Prescriber Uncertainty as Opportunity to Improve Care of Type 2 Diabetes with Chronic Kidney Disease: Mixed Methods Study

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BACKGROUND: Over 5 million patients in the United States have type 2 diabetes mellitus (T2D) with chronic kidney disease (CKD); antidiabetic drug selection for this population is complex and has important implications for outcomes.

OBJECTIVE: To better understand how providers choose antidiabetic drugs in T2D with CKD

DESIGN: Mixed methods. Interviews with providers underwent qualitative analysis using grounded theory to identify themes related to antidiabetic drug prescribing. A provider survey used vignettes and direct questions to quantitatively assess prescribers' knowledge and preferences. A retrospective cohort analysis of real-world prescribing data assessed the external validity of the interview and survey findings.

PARTICIPANTS: Primary care physicians, endocrinologists, nurse-practitioners, and physicians' assistants were eligible for interviews; primary care physicians and endocrinologists were eligible for the survey; prescribing data were derived from adult patients with serum creatinine data.

MAIN MEASURES: Interviews were qualitative; for the survey and retrospective cohort, proportion of patients receiving metformin was the primary outcome.

KEY RESULTS: Interviews with 9 providers identified a theme of uncertainty about guidelines for prescribing antidiabetic drugs in patients with T2D and CKD. The survey had 105 respondents: 74 primary care providers and 31 endocrinologists. Metformin was the most common choice for patients with T2D and CKD. Compared to primary care providers, endocrinologists were less likely to prescribe metformin at levels of kidney function at which it is contraindicated and more likely to correctly answer a question about metformin's contraindications (71% versus 41%) ($p < .05$). Real-world data were consistent with survey findings, and further showed low rates of use of sodium-glucose cotransporter 2 inhibitors and glucagon-like peptide 1 receptor agonists (<10%) in patients with eGFR below 60 ml/min/1.73m^2.

CONCLUSIONS: Providers are unsure how to treat T2D with CKD and incompletely informed as to existing guidelines. This suggests opportunities to improve care.

KEY WORDS: type 2 diabetes; chronic kidney disease; metformin; drugs; provider preference.

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Key Points

Question: How do providers choose which antidiabetic drug to use first in patients with type 2 diabetes and chronic kidney disease?

Findings: Providers are unsure whether they can use metformin in patients with intermediate levels of kidney disease. Providers are similarly unsure as to alternatives to metformin in patients with kidney disease.

Meaning: Providers' uncertainty when prescribing antidiabetic drugs for patients with diabetes and chronic kidney disease may adversely affect care for a population of over 5 million patients in the United States, and is an important target for quality improvement activities.

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INTRODUCTION

Metformin is the traditional first-line drug for type 2 diabetes mellitus (T2D). However, guidelines now recommend sodium-glucose cotransporter 2 inhibitors (SGLT2-I) and glucagon-like peptide 1 receptor agonists (GLP1-RA) as first-line in some scenarios.[1] Potential benefits from these newer drug classes are especially relevant in the over 5 million patients with T2D and chronic kidney disease (CKD) stage 3 or higher in the United States (US)[2,3], both because SGLT2-I and GLP1-RA can be renally protective and because metformin is discouraged or contraindicated in many of these patients.[1,4–6] The US Food and Drug Administration (FDA) label permits metformin to be started in patients with estimated glomerular filtration rate (eGFR) > 45 ml/min/1.73m^2 (stage 3a or better CKD), permits metformin to be continued but not started in patients with eGFR between 30 and 45 (stage 3b), and contraindicates metformin below eGFR 30 (stage 4 or worse).[7]

Prescribing patterns in CKD and T2D are not well characterized because CKD stage is best defined using laboratory data, which is not widely available in most large US administrative datasets. Cross-sectional studies using National Health and Nutrition Examination Survey data have shown the prevalence of metformin use declines with decreasing eGFR, from 50% of patients with eGFR > 60 ml/min/1.73m^2 to 8.8% of

patients with eGFR < 30.[2] Fewer data are available on adoption of newer agents by eGFR.[8,9]

