eAppendix A. Net Reclassification from KDIGO Risk Strata to KidneyIntelX Risk Strata in Derivation and Validation Sample (Chan et al., 2021)\textsuperscript{11}

<table>
<thead>
<tr>
<th>Derivation Sample</th>
<th>KidneyIntelX Score</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>KDIGO Strata</td>
<td>Low</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Composite Kidney Event</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderately increased risk</td>
<td>15</td>
<td>35</td>
</tr>
<tr>
<td>High Risk</td>
<td>1</td>
<td>17</td>
</tr>
<tr>
<td>Very high risk</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Total events</td>
<td>17</td>
<td>57</td>
</tr>
<tr>
<td>No Kidney Event</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderately Increased Risk</td>
<td>198</td>
<td>126</td>
</tr>
<tr>
<td>High Risk</td>
<td>79</td>
<td>73</td>
</tr>
<tr>
<td>Very high risk</td>
<td>13</td>
<td>20</td>
</tr>
<tr>
<td>Total Non-Events</td>
<td>290</td>
<td>219</td>
</tr>
</tbody>
</table>

Reclassified – Derivation sample

<table>
<thead>
<tr>
<th>Event</th>
<th>Higher</th>
<th>Lower</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Event</td>
<td>83</td>
<td>60.6</td>
</tr>
<tr>
<td>Non-event</td>
<td>157</td>
<td>28.6</td>
</tr>
</tbody>
</table>

Validation Sample

<table>
<thead>
<tr>
<th>KDIGO Strata</th>
<th>KidneyIntelX Score</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Intermediate</td>
<td>High</td>
</tr>
<tr>
<td>Composite Kidney Event</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderately increased risk</td>
<td>14</td>
<td>21</td>
</tr>
<tr>
<td>High Risk</td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td>Very high risk</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Total events</td>
<td>20</td>
<td>37</td>
</tr>
<tr>
<td>No Kidney Event</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderately Increased Risk</td>
<td>132</td>
<td>80</td>
</tr>
<tr>
<td>High Risk</td>
<td>53</td>
<td>39</td>
</tr>
<tr>
<td>Very high risk</td>
<td>7</td>
<td>16</td>
</tr>
<tr>
<td>Total Non-Events</td>
<td>192</td>
<td>135</td>
</tr>
</tbody>
</table>

Reclassified – Validation sample

<table>
<thead>
<tr>
<th>Event</th>
<th>Higher</th>
<th>Lower</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Event</td>
<td>53</td>
<td>51.0</td>
</tr>
<tr>
<td>Non-event</td>
<td>104</td>
<td>29.2</td>
</tr>
</tbody>
</table>
## eAppendix B. KidneyIntelX treatment and management recommendations by risk result

<table>
<thead>
<tr>
<th>Recommendations by Test X Risk Result</th>
<th>Low</th>
<th>Intermediate</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>• Monitor 1x/year&lt;br&gt;• Maintain current level of treatment with ACEi/ARBs, antihypertensives, and anti-hyperglycemic agents</td>
<td>• Monitor 2x/year&lt;br&gt;• Medication intensification:&lt;br&gt;  o Treat with ACEi or ARB and anti-hypertensives&lt;br&gt;  o Consider SGLT2 inhibitors (if clinically indicated)</td>
<td>• Monitor 3x/year&lt;br&gt;• Medication intensification:&lt;br&gt;  o Titrate ACEi or ARBs to maximally tolerated dose&lt;br&gt;  o Strongly consider SGLT2 inhibitors (unless contraindicated)&lt;br&gt;  • Refer patient to nephrologist</td>
</tr>
</tbody>
</table>
eAppendix C. Screener and Survey Questions

