



REVIEW

Trajectory of Kidney Function in T1D over Time: A Scoping Review

Favian Co · Reid Whitlock · Arvind Katta · Carolina Aldworth · Jon Mares ·

Zihe Zheng · Mauricio Ferri · Nicole Askin · Navdeep Tangri

Received: April 15, 2026 / Accepted: June 25, 2026
© The Author(s) 2026

ABSTRACT

Introduction: Type 1 diabetes (T1D) is associated with chronic kidney disease (CKD) and major adverse cardiovascular events (MACE). Contemporary data on the natural history of kidney function decline and the effect of therapies on slowing disease progression in T1D-related CKD are limited. We conducted a scoping review to describe the natural trajectory of kidney function and its effects in individuals with T1D in the USA.

Methods: In our scoping review of observational studies and grey literature, we searched

EMBASE (Ovid), Cumulative Index to Nursing and Allied Health Literature [CINAHL; Elton B. Stephens Company (EBSCO)], MEDLINE (Ovid), Scopus (Elsevier), Global Health (Ovid), and the Food and Drug Administration from inception to 25 April 2025. The study population included adults (age ≥ 18 years) with T1D in the USA. Our outcomes were change in estimated glomerular filtration rate (eGFR), urine albumin-to-creatinine ratio (UACR), MACE (myocardial infarction, ischemic stroke, cardiovascular death, unstable angina, or heart failure hospitalization), and healthcare resource use (HCRU). We screened 6437 abstracts and selected 22 texts that matched our criteria.

Results: In one cohort, more than 50.0% of individuals with T1D developed moderately increased albuminuria (UACR > 30 – 299 mg/g) after 20 years and two cohort studies in T1D observed a progressive annual eGFR decline of 3 mL/min/ 1.73 m². Five cohort studies found higher proportions of individuals with T1D experienced MACE or kidney failure versus those without T1D. Cross-sectional studies estimated total annual cost of HCRU in the USA at \$17–27.8 billion for those with T1D, with annual per-patient costs ranging from \$73,534–\$112,833 for kidney failure and \$40,889–\$86,417 for components of MACE.

Conclusions: T1D is associated with a high burden of CKD, MACE, and healthcare costs. A clearer understanding of the trajectory of kidney

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s13300-026-01899-9>.

F. Co · R. Whitlock (✉) · N. Tangri
Seven Oaks General Hospital Chronic Disease
Innovation Centre, 2LB19-2300 McPhillips St,
Winnipeg, MB R2V 3M3, Canada
e-mail: rwhitlock@sogh.mb.ca

A. Katta · C. Aldworth · J. Mares · Z. Zheng · M. Ferri
Medical Affairs, Bayer US, LLC, Whippany, NJ, USA

N. Askin
WRHA Virtual Library, University of Manitoba,
Winnipeg, MB, Canada

N. Tangri
Department of Internal Medicine, University
of Manitoba, Winnipeg, MB, Canada

function decline in T1D would help providers and policymakers understand the impact potential therapies to treat T1D-related CKD may have on reducing the risk of kidney failure, MACE, and HCRU.

Keywords: Type 1 diabetes; Natural history; UACR; eGFR; MACE; Pharmacotherapies

Key Summary Points

A significant proportion of individuals with type 1 diabetes (T1D) will develop moderately increased albuminuria.

Individuals with T1D experience a higher progressive annual kidney function decline than the general population.

Patients with T1D will experience a high burden of major adverse cardiovascular events, healthcare costs, and resource use.

A clearer understanding of the trajectory of kidney function decline in T1D would help providers and policymakers understand the impact potential therapies to treat T1D-related chronic kidney disease may have on reducing the risk of kidney failure and major adverse cardiovascular events.

INTRODUCTION

Diabetes is distinguished by hyperglycemia, which is driven by complications in insulin secretion, insulin activity, or both [1]. The two main classes of diabetes are type 1 diabetes (T1D), and (2) type 2 diabetes (T2D) [2]. T1D is normally diagnosed in childhood and caused by autoimmune destruction of pancreatic β -cells [3]. Patients with T1D must be administered exogenous insulin. In contrast, T2D is normally diagnosed in adulthood and is marked by insulin resistance and/or unusual insulin secretion [4]. Patients with T2D may require exogenous insulin if blood glucose

levels cannot be controlled by dietary means or oral hypoglycemic agents [5].

Both T1D and T2D are associated with microvascular and macrovascular complications, and increased risk of mortality [6, 7]. Microvascular complications affect several tissues, including the kidneys. However, macrovascular complications affect arteries and veins, including the cardiovascular system [8].

Diabetes is the primary cause of kidney failure [9]. Diabetic kidney disease (DKD) occurs in 20–40% of individuals with T1D and is characterized by albuminuria, reduction in estimated glomerular filtration rate (eGFR), high blood pressure, and higher cardiovascular risk [9, 10].

Overall, there is a paucity of data on the natural history of changes in kidney function in those with T1D compared with T2D as well as fewer treatment options to slow CKD progression. Studies have reported that approximately 85% of patients with DKD and moderately increased albuminuria [urine albumin-to-creatinine ratio (UACR) >30–299 mg/g] develop severely increased albuminuria (UACR $\geq$ 300 mg/g) within the next 10–15 years [11]. Further, 50% of individuals with T1D and severely increased albuminuria progress to kidney failure within 10 years, and at least 75% within 20 years, compared with only 20% of those with T2D and macroalbuminuria [12, 13]. Although the association between T1D and CVD is well known [14, 15], the specific rate and trajectory of decline in kidney function over time in that association is less understood.

Understanding the natural history of kidney function decline in patients with T1D can help healthcare providers and policymakers identify clinical phenotypes based on patterns of T1D-related CKD and devise treatment plans that slow or halt kidney function decline. As such, we conducted a scoping review to investigate the natural history, cardiovascular burden, regulatory considerations, and health care resource use (HRCU) outcomes associated with CKD in individuals with T1D in the USA.

METHODS

Literature Search

Articles published on EMBASE (Ovid), Cumulative Index to Nursing and Allied Health Literature [CINAHL; Elton B. Stephens Company (EBSCO)], MEDLINE (Ovid), Scopus (Elsevier), and Global Health (Ovid) were captured. Additionally, grey literature published by the Food and Drug Administration (FDA) was included. The search included articles published from inception to 25 April 2025. We adapted a search strategy from our prepared protocol which included keywords and Medical Subject Headings (MeSH) terms related to type 1 diabetes, urine albumin to creatinine ratio, and estimated glomerular filtration rate. The full search strategy used for each database is provided in the Supplementary Material.

Study Selection

Citations were eligible if they met the following criteria: (1) adults (age ≥ 18 years) with T1D and (2) observational studies in a USA setting. We also included materials from our search of the FDA related to pharmacological safety in T1D-related CKD. We excluded articles where the study population was on kidney replacement therapy. There were no restrictions due to language or sample size.

