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Evaluation of Payer Budget Impact Associated with the Use of an Artificial Intelligence *In Vitro* Kidney Diagnostic to Modify DKD Progression

Abstract # 479
National Kidney Foundation® 2020 Spring Clinical Meetings

Agenda and Disclosures

Agenda

- Background and Aim of our Study
- Methods
- Key Results
- Conclusions

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Background and Aim of Study

Diabetic Kidney Disease can progressively lead to poor health outcomes and increased costs if timely interventions are not employed

Background:

- It is estimated that 15% (~37 million) of US adults have Chronic kidney disease (CKD)[1]
- Over 30% of patients with CKD (~12 million) have type 2 diabetes (T2DM) and existing kidney disease (referred to as diabetic kidney disease or DKD)
- DKD accounts for ~50% of patients who will experience rapid kidney function decline (RKFD) and are at the highest risk for progressing to end-stage renal disease (ESRD) requiring dialysis and kidney transplants[2]
- DKD and ESRD costs in the United States Medicare system alone are estimated to exceed $114 billion annually[4]

Unmet Need:

- The current method for DKD risk stratification fails to identify ~50% of patients who will have RKFD
- Up to 63% of existing DKD patients initiate dialysis acutely due to a “crash”[3]
- Many high-risk patients are not referred from their Primary Care Physician (PCP) or Endocrinologist to a Nephrologist and do not undergo the necessary treatment changes that are proven to delay DKD progression to ESRD[3]
- There is an important need for a predictive tool that can assess the risk of developing DKD before substantial damage occurs

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3. Mendelssohn DC, Curtis B, Yeates K, et al. Suboptimal initiation of dialysis with and without early referral to a nephrologist. Nephrol Dial Transplant. 2011;26:2959–65. doi
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The Artificial Intelligence *In Vitro* Kidney Diagnostic (AIKD) Solution

The test is an artificial intelligence-enabled clinical diagnostic that uses an advanced machine learning algorithm to generate a patient-specific score for assessing the five-year risk of RKFD or kidney failure in DKD patients

- Analyzes biomarkers and electronic health record (EHR) features to categorize patients as low, intermediate or high risk of developing DKD
- Currently indicated in patients with T2DM and DKD stages 1-3b (excluding G1&A1 and G2&A1)
- Has been granted Breakthrough Device designation by the US Food and Drug Administration (FDA)

CKD Staging based on Kidney Disease Improving Global Outcomes (KDIGO) Guidelines

Targets ambiguous area of clinical decision making & treatment in Stages 1, 2, 3

				Albuminuria stages, description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<3 mg/mmol	3-29 mg/mmol	≥30 mg/mmol
GFR stages, descriptions and range (ml/min per 1.73m²)	Stage 1 (G1)	Normal or high	≥90			
	Stage 2 (G2)	Mildly decreased	60-90			
	Stage 3 (G3a)	Mildly to moderately decreased	45-59			
	Stage 3 (G3b)	Moderately to severely decreased	30-44			
	Stage 4 (G4)	Severely decreased	15-29			
	Stage 5 (G5)	Kidney failure	<15			

~25 million U.S. patients fall into the AIKD intended use population[1]

