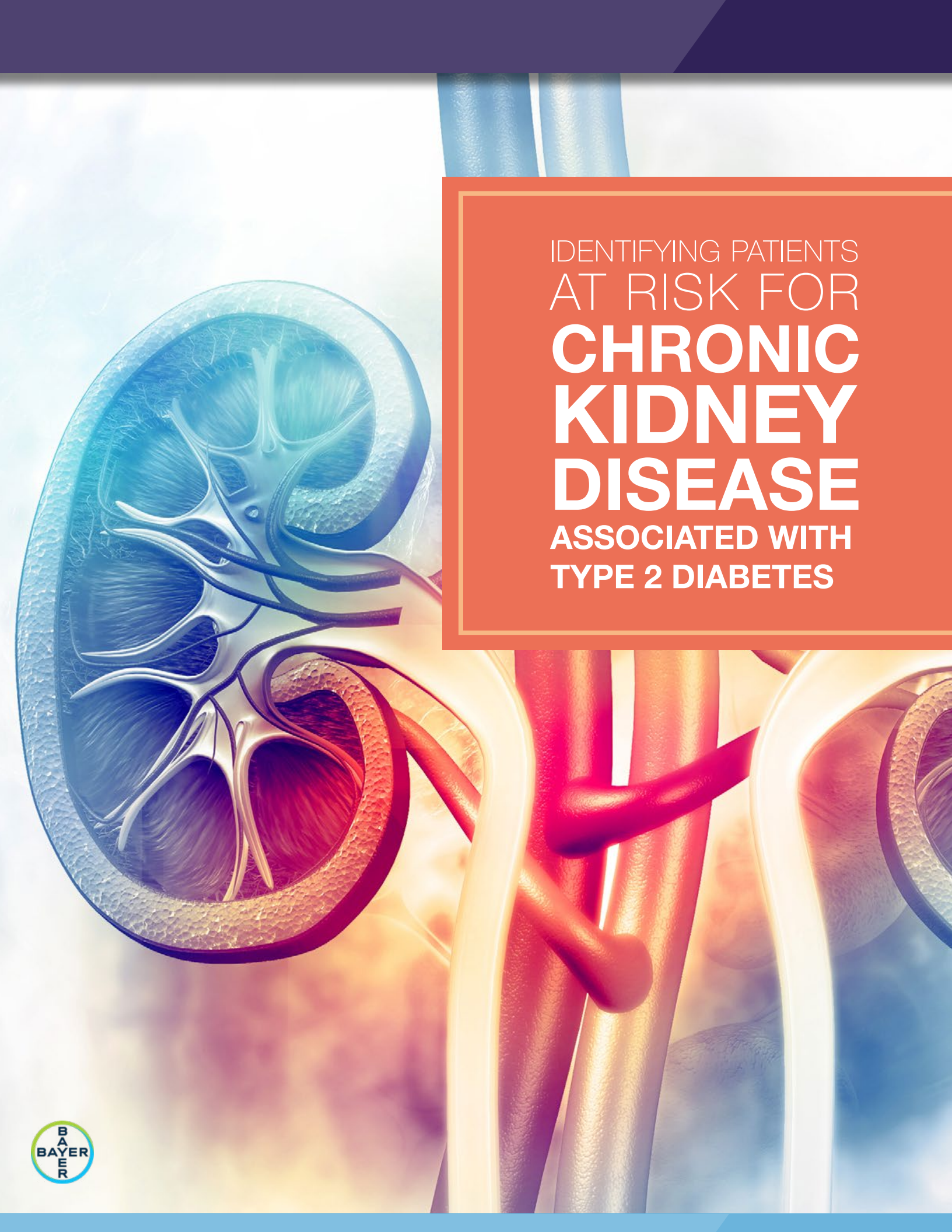
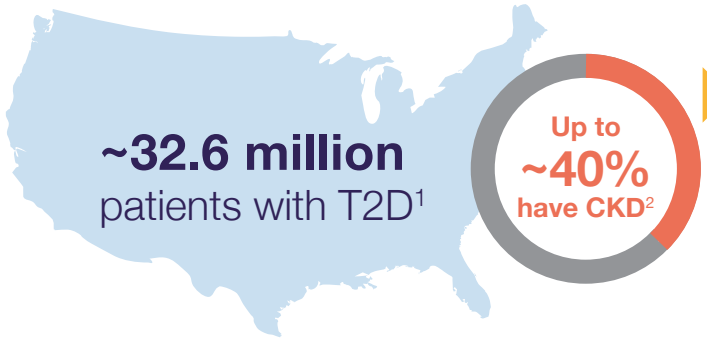


