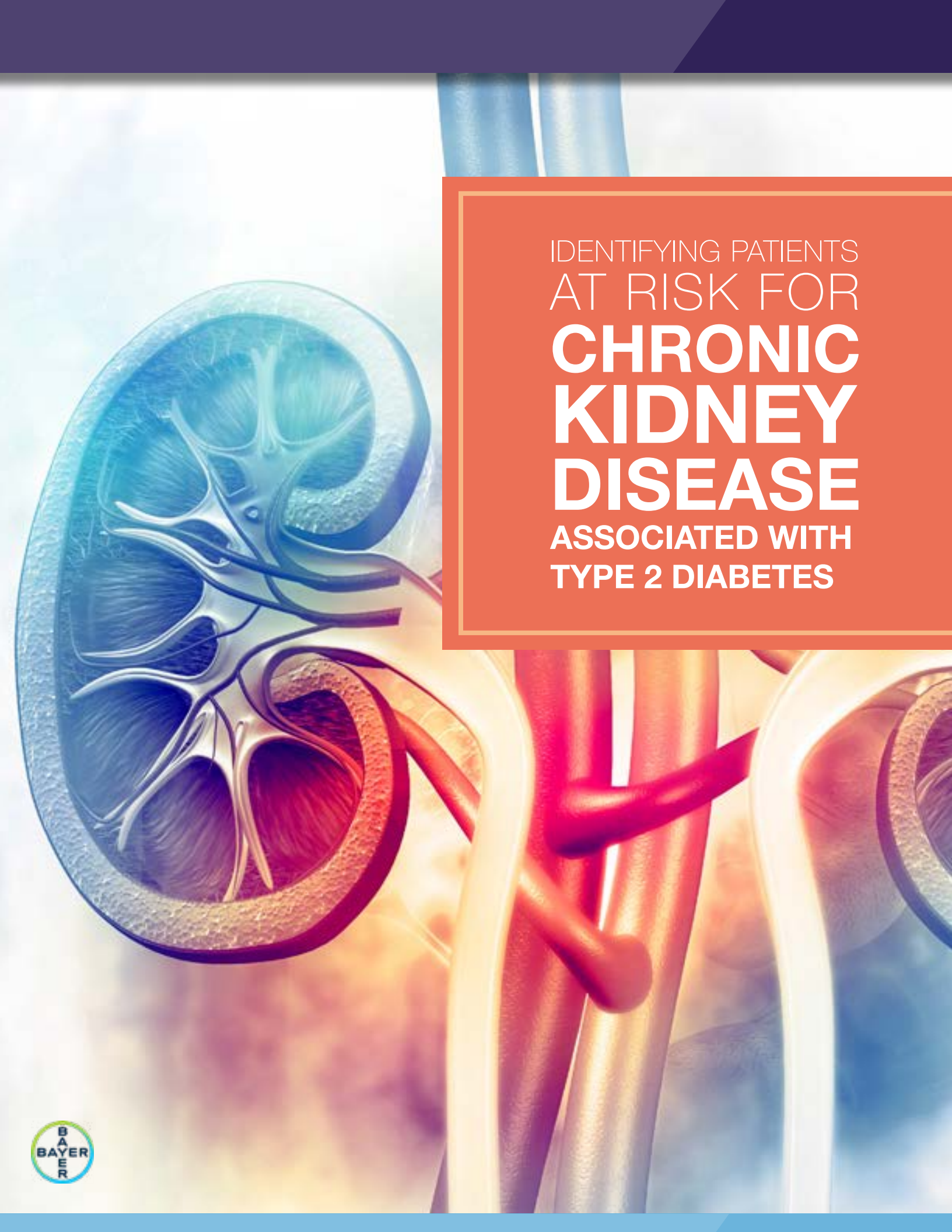
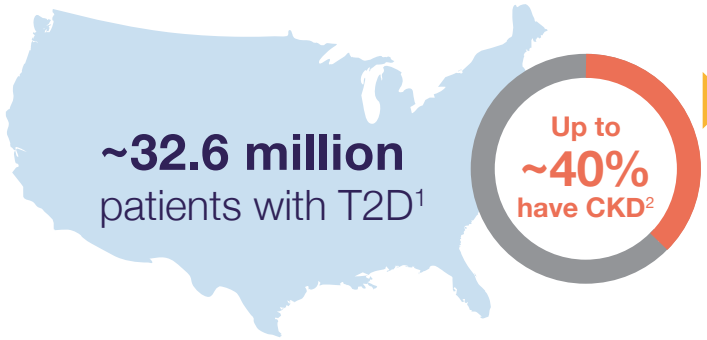


IDENTIFYING PATIENTS AT RISK FOR CHRONIC KIDNEY DISEASE ASSOCIATED WITH TYPE 2 DIABETES

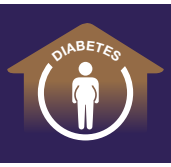
BAYER

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

Members 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] For more information on the NCQA Kidney Health Toolkit, please click here.