We aimed to describe temporal changes in kidney function in patients with T1D and the associated cardiovascular events and HCRU. Our outcomes included (1) changes in eGFR, (2) changes in UACR, (3) major adverse cardiovascular events (MACE), and (4) HCRU including costs of treatment, hospitalizations, and emergency room visits. We defined MACE as a composite outcome of myocardial infarction, ischemic stroke, cardiovascular death, unstable angina, or heart failure hospitalization [16]. We also evaluated the individual components of MACE. Additionally, we sought citations that compared all outcomes in T1D to those with T2D.

Once the search results were inputted into Covidence by the medical librarian, one

reviewer (F.C.) screened through the abstracts and selected articles for full text review. From there, the full texts were reviewed to be selected for data extraction. The reviewer consulted with the senior author (N.T.) before finalizing all articles for inclusion at each stage.

Data Extraction

We extracted the author, title, journal, year of publication, study setting and duration, diagnosis of diabetes, and relevant outcomes with magnitude of change and association.

Ethics Statement

This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

RESULTS

The citations were imported into Covidence. The search captured 10,190 citations. After removing duplicates, 6437 abstracts were screened. In addition to the captured citations, three articles were manually added. Following full-text screening, 22 articles satisfied the inclusion criteria. Figure 1 provides the search results and study selection using an adapted Preferred Reporting Items for Systematic Reviews and Meta-analyses Extension for Scoping Reviews (PRISMA ScR) flow diagram [17].

Theme 1: Changes in UACR in Patients with T1D

Table 1 contains four citations that explored the changes in UACR in patients with T1D. Three studies found that longer diabetes duration is associated with higher levels of protein in the urine (i.e., severely or moderately increased albuminuria) [18, 19]. Conversely, another study found that hyperfiltration was not associated

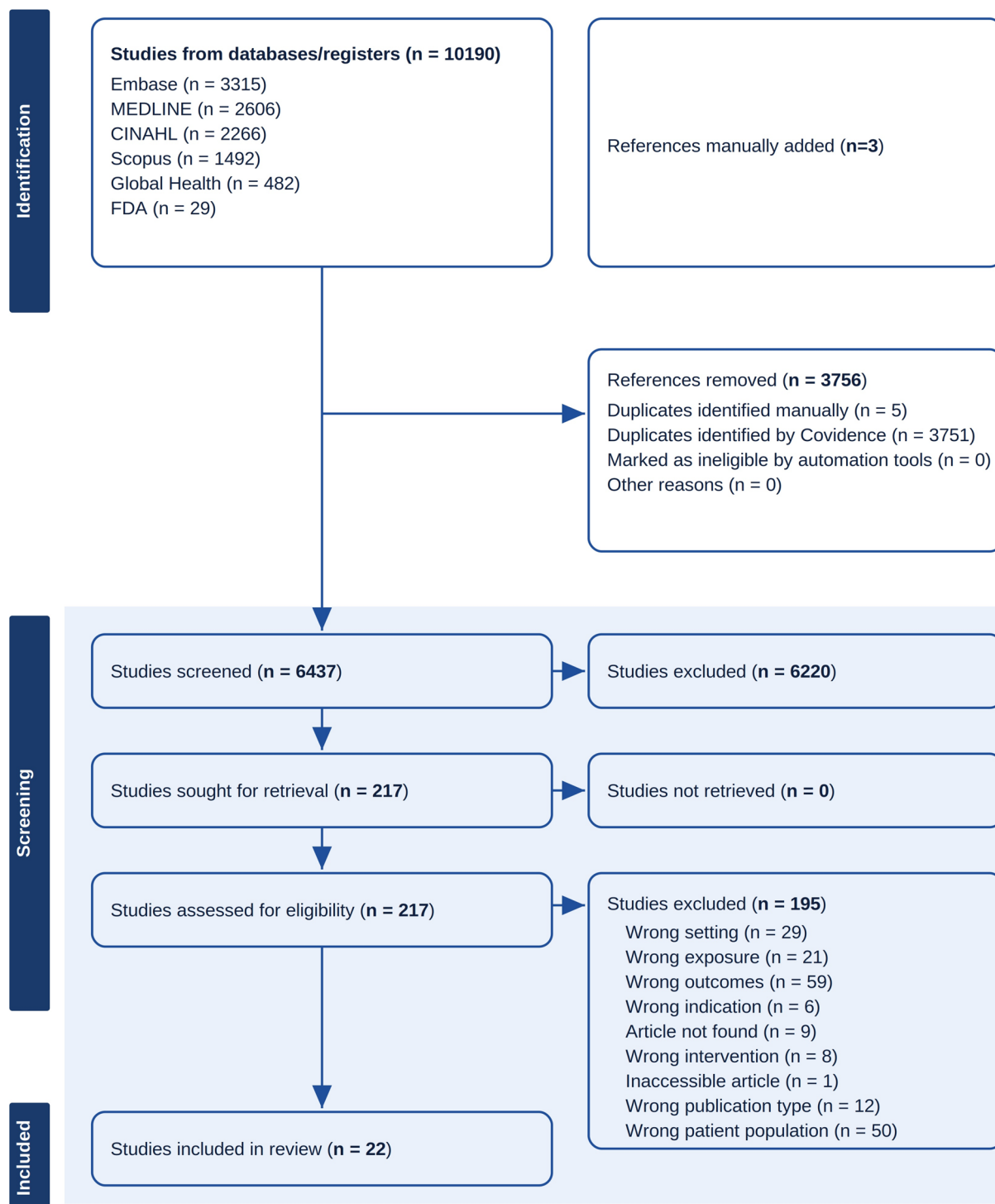


Fig. 1 Flow diagram of the literature search

Table 1 Changes in UACR in patients with T1D

Author (year)	Location	Population	Study design	Findings
Caramori et al. (2003) [18]	Minnesota	T1D patients with diabetes for at least 10 years with UACR < 30 mg/g (<i>n</i> = 105)	Cross-sectional study	A GFR less than 90 mL/min/1.73 m ² was identified in 23 of 105 (21.9%) patients with UACR < 30 mg/g with diabetes for at least 10 years, which could increase the risk of progression to microalbuminuria.
Costacou et al. (2018) [19]	Pittsburgh	T1D diagnosis between 1950 and 1980, living within 2.5 h or 100 miles from Pittsburgh (<i>n</i> = 932)	Prospective cohort study with 25–50 years of follow-up	At least 50.0% and 88.0% of the cohort developed microalbuminuria by 20 and 50 years of diabetes duration, respectively. Similarly, at least 27.1% and almost 71.8% of the cohort would develop macroalbuminuria by 20 and 50 years of diabetes duration, respectively.
Ficociello et al. (2009) [20]	Massachusetts	Patients with T1D (<i>n</i> = 426)	Prospective cohort study with 15 years of follow-up	Hyperfiltration did not contribute to microalbuminuria during the 5, 10, or 15 years of follow-up.
Roy et al. (2007) [21]	New Jersey	Diabetes diagnosis at < 30 years and taking insulin (<i>n</i> = 483)	Prospective cohort study with 6 years of follow-up	In African Americans with T1D, the 6-year incidence of overt albuminuria (albumin excretion rate > 200 µg/min) was 27.5%.

