Type 1 diabetes mellitus (T1DM) is a complex, heterogeneous disorder characterized by selective pancreatic beta cell destruction resulting in absolute insulin deficiency.\(^1\,\(^2\) T1DM is further categorized by the presence (Type 1A) or absence (Type 1B) of autoimmunity.\(^2\,\(^3\) For the purpose of this article, T1DM is referred to as a chronic autoimmune-mediated disorder characterized by selective pancreatic beta cell destruction with severe insulin deficiency, resulting in hyperglycemia.

T1DM is thought to be triggered by environmental factors in those with a genetic predisposition.\(^3\) Although there are proposed environmental factors, such as cow’s milk protein, vitamin D deficiency, viral infections, toxins, and stress, no single factor has been identified.\(^2\) However, because T1DM has been frequently discovered during illness, there is suspicion that the onset may be triggered by an infection.\(^5\)

Individuals with T1DM are at higher risk for developing cardiovascular disease (CVD) than the general population. This article discusses risk factors for CVD in adults with T1DM and ways the NP can help patients modify risk factors associated with the development of CVD.

**Incidence and prevalence**
T1DM is commonly known as a childhood disease. However, the age of onset varies and usually occurs before age 30, with a peak onset during puberty.\(^1\) The rate of beta cell destruction varies, with a more rapid rate in younger patients.\(^3\) Large registry studies show an increased incidence

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**Abstract**: Individuals with type 1 diabetes mellitus (T1DM) have a high risk of developing cardiovascular disease (CVD), but some risk factors can be mediated by lifestyle modification and medication. NPs should understand evidence-based management approaches to counsel patients with T1DM on appropriate self-management interventions to reduce the likelihood of CVD.

**Keywords**: cardiovascular disease, cardiovascular disease prevention, CVD, health promotion, T1DM, type 1 diabetes mellitus

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of T1DM worldwide. Although an increase in incidence is reported in most continents, Europe, Asia, and North America (3.2%, 4%, and 5.3%, respectively) have the highest incidence rates. 8 During 1990 to 2008, the global incidence of T1DM increased annually by 2.85% to 4%. 7 A similar increase was noted in the United States, and it is projected to increase further from 2.13/1,000 to 5.20/1,000 in individuals 20 and younger. 8

The prevalence of T1DM is not well documented. However, a recent study noted an increase in prevalence of T1DM in the United States in all gender, age, and race/ethnicity groups. 9 The increase in prevalence has been especially noted among racial/ethnic groups, as T1DM has been historically noted among White youths. 9 Although T1DM is commonly diagnosed in children and adolescents, it is important to note that the diagnosis can occur across the lifespan, including older adults. Although the incidence of new-onset T1DM in individuals over age 20 is not known, most individuals living with T1DM are adults.

- CVD risk in T1DM

It is well established that patients with uncontrolled T1DM are at higher risk for adverse health outcomes, including both micro- and macrovascular disease. 10 CVD is the leading cause of death in adults with both T1DM and type 2 diabetes mellitus (T2DM), and risk factors may begin to manifest as early as adolescence. 11 In addition, individuals with diabetes have a two- to fourfold increase in developing CVD compared with the general population. 12 Although those with T1DM have lower rates of obesity, hypertension,
and dyslipidemia than those with T2DM, they are still at high risk for developing CVD throughout life.\textsuperscript{13} Optimizing glycemic control may be the most important factor for CVD prevention in T1DM.\textsuperscript{13} Although some nonmodifiable risk factors (such as genetic polymorphisms) may influence the progression of CVD in patients with T1DM, certain modifiable risk factors should be considered in addition to optimizing glycemic control; for most patients, this means targeting a hemoglobin A1c (A1c) of less than 7% for most patients.\textsuperscript{14} Addressing these factors early in the disease course is essential. The American Diabetes Association (ADA) recommends that all patients with diabetes be assessed at least annually for cardiovascular risk factors (see Risk factors associated with CVD for patients with T1DM).\textsuperscript{14,15}

<table>
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<th>Nonmodifiable versus modifiable risk factors</th>
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| Nonmodifiable risk factors for CVD include gender, age, and family history of CVD. Men are at higher risk for CVD than women, and the risk of CVD increases substantially with age (men over age 55 and women over age 65).\textsuperscript{15} Premenopausal women are not protected against CVD and should be screened for risk factors and early signs and symptoms. Individuals with T1DM who also have a family history of early onset CVD (myocardial infarction [MI] or stroke) should be even more vigilant about mediating other risk factors. Most CVD risk factors are modifiable. Some authors suggest that the incidence of MI could be reduced up to 63% if lifestyle modifications and recommended treatments were followed.\textsuperscript{16} Modifiable risk factors include smoking (approximately one-third of deaths related to CVD are related to tobacco use and secondhand smoke), hypertension, dyslipidemia, obesity, and a sedentary lifestyle.\textsuperscript{17} Although obesity, hypertension, and dyslipidemia carry significant genetic components, these chronic diseases have direct correlations with CVD and the risk can be significantly reduced through medication therapy and lifestyle interventions.