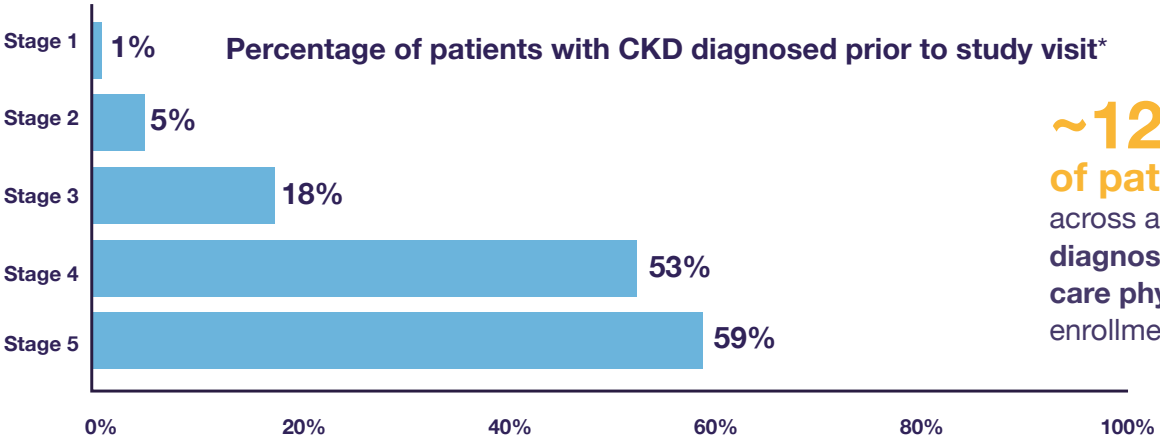
The National Kidney Foundation (NKF) has launched the NKF Patient Network, the first nationwide, kidney disease patient registry, to improve the lives of people with kidney disease through research, clinical care, drug development, and supportive health policies.[10] The NKF has also teamed up with actress 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 Members 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 member outcomes**[15]

UACR and eGFR Are **Critical for CKD Diagnosis in Members 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]

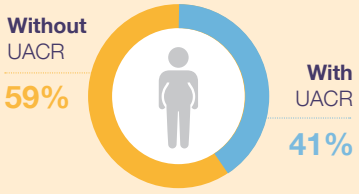
UACR and eGFR are important diagnostic and prognostic indicators of kidney health and can be predictive of CKD progression.[16]

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 members with T2D[4]:

At least once a year, kidney health should be evaluated through spot **UACR and eGFR testing in all members 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 members 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]

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]

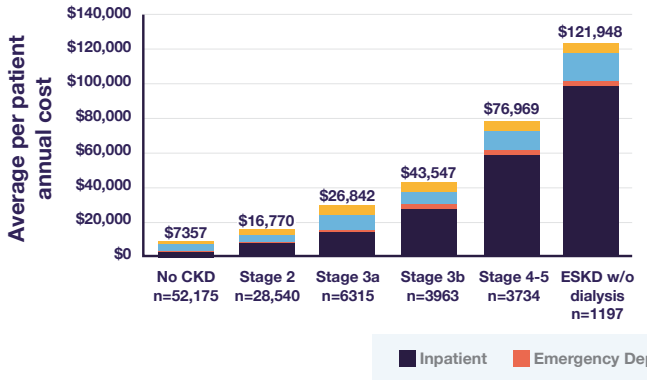
CKD Poses a Considerable **Economic Burden** and Accounts for ~$120 Billion in Annual Medicare Spending[23]

As Kidney Function Declines, Per-Member Costs Increase Exponentially

Commercial costs for patients with CKD (aged <65 years)[24]

Mean annualized costs by CKD stage (2007-2012)

