

# Exercise and Type 2 Diabetes

## SUMMARY

Although physical activity (PA) is a key element in the prevention and management of type 2 diabetes mellitus (T2DM), many with this chronic disease do not become or remain regularly active. High-quality studies establishing the importance of exercise and fitness in diabetes were lacking until recently, but it is now well established that participation in regular PA improves blood glucose control and can prevent or delay T2DM, along with positively affecting lipids, blood pressure, cardiovascular events, mortality, and quality of life. Structured interventions combining PA and modest weight loss have been shown to lower T2DM risk by up to 58% in high-risk populations. Most benefits of PA on diabetes management are realized through acute and chronic improvements in insulin action, accomplished with both aerobic and resistance training. The benefits of physical training are discussed, along with recommendations for varying activities, PA-associated blood glucose management, diabetes prevention, gestational diabetes, and safe and effective practices for PA with diabetes-related complications.

## INTRODUCTION

Diabetes has become a widespread epidemic, primarily because of the increasing prevalence and incidence of type 2 diabetes mellitus (T2DM). According to the Centers for Disease Control and Prevention, in 2007, almost 24 million Americans had diabetes, with one quarter of those, or 6 million, undiagnosed (261). Currently, it is estimated that almost 60 million US residents also have prediabetes, a condition in which blood glucose (BG) levels are above normal, thus greatly increasing their risk for T2DM (261). Lifetime risk estimates suggest that one in three Americans born in 2000 or later will develop diabetes, but in high-risk ethnic populations, closer to 50% may develop it (200). T2DM is a significant cause of premature mortality and morbidity related to cardiovascular disease (CVD), blindness, kidney and nerve

disease, and amputation (261). Although regular physical activity (PA) may prevent or delay diabetes and its complications (10,46,89,112,176,208,259,294), most people with T2DM are not active (193).

In this article, the broader term “physical activity” (defined as “bodily movement produced by the contraction of skeletal muscle that substantially increases energy expenditure”) is used interchangeably with “exercise,” which is defined as “a subset of PA done with the intention of developing physical fitness (i.e., cardiovascular, strength, and flexibility training).” The intent is to recognize that many types of physical movement may have a positive effect on physical fitness, morbidity, and mortality in individuals with T2DM.

### Diagnosis, classification, and etiology of diabetes.

Currently, the American Diabetes Association (ADA) recommends the use of any of the following four criteria for diagnosing diabetes: 1) glycated hemoglobin ( $A_{1c}$ ) value of 6.5% or higher, 2) fasting plasma glucose  $\geq 126$  mg·dL<sup>-1</sup> (7.0 mmol·L<sup>-1</sup>), 3) 2-h plasma glucose  $\geq 200$  mg·dL<sup>-1</sup> (11.1 mmol·L<sup>-1</sup>) during an oral glucose tolerance test using 75 g of glucose, and/or 4) classic symptoms of hyperglycemia (e.g., polyuria, polydipsia, and unexplained weight loss) or hyperglycemic crisis with a random plasma glucose of 200 mg·dL<sup>-1</sup> (11.1 mmol·L<sup>-1</sup>) or higher. In the absence of unequivocal hyperglycemia, the first three criteria should be confirmed by repeat testing (4). Prediabetes is diagnosed with an  $A_{1c}$  of 5.7%–6.4%, fasting plasma glucose of 100–125 mg·dL<sup>-1</sup> (5.6–6.9 mmol·L<sup>-1</sup>; i.e., impaired fasting glucose, or IFG), or 2-h postload glucose of 140–199 mg·dL<sup>-1</sup> (7.8–11.0 mmol·L<sup>-1</sup>; i.e., impaired glucose tolerance, or IGT) (4).

The major forms of diabetes can be categorized as type 1 or type 2 (4). In type 1, which accounts for 5%–10% of cases, the cause is an absolute deficiency of insulin secretion resulting from autoimmune destruction of the insulin-producing cells in the pancreas. T2DM (90%–95% of cases) results from a combination of the inability of muscle cells to respond to insulin properly (insulin resistance) and inadequate compensatory insulin secretion. Less common forms include gestational diabetes (GDM), which is associated with a 40%–60% chance of developing T2DM in the next 5–10 yr (261). Diabetes can also result from genetic defects in insulin action, pancreatic disease, surgery, infections, and drugs or chemicals (4,261).

Genetic and environmental factors are strongly implicated in the development of T2DM. The exact genetic defects are

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complex and not clearly defined (4), but risk increases with age, obesity, and physical inactivity. T2DM occurs more frequently in populations with hypertension or dyslipidemia, women with previous GDM, and non-Caucasian people including Native Americans, African Americans, Hispanic/Latinos, Asians, and Pacific Islanders.

**Treatment goals in T2DM.** The goal of treatment in T2DM is to achieve and maintain optimal BG, lipid, and blood pressure (BP) levels to prevent or delay chronic complications of diabetes (5). Many people with T2DM can achieve BG control by following a nutritious meal plan and exercise program, losing excess weight, implementing necessary self-care behaviors, and taking oral medications, although others may need supplemental insulin (261). Diet and PA are central to the management and prevention of T2DM because they help treat the associated glucose, lipid, BP control abnormalities, as well as aid in weight loss and maintenance. When medications are used to control T2DM, they should augment lifestyle improvements, not replace them.

## ACUTE EFFECTS OF EXERCISE

### Fuel Metabolism during Exercise

**Fuel mobilization, glucose production, and muscle glycogenolysis.** The maintenance of normal BG at rest and during exercise depends largely on the coordination and integration of the sympathetic nervous and endocrine systems (250). Contracting muscles increase uptake of BG, although BG levels are usually maintained by glucose production via liver glycogenolysis and gluconeogenesis and mobilization of alternate fuels, such as free fatty acids (FFA) (250,268).

Several factors influence exercise fuel use, but the most important are the intensity and duration of PA (9,29,47,83, 111,133,160,181,241). Any activity causes a shift from predominant reliance on FFA at rest to a blend of fat, glucose, and muscle glycogen, with a small contribution from amino acids (15,31). With increasing exercise intensity, there is a greater reliance on carbohydrate as long as sufficient amounts are available in muscle or blood (21,23, 47,133). Early in exercise, glycogen provides the bulk of the fuel for working muscles. As glycogen stores become depleted, muscles increase their uptake and use of circulating BG, along with FFA released from adipose tissue (15,132,271). Intramuscular lipid stores are more readily used during longer-duration activities and recovery (23,223, 270). Glucose production also shifts from hepatic glycogenolysis to enhanced gluconeogenesis as duration increases (250,268).

**Evidence statement.** PA causes increased glucose uptake into active muscles balanced by hepatic glucose production, with a greater reliance on carbohydrate to fuel muscular activity as intensity increases. *ACSM evidence category A* (see Tables 1 and 2 for explanation).