### Cardiovascular risk reduction

**Optimizing glucose control.** Several landmark, randomized controlled trials have changed the way T1DM is managed. The Diabetes Control and Complications Trial (DCCT) suggested that intensive glycemic control significantly reduced the incidence and progression of microvascular disease (such as retinopathy, neuropathy, and nephropathy) compared with patients in the standard group in patients with T1DM.\textsuperscript{18}

The Epidemiology of Diabetes Interventions and Complications (EDIC) study further suggested that the intensive group had a 42% risk reduction in cardiovascular events 10 years after the intervention component of the study had ended. Similarly, when combined with nonfatal MI, stroke, and CVD-related death, the intensive group had a 57% risk reduction compared with the standard group. These results suggest that early, aggressive diabetes management is essential in preventing complications later in the course of diabetes. Although these studies did not specifically evaluate cardiovascular outcomes, it is well understood that both micro- and macrovascular diseases coexist and share many of the same mechanisms that promote vascular dysregulation.\textsuperscript{19}

The United Kingdom Prospective Diabetes Study (UKPDS) evaluated over 4,200 patients recently diagnosed with T2DM over an 11-year period. The intervention group had a mean A1c of 7%, while the standard group had an A1c of 7.9%. Over the 10-year follow-up period, compared with the standard group, the intensive group had a 10% reduction in diabetes-related death and a 6% reduction in all-cause mortality. The study results also suggested that for each 1% reduction in A1c, participants had a 21% reduction in death and 14% reduction in MI.\textsuperscript{20}

The study suggested that participants in the intervention group (metformin treatment) had a cardiovascular risk reduction of up to 33% even 10 years after the intervention period concluded. This “legacy effect” noted by both EDIC and UKPDS suggests that early, aggressive diabetes management can reduce the risk of both micro- and macrovascular disease later in life, even if glycemia is no longer as tightly controlled. It is important to note that optimal glycemic control involves more than optimizing A1c or fasting blood glucose level, as glucose variability and hypoglycemia can play a significant role in patient quality of life.
Avoiding hypoglycemia. Hypoglycemia occurs when blood glucose falls below 70 mg/dL and is a feared consequence of well-controlled blood glucose levels. Although patients with T1DM may experience symptoms such as shakiness and weakness, the physiologic response to hypoglycemia includes a marked stress on cardiac function, including increased heart rate, peripheral BP, myocardial contractility, stroke volume, and cardiac output. Additionally, hypoglycemia can cause ECG changes, specifically prolonged QT interval changes, which may also be a factor in some of the “sudden death” case studies noted in patients with T1DM. Although these short-term cardiac effects of hypoglycemia may have little impact on younger and healthier patients, those patients with preexisting CVD may be significantly impacted over time.

The Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial involved 10,251 participants and was designed to evaluate if patients with T2DM maintaining normal blood glucose levels in diabetes (A1c less than 6%) led to fewer cardiovascular events than participants who maintained A1c levels between 7% and 7.9%. Participants in the intensive group achieved a mean A1c of 6.4% (standard group mean was 7.5%) but had a 22% higher all-cause mortality after 3.4 years than the standard group.

The intensive group was stopped prematurely due to excessive risk. Although the reason for the excess risk remains unknown, some hypotheses include hypoglycemia, rapid reduction of glucose levels, drugs or drug combinations, or weight gain. Although the ACCORD study was designed for patients with T2DM, similar principles may apply to the treatment of patients with T1DM.

Current ADA practice recommendations suggest targeting an A1c of less than 7% for most nonpregnant adults while avoiding severe hypoglycemia. Some patients may tolerate a more stringent A1c goal (less than 6.5%) if they are able to achieve that goal without hypoglycemia. Patients who have advanced micro- or macrovascular disease, limited life expectancy, or a history of severe hypoglycemia may target an A1c up to 8%. Any episodes of hypoglycemia should be addressed promptly to prevent recurrence. Continuous glucose monitoring is an effective method of reducing the incidence of hypoglycemia in patients with T1DM.