GFR glomerular filtration rate, T1D type 1 diabetes, UACR urine albumin-to-creatinine ratio

Table 2 Changes in eGFR in patients with T1D

Author (year)	Location	Population	Study design	Findings
Costacou et al. (2007) [22]	Pittsburgh	Patients with childhood-onset (< 17 years) T1D with eGFR $\geq$ 60 mL/min/1.73 m ² at baseline (<i>n</i> = 480)	Prospective cohort study with 16 years of follow-up	Over 16 years of follow-up, 71 of 480 (14.8%) developed an eGFR < 60 mL/min/1.73 m ² .
Klein et al. (1999) [23]	Wisconsin	Diabetes diagnosis at < 30 years and taking insulin (<i>n</i> = 2290)	Prospective cohort study with 10 years of follow-up	In patients with T1D, 52.5% reported at least 3 mL/min/1.73 m ² /year decline in creatinine clearance, and 14% developed CKD or kidney failure over 10 years.
Perkins et al. (2007) [24]	Massachusetts	Patients with T1D (<i>n</i> = 568)	Prospective cohort study with 8–12 years of follow-up	Progressive renal decline (i.e., decrease between 3.3 and 2.8 mL/min/1.73 m ² per year) in eGFR usually begins during microalbuminuria. eGFR may be higher than normal when the decline starts.
Roy et al. (2007) [21]	New Jersey	T1D diagnosis at < 30 years and taking insulin (<i>n</i> = 483)	Prospective cohort study with 6 years of follow-up	In African American patients with T1D, the 6-year incidence of kidney failure was 8.7%.

CKD chronic kidney disease, eGFR estimated glomerular filtration rate, T1D type 1 diabetes

with developing microalbuminuria within 5, 10, or 15 years of follow-up [20].

Theme 2: Changes in eGFR in Patients with T1D

Table 2 contains four citations that explored the changes in eGFR in patients with T1D. Over 16 years of follow-up, 71 of 480 (14.8%) participants in the Pittsburgh Epidemiology of Diabetes Complications Study developed an $\text{eGFR} < 60 \text{ mL/min/1.73 m}^2$; of those, 66 (93.0%) had prior/concurrent albuminuria [22]. Two cohort studies found an approximate annual eGFR or creatinine clearance decline of $3 \text{ mL/min/1.73 m}^2$, and another study found 8.7% of individuals with T1D developed kidney failure within 6 years [23, 24].

Theme 3: Comparing the Changes in UACR in Patients with T1D to Those with T2D

We did not capture citations that compared the changes in UACR in patients with T1D with patients with T2D.

Theme 4: Comparing the Changes in eGFR in Patients with T1D to Those with T2D

Table 3 reports a study that compared the changes in eGFR in patients with diabetes who use insulin versus patients with diabetes who only use oral medications for glycemic control. The group who used insulin experienced a greater annual decline in eGFR versus the group who used oral medications (unadjusted: -1.8 versus $-0.7 \text{ mL/min/1.73 m}^2$; adjusted: -1.1 versus $-0.3 \text{ mL/min/1.73 m}^2$). [25]

Theme 5: The Effect of Worsening Kidney Function on Major Adverse Cardiovascular Events in Patients with T1D

Table 4 includes five articles that reported the effects of kidney function decline on MACE in patients with T1D. These observational studies showed that lower levels of kidney function were associated with higher risks of heart failure,

Table 3 Comparison of change in eGFR in patients with T1D to those with T2D

Author (year)	Location	Population	Study design	Findings
Warren et al. (2018) [25]	North Carolina, Mississippi, Minnesota, and Maryland	Patients with diabetes ($n = 15,517$)	Prospective cohort study with 26 years of follow-up	The unadjusted and adjusted mean annual change in eGFR in patients who use insulin was -1.8 and $-1.1 \text{ mL/min/1.73 m}^2$, respectively. On the other hand, the use of only oral medications reported an unadjusted and adjusted mean annual eGFR change of -0.7 and $-0.3 \text{ mL/min/1.73 m}^2$, respectively

eGFR estimated glomerular filtration rate, *T1D* type 1 diabetes, *T2D* type 2 diabetes

Table 4 The effect of renal decline on major adverse cardiovascular events in patients with T1D

Author (year)	Location	Population	Study Design	Implications
Guo et al. (2022) [26]	Pittsburgh	Patients with childhood-onset (< 17 years) T1D ($n = 655$) Mean age: 27 ± 8 years; 49.3% female	Prospective cohort study with 25–50 years of follow-up	Over 25 years of follow-up, 43 of 655 (6.6%) experienced heart failure. Higher eGFR at baseline was associated with heart failure risk reduction (HR 0.6; 95% CI 0.4–0.9; $p = 0.038$)
Klein et al. (2004) [27]	Wisconsin	Patients with T1D ($n = 996$)	Prospective cohort study with 20 years of follow-up	The 20-year age-adjusted cumulative incidence for angina, myocardial infarction, and stroke were 18.1%, 14.8%, and 5.9%, respectively. Diabetic kidney disease was associated with higher risk of cardiovascular events
Manske et al. (1997) [28]	Minnesota	Patients with T1D and creatinine clearance less than 30 mL/min ($n = 198$)	Prospective cohort study with a median follow-up of 41 months	During a median follow-up of 41 months, 28 of 198 patients (14.1%) experienced a myocardial infarction and 7 experienced a cerebrovascular event
Mondesir et al. (2016) [29]	North Carolina, South Carolina, Georgia, Alabama, Arkansas, Louisiana, Mississippi, and Tennessee	Patients with T1D and T2D ($n = 5541$)	Prospective cohort study with a mean follow-up of 5 years	Patients with diabetes using insulin and/or with albuminuria with no history of CHD experienced a similar rate of incident CHD events to patients with prevalent CHD and no diabetes

Table 4 continued

Author (year)	Location	Population	Study Design	Implications
Norby et al. (2022) [30]	Oregon	Patients with T1D and T2D (<i>n</i> = 2997)	Case-control study	In this case-control study, patients with T1D, SCA was 2/41 times more likely than in patients with T2D. In T1D, those with SCA had a higher proportion of CKD than controls (63.6% versus 45.0%)

CHD coronary heart disease, CKD chronic kidney disease, MI myocardial infarction, SCA sudden cardiac arrest, T1D type 1 diabetes, T2D type 2 diabetes

angina, myocardial infarction, cerebrovascular events, coronary heart disease, and sudden cardiac arrests [26–30]. However, the magnitude of annual kidney function decline and its longitudinal relationship with MACE in T1D was not quantified.

Theme 6: Healthcare Resource Utilization in Patients with T1D

Table 5 includes four articles that reported HCRU and costs in patients with T1D. Cross-sectional studies estimated total annual cost of HRCU at \$17–27.8 billion for those with T1D with annual per-patient costs ranging from \$73,534–\$112,833 for kidney failure and \$40,889–\$86,417 for components of MACE, depending on whether the costs were for maintenance of existing comorbidities or for experiencing events.