**Insulin-independent and insulin-dependent muscle glucose uptake during exercise.** There are two well-defined pathways that stimulate glucose uptake by muscle (96). At rest and postprandially, its uptake by muscle is insulin-dependent and serves primarily to replenish muscle glycogen stores. During exercise, contractions increase BG uptake to supplement intramuscular glycogenolysis (220,227). As the two pathways are distinct, BG uptake into working muscle is normal even when insulin-mediated uptake is impaired in T2DM (28,47,293). Muscular BG uptake remains elevated postexercise, with the contraction-mediated pathway persisting for several hours (86,119) and insulin-mediated uptake for longer (9,33,141,226).

Glucose transport into skeletal muscle is accomplished via glucose transporter proteins, with glucose transporter 4 (GLUT4) being the main isoform in muscle modulated by both insulin and contractions (110,138). Insulin activates GLUT4 translocation through a complex signaling cascade (256,293). Contractions, however, trigger GLUT4 translocation at least in part through activation of 5'-AMP-activated protein kinase (198,293). Insulin-stimulated GLUT4 translocation is generally impaired in T2DM (96). Both aerobic and resistance exercises increase GLUT4 abundance and BG uptake, even in the presence of T2DM (39,51,204,270).

**Evidence statement.** Insulin-stimulated BG uptake into skeletal muscle predominates at rest and is impaired in T2DM, while muscular contractions stimulate BG transport via a separate additive mechanism not impaired by insulin resistance or T2DM. *ACSM evidence category A*.

### Postexercise Glycemic Control/BG Levels

**Aerobic exercise effects.** During moderate-intensity exercise in nondiabetic persons, the rise in peripheral glucose uptake is matched by an equal rise in hepatic glucose production, the result being that BG does not change except during prolonged, glycogen-depleting exercise. In individuals with T2DM performing moderate exercise, BG utilization by muscles usually rises more than hepatic glucose production, and BG levels tend to decline (191). Plasma insulin levels normally fall, however, making the risk of exercise-induced hypoglycemia in anyone not taking insulin or insulin secretagogues very minimal, even with prolonged PA (152). The effects of a single bout of aerobic exercise on insulin action vary with duration, intensity, and subsequent diet; a single session increases insulin action and glucose tolerance for more than 24 h but less than 72 h (26,33,85,141). The effects of moderate aerobic exercise are similar whether the PA is performed in a single session or multiple bouts with the same total duration (14).

During brief, intense aerobic exercise, plasma catecholamine levels rise markedly, driving a major increase in glucose production (184). Hyperglycemia can result from such activity and persist for up to 1–2 h, likely because plasma catecholamine levels and glucose production do not return to normal immediately with cessation of the activity (184).

TABLE 1. Evidence categories for the ACSM and evidence-grading system for clinical practice recommendations for the ADA.

I. ACSM Evidence Categories		
Evidence Category	Source of Evidence	Definition
A	Randomized, controlled trials (overwhelming data)	Provides a consistent pattern of findings with substantial studies
B	Randomized, controlled trials (limited data)	Few randomized trials exist, which are small in size and results are inconsistent
C	Nonrandomized trials, observational studies	Outcomes are from uncontrolled, nonrandomized, and/or observational studies
D	Panel consensus judgment	Panel's expert opinion when the evidence is insufficient to place it in categories A–C
II. ADA Evidence-Grading System for Clinical Practice Recommendations		
Level of Evidence	Description	
A	Clear evidence from well-conducted, generalizable, randomized controlled trials that are adequately powered, including the following: <ul style="list-style-type: none"> <li>• Evidence from a well-conducted multicenter trial</li> <li>• Evidence from a meta-analysis that incorporated quality ratings in the analysis</li> </ul> Compelling nonexperimental evidence, i.e., the “all-or-none” rule developed by the Centre for Evidence-Based Medicine at Oxford	
B	Supportive evidence from well-conducted randomized controlled trials that are adequately powered, including the following: <ul style="list-style-type: none"> <li>• Evidence from a well-conducted trial at one or more institutions</li> <li>• Evidence from a meta-analysis that incorporated quality ratings in the analysis</li> </ul> Supportive evidence from well-conducted cohort studies, including the following: <ul style="list-style-type: none"> <li>• Evidence from a well-conducted prospective cohort study or registry</li> <li>• Evidence from a well-conducted meta-analysis of cohort studies</li> </ul> Supportive evidence from a well-conducted case-control study	
C	Supportive evidence from poorly controlled or uncontrolled studies, including the following: <ul style="list-style-type: none"> <li>• Evidence from randomized clinical trials with one or more major or three or more minor methodological flaws that could invalidate the results</li> <li>• Evidence from observational studies with high potential for bias (such as case series with comparison to historical controls)</li> <li>• Evidence from case series or case reports</li> </ul> Conflicting evidence with the weight of evidence supporting the recommendation	
E	Expert consensus or clinical experience	

**Evidence statement.** Although moderate aerobic exercise improves BG and insulin action acutely, the risk of exercise-induced hypoglycemia is minimal without use of exogenous insulin or insulin secretagogues. Transient hyperglycemia can follow intense PA. *ACSM evidence category C.*

**Resistance exercise effects.** The acute effects of a single bout of resistance training on BG levels and/or insulin action in individuals with T2DM have not been reported. In individuals with IFG (BG levels of 100–125 mg·dL<sup>-1</sup>), resistance exercise results in lower fasting BG levels 24 h after exercise, with greater reductions in response to both volume (multiple- vs single-set sessions) and intensity of resistance exercise (vigorous compared with moderate) (18).

**Evidence statement.** The acute effects of resistance exercise in T2DM have not been reported, but result in lower fasting BG levels for at least 24 h after exercise in individuals with IFG. *ACSM evidence category C.*

**Combined aerobic and resistance and other types of training.** A combination of aerobic and resistance training may be more effective for BG management than either type of exercise alone (51,238). Any increase in muscle mass that may result from resistance training could contribute to BG uptake without altering the muscle's intrinsic capacity to respond to insulin, whereas aerobic exercise enhances its uptake via a greater insulin action, independent of changes in muscle mass or aerobic capacity (51). However, all reported combination training had a greater total duration of exercise and caloric use than when each type of training was undertaken alone (51,183,238).

Mild-intensity exercises like tai chi and yoga have also been investigated for their potential to improve BG management, with mixed results (98,117,159,257,269,286,291). Although tai chi may lead to short-term improvements in BG levels,

effects from long-term training (i.e., 16 wk) do not seem to last 72 h after the last session (257). Some studies have shown lower overall BG levels with extended participation in such activities (286,291), although others have not (159,257). One study suggested that yoga's benefits on fasting BG, lipids, oxidative stress markers, and antioxidant status are at least equivalent to more conventional forms of PA (98). However, a meta-analysis of yoga studies stated that the limitations characterizing most studies, such as small sample size and varying forms of yoga, preclude drawing firm conclusions about benefits to diabetes management (117).

**Evidence statement.** A combination of aerobic and resistance exercise training may be more effective in improving BG control than either alone; however, more studies are needed to determine if total caloric expenditure, exercise duration, or exercise mode is responsible. *ACSM evidence category B.* Milder forms of exercise (e.g., tai chi, yoga) have shown mixed results. *ACSM evidence category C.*

## Insulin Resistance

**Acute changes in muscular insulin resistance.** Most benefits of PA on T2DM management and prevention are realized through acute and chronic improvements in insulin action (29,46,116,118,282). The acute effects of a recent bout of exercise account for most of the improvements in insulin action, with most individuals experiencing a decrease in their BG levels during mild- and moderate-intensity exercise and for 2–72 h afterward (24,83,204).

