



Assessing and Preventing Microvascular Complications of Type 2 Diabetes

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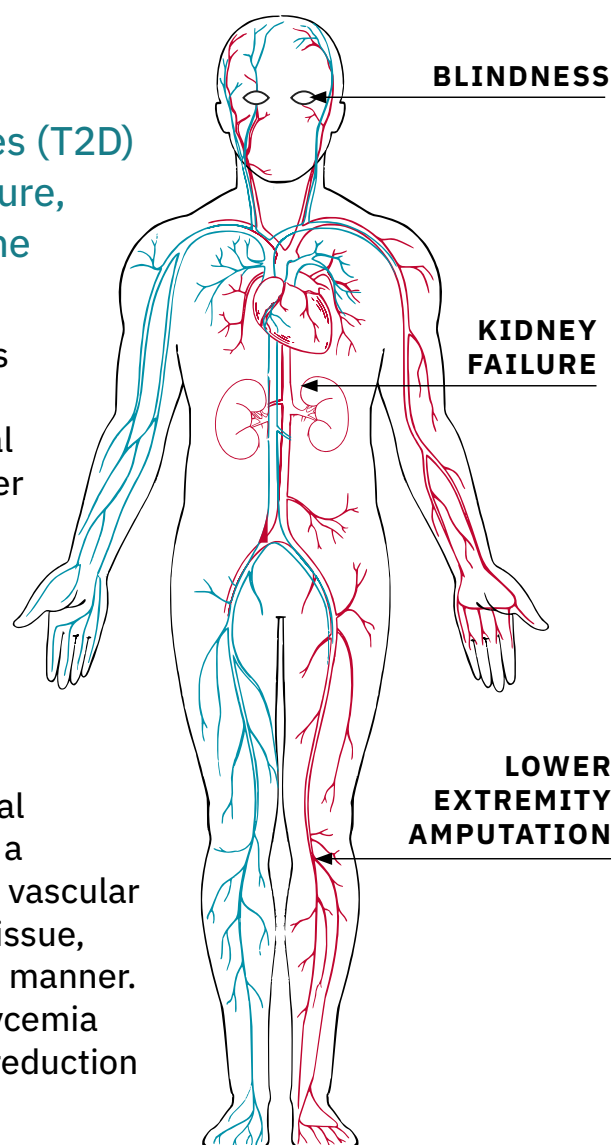
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Microvascular complications of type 2 diabetes (T2D) are the leading cause of blindness, kidney failure, and lower extremity amputation in adults in the United States.¹

These complications typically occur over many years but can be present prior to the time of diagnosis. Complications disproportionately occur among racial and ethnic minority groups and individuals with lower socioeconomic status, in part due to disparities in screening practices and risk factor management.²⁻⁴ This document reviews evidence-based recommendations for screening and prevention of retinopathy, nephropathy, and peripheral neuropathy.

Chronic glycemia, often measured by A1C, is a critical risk factor for microvascular complications. There is a predilection for hyperglycemia-mediated damage to vascular endothelial cells of the retina, kidney, and nervous tissue, which allow glucose entry in an insulin-independent manner. In people with recently diagnosed T2D, intensive glycemia management (A1C 7% vs. 7.9%) resulted in a 25% reduction in microvascular complications.^{5,6}



Importantly, early intervention for hyperglycemia has an enduring effect, which leads to continued benefit on microvascular risk and emerging reductions in macrovascular (cardiovascular) events

during long-term follow-up.⁷ Other risk factors include duration of diabetes, family history of complications, hypertension, dyslipidemia, and tobacco use (Table 1).

Patients with microvascular complications are also at greater risk for cardiovascular complications,⁸ but the preventive role for A1C reduction is comparatively weak.^{6,7} In established T2D, stricter targets of 6% to 6.5% (typically achieved with insulin therapy) resulted in modest additional microvascular benefit at the expense of more severe hypoglycemia and no cardiovascular or mortality benefit.⁹⁻¹¹

Screening

Clinical guidelines reflect the need for early recognition of microvascular disease to allow for therapeutic intervention (Table 2).^{13,14} Notably, guidelines recommend screening for microvascular complications in T2D at the time of diagnosis regardless of diabetes duration, whereas in type 1 diabetes (T1D), screening is initiated 5 years after diagnosis.

Retinopathy

Initial screening should include a dilated retinal fundus examination performed by an ophthalmologist or an optometrist. If access to these providers is limited, screening with retinal cameras in primary care and other offices with remote reading or using a validated assessment tool are acceptable alternatives. The frequency for rescreens should be individualized based on the stage of diabetic retinopathy at the initial/prior screening and the management of risk factors for progression, largely target range glycemia, blood pressure, and lipids.