**SCREENER**

i. What is your main specialty? [Randomize]
   - a. Family medicine physician [CONTINUE]
   - b. Primary care/INTERNAL medicine physician [CONTINUE]
   - c. Diabetologist
   - d. Endocrinologist
   - e. Gastroenterologist
   - f. Urologist
   - g. None of the above [Exclusive, Anchor] [TERMINATE IMMEDIATELY]

ii. Are you board-certified in your specialty?
   - a. Yes [CONTINUE]
   - b. No [TERMINATE at end of screener]

iii. Approximately how many type 2 diabetes patients have you seen in the past 6 months?
   - ___________ type 2 diabetes patient(s) in the past 6 months
   - [RANGE for text box 0 – 99,999. No decimals] [TERMINATE at end of screener IF 0-20] Error message: please provide a number between 0 and 99,999

iv. [If question iii is >0] Approximately how many type 2 diabetes patients have you **tested for indications of kidney disease** in the past 6 months?
   - I have tested ___________ type 2 diabetes patient(s) for indications of kidney disease in the past 6 months
   - [RANGE for text box 0 – value provided in prior question. No decimals] [TERMINATE at end of screener IF 0-10] Error message: Please provide a number no greater than [fill in prior response], the number of type 2 diabetes patients you saw in the past 6 months

v. [If question iii >0] Approximately what percentage of your type 2 diabetes patients have **diabetic kidney disease (DKD)?**
   - _________% of my type 2 diabetes patients have DKD
   - [RANGE for text box 0 – 100. No decimals] [TERMINATE at end of screener IF 0] [Error message: please provide a number between 0 and 100]

vi. Approximately how long have you been practicing in your current specialty?
   - ___________ year(s) [TERMINATE at end of screener IF <2] [RANGE for text box 0 – 99; no decimals]

vii. In what setting of care do you treat **the majority** of your patients? **Select only one** response. [Randomize]
    - a. Office-Based Private Practice [CONTINUE]
    - b. Community Hospital [CONTINUE]
    - c. Academic Medical Center [CONTINUE]

viii. Approximately what percentage of your time is spent performing direct clinical care (versus administrative duties)?
   - _____% of my time is spent performing direct clinical care
   - [Range for text box: 0-100; no decimals]
   - IF clinical care ≥50% [CONTINUE]
   - IF clinical care ≥0% and <50% [TERMINATE AT END OF SCREENER]

ix. In which state is your practice located? [No hard quotas, but range of responses desired.]
a. Alabama  
b. Alaska  
c. Arizona  
d. Arkansas  
e. California  
f. Colorado  
g. Connecticut  
h. Delaware  
i. District of Columbia  
j. Florida  
k. Georgia  
l. Hawaii  
m. Idaho  
n. Illinois  
o. Indiana  
p. Iowa  
q. Kansas  
r. Kentucky  
s. Louisiana  
t. Maine  END IMMEDIATELY (because of restrictive market research rules in this state)  
u. Maryland  
v. Massachusetts  
w. Michigan  
x. Minnesota  
y. Mississippi  
z. Missouri  
aa. Montana  
bb. Nebraska  
cc. Nevada  
 dd. New Hampshire  
ees. New Jersey  
ff. New Mexico  
gg. New York  
hh. North Carolina  
ii. North Dakota  
jj. Ohio  
kk. Oklahoma  
ll. Oregon  
mm. Pennsylvania  
nn. Rhode Island  
oo. South Carolina  
pp. South Dakota  
qq. Tennessee  
rr. Texas  
ss. Utah  
tt. Vermont END IMMEDIATELY (because of restrictive market research rules in this state)  
 uu. Virginia  
 vv. Washington  
ww. West Virginia  
xx. Wisconsin  
 yy. Wyoming

Target regions for programmer to create:
-Northeast (CT, ME, MA, NH, NJ, NY, PA, RI, VT)
-Midwest (IL, IN, IA, KS, MI, MN, MO, NE, ND, OH, SD, WI)
WELCOME

The purpose of this survey is to obtain your insights on a test that assesses the risk of progressive decline in kidney function in patients with diabetic kidney disease (DKD).

The survey is confidential and should take about 15 minutes. We combine all answers we receive to help us understand clinicians’ overall perspectives. We recommend you finish the survey in one sitting. If you are unable to complete the survey in one sitting, you may save your work and return at any time. Once you have completed the study, please allow time for us to process your incentive. You must fully complete the survey to receive the incentive.

Please do NOT use the arrow in your browser to return to a previous page in the survey. (Using this arrow may prevent you from completing the survey.)

Thank you for your time and opinions!