Even less is known about the provider decision-making underlying these trends. Lower rates of metformin use at lower eGFR could be explained in several ways with different implications. Does the trend reflect providers' knowing and implementing the FDA guidelines, or are providers largely unaware of the label content? If providers are not following FDA guidelines, do they have their own consistent practices for metformin use in CKD, or is decision-making more haphazard? Findings from two focus groups conducted prior to 2016 suggested that provider decisions on metformin use in particular are not aligned with evidence, but data on more recent prescribing practices are needed.[10]

Mixed-methods approaches may provide the qualitative information needed to understand the underlying causes and meaning of quantitative prescribing data.[11–16] Our aim was to use mixed methods to better understand how providers think about choice of antidiabetic drugs in T2D with CKD, and to identify possible ways to improve decision making in this common, important clinical scenario.

METHODS

This mixed methods project incorporated qualitative interviews with health care professionals in New York State (NYS), a quantitative survey of providers from across the US, and a retrospective cohort analysis of prescribing data in the New York City (NYC) area.

Provider interviews were conducted with a convenience sample recruited from across NYS but mainly from academic medical practices in NYC. Due to the technical content, all interviews were conducted by an interviewer with a medical doctorate (VLM). Any general internist, family practitioner, nurse practitioner, physician's assistant, or endocrinologist was eligible. Individuals were approached via email and interviews were conducted over remote telephone or videoconferencing. Interviews were recorded and transcribed. Recruitment included circulation of invitations to multiple large email lists and precise statistics on non-participation were not kept, but the non-participation rate exceeded 90%.

A sample size of 9 was targeted a priori, based on limited study resources and empirical evidence that very common themes are very likely to be identified after approximately 6 interviews.[17]

Analysis applied grounded theory to identify themes related to antidiabetic drug use, although inclusion of specific questions about prescribing at different CKD stages made the interview likely to identify themes related to those topics (Supplementary Appendix).[18] A code list was developed independently by two reviewers based on review of one transcript. This code list was consolidated and applied to an additional transcript by both reviewers. After a second round of review and confirmation that each reviewer was obtaining consistent results, all transcripts were coded using the code list. The coded transcripts were then reviewed by the study team and emergent themes and sub-themes were identified.[19]

The provider survey was conducted electronically between 6/10/2020 and 8/28/2020, through the survey firm SSRS, which recruited respondents through a third-party opt-in web panel (the Dynata physician panel), which partners with organizations including the American Medical Association to recruit healthcare providers to join the panel through direct mail. Members of the panel were then contacted electronically and offered participation in this specific survey.[20] Endocrinologists and primary care providers currently in clinical practice in the US were eligible. The survey included 17 questions (apart from introductory questions to collect demographic covariates). These included four patient vignettes (drawn at random for each respondent from a library of 40 vignettes) in which respondents were asked to choose an antidiabetic drug for monotherapy in a hypothetical patient, with the option to choose metformin, sulfonylurea, SGLT2-I, GLP1-RA, insulin, dipeptidyl-peptidase 4 inhibitor (DPP4-I), other (free text), and no medication. Vignettes have been previously found to be effective in predicting actual prescribing behavior.[21–23] In each vignette, the patient's serum creatinine and eGFR (calculated using the CKD-EPI 2009 equation, as the survey was developed and implemented prior to 2021 revisions to the formula[24]) was presented, with values ranging from 24 ml/min/1.73m^2 to 99. The primary outcome for the survey was the proportion of vignettes to which the response was "metformin," stratified by stage of CKD. The survey also included direct questions about how providers chose antidiabetic medications in T2D and CKD; two questions assessing the provider's level of knowledge of current FDA rules on metformin use in CKD; and two eliciting preferences among hypothetical future studies to inform antidiabetic drug use in CKD (Supplementary Appendix).

For responses to questions other than the patient vignettes, *t*-test or chi-square tests were used for significance testing. Tests related to vignette responses were conducted by hierarchical logistic regression to account for clustering within respondents. Multivariable modeling using hierarchical logistic regression of the association between vignette characteristics and medication choice included as independent variables provider (respondent) specialty and the hypothetical patient's age, body mass index (BMI), eGFR, history of heart failure, history of "stomach upset," and history of "frailty."