Kidney Disease

Screening for diabetic kidney disease focuses on monitoring for albuminuria (i.e., urinary albumin to creatinine ratio [UACR]) and the estimated glomerular filtration rate [eGFR] using standardized equations). Repeat screens should occur 1 to 4 times per year, depending on the presence of albuminuria (UACR \geq 30 mg/g on 2 of 3 assessments within 6 months) and/or decline in eGFR ($<$ 60 mL/min/1.73 m²). For accurate UACR assessments, it is critical for patients to avoid heavy exercise or illness in the preceding 24 hours, as these can falsely elevate UACR. Cystatin C may be used in combination with eGFR to improve clinical decision making. Classification of kidney disease and recommendations for referral are shown in Figure 1.

Table 1. Modifiable Risk Factors for Complications Related to Diabetes

	Microvascular			Macrovascular (Cardiovascular Disease)
	Nephropathy	Neuropathy	Retinopathy	
Glycemia	✓	✓	✓	?
Blood Pressure	✓	✓	✓	✓
Lipids*	?	?	✓	?
Smoking	✓	✓	✓	?

? = limited evidence.

*Dyslipidemia is associated with the development of microvascular complications, but there is limited or conflicting high-quality evidence for the impact of intervention in primary prevention.¹²

Figure 1. Classification of Kidney Disease and Recommendations for Referral

CKD is Classified Based On: <ul style="list-style-type: none"> ■ Cause (C) ■ GFR (G) ■ Albuminuria (A) 				Albuminuria Categories Description and Range		
				A1	A2	A3
				Normal to Mildly Increased	Moderately Increased	Severely Increased
				<30 mg/g <3 mg/mmol	30-299 mg/g 3-29 mg/mmol	≥300 mg/g ≥30 mg/mmol
GFR Categories (mL/min/1.73m ²) Description and Range	G1	Normal to High	≥90	1 if CKD	Treat 1	Refer* 2
	G2	Mildly Decreased	60-89	1 if CKD	Treat 1	Refer* 2
	G3a	Mildly to Moderately Decreased	45-59	Treat 1	Treat 2	Refer 3
	G3b	Moderately to Severely Decreased	30-44	Treat 2	Refer 3	Refer 3
	G4	Severely Decreased	15-29	Refer* 3	Refer* 3	Refer 4+
	G5	Kidney Failure	<15	Refer 4+	Refer 4+	Refer 4+

Risk of chronic kidney disease (CKD) progression, frequency of visits, and referral to nephrology according to glomerular filtration rate (GFR) and albuminuria. The GFR and albuminuria grid depicts the risk of progression, morbidity, and mortality by color, from best to worst (green, yellow, orange, red, dark red). The numbers in the boxes are a guide to the frequency of visits (number of times per year). "Refer" indicates that nephrology services are recommended.

Adapted from *Chronic kidney disease and risk management: Standards of Care in Diabetes—2024*¹⁴

Peripheral Neuropathy

Screening for peripheral neuropathy should occur at least annually and is essential, as disease can be asymptomatic and place patients at risk for injuries and amputations. Patients may or may not report symptoms of pain, burning, or tingling. Visual inspection for any areas of skin breakdown, along with palpation of pulses, can identify vascular compromise. Provocative testing includes small fiber (e.g., temperature and/or pinprick) and large fiber (e.g., vibration, monofilament) assessments. Monofilament testing also detects loss of protective sensation (LOPS), which is a risk factor for ulceration. Abnormalities in these screening assessments indicate the need for more frequent assessment and follow-up or referral to podiatry. Consider electrophysiologic testing in people with atypical features (e.g., asymmetry, rapid progression). Other etiologies for peripheral neuropathy should be considered.¹⁵

