLP-1RAs,[17–20] SGLT2is,[21–26] and finerenone[27–29] as emerging kidney therapies for the management of CKD in T2D. Both GLP-1RAs and SGLT2is demonstrated a reduced risk of CKD progression[17–23,25,26] as well as major adverse cardiovascular events.[19,21,22,24–26,30–33] The data on current steroidal MRAs, such as spironolactone and eplerenone, for CKD in T2D, which are not currently indicated for treating CKD in T2D, have not yet demonstrated a clear kidney benefit in a dedicated outcome trial. Steroidal MRAs are currently used for primarily treating resistant hypertension,[34,35] primary aldosteronism,[36] or advanced heart failure[37]; however, they remain underused because of the potential adverse effects of gynecomastia, reduced libido, and hyperkalemia.[38] Finerenone, a new, nonsteroidal, and selective MRA, is of recent clinical interest. The Finerenone in Reducing Kidney Failure and Disease Progression in Diabetic Kidney Disease (FIDELIO-DKD) trial found that finerenone resulted in lower risks of CKD progression and cardiovascular events among patients with T2D and advanced CKD and had a acceptable adverse effect profile.[27,28] The recently completed Finerenone in Reducing Cardiovascular Mortality and Morbidity in Diabetic Kidney Disease (FIGARO-DKD) trial provides insight into the efficacy and tolerability of finerenone among patients with T2D and less advanced CKD.[29] Finerenone is not yet approved for use in Canada but may provide an additional therapeutic option in the future.

Because the treatment of CKD in T2D has evolved during the past few years, an up-to-date analysis of the burden of disease, distribution of therapies, and cardiovascular, kidney, and diabetes-related complications among patients is necessary. Thus, the primary objective of this study is to assess the prevalence of CKD in T2D and describe the therapies used in a cohort of patients from an endocrinology-led Canadian registry. Although Canada has nationally endorsed clinical practice guidelines in CKD care, many of the recommended therapies for CKD in T2D have multiple indications, and health care practitioner (HCP) rationale for prescribing therapies for CKD in patients with T2D is not well described. Therefore, understanding HCP rationale and satisfaction with currently available therapies for CKD in T2D was a secondary objective of the study.

PARTICIPANTS AND METHODS

This study was a retrospective, observational study (module A) with a prospective survey component (module B). For module A, data were retrieved from the LMC Diabetes Registry which holds the electronic medical records of >42,000 patients with diabetes in Canada's largest single-speciality group of 13 endocrinology clinics in Ontario, Quebec, and Alberta. Patients who were seen by an endocrinologist between January 2019 and December 2019 were included and followed up until June 30, 2020, to capture and allow the consideration of emerging therapies that may have been recently prescribed. The patients received care based on current Diabetes Canada clinical practice guidelines[39] within Canada's publicly funded health care system from approximately 100 endocrinologists, physician assistants, and certified diabetes educators. The registry provided medical history and sociodemographic, medication, and laboratory data. A detailed description of this registry has been previously reported.[40–42]

An independent ethics committee approved the protocol, and all patients included in the cohort provided consent for their medical data to be used for research purposes. Informed consent was obtained from HCPs for module B to collect survey responses. The study was conducted in accordance with the ethics principles of the Declaration of Helsinki and registered on ClinicalTrials.gov (NCT04445181).

Module A

T2D and comorbidities were reported if indicated in the patient's medical problem history in the LMC Diabetes Registry. The comorbidities reported were hypertension, dyslipidemia, microvascular disease (retinopathy and neuropathy), and macrovascular disease, including cerebrovascular accident and cardiovascular disease (CVD). CVD was defined as including ≥1 of the following conditions in the patient's electronic medical record: angina, congestive heart failure, cardiovascular disease, coronary artery disease, coronary vascular disease, coronary angioplasty, coronary artery bypass grafting, percutaneous coronary intervention, and/or myocardial infarction.

CKD stage was based on the most recent laboratory results for eGFR and albuminuria (urine albumin-to-creatinine ratio [uACR]) within 18 months before the index date (July 1, 2020): eGFR ≥90 mL/min/1.73 m^2 and uACR ≥2 mg/mmol (stage 1), eGFR 60 to 89 mL/min/1.73 m^2 and uACR ≥2 mg/mmol (stage 2), eGFR 45 to 59 mL/min/1.73 m^2 (stage 3a), eGFR 30 to 44 mL/min/1.73 m^2 (stage 3b), eGFR 15 to 29 mL/min/1.73 m^2 (stage 4), and eGFR <15 mL/min/1.73 m^2 (stage 5). eGFR was calculated using the CKD-EPI (CKD Epidemiology Collaboration) equation. Albuminuria (uACR) was retrieved from laboratory results. Individuals with missing values for uACR were assumed to not have albuminuria when categorized by CKD stage.

Sociodemographic variables retrieved from the LMC Diabetes Registry were age, sex, diabetes duration, ethnicity, educational level, household income, health coverage, and smoking status. Additional anthropometric and laboratory measurements collected within 18 months of the index date included weight, body mass index (BMI), blood pressure, glycated hemoglobin (HbA_{1c}), and lipid panel (LDL-C, triglycerides, HDL-C, and non–HDL-C).