BG reductions are related to the duration and intensity of the exercise, preexercise control, and state of physical training (24,26,47,238). Although previous PA of any intensity generally exerts its effects by enhancing uptake of BG for glycogen synthesis (40,83) and by stimulating fat

TABLE 2. Summary of ACSM evidence and ADA clinical practice recommendation statements.

Section Heading	ACSM Evidence and ADA Clinical Practice Recommendation Statements	ACSM Evidence Category (A = highest; D = lowest)/ADA Level of Evidence (A = highest; E = lowest; *No Recommendation Given)
Acute effects of exercise	<ul style="list-style-type: none"> <li>PA causes increased glucose uptake into active muscles balanced by hepatic glucose production, with a greater reliance on carbohydrate to fuel muscular activity as intensity increases.</li> <li>Insulin-stimulated BG uptake into skeletal muscle predominates at rest and is impaired in T2DM, while muscular contractions stimulate BG transport via a separate, additive mechanism not impaired by insulin resistance or T2DM.</li> <li>Although moderate aerobic exercise improves BG and insulin action acutely, the risk of exercise-induced hypoglycemia is minimal without use of exogenous insulin or insulin secretagogues. Transient hyperglycemia can follow intense PA.</li> <li>The acute effects of resistance exercise in T2DM have not been reported, but result in lower fasting BG levels for at least 24 h postexercise in individuals with IFG.</li> <li>A combination of aerobic and resistance exercise training may be more effective in improving BG control than either alone; however, more studies are needed to determine if total caloric expenditure, exercise duration, or exercise mode is responsible.</li> <li>Milder forms of exercise (e.g., tai chi, yoga) have shown mixed results.</li> <li>PA can result in acute improvements in systemic insulin action lasting from 2 to 72 h.</li> </ul>	<p>A/*</p> <p>A/*</p> <p>C/*</p> <p>C/*</p> <p>B/*</p> <p>C/*</p> <p>A/*</p>
Chronic effects of exercise training	<ul style="list-style-type: none"> <li>Both aerobic and resistance training improve insulin action, BG control, and fat oxidation and storage in muscle.</li> <li>Resistance exercise enhances skeletal muscle mass.</li> <li>Blood lipid responses to training are mixed but may result in a small reduction in LDL-C with no change in HDL-C or triglycerides. Combined weight loss and PA may be more effective than aerobic exercise training alone on lipids.</li> <li>Aerobic training may slightly reduce systolic BP, but reductions in diastolic BP are less common, in individuals with T2DM.</li> <li>Observational studies suggest that greater PA and fitness are associated with a lower risk of all-cause and CV mortality.</li> <li>Recommended levels of PA may help produce weight loss. However, up to 60 min·d<sup>-1</sup> may be required when relying on exercise alone for weight loss.</li> <li>Individuals with T2DM engaged in supervised training exhibit greater compliance and BG control than those undertaking exercise training without supervision.</li> <li>Increased PA and physical fitness can reduce symptoms of depression and improve health-related QOL in those with T2DM.</li> </ul>	<p>B/*</p> <p>A/*</p> <p>C/*</p> <p>C/*</p> <p>C/*</p> <p>B/*</p> <p>B/*</p>
PA and prevention of type 2 diabetes	<ul style="list-style-type: none"> <li>At least 2.5 h·wk<sup>-1</sup> of moderate to vigorous PA should be undertaken as part of lifestyle changes to prevent T2DM onset in high-risk adults.</li> </ul>	<p>A/A</p>
PA in prevention and control of gestational diabetes	<ul style="list-style-type: none"> <li>Epidemiologic studies suggest that higher levels of PA may reduce risk of developing GDM during pregnancy.</li> <li>RCTs suggest that moderate exercise may lower maternal BG levels in GDM.</li> </ul>	<p>C/*</p> <p>B/*</p>
Preexercise evaluation	<ul style="list-style-type: none"> <li>Before undertaking exercise more intense than brisk walking, sedentary persons with T2DM will likely benefit from an evaluation by a physician. ECG exercise stress testing for asymptomatic individuals at low risk of CAD is not recommended but may be indicated for higher risk.</li> </ul>	<p>C/C</p>
Recommended PA participation for persons with type 2 diabetes	<ul style="list-style-type: none"> <li>Persons with T2DM should undertake at least 150 min·wk<sup>-1</sup> of moderate to vigorous aerobic exercise spread out during at least 3 d during the week, with no more than two consecutive days between bouts of aerobic activity.</li> <li>In addition to aerobic training, persons with T2DM should undertake moderate to vigorous resistance training at least 2–3 d·wk<sup>-1</sup>.</li> <li>Supervised and combined aerobic and resistance training may confer health additional benefits, although milder forms of PA (like yoga) have shown mixed results. Persons with T2DM are encouraged to increase their total daily unstructured PA. Flexibility training may be included but should not be undertaken in place of other recommended types of PA.</li> </ul>	<p>B/B</p> <p>B/B</p> <p>B/C</p>
Exercise with nonoptimal BG control	<ul style="list-style-type: none"> <li>Individuals with T2DM may engage in PA, using caution when exercising with BG levels exceeding 300 mg·dL<sup>-1</sup> (16.7 mmol·L<sup>-1</sup>) without ketosis, provided they are feeling well and are adequately hydrated.</li> <li>Persons with T2DM not using insulin or insulin secretagogues are unlikely to experience hypoglycemia related to PA. Users of insulin and insulin secretagogues are advised to supplement with carbohydrate as needed to prevent hypoglycemia during and after exercise.</li> </ul>	<p>C/E</p> <p>C/C</p>
Medication effects on exercise responses	<ul style="list-style-type: none"> <li>Medication dosage adjustments to prevent exercise-associated hypoglycemia may be required by individuals using insulin or certain insulin secretagogues. Most other medications prescribed for concomitant health problems do not affect exercise, with the exception of <math>\beta</math>-blockers, some diuretics, and statins.</li> </ul>	<p>C/C</p>

(continued on next page)



TABLE 2. (Continued)

Section Heading	ACSM Evidence and ADA Clinical Practice Recommendation Statements	ACSM Evidence Category (A = highest; D = lowest)/ADA Level of Evidence (A = highest; E = lowest; *No Recommendation Given)
Exercise with long-term complications of diabetes	• Known CVD is not an absolute contraindication to exercise. Individuals with angina classified as moderate or high risk should likely begin exercise in a supervised cardiac rehabilitation program. PA is advised for anyone with PAD.	C/C
	• Individuals with peripheral neuropathy and without acute ulceration may participate in moderate weight-bearing exercise. Comprehensive foot care including daily inspection of feet and use of proper footwear is recommended for prevention and early detection of sores or ulcers. Moderate walking likely does not increase risk of foot ulcers or reulceration with peripheral neuropathy.	B/B
	• Individuals with CAN should be screened and receive physician approval and possibly an exercise stress test before exercise initiation. Exercise intensity is best prescribed using the HR reserve method with direct measurement of maximal HR.	C/C
	• Individuals with uncontrolled proliferative retinopathy should avoid activities that greatly increase intraocular pressure and hemorrhage risk.	D/E
	• Exercise training increases physical function and QOL in individuals with kidney disease and may even be undertaken during dialysis sessions. The presence of microalbuminuria per se does not necessitate exercise restrictions.	C/C
Adoption and maintenance of exercise by persons with diabetes	• Efforts to promote PA should focus on developing self-efficacy and fostering social support from family, friends, and health care providers. Encouraging mild or moderate PA may be most beneficial to adoption and maintenance of regular PA participation. Lifestyle interventions may have some efficacy in promoting PA behavior.	B/B

oxidation and storage in muscle (21,64,95), more prolonged or intense PA acutely enhances insulin action for longer periods (9,29,75,111,160,238).