$42 billion per year currently spent by Medicare on this population

1. Based on Company analysis.

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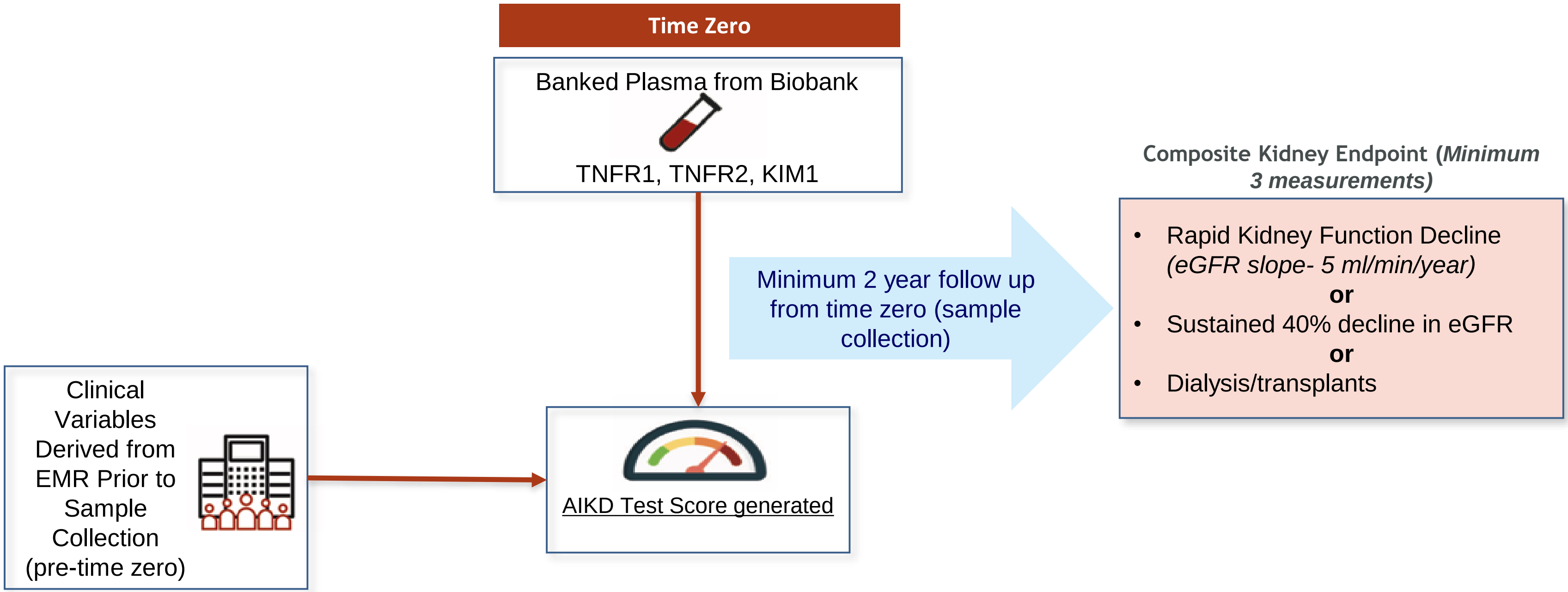
AIKD Score Generation from Mount Sinai and UPenn Biobanks