Medications were categorized into the following treatment classes: ACEi/ARB, steroidal MRA, SGLT2i, GLP-1RA, sulfonylurea, biguanide (metformin), and dipeptidyl peptidase-4 inhibitor (DPP-4i). Use of at least 1 antihyperglycemic agent (AHA) was defined as at least 1 active prescription identified at the study index date for a sulfonylurea, biguanide (metformin), DPP-4i, SGLT2i, or GLP-1RA therapy. Data on the use of insulin; other cardiovascular medications, including antiplatelet agents, anticoagulants, β-blockers, calcium channel blockers, fibrates, and bile acid sequestrants; and weight loss therapies were also retrieved.

Module B

Module B followed a prospective, cross-sectional study design. A subset of 500 patients with CKD and T2D were randomly selected for the HCP surveys. The patient's endocrinologist was asked questions about rationale and satisfaction with the treatment classes of interest (ACEI/ARB, steroidal MRA, SGLT2i, and/or GLP-1RA therapy), which were prescribed for the selected patients with CKD and T2D. The patients were grouped by their total number of AHAs plus ACEi/ARB and/or steroidal MRA and randomly selected for module B using R statistical software, version 3.5.3 (R Foundation for Statistical Computing, Vienna, Austria)[43] with the dplyr package[44] to target a subgroup of patients with a similar proportion of AHA, ACEi/ARB, and steroidal MRA use as in module A. HCPs completed the survey responses for all the

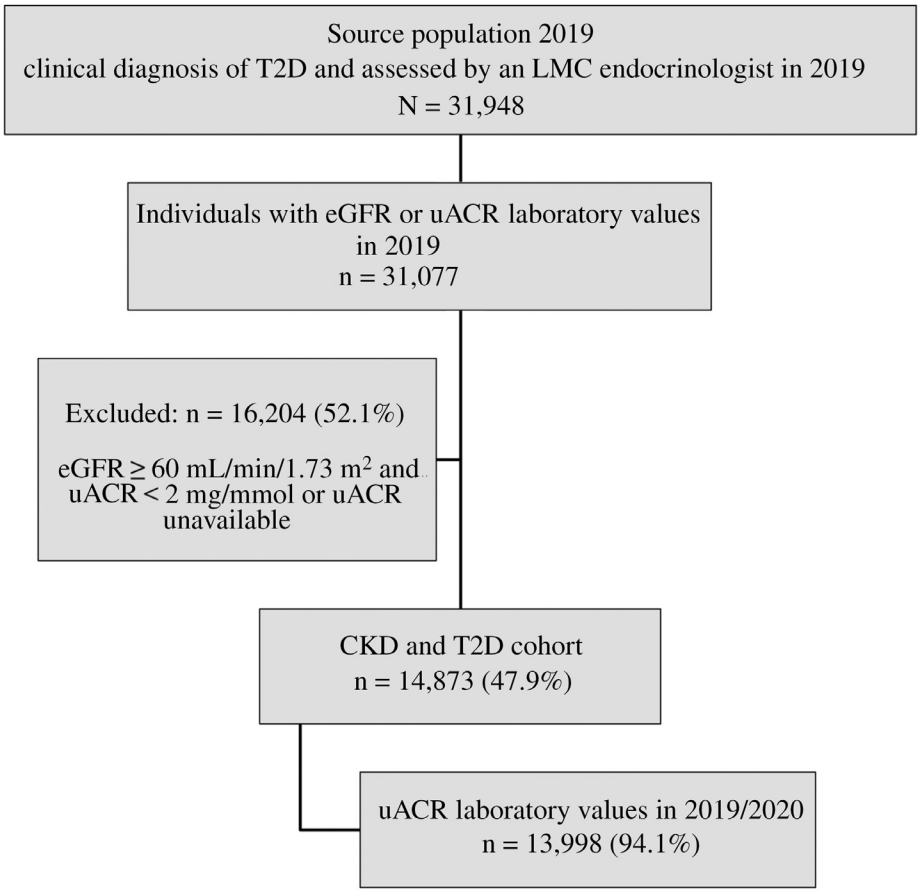

Figure 1. Flowchart of patient disposition of the final cohort of patients with chronic kidney disease (CKD) and type 2 diabetes (T2D). eGFR = estimated glomerular filtration rate; LMC = LMC Diabetes & Endocrinology; uACR = urine albumin-to-creatinine ratio.

medications of interest, if >1 of the 4 treatment classes were prescribed for the selected patient.

Statistical Analysis

The descriptive statistical analyses were performed using R software, version 3.5.3.[43] Sociodemographic data and clinical variables were summarized as number (percentage), mean (SD), or median (interquartile range). All data were inspected for outliers and potential data entry errors. The analysis population included people with evaluable data, and missing data were not replaced. Data were presented in the full cohort and by CKD stage for module A and in a subset of 500 patients for module B. Exploratory analyses for module A included describing history of cardiovascular events and CKD progression within 3 years before the index date.