SURVEY

Diabetic Kidney Disease Care Pathway

1. Please estimate the percentage of your type 2 diabetes patients with DKD who have the following types of health insurance. (The total must equal 100%.) [Allowable answers 0-100; no decimals]
   a. _____ % Private payer/commercial plans
   b. _____ % Medicare
   c. _____ % Medicaid
   d. _____ % VA/DOD/Military (e.g. Tricare)
   e. _____ % Other insurance
   f. _____ % Self-pay/uninsured
   g. I don’t know [exclusive]

2. Which test(s) do you conduct/request for your type 2 diabetes patients with DKD? Select all that apply. [Randomize]
   a. eGFR
   b. Urine albumin-to-creatinine ratio/Albuminuria/Microalbumin
   c. Blood urea nitrogen
   d. HbA1c
   e. Blood pressure
   f. Other _____ [Anchor, show text box]

For your reference, the stages of DKD are outlined below:

<table>
<thead>
<tr>
<th>Stages</th>
<th>GFR Descriptions</th>
<th>eGFR range (ml/min per 1.73m²)</th>
<th>Albuminuria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>Normal or high</td>
<td>$\geq 90$</td>
<td>Moderately or severely increased</td>
</tr>
<tr>
<td>Stage 2</td>
<td>Mildly decreased</td>
<td>60-89</td>
<td></td>
</tr>
<tr>
<td>Stage 3a</td>
<td>Mildly to moderately decreased</td>
<td>45-59</td>
<td>Any level</td>
</tr>
<tr>
<td>Stage</td>
<td>Description</td>
<td>Value</td>
<td></td>
</tr>
<tr>
<td>----------</td>
<td>-------------------------</td>
<td>-------</td>
<td></td>
</tr>
<tr>
<td>Stage 3b</td>
<td>Moderately to severely decreased</td>
<td>30-44</td>
<td></td>
</tr>
<tr>
<td>Stage 4</td>
<td>Severely decreased</td>
<td>15-29</td>
<td></td>
</tr>
<tr>
<td>Stage 5</td>
<td>Kidney failure</td>
<td>&lt;15</td>
<td></td>
</tr>
</tbody>
</table>

Please consider your type 2 diabetes patients with DKD.

What is the percent distribution by stage at DKD diagnosis? Note total must add to 100%.

a. Stage 1 _____ %  
b. Stage 2 _____ %  
c. Stage 3a _____ %  
d. Stage 3b _____ %  
e. Stage 4 _____ %  
f. Stage 5 _____ %  

=100%  

[Whole numbers only 0-100, no decimals] [Show running total] [% should add up to 100%.]  

3. Overall, how satisfied are you with current tests/methods for assessing a type 2 diabetes patient’s risk for kidney function decline on a scale of 1 to 5, where 1 is “extremely dissatisfied” and 5 is “extremely satisfied”?

[Radio buttons provided]  

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extremely dissatisfied</td>
<td>Somewhat dissatisfied</td>
<td>Neither satisfied nor dissatisfied</td>
<td>Somewhat satisfied</td>
<td>Extremely satisfied</td>
</tr>
</tbody>
</table>

4. What are the diagnostic challenges pertaining to DKD in type 2 diabetes patients? Select all that apply.

[Randomize]  
a. No test is available to predict accurately whether the patient will develop kidney function decline before clinical symptoms appear  
b. Difficult to detect existing diabetic kidney disease in early stages (e.g., at stage 1 and 2)  
c. No test to clearly identify what stage of DKD the patient is in  
d. Other _____ [Anchor, show text box]  
e. None of the above [Anchor; exclusive]  

5. At what point would you typically refer a type 2 diabetes patient to a nephrologist, if at all?

a. At diagnosis of type 2 diabetes  
b. At diagnosis of DKD, irrespective of the stage at diagnosis  
c. When the patient is in early-stage DKD (eGFR levels >59)  
d. When the patient is in mid-stage DKD (eGFR levels 30-59)  
e. Upon progression to late-stage DKD (eGFR levels <30)  
f. I do not refer to a nephrologist  
g. Other _____ [show text box]
6. What would be the primary clinical benefits of accurately assessing the risk of **progressive decline in kidney function** in type 2 diabetes patients with DKD, if any? Select all that apply. [Randomize]
   a. Higher-risk patients could receive aggressive clinical action early
   b. Higher-risk patients with comorbid conditions could avoid drugs that might cause further kidney damage
   c. Higher-risk patients could be monitored more frequently
   d. Lower-risk patients could be managed without intervention from a nephrologist
   e. Other _____ [Anchor, show text box]

7. For the next set of questions, please assume you have tools at your disposal that allow you to determine the risk of **progressive decline in kidney function** in type 2 diabetes patients with DKD.