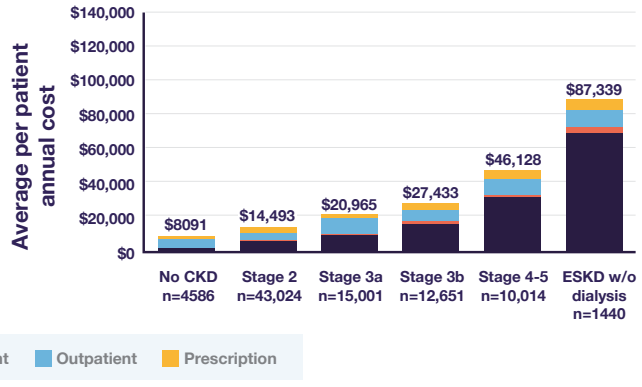
- Diabetes was present in 38% of commercially insured study participants with CKD[24,*]

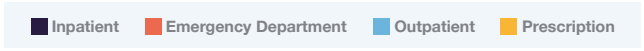


Medicare costs for patients with CKD (aged ≥65 years)[24]

Mean annualized costs by CKD stage (2007-2012)

- Diabetes was present in 42% of Medicare study participants with CKD[24,*]





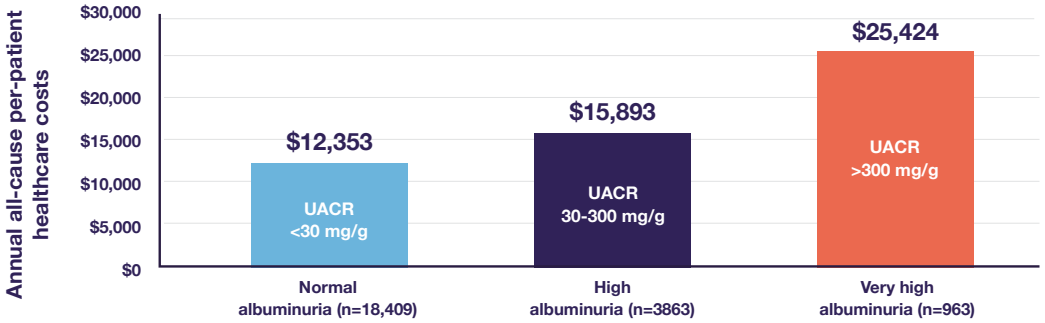
ESKD=end-stage kidney disease.

*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]

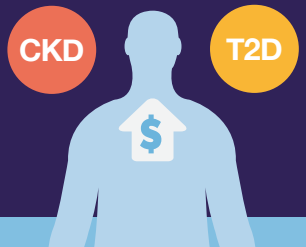
CKD stage 3 continues to be the most widely prevalent stage of disease in the United States and direct medical costs associated with CKD stage 3 range between ~$21,000 to nearly ~$45,000 per member per year.[24,25]

Per-Member Costs Increase Substantially as Kidney Damage Worsens

Members 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 members with T2D and normal albuminuria (UACR <30 mg/g)[26,†]



†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.[26]



As CKD worsens, members 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**[27]

Failure to diagnose and properly code CKD stages 3-5 or ESKD **may impact risk-adjusted performance measures**[22,28,29]

Real-world Study: Vigilant Monitoring, Multidisciplinary Care, and Member Education According to CKD Risk May Improve Outcomes

A real-world, CKD quality improvement study was incorporated into the CareFirst primary care patient-centered medical home (PCMH) initiative for a group of 7420 individuals aged 18 years or older with diagnosed CKD, hypertension, and/or diabetes between 2015 and 2017.*† Investigators assigned participants to an appropriate CKD class using the heat map included in the 2012 National Kidney Foundation's Kidney Disease Outcomes Quality Initiative guidelines and implemented treatment and **screening recommendations according to CKD stage and risk level.**[28]

Please refer to page x of the KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease for more information about CKD risk levels and the investigator's stratification protocol.

*Continuous enrollment in the CKD study and PCMH panel was required throughout the 24-month study period. The study excluded people who used Medicare as their primary form of health insurance and those with a history of kidney transplantation or dialysis during the study period.[28]

†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]

Summary of Interventions Performed in CareFirst Quality Improvement Study[28]

Vigilant Monitoring

Encourage network providers to order UACR and eGFR testing to understand member risk and monitor kidney function frequently for high-risk members

Multidisciplinary Care

Provide care management support on nutrition, smoking cessation, diabetes, and other topics according to member risk

Member Education

Remind members to schedule regular follow-ups and enable consultation or referral to a nephrologist for advanced stages

Study interventions promoted substantial reductions in[28,‡]:

