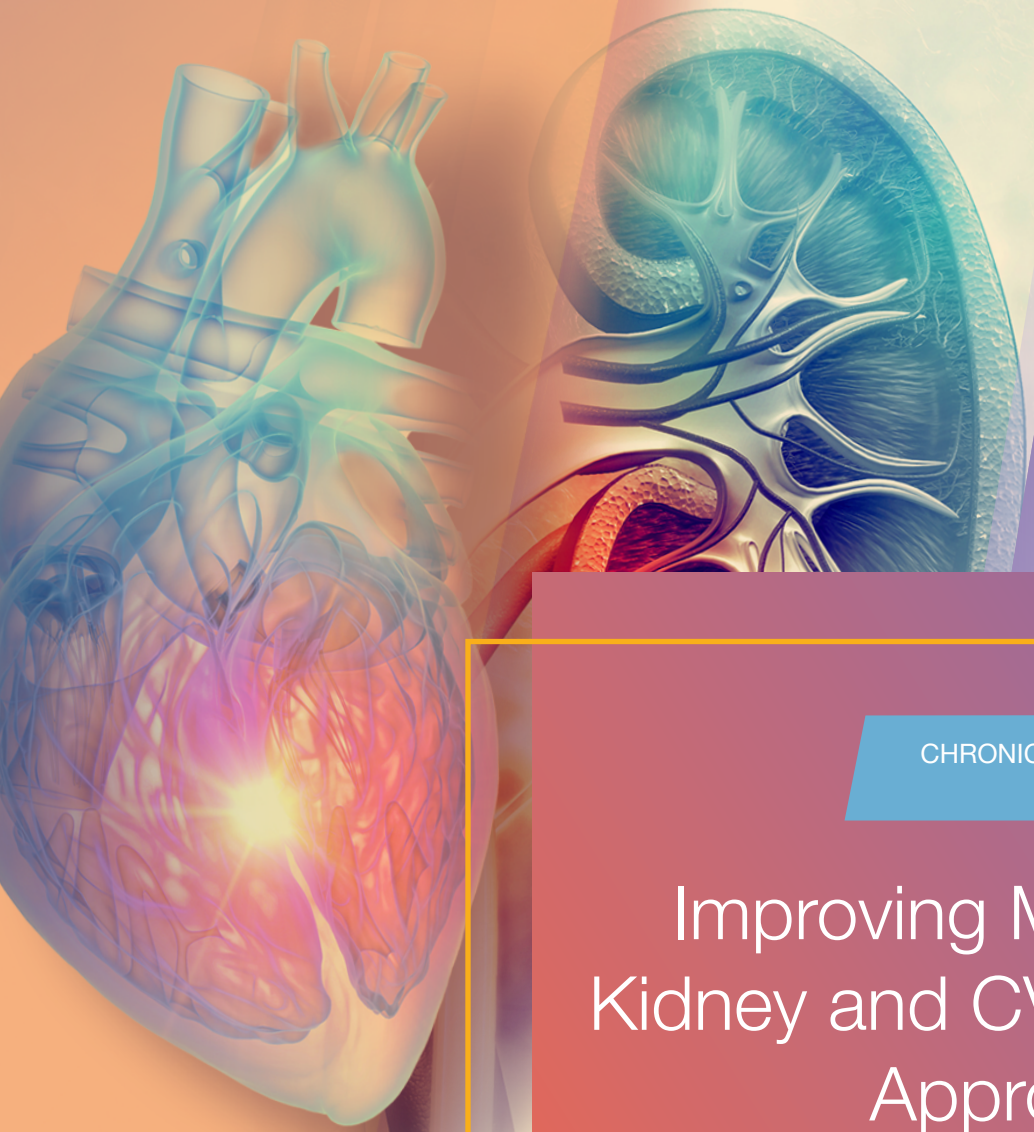


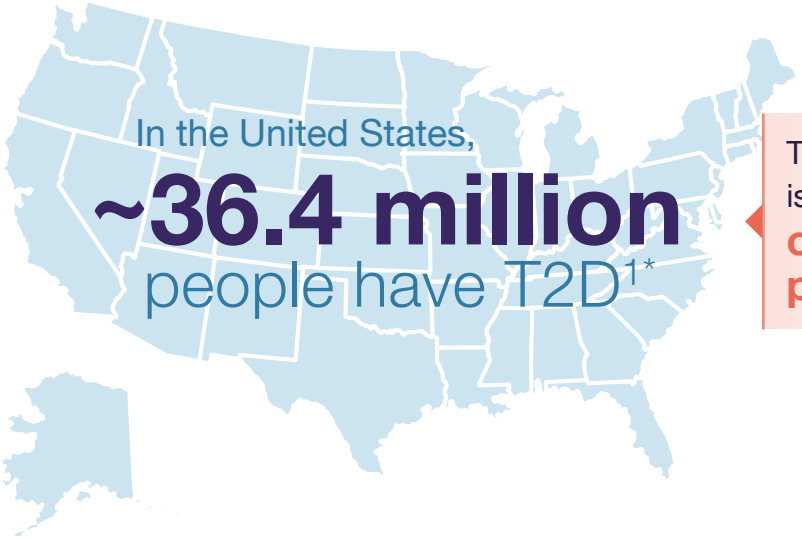
CHRONIC KIDNEY DISEASE (CKD) ASSOCIATED WITH TYPE 2 DIABETES (T2D)