   How would you treat most type 2 diabetes patients in early stages (1-3) of DKD who are considered to be at **low risk of progressive decline in kidney function**, specifically with respect to their diabetes medications? Select all that apply.
   a. Metformin
   b. Meglitinides (e.g., nateglinide)
   c. Thiazolidinediones (e.g., pioglitazone)
   d. DPP4 inhibitors (e.g., sitagliptin)
   e. Sulfonylureas (e.g., glipizide)
   f. GLP1-RAs (e.g., exenatide)
   g. SGLT2 inhibitors (e.g., canagliflozin)
   h. Alpha-glucosidase inhibitors (e.g., acarbose)
   i. Insulin
   j. None of the above [exclusive]

8. How would you treat type 2 diabetes patients in the early stages (1-3) of DKD once they are identified as being at **increased risk of progressive decline in kidney function**, specifically with respect to their diabetes medications? [If 9a is visible] Select all that apply.
   a. [Show if prior question is not “none of the above” (8j)] I would increase the dose of current diabetes medications to maximum tolerated
   b. [Show if respondent did not select “SGLT2 inhibitors” in prior question (8g)] I would start SGLT2 inhibitor
   c. [Show if respondent did select “SGLT2 inhibitors” in prior question (8g)] I would increase/optimize dose of SGLT2 inhibitor
   d. I would not recommend the treatment option(s) described [Anchor, exclusive]

9. How would you treat most type 2 diabetes patients in the early stages (1-3) of DKD who are considered to be at **low risk of progressive decline in kidney function**, specifically with respect to their blood pressure medications? Select all that apply. [Randomize]
   a. ACE/ARB inhibitors
   b. Thiazide diuretics
   c. Mineralocorticoid Receptor Antagonists (MRAs) (e.g., eplerenone)
   d. Calcium channel blockers
   e. Beta blockers
   f. None of the above [Anchor, exclusive]

10. How would you treat type 2 diabetes patients in the early stages (1-3) of DKD once they are identified as being at **increased risk of progressive decline in kidney function**, specifically with respect to their blood pressure medications? Select all that apply. [Randomize]
a. [Show if ACE/ARB selected in prior question] Increase ACE/ARB inhibitor dose (if not already at the maximum tolerated dose)

b. [Show if ACE/ARB not selected in prior question] Start ACE/ARB inhibitor

c. [Show if at least one of the following (thiazide diuretics, selective MRAs, calcium channel blockers, beta blockers) was selected in prior question] Increase dose of other blood pressure medications other than ACE/ARB inhibitors

d. [Show if not one of the following were selected: (thiazide diuretics or selective MRAs or calcium channel blockers or beta blockers) was selected in prior question] Start thiazide diuretics, selective MRAs, calcium channel blockers, or beta blockers

e. None of the above [Anchor, exclusive]

11. About what percentage of your type 2 diabetes patients in the early-to-mid stages of DKD (eGFR ≥30) follow the treatment protocol you recommend for managing DKD? ________% of patients [Whole numbers only 0-100, no decimals]

Adoption of Test X

Please review the information about diabetic kidney disease and Test X.

As you continue taking the survey, you will be able to click on a link to refer back to this test description. (If you do click on the link to view the test description again, you can return to the survey questions by clicking on the “X” at the top right of the test description.) [Show profile, including background.]

[Present subsequent questions about Test X through the conjoint with a link to description of Test X (test description only (pages 2 and 3), not background). Questions after the conjoint do not need this link.]

12. [New page] For the remainder of the survey, please assume the following unless otherwise specified:

- Test X is commercially available and has been FDA-cleared.
- The cost of Test X is not an issue for you or your patients.

On a scale of 1-5, where 1 is “not at all likely” and 5 is “extremely likely”, what is your likelihood of ordering this test for predicting the risk of progressive decline in kidney function in your patients with type 2 diabetes with DKD?