One study found that starting treatment with an angiotensin-converting enzyme (ACE) inhibitor (captopril) in patients with T1D at the onset of diagnosis is cost effective at \$27,143/QALY (2004 USD cost) it provides the benefit of a cumulative lifetime risk reduction of incidence of kidney failure by 0.5%.

Theme 7: The FDA’s Safety Justifications for T1D Indications

The citations included 2 drug labels, 1 guidance draft, 1 safety communication, and 1 drug development resource [35–38]. We captured two sodium-glucose cotransporter-2 (SGLT2) inhibitors labels [35, 38]. The use of SGLT2 inhibitors in patients with T1D is not recommended due to the increased risk of diabetic ketoacidosis [35, 38], and their safety is not established [37]. The end points of T1D indications are a statistically significant reduction in blood glucose levels [36] (Table 6).

DISCUSSION

In this scoping review of the natural trajectory of kidney function and its effects in individuals with T1D in the USA, we found consistent

Table 5 Healthcare resource use and costs of kidney and cardiovascular events in patients with T1D

Author (year)	Location	Population	Study design	Implications
Dong et al. (2004) [31]	Nationwide	Newly diagnosed T1D assigned to captopril after 1 year of diagnosis and another cohort screened annually for moderately increased albuminuria and treated with captopril only after diagnosis of moderately increased albuminuria	Health economic simulation study with a semi-Markov model and lifetime horizon	Treatment with captopril one year after T1D onset reduces lifetime incidence of kidney failure by 0.5%. Incremental cost-effectiveness of \$27,143/QALY
Willey et al. (2018) [32]	Nationwide	Patients with T1D	Cross-sectional study over an 8-year cohort entry period	The rates of CKD marginally increased from 19.4% in 2007 to 22.0% in 2014 The all-cause hospitalization rate among patients with T1D was 23.7% in 2007, and 20.8% in 2014 The rate of all-cause emergency department visits fluctuated between 23.2% and 24.4% from 2007 to 2014 Overall costs incurred by patients with T1D was estimated at between \$17.9–25.0 billion in 2007 and \$18.8–27.8 billion in 2014
Yang et al. (2020) [33]	Nationwide	Patients with T1D	Retrospective cohort study with a mean follow-up between 1 and 4 years depending on year of cohort entry	The annual per-patient cost was highest for those with T1D and a history of kidney failure (\$112,833) and stroke (\$86,417) The first-year complication costs were highest for those who experienced a kidney failure event (\$73,534), CHF event (\$41,681) and MI event (\$40,899) respectively

Table 5 continued

Author (year)	Location	Population	Study design	Implications
Yeaw et al. (2014) [34]	Nationwide	Patients with T1D	Retrospective cohort study with 2 years of follow-up	Patients with diabetes using insulin and/or with albuminuria with no history of CHD experienced a similar rate of incident CHD events to patients with prevalent CHD and no diabetes
CHD coronary heart disease, CHF congestive heart failure, CKD chronic kidney disease, HR hazard ratio, MI myocardial infarction, QALY quality adjusted life-years, T1D type 1 diabetes				

themes that showed many patients with T1D experience significant increases in UACR and decreases in eGFR throughout their diabetes duration which over time may lead to experiencing kidney failure and MACE. These are contributing factors to an environment where the estimated annual HCRU cost of individuals with T1D is \$27.8 billion in the USA. Notable findings include cohort studies which have found that more than 50% of individuals with T1D develop moderately increased albuminuria after 20 years, a progressive annual decline of eGFR in individuals with T1D up to 3 times higher than what would normally be expected [19, 22, 23], and high rates of MACE. The higher rates of kidney failure and cardiovascular events in patients with T1D contribute to high per-person healthcare costs and total HCRU costs of \$18–28 billion a year in the USA. These facts underscore the urgency to ensure individuals with T1D have access to therapies that can slow the decline of kidney function and reduce the risk of MACE.

Our review could not find direct comparisons of kidney function decline trajectory between T1D and T2D in an American setting. One observational study found that individuals with diabetes using insulin experienced a greater decline in eGFR relative compared to individuals with diabetes using oral medications (unadjusted: −1.8 versus −0.7 mL/min/1.73 m²; adjusted: −1.1 versus −0.3 mL/min/1.73 m²) [25]. Although this may be an indicator that CKD progresses faster in those with T1D versus T2D, there was not enough information in that study to make that conclusion, as the proportion of those with diabetes using insulin who were diagnosed with T1D was not provided. A Danish study found similar trajectories in T1D and T2D that were higher than a normal annual decline of 1 mL/min/1.73 m². The mean annual eGFR declines in patients without albuminuria, moderately increased albuminuria, and severely increased albuminuria after 10 years of CKD G3 diagnosis were 1.9, 2.3, and 3.3 mL/min/1.73 m² in patients with T1D and 1.9, 2.1, and 3.0 mL/min/1.73 m² in patients with T2D, respectively [40].

Over the past decade, more novel therapies, including GLP-1 receptor agonists, nonsteroidal mineralocorticoid receptor antagonists

Table 6 Safety data for T1D indications

Citation title	Citation type	Implications
Dapagliflozin FDA label [35]	Drug label	There is a limitation of use restriction in T1D due to the increased risk of diabetic ketoacidosis
Diabetes mellitus: efficacy endpoints for clinical trials investigating antidiabetic drugs and biological products [36]	Guidance Draft	The efficacy endpoints for patients with T1D or T2D are A_{1C} and hypoglycemia. The decrease from baseline A_{1C} must be statistically significant across trials and subgroups. The risks associated with the extent of reduction in A_{1C} should be evaluated. Hypoglycemia is primarily a safety endpoint. If a hypoglycemia claim is made, the incidence of level 3 hypoglycemia (i.e., altered mental and/or physical state, which, if not treated, may result in fainting, seizures, coma, or death) must be reported
FDA revises labels of SGLT2 inhibitors for diabetes to include warnings about too much acid in the blood and serious urinary tract infections [37]	Safety communication	SGLT2 inhibitors are not prescribed for patients with T1D because their safety and efficacy have not been proven
Sotagliflozin FDA label [38]	Drug label	In patients with T1D, sotagliflozin significantly increased the risk of diabetic ketoacidosis. As such, ketone monitoring should be considered in patients with T1D and sotagliflozin should be discontinued if ketoacidosis is suspected
Table of surrogate endpoints that were the basis of drug approval or licensure [39]	Drug development resource	The surrogate endpoint for adults with T1D that is the basis for drug approval or licensure is A_{1C} through a glucose lowering mechanism of action and is appropriate for traditional approval

A_{1C} hemoglobin A_{1C} , *CGM* continuous glucose monitoring, *FDA* Food and Drug Administration, *SGLT2* sodium-glucose cotransporter 2, *T1D* type 1 diabetes

(MRAs), and SGLT-2 inhibitors have been proven to slow the progression of kidney function and reduce the risk of cardiovascular events in individuals with CKD and T2D [41–46]. However, their safety and effectiveness in T1D have yet to be firmly established. There are key differences in the pathophysiology

of the types of diabetes due to the complete inability of those with T1D to produce insulin, such as increased hepatic glucose production, suppressed capacity of the kidneys to absorb glucose, and inhibited lipid and protein metabolism [47]. Additionally, T2D represents over 90% of all patients with diabetes [48] and

therefore attracts more investment in research compared to T1D.