Table 2. Screening for Microvascular Complications

	Screening	Initial	Follow-Up
Retinopathy	<ul style="list-style-type: none"> ▪ Dilated retinal exam performed by ophthalmologist or optometrist <p>OR</p> <ul style="list-style-type: none"> ▪ Retinal fundus photography captured by in-office camera with remote reading or validated assessment tool 	<ul style="list-style-type: none"> ▪ T2D: At diagnosis ▪ T1D: ≥5 year duration 	<ul style="list-style-type: none"> ▪ If initial exam is normal and glycemia is at goal, rescreen every 1-2 years ▪ If initial exam is abnormal, rescreen at least yearly and more frequently as guided by diabetic retinopathy stage and retinal specialist ▪ If remote retinal screening is abnormal, perform dilated exam ▪ Pregnancy: each trimester
Nephropathy	<ul style="list-style-type: none"> ▪ Spot UACR <ul style="list-style-type: none"> ▪ Normal: UACR <30 mg/g ▪ Moderate: UACR ≥30-299 mg/g ▪ Severe: UACR ≥300 mg/g ▪ Diagnosis only if 2 of 3 tests within 3-6 months is abnormal ▪ Avoid within 24 hours of heavy exercise or during illness <p>AND</p> <ul style="list-style-type: none"> ▪ eGFR <ul style="list-style-type: none"> ▪ Normal ≥60 mL/min/1.73 m² ▪ +/- Cystatin C (suggested) ▪ CKD is defined by elevated UACR or reduced eGFR 	<ul style="list-style-type: none"> ▪ T2D: At diagnosis ▪ T1D: ≥5 year duration 	<ul style="list-style-type: none"> ▪ Annual if normal UACR and eGFR ▪ Up to 4 times/year with elevations in UACR or decline in eGFR or established kidney disease ▪ Refer to Table 3 for monitoring recommendations in patients with established kidney disease
Peripheral Neuropathy	<p>Examination should include all of the following:</p> <ul style="list-style-type: none"> ▪ Visual inspection, pulse ▪ Small fiber: Either temperature or pinprick ▪ Large fiber: Vibration (128 Hz tuning fork) ▪ 10-g monofilament 	<ul style="list-style-type: none"> ▪ T2D: at diagnosis ▪ T1D: ≥5 year duration 	<ul style="list-style-type: none"> ▪ At least yearly if normal ▪ Every 1-6 months or referral to podiatry if abnormal ▪ Electrophysiologic testing if atypical (e.g., asymmetric, rapid progression) ▪ Consider testing to rule out other causes

eGFR = estimated glomerular filtration rate; T1D = type 1 diabetes; T2D = type 2 diabetes; UACR = urine albumin/creatinine.

Primary Prevention

The goals for primary prevention of microvascular complications should be individualized according to a shared decision making approach (see Table 3 below and [resources](#) at the end of document). The benefits of multiple risk factor management are widely recognized for preventing cardiovascular disease but are also important for preventing microvascular complications.¹⁶ In the United States, only 51% of patients achieve A1C < 7%; 56% achieve non-HDL cholesterol < 130 mg/dL; 74% achieve blood pressure < 140/90 levels; and only 22% achieve all three targets.¹⁷ Clinical inertia is common, and a delay of only 1 year in intensification of glucose-lowering therapy after diagnosis of T2D is associated with increased odds of microvascular and macrovascular complications.^{18,19} Weight loss is beneficial for managing risk factors, and a healthy lifestyle is associated with a lower risk of microvascular complications.²⁰ Newer therapies for T2D, such as sodium-glucose cotransporter-2 inhibitors (SGLT2i) and glucagon-like peptide-1 (GLP-1) based therapies, offer additional cardiovascular and renal benefits beyond A1C reduction.²¹

Table 3. Primary Prevention of Microvascular Complications

A1C/Glycemia* ²²	Blood Pressure*	Lipids ^{23,24}
<ul style="list-style-type: none"> ▪ A1C <7% ▪ CGM measures <ul style="list-style-type: none"> ▪ Glycemic Management Index <7% ▪ % Time in Range (70-180 mg/dL): 70% (50% if high risk) ▪ % Time Below Range (<70 mg/dL): 4% (1% if high risk) 	<ul style="list-style-type: none"> AHA criteria²³ <ul style="list-style-type: none"> ▪ Initiation of therapy <ul style="list-style-type: none"> ▪ Low risk: 140/90 mmHg ▪ High risk: ^130/80 mmHg ▪ Therapeutic target: <130/80 mmHg ADA criteria²⁴ <ul style="list-style-type: none"> ▪ Initiation of therapy: Persistently elevated blood pressure >130/80 mmHg ▪ Therapeutic target: <130/80 mmHg 	<p>Statin therapy according to cardiovascular risk (risk enhancers include microvascular complications)</p>

*Individualized based upon shared decision making considering potential benefit, treatment burden, side effects, costs/access, and preferences.

^Limited evidence to establish treatment targets for prevention of microvascular complications.

ADA = American Diabetes Association; AHA = American Heart Association; CGM = continuous glucose monitoring.