Dyslipidemia. Dyslipidemia is a noted risk factor for CVD in patients with diabetes. Although evidence supports the benefits of HMG-CoA reductase inhibitors (statin therapy) in adults with hypercholesterolemia or with a history of CVD, few studies have been done on adults with T1DM. Fasting lipid profile should be measured annually or every 2 years in adults with a low-risk lipid profile (low-density lipoprotein [LDL] 100 mg/dL or less, high-density lipoprotein [HDL] 50 mg/dL or greater, and triglycerides 150 mg/dL or less). The current recommendations suggest targeting moderate- or high-intensity statin doses based on CVD risk factors rather than lipoprotein levels (see Recommendations for statin therapy).

Aspirin therapy. In 2010, a position statement of the ADA, the American Heart Association (AHA), and the American College of Cardiology (ACC) Foundation recommended a low dose of aspirin therapy (75 mg to 162 mg/day) as a primary prevention in adults with diabetes.
Type 1 diabetes & cardiovascular disease

with no history of vascular disease who have a 10-year risk of CVD events over 10% and who are not at risk for bleeding.22 These adults include most men over age 50 and women over age 60 and who have one or more risk factors (smoking, hypertension, dyslipidemia, family history of premature CVD, and albuminuria). The 2016 ADA Standard of Practice continues to recommend aspirin therapy as primary prevention.14

Hypertension management. The presence of hypertension as a comorbid condition is usually found in individuals with diabetes mellitus. Hypertension affects approximately 30% of patients with T1DM, and it is usually the result of underlying nephropathy.26 Other factors such as obesity and hyperglycemia are associated with hypertension in T1DM.13 Adults with diabetes and hypertension should be treated to a systolic BP (SBP) goal of less than 140 mm Hg over a diastolic BP (DBP) less than 90 mm Hg.27 A slightly lower BP target (<130 SBP) may be appropriate in certain populations, such as younger patients, those without comorbid conditions, or those with albuminuria.14

Pharmacologic therapy should include antihypertensive drugs, specifically an angiotensin-converting enzyme inhibitor or an angiotensin II receptor blocker.14 Thiazide diuretics and calcium channel blockers may be helpful in multiple-drug therapy for patients with diabetes.14,27 In addition, the following lifestyle modifications should be encouraged: weight loss, low dietary sodium intake (1,500 mg/day), increased fruit and vegetable consumption (8 to 10 servings a day), low-fat dairy products (2 to 3 servings per day), increase in physical activity, and avoiding excessive alcohol consumption (men 2 servings and women 1 serving per day).14

Lifestyle interventions

Diet. There is no "gold standard" diet for optimal cardiovascular health, but multiple studies have suggested that diets such as the Dietary Approaches to Stop Hypertension (DASH) diet as well as the Mediterranean diet may contribute to cardiovascular protection (see Recommended diets to reduce cardiovascular risk).14,28,31

Other dietary recommendations include limiting the amount of fat consumed (less than 35% of total energy intake), limited saturated and trans fats, and increasing intake of omega-3 fatty acids, fiber, and plant stenols/sterols.14,32 For adults who need to lower LDL cholesterol or BP, joint guidelines from the AHA and American College of Cardiology suggest emphasizing a diet including vegetables, fruits, whole grains, dairy, poultry, nuts, and fish, and limiting sugar-sweetened items and red meat.

One of the main limiting factors of special diets is cost, with higher prices of produce and fresh products causing difficulty in dietary adherence.33 Modifications can be taken with the diets to increase affordability while maintaining health benefits. Patients with T1DM should receive individualized counseling from a registered dietitian to assist in meal planning and reaching dietary targets.14

Ongoing research is exploring the importance of the type of carbohydrate consumed. High-glycemic foods (such as regular soda and white starches) may contribute to oxidant stress including short-term inflammation, hypercoaguability, endothelial dysfunction, and fibrinolysis, in addition to elevating blood glucose levels.14 This "postprandial dysregulation" is an independent risk factor for CVD that can be mediated with a modified diet.14 For optimal glucose control and cardiovascular protection, patients with diabetes mellitus should be encouraged to choose quality, high-fiber carbohydrates.