RESULTS

Module A

The overall prevalence of CKD in patients with T2D was 47.9%. Among 31,077 patients with active T2D in the Canadian diabetes registry who were assessed by an endocrinologist in 2019, with eGFR and uACR measured within 18 months before July 1, 2020, 14,873 patients had an eGFR <60 mL/min/1.73 m^2 and/or a uACR ≥2 mg/mmol, forming the final cohort with CKD and T2D. A flowchart of the patient disposition is presented in Figure 1. The proportion of individuals in each CKD stage and albuminuria

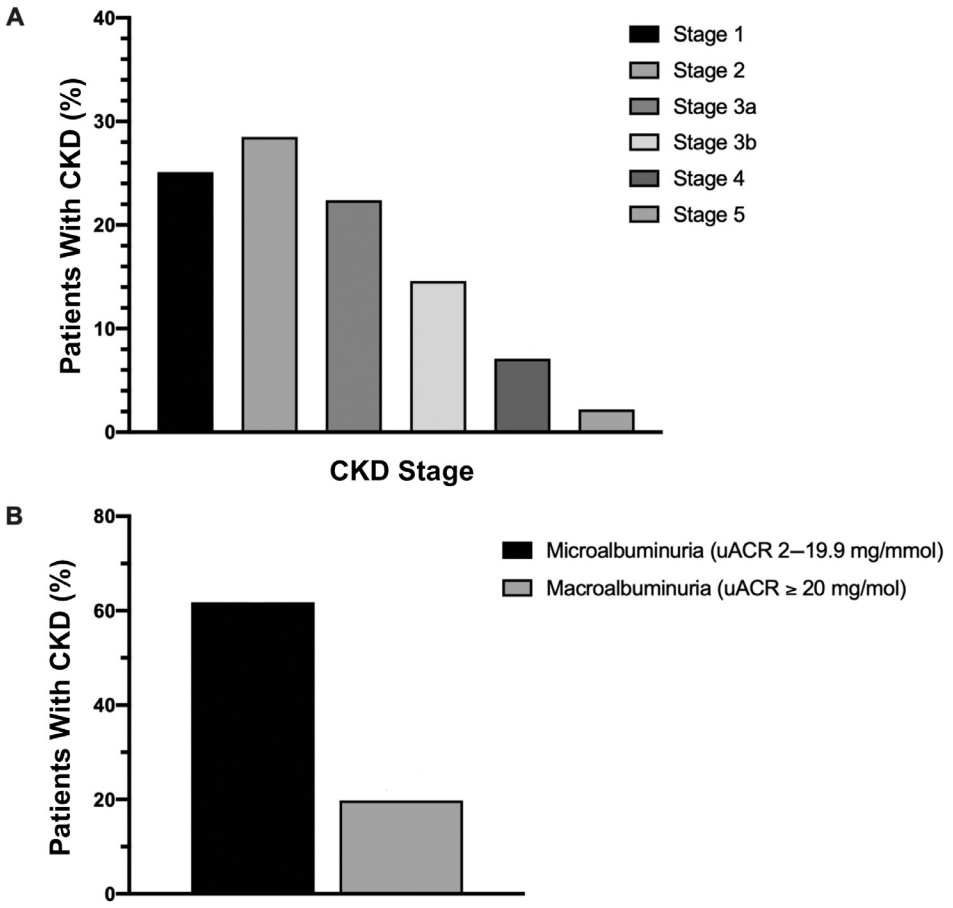

Figure 2. (A) Chronic kidney disease (CKD) stage and (B) albuminuria as a proportion of patients with CKD and type 2 diabetes in the cohort. uACR = urine albumin-to-creatinine ratio.

group are reported in Figure 2. A small proportion of individuals (n = 875) in the final cohort did not have uACR measured in 2019 or 2020 and were assumed to not have albuminuria.

The cohort with CKD and T2D was 59% male, with a mean age of 67 years, a BMI of 31 kg/m^2, an HbA_{1c} level of 7.1%, and a diabetes duration of 16 years. Sociodemographic and clinical data are summarized in Table I. The most common comorbidities were hypertension (76.1%) and dyslipidemia (71.3%). There was also a high prevalence of obesity (approximately 51%), and 58.7% of patients were treated with an AHA associated with weight loss (SGLT2i and/or GLP-1RA). Less than 1% of the patients were using an active weight loss medication indicated primarily for the treatment of obesity (liraglutide >1.8 mg, naltrexone hydrochloride/buproprion hydrochloride, or orlistat) and/or had a history of bariatric surgery. CVD was reported in 21.7% of the population, and 2.9% had experienced a cerebrovascular accident. Additional microvascular complications were found in 10.1% and 9.6% of individuals for neuropathy and retinopathy, respectively.

ACEis and ARBs were the most widely used agent among the cohort (75.8%), with 39.1% of patients using an ACEi and 36.7% of patients using an ARB, whereas steroidal MRAs were used by the smallest proportion (3.0%) of patients. SGLT2i and GLP-1RA therapies were used by 47.6% and 29.6% of the group, respectively. Use of guideline-recommended and emerging kidney medications by treatment class and CKD stage are reported in Figure 3. The proportion

Table I. Population characteristics.