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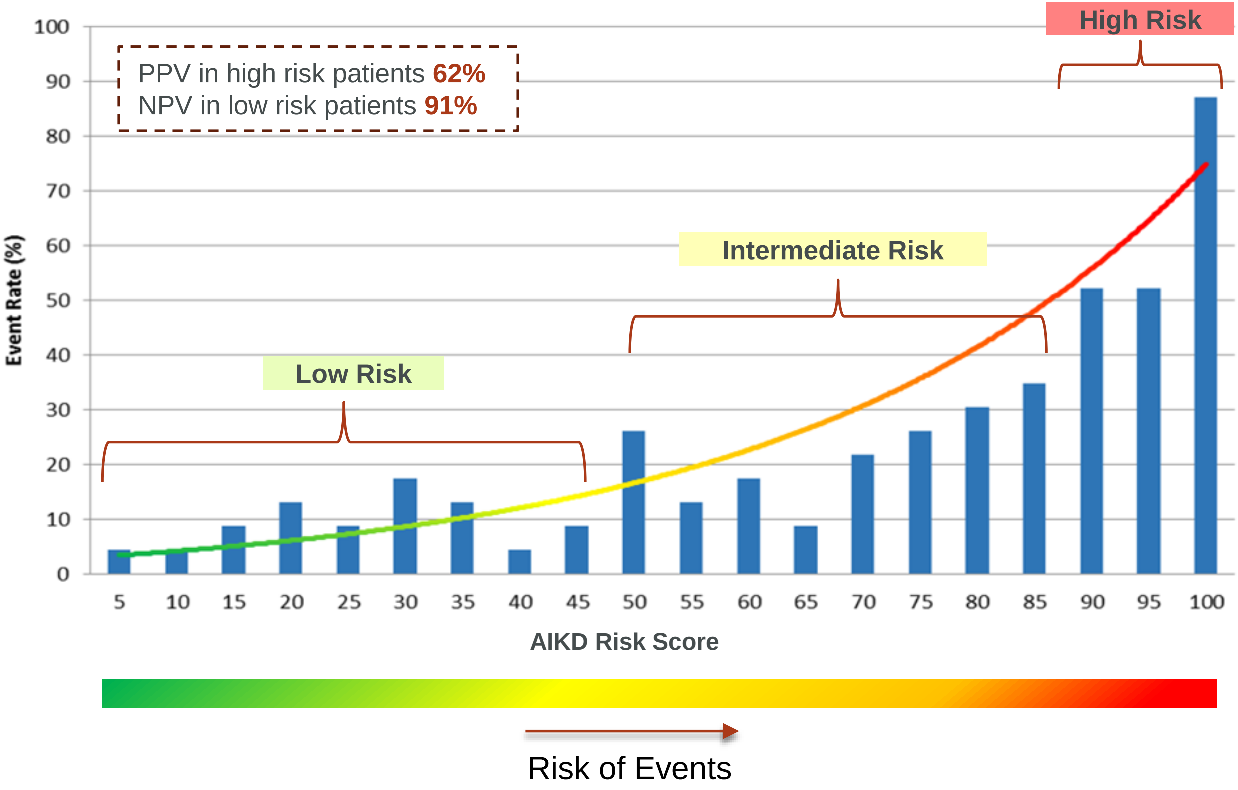
Probability of the composite kidney endpoint by quantile of the AIKD score in validation study



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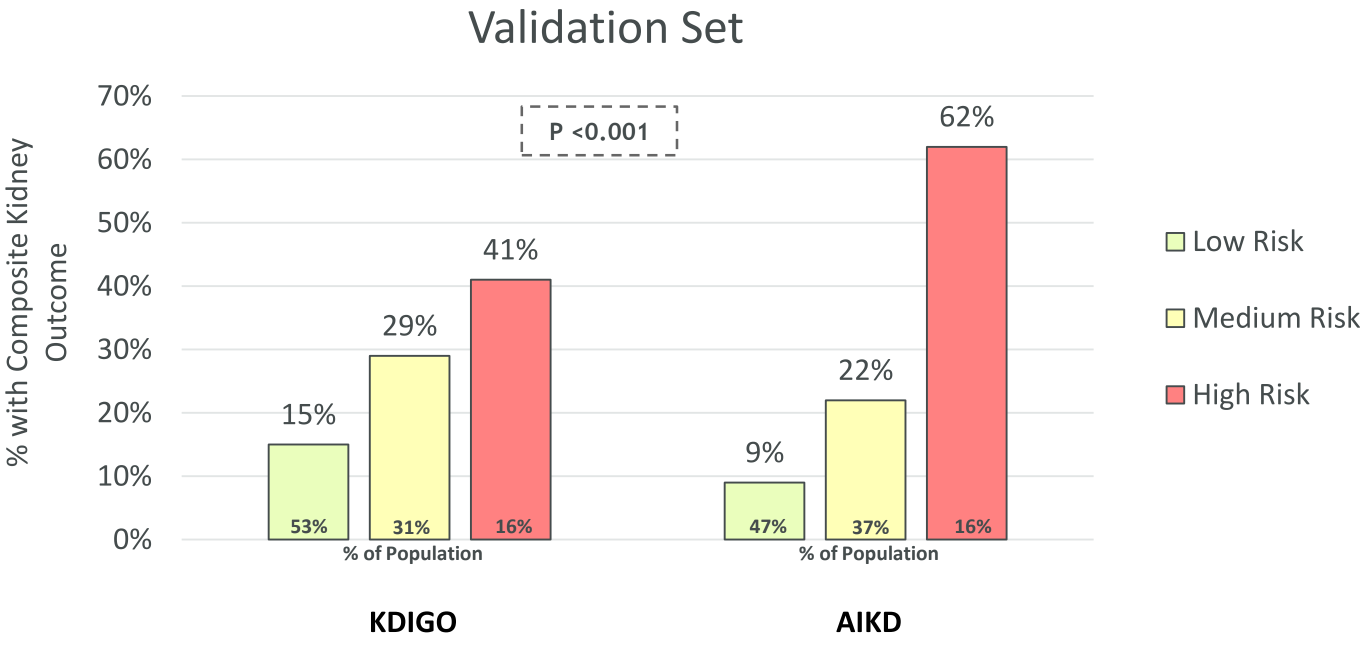
Kidney event rates for KDIGO strata vs. AIKD Stratification