[Radio buttons provided]

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Not at all likely</td>
<td>Not very likely</td>
<td>Somewhat likely</td>
<td>Very likely</td>
<td>Extremely likely</td>
</tr>
</tbody>
</table>

13. For what percentage of your type 2 diabetes patients with DKD would you order Test X in a typical year? ______ % [Whole number 0-100 only, no decimals]

14. [If test use (q14) > 0% AND if more than 1 stage in q3 shows a value >0] Please indicate the distribution, by stage, of the type 2 diabetes patients with DKD for whom you would you use Test X. The total must equal 100%.

[Values 0-100 allowed, no decimals. Total must =100] [Show running total]

a. [Show if q3a>0] Stage 1 (normal or high GFR and moderately or severely increased albuminuria) ______ %

b. [Show if q3b>0] Stage 2 (mildly decreased GFR and moderately or severely increased albuminuria) ______ %
c. \[\text{Show if } q3c>0\] Stage 3a (mildly-to-moderately decreased GFR, regardless of albuminuria level) _____%  
d. \[\text{Show if } q3d>0\] Stage 3b (moderately-to-severely decreased GFR, regardless of albuminuria level) _____% 
\[=100\% \text{ or}\]
e. I don’t know [Exclusive]

Conjoint Analysis

Current Practice Patterns and Clinical Positioning [Aim: Understand the influence of specific risk factors on clinician decision-making]

It is advisable and preferred that you finish the rest of the survey in one sitting if possible.

15. [new page] For the following questions you will be presented with hypothetical profiles of type 2 diabetes patients with DKD. You will be asked about your clinical recommendations based on descriptions of the following risk factors: eGFR, albuminuria, HbA1c, age, and blood pressure, as well as the results of Test X, where applicable.

Please assume the following:
- The cost of Test X is not an issue for you and your patients
- Test X is commercially available and has been FDA-cleared
- Your practice has adopted Test X
- Patients have not been consulting a nephrologist
- Patients have normal potassium levels

Please pay close attention and answer as you believe you would act in clinical practice. This will help ensure the test is optimized for the patients where it is needed most.

- You will see 8 screens with 1 patient per screen.

You will be able to click on the link to refer back to the test description as necessary. (If you do click on the link to view the test description again, you can return to the survey questions by clicking on the “X” at the top right of the test description.)

[new page and keep this text here until all questions under this section have been answered]

[For patient 1] You will be asked 3 clinical decision questions about the patient on this page.

For this type 2 diabetes patient with DKD and for all patients presented on subsequent pages, please assume the following:

The patients
- Have been receiving 1000 mg of metformin twice a day
- Have been receiving 50 mg of losartan per day
- Have no contraindications to or higher-than-average risk of side-effects from SGLT2 inhibitors or ACE inhibitors

[For patients 2-8]
You will be asked 3 clinical decision questions about the new patient on this page.

(For your reference, the “Recommendations by Test X Risk Result” table you have already seen is presented again below.) If needed, you can also click on the link below to review the patient assumptions that apply to all patients in this exercise. [Show link to the paragraph above starting “The patients’”]

<table>
<thead>
<tr>
<th>Recommendations by Test X Risk Result</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low</strong></td>
</tr>
<tr>
<td>• Monitor 1x/year</td>
</tr>
<tr>
<td>• Maintain current level of treatment with ACEi/ARBs, antihypertensives, and antihyperglycemic agents</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albuminuria</td>
</tr>
<tr>
<td>Glycemic control (HbA1c)</td>
</tr>
</tbody>
</table>

[1]

Based on the clinical data provided, would you:

- □ Prescribe SGLT2s that have a DKD indication
- □ Not prescribe SGLT2s that have a DKD indication

[2]

Based on the clinical data provided, would you:

- □ Increase losartan dose to 100 mg per day
- □ Continue losartan dose of 50 mg per day

[3]

Based on the clinical data provided, would you:

- □ Refer to a nephrologist
- □ Not refer to a nephrologist
“You have answered questions about 4 patients and are halfway through this patient treatment exercise. We understand that these questions can be a bit tedious, but please pay close attention and answer as you believe you would act in clinical practice.”