Acute improvements in insulin sensitivity in women with T2DM have been found for equivalent energy expenditures whether engaging in low-intensity or high-intensity walking (29) but may be affected by age and training status (24,75,100,101,228). For example, moderate- to heavy-intensity aerobic training undertaken three times a week for 6 months improved insulin action in both younger and older women but persisted only in the younger group for 72–120 h.

**Acute changes in liver's ability to process glucose.** Increases in liver fat content common in obesity and T2DM are strongly associated with reduced hepatic and peripheral insulin action. Enhanced whole-body insulin action after aerobic training seems to be related to gains in peripheral, not hepatic, insulin action (146,282). Such training not resulting in overall weight loss may still reduce hepatic lipid content and alter fat partitioning and use in the liver (128).

**Evidence statement.** PA can result in acute improvements in systemic insulin action lasting from 2 to 72 h. *ACSM evidence category A.*

## CHRONIC EFFECTS OF EXERCISE TRAINING

**Metabolic control: BG levels and insulin resistance.** Aerobic exercise has been the mode traditionally prescribed for diabetes prevention and management. Even 1 wk of aerobic training can improve whole-body insulin sensitivity in individuals with T2DM (282). Moderate and vigorous aerobic training improve insulin sensitivity (9,75,83,111), albeit for only a period of hours to days (141), but a lesser intensity may also improve insulin action to

some degree (111). Training can enhance the responsiveness of skeletal muscles to insulin with increased expression and/or activity of proteins involved in glucose metabolism and insulin signaling (39,110,204,270). Moderate training may increase glycogen synthase activity and GLUT4 protein expression but not insulin signaling (39). Fat oxidation is also a key aspect of improved insulin action, and training increases lipid storage in muscle and fat oxidation capacity (64,95,136,223).

An individual's training status will affect the use of carbohydrate during an aerobic activity. Aerobic training increases fat utilization during a similar duration bout of low- or moderate-intensity activity done after training, which spares muscle glycogen and BG and results in a lesser acute decrease in BG (28,83,223). T2DM may be associated with a decrease in lipid oxidation and shift toward greater carbohydrate oxidation at all exercise intensities (87).

Resistance exercise training also benefits BG control and insulin action in T2DM (46,65,115,116,118,246). In a randomized controlled trial (RCT), twice-weekly progressive resistance training for 16 wk by older men with newly diagnosed T2DM resulted in a 46.3% increase in insulin action, a 7.1% reduction in fasting BG levels, and significant loss of visceral fat (116). An increase in muscle mass from resistance training may contribute to BG uptake from a mass effect, and heavy weight training in particular may reverse or prevent further loss of skeletal muscle due to disuse and aging (34,276). In another RCT, all 20 men with T2DM who participated in either resistance or aerobic exercise thrice weekly for 10 wk improved their overall BG control, but those doing resistance training had significantly lower  $A_{1c}$  values (32). Diabetic women undergoing 12 wk of low-intensity training with resistance bands had gains in

strength and muscle mass and loss of fat mass but had no change in insulin sensitivity (157).

**Evidence statement.** Both aerobic and resistance training improve insulin action, BG control, and fat oxidation and storage in muscle. *ACSM evidence category B.* Resistance exercise enhances skeletal muscle mass. *ACSM evidence category A.*

**Lipids and lipoproteins.** Small RCTs involving T2DM have reported that aerobic training decreases total and LDL-C (low-density lipoprotein-cholesterol) and raises HDL-C (high-density lipoprotein-cholesterol) (130,229). One larger RCT found decreases in total cholesterol with both aerobic and yoga training but no changes in HDL-C or LDL-C (98), although most have found no effect of any form of exercise training on lipids (6,175,178,238,258,267). RCTs designed to increase PA also had no effect on the cholesterol profile in T2DM, with most also finding no change in triglycerides (6,175,238,258,267). A meta-analysis of training effects on blood lipids in adults with T2DM found, however, that LDL-C may be reduced by approximately 5% (136).

Lipid profiles may benefit more from concomitant exercise training and weight reduction. Some studies using intensive diet and aerobic exercise interventions reported large reductions in total cholesterol and triglycerides but failed to include controls (12,13). In the Look AHEAD (Action for Health in Diabetes) study, intensive lifestyle participants exhibited greater decreases in triglycerides and increases in HDL-C than the control group, while both the intensive lifestyle and usual care groups decreased LDL-C (218). Most lifestyle interventions have been accompanied by an approximate 5-kg weight loss.

**Evidence statement.** Blood lipid responses to training are mixed but may result in a small reduction in LDL-C with no change in HDL-C or triglycerides. Combined weight loss and PA may be more effective than aerobic exercise training alone on lipids. *ACSM evidence category C.*

**Hypertension.** Hypertension is a common comorbidity affecting more than 60% of individuals with T2DM (201,249). The risk of vascular complications in hypertensive individuals with T2DM is 66%–100% higher than with either condition alone (103,195). Both aerobic and resistance training can lower BP in nondiabetic individuals, with slightly greater effects observed with the former (49,134,135,137). Most observational studies show that both exercises lower BP in diabetic individuals (35,46,78,208,267). Several RCTs have shown reductions in systolic BP (4–8 mm Hg), but only one reported a slightly lower diastolic BP (11,130,140,176). The Look AHEAD trial found reductions in both systolic and diastolic BP with exercise and weight loss (218), but several studies have reported no changes in BP with training in T2DM (175,238,283). Carefully designed RCTs using increasing levels of PA also failed to show any change in BP despite substantially increased PA (6,258).

**Evidence statement.** Aerobic training may slightly reduce systolic BP, but reductions in diastolic BP are less common, in individuals with T2DM. *ACSM evidence category C.*

**Mortality and cardiovascular risk.** Higher levels of physical fitness and PA are associated with lower cardiovascular (CV) risk and mortality in both healthy and clinical populations (19,153,164,207). Increases in PA and physical fitness are also associated with reduced early mortality in both populations as well (19,42,153,163,164,186,272). All-cause and CV mortality risk was 1.7–6.6 times higher in low-fit compared with high-fit men with T2DM, with the fittest men exhibiting the lowest risk (42,43). A work capacity >10 METs (where 1 MET is defined as the equivalent of resting metabolic rate) carries the lowest risk, independent of obesity (42,153,186). No RCT data on the effects of changes in physical fitness on mortality in diabetes exist.