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Recommendations for care management associated with risk categories are stratified by the AIKD score and align with published KDIGO guideline recommendations

KDIGO Guideline Recommendations

- *High risk patients:* >60% risk of RKFD or kidney failure in 5 years; should be considered for more intensive therapy and/or referral to a nephrologist and aggressive medical management
- *Intermediate risk patients:* Risk of progression is at population level (≈20%); can be considered for PCP or endocrinologist monitoring 2 to 3 times per year
- *Low risk patients:* < 10% progress over 5 years; can be considered for monitoring by their PCP or endocrinologist on at least an annual basis

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The goal of this study is to develop a 5-year payer budget-impact model to assess potential cost impact associated with the AIKD

Specific objectives of this study are as follows:

1. Identify incremental costs to payers associated with the AIKD implementation [compared to standard-of-care(SOC)]
2. Identify incremental benefit from the use of the AIKD (compared to SOC) and monetize this benefit
3. Calculate savings associated with the AIKD use

Three core areas for benefits achieved through the use of the AIKD

- **Slowed progression through DKD stages**
- **Delayed or prevented dialysis and transplants**
- **Reduction in dialysis crashes**

A hypothetical cohort of 100,000 patients with T2DM and DKD stages 1-3b (excluding stages G1&A1 and G2&A1) was modeled for up to 5 years

Savings in the 3 core areas were calculated and added together to calculate total savings

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Methods

AIKD Target Population and Movement Through DKD Stages

- **The model uses population distribution data from the literature to place patients in various stages of DKD[1]**
- **This is the distribution of patients assumed at T0**
- **Progression rate data for SOC was obtained from the AIKD validation studies. A sensitivity analysis was conducted using three different definitions of 'progression' to the next DKD stage**
  - ***Least Stringent****:* ≥1 eGFR value(s) in the next stage
  - ***Stringent****:* ≥2 eGFR values 3 months apart in next stage
  - ***Most Stringent****:* ≥2 eGFR values 3 months apart in the next stage, only in the 21% of patients that ultimately experienced RKFD or kidney failure (79% stable)

Thus, in the least stringent definition of progression, more patients were assumed to progress through DKD stages, resulting in more potential cost savings compared to the most stringent definition

Distribution of patients into DKD stages[1]

Stage	Number of patients
Total Target Patients, DKD Stage 1 (Excluding A1)	28,235
Total Target Patients, DKD Stage 2 (Excluding A1)	25,294
Total Target Patients, DKD Stage 3a	30,588
Total Target Patients, DKD Stage 3b	15,882
Total	**100,000**

Cumulative progression rates for movement through the stages by year (SOC)

Movement through stages	Year 1	Year 2	Year 3	Year 4	Year 5
1 (excluding A1) --> 2 (excluding A1)	54.0%	63.0%	69.0%	72.0%	72.8%
2 (excluding A1) --> 3a	34.0%	44.0%	49.0%	51.0%	51.7%
3a ---> 3b	38.0%	48.0%	51.0%	52.0%	52.9%
3b ---> 4	26.0%	34.0%	39.0%	40.0%	41.4%
4 ---> 5	13.0%	25.0%	29.0%	33.0%	33.7%
5 ---> Dialysis	50.0%	55.0%	60.0%	65.0%	70.0%

1. Wang T, Xi Y, Lubwama R, Hannanchi H, Iglay K, Koro C: Chronic kidney disease among US adults with type 2 diabetes and cardiovascular diseases: A national estimate of prevalence by KDIGO classification. Diabetes Metab Syndr. 2019;13:612–615.