Characteristic	All* (N = 14,873)	Missing, No. (%)
Age, mean (SD), y	66.9 (12.5)	0 (0.0)
Male sex	8809 (59.2)	0 (0.0)
Diabetes duration, mean (SD), y	15.9 (9.8)	52 (0.4)
Race/ethnicity		0 (0.0)
Black	1160 (7.8)	
East/Southeast Asian	1234 (8.3)	
Indigenous	81 (0.5)	
Latino	216 (1.5)	
South Asian	2353 (15.8)	
White	7064 (47.5)	
Other (Middle Eastern, Pacific Islander)	366 (2.5)	
Not specified	2399 (16.1)	
Educational level		0 (0.0)
Secondary school	3978 (26.7)	
College	2093 (14.1)	
University	3815 (25.7)	
Not specified/declined response	4987 (33.5)	
Additional health coverage		1782 (12.0)
Private	4419 (33.8)	
Public	7524 (57.5)	
No benefit	1148 (8.8)	
Smoking status		1221 (8.2)
Nonsmoker	8569 (62.8)	
Ex-smoker	3733 (27.3)	
Current smoker	1350 (9.9)	
Clinical data		
eGFR, mean (SD), mL/min/1.73 m^2	67.0 (28.0)	23 (0.2)
uACR, median (interquartile range), mg/mmol	5.1 (2.6,15.5)	882 (5.9)
Weight, mean (SD), kg	86.3 (21.4)	87 (0.6)
BMI, mean (SD), kg/m^2	31.2 (6.8)	94 (0.6)
25.0–29.9	4,970 (33.6)	
30.0–34.9	4,045 (27.4)	
≥35.0	3,493 (23.6)	
Systolic blood pressure, mean (SD), mm Hg	126 (15)	30 (0.2)
Diastolic blood pressure, mean (SD), mm Hg	70 (10)	29 (0.2)
HbA_{1c}, mean (SD), %	7.6 (1.4)	15 (0.1)
Fasting glucose, mean (SD), mmol/L	8.1 (2.9)	3597 (24.2)
Serum electrolytes		
Sodium, mean (SD), mmol/L	140.0 (3.0)	1973 (13.3)
Potassium, mean (SD), mmol/L	4.6 (0.5)	1368 (9.2)
Incidence of hyperkalemia (potassium >5.5 mmol/L)†	502 (3.4)	1368 (9.2)
Lipids		
LDL-C, mean (SD), mmol/L	1.7 (1.4)	797 (5.4)

(*continued on next page*)

Table I. (*continued*)

Characteristic	All* (N = 14,873)	Missing, No. (%)
HDL-C, mean (SD), mmol/L	1.2 (0.3)	514 (3.5)
Non–HDL-C, mean (SD), mmol/L	2.5 (0.9)	661 (4.4)
Triglycerides, mean (SD), mmol/L	1.9 (1.5)	505 (3.4)

BMI = body mass index; eGFR = estimated glomerular filtration rate; HbA_{1c} = glycated hemoglobin; uACR = urine albumin-to-creatinine ratio.

* Data in this column are presented as number (percentage) of patients unless otherwise indicated. †Incidence of hyperkalemia was defined as at least 1 value of potassium >5.5 mmol/L during the observation period

of ACEis/ARBs, SGLT2is, and GLP-1RAs decreased with worsening CKD severity. Steroidal MRA use for patients with stage 3a, 3b, and 4 CKD was proportionately higher than steroidal MRA use for patients with stage 1 and 5 CKD.

Among other diabetes medications, a large proportion of patients were using metformin (74.6%), which decreased with worsening CKD severity, in keeping with the product monograph and the contraindication of use for patients with eGFR <30 mL/min/1.73 m^2. At least 1 AHA was used in 91.5% of the cohort. With increasing CKD severity, the treatment pattern favored less AHA and increased insulin use. A total of 50.8% of the group was treated with insulin; 23.3% of patients were using basal insulin only (with or without additional AHAs), and 27.4% of patients were using multiple daily injections (with or without additional AHAs).

The use of other cardiovascular medications is summarized in the Supplementary Materials (Figure S1). There was a high proportion of statin use (87.7%). The exploratory analyses describing history of cardiovascular events and CKD progression within 3 years before the index date are summarized in Table II. At least 1 prior cardiovascular event was reported among 23.4% of the population. Furthermore, 2.1% of the CKD in T2D cohort had history of ESKD requiring dialysis or kidney transplantation, indicating impaired eGFR or the presence of albuminuria, even with kidney replacement therapies.

Module B

HCP rationale and satisfaction results for prescribed medications by treatment class (ACEis/ARBs, steroidal MRAs, SGLT2is, and GLP-1RAs) are summarized in Table III. The results of HCP rationale for both guideline-recommended and emerging kidney therapies for a subgroup of 500 patients indicated that SGLT2i and GLP-1RA therapies were primarily prescribed for glycemic control for patients with CKD and T2D. The data indicate that 12% of SGLT2is were identified as primarily prescribed to treat CKD, whereas 33% of ACEis/ARBs were primarily prescribed to treat CKD, with 61% of prescriptions intended to lower blood pressure. Only 4% of steroidal MRAs were prescribed to treat CKD. More prescribers identified blood pressure (57%) and heart failure (21%) as their primary considerations for steroidal MRA use. Mean HCP satisfaction was scored ≥3 of 5 across all treatment classes.