T1D is also associated with an increased risk of diabetic ketoacidosis, other autoimmune diseases, and severe hypoglycemia compared with T2D, which manifests in more cautious approaches to safety in T1D [49–51]. For example, current FDA guidance issues warnings for SGLT2 inhibitor use in patients with T1D due to the increased risk for diabetic ketoacidosis [35, 38]. However, it is promising that phase 3 clinical trials evaluating new medications in T1D and CKD are either ongoing [52, 53] or have been recently completed, such as the FINE-ONE trial investigating finerenone and participants with T1D and CKD, which found that finerenone was associated with a 25% greater reduction of UACR after 6 months compared with placebo [54].

Our scoping review showed that the early stages of CKD can quickly progress to major adverse kidney and cardiovascular events in patients with T1D. In one study, 33% of individuals progressed to severely increased albuminuria from moderately increased albuminuria over 10 years [55]. Whereas another study found that, in patients with T1D and diabetes diagnosis younger than 30 years of age, 8.7% of patients with T1D and CKD progressed to kidney failure over 6 years [21]. These results are consistent with results found in two analyses of retrospective cohorts of adults with T1D. One study found that 8% developed CKD over a median duration of 24 years, and another found that 9% of those with rapid decline of eGFR developed CKD in at least 6 years [56, 57]. Both studies showed a significant number of individuals with rapid eGFR decline.

Our scoping review also found those with T1D and CKD experienced higher rates heart failure, angina, myocardial infarction, cerebrovascular events, and coronary heart disease than those without. Furthermore, there was evidence to suggest a higher likelihood of sudden cardiac arrest for those with T1D compared with T2D. However, the nature of the relationship between annual eGFR decline and MACE could not be quantified. An analysis of the Diabetes Control and Complications Trial (DCCT) attempted to analyze this temporal relationship. The study results showed that early rapid eGFR loss in T1D

was predictive of CKD, but not MACE, in later years [58].

Longer diabetes duration, with moderately or severely increased albuminuria, was associated with higher mortality risk from cardiovascular disease, coronary heart disease, and stroke relative to patients without albuminuria in both T1D and T2D, possibly indicative of a biomarker as a risk factor for MACE for both types of diabetes [59, 60]. Similarly, a low eGFR forecasted the risk of heart failure endpoints [26]. In an analysis of the Swedish Diabetes Registry where 2.4% of individuals with T1D with a mean age of 41 years were hospitalized with heart failure (HF) over a median of 7 years, the risk of hospitalization for HF was at least twofold higher at eGFR between 45 and 60 mL/min/1.73 m² and at least threefold higher at eGFR less than 30 mL/min/1.73 m² relative to an eGFR of at least 90 mL/min/1.73 m² [61]. In a study of patients with T1D in Finland, the relative risks for CHD, stroke, and any CVD in those with CKD versus those without were 10.3, 10.9, and 10.0, respectively, over a 24-year follow-up period [62].

Clinical variables such as hemoglobin A_{1C} (HbA_{1C}) and hypoglycemia are vital endpoints that reflect the therapeutic benefits of new T1D therapies [63]. Regulatory assessments prioritize these outcomes, as an HbA_{1C} of less than 7% is associated with a lower risk of cardiovascular mortality [64]. However, hypoglycemia remains a critical safety endpoint [36] that can cause sweating, shakiness, dizziness, blurred vision, confusion, and in extreme cases, seizures, coma, or death [65]. Therefore, understanding the balance between achieving glycemic control and minimizing hypoglycemia is essential for the safe management of T1D.

While the above endpoints are crucial, managing T1D with insulin replacement therapy presents significant challenges. Insulin replacement therapies are modalities to control blood glucose levels in individuals with T1D [66]. Hypoglycemia is the predominant adverse event in insulin therapy [67]. Additionally, insulin promotes weight gain, which may decrease the dosage of insulin in individuals with T1D [67]. Noninsulin adjunct medications should (1) mitigate hypoglycemia, (2) prevent insulin-driven weight gain, and (3) promote

cardiovascular outcomes [68]. The prospective adjunct therapies for patients with T1D and CKD are nonsteroidal MRAs, SGLT2 inhibitors, and glucagon-like peptide 1 receptor agonists (GLP-1 RAs) [69, 70].

Our search of FDA literature captured SGLT2 inhibitors but not nonsteroidal MRAs or GLP-1 RAs. There are data available for some of these medications in T1D. A meta-analysis of sotagliflozin as adjunct therapy in patients with T1D reported a reduction in blood glucose levels, blood pressure, and weight; however, the risk of diabetic ketoacidosis needs to be assessed [71]. Similarly, dapagliflozin adjunct therapy in patients with T1D decreased HbA_{1C} and weight; however, diabetic ketoacidosis was higher [72]. Empagliflozin reduced HbA_{1C} [73–75] and weight [73–75], ketoacidosis increased with higher dosage [73], and it did not contribute to increasing the risk for hypoglycemia [75]. A meta-analysis of liraglutide as adjunct treatment in T1D reported reductions in HbA_{1C}, weight, and risk of severe hypoglycemia; however, the odds for nausea and vomiting increased [76]. Additionally, liraglutide was not associated with diabetic ketoacidosis [76]. When exenatide was used as adjunct therapy in patients with T1D, gastrointestinal adverse events, primarily nausea, were reported [77].

To our knowledge, this is the first scoping review to assess the natural longitudinal trajectory of kidney function and UACR in individuals with T1D in the USA. This scoping review has limitations. Many of the studies we assessed did not differentiate between T1D or T2D or intentionally combined data in individuals with T1D and T2D. As a result, we had to exclude studies where we could not report on T1D specifically. Additionally, we could not definitively quantify the extent to which the burden of CKD, MACE, and HCRU is increased in individuals with T1D compared with the general population due to the limited availability of direct longitudinal comparative evidence. However, the available evidence does suggest that individuals with T1D are disproportionately affected by faster progression of CKD and its downstream effects including MACE and healthcare costs.

CONCLUSIONS

T1D is associated with a high burden of CKD, MACE, and healthcare costs, which underscores the need for therapies to treat T1D-related CKD. A clearer understanding of the natural trajectory of the loss of kidney function in patients with T1D would help providers and policymakers better understand the long-term impact potential therapies to treat CKD may have on reducing the risk of kidney failure, MACE, and HCRU in this population.

Author Contributions. Favian Co, Reid Whitlock, Arvind Katta, Carolina Aldworth, Jon Mares, Zihe Zheng, Mauricio Ferri, Nicole Askin, and Navdeep Tangri contributed to the study conception and design. The literature search was performed by Nicole Askin. Data analysis was performed by Favian Co. The first draft of the manuscript was written by Favian Co, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Funding. The Seven Oaks Hospital Chronic Disease Innovation Centre received funding provided by Bayer US to conduct the research and final report. The journal's rapid service fees are funded by Bayer US.