**Evidence statement.** Observational studies suggest that greater PA and fitness are associated with a lower risk of all-cause and CV mortality. *ACSM evidence category C.*

**Body weight: maintenance and loss.** The most successful programs for long-term weight control have involved combinations of diet, exercise, and behavior modification (281). Exercise interventions undertaken with volumes typically recommended to improve BG control and reduce CVD risk (e.g., 150 min·wk<sup>-1</sup> of brisk walking) are usually insufficient for major weight loss (24), likely because obese and older people frequently have difficulty performing sufficient exercise to create a large energy deficit and can easily counterbalance expenditures by eating more (281). However, in RCTs, about 1 h of daily moderate aerobic exercise produces at least as much fat loss as equivalent caloric restriction, with resultant greater insulin action (231,232).

The optimal volume of exercise to achieve sustained major weight loss is probably much larger than the amount required to achieve improved BG control and CV health (24,217). In observational studies (234,235,274), individuals who successfully maintained large weight loss during at least a year typically engaged in approximately 7 h·wk<sup>-1</sup> of moderate- to vigorous-intensity exercise (62). Two RCTs found that higher exercise volumes (2000 and 2500 kcal·wk<sup>-1</sup>) produced greater and more sustained weight loss than 1000 kcal·wk<sup>-1</sup> of exercise (123,124).

**Evidence statement.** Recommended levels of PA may help produce weight loss. However, up to 60 min·d<sup>-1</sup> may be required when relying on exercise alone for weight loss. *ACSM evidence category C.*

**Supervision of training.** Exercise intervention studies showing the greatest effect on BG control have all involved supervision of exercise sessions by qualified exercise trainers (34,65,196,238). The most direct test of the incremental benefits of supervised training was the Italian Diabetes and Exercise Study (11). In this 1-yr trial, all 606 participants with T2DM (both intervention and control) received high-quality exercise counseling that increased self-reported PA substantially. The intervention group also received supervised, facility-based combined aerobic and resistance exercise training twice weekly, resulting in greater improvements in overall BG control, BP, body

mass index, waist circumference, HDL-C, and estimated 10-yr CVD risk. A recent systematic review of 20 resistance training studies on T2DM (97) found that supervised training of varying volume, frequency, and intensity improved BG control and insulin sensitivity, but that when supervision was removed, compliance and BG control both deteriorated.

**Evidence statement.** Individuals with T2DM engaged in supervised training exhibit greater compliance and BG control than those undertaking exercise training without supervision. *ACSM evidence category B.*

**Psychological effects.** Exercise likely has psychological benefits for persons with T2DM, although evidence for acute and chronic psychological benefits is limited. In the Look AHEAD trial, participants in the intensive lifestyle intervention attempted to lose more than 7% of their initial weight and increase moderately intense PA to greater than 175 min·wk<sup>-1</sup>. They had improvements in health-related (SF-36 physical component scores) quality of life (QOL) and depression symptoms after 12 months that were mediated by enhanced physical fitness (280).

However, it seems that individuals who undertake exercise to prevent a chronic disease fare better than those who undertake it to manage an existing one. A recent meta-analysis found that while psychological well-being was significantly improved among individuals who exercised for disease prevention, it deteriorated significantly when undertaken for management of CVD, end-stage renal disease, pulmonary disease, neurological disorders, and cancer (90). These findings suggest that benefits may vary, with those with fewer existing complications benefiting the most.

Meta-analyses of clinically depressed men and women of all age groups found substantial decreases in depressive symptoms after both short and long courses of exercise (50) and clinical depression and depressive symptoms among the aged (243). Potential mechanisms of exercise include psychological factors, such as increased self-efficacy, a sense of mastery, distraction, and changes in self-concept, as well as physiological factors like increased central norepinephrine transmission, changes in the hypothalamic adrenocortical system (63), serotonin synthesis and metabolism (61), and endorphins. Regular PA may improve psychological well-being, health-related QOL, and depression in individuals with T2DM, among whom depression is more common than in the general population (73).

**Evidence statement.** Increased PA and physical fitness can reduce symptoms of depression and improve health-related QOL in those with T2DM. *ACSM evidence category B.*

## PA AND PREVENTION OF T2DM

Participation in regular PA improves BG control and can prevent or delay onset of T2DM (64,104,149,158,170,260). Prospective cohort and cross-sectional observational studies that assessed PA with questionnaires showed that higher PA levels are associated with reduced risk for T2DM, regardless

of method of activity assessment, ranges of activity categories, and statistical methods (108,113,182). Both moderate walking and vigorous activity have been associated with a decreased risk, and greater volumes of PA may provide the most prevention (113). Observational studies have reported that greater fitness is associated with a reduced risk of developing T2DM (251,273), even if only moderate-intensity exercise is undertaken.

The Da Qing study in China (211) included an exercise-only treatment arm and reported that even modest changes in exercise (20 min of mild or moderate, 10 min of strenuous, or 5 min of very strenuous exercise one to two times a day) reduced diabetes risk by 46% (compared with 42% for diet plus exercise and 31% for diet alone). The Finnish Diabetes Prevention Study (74,260) and the US Diabetes Prevention Program (DPP) (149) included intensive, lifestyle modifications with both diet and increased PA. In the former, 522 middle-aged, overweight adults with IGT completed either lifestyle modifications of at least 30 min of daily, moderate PA, or no change in behavior (74,260). The DPP randomized 3234 men and women with IGT or IFG into control, medication (metformin), or lifestyle modification groups, composed of dietary and weight loss goals and 150 min of weekly aerobic activity (149). Lifestyle modification in both studies reduced incident diabetes by 58% and, in the DPP, had a greater effect than metformin (31%). Weight loss was the dominant predictor of a lower incidence, but increased PA reduced risk of T2DM even when weight loss goals were not achieved (104,158,173). PA seems to play a role in preventing T2DM across ethnic groups and in both sexes (154,224).

Data show that moderate exercise like brisk walking reduces risk of T2DM (108,113,114,154,224), and all studies support the current recommendation of 2.5 h·wk<sup>-1</sup> of a moderate aerobic activity or typically 30 min·d<sup>-1</sup> for 5 d·wk<sup>-1</sup> for prevention. A meta-analysis of 10 cohort studies (125) that assessed the preventive effects of moderate-intensity PA found that risk reduction for T2DM was 0.70 (0.58–0.84) for walking on a regular basis (typically briskly for ≥2.5 h·wk<sup>-1</sup>). The preventive effects of resistance training have not been studied.