Improving Management of Kidney and CV Risk Through Appropriate Testing, Diagnosis, and Treatment

Click to begin

CV, cardiovascular.

CKD Associated With T2D Is a Major Population Health Concern



In the United States,

~36.4 million

people have T2D[1*]

The diabetes population is expected to double to **over 60 million people by 2060**[2]

Up to **40%** of patients with T2D have CKD[3]

But a vast majority, **~90%** of patients with diabetes and CKD, are **unaware of their kidney disease**[4†‡]

*Data from 2021.

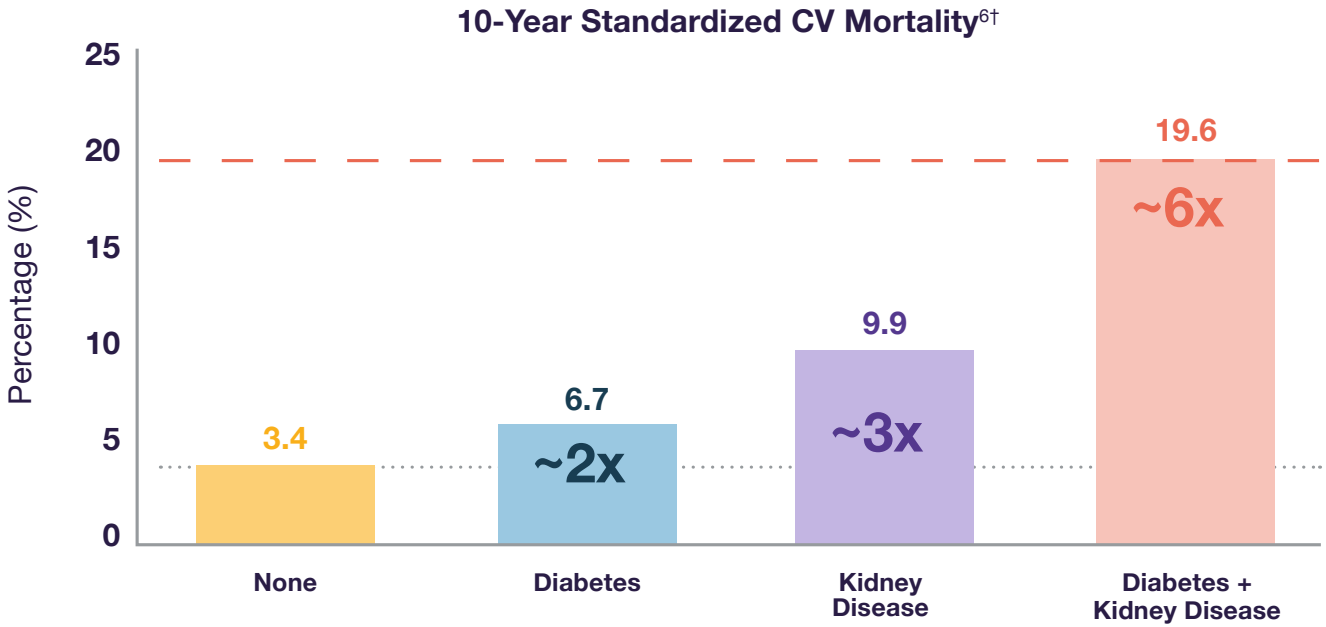
†Data from the National Health and Nutrition Examination Survey (NHANES), 2015-2018 participants.[4]

‡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.[5]

CKD, chronic kidney disease; T2D, type 2 diabetes.

Kidney Disease Approximately **Triples the Risk** of CV Mortality in Patients With Diabetes

Study results based on NHANES III participant data* suggested that excess risk for CV mortality among patients with T2D was concentrated in patients with CKD—defined as elevated UACR (albuminuria), impaired eGFR, or both[6]



*NHANES III was conducted between 1988 and 1994. This study used data from NHANES III participants aged ≥20 years who had follow-up mortality data through 2006.[6]

†N=15,046.

eGFR, estimated glomerular filtration rate; NHANES, National Health and Nutrition Examination Survey; UACR, urinary albumin-to-creatinine ratio.