IDENTIFYING PATIENTS AT RISK FOR CHRONIC KIDNEY DISEASE ASSOCIATED WITH TYPE 2 DIABETES

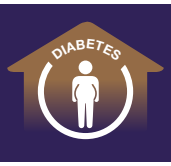
BAYER

Chronic Kidney Disease Associated With Type 2 Diabetes Is a Population Health Concern Throughout the United States



Diabetes is a major cause of chronic kidney disease (CKD) in the United States, and of the ~32.6 million patients with type 2 diabetes (T2D), **up to 40% have evidence of CKD**.[1,2] Despite this high prevalence, ~90% of patients with diabetes and CKD are unaware of their kidney disease.[3,*]

***Estimates of diabetes may not delineate between type 1 and type 2 diabetes. According to the American Diabetes Association, type 2 diabetes accounts for 90%-95% of all diabetes cases. Therefore, statistics that describe diabetes may be more characteristic of type 2 diabetes.[4]**



60 MILLION BY 2060

As the population with diabetes is projected to increase to over **60 million by 2060**,[5] the estimated, corresponding rise in CKD cases may make **CKD associated with T2D** an even bigger **population health priority**

CKD Is an Independent Risk Factor for CV Events and Death in Patients With CKD Associated With T2D

Patients with CKD associated with T2D are at an increased risk of cardiovascular (CV) events, and are at a greater risk of CV-related death, when compared with patients with type 2 diabetes alone[6-8]

~2x MORE

patients with CKD associated with T2D reported myocardial infarction vs patients with T2D alone[6,†]

83% GREATER RISK

of CV death in patients with CKD associated with T2D vs patients with T2D alone[8,‡]

†As evidenced by a cross-sectional analysis of self-reported patient data collected between 2007 and 2012 from 2006 patients with type 2 diabetes who completed the US National Health and Nutrition Examination Surveys (NHANES).[6]

‡As evidenced by a subgroup analysis that aimed to examine the impact of early CKD and insulin glargine (in patients with and without early CKD) on cardiovascular outcomes among 12,537 participants enrolled in the multicenter, randomized controlled trial, ORIGIN. Hazard risk based on a comparison of patients with early T2D and CKD stages 1-3 (n=3695) and those with T2D alone (n=7057). Hazard ratios calculated after adjustment for treatment, glycemic status, and prior cardiovascular events.[8]

Significant Public and Private Initiatives Focused on Improving CKD Associated With T2D Outcomes Are Underway

The National Committee for Quality Assurance (NCQA) released an educational resource on the importance of testing patients with T2D for CKD called the Kidney Health Toolkit.[9] Click here to navigate to the section of this brochure that provides further details on the Toolkit.

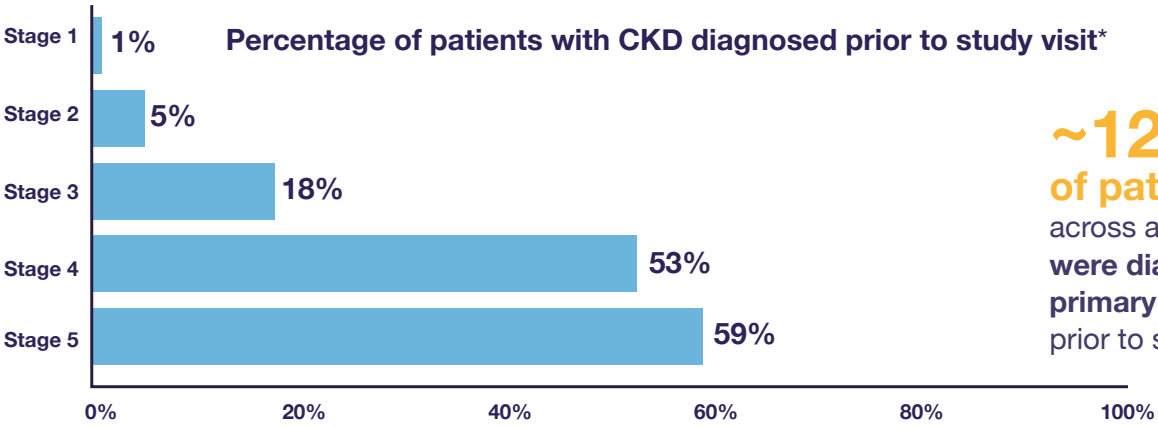
The National Kidney Foundation (NKF) has launched the NKF Patient Network, the first nationwide, kidney disease patient registry, to improve the lives of people with kidney disease through research, clinical care, drug development, and supportive health policies.[10] The NKF has also teamed up with actress Debbie Allen on "Are You the 33%?", a campaign designed to raise awareness that 1 in 3 adults in the United States are at risk for life-threatening kidney disease.[11,12,§]