T2DM is also increasing in prevalence in children and adolescents, with increasingly sedentary behavior and obesity as key contributors. No RCTs have been completed that address whether PA or exercise prevents T2DM in youth. However, limited studies suggest that, to prevent and manage T2DM, goals for youth should include limiting daily screen time (television, computer, or video game) to less than 60 min·d<sup>-1</sup> and doing at least 60 min·d<sup>-1</sup> of PA (188). A multicenter trial (the TODAY study) is currently underway to assess the role of PA as part of a behavioral lifestyle intervention aimed at preventing T2DM in youth (254).

**Evidence statement.** At least 2.5 h·wk<sup>-1</sup> of moderate to vigorous PA should be undertaken as part of lifestyle changes to prevent T2DM onset in high-risk adults. *ACSM evidence category A. ADA A level recommendation.*



## PA AND PREVENTION AND CONTROL OF GDM

As the prevalence of diabetes continues to rise worldwide, it becomes increasingly important to identify high-risk populations and to implement strategies to delay or prevent diabetes onset. Women diagnosed with GDM are at substantially increased risk of developing T2DM; therefore, PA may be considered a tool to prevent both GDM and possibly T2DM at a later date (70). Prepregnancy PA has been consistently associated with a reduced risk of GDM (57,58,69,206,290). Studies during pregnancy are sparse, with only one case-control study (57), one retrospective study (174), and one study of a cohort of Hispanic women (37) observing significant protective effects of PA, while others have not (58,69,206).

Engaging in 30 min of moderate-intensity PA (e.g., brisk walking) during most days of the week (e.g., 2.5 h·wk<sup>-1</sup>) has been adopted as a recommendation for pregnant women without medical or obstetrical complications (222). However, few primary prevention studies have examined whether making a change in PA reduces risk of developing GDM. In 2006, a meta-analysis reviewed four RCTs on GDM in which pregnant women in their third trimester exercised on a cycle or arm ergometer or performed resistance training three times a week for 20–45 min compared with doing no specific program (36). The women involved in exercise had better BG control, lower fasting and postprandial glucose concentrations, and improved cardiorespiratory fitness, although frequency of prescription of insulin to control BG did not differ from nonexercisers, and pregnancy outcomes were unchanged.

**Evidence statement.** Epidemiologic studies suggest that higher levels of PA may reduce risk of developing GDM during pregnancy. *ACSM evidence category C.* RCTs suggest that moderate exercise may lower maternal BG levels in GDM. *ACSM evidence category B.*

## PREEXERCISE EVALUATION

Safe exercise participation can be complicated by the presence of diabetes-related health complications like CVD, hypertension, neuropathy, or microvascular changes (239). For individuals desiring to participate in low-intensity PA like walking, health care providers should use clinical judgment in deciding whether to recommend preexercise testing (3). Conducting exercise stress testing before walking is unnecessary. No evidence suggests that it is routinely necessary as a CVD diagnostic tool, and requiring it may create barriers to participation.

For exercise more vigorous than brisk walking or exceeding the demands of everyday living, sedentary and older diabetic individuals will likely benefit from being assessed for conditions that might be associated with risk of CVD, contraindicate certain activities, or predispose to injuries, including severe peripheral neuropathy, severe autonomic

neuropathy, and preproliferative or proliferative retinopathy (240). Before undertaking new higher-intensity PA, they are advised to undergo a detailed medical evaluation and screening for BG control, physical limitations, medications, and macrovascular and microvascular complications (3).

This assessment may include a graded exercise test depending on the age of the person, diabetes duration, and the presence of additional CVD risk factors (3,240). The prevalence of symptomatic and asymptomatic CAD is greater in individuals with T2DM (72,155), and maximal graded exercise testing can identify a small proportion of asymptomatic persons with severe coronary artery obstruction (52).

Most young individuals with a low CAD risk may not benefit from preexercise stress testing. In the Look AHEAD trial, although exercise-induced abnormalities were present in 1303 (22.5%) participants, only older age was associated with increased prevalence of all abnormalities during maximal testing (52). A systematic review of the US Preventive Services Task Force concluded that stress testing should not be routinely recommended to detect ischemia in asymptomatic individuals with a low CAD risk (<10% risk of a cardiac event more than 10 yr) because the risks from invasive testing done after a false-positive test outweigh the benefits of its detection (79,262). The lower the CAD risk, the higher the chance of a false positive (79,248).

Current guidelines attempt to avoid automatic inclusion of lower-risk individuals with T2DM, stating that exercise stress testing is advised primarily for *previously sedentary* individuals with diabetes who want to undertake activity *more intense than brisk walking*. The goal is to more effectively target individuals at higher risk for underlying CVD (239). The UKPDS Risk Engine (<http://www.dtu.ox.ac.uk/riskengine/download.htm>) (248) can also be used to calculate expected 10-yr CV risk based on age, sex, smoking, A<sub>1c</sub>, diabetes duration, lipids, BP, and race.

In general, ECG stress testing may be indicated for individuals matching one or more of these criteria:

- Age > 40 yr, with or without CVD risk factors other than diabetes
- Age > 30 yr and
  - Type 1 or 2 diabetes of >10 yr in duration
  - Hypertension
  - Cigarette smoking
  - Dyslipidemia
  - Proliferative or preproliferative retinopathy
  - Nephropathy including microalbuminuria
- Any of the following, regardless of age
  - Known or suspected CAD, cerebrovascular disease, and/or peripheral artery disease (PAD)
  - Autonomic neuropathy
  - Advanced nephropathy with renal failure

Use of these criteria does not exclude the possibility of conducting ECG stress testing on individuals with a low



CAD risk or those who planning to engage in less intense exercise (248). In the absence of contraindications to maximal stress testing, it can still be considered for anyone with T2DM. Although clinical evidence does not definitively determine who should undergo such testing, potential benefits should be weighed against the risk associated with unnecessary procedures for each individual (155,239).

In individuals with positive or nonspecific ECG changes in response to exercise, or with nonspecific ST and T wave changes at rest, follow-up testing may be performed (236). However, the DIAD trial involving 1123 individuals with T2DM and no symptoms of CAD found that screening with adenosine-stress radionuclide myocardial perfusion imaging for myocardial ischemia more than 4.8 yr did not alter rates of cardiac events (288); thus, the cost-effectiveness and diagnostic value of more intensive testing remains in question.

There is no evidence available to determine whether pre-exercise evaluation involving stress testing is necessary or beneficial before participation in anaerobic or resistance training. At present, most testing centers are equipped for maximal stress testing but not for an alternate form of testing involving resistance exercise. Moreover, coronary ischemia is less likely to occur during resistance compared with aerobic exercise eliciting the same HR, and some doubt exists as to whether resistance exercise induces ischemia (77,88). A review of 12 studies of resistance exercise in men with known CAD found no angina, ST depression, abnormal hemodynamics, ventricular dysrhythmias, or other complications during such exercise (275).

**Evidence statement.** Before undertaking exercise more intense than brisk walking, sedentary persons with T2DM will likely benefit from an evaluation by a physician. ECG exercise stress testing for asymptomatic individuals at low risk of CAD is not recommended but may be indicated for higher risk. *ACSM evidence category C. ADA C level recommendation.*

## RECOMMENDED PA PARTICIPATION FOR PERSONS WITH T2DM

Just 39% of adults with diabetes are physically active compared with 58% of other American adults (193). However, for most people with T2DM, exercise is recommended for diabetes management and can be undertaken safely and effectively.