The retrospective cohort analysis used data from the INSIGHT Clinical Research Network (CRN), which includes longitudinal data for a large, diverse urban patient population across five academic medical centers in New York City.[25,26] The INSIGHT-CRN includes electronic prescribing data, patient demographic information, diagnosis codes, and laboratory values. Patients were eligible to contribute data from 1/1/2019–12/31/2020 to the primary analysis. To maximize

comparability with the results of the provider survey, the cohort was constrained to the same eGFR range (24–99), HbA1c range (6.5–9.5), and age range (47–86) as found in the survey vignettes. Patients were required to have at least one previous diagnosis code for T2D, no previous diagnosis code for type 1 diabetes, at least one outpatient visit prior to the prescription date, and no previous codes for diabetic complications or prescriptions for antidiabetic drugs. Electronic prescriptions for antidiabetic medications occurring within 30 days after a serum creatinine measurement were classified according to that serum creatinine, which was converted to eGFR using the CKD-EPI 2021 equation.[24] The proportion of prescriptions for each antidiabetic drug class at each eGFR level is reported and is interpretable as the probability that a given drug class was a provider's first choice of initial antidiabetic therapy, contingent on recently measured eGFR. Sensitivity analysis included relaxation of inclusion criteria, inclusion of data from 1/1/2012 until 12/31/2020, and use of the CKD-EPI 2009 equation (Supplementary Data). Unadjusted linear models were used to assess the relationship between eGFR and use of each drug class.

R 4.0.0 was used for analysis. These studies were approved by the Memorial Sloan Kettering Cancer Center, Weill-Cornell, Mt. Sinai, and Biomedical Research Alliance of New York Institutional Review Boards. De-identified data from the provider survey are available on request. Interview transcripts or prescribed data cannot be shared due to IRB standards and the need to protect patient confidentiality.

RESULTS

Interviews

Qualitative interviews were conducted with 9 providers — 2 endocrinologists, 6 general internists, and 1 nurse practitioner — between 1/1/2020 and 6/1/2021. Inductive coding identified the following themes related to prescribing in T2D and CKD. Exemplar quotations are followed by a bracketed number indicating which interview they are taken from.

Metformin as first-line drug: All interviewees viewed metformin as the first-line treatment for T2D overall (without taking CKD into account).

Change in practice: Interviewees noted that practice patterns were changing, with two sub-themes. The first was *rising interest in newer medications over older*, both as first-line ("I'm seeing more and more that the newer class of medications such as GLP1's and SGLT2's which come with renal benefits, cardiovascular benefits, weight loss benefits. And I'm actually starting to consider implementing those more often as first line" [6]) and second-line ("tend not to use sulfonylureas anymore" [8]). The second was *changes in guidelines*, particularly for metformin's use in CKD ("I think it's [the cutoff for metformin use] is down to a GFR of 30, if I'm not mistaken … so that's quite a shock because I remember when it went to like 45" [2]).

Uncertainty about prescribing for patients with T2D and CKD included sub-themes of *uncertainty in metformin prescribing*, which emerged when providers were describing whether they would use metformin at eGFRs between 30 and 60 ml/min/1.73m^2 and *uncertainty in SGLT2 prescribing*, which emerged in questions focused on the same eGFR range (Table 1).

Safety concerns about antidiabetic drugs in patients with CKD had two sub-themes: *hypoglycemia with sulfonylureas and insulin*, and *lactic acidosis with metformin*: "hypoglycemia for sure. That's definitely the first [safety concern]. And then after that would be thinking about metformin, I worry about lactic acidosis" [6].

Individualization of treatment was a theme, with one interviewee stating that antidiabetic drug choice was "very, very, very individual" [2]; multiple interviewees gave as an example that they would avoid metformin in patients with a history of gastrointestinal problems ("people having very severe IBS [irritable bowel syndrome], IBD [inflammatory bowel disease] … [metformin] wouldn't be like my first choice because [of] the tolerability" [3]).