Incidence of Costly CV Events Increases Substantially in Patients With CKD Associated With T2D vs Those With T2D Alone

Incidence of CV Events

in Patients With CKD Associated With T2D vs T2D alone

~2x more

Myocardial infarction (MI) cases[7*]

~3-6x greater risk of

Hospitalization for heart failure (HHF)[8†]

~3x more

Cardiovascular (CV) deaths[6‡]

Cost of CV Events

in Patients With CKD Associated With T2D (2023 USD)[6-10§]

ANNUALIZED MI: $26,193

ANNUALIZED HHF: $43,053

1-MONTH COST CV-related death: $17,917

Promptly identifying elevated UACR informs evidence-based treatment in patients with T2D and may help to reduce or defer costly complications[11]

*As evidenced by a cross-sectional analysis of self-reported patient data collected between 2007 and 2012 from 2,006 patients with type 2 diabetes who completed NHANES.[7]

†Randomized, double-blind, placebo-controlled SAVOR TIMI 53 trial conducted from 2010-2013 in 16,492 patients with T2D and a glycated hemoglobin (HbA1c) of 6.5%-12.0% within 6 months of randomization and either a history of atherosclerotic cardiovascular disease (ASCVD) or multiple cardiovascular disease (CVD) risk factors. Baseline UACR was available in 15,760 patients.[8]

‡This study used data from NHANES III participants aged ≥20 years, who participated in a health examination and had available data on medications used, serum creatinine, and urine albumin and creatinine concentrations. Of these, the only participants who were included were those who had follow-up mortality data through 2006 (15,046 of 15,762 of NHANES III participants, 95.5%); 1,430 (9.5%) of the 15,046 participants had T2D.[6]

§Costs inflated to 2023 USD using MCPI from the US Bureau of Labor Statistics. MCPI from Half 2 of relevant years used in calculations. Difference of MCPI 2023 (Half 1) and originating MCPI was taken and divided by originating MCPI, and then multiplied by 100 to generate inflation factor percentage. Inflation factor percentage was multiplied by originating cost to generate inflated cost in 2023 USD. Values rounded to nearest dollar.[10]

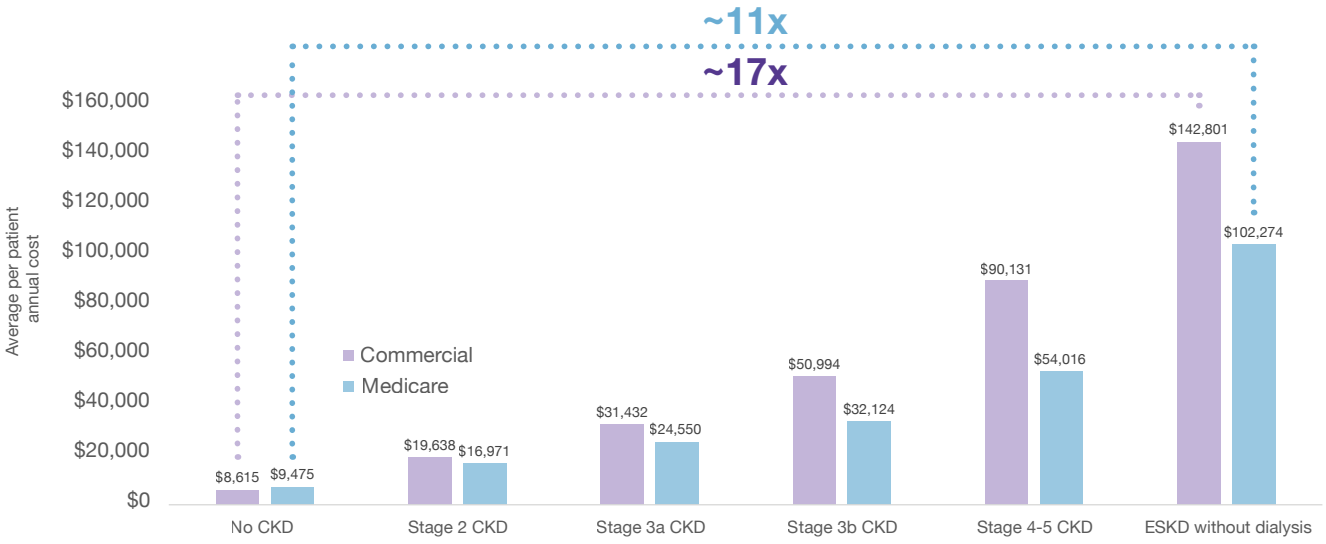
MCPI, Medical Care Price Index; USD, US dollars.