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Impact of the AIKD and other assumptions

The model assumes the following benefit associated with the AIKD patients compared to SOC:

- 20% slowed progression rate through DKD stages upon using the AIKD compared to SOC was assumed (A sensitivity analysis was conducted by varying the rate of delayed progression between 5% and 35%). This was the base-case scenario for all analyses
- Of the 100,000 patients tested with AIKD, 16% patients were assumed to have a high-risk test result[1]

Other Assumptions:

- Since this was a 5-year model, a discount rate of 3%[2] was applied to future savings to estimate present savings
- Proportion of patients insured by Medicare vs. Commercial insurance was assumed to be 60% vs. 40%
- 100% adherence to preventative measures was assumed in these patients

Cumulative progression rates for movement through the stages by year (AIKD)

Movement through stages	Year 1	Year 2	Year 3	Year 4	Year 5
1 (excluding A1) --> 2 (excluding A1)	43.2%	50.4%	55.2%	57.6%	58.2%
2 (excluding A1) --> 3a	27.2%	35.2%	39.2%	40.8%	41.4%
3a ---> 3b	30.4%	38.4%	40.8%	41.6%	42.3%
3b ---> 4	20.8%	27.2%	31.2%	32.0%	33.1%
4 ---> 5	10.4%	20.0%	23.2%	26.4%	27.0%
5 ---> Dialysis	47.5%	52.3%	57.0%	61.8%	66.5%

1. Nadkarni, G. N., Fleming, F., McCullough, J. R., Chauhan, K., Verghese, D. A., John, … Coca, S. G. (2019, January 1). Prediction of rapid kidney function decline using machine learning combining blood biomarkers and electronic health record data. Retrieved from https://www.biorxiv.org/content/10.1101/587774v1
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Cost Categories, Sources, and Assumptions

The model compares differences in the following treatment costs between the AIKD and SOC patients:

- **Costs of each stage of DKD:** Medicare and Commercial plan CKD costs were identified from multiple sources to derive the costs in each stage of DKD in this model
- **Costs of preventative measures in high-risk patients:** Plan costs of prescription medications, nephrologist visits, and behavioral and dietary office visit costs identified from the literature. Only considered in patients identified as 'high-risk' by the AIKD
- **Costs of dialysis, transplants (including post-transplant care), and crashes:** Plan costs identified from the literature
- **Cost of the AIKD test:** $1,050 ($950 test cost + $100 administration cost)

Annual Costs per Patient at Each CKD Stage[1-4]

CKD Stage	Cost of CKD stage (USD)	Cost of preventative measures by CKD stage (AIKD high-risk cohort only) (USD)
CKD Stage 1 (Excluding G1&A1)	$16,612	$1,562
CKD Stage 2 (Excluding G2&A1)	$18,807	$2,024
CKD Stage 3a	$21,861	$2,003
CKD Stage 3b	$31,978	$2,662
CKD Stage 4	$42,239	N/A
CKD Stage 5	$72,768	N/A
ESRD (treatment cost, not including dialysis)	$118,181	N/A

Costs for Dialysis, Transplants, Crashes per Patient

Event	Cost
Cost of dialysis[5]	$88,000 per year
Additional cost of an initial unplanned dialysis (crash)[6]	$49,199 one time
Cost of a transplant[7]	$262,000 one time
Annual cost of post-transplant care[8]	$40,000 per year