Know Diabetes by Heart, a program sponsored by the American Diabetes Association (ADA) and the American Heart Association aligns with Bayer's mission to promote a comprehensive approach to the management of patients with diabetes by addressing glucose control as well as heart and kidney health.[13,§]

§Bayer is a Corporate Sponsor of NKF and National Sponsor of Know Diabetes by Heart.

Despite the Associated Clinical Burden, **CKD Is Underdiagnosed in Patients With T2D**

A multicenter, observational study conducted in primary care practices in the United States assessed CKD prevalence in a population of patients with T2D. Investigators assessed the rate of appropriate, clinical CKD diagnosis, as measured through UACR and eGFR testing, and concluded that underdiagnosis was observed most frequently in patients with earlier stages of CKD[14]



~12% of patients across all stages of CKD **were diagnosed by their primary care physicians** prior to study enrollment[14]

*As evidenced by a multicenter, observational study conducted in 466 primary care practices in the United States that assessed CKD prevalence within an adult, T2D population between 2011 and 2012. Investigators assessed the rate of appropriate CKD diagnosis, which was determined by conducting eGFR tests; glycated hemoglobin (HbA1c) evaluations, a urine analysis to detect proteinuria, a urine measurement for UACR, 2 patient health-related quality-of-life questionnaires, and a 15-month medical review were also performed. CKD stages 3-5 were based on eGFR value alone. Units for eGFR are mL/min/1.73 m^2.

Early identification of CKD associated with T2D through improved diagnostic and screening practices may be a **crucial step in improving patient outcomes**[15]

UACR and eGFR Are **Critical for CKD Diagnosis in Patients With T2D**

CKD is diagnosed via assessment of albuminuria (elevated UACR) **and/or reduced kidney function** (decreased eGFR) **in the absence of signs or symptoms** of other primary causes of kidney damage.[4]

UACR and eGFR are important diagnostic and prognostic indicators of kidney health and can be predictive of CKD progression.[16]

Furthermore, albuminuria, which is measured through UACR assessment, is an independent and early predictor of CV mortality.[17,18]

One study concluded that 10-year mortality risk is 4x higher for people with T2D with increased UACR vs people without kidney disease.[7]

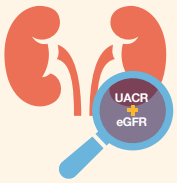
A retrospective analysis of patients included in the OPTUM EHR database assessed the proportion of patients with T2D who had eGFR and UACR recorded between 12 months pre- and 36 months post-index (T2D diagnosis) date.[19]

While most patients had the eGFR test performed, the study found that **only 41%** of patients also had a UACR test performed within the past 3 years post T2D diagnosis.[19]

eGFR=estimated glomerular filtration rate; EHR=electronic health record; UACR=urine albumin-to-creatinine ratio.