Data Availability. No new data were created or analyzed in this article. All data included in this scoping review are from previously published studies. The full search strategy is available in the supplementary materials. All inquiries about the data presented in this article can be sent to the corresponding author.

Declarations

Conflict of Interest. Navdeep Tangri has received research support and honoraria from Bayer US. Arvind Katta, Carolina Aldworth, Jon Mares, Zihe Zheng, and Mauricio Ferri are employees of Bayer US or were employed by Bayer US at the time of this research. Favian Co, Reid Whitlock, and Nicole Askin have no conflicts of interest to declare. There are no other

relationships or activities that could appear to have influenced the submitted work.

Ethical Approval. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Open Access. This article is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License, which permits any non-commercial use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc/4.0/>.

REFERENCES

1. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2014;37(Supplement_1):S81–90. <https://doi.org/10.2337/dc14-S081>.
2. Punthakee Z, Goldenberg R, Katz P. Definition, classification and diagnosis of diabetes, prediabetes and metabolic syndrome. *Can J Diabetes*. 2018;42:S10–5. <https://doi.org/10.1016/j.cjcd.2017.10.003>.
3. Green A, Hede SM, Patterson CC, et al. Type 1 diabetes in 2017: global estimates of incident and prevalent cases in children and adults. *Diabetologia*. 2017;64(12):2741–50. <https://doi.org/10.1007/s00125-021-05571-8>.
4. Galicia-Garcia U, Benito-Vicente A, Jebbari S, et al. Pathophysiology of type 2 diabetes mellitus. *IJMS*. 2020;21(17):6275. <https://doi.org/10.3390/ijms21176275>.
5. Zimmet P, Alberti KGMM, Shaw J. Global and societal implications of the diabetes epidemic. *Nature*. 2001;414(6865):782–7. <https://doi.org/10.1038/414782a>.
6. Vergès B. Cardiovascular disease in type 1 diabetes: a review of epidemiological data and underlying mechanisms. *Diabetes Metab*. 2020;46(6):442–9. <https://doi.org/10.1016/j.diabet.2020.09.001>.
7. Borén J, Öörni K, Catapano AL. The link between diabetes and cardiovascular disease. *Atherosclerosis*. 2024;394:117607. <https://doi.org/10.1016/j.atherosclerosis.2024.117607>.
8. Lu Y, Wang W, Liu J, Xie M, Liu Q, Li S. Vascular complications of diabetes: a narrative review. *Medicine (Baltimore)*. 2023;102(40):e35285. <https://doi.org/10.1097/MD.00000000000035285>.
9. Ibrahim HAA, Vora JP. Diabetic nephropathy. *Best Pract Res Clin Endocrinol Metab*. 1999;13(2):239–64. <https://doi.org/10.1053/beem.1999.0018>.
10. Ruggenenti P, Remuzzi G. Nephropathy of type 1 and type 2 diabetes: diverse pathophysiology, same treatment? *Nephrol Dial Transplant*. 2000;15(12):1900–2. <https://doi.org/10.1093/ndt/15.12.1900>.
11. Marshall SM. Natural history and clinical characteristics of CKD in type 1 and type 2 diabetes mellitus. *Adv Chronic Kidney Dis*. 2014;21(3):267–72. <https://doi.org/10.1053/j.ackd.2014.03.007>.
12. American Diabetes Association. Nephropathy in diabetes. *Diabetes Care*. 2004;27(suppl_1):s79–83. <https://doi.org/10.2337/diacare.27.2007.s79>.
13. Van Dril E. Chronic kidney disease in patients with diabetes. In: *PSAP 2023 Book 1 (endocrinology and nephrology)*. 2023. https://www.accp.com/docs/bookstore/psap/p2023b1_sample.pdf.
14. Schnell O, Cappuccio F, Genovese S, Standl E, Valensi P, Ceriello A. Type 1 diabetes and cardiovascular disease. *Cardiovasc Diabetol*. 2013;12(1):156. <https://doi.org/10.1186/1475-2840-12-156>.
15. Ducluzeau PH, Fauchier G, Herbert J, et al. Prevalence and incidence of cardiovascular and renal diseases in type 1 compared with type 2 diabetes: a nationwide French observational study of hospitalized patients. *Diabetes Metab*. 2023;49(3):101429. <https://doi.org/10.1016/j.diabet.2023.101429>.
16. Bosco E, Hsueh L, McConeghy KW, Gravenstein S, Saade E. Major adverse cardiovascular event definitions used in observational analysis of administrative databases: a systematic review. *BMC Med*.