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1. Honeycutt, A. A., Segel, J. E., Zhuo, X., Hoerger, T. J., Imai, K., & Williams, D. (2013, September 1). Medical Costs of CKD in the Medicare Population. JASN, 24, 9. Retrieved from https://jasn.asnjournals.org/content/24/9/1478.
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3. Knight, T., Schaefer, C., Krasa, H., Oberdhan, D., Chapman, A., & Perrone, R. D. (2015, February 20). Medical resource utilization and costs associated with autosomal dominant polycystic kidney disease in the USA: a retrospective matched cohort analysis of private insurer data. ClinicoEconomics and Outcomes Research, 7, 123-132. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/25759590.
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6. Lui, F.X, Ghaffari, A., Dhatt, H., Kumar, V., Balsera, C., Wallace, E,…Guest, S. (2014, December). Economic Evaluation of Urgent-Start Peritoneal Dialysis Versus Urgent-Start Hemodialysis in the United States. Medicine, 93, 28. Retrieved from https://journals.lww.com/md-journal/Fulltext/2014/12030/Economic_Evaluation_of_Urgent_Start_Peritoneal.41.aspx
7. NEPHCURE Kidney International. Transplant. Retrieved from https://nephcure.org/livingwithkidneydisease/kidney-failure/transplant/
8. National Kidney Foundation. Comprehensive Immunosuppressive Drug Coverage for Kidney Transplant Patients Act. Retrieved from https://www.kidney.org/sites/default/files/ImmunosuppressiveFactSheet-HR6139-20160930.pdf

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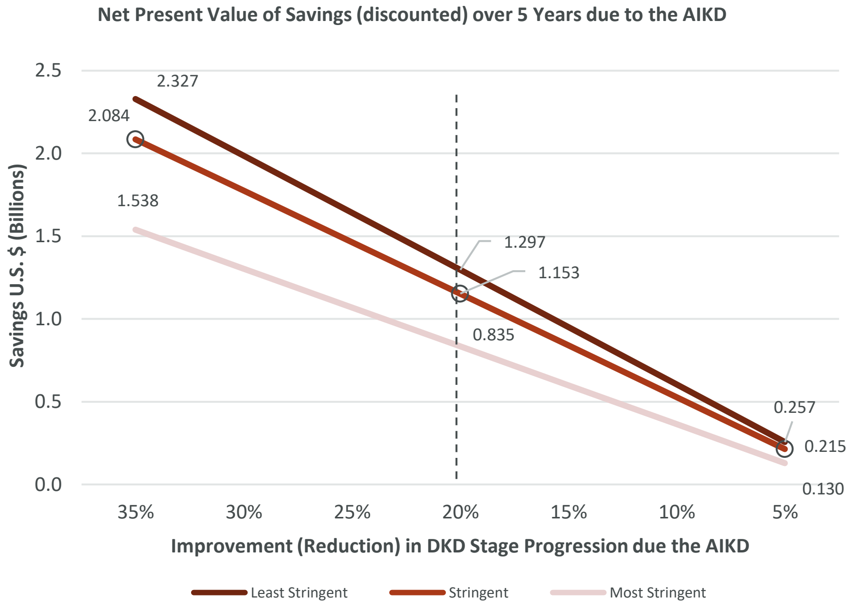
Results

The net present value of 5-year payer savings associated with AIKD adoption is estimated to be $1.153B (base-case) for 100,000 patients tested

- The net present of savings due to slowed progression, delayed/avoided dialysis & transplants, and fewer crashes over 5 years is expected to be
  - **$835 million** for the most-stringent definition of progression
  - **$1.297 billion** for the least-stringent definition of progression
- When the slowed progression resulting from improved medical management associated with the AIKD was changed from 20% to 5% and 35%, the highest cost savings were seen in the 'Least Stringent'/ '35% progression decline' scenario **($2.327B savings),** while the lowest cost savings were seen in the 'Most Stringent'/ '5% progression decline' scenario **($130M savings)**