**Reaction to Test X**

16. What are the benefits of Test X, if any? Select all that apply. [Randomize]
   a. Test X’s positive predictive value (i.e., ability to avoid false positives) is 69%
   b. Test X’s negative predictive value (i.e., ability to avoid false negatives) is 93%
   c. Test X has a fast turnaround time (7 days)
   d. Test X can serve as motivation for patients to make lifestyle changes
   e. Test X can increase patient compliance with treatment recommendations
   f. Test X can rule out patients at low risk of progressive decline in kidney function
   g. Test X can inform treatment changes for diabetes and hypertension
   h. Test X can improve clinical outcomes in DKD patients through appropriate therapeutic interventions
   i. Test X can save health care costs by reducing inappropriate treatment and/or DKD progression, dialysis, and kidney transplants
   j. Other ______ [Anchor, show text box]
   k. None of the above [anchor; exclusive]

17. What are the limitations of Test X, if any? Select all that apply. [Randomize]
   a. Test X requires a blood draw
   b. [Do not show if q17=a] Test X’s positive predictive value (i.e., ability to avoid false positives) is 69%, which is not high enough
   c. [Do not show if q17=b] Test X’s negative predictive value (i.e., ability to avoid false negatives) is 93%, which is not high enough
   d. [Do not show if q17=c] Test X has a slow turnaround time (7 days)
   e. I am concerned about the potentially high cost or lack of coverage of Test X
   f. Test X is not included in guidelines
   g. Patient data such as UACR, eGFR, serum calcium, HbA1c, systolic blood pressure, platelets, and AST are needed as an input for the Test X algorithm
   h. Test X is not included in guidelines
   i. Test X might not change patient management
   j. I am skeptical of artificial intelligence
   k. Other ______ [Anchor, show text box]
   l. None of the above [anchor; exclusive]

18. [If concerned about turnaround time q18d] What is the maximum acceptable turnaround time for you to order Test X? [Show error message “The maximum turnaround time must be less than 7 days.”]
   a. _____ Day(s) [must be less than 7; 1 decimal allowed]

19. [If test use q14 > 0%] How often do you expect you would you re-test type 2 diabetes patients with DKD who have the following results with Test X (assuming the cost of Test X is not an issue for you and your patients)? [values from >0 to 99. One decimal allowed]
   a. Low risk result: Every _____ month(s) [Show error message if low risk result number is not smaller than the intermediate and high risk result numbers]
b. Intermediate risk result: Every _____ month(s) [Show error message if intermediate risk result number is not smaller than high risk result number]

c. High risk result: Every _____ month(s)

d. I don’t know [Exclusive]

Follow-up

20. [Optional] If you have any additional comments about Test X or your experience taking this survey, please let us know.

____________ [Show text box]

[Show on same page as above.] Thank you for your time and thoughtfulness in responding to our survey.
Diabetic Kidney Disease (DKD) Background

The Problem

Current Methods of DKD Diagnosis and Assessment of Risk of Kidney Function Decline

DKD is currently diagnosed and monitored through two primary methods recommended in the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines:

- **Albuminuria Measurement**
  Measures the extent of albumin elevation through Albumin to Creatinine ratio (ACR)

- **Estimated Glomerular Filtration Rate (eGFR)**
  eGFR is a formula comprised of: Serum creatinine level, age, sex, and race

These tests fail to accurately identify up to 50% of patients with DKD who will experience progressive decline in kidney function in the future

Outcomes

- DKD progression can lead to adverse outcomes, including cardiovascular events, and increased costs at each stage
- Unmanaged DKD can ultimately lead to end stage kidney disease (ESKD), which requires dialysis or a kidney transplant
- DKD patients in any stage can progress to dialysis if their DKD is not appropriately managed
**Test X: Artificial Intelligence (AI) In Vitro Kidney Diagnostic**

**Test X Description**
- Validated blood-based protein biomarkers (sTNFR-1, sTNFR-2, and KIM-1) from a standard blood draw.
- Personalized patient data (eGFR, UACR, serum calcium, HbA1c, systolic blood pressure, platelets, and AST) from the electronic health record (EHR).
- An artificial intelligence-enabled algorithm to stratify patients as high, intermediate, or low risk for progressive decline in kidney function including end stage kidney disease (ESKD).