DISCUSSION

This study provides current epidemiologic data on the treatment of CKD in T2D, describing the prevalence of CKD, associated comorbidities, current treatment patterns, and HCP rationale and satisfaction for prescribing therapy among patients with T2D and CKD. The prevalence of CKD in a large, Canadian T2D endocrinology-led registry was 47.9%. Among the cohort of 14,873 patients, there was a high prevalence of hypertension, dyslipidemia, and obesity, and >20% had history of a prior cardiovascular event. These data highlight the importance of considering treatments that will provide a comprehensive strategy for kidney and cardiovascular risk protection, as noted by recent clinical practice guidelines for CKD in T2D.[8] Obesity management is also essential for diabetes management and the prevention of related complications. New Canadian obesity clinical practice guidelines emphasize the need for better access and

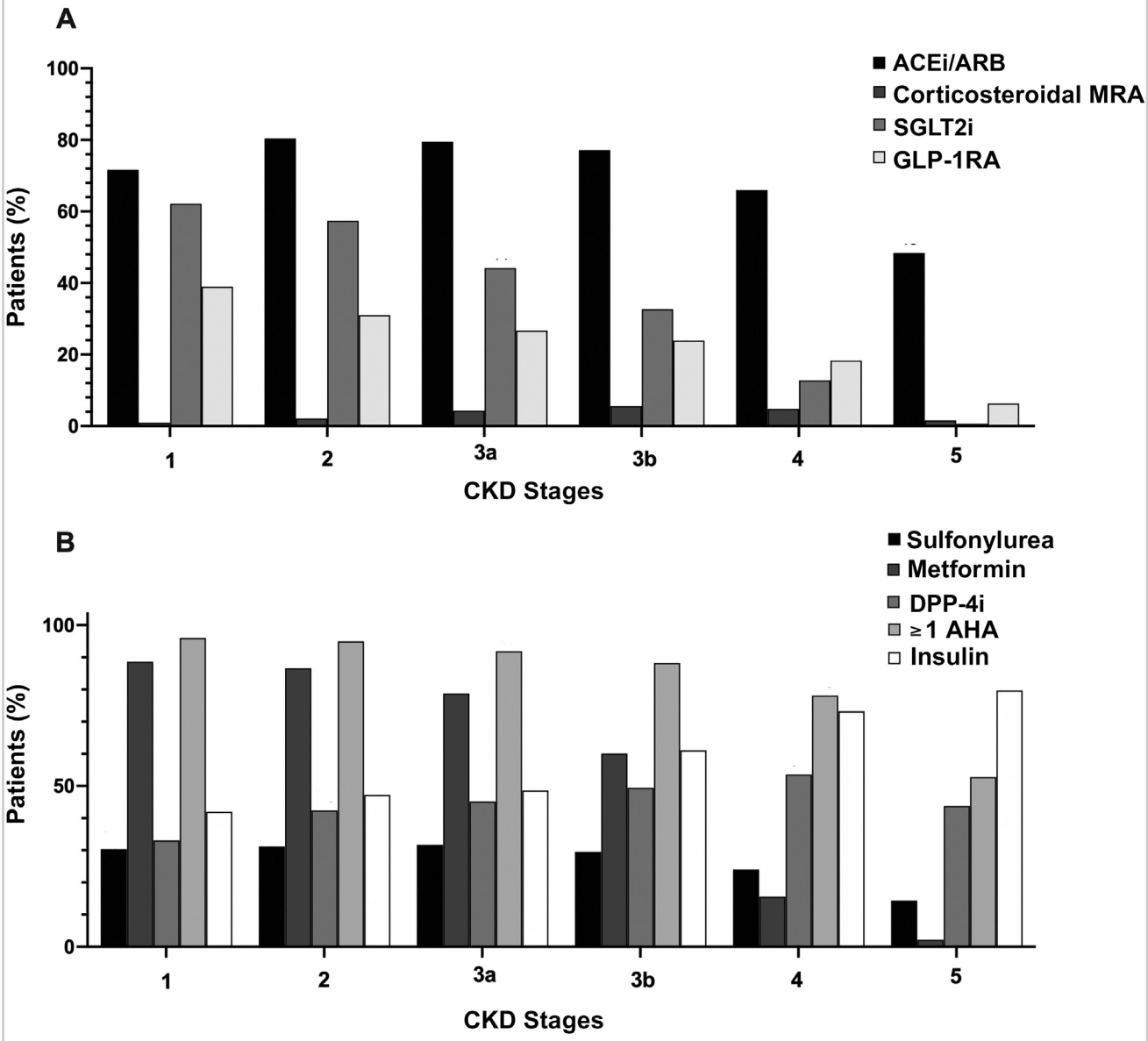

Figure 3. (A) Guideline-recommended kidney medications and emerging kidney medications by chronic kidney disease (CKD) stage and (B) other antihyperglycemic agents by CKD stage. ACEi = angiotensin-converting enzyme inhibitor; AHA = antihyperglycemic agent; ARB = angiotensin receptor blocker; MRA = mineralocorticoid receptor antagonist; SGLT2i = sodium-glucose cotransporter 2 inhibitor; GLP-1RA, glucagon-like peptide 1 receptor agonist; DPP-4i = dipeptidyl peptidase-4 inhibitor.