Secondary Prevention

Microvascular complications are generally irreversible, except possibly at the earliest stages. Interventions to achieve target A1C slow the progression of retinopathy and nephropathy,²⁵⁻²⁷ but there is inconclusive evidence for peripheral neuropathy. Recommendations for secondary and tertiary prevention are addressed below and detailed in [Table 4](#).

Retinopathy

Any level of diabetic retinopathy necessitates at least annual dilated retinal fundus examination.¹³ Improvement in A1C is beneficial but rapid reduction in A1C (> 1.5% over 6 months) should be avoided in persons with established retinopathy, as it may increase the risk of retinal events.^{13,28,29} Blood pressure management also reduces the progression of retinopathy,³⁰ but tight targets < 120 mmHg do not provide additional benefit.³¹

Lipid-lowering therapy, including statins and fenofibrate, may slow retinopathy progression.³² Panretinal laser photocoagulation (PRP) or intravitreal anti-vascular endothelial growth factor (VEGF) injection may be indicated for high-risk proliferative diabetic retinopathy, severe nonproliferative diabetic retinopathy, or sight-threatening diabetic macular edema to reduce the risk of vision loss.¹³

Nephropathy

In general, the target blood pressure is < 130/80 mmHg, blood pressure goal is < 130/80 mmHg, with lower targets in some individuals with UACR > 300 mg/g creatinine.¹⁴ Angiotensin converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARB) are first line therapies to slow progression.¹⁴ Titrate these drugs to the maximally tolerated dose (considering orthostatic symptoms and presence of hyperkalemia) and continue with modest increases in creatinine of up to 30%. In people with UACR ≥ 300 mg/g, the goal is at least a 30% reduction in UACR.

In T2D complicated by chronic kidney disease (CKD), defined as UACR ≥ 30 mg/g or eGFR < 60 mL/min/1.73m², SGLT2i reduce progression of composite renal outcomes by about 30% when added to maximally tolerated ACEi or ARB.³³ Thus, treatment with SGLT2i is indicated regardless of A1C goals or concomitant glucose lowering therapy and should be continued until dialysis is needed.^{14,34} If additional glycemia reduction is required, GLP-1-based therapies are preferred. The nonsteroidal mineralocorticoid receptor antagonist finerenone is also recommended to reduce CKD progression and cardiovascular events in individuals with T2D and albuminuria despite maximally tolerated doses of ACEi or ARB.^{14,34} Referral to nephrology should be considered for eGFR < 30 mL/min/1.73m², UACR ≥ 300 mg/g, or in the setting of CKD complications or diagnostic uncertainty.^{14,35}

Peripheral Neuropathy

Secondary and tertiary prevention of peripheral neuropathy focuses on risk for foot ulcers and amputation. LOPS, peripheral arterial disease (PAD), foot deformities, personal history of ulceration and/or amputation, pre-ulcerative corns or calluses, tobacco use, and established retinopathy and nephropathy (particularly kidney failure) are risk factors for foot ulceration. Foot examinations should be performed based upon degree of risk.³⁶ Individuals with peripheral neuropathy should be instructed to perform daily foot examination. Management of the at-risk foot may necessitate a multidisciplinary approach, including referral to foot care specialists who can provide surveillance and management of foot deformities, ongoing preventative care, and recommendations for therapeutic footwear.¹⁴

