Evaluation of the Clinical Utility of PromarkerD In-Vitro Test in Predicting Diabetic Kidney Disease and Rapid Renal Decline

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Background

- Diabetic kidney disease (DKD) develops in 1 in 3 people with type 2 diabetes (T2D)[1] and is the leading cause of end-stage renal disease (ESRD), associated with increased morbidity and mortality.[2,3]
- DKD and ESRD impose economic burdens and lower quality of life, costing the US Medicare system $50 billion annually.[4]
- Existing standard-of-care tests for detecting DKD are the estimated glomerular filtration rate (eGFR) blood test and the urinary albumin-to-creatinine ratio (ACR). Despite the well established KDIGO (Kidney Disease Improving Global Outcomes) guidelines,[5] currently 80% of at-risk patients do not receive adequate testing.[6]
- Early identification of patients at risk of developing DKD or rapid renal decline is imperative for selecting appropriate patient interventions and treatment,[7] however, both the eGFR and ACR tests have limited accuracy in predicting the risk of developing DKD.[8]
- PromarkerD is an innovative protein biomarker-based blood test that can predict future renal function decline within the next 4 years in people with T2D, including in those with no existing DKD.

Aim

- To evaluate the impact of PromarkerD on clinical treatment decisions for T2D patients.

Methods

- A conjoint analysis was used to infer the importance of PromarkerD and other patient attributes on physician decision-making via a web-based survey administered to a convenience sample of 400 primary care physicians (PCPs) and endocrinologists.
- 42 hypothetical patient profiles were generated, with varying levels of the following attributes: PromarkerD result (low-, moderate-, or high-risk), albuminuria (as measured by ACR), eGFR, blood pressure (BP), glycemic control (HbA1c), and age (Table 1).
- A web-based survey asked each physician to make monitoring and treatment selection/dosing decisions for eight randomly selected profiles.
- Respondents were shown a blinded description of PromarkerD (which was described throughout the survey as "Test X").

Table 1. Detailed attributes and levels

Attributes and Levels				
Attribute	**Level 1**	**Level 2**	**Level 3**	**Level 4**
PromarkerD result	No test	Low risk	Moderate risk	High risk
Albuminuria	15 mcg/mg (mildly increased)	165 mcg/mg (moderately increased)	500 mcg/mg (severely increased)	N/A
eGFR	110 ml/min/1.73m^2 (normal)	75 ml/min/1.73m^2 (mildly decreased)	45 ml/min/1.73m^2 (moderately decreased)	N/A
Blood pressure (BP)	120/70 mmHg	135/90 mmHg	150/95 mmHg	N/A
Glycemic control (HbA1c)	6.3%	7.5%	8.4%	N/A
Age	48 years	66 years	83 years	N/A

N/A = not applicable

- For each patient, physicians indicated with their decision-making outcomes about monitoring frequency (increase/decrease/same), treatment selection (Sodium-Glucose Cotransporter-2 [SGLT2] inhibitors, renotoxic medication), and dosing (ACE inhibitors) (Table 2).

Methods

Table 2. Detailed decision-making outcomes

Outcomes	
Outcome	**Operationalisation (Single select for each outcome)**
Monitoring frequency of risk factors (albuminuria, eGFR, blood pressure, and HbA1c)	Increase, decrease, or maintain standard monitoring frequency*
Prescribe SGLT2 inhibitors	Yes or no
Replace ibuprofen	Yes or no
Increase lisinopril dose to 20mg per day	Yes or no

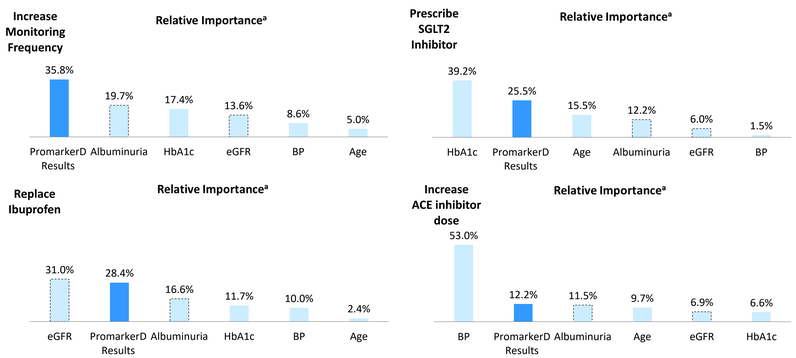
*In the analysis, the categories "decrease monitoring frequency" and "maintain standard monitoring frequency" of the monitoring frequency outcome variable were combined due to sparse data, as "decrease monitoring frequency" was selected as an option for only 5% of the patient profiles. Consequently, this monitoring outcome was analyzed as a binary variable (increase in monitoring frequency versus no increase in monitoring frequency).