Table 1 Exemplar Quotations Regarding Diabetes Drug Choice by eGFR Category

Question	Stage 2 (eGFR > 60)	Stage 3a (eGFR 45–59)	Stage 3b (eGFR 30–44)	Stage 4 (eGFR < 30)
What is your preferred diabetes medication in stage [blank] CKD?	"just metformin" [9] "start with metformin" [7] "SGLT 2 in addition to metformin" [2] "probably still be metformin" [4] "I try and add on an SGLT2" [6] "use an SGLT 2 in addition to metformin" [2] "entertain an SGLT2" [4]	"probably metformin" [8] "might do a lower dose of metformin" [7] "break the rules and still sometimes start metformin" [5] "forget where the [eGFR] cutoff is for SGLT 2s … otherwise maybe … DPP4 or GLP1" [6] "I think this is where most of the SGLT-2s are recommended … Off the top of my head, I'm not totally sure" [9] "still be among the SGLT2s … open to using of course the GLP-1 receptor agonist"" [3]	"If they're already on metformin, I would lower the dose… would not start metformin" [9] "not totally sure about starting metformin" [1] "okay to actually use a small dose [of metformin] … nothing more" [3] "possibly an SGLT2" [4] "definitely stay away from the SGLT-2s" [9] "maybe a DPP 4 … adding a low dose sulfonylurea" [6] "I might try a GLP-1 for this patient" [8]	"taking them off [metformin] for sure" [9] "tend not to start metformin" [8] "metformin is out" [6] "I might just go to insulin" [5] "I'd probably say the GLP-1s again" [8] "use low dose DPP-4s or insulin as needed … even consider a very, very short-acting sulfonylurea" [3] "double check and see if you can give a sulfonylurea … check an SGLT2, because don't know that one off the top of my head" [1]

Note: eGFR, estimated glomerular filtration rate, expressed in ml/min/1.73m^2

Specific questions about provider's approach to identifying CKD ensured that *defining and monitoring CKD* would be present as a theme. Within this theme two sub-themes emerged: *eGFR versus creatinine* ("creatinine and eGFR … I look more at the creatinine, I think"[6] versus "[I] tend to use the estimated GFR but certainly, I'm going to look at the creatinine" [8]) and the *influence of presentation* ("I use [eGFR] greater than 60 and consider that to be normal, because I think [our electronic medical record] only reports greater than 60" [1]).

Specific questions about providers' willingness to use metformin and their preferred alternative agents at different eGFR ranges almost ensured that *changing prescribing patterns with eGFR* would be a theme. Sub-themes were *metformin dose reduction at low eGFR*, *reluctance to use metformin at low eGFR*, *interest in SGLT2-I at high eGFR* and *uncertainty about SGLT2-I use at lower eGFR*, *and increasing use of insulin and sulfonylureas at lower eGFR* (Table 1).

Survey

The survey had 105 respondents including 74 primary care providers and 31 endocrinologists, between 6/10/2020 and 8/28/2020. Respondents were most commonly age 35–50 (interquartile range) and evenly divided between men and women, with representation from all regions of the US (Supplementary Data). For this non-probability web sample, response rates cannot be calculated, so the American Association for Public Opinion Research (AAPOR) response rate #3 is reported; it was 25%, meaning that 25% of panel members approached participated.[27] All statements of difference are nominally statistically significant at the $p < 0.05$ level.

Survey responses are summarized in Table 2. Results are stratified by specialty (endocrinologist versus primary care provider). Endocrinologists were more likely to give the correct answer when asked a multiple-choice question about the current FDA guidelines (71% versus 41%). Endocrinologists were also more likely to endorse being comfortable prescribing metformin at eGFR 50 ml/min/1.73m^2 (90% versus 61%) and eGFR 40 (65% versus 35%).