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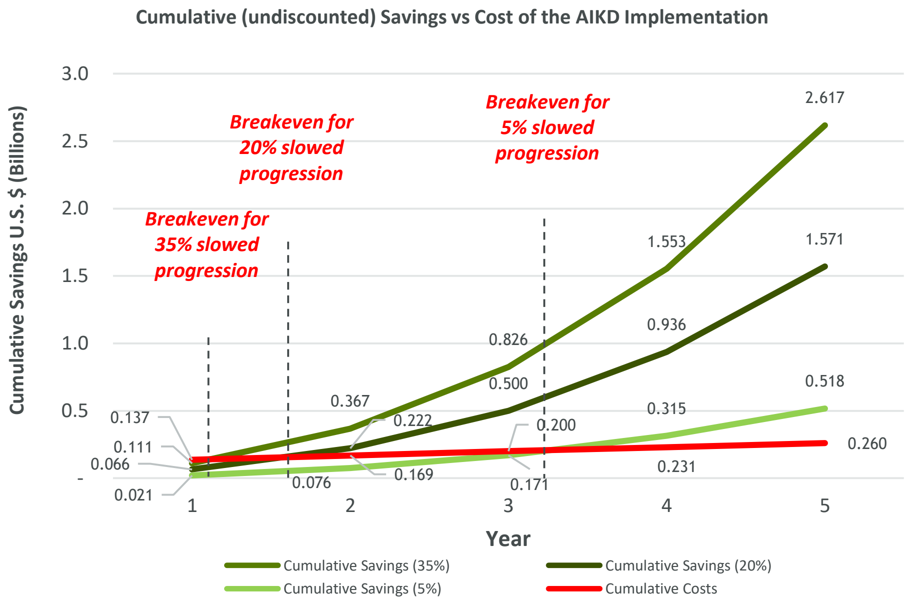
The estimated time to breakeven for the AIKD adoption occurs between 1 and 2 years (base-case) for 100,000 patients tested

- After this point, the **cumulative savings** are **expected to start increasing** compared to costs of implementation

- The expected breakeven point varies **between years 1 and 4** when slowed progression rates are varied from 20% to 5% and 35% assuming the 'Stringent' definition of progression
  - *35% slowed progression:* Slightly after year 1
  - *5% slowed progression:* Between year 3 and 4



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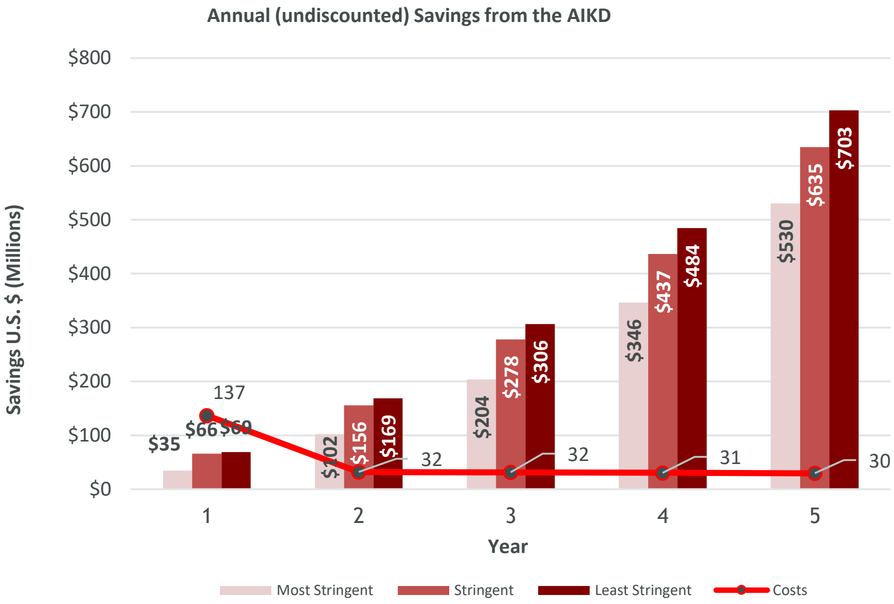
Estimated annual savings associated with AIKD use are expected to increase by year, with year 5 yielding the most savings ($635 million in base-case)

- The increase in savings by year is a function of more patients progressing to more severe (and costly) DKD stages and requiring dialysis and transplants over time if the AIKD were not implemented