care and support for patient-centered behavioral interventions and appropriate treatment for adults with obesity.[45] Adjunctive pharmacotherapy for weight loss or weight maintenance is recommended for adults with BMIs ≥27 kg/m^2 with adiposity-related complications or adults with BMIs ≥30 kg/m^2.[45]

Despite the high prevalence of obesity, there was a very low use of therapies primarily indicated for treating obesity reported in this study. However, AHAs associated with weight loss were being used. Weight loss interventions for people living with obesity in addition to CKD and T2D remains a critical area that

Table II. History of cardiovascular events and **CKD progression**.

Event	No. (%) of Patients	
	All (N = 14,873)	Missing
History of cardiovascular events	3484 (23.4)	0 (0.0)
Myocardial infarction	1006 (6.8)	
Congestive heart failure	852 (5.7)	
Percutaneous coronary intervention	645 (4.3)	
Coronary artery bypass grafting	1068 (7.2)	
Cerebrovascular accident	428 (2.9)	
CKD progression		
Impaired eGFR (eGFR <60 mL/min/1.73 m^2) for ≥1–3 years from index date	5975 (40.2)	283 (1.9)*
Microalbuminuria or macroalbuminuria (uACR ≥2 mg/mmol) for ≥1–3 years from index date	6717 (48.0)	1291 (9.2)*
Macroalbuminuria (uACR ≥20 mg/mmol) for ≥1–3 years from index date	1688 (12.1)	326 (2.3)*
ESKD		
History of **ESKD**, dialysis, or kidney transplant at index	313 (2.1)	
ESKD/initiated dialysis or kidney transplant within prior 1–3 years	159 (1.1)	
History of kidney transplant at index	116 (0.8)	
Kidney transplant within prior 1–3 years	42 (0.3)	

eGFR = estimated glomerular filtration rate; **ESKD** = end-stage kidney disease; uACR = urine albumin-to-creatinine ratio.
* Data are the number (percentage) of patients who did not have laboratory values available in the prior 1 to 3 years for each specified variable.

requires further research because there are no current clinical recommendations.[8]

The treatment patterns reported in this study appear to reflect the trajectory of new insights from clinical trials and clinical care guidelines for T2D and CKD promoting treatments with kidney and/or cardiovascular benefits.[8,46] Study findings confirmed that a large proportion of patients (76%) were prescribed an ACEi/ARB, which are the mainstay for treating CKD. Of the ACEi/ARB prescriptions in module B, 33% were identified as prescribed to primarily treat CKD. In addition, module B results suggested that SGLT2i prescriptions were recognized as a treatment option for kidney protection and glycemic management. HCPs may have also considered the benefits of SGLT2is for CVD risk prevention, but this was not the primary reason for prescribing an SGLT2i. Despite recent findings,[17] no GLP-1RAs were primarily prescribed to treat CKD. As expected, steroidal MRAs were prescribed in only a small proportion of patients with T2D and CKD (3%) in this endocrinology-led cohort, primarily for treating hypertension (57%) or heart failure (21%), as described by module B results. Generally, HCP satisfaction was fairly positive and similar across treatment classes.

The prevalence of CKD in T2D was found to be higher in this study (47.9%) compared with the US Renal Data System estimates of 34% to 38%[47] and compared with Canadian data from a retrospective, population-based, cross-sectional study using the Alberta Kidney Disease Network database, which reported 33% of patients with T2D had CKD as of March 2017 (index date).[48] The difference in prevalence for this study compared with the Alberta study could be explained by the inclusion of a population entirely followed by endocrinology specialists and, possibly, differences across provinces and study index date. Another population-based study using linked health care databases in Ontario, Canada, which explored health care use in adults 50 years or older with diabetes,[49] provides additional insight on CKD prevalence. Although CKD stage

Table III. Health care practitioner rationale and satisfaction for prescribed medications.*