### Aerobic Exercise Training

**Frequency.** Aerobic exercise should be performed at least 3 d·wk<sup>-1</sup> with no more than two consecutive days between bouts of activity because of the transient nature of exercise-induced improvements in insulin action (26,141). Most clinical trials evaluating exercise interventions in T2DM have used a frequency of three times per week (24,238, 246,255), but current guidelines for adults generally recommend five sessions of moderate activity (105,202,217).

**Intensity.** Aerobic exercise should be at least at moderate intensity, corresponding approximately to 40%–60% of  $\dot{V}O_{2\max}$  (maximal aerobic capacity). For most people with T2DM, brisk walking is a moderate-intensity exercise. Additional benefits may be gained from vigorous exercise (>60% of  $\dot{V}O_{2\max}$ ). A meta-analysis (25) showed that exercise intensity predicts improvements in overall BG control to a greater extent than exercise volume, suggesting that those already exercising at a moderate intensity should consider undertaking some vigorous PA to obtain additional BG (and likely CV) benefits.

**Duration.** Individuals with T2DM should engage in a minimum of 150 min·wk<sup>-1</sup> of exercise undertaken at moderate intensity or greater. Aerobic activity should be performed in bouts of at least 10 min and be spread throughout the week. Around 150 min·wk<sup>-1</sup> of moderate-intensity exercise is associated with reduced morbidity and mortality in observational studies in all populations (217). The average weekly duration in meta-analyses of exercise interventions in T2DM (24,246,255), including higher-intensity aerobic exercise (196), has been in a similar range. Recent joint American College of Sports Medicine/American Heart Association guidelines (105,202) recommended 150 min of moderate activity (30 min, 5 d·wk<sup>-1</sup>) or 60 min of vigorous PA (20 min on 3 d) for all adults, whereas recent US federal guidelines (217) recommended 150 min of moderate or 75 min of vigorous activity, or an equivalent combination, spread throughout each week.

The US federal guidelines (217) suggest that an exercise volume of 500–1000 MET·min·wk<sup>-1</sup> (MET equivalent of PA × number of minutes) is optimal and can be achieved, for example, with 150 min·wk<sup>-1</sup> of walking at 6.4 km·h<sup>-1</sup> (4 mph; intensity of 5 METs) or 75 min of jogging at 9.6 km·h<sup>-1</sup> (6 mph; 10 METs). Unfortunately, most people with T2DM do not have sufficient aerobic capacity to jog at 9.6 km·h<sup>-1</sup> for that weekly duration, and they may have orthopedic or other limitations. In a meta-analysis, the mean maximal aerobic capacity in diabetic individuals was only 22.4 mL·kg<sup>-1</sup>·min<sup>-1</sup>, or 6.4 METs (25), making 4.8 METs (75% of maximal) the highest sustainable intensity. Therefore, most diabetic individuals will require at least 150 min of moderate to vigorous aerobic exercise per week to achieve optimal CVD risk reduction. Some CV and BG benefits may be gained from lower exercise volumes (a minimum dose has not been established), whereas further benefit likely results from engaging in durations beyond recommended amounts. Individuals with higher aerobic capacities (>10 METs) may be able to exercise at a higher absolute intensity for less time and achieve the same benefits.

**Mode.** Any form of aerobic exercise (including brisk walking) that uses large muscle groups and causes sustained increases in HR is likely to be beneficial (114), and undertaking a variety of modes of PA is recommended (217).

**Rate of progression.** At present, no study on individuals with T2DM has compared rates of progression in exercise intensity or volume. Gradual progression of both is

advisable to minimize the risk of injury, particularly if health complications are present, and to enhance compliance.

**Body weight loss and maintenance.** The most successful weight control programs involve combinations of exercise, diet, and behavior modification. People who successfully maintain a large weight loss report exercising about 7 h·wk<sup>-1</sup> (62,212,234,235,274).

**Evidence statement.** Persons with T2DM should undertake at least 150 min·wk<sup>-1</sup> of moderate to vigorous aerobic exercise spread out during at least 3 d during the week, with no more than two consecutive days between bouts of aerobic activity. *ACSM evidence category B. ADA B level recommendation.*

## Resistance Exercise Training

**Frequency.** Resistance exercise should be undertaken at least twice weekly on nonconsecutive days (1,105,202,217, 239,240), but more ideally three times a week (65,246), as part of a PA program for individuals with T2DM, along with regular aerobic activities.

**Intensity.** Training should be moderate (50% of 1-repetition maximum, or 1-RM) or vigorous (75%–80% of 1-RM) for optimal gains in strength and insulin action (1,97,239,240,263). Home-based resistance training following supervised, gym-based training may be less effective for maintaining BG control but adequate for maintaining muscle mass and strength (66).

**Duration.** Each training session should minimally include 5–10 exercises involving the major muscle groups (in the upper body, lower body, and core) and involve completion of 10–15 repetitions to near fatigue per set early in training (1,97,239,240,263), progressing over time to heavier weights (or resistance) that can be lifted only 8–10 times. A minimum of one set of repetitions to near fatigue, but as many as three to four sets, is recommended for optimal strength gains.

**Mode.** Resistance machines and free weights (e.g., dumbbells and barbells) can result in fairly equivalent gains in strength and mass of targeted muscles (66). Heavier weights or resistance may be needed for optimization of insulin action and BG control (276).

**Rate of progression.** To avoid injury, progression of intensity, frequency, and duration of training sessions should occur slowly. In most progressive training, increases in weight or resistance are undertaken first and only once when the target number of repetitions per set can consistently be exceeded, followed by a greater number of sets and lastly by increased training frequency. Progression for 6 months to thrice-weekly sessions of three sets of 8–10 repetitions done at 75% to 80% of 1-RM on 8–10 exercises may be an optimal goal (65).

**Evidence statement.** In addition to aerobic training, persons with T2DM should undertake moderate to vigorous resistance training at least 2–3 d·wk<sup>-1</sup>. *ACSM evidence category B. ADA B level recommendation.*

## Supervised Training

Initial instruction and periodic supervision by a qualified exercise trainer is recommended for most persons with T2DM, particularly if they undertake resistance exercise training, to ensure optimal benefits to BG control, BP, lipids, and CV risk and to minimize injury risk (11).

## Combined Aerobic and Resistance and Other Types of Training

Inclusion of both aerobic and resistance exercise training is recommended. Combined training thrice weekly in individuals with T2DM may be of greater benefit to BG control than either aerobic or resistance exercise alone (238). However, the total duration of exercise and caloric expenditure was greatest with combined training in all studies done to date (51,183,238), and both types of training were undertaken together on the same days. No studies have yet reported whether daily, but alternating, training is more effective or the BG effect of isocaloric combinations of training. Milder forms of PA, like yoga and tai chi, may benefit control of BG (98,117,269,286,291), although their inclusion is not supported conclusively at this time.