Table 4. Secondary and Tertiary Prevention of Microvascular Complications

	Surveillance	Interventions
Retinopathy	<p>Annual dilated exam, more frequent if retinopathy is progressing or other risk factors are above targets</p>	<ul style="list-style-type: none"> ▪ Optimize glycemia gradually (avoid >1.5% reduction in A1C in any 6-month period) ▪ Optimize blood pressure and lipids ▪ Refer to retinal specialist <ul style="list-style-type: none"> ▪ High-risk proliferative diabetic retinopathy: PRP or VEGF ▪ Consider PRP for severe nonproliferative diabetic retinopathy ▪ Sight-threatening diabetic macular edema: VEGF
Nephropathy	<ul style="list-style-type: none"> ▪ Annual serum creatinine, UACR, every 3-6 months if eGFR <60 mL/min/1.73 m² or UACR ≥300 mg/gm ▪ Potassium (if eGFR <60 mL/min/1.73 m² or receiving relevant medications); check potassium ▪ Screen for complications of CKD (volume overload, metabolic bone disease, electrolyte abnormalities, anemia, acidosis); if eGFR <60 mL/min/1.73 m²: physical exam, electrolytes, CBC, serum calcium, phosphate, PTH, vitamin 25(OH)D 	<ul style="list-style-type: none"> ▪ Optimize glycemia, blood pressure, and lipid management ▪ ACEi/ARB titrated to maximum tolerated dose, continue in setting of modest increase in serum creatinine <30% ▪ If UACR ≥300 mg/g, goal to reduce by 30% ▪ SGLT2i (T2D and eGFR 20-60 mL/min/1.73 m²) – continue until dialysis ▪ Finerenone if persistent albuminuria on above, serum potassium <5 mEq/L and eGFR ≥25 mL/min/1.73 m² (start 10 mg/20 mg if eGFR 25-59 or ≥60 mL/min/ 1.73m², respectively) ▪ Referral to nephrology for eGFR <30 mL/min/1.73 m², UACR ≥300 mg/g, CKD complications, or diagnostic uncertainty
Peripheral Neuropathy	<ul style="list-style-type: none"> ▪ Daily self-exam ▪ Health care provider foot exam <ul style="list-style-type: none"> ▪ LOPS or PAD: every 6-12 months ▪ 2 or more (LOPS, PAD, foot deformity): 3-6 months ▪ 2 or more (LOPS or PAD + amputation, prior foot ulcer, or ESRD): 1-3 months 	<ul style="list-style-type: none"> ▪ Optimize glycemia, blood pressure, and lipid management ▪ Referrals for high-risk foot, therapeutic foot wear

ACEi = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; CBC = complete blood count; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; ESRD = end stage renal disease; LOPS = loss of protective sensation; PAD = peripheral artery disease; PRP = panretinal photocoagulation; PTH = parathyroid hormone; SGLT2i = sodium-glucose cotransporter-2 inhibitor; UACR = urine albumin/creatinine; VEGF = vascular endothelial growth factor based therapy.

Clinical Practice Implementation

Only 33% to 68% of individuals with diabetes in the United States undergo a dilated eye exam, and rates are lowest in Black and Latino groups.³⁷ UACR testing is only 52%, with similar rates across racial and ethnic groups,³⁸ but there are disparities in the use of evidence-based therapies.³⁹⁻⁴¹ Barriers to chronic disease management are complex and include factors such as access to care and geographic disparities (e.g., transportation, availability of specialists), finances (e.g., underinsured status, low income), systemic and unconscious bias, and education level.^{3,42}

The majority of diabetes management is done by primary care providers, therefore, strategies to address these issues must

be collaborative and, ultimately, start at the organizational level.⁴²⁻⁴⁴ The Community Preventive Services Task Force reviewed studies on team-based interventions for people with T2D and found that the best outcomes were achieved when the team included a pharmacist; team members made recommendations to the primary care provider; all team members had medical record access; and communication was through direct means, such as team meetings.⁴³ Patients managed with a team-based approach ultimately had clinically significant improvements in glycemia, lipids, and blood pressure.⁴³ Co-management with a specialist in diabetes care is also effective at improving outcomes. Additional practice-based solutions are presented in Table 5.

Table 5. Interventions to Promote Chronic Care Management for Type 2 Diabetes

- Team-based care that includes virtual care options and remote monitoring services
- Specialist co-management
- Assess and address social determinants of health
- Onsite services (point-of-care A1C, urine albumin/creatinine, blood draws, retinal cameras, and foot exams)
- Self-management education and support
- Decision support (at the point of care)
- Clinical information systems/registries

Access Cardi-OH's Expanded Resources

- **Managing Diabetes in Older Populations: Targets, Challenges, and Medications**
cardi-oh.org/resources/managing-diabetes-in-older-populations-targets-challenges-and-medications
- **Beyond the A1C: Targets for Blood Glucose and Methods of Measurement**
cardi-oh.org/resources/beyond-the-a1c-targets-for-blood-glucose-and-methods-of-measurement
- **Managing Patients with Concomitant Hypertension and Diabetes**
cardi-oh.org/resources/managing-patients-with-concomitant-hypertension-and-diabetes
- **Atherosclerotic Cardiovascular Disease Risk Reduction: Management of Lipids**
cardi-oh.org/resources/atherosclerotic-cardiovascular-disease-risk-reduction-management-of-lipids
- **Utilizing Huddles to Improve Team-Based Care**
cardi-oh.org/resources/utilizing-huddles-to-improve-team-based-care
- **Diabetes QIP Clinical Toolkit**
cardi-oh.org/about/quality-improvement

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