Current Rates of UACR Testing Are Suboptimal and Do Not Align With ADA Recommendations

The American Diabetes Association and the Kidney Disease: Improving Global Outcomes (KDIGO) Work Group define appropriate kidney health evaluation as the assessment of both UACR and eGFR.[4,20]



In its 2021 Standards of Medical Care in Diabetes, the American Diabetes Association recommends the following kidney screening process for patients with T2D[4]:

At least once a year, kidney health should be evaluated through spot **UACR and eGFR testing in all patients with T2D**, regardless of treatment

Members with diabetes and urinary albumin >300 mg/g and/or eGFR 30-60 mL/min/1.73 m^2 should be monitored at **least twice annually** to guide therapy

In the 2020 KDIGO Clinical Practice Guideline for Diabetes Management in CKD, KDIGO tailors its monitoring and pharmacotherapeutic recommendations according to a patient's UACR and eGFR levels,[20] which makes assessment of these markers critical to ensuring appropriate, evidence-based care

The Healthcare Effectiveness Data and Information Set (HEDIS®) Quality Measure Requires Reporting of **Annual UACR Screening**

The NCQA has approved a measure of Kidney Health Evaluation for Patients with Diabetes, which requires annual screening for both UACR and eGFR.[21] Studies have demonstrated substantial gaps in UACR screening, and ensuring alignment of quality measures to evidence-based UACR screening recommendations may promote improved management of patients with CKD associated with T2D.[4,19]

The Kidney Health Evaluation quality measure requires both UACR and eGFR screenings annually, while prior to this measure, UACR was included as one of many ways to meet the NCQA HEDIS® Medical Attention for Nephropathy indicator in the Comprehensive Diabetes Care measure. Prioritizing both UACR and eGFR screenings may help organizations when they are evaluated under the Kidney Health Evaluation metric.[21,22]

CERTIFIED NCQA HEDIS® MEASURES

HEDIS® MEASUREMENT YEAR 2020/2021

Kidney Health Evaluation for Patients with Diabetes HEDIS® Measurement Years 2020 and 2021

The measure **assesses the percentage of people aged 18 to 85 years with a diagnosis of diabetes** who receive a kidney health evaluation, defined as both UACR and eGFR assessment within a 12-month measurement period.[21]

This **standalone measure** was first published in the HEDIS® Measurement Year 2020 and Measurement Year 2021 publications, with first reporting beginning in 2021.[21]

Accurately identifying patients with CKD associated with T2D may help providers intervene earlier in the course of disease, improve kidney-related outcomes, and reduce associated costs[15,23,24]

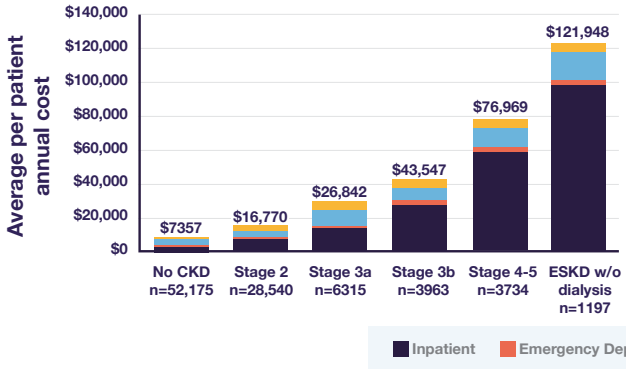
CKD Poses a Considerable **Economic Burden** and Accounts for ~$120 Billion in Annual Medicare Spending[25]

As Kidney Function Declines, Per-Patient Costs Increase Exponentially

Commercial costs for patients with CKD (aged <65 years)[23]

Mean annualized costs by CKD stage (2007-2012)

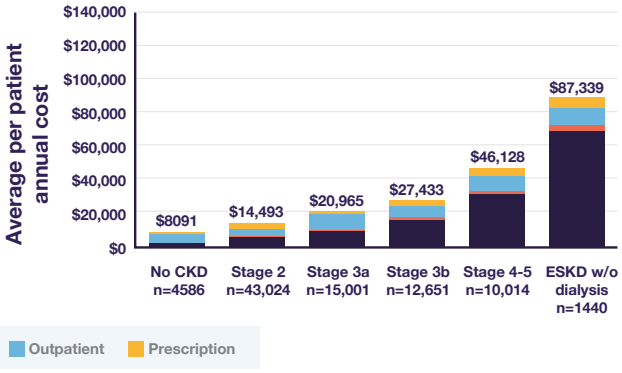
- Diabetes was present in 38% of commercially insured study participants with CKD[23,*]