Medication	Glycemic Management	Hypertension	Heart Failure	CAD	CKD	Other
ACEi/ARB (n = 442)						
Rationale†		269 (60.9)	3 (0.7)	22 (5.0)	146 (33.0)	2 (0.5)
Satisfaction score, mean (SD) (total of 5)		3.9 (0.8)	3.7 (0.6)	4.0 (0.3)	3.8 (0.8)	
No. dissatisfied		19	0	0	13	
Because of efficacy		15	0	0	11	
Because of poor access		1	0	0	0	
Because of tolerability or adverse effects		0	0	0	1	
Because of poor adherence		3	0	0	1	
Steroidal MRA (n = 47)						
Rationale†		27 (57.4)	10 (21.3)	2 (4.3)	2 (4.3)	6(12.8)
Satisfaction score, mean (SD) (total of 5)		3.8 (0.7)	3.1 (0.4)	4.5 (0.7)	4 (0)	
No. dissatisfied		1	0	0	0	
Because of efficacy		1	0	0	0	
Because of poor access		0	0	0	0	
Because of tolerability or adverse effects		0	0	0	0	
Because of poor adherence		0	0	0	0	
SGLT2i (n = 277)						
Rationale†	226 (81.6)	0 (0.0)	2 (0.7)	11 (4.0)	34 (12.3)	4 (1.4)
Satisfaction score, mean (SD) (total of 5)	3.8 (0.9)		4.5 (0.7)	3.9 (0.5)	4.1 (0.6)	
No. dissatisfied	23	0	0	0	0	
Because of efficacy	15	0	0	0	0	
Because of poor access	2	0	0	0	0	
Because of tolerability or adverse effects	2	0	0	0	0	
Because of poor adherence	4	0	0	0	0	
GLP-1RA (n = 157)						
Rationale†	146 (93.0)	0 (0.0)	0 (0.0)	2 (1.3)	0 (0.0)	9 (5.7)
Satisfaction score, mean (SD) (total of 5)	3.9 (1.1)			3 (0)		
No. dissatisfied	19	0	0	0	0	
Because of efficacy	11	0	0	0	0	
Because of poor access	2	0	0	0	0	
Because of tolerability or adverse effects	5	0	0	0	0	
Because of poor adherence	1	0	0	0	0	

ACEi = angiotensin-converting enzyme inhibitors; ARB = angiotensin receptor blocker; CAD = coronary artery disease; CKD = chronic kidney disease; GLP-1RA = glucagon-like peptide 1 receptor agonist; MRA = mineralocorticoid receptor antagonist; SGLT2i, sodium-glucose cotransporter 2 inhibitor.

* Data are presented as number (percentage) of patients unless otherwise indicated.

† Rationale was defined as the primary condition that the medication was intended to treat based on the judgment of the patient's health care practitioner.

was not reported in the article, the prevalence of CKD for stage 1, 2, 3a/3b, and 4/5 CKD, as of January 2014 (index date), could be calculated from eGFR values in the Ontario study as 35%, 45%, 17%, and 2.3%, respectively.[48,49] Insights from the Discovering Treatment Reality of Type 2 Diabetes in Real World Settings (DISCOVER) study, a multicenter, observational, prospective, longitudinal cohort study that included study sites in 38 countries, reported baseline prevalences of 51.4% for stage 0-1, 37.7% for stage 2, 9.4% for stage 3, and 1.4% for stage 4-5 CKD.[50] Thus, the prevalence of severe CKD in our endocrinology specialist–led population (9.3%) was higher compared with the prevalence of severe CKD previously reported in the Ontario population-based study (2.3%)[49] and the DISCOVER study (1.4%).[50]

In addition to a higher prevalence of CKD, there could be greater use of pharmacotherapy within a T2D population entirely followed by endocrinology specialists. The most common AHAs prescribed among patients with T2D and CKD in this study were metformin (75%) and insulin (51%), followed closely by SGLT2i (48%) and DPP-4i (43%). These data are aligned with trends supporting the increased use of AHAs for CKD in T2D.[51] Compared with the Alberta study by Tonelli et al,[48] SGLT2i and GLP-1RA use appeared substantially higher in our T2D specialist population by at least 40% for SGLT2i use and 25% for GLP-1RA use. Because the Alberta study had an earlier index date of March 2017, the higher prevalence of AHA use in the present study may be related to more published data from clinical trials and promotional efforts within the past few years on the use of AHAs for CKD and CVD risk prevention. Although a higher use of SGLT2is was observed in this study compared with the study by Tonelli et al,[48] SGLT2is remain underused among patients with CKD and T2D, especially considering recent clinical trial data supporting SGLT2i use.[23,30]

ACEis/ARBs were also underused, which has been reported in other countries by the Chronic Kidney Disease Outcomes and Practice Patterns Study (CKDopps).[52,53] CKDopps reported that the use of ACEis/ARBs, direct renin inhibitors, or aldosterone receptor antagonists was 71% to 85% among people with diabetes and albuminuria in Brazil, France, and Germany, with even lower use in the United States (57%), despite patients having strong class-specific guideline-directed eligibility for renin angiotensin aldosterone system inhibitor use.[52,53] Data from the Center for Kidney Disease Research, Education, and Hope registry also reported lower use of ACEis/ARBs among patients with CKD, hypertension, and prediabetes or diabetes (approximately 25%).[54] Although differences exist when comparing health systems, countries, and primary care and specialist care practices, the data have repeatedly found gaps in patient care for CKD and the need for comprehensive surveillance of trends and treatment patterns.