CKD Progression Exponentially Increases Costs for Commercial and Medicare Patients, Including Those With T2D

COST OF CARE FOR *COMMERCIAL* AND *MEDICARE* PATIENTS[10,12*]

Diabetes was present in 38% of commercially insured and 42% of Medicare study participants with CKD[12]

Costs shown in 2023 USD[†]



*Based on a study conducted between 2007 and 2012 that analyzed all-cause, prescription, outpatient, emergency department, and inpatient costs according to CKD stage. Diabetes present in 38% and 42% of commercial and Medicare participants, respectively. Sample sizes (n) for the cohorts in this study are as follows: No CKD (Medicare: 4,586; commercial: 52,175); Stage 2 (Medicare: 43,024; commercial: 28,540); Stage 3a (Medicare: 15,001; commercial: 6,315); Stage 3b (Medicare: 12,651; commercial: 3,963); Stages 4-5 (Medicare: 10,014; commercial: 3,734); end-stage kidney disease without dialysis (Medicare: 1,440; commercial: 1,197).[12]

†Costs inflated to 2023 USD using MCPI from the US Bureau of Labor Statistics. MCPI from Half 2 of relevant years used in calculations. Difference of MCPI 2023 (Half 1) and originating MCPI was taken and divided by originating MCPI, and then multiplied by 100 to generate inflation factor percentage. Inflation factor percentage was multiplied by originating cost to generate inflated cost in 2023 USD. Values rounded to nearest dollar.[10]

ESKD, end-stage kidney disease.

Most Patients With CKD Associated With T2D Do Not Receive the Appropriate Tests, Specifically UACR

CKD diagnosis in patients with T2D is established by eGFR, an evaluation of kidney function, and UACR, an evaluation of kidney damage, over a 12-month period[13]

Despite guideline recommendations from the ADA, AACE, ESC, and KDIGO to test eGFR and UACR **at least annually** in all patients with T2D[5,14-16]:

eGFR testing rates are

>94%[11*†]

HOWEVER

UACR testing rates are only

38.7%[11*†]

Low testing rates indicate failure to achieve quality measures[11,17]

The National Committee for Quality Assurance (NCQA) has developed a Healthcare Effectiveness Data and Information Set (HEDIS®) measure called KIDNEY HEALTH EVALUATION FOR PATIENTS WITH DIABETES (KED), which **assesses whether patients aged 18 to 85 years with diabetes received annual UACR and eGFR testing.**

*As evidenced by a retrospective analysis of 101,057 patients with CKD associated with T2D across the US who had data in the Optum Clinformatics database. Investigators sought to evaluate eGFR and UACR testing rates over a 1-year period.[11]

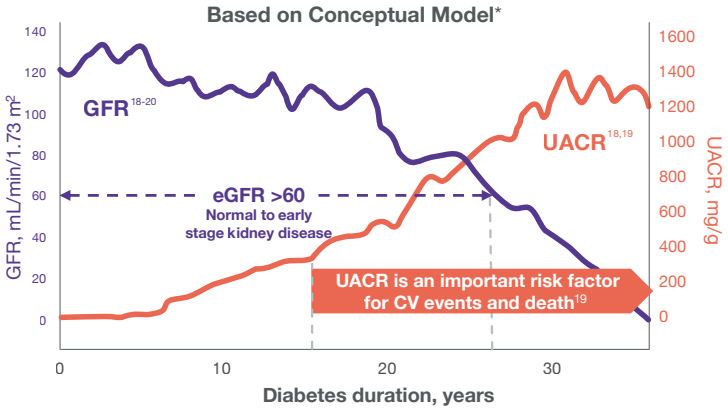
†Estimates of diabetes may not delineate between T1D and T2D. According to the American Diabetes Association, T2D accounts for 90% to 95% of all diabetes cases. Therefore, statistics that describe diabetes may be more characteristic of T2D.[5]

AACE, American Association of Clinical Endocrinology; ADA, American Diabetes Association; ESC, European Society of Cardiology; KDIGO, Kidney Disease: Improving Global Outcomes; T1D, type 1 diabetes.

HEDIS® is a registered trademark of the National Committee for Quality Assurance (NCQA).

Albuminuria, Measured Through UACR, Is an Independent Predictor of Poor CV Outcomes and a Major Cost Driver

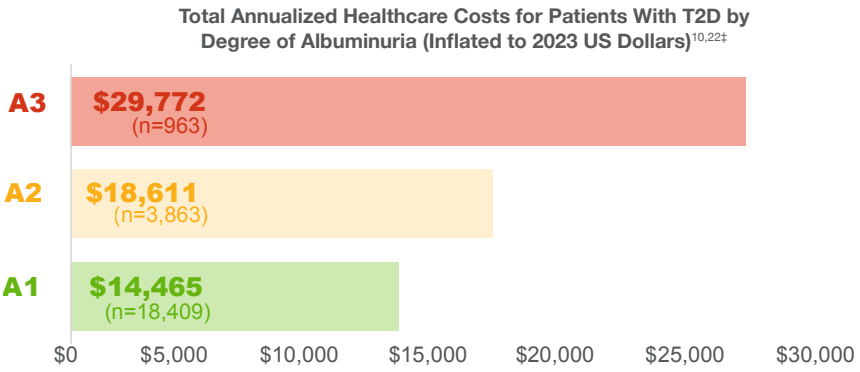
Elevated UACR is often the earliest indicator of CKD and associated CV and kidney risk, and can occur years before eGFR decline[18-20]