Exercise. Exercise is essential for cardiovascular protection by positively affecting BP, lipids, weight, and generalized inflammation associated with diabetes.11 Most of the research surrounding physical activity in diabetes has been done on patients with T2DM. There is no clear benefit to improved glycemic control for patients with T1DM, and hypoglycemia during exercise can be a barrier to exercise adherence.35 A 2012 meta-analysis of 48 articles studying exercise in T1DM noted a measurable benefit from activity in fitness level, insulin requirement, lipid levels, endothelial function, mortality, insulin resistance, well-being, and CVD protection. Variables of unclear benefit include glycemic control, microvascular disease, BP, and beta cell function.36 The current ADA recommendations are to exercise at least 150 minutes per week at a moderate intensity level with at least 2 days per week of resistance training.14

Weight reduction. Patients with T1DM are not typically overweight, but an increase in body mass can occur during the natural course of life or with insulin treatment or intensification. One study (n = 658) suggested that the presence of overweight patients with T1DM has increased 47% since the mid-1980s, and the presence of obesity (body mass index [BMI] over 30) has increased sevenfold since that time.37 Results from the DCCT trial suggested that a
Pharmacologic therapy should include an angiotensin-converting enzyme inhibitor or an angiotensin II receptor blocker.

BMI over 27 may increase risk for the CVD development in some individuals with T1DM.38,39 Maintaining a normal body weight and exercising regularly can lower overall CVD risk. Similar to treatment of patients with T2DM, even a modest weight reduction can improve lipids, BP, and blood glucose levels in patients with T1DM.14,40,41 Weight management can be achieved more readily in patients who eat modest carbohydrate counts (less than 60 g per meal) and who balance calorie intake with energy expenditure.

Smoking cessation. Tobacco use continues to be the largest preventable cause of mortality in the United States, with cigarette smoking claiming approximately 480,000 lives annually.42 The adverse reactions of smoking and risk for CVD are well documented.25 Patients with T1DM who smoke are at even higher cardiovascular risk.43-45 A recent study comparing T1DM smokers with nonsmokers found smokers had higher A1c and required more intensive insulin therapy than nonsmokers.43 In addition, the number of patients who achieved target A1c goal (7% or less) were twice as high in nonsmokers, suggesting smoking affects glucose metabolism.43 Gender differences were also noted in this study, with females having slightly worse glycemic control than their male counterparts.43

<table>
<thead>
<tr>
<th>Recommended diets to reduce cardiovascular risk30,31</th>
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### DASH

<table>
<thead>
<tr>
<th>Food category</th>
<th>Servings per day</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1,600 calories per day</td>
</tr>
<tr>
<td>Grains</td>
<td>6</td>
</tr>
<tr>
<td>Vegetables</td>
<td>3 to 4</td>
</tr>
<tr>
<td>Fruits</td>
<td>4</td>
</tr>
<tr>
<td>Fat free/low-fat dairy</td>
<td>2 to 3</td>
</tr>
<tr>
<td>Lean meat/poultry</td>
<td>3 to 6</td>
</tr>
<tr>
<td>Nuts, seeds, legumes</td>
<td>3 per week</td>
</tr>
<tr>
<td>Fats/oils</td>
<td>2</td>
</tr>
<tr>
<td>Sweets/added sugars</td>
<td>0</td>
</tr>
</tbody>
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### Mediterranean

**Foods to include**
- Fish and seafood
- Plant-based meals with small amounts of lean meat or chicken
- Whole grains
- Nuts, seeds, legumes
- Fresh fruits and vegetables
- Olive oil (main source of fat)

**Foods to avoid**
- Red meat
- Eggs
- Butter
- Sweets

Smoking cessation is especially important for patients with T1DM, as vascular complications is common in this population—especially in young adults.41 A previous study found an increase in smokers in the pediatric population with T1DM during adolescence and young adulthood.46 Based on these findings, smoking education, prevention, and assistance in cessation were recommended during early ages in those with T1DM.46 A recent study echoed these recommendations, suggesting that smoking cessation should be emphasized during diabetes follow-up care—especially among younger patients with T1DM who may find smoking appealing.45
Moving forward

As healthcare systems move toward a patient-centered approach, NPs should assess readiness for lifestyle modifications as well as involving patients in decision-making. Diabetes guidelines recommend that all patients should be advised on smoking cessation and the use of tobacco products as part of a routine visit for diabetes care. Pharmacologic and nonpharmacologic interventions should be discussed, allowing the patient to be proactive in the decision-making. However, clinicians should also gauge the patient’s preferred level of involvement.

Patients with T1DM are at high risk for CVD development throughout the lifespan. This risk can be mediated through lifestyle modifications as well as optimizing glucose levels and modifying other risk factors, such as high cholesterol and BP. NPs are in an ideal position to positively influence patients with T1DM by reinforcing self-management behaviors and delivering evidence-based patient education regarding CVD prevention.

REFERENCES


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