- Data analysis was conducted with Sawtooth Software (Conjoint Value Analysis Module, version 3). A multivariable logit model for each outcome was used to analyze the impact of PromarkerD and other patient attributes on physician decision-making.
- Additionally, the survey included questions about current management of T2D patients and physicians' expected use of PromarkerD.

Results

- Four hundred physicians (203 PCPs; 197 endocrinologists) completed the survey.
- Sixty-three percent of endocrinologists (124/197) and 67% of PCPs (136/203) acknowledged the difficulty of using current tools to predict the progression of DKD, and 44% of endocrinologists (87/197) and 46% of PCPs (93/203) indicated predicting the onset of DKD in the near future for T2D patients is a challenge.
- Seventy-eight percent of physicians reported they are very or extremely likely to use PromarkerD.
- The conjoint analysis indicated that the PromarkerD test result was the most important attribute for the decision to increase the frequency of risk factor monitoring (Figure 1).
- PromarkerD was second to HbA1c for the decision to prescribe SGLT2 inhibitors with a DKD indication, second to eGFR for replacing ibuprofen with a non-nephrotoxic medication, and second to blood pressure (BP) for increasing the dose of lisinopril (ACE inhibitor) (Figure 1).

Figure 1. The relative importance of each attribute in influencing measured outcomes

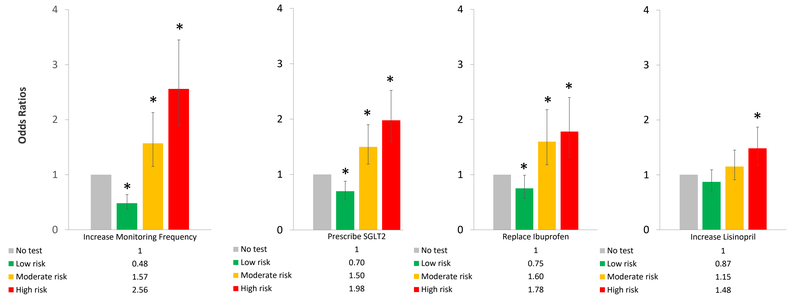


[a] While attribute importance values sum to 100% across attributes for each outcome assessed, percentages listed may not add to 100% as a result of rounding.

Results

- Compared with no PromarkerD test results, a high-risk PromarkerD result was associated with significantly higher odds of increasing monitoring frequency (odds ratio [OR]: 2.56, 95% confidence interval: 1.90-3.45), prescribing SGLT2 inhibitors (OR: 1.98 [1.56-2.52]), replacing ibuprofen (OR: 1.78 [1.32-2.40]), and increasing ACE inhibitors dose (OR: 1.48 [1.17-1.87]) (Figure 2).
- Compared with no PromarkerD test results, a moderate-risk PromarkerD result was also associated with significantly higher odds of increasing monitoring frequency (OR: 1.57 [1.15-2.13]), prescribing SGLT2 inhibitors (OR: 1.50 [1.19-1.90]), and replacing ibuprofen (OR: 1.60 [1.18-2.18]) (Figure 2).
- Compared with no PromarkerD test results, a low-risk PromarkerD result was associated with significantly lower odds of increasing monitoring frequency (OR: 0.48 [0.37-0.64]), prescribing SGLT2s (OR: 0.70 [0.56-0.88]), and replacing ibuprofen (OR: 0.75 [0.57-0.99]) (Figure 2).

Figure 2. Impact of PromarkerD test results on physician decision-making [a]



[a] Vertical lines represent the 95% confidence interval for the odds ratio estimates.
* Significant at α=0.05, compared to no PromarkerD test results.
"No test" was the reference level.

Conclusions

- The study suggests implementing PromarkerD testing would significantly impact physicians' prescribing and monitoring decisions for T2D patients.
- PromarkerD results were relatively more important to physicians than the current standard-of-care tests, eGFR and ACR (albuminuria) for three of four outcomes.
- PromarkerD could help inform T2D management decisions, with physicians viewing moderate- and high-risk PromarkerD results as expected to increase the likelihood of renoprotective changes in management of T2D patients at risk of DKD or rapid renal decline compared with no test results, while low-risk results were expected to lower the likelihood of aggressive treatment and health care resource utilization.
- Physician data from this study indicate PromarkerD could provide clinical utility in the management of DKD in patients with T2D and offer a cost-effective personalized approach to improving patient outcomes by earlier targeted treatment of those patients at highest risk of DKD.

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