Albuminuria has been identified as a contributing factor to rapidly progressing kidney disease (ie, >4 mL/min/1.73 m² eGFR reduction per year) in patients with T2D, with ~25% experiencing rapid progression within just 2 years[21†]

Healthcare costs increase as albuminuria worsens[22,23]:

Albuminuria Catagories[23]	UACR, mg/g
A3 Severely increased	≥300
A2 Moderately increased	30-299
A1 Normal to mildly increased	<30



*Timeline is well characterized for T1D. For T2D, timeline may depart from the illustration due to the variable timing of hyperglycemia onset.[19]

†Estimates of diabetes may not delineate between T1D and T2D. According to the American Diabetes Association, T2D accounts for 90% to 95% of all diabetes cases. Therefore, statistics that describe diabetes may be more characteristic of T2D.[5]

‡$P<0.0001$ for adjusted cost differences.[22]

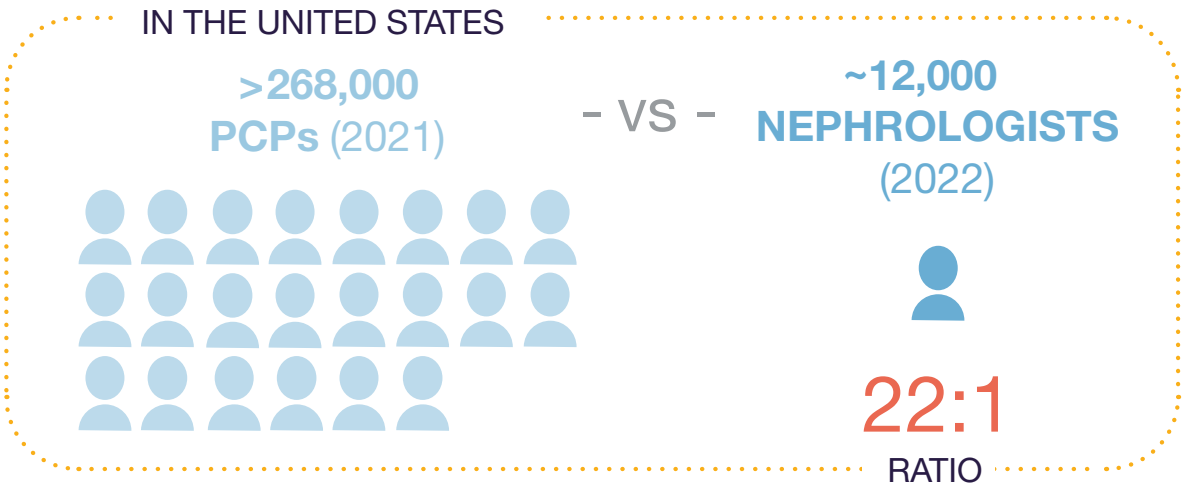
GFR, glomerular filtration rate.

Early UACR Evaluation by PCPs May Improve CKD Diagnosis, Monitoring, and Treatment

PCPs are key players in CKD detection and management:

- Patients with T2D and CKD stages 1 to 3 are often evaluated in the primary care setting, but are often not diagnosed or actively managed by PCPs[24-26]
- Activating PCPs to diagnose and treat patients with early stages of CKD may help ensure nephrologists can focus on treating later-stage patients with more acute treatment needs[24,25]
- Incorporating UACR testing into routine PCP examinations of patients with T2D can help improve awareness, diagnosis, and monitoring of CKD—and subsequently guide evidence-based treatment[11,23,27]

Limited number of nephrologists underscores the need for management of patients with early stage CKD by PCPs[28,29]:



PCP, primary care physician.