- Res Methodol. 2021;21(1):241. <https://doi.org/10.1186/s12874-021-01440-5>.
17. Tricco AC, Lillie E, Zarin W, et al. PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. *Ann Intern Med*. 2018;169(7):467–73. <https://doi.org/10.7326/m18-0850>.
 18. Caramori ML, Fioretto P, Mauer M. Low glomerular filtration rate in normoalbuminuric type 1 diabetic patients. *Diabetes*. 2003;52(4):1036–40. <https://doi.org/10.2337/diabetes.52.4.1036>.
 19. Costacou T, Orchard TJ. Cumulative kidney complication risk by 50 years of type 1 diabetes: the effects of sex, age, and calendar year at onset. *Diabetes Care*. 2018;41(3):426–33. <https://doi.org/10.2337/dc17-1118>.
 20. Ficociello LH, Perkins BA, Roshan B, et al. Renal hyperfiltration and the development of microalbuminuria in type 1 diabetes. *Diabetes Care*. 2009;32(5):889–93. <https://doi.org/10.2337/dc08-1560>.
 21. Roy MS, Affouf M, Roy A. Six-year incidence of proteinuria in type 1 diabetic African Americans. *Diabetes Care*. 2007;30(7):1807–12. <https://doi.org/10.2337/dc06-2534>.
 22. Costacou T, Ellis D, Fried L, Orchard TJ. Sequence of progression of albuminuria and decreased GFR in persons with type 1 diabetes: a cohort study. *Am J Kidney Dis*. 2007;50(5):721–32. <https://doi.org/10.1053/j.ajkd.2007.08.005>.
 23. Klein R, Klein BE, Moss SE, Cruickshanks KJ, Brazy PC. The 10-year incidence of renal insufficiency in people with type 1 diabetes. *Diabetes Care*. 1999;22(5):743–51. <https://doi.org/10.2337/diacare.22.5.743>.
 24. Perkins BA, Ficociello LH, Ostrander BE, et al. Microalbuminuria and the risk for early progressive renal function decline in type 1 diabetes. *J Am Soc Nephrol*. 2007;18(4):1353–61. <https://doi.org/10.1681/asn.2006080872>.
 25. Warren B, Rebholz CM, Sang Y, et al. Diabetes and trajectories of estimated glomerular filtration rate: a prospective cohort analysis of the atherosclerosis risk in communities study. *Diabetes Care*. 2018;41(8):1646–53. <https://doi.org/10.2337/dc18-0277>.
 26. Guo J, Costacou T, Orchard TJ. Long term risk of heart failure in individuals with childhood-onset type 1 diabetes. *J Diabetes Complications*. 2022;36(8):108233. <https://doi.org/10.1016/j.jdiacomp.2022.108233>.
 27. Klein BEK, Klein R, McBride PE, et al. Cardiovascular disease, mortality, and retinal microvascular characteristics in type 1 diabetes: Wisconsin epidemiologic study of diabetic retinopathy. *Arch Intern Med*. 2004;164(17):1917. <https://doi.org/10.1001/archinte.164.17.1917>.
 28. Manske CL, Wilson RF, Wang Y, Thomas W. Atherosclerotic vascular complications in diabetic transplant candidates. *Am J Kidney Dis*. 1997;29(4):601–7. [https://doi.org/10.1016/s0272-6386\(97\)90344-9](https://doi.org/10.1016/s0272-6386(97)90344-9).
 29. Mondesir FL, Brown TM, Muntner P, et al. Diabetes, diabetes severity, and coronary heart disease risk equivalence: Reasons for Geographic and Racial Differences in Stroke (REGARDS). *Am Heart J*. 2016;181:43–51. <https://doi.org/10.1016/j.ahj.2016.08.002>.
 30. Norby FL, Reinier K, Uy-Evanado A, et al. Sudden cardiac death in patients with type 1 versus type 2 diabetes. *Mayo Clin Proc*. 2022;97(12):2271–81. <https://doi.org/10.1016/j.mayocp.2022.05.021>.
 31. Dong FB, Sorensen SW, Manninen DL, et al. Cost effectiveness of ACE inhibitor treatment for patients with type 1 diabetes mellitus. *Pharmacoeconomics*. 2004;22(15):1015–27. <https://doi.org/10.2165/00019053-200422150-00005>.
 32. Willey VJ, Kong S, Wu B, et al. Estimating the real-world cost of diabetes mellitus in the United States during an 8-year period using 2 cost methodologies. *Am Health Drug Benef*. 2018;11(6):310–8.
 33. Yang W, Cintina I, Hoerger T, et al. Estimating costs of diabetes complications in people <65 years in the U.S. using panel data. *J Diabetes Complic*. 2020;34(12):107735. <https://doi.org/10.1016/j.jdiacomp.2020.107735>.
 34. Yeaw J, Halinan S, Hines D, et al. Direct medical costs for complications among children and adults with diabetes in the US commercial payer setting. *Appl Health Econ Health Policy*. 2014;12(2):219–30. <https://doi.org/10.1007/s40258-014-0086-9>.
 35. FDA. FARXIGA (dapagliflozin). Published online May 2023. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/202293s026lbl.pdf.
 36. FDA. Diabetes mellitus: efficacy endpoints for clinical trials investigating antidiabetic drugs and biological products. Published online May 2023. <https://www.fda.gov/media/168475/download>.
 37. FDA. FDA revises labels of SGLT2 inhibitors for diabetes to include warnings about too much acid in the blood and serious urinary tract infections. March 16, 2022. <https://www.fda.gov/drugs/drug-safety-and-availability/fda-revis>

- es-labels-sglit2-inhibitors-diabetes-include-warnings-about-too-much-acid-blood-and-serious.
38. FDA. INPEFA (Sotagliflozin). Published online May 2023. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/216203s000lbl.pdf.
 39. FDA. Table of surrogate endpoints that were the basis of drug approval or licensure. December 17, 2024. <https://www.fda.gov/drugs/development-resources/table-surrogate-endpoints-were-basis-drug-approval-or-licensure>.
 40. Vistisen D, Andersen GS, Hulman A, Persson F, Rossing P, Jørgensen ME. Progressive decline in estimated glomerular filtration rate in patients with diabetes after moderate loss in kidney function—even without albuminuria. *Diabetes Care*. 2019;42(10):1886–94. <https://doi.org/10.2337/dc19-0349>.
 41. Pitt B, Filippatos G, Agarwal R, et al. Cardiovascular events with finerenone in kidney disease and type 2 diabetes. *N Engl J Med*. 2021;385(24):2252–63. <https://doi.org/10.1056/NEJMoa2110956>.
 42. Bakris GL, Agarwal R, Anker SD, et al. Effect of finerenone on chronic kidney disease outcomes in type 2 diabetes. *N Engl J Med*. 2020;383(23):2219–29. <https://doi.org/10.1056/NEJMoa2025845>.
 43. Perkovic V, Tuttle KR, Rossing P, et al. Effects of semaglutide on chronic kidney disease in patients with type 2 diabetes. *N Engl J Med*. 2024;391(2):109–21. <https://doi.org/10.1056/NEJMoa2403347>.
 44. Heerspink HJL, Stefánsson BV, Correa-Rotter R, et al. Dapagliflozin in patients with chronic kidney disease. *N Engl J Med*. 2020;383(15):1436–46. <https://doi.org/10.1056/NEJMoa2024816>.
 45. Perkovic V, Jardine MJ, Neal B, et al. Canagliflozin and renal outcomes in type 2 diabetes and nephropathy. *N Engl J Med*. 2019;380(24):2295–306. <https://doi.org/10.1056/NEJMoa1811744>.
 46. The EMPA-KIDNEY Collaborative Group. Empagliflozin in patients with chronic kidney disease. *N Engl J Med*. 2023;388(2):117–27. <https://doi.org/10.1056/NEJMoa2204233>.
 47. Ozougwu O. The pathogenesis and pathophysiology of type 1 and type 2 diabetes mellitus. *J Physiol Pathophysiol*. 2013;4(4):46–57. <https://doi.org/10.5897/JPA2013.0001>.
 48. Chatterjee S, Khunti K, Davies MJ. Type 2 diabetes. *Lancet*. 2017;389(10085):2239–51. [https://doi.org/10.1016/S0140-6736\(17\)30058-2](https://doi.org/10.1016/S0140-6736(17)30058-2).
 49. Nederstigt C, Uitbeijerse BS, Janssen LGM, Corssmit EPM, De Koning EJP, Dekkers OM. Associated auto-immune disease in type 1 diabetes patients: a systematic review and meta-analysis. *Eur J Endocrinol*. 2019;180(2):135–44. <https://doi.org/10.1530/EJE-18-0515>.
 50. Farsani SE, Brodovicz K, Soleymanlou N, Marquard J, Wissinger E, Maiese BA. Incidence and prevalence of diabetic ketoacidosis (DKA) among adults with type 1 diabetes mellitus (T1D): a systematic literature review. *BMJ Open*. 2017;7(7):e016587. <https://doi.org/10.1136/bmjopen-2017-016587>.
 51. Briscoe VJ, Davis SN. Hypoglycemia in type 1 and type 2 diabetes: physiology, pathophysiology, and management. *Clin Diabetes*. 2006;24(3):115–21. <https://doi.org/10.2337/diaclin.24.3.115>.
 52. deBoer I. Trial of semaglutide for diabetic kidney disease in type 1 diabetes. *clinicaltrials.gov*; 2025. <https://clinicaltrials.gov/study/NCT05822609>. Accessed March 10, 2026.
 53. Doria A. Sotagliflozin to slow kidney function decline in persons with type 1 diabetes and diabetic kidney disease. *clinicaltrials.gov*; 2025. <https://clinicaltrials.gov/study/NCT06217302>. Accessed 10 Mar 2026.
 54. Heerspink HJL, Birkenfeld AL, Cherney DZI, et al. Finerenone in type 1 diabetes and chronic kidney disease. *N Engl J Med*. 2026;394(10):947–57. <https://doi.org/10.1056/NEJMoa2512854>.
 55. Rossing P, Hougaard P, Parving HH. Progression of microalbuminuria in type 1 diabetes: ten-year prospective observational study. *Kidney Int*. 2005;68(4):1446–50. <https://doi.org/10.1111/j.1523-1755.2005.00556.x>.
 56. Bjornstad P, Cherney DZ, Snell-Bergeon JK, et al. Rapid GFR decline is associated with renal hyperfiltration and impaired GFR in adults with type 1 diabetes. *Nephrol Dial Transplant*. 2015;30(10):1706–11. <https://doi.org/10.1093/ndt/gfv121>.
 57. Favel K, Bone JN, Elliott T, Panagiotopoulos C, Mammen C. Classification of longitudinal estimated glomerular filtration rate trajectories in Canadian adults with type 1 diabetes. *J Diabetes Complications*. 2024;38(11):108864. <https://doi.org/10.1016/j.jdiacomp.2024.108864>.
 58. Perkins BA, Bebu I, Gao X, et al. Early trajectory of estimated glomerular filtration rate and long-term advanced kidney and cardiovascular complications in type 1 diabetes. *Diabetes Care*. 2022;45(3):585–93. <https://doi.org/10.2337/dc21-1883>.