**Target Population**
- Type 2 diabetes patients with DKD (Stages 1-3b, excluding G1&A1 and G2&A1).

<table>
<thead>
<tr>
<th>Target Population</th>
<th>GFR stages, descriptions, and range (mL/min per 1.73m²)</th>
<th>Albuminuria stages, descriptions, and range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1 (G1)</td>
<td>Normal or high</td>
<td>≤30</td>
</tr>
<tr>
<td>Stage 2 (G2)</td>
<td>Mildly decreased</td>
<td>30-90 mg/g</td>
</tr>
<tr>
<td>Stage 3 (G3a)</td>
<td>Mildly to moderately decreased</td>
<td>&gt;90 mg/g</td>
</tr>
<tr>
<td>Stage 3 (G3b)</td>
<td>Moderately to severely decreased</td>
<td>≤30 mg/g</td>
</tr>
<tr>
<td>Stage 4 (G4)</td>
<td>Severely decreased</td>
<td>&gt;30 mg/g</td>
</tr>
<tr>
<td>Stage 5 (G5)</td>
<td>Kidney failure</td>
<td>&lt;15</td>
</tr>
</tbody>
</table>

**Turnaround Time**
- 7 days

**Value Proposition**
- Delays/prevents progression to ESKD through more accurate assessment of risk of progressive decline in kidney function and earlier use of medical interventions proven to slow progression.
  - Identifies high-risk DKD patients who are candidates for early, more aggressive clinical action and preventive measures.
  - Allows low-risk DKD patients to be managed at primary care level.
  - Maximizes patient compliance by educating patients and clinicians.
Test X Delivers Actionable Assessment of the Risk of Kidney Function Decline

**Test X Validation Study Results**

- **93% negative predictive value (NPV)** for progression in patients scored as low-risk with test X versus 85% with Standard Risk Scoring based on KDIGO
  - In other words, **low scoring patients have a 93% chance of not experiencing progression** within 5 years

- **69% positive predictive value (PPV)** for progression in patients scored as high-risk by test X versus 40% with Standard Risk Scoring based on KDIGO
  - In other words, **high scoring patients have a 69% chance of experiencing progression** within 5 years

- **High scoring patients** are **10 times more likely to experience progression of DKD** than low-risk patients

**A Holistic Approach Based on Risk-specific Recommendations**

**Test X Score**

- The test score ranges from 0 (lowest risk) to 100 (highest risk) and correlates with the probability of progressive decline in kidney function in the tested population

**Low score recommendations:**

- Monitor 1x/year
- Maintain current level of treatment with ACEi/ARBs, antihypertensives, and anti-hyperglycemic agents

**Intermediate score recommendations:**

- Monitor 2x/year
- Medication intensification:
  - Treat with ACEi or ARB and anti-hypertensives
  - Consider SGLT2 inhibitors (if clinically indicated)

**High score recommendations:**

- Monitor 3x/year
- Medication intensification:
  - Titrate ACEi or ARBs to maximally tolerated dose
  - Strongly consider SGLT2 inhibitors (unless contraindicated)
- Refer patient to nephrologist
eAppendix E. Sample Attrition

Attrition of respondents from outreach to final survey is presented. A total of 6,104 invitations were sent out. 8.8% of the physicians who received the invitations entered the survey, and 401 of those (74.2%) qualified and completed the survey.

PCP = Primary care physicians
**eAppendix F. Table Study population characteristics (N=401)**

<table>
<thead>
<tr>
<th>Provider/ Practice Variables</th>
<th>Respondents</th>
<th>Percentage (%)&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Specialty</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family Medicine</td>
<td>146</td>
<td>64%</td>
</tr>
<tr>
<td>Primary Care/ Internal Medicine</td>
<td>255</td>
<td>36%</td>
</tr>
<tr>
<td><strong>Settings of Care</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Office-Based Private Practice</td>
<td>284</td>
<td>71%</td>
</tr>
<tr>
<td>Community Hospital</td>
<td>66</td>
<td>16%</td>
</tr>
<tr>
<td>Academic Medical Center</td>
<td>51</td>
<td>13%</td>
</tr>
<tr>
<td><strong>Geographic Distribution</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Midwest</td>
<td>100</td>
<td>25%</td>
</tr>
<tr>
<td>Northeast</td>
<td>85</td>
<td>21%</td>
</tr>
<tr>
<td>South</td>
<td>125</td>
<td>31%</td>
</tr>
<tr>
<td>West</td>
<td>91</td>
<td>23%</td>
</tr>
</tbody>
</table>

<sup>a</sup>Percentages may not add to 100% as a result of rounding