- **The savings for year 5 are expected to be:**
  - **$530 million** for most stringent definition of progression
  - **$703 million** for least stringent definition of progression



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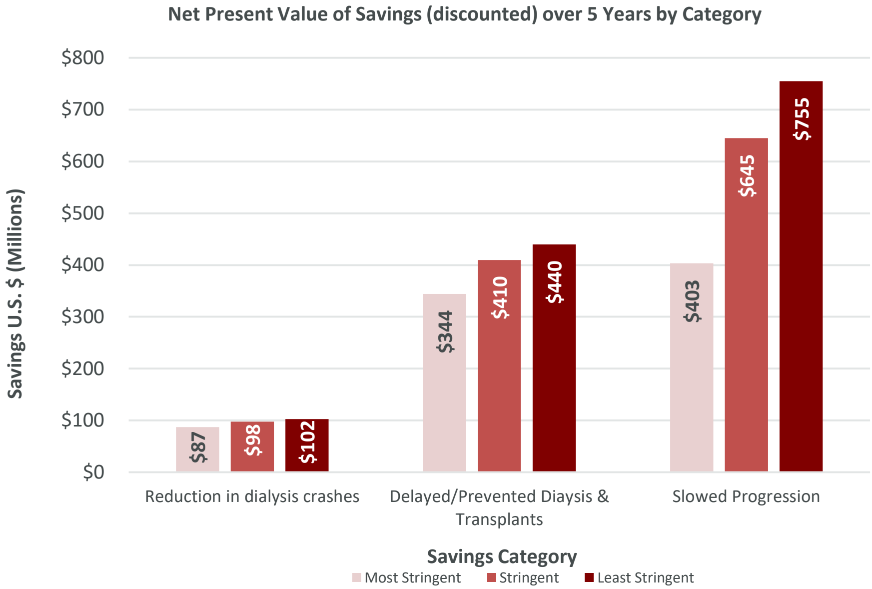
Highest net savings ($645 million for base case) are attributable to slowed progression owing to the use of AIKD compared to savings from other categories

- Base-case 5 year net savings for other categories are expected to be:
  - **$98 million** from reduction in dialysis crashes
  - **$410 million** from delayed/prevented dialysis/transplants

- Range of net present value of 5 year savings from slowed progression:
  - Least stringent definition of progression: **$755 million**
  - Stringent definition of progression: **$645 million**
  - Most stringent definition of progression: **$403 million**



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Conclusions

The use of the AIKD is expected to achieve significant cost savings for payers, primarily from delayed progression of beneficiaries with DKD

- Through early and accurate risk stratification of patients with DKD who are likely to experience RKFD or kidney failure, the AIKD has the ability to generate significant cost savings for payers through improved care management at earlier stages of DKD

- The AIKD will support the primary care physician and/or endocrinologist in identifying appropriate monitoring and interventions for patients determined to be high risk for RKFD; timely referral to a specialist/nephrologist will further improve outcomes

- Improving the health care systems' ability to provide care that conforms to KDIGO guideline recommendations will help reduce the rate of progression from DKD to ESRD and have a substantial clinical and economic impact

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Questions?

- **Abstract #407: AURORA Phase 3 Trial Demonstrates Voclosporin Statistical Superiority Over Standard of Care in Lupus Nephritis (LN)**
  - Keisha Gibson, MD, MPH, FASN - keisha_gibson@med.unc.edu

- **Abstract #409: Efficacy and Safety of Oral Difelikefalin in Stage 3-5 Chronic Kidney Disease Patients with Moderate-to-Severe Pruritus: A Response Analysis from a Randomised, Placebo-Controlled, Phase 2 Trial**
  - Ahmed Awad, DO, FACP, FASN - awada@crckcmo.com

- **Abstract #479: Evaluation of Payer Budget Impact Associated with the Use of Artificial Intelligence in Vitro Diagnostic, KidneyIntelX, to Modify DKD Progression**
  - Thomas Goss, PharmD - tgoss@bostonhealthcare.com

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