- **Institutional PMPM costs** in classes 3-5§
- **Medical PMPM costs** in classes 3 and 5
- **Admissions** in classes 3-5‖
- **Readmissions** in classes 4 and 5‖
- **Emergency department visits** in classes 1 and 2‖

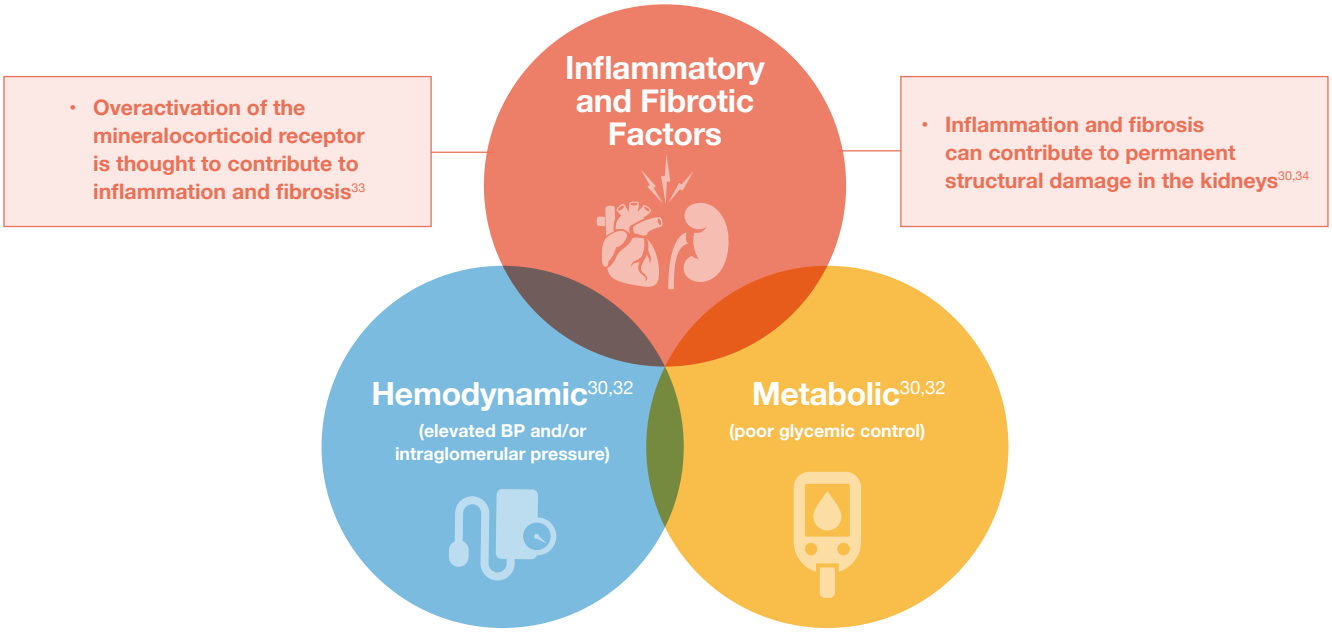
PMPM=per member per month.

‡Expenditures are not adjusted for inflation during the study period.
§Institutional or hospitalization expenditures.
‖Per 1000 members.

In addition to those instituted in the CareFirst study, **organizations may want to consider the approaches below** in managing members with CKD associated with T2D:

- **Leverage pharmacists to counsel patients** about the importance of eGFR and UACR screenings, in addition to the risks associated with CKD progression
- **Implement CKD awareness and screening** into existing diabetes education platforms
- Ask contracted labs to **implement the kidney health panel** in their order sets
- Support primary care and accountable care providers **with information about their current testing status** and potential gaps in care
- Incorporate the new claims-based measure into your value-based payment programs **to reward clinical excellence and encourage quality improvement**[21]

There Are Multiple Drivers of CKD Progression in Members With CKD Associated With T2D[30-32]



BP=blood pressure.

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[33]

Take Action: Optimize Management of Members With CKD Associated With T2D

Accurately identifying members with CKD **may help providers intervene earlier** in the course of disease and improve kidney-related outcomes.[15]

Ensuring that members receive both eGFR and UACR screenings **will help prepare your organization to meet the updated HEDIS quality measure**.

As worsening of eGFR and UACR are associated with greater expenditure in members with CKD associated with T2D, **early intervention may help delay progression of the illness and associated costs**.[24,26,28]

Improving CKD management and utilizing guideline-based treatment plans in your members **may reduce the PMPM costs and healthcare resource utilization associated with CKD**.[28]

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