To the best of our knowledge, no other studies have reported treatment patterns and HCP rationale for ACEi/ARB or new AHA or steroidal MRA use for CKD in patients with T2D in Canada. Thus, the present study extends our knowledge of treatment patterns beyond AHAs, as reported by Tonelli et al,[48] to include ACEis/ARBs, steroidal MRAs, and cardiovascular medication classes and provides insight on treatment patterns of patients seen within a large endocrinology practice group. The use of steroidal MRAs to treat CKD in patients with T2D is expectedly low in the present study, reflecting the scarcity of data and lack of indication for steroidal MRAs in this patient population.

If finerenone is approved, the use of nonsteroidal MRAs for CKD in patients with T2D may increase in the future. Recent results from the FIDELIO-DKD trial have been encouraging, finding that finerenone, a new nonsteroidal and selective MRA, is effective in reducing the risk of CKD progression and cardiovascular events in this patient population, with a low incidence of treatment discontinuation because of hyperkalemia.[27,28] The recently completed FIGARO-DKD trial provides further support on the efficacy and tolerability of finerenone among patients with T2D and less advanced CKD.[29]

The study results should be interpreted with the consideration of a few limitations. The patients were under specialist care by a large endocrinology group; thus, results may not be generalizable to all individuals followed up by primary care or other specialist physicians. The HCPs surveyed in module B are representative of urban and suburban community endocrinology specialists. Registry limitations include the possibility of incomplete data collection of medical history such that comorbidities diagnosed by a physician outside the practice group could be underreported.

The interpretation of module B may be limited by survey restrictions that allow 1 response per question and no text fields. For example, HCPs were asked to select only 1 response for each prescribed medication class, and they could not select >1 condition even if the medication was chosen for its multiple benefits, including kidney and/or cardiovascular risk protection, glycemic control, or weight loss. Hence, use of SGLT2i and/or GLP-1RA therapies for kidney protection could have been underreported secondary benefits, overshadowed by a focus on glycemic control shared by endocrinologists.

Strengths of the study include its large size in a community-based setting within Canada's public health care system. The Canadian diabetes registry provided the capacity to report new data among patients with CKD and T2D in Canada, including ACEi/ARB, steroidal MRA, AHA, and cardiovascular medication use by CKD stage, and presented exploratory end points on CKD progression and history of cardiovascular events. In addition, module B provided unique insights on HCP rationale and satisfaction with available treatments for CKD in T2D. To the best of our knowledge, no data on HCP rationale and satisfaction for prescribed medications for CKD in patients with T2D have been previously reported.

CONCLUSIONS

The study findings describe the current landscape of CKD in T2D and provide valuable data on the burden of disease, treatment patterns, and gaps for patient care. CKD in T2D is extremely prevalent within community-based specialist care and often occurs concomitantly with other comorbidities and risk factors for CKD progression, CKD events, and cardiovascular events. This study presents further evidence of the need for individualized treatment that considers kidney benefits, glycemia, and weight management as well as primary and secondary cardiovascular risk reduction. The relatively high prevalence of obesity in this cohort of patients with CKD and T2D suggests behavioral intervention and investigation of therapies for weight loss or weight maintenance are crucial and should be considered as part of the standard of care. Only in the last couple of years has there been a wealth of positive data supporting different potential therapies for CKD in T2D after very little change since 2001. It will be important for clinicians to be well-informed about the new treatment options for CKD in T2D and to understand where the therapies fit within the treatment landscape so they can be used appropriately. With such an immense burden of CKD progression and ESKD among patients with T2D, the use of treatments that provide a comprehensive strategy for kidney protection will transform the landscape of CKD and T2D.

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DISCLOSURES

M. Fuller, K. Jervis, and A. Ciaccia are current employees of Bayer Inc. A. Abitbol reports receiving grants and personal fees outside the submitted work from Amgen, Bayer Inc, Sanofi, Novo Nordisk, Janssen, AstraZeneca, Eli Lilly, Boehringer-Ingelheim, Merck, and Senseonics, personal fees from Dexcom and Insulet, and grants from Gilead, Glaxo-Smith-Kline, Lexicon, Pfizer, Xeris, Zealand, and Zucara. The authors have indicated that they have no other conflicts of interest regarding the content of this article.

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APPENDIX. SUPPLEMENTARY MATERIALS

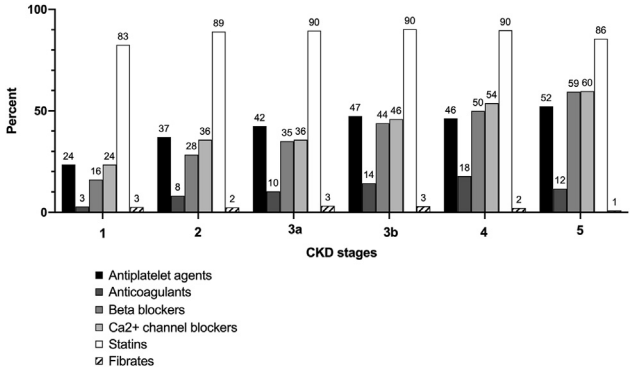

Figure S1. **Other cardiovascular medications by CKD stage.** Abbreviations: CKD, chronic kidney disease; Ca^{2+}, calcium.