High Costs of Care for Patients With CKD Associated With T2D Emphasizes the Need to Accurately Diagnose and Code Conditions

LACK OF DIAGNOSIS[30]

Patients may have lab-indicated CKD without corresponding diagnosis codes

Nearly 75% of Medicare Advantage patients with lab-indicated CKD did not have a corresponding diagnosis code

Importance of Coding on Risk Scores

Risk-adjusted scoring represents a plan or health system population's burden of illness (as defined by diagnosis code/stage). In the illustrative examples below, the risk-adjusted scores are based on diagnoses of CKD stage 3 or 4 in non-institutional, non-dual, non-disabled female patients aged 67 years with other common comorbidities[31]

		Patient A **(Undiagnosed CKD)**	Patient B **(Diagnosed CKD Stage 3)**	Patient C **(Diagnosed CKD Stage 4)**
Gender, Age	Female, 67	0.330	0.330	0.330
Conditions	Diabetes with Chronic Complications	0.166	0.166	0.166
	Congestive Heart Failure (CHF)	0.360	0.360	0.360
	CKD Stage	N/A	0.127	0.514
	Diabetes with CHF	0.112	0.112	0.112
	CHF*Renal	N/A	0.176	0.176
	Total Raw Risk Score	**0.968**	**1.271**	**1.658**
Parameters	Normalization Factor	1.015	1.015	1.015
	Coding Pattern Differences	0.941	0.941	0.941
	Final Risk Score	**0.897**	**1.178**	**1.537**

Guideline-Directed Medical Therapy Is Informed by Comprehensive Kidney Health Evaluation, Including eGFR and UACR

At-risk patients should receive testing, treatment, and referral according to their individual risk[23]

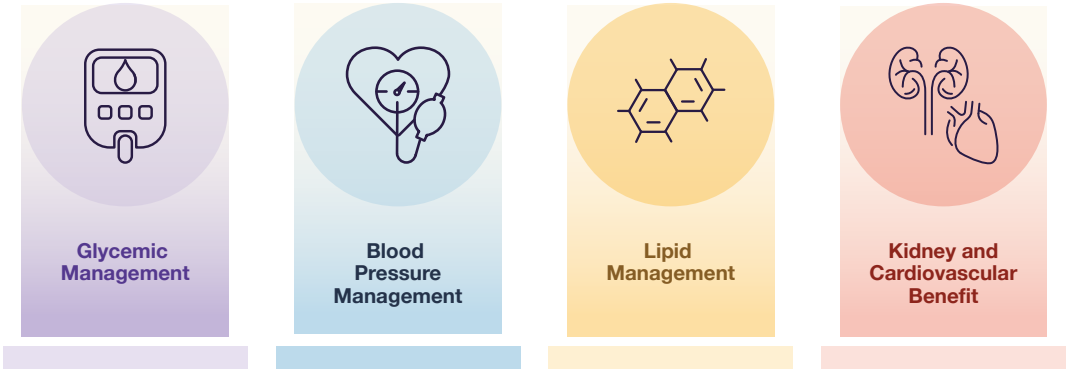
ADA-KDIGO Consensus Statement: Risk of Progression, Frequency of Visits, and Referral to Nephrology According to eGFR and UACR[23]

GFR Categories (mL/min/1.73 m²), Description and Range			Albuminuria Categories, Description and Range: A1 — Normal to mildly increased, <30 mg/g, <3 mg/mmol	A2 — Moderately increased, 30-299 mg/g, 3-29 mg/mmol	A3 — Severely increased, ≥300 mg/g, ≥30 mg/mmol	
G1	Normal or high	>90	Screen 1	Treat 1	Treat and refer 2	Low risk (if no other markers of kidney disease, no CKD)
G2	Mildly decreased	60–89	Screen 1	Treat 1	Treat and refer 2	
G3a	Mildly to moderately decreased	45–59	Treat 1	Treat 2	Treat and refer 3	Moderately increased risk
G3b	Moderately to severely decreased	30–44	Treat 2	Treat and refer 3	Treat and refer 3	High risk
G4	Severely decreased	15–29	Treat and refer 3	Treat and refer 3	Treat and refer 4+	Very high risk
G5	Kidney failure	<15	Treat and refer 4+	Treat and refer 4+	Treat and refer 4+	

Delayed identification of CKD in patients with T2D impedes timely initiation of evidence-based treatment[26]

Treatment Guidelines for CKD Associated With T2D Focus on Risk Reduction and Semi-Annual Assessment of UACR

GUIDELINE-DIRECTED CARE INCLUDES[5,23]:



LIFESTYLE MODIFICATION AND DIABETES EDUCATION

Risk Factor Reassessment

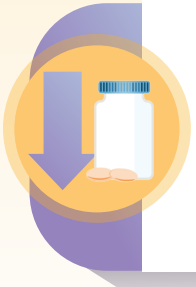
every 3-6 months[23]

The American Diabetes Association recommends a ≥30% reduction in urinary albumin for patients who have CKD and urinary albumin ≥300 mg/g.[5] A 30% decrease in albuminuria corresponded to a 27% decrease in CKD progression for patients with UACR ≥30 mg/g[32]*

*As evidenced by a prediction model analysis that evaluated 6-month change in albuminuria and a composite kidney endpoint (defined as end-stage kidney disease [initiation of chronic treatment with dialysis or kidney transplantation], eGFR <15 mL/min/1.73 m^2, or doubling of serum creatinine sustained at the subsequent visit) across 41 clinical trials in 22,544 patients with UACR ≥30 mg/g.[32]

Guideline-Directed Medical Therapies for CKD Associated With T2D Are Broadly Underutilized

Real-World Utilization of Guideline-Directed Medical Therapies[33*]



30%
No GDMT

41%
ACEi/ARB only

19%
ACEi/ARB + additional GDMT

American Diabetes Association.