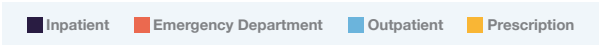


Medicare costs for patients with CKD (aged ≥65 years)[23]

Mean annualized costs by CKD stage (2007-2012)

- Diabetes was present in 42% of Medicare study participants with CKD[23,*]





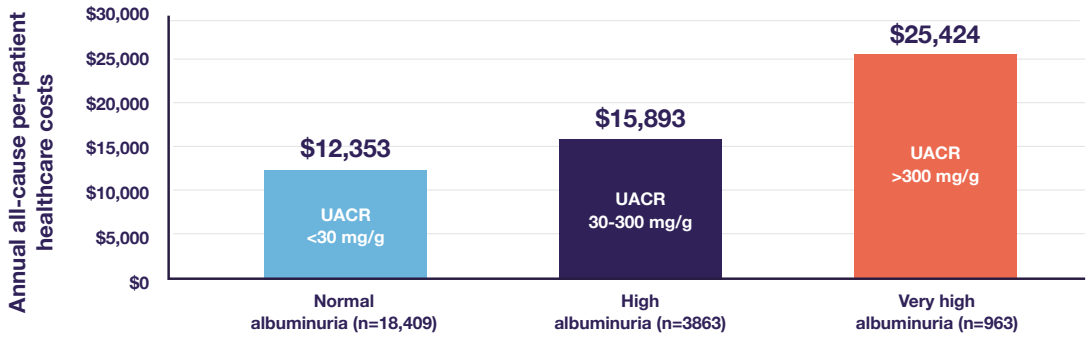
ESKD=end-stage kidney disease.

*Estimates of diabetes may not delineate between type 1 and type 2 diabetes. According to the American Diabetes Association, type 2 diabetes accounts for 90%-95% of all diabetes cases. Therefore, statistics that describe diabetes may be more characteristic of type 2 diabetes.[4]

On average, inpatient costs were the largest cost contributor, followed by costs associated with outpatient care, emergency department visits, and prescriptions. A key driver for inpatient costs were 30-day readmissions—more than 1 in 5 commercial and Medicare beneficiaries with CKD stages 4-5 or ESKD were readmitted within 30 days.[23]

Per-Patient Costs Increase Substantially as Kidney Damage Worsens

Patients with T2D and high albuminuria (UACR 30-300 mg/g) or very high albuminuria (UACR >300 mg/g) incurred significantly higher annual all-cause healthcare costs when compared with patients with T2D and normal albuminuria (UACR <30 mg/g)[24,†]

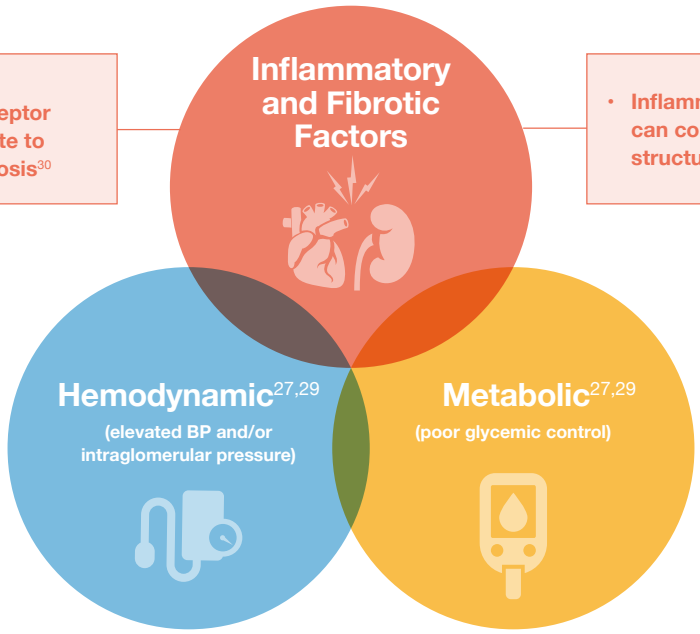


†As evidenced by a retrospective database analysis conducted between 2004 and 2014 that enrolled 23,235 patients ages 18 and older with T2D and at least 2 urine albumin tests. Albuminuria was characterized as follows: Normal albuminuria (UACR <30 mg/g), high albuminuria (30-300 mg/g), very high albuminuria (UACR >300 mg/g). UACR was found to be an important cost driver as other clinical measures (eg, A1C, eGFR) were not included in the analysis.[24]