Asked what eGFR range would be most appropriate for participants in a randomized trial comparing metformin to an alternative drug in patients with diabetic kidney disease, participants most commonly chose eGFR 45–59 ml/min/1.73m^2 (43%), followed by eGFR 30–44 (37%). In response to a

Table 2 Survey Responses

Characteristic	Endocrinologist, $N = 31^1$	Primary care provider, $N = 74^1$	p-value^2
Factor at least "fairly important" in prescribing:			
Age	19 (61%)	43 (58%)	0.8
Race	7 (23%)	30 (41%)	0.079
Kidney function	29 (94%)	71 (96%)	0.6
HbA1c	31 (100%)	72 (97%)	>0.9
BMI	29 (94%)	58 (78%)	0.060
At least "moderately" comfortable prescribing metformin at:			
eGFR 30 ml/min/1.73m^2	10 (32%)	26 (35%)	0.8
eGFR 40 ml/min/1.73m^2	20 (65%)	26 (35%)	0.006
eGFR 50 ml/min/1.73m^2	28 (90%)	45 (61%)	0.003
FDA guidelines for metformin use in decreased kidney function:			0.025
No restriction	0 (0%)	2 (2.7%)	
Contraindicated for serum creatinine > 1.4 mg/dl in women or 1.5 mg/dl in men	5 (16%)	15 (20%)	
Contraindicated at eGFR < 60 ml/min/1.73m^2	0 (0%)	11 (15%)	
Contraindicated at eGFR< 45 ml/min/1.73m^2	4 (13%)	16 (22%)	
Contraindicated at eGFR< 30 ml/min/1.73m^2	22 (71%)	30 (41%)	
Metformin prescription is not advisable at eGFR below:	30 (IQR 30, 36)	40 (IQR 29, 52)	0.13
Imagine that you are referring patients to a study that would compare metformin to an alternative drug in patients with diabetic kidney disease, with major adverse cardiovascular events and progression of kidney disease as the primary outcomes. What do you think would be the most appropriate comparator group?			0.013
Sulfonylurea	2 (6.5%)	10 (14%)	
SGLT2 inhibitor	21 (68%)	21 (28%)	
GLP1 receptor agonist	4 (13%)	16 (22%)	
Insulin	0 (0%)	5 (6.8%)	
DPP4 inhibitor	3 (9.7%)	10 (14%)	
Placebo	0 (0%)	4 (5.4%)	
Other	1 (3.2%)	1 (1.4%)	
None	0 (0%)	7 (9.5%)	
Imagine that you are referring patients to a study that would compare metformin to an alternative drug in patients with diabetic kidney disease, with major adverse cardiovascular events and progression of kidney disease as the primary outcomes. What eGFR range would you consider most appropriate for recruitment?			0.6
15–29 ml/min/1.73m^2	2 (6.5%)	1 (1.4%)	
30–44 ml/min/1.73m^2	11 (35%)	28 (38%)	
45–59 ml/min/1.73m^2	14 (45%)	31 (42%)	
60–89 ml/min/1.73m^2	3 (9.7%)	11 (15%)	
None	1 (3.2%)	3 (4.1%)	

[1]n (%); Median (IQR). [2]Pearson's chi-squared test; Fisher's exact test; Wilcoxon rank sum test

question asking for the most appropriate comparator, SGLT2 inhibitors were the most common choice for both endocrinologists and generalists (Table 2).

In the responses to vignettes, metformin was the single most common drug selected, although it was chosen more often by primary care providers than by endocrinologists (48% versus 31%). The second most common choices were SGLT2-I and GLP1-RA (16% and 14% overall), with endocrinologists more likely than primary care providers to choose these agents. Providers were less likely to choose metformin in vignettes with a low eGFR (Fig. 1). Endocrinologists' willingness to use metformin declined more rapidly with eGFR than generalists'. Lower BMI and a history of gastrointestinal complaints were also independently associated with less metformin use (Table 3).

Table 3 Results of Multivariable Logistic Regression for Predictors of Choice of Metformin in Responses to Patient Vignettes

Predictor variable	Odds ratio
Provider characteristics:	
Endocrinologist	0.30 (0.13–0.66)
Patient characteristics:	
HbA1c (per %)	1.25 (0.89–2.76)
Age (per 10 years)	0.73 (0.53–1.01)
Body Mass Index (per 5 kg/m^2)	1.93 (1.02–3.63)
eGFR (per 30 ml/min/1.73m^2)	1.53 (1.23–1.90)
Frailty	0.59 (0.26–1.32)
Stomach upset	0.45 (0.24–0.84)
Heart failure	1.18 (0.58–2.38)