AACE
American Association of Clinical Endocrinology

ESC
European Society of Cardiology

KDIGO
Kidney Disease: Improving Global Outcomes

Clinical practice guidance from the ADA, AACE, ESC, and KDIGO recommend the use of pharmacotherapies to reduce risk in patients with CKD associated with T2D, although real-world data in diagnosed patients show that use is insufficient and there is unchecked disease progression for patients with CKD associated with T2D[5,11,14-16,23,33]

An analysis showed that 94% of patients diagnosed with CKD and T2D were not gaining access to more recently approved therapies indicated to reduce risks of renal and cardiovascular outcomes, with the largest obstacle being restrictions in payer coverage[34]

*Based on Bayer analysis of patient-level claims data encompassing nearly 3.3 million unique adult patients nationally with a diagnosis of CKD and T2D in calendar year 2022.[33]

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; GDMT, guideline-directed medical therapy.

IN PATIENTS WITH CKD ASSOCIATED WITH T2D

Improved Testing, Diagnosis, and Use of GDMT May Reduce the Risk of CV Events, CKD Progression, and High Associated Costs

Improve Testing

UACR is the guideline-preferred method for **albuminuria testing, which is critical to diagnosing CKD,** but is underutilized in patients with T2D[5,11,35]

Increase Diagnosis

Disease identification is crucial to guiding appropriate management of patients with CKD associated with T2D[11,23]

Use Evidence-Based Treatment

Guideline-directed medical therapies are vital, but underutilized, drivers of risk reduction[23,33]