As CKD worsens, patients with CKD associated with T2D represent an increased risk of spend and are at a greater risk of progressing to more advanced, **more costly stages of disease**[26]

There Are Multiple Drivers of CKD Progression in Patients With CKD Associated With T2D[27-29]

- Overactivation of the mineralocorticoid receptor is thought to contribute to inflammation and fibrosis[30]



- Inflammation and fibrosis can contribute to permanent structural damage in the kidneys[27,31]

Patients with CKD associated with T2D may be at risk for CKD progression despite receiving standard of care treatment to control blood pressure and blood glucose[30]

BP=blood pressure.

Utilizing Electronic Health Records to Improve Outcomes in Patients With CKD Associated With T2D

There is currently no standardized way to identify patients with CKD, ESKD, and kidney transplant through EHR review.[32]

With HEDIS quality measures reporting for patients with CKD associated with T2D, it is important to develop protocols to identify and monitor patients at risk for kidney disease progression, and to ensure patients with T2D are screened for CKD using UACR and eGFR testing.

Additionally, since CKD is typically diagnosed through evaluation of laboratory metrics,[4] leveraging the clinical support functionalities of your organization's EHR may facilitate improved intervention.

Developing policies that reflect **appropriate screening practices may enable providers to better identify patients with CKD associated with T2D** and improve the health of your organization's entire CKD associated with T2D population

Population Health Initiatives and Clinical Decision Support Considerations **May Drive Improved Identification of CKD Associated With T2D**

Electronic Health Record Solutions[33,34]

The clinical decision support functionalities contained within your organization's EHR may provide valuable opportunities to ensure your providers are acting in accordance with evidence-based guidance.

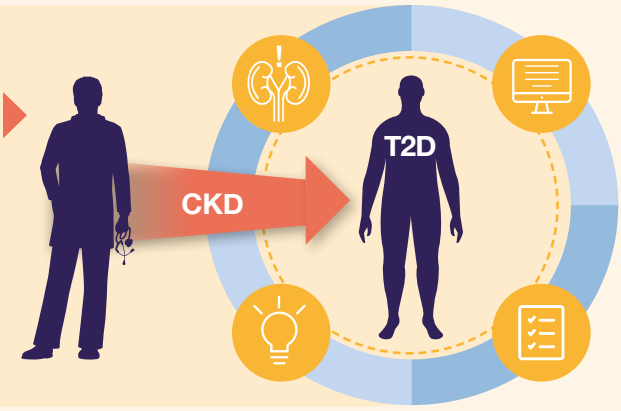
Some examples include:

- **Constructing patient lists to facilitate case management review and closing gaps of care**
- **Embedding concise guideline recommendations and protocols**
- **Utilizing electronic care prompts**
- **Data generation collaborations for registries**
- **Providing best practice support within lab reports**
- **Mobile patient platform outreach**

This information can then be analyzed to evaluate how your organization's identification, monitoring, and screening parameters are impacting the patient's care.

Educating Key Stakeholders About CKD Associated With T2D[4,33,34]

Promoting education among healthcare providers (HCPs) can help to ensure that patients with CKD associated with T2D receive appropriate, evidence-based intervention.



Because the ADA recommends that providers manage patients on an individualized basis, **improving patient-level awareness of CKD associated with T2D through educational and self-management resources available through patient portals can foster more informed, shared decision making.**

Utilizing the NCQA Kidney Health Toolkit[9]

Bayer is proud to have sponsored NCQA to develop the Kidney Health Toolkit in support of raising awareness for the HEDIS® Kidney Health Evaluation quality measure.

This resource includes information and resources about assessing and monitoring kidney health, interpreting eGFR and UACR test results, and diagnosis and staging of CKD. For more information on the NCQA Kidney Health Toolkit, please click here.

By promoting earlier identification, monitoring, and screening for patients with CKD associated with T2D, **you may drive improved outcomes and mitigate disease-related costs**[15,23,35,36]

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