Prescribing Data

After exclusion criteria, the INSIGHT-CRN data included 3145 first outpatient prescriptions for antidiabetic medication in 2019–2020, prescribed within 30 days after measurement of a serum creatinine (Supplementary Data). Recipients were 51.1% female; 32.3% white, 19.1% Black, and 6.0% Asian, with the rest reported as "other," "mixed race," or missing data; median age at prescription was 67.1 years (IQR 60.4–73.7). Across eGFR categories, 80.6% of prescriptions were in patients with eGFR ≥ 60 ml/min/1.73m^2, 13.5% to eGFR 45–59; 5.0% to eGFR 30–44, and 0.8% to eGFR 15–29. Rates of prescribing of each antidiabetic drug class by eGFR are shown in Figure 2. All drugs except for GLP1-RA and SGLT2-I showed a relationship between prescribing probability and eGFR significant at $p < 0.001$. Rates of use of GLP1-RA and SGLT2-I were comparatively low (<10%). Metformin was more likely to be used at higher eGFR and insulin, sulfonylureas, and DPP4 inhibitors were less likely. Across a range of sensitivity analyses, these results were consistent except that rates of insulin use, especially at low eGFR, were higher when patients with diabetes complications were not excluded (Supplementary Data).

CONCLUSIONS

This mixed methods approach combines qualitative interviews, survey data, and real-world prescribing data. Consistent with prior literature, we find that metformin use is lower with reduced kidney function. The major study finding is that this seemingly orderly prescribing pattern belies substantial uncertainty among providers about how to treat diabetes in CKD patients.

The finding that lower eGFR is related to less metformin use was seen using all three methods and across sensitivity analyses. Among interviewees, metformin was a universal first-line choice at eGFR > 60 ml/min/1.73m^2, was less likely to be endorsed as a treatment option between eGFR 30 and 60, and was not considered an option below eGFR of 30. Among survey respondents and real-world prescribing data, a similar decline in willingness to use metformin was seen. Figure 1 suggests that many survey respondents would start metformin at eGFR < 30 ml/min/1.73m^2, but this finding is likely due to

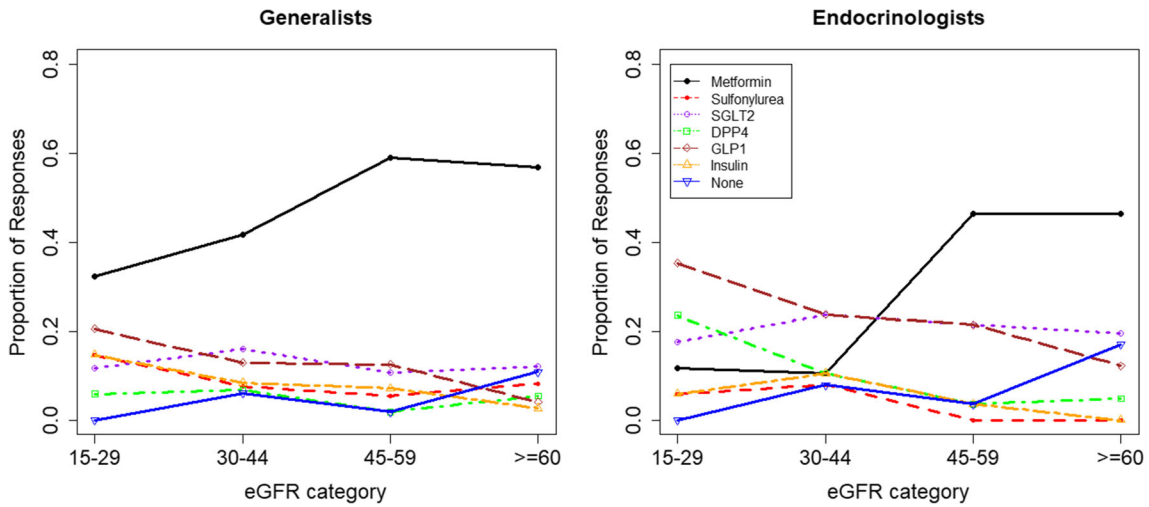

Figure 1 Survey results for prescribing preference in responses to vignettes, by estimated glomerular filtration rate (eGFR).