References: 1. Statistics about diabetes. American Diabetes Association. Accessed February 2, 2024. https://diabetes.org/about-diabetes/statistics/about-diabetes **2.** Lin J, Thompson TJ, Cheng YJ, et al. Projection of the future diabetes burden in the United States through 2060. *Popul Health Metr.* 2018;16(1):9. **3.** Bailey RA, Wang Y, Zhu V, Rupnow MFT. Chronic kidney disease in US adults with type 2 diabetes: an updated national estimate of prevalence based on Kidney Disease: Improving Global Outcomes (KDIGO) staging. *BMC Res Notes.* 2014;7:415. **4.** CKD in the general population. United States Renal Data System. 2020 USRDS annual data report. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2020. Accessed February 2, 2024. https://usrds-adr.niddk.nih.gov/2020/chronic-kidney-disease/1-ckd-in-the-general-population **5.** American Diabetes Association. Standards of care in diabetes—2024. *Diabetes Care.* 2024;47(suppl 1):S1-S321. **6.** Afkarian M, Sachs MC, Kestenbaum B, et al. Kidney disease and increased mortality risk in type 2 diabetes. *J Am Soc Nephrol.* 2013;24(2):302-308. **7.** Wu B, Bell K, Stanford A, et al. Understanding CKD among patients with T2DM: prevalence, temporal trends, and treatment patterns–NHANES 2007-2012. *BMJ Open Diabetes Res Care.* 2016;4(1):e000154. **8.** Scirica BM, Mosenzon O, Bhatt DL, et al. Cardiovascular outcomes according to urinary albumin and kidney disease in patients with type 2 diabetes at high cardiovascular risk: observations from the SAVOR-TIMI 53 trial. *JAMA Cardiol.* 2018;3(2):155-163. **9.** Betts KA, Song J, Faust E, et al. Medical costs for managing chronic kidney disease and related complications in patients with chronic kidney disease and type 2 diabetes. *Am J Manag Care.* 2021;27(20 suppl):S369-S374. **10.** U.S. Bureau of Labor Statistics. Databases, tables & calculators by subject. Accessed February 2, 2024. https://data.bls.gov/timeseries/CUUR0000SAM?output_view=data **11.** Betts KA, Song J, Elliott J, et al. Geographical variation in kidney function testing and associations with health care costs among patients with chronic kidney disease and type 2 diabetes. *Am J Manag Care.* 2022;28(6 suppl):S112-S119. **12.** Golestaneh L, Alvarez PJ, Reaven NL, et al. All-cause costs increase exponentially with increased chronic kidney disease stage. *Am J Manag Care.* 2017;23(suppl 10):S163-S172. **13.** National Institute of Diabetes and Digestive and Kidney Diseases. Chronic kidney disease tests & diagnosis. Accessed February 2, 2024. https://www.niddk.nih.gov/health-information/kidney-disease/chronic-kidney-disease-ckd/tests-diagnosis **14.** Marx N, Federici M, Schütt K, et al; for the ESC Scientific Document Group. 2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes. *Eur Heart J.* 2023;44(39):4043-4140. **15.** Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group. KDIGO 2022 clinical practice guideline for diabetes management in chronic kidney disease. *Kidney Int.* 2022;102(5S):S1-S127. **16.** Blonde L, Umpierrez GE, Reddy SS, et al. American Association of Clinical Endocrinology clinical practice guideline: developing a diabetes mellitus comprehensive care plan–2022 update. *Endocr Pract.* 2022;28(10):923-1049. **17.** Kidney health evaluation for patients with diabetes (KED). National Committee for Quality Assurance. Accessed February 2, 2024. https://www.ncqa.org/hedis/measures/kidney-health-evaluation-for-patients-with-diabetes **18.** Afkarian M. Diabetic kidney disease in children and adolescents. *Pediatr Nephrol.* 2015;30(1):65-74. **19.** Alicic RZ, Rooney MT, Tuttle KR. Diabetic kidney disease: challenges, progress, and possibilities. *Clin J Am Soc Nephrol.* 2017;12(12):2032-2045. **20.** Altemtam N, Russell J, El Nahas M. A study of the natural history of diabetic kidney disease (DKD). *Nephrol Dial Transplant.* 2012;27(5):1847-1854. **21.** Go AS, Yang J, Tan TC, et al. Contemporary rates and predictors of fast progression of chronic kidney disease in adults with and without diabetes mellitus. *BMC Nephrol.* 2018;19(1):146. **22.** Zhou Z, Chaudhari P, Yang H, et al. Healthcare resource use, costs, and disease progression associated with diabetic nephropathy in adults with type 2 diabetes: a retrospective observational study. *Diabetes Ther.* 2017;8(3):555-571. **23.** de Boer IH, Khunti K, Sadusky T, et al. Diabetes management in chronic kidney disease: a consensus report by the American Diabetes Association (ADA) and Kidney Disease: Improving Global Outcomes (KDIGO). Diabetes Care. 2022;45(12):3075-3090. **24.** Vassalotti JA, Centor R, Turner BJ, et al. Practical approach to detection and management of chronic kidney disease for the primary care clinician. *Am J Med.* 2016;129(2):153-162. **25.** Gaitonde DY, Cook DL, Rivera IM. Chronic kidney disease: detection and evaluation. *Am Fam Physician.* 2017;96(12):776-783. **26.** Szczech LA, Stewart RC, Su H-L, et al. Primary care detection of chronic kidney disease in adults with type-2 diabetes: the ADD-CKD Study (Awareness, Detection and Drug Therapy in Type 2 Diabetes and Chronic Kidney Disease). *PLoS One.* 2014;9(11):e110535. **27.** Kidney failure risk factor: urine albumin-creatinine ratio (uACR). National Kidney Foundation. Accessed February 2, 2024. https://www.kidney.org/content/kidney-failure-risk-factor-urine-albumin-to-creatinine-ration-uacr **28.** State of the primary care workforce, 2023. Health Resources and Services Administration. Accessed April 30, 2024. https://bhw.hrsa.gov/sites/default/files/bureau-health-workforce/data-research/state-of-primary-care-workforce-2023.pdf **29.** Ibrahim T. Top 10 predictions about US nephrologists in 2035. American Society of Nephrology Kidney News. July 2022. Accessed April 30, 2024. https://www.kidneynews.org/downloadpdf/journals/kidney-news/14/7/article-p8_3.xml **30.** Chronic kidney disease often undiagnosed in Medicare beneficiaries. Centers for Medicare & Medicaid Services. Updated September 2021. Accessed March 18, 2024. https://www.cms.gov/files/document/ckd-data-highlight102020-2.pdf **31.** Announcement of calendar year (CY) 2024 Medicare Advantage (MA) capitation rates and Part C and Part D payment policies. Centers for Medicare & Medicaid Services. Accessed April 25, 2024. https://www.cms.gov/files/document/2024-announcement-pdf.pdf **32.** Heerspink HJL, Greene T, Tighiouart H, et al; for the Chronic Kidney Disease Epidemiology Collaboration. Change in albuminuria as a surrogate endpoint for progression of kidney disease: a meta-analysis of treatment effects in randomised clinical trials. *Lancet Diabetes Endocrinol.* 2019;7(2):128-139. **33.** Data on file. Bayer. **34.** The impact of payer access controls in chronic kidney disease for patients with type II diabetes. IQVIA. Accessed March 18, 2024. https://www.iqvia.com/locations/united-states/blogs/2022/03/impact-of-payer-access-controls-chronic-kidney-disease-patients-type-ii-diabetes **35.** Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int.* 2024;105(4S):S117-S314.