59. Valmadrid CT, Klein R, Moss SE, Klein BEK. The risk of cardiovascular disease mortality associated with microalbuminuria and gross proteinuria in persons with older-onset diabetes mellitus. *Arch Intern Med*. 2000;160(8):1093. <https://doi.org/10.1001/archinte.160.8.1093>.
60. De Boer IH, Gao X, Cleary PA, et al. Albuminuria changes and cardiovascular and renal outcomes in type 1 diabetes: the DCCT/EDIC study. *CJASN*. 2016;11(11):1969–77. <https://doi.org/10.2215/cjn.02870316>.
61. Vestberg D, Rosengren A, Olsson M, et al. Decreased eGFR as a risk factor for heart failure in 13 781 individuals with type 1 diabetes. *J Diabetes Sci Technol*. 2016;10(1):131–6. <https://doi.org/10.1177/1932296815596174>.
62. Tuomilehto J, Borch-Johnsen K, Molarius A, et al. Incidence of cardiovascular disease in type 1 (insulin-dependent) diabetic subjects with and without diabetic nephropathy in Finland. *Diabetologia*. 1998;41(7):784–90. <https://doi.org/10.1007/s001250050988>.
63. Ehlers MR. Strategies for clinical trials in type 1 diabetes. *J Autoimmun*. 2016;71:88–96. <https://doi.org/10.1016/j.jaut.2016.03.008>.
64. Lind M, Svensson AM, Kosiborod M, et al. Glycemic control and excess mortality in type 1 diabetes. *N Engl J Med*. 2014;371(21):1972–82. <https://doi.org/10.1056/nejmoa1408214>.
65. Starr L, Dutta S, Danne T, Karpen SR, Hutton C, Kowalski A. The urgent need for breakthrough therapies and a world without type 1 diabetes. *Diabetes Ther*. 2025;16(6):1063–76. <https://doi.org/10.1007/s13300-025-01735-6>.
66. Lucier J, Mathias P. Type 1 diabetes. Published online January 2025. <https://www.ncbi.nlm.nih.gov/books/NBK507713/>.
67. Holt RIG, DeVries JH, Hess-Fischl A, et al. The management of type 1 diabetes in adults. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care*. 2021;44(11):2589–625. <https://doi.org/10.2337/dci21-0043>.
68. Petrie JR. SGLT2 inhibitors in type 1 diabetes: knocked down, but up again? *Lancet Diabetes Endocrinol*. 2017;5(11):841–3. [https://doi.org/10.1016/s2213-8587\(17\)30315-7](https://doi.org/10.1016/s2213-8587(17)30315-7).
69. Heerspink HJL, Birkenfeld AL, Cherney DZI, et al. Rationale and design of a randomised phase III registration trial investigating finerenone in participants with type 1 diabetes and chronic kidney disease: the FINE-ONE trial. *Diabetes Res Clin Pract*. 2023;204:110908. <https://doi.org/10.1016/j.diabres.2023.110908>.
70. Timmons JG, Littlejohn L, Boyle JG, Petrie JR. Recent developments in adjunct therapies for type 1 diabetes. *Expert Opin Investig Drugs*. 2022;31(12):1311–20. <https://doi.org/10.1080/13543784.2022.2159806>.
71. Lei Y, Yao S, Wang Z, Tu Q, Yuan Z, Jiang Q. Safety and efficacy of adjuvant sotagliflozin therapy in patients with T1D—an update and systematic review and meta-analysis. *Front Endocrinol*. 2025. <https://doi.org/10.3389/fendo.2025.1506652>.
72. Phillip M, Mathieu C, Lind M, et al. Long-term efficacy and safety of dapagliflozin in patients with inadequately controlled type 1 diabetes: pooled 52-week outcomes from the DEPICT-1 and -2 studies. *Diabetes Obes Metab*. 2021;23(2):549–60. <https://doi.org/10.1111/dom.14248>.
73. Rosenstock J, Marquard J, Laffel LM, et al. Empagliflozin as adjunctive to insulin therapy in type 1 diabetes: the EASE trials. *Diabetes Care*. 2018;41(12):2560–9. <https://doi.org/10.2337/dc18-1749>.
74. Najafipour M, Najafipour F, Ostadrahimi A, et al. The effects of empagliflozin in patients with type 1 diabetes: results of a 12-week, double-blind, randomized, placebo-controlled clinical trial. *Health Promot Perspect*. 2024;14(4):380–7. <https://doi.org/10.34172/hpp.42486>.
75. Pieber TR, Famulla S, Eilbracht J, et al. Empagliflozin as adjunct to insulin in patients with type 1 diabetes: a 4-week, randomized, placebo-controlled trial (EASE-1). *Diabetes Obes Metab*. 2015;17(10):928–35. <https://doi.org/10.1111/dom.12494>.
76. Dimitrios P, Michael D, Vasilios K, et al. Liraglutide as adjunct to insulin treatment in patients with type 1 diabetes: a systematic review and meta-analysis. *CDR*. 2020;16(4):313–26. <https://doi.org/10.2174/1573399815666190614141918>.
77. Johansen NJ, Dejgaard TF, Lund A, et al. Efficacy and safety of meal-time administration of short-acting exenatide for glycaemic control in type 1 diabetes (MAG1C): a randomised, double-blind, placebo-controlled trial. *Lancet Diabetes Endocrinol*. 2020;8(4):313–24. [https://doi.org/10.1016/s2213-8587\(20\)30030-9](https://doi.org/10.1016/s2213-8587(20)30030-9).