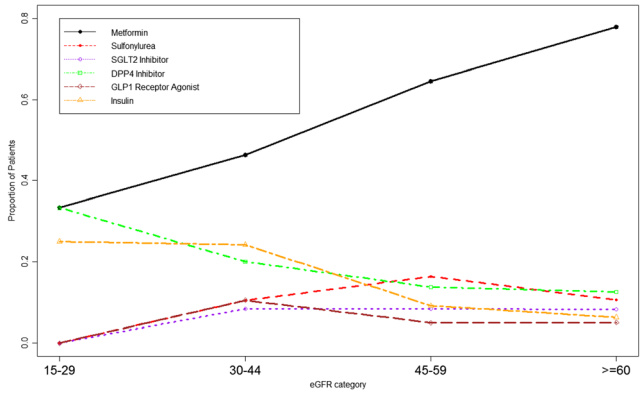

Figure 2 Real-world prescribing patterns for antidiabetic drugs according to estimated glomerular filtration rate (eGFR), 2019–2020.

the distribution of eGFRs in the patient vignettes, in which no eGFR was lower than 24.

The qualitative data show that the seemingly orderly decline in metformin use with falling eGFR is accompanied by considerable uncertainty. Interview participants gave tentative, variable, and sometimes factually incorrect responses when asked about using metformin use in stage 3a and 3b CKD. In the survey, there was a striking difference between the generalists — who often chose metformin as a treatment in vignettes with stage 4 CKD, and fewer than half of whom gave the correct answer to a factual question about metformin's contraindications — and the endocrinologists, who were more likely to give answers consistent with FDA recommendations.

The interview data also show providers to be considering the newer drug classes over sulfonylurea in kidney disease, unsure of the safety of SGLT2-I in patients with stage 3 or worse kidney disease, and more likely to use insulin and sulfonylureas in advanced kidney disease. Survey data were consistent with this, except that they did not show increased rates of insulin use at low eGFR, again likely in part because survey data did not extend below eGFR 24 ml/min/1.73m^2. Real-world data were aligned with the qualitative findings and had the statistical precision to show that use of SGLT2-I and GLP1-RA in patients with stage 3 or higher CKD remains low, an important finding given the benefits of these drugs in those populations and one consistent with other recent research.[28]

One discrepancy between real-world and qualitative data was higher use of insulin at low eGFR in the real-world prescribing data. Although the discrepancy was small in the primary analysis, it was larger in sensitivity analyses. A likely explanation is that the low-eGFR patients in the real-world data were more complex patients with more comorbidities than their hypothetical counterparts in the survey, which could drive higher rates of insulin prescribing.[29] Other possible explanations point to broader study limitations. The convenience samples may not have been representative of typical prescribers; responses to hypothetical scenarios might differ from real decisions; or real-world data might have missingness and other sources of bias. In future research, a survey distributed to providers within a health system with high response rates and linkage to prescribing data would address many of these limitations. Additional limitations of this study include exclusion of other subspecialties that frequently prescribe antidiabetic medications, including nephrology and cardiology, and the relatively small number of interviews conducted. Finally, this study does not address the patient perspective on diabetes drug selection.[30] However, prior work has found patients pay little attention to quantitative assessment or staging of kidney function, making it reasonable to focus on the provider perspective here.[31,32]

Despite its limitations, this study provides useful insights into how providers treat T2D with CKD. Providers are aware that kidney function has significant implications for whether metformin and other drugs can be used to treat T2D. However, non-endocrinologists are often uncertain of the specific standards for prescribing in T2D with CKD. This implies that patient care is probably not optimal, since most patients with T2D are not cared for by endocrinologists.[33] In particular, the data suggest potential underuse of metformin in stage 3 CKD and overuse in stage 4; underuse of GLP1-RA and SGLT2-I; and perhaps overuse of insulin and sulfonylurea in patients with advanced CKD.[34,35] Interventions including programs of provider education, increased access to specialist care, and electronic decision support to address this uncertainty might bring prescribing more into line with guidelines and recent evidence, with large potential benefits for a vulnerable, growing population of over 5 million US patients with T2D and CKD[2,36–43]

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