## Daily Movement (Unstructured Activity)

Individuals with T2DM are encouraged to increase their total daily, unstructured PA to gain additional health benefits. Nonexercise activity thermogenesis (i.e., energy expending for activities of daily living) can create a large daily caloric deficit to prevent excessive weight gain (168,169). In an observational study, obese individuals sat for about 2.5 h more and walked an average of 3.5 miles·d<sup>-1</sup> or less than their lean counterparts do. Most of the lean subjects' greater activity came from walks of short duration (<15 min) and low velocity (~1 mph) (168).

Moreover, use of objective measures like step counters may enhance reaching daily goals. A meta-analysis of 26 studies with a total of 2767 (primarily nondiabetic) participants (8 RCTs and 18 observational studies) found that pedometer users increased PA by 26.9% over baseline in studies having an average intervention of 18 wk (30). An important predictor of increased PA was the use of a goal, such as to take 10,000 steps per day (30).

## Flexibility Training

Flexibility training may be included as part of a PA program, although it should not substitute for other training. Older adults are advised to undertake exercises that maintain or improve balance (202,217), which may include some flexibility training, particularly for many older individuals with T2DM with a higher risk of falling (194). Although flexibility exercise (stretching) has frequently been recommended as a means of increasing joint range of motion (ROM) and reducing risk of injury, two systematic reviews found that flexibility exercise does not reduce risk of exercise-induced

injury (237,287). A small RCT found that ROM exercises modestly decreased peak plantar pressures (94), but no study has directly evaluated whether such training reduces risk of ulceration or injury in T2DM. However, flexibility exercise combined with resistance training can increase ROM in individuals with T2DM (109) and allow individuals to more easily engage in activities that require greater ROM around joints.

**Evidence statement.** Supervised and combined aerobic and resistance training may confer health additional benefits, although milder forms of PA (like yoga) have shown mixed results. Persons with T2DM are encouraged to increase their total daily unstructured PA. Flexibility training may be included but should not be undertaken in place of other recommended types of PA. *ACSM evidence category B. ADA C level recommendation.*

## EXERCISE WITH NONOPTIMAL BG CONTROL

**Hyperglycemia.** While hyperglycemia can be worsened by exercise in type 1 diabetic individuals who are insulin-deficient and ketotic (due to missed or insufficient insulin), very few persons with T2DM develop such a profound degree of insulin deficiency. Therefore, individuals with T2DM generally do not need to postpone exercise because of high BG, provided that they are feeling well. If they undertake strenuous physical activities with elevated glucose levels ( $>300 \text{ mg}\cdot\text{dL}^{-1}$  or  $16.7 \text{ mmol}\cdot\text{L}^{-1}$ ), it is prudent to ensure that they are adequately hydrated (3). If hyperglycemic after a meal, individuals with T2DM will still likely experience a reduction in BG during aerobic work because endogenous insulin levels will likely be higher at that time (221).

**Evidence statement.** Individuals with T2DM may engage in PA, using caution when exercising with BG levels exceeding  $300 \text{ mg}\cdot\text{dL}^{-1}$  ( $16.7 \text{ mmol}\cdot\text{L}^{-1}$ ) without ketosis, provided they are feeling well and are adequately hydrated. *ACSM evidence category C. ADA E level recommendation.*

**Hypoglycemia: causes and prevention.** Of greatest concern to many exercisers is the risk of hypoglycemia. In individuals whose diabetes is being controlled by lifestyle alone, the risk of developing hypoglycemia during exercise is minimal, making stringent measures unnecessary to maintain BG (239). Glucose monitoring can be performed before and after PA to assess its unique effect. Activities of longer duration and lower intensity generally cause a decline in BG levels but not to the level of hypoglycemia (9,29,75,111,160). While very intense activities can cause transient elevations in BG (156,252,253), intermittent high-intensity exercise done immediately after breakfast in individuals treated with diet only reduces BG levels and insulin secretion (160).

In insulin or insulin secretagogue users, who frequently have the effects of both exercise and insulin to increase glucose uptake, PA can complicate diabetes management (138,198,230,293). For preexercise BG levels of less than  $100 \text{ mg}\cdot\text{dL}^{-1}$  ( $5.5 \text{ mmol}\cdot\text{L}^{-1}$ ), the ADA recommends that

carbohydrate be ingested before any PA (3), but this applies only to individuals taking insulin or the secretagogues more likely to cause hypoglycemia (e.g., sulfonylureas like glyburide, glipizide, and glimepiride, as well as nateglinide and repaglinide) (161,230). If controlled with diet or other oral medications, most individuals will not need carbohydrate supplements for exercise lasting less than an hour. Insulin users should likely consume up to  $15 \text{ g}$  of carbohydrate before exercise for an initial BG level of  $100 \text{ mg}\cdot\text{dL}^{-1}$  or lower, with the actual amount dependent on injected insulin doses, exercise duration and intensity, and results of BG monitoring. Intense, short exercise requires lesser or no carbohydrate intake (156).

Later-onset hypoglycemia is a greater concern when carbohydrate stores (i.e., muscle and liver glycogen) are depleted during an acute bout of exercise. In particular, high-intensity exercise (e.g., repeated interval or intense resistance training) can result in substantial depletion of muscle glycogen, thereby increasing risk for postexercise hypoglycemia in users of insulin or insulin secretagogues (161). In such cases, the consumption of  $5\text{--}30 \text{ g}$  of carbohydrate during and within 30 min after exhaustive, glycogen-depleting exercise will lower hypoglycemia risk and allow for more efficient restoration of muscle glycogen (31,247).

**Evidence statement.** Persons with T2DM not using insulin or insulin secretagogues are unlikely to experience hypoglycemia related to PA. Users of insulin and insulin secretagogues are advised to supplement with carbohydrate as needed to prevent hypoglycemia during and after exercise. *ACSM evidence category C. ADA C level recommendation.*

## MEDICATION EFFECTS ON EXERCISE RESPONSES

Current treatment strategies promote combination therapies to address the three major defects in T2DM: impaired peripheral glucose uptake (liver, fat, and muscle), excessive hepatic glucose release (with glucagon excess), and insufficient insulin secretion. Medication adjustments for PA are generally necessary only with use of insulin and other insulin secretagogues (161,230). To prevent hypoglycemia, individuals may need to reduce their oral medications or insulin dosing before (and possibly after) exercise (83,161). Before planned exercise, short-acting insulin doses will likely have to be reduced to prevent hypoglycemia. Newer, synthetic, rapid-acting insulin analogs (i.e., lispro, aspart, and glulisine) induce more rapid decreases in BG than regular human insulin. Individuals will need to monitor BG levels before, occasionally during, and after exercise and compensate with appropriate dietary and/or medication regimen changes, particularly when exercising at insulin peak times. If only longer-acting insulins like glargine, detemir, and Neutral Protamine Hagedorn (NPH) are being absorbed from subcutaneous depots during PA, exercise-induced hypoglycemia is not as likely (219), although doses may need to be reduced to accommodate regular



participation in PA. Doses of select oral hypoglycemic agents (glyburide, glipizide, glimepiride, nateglinide, and repaglinide) may also need to be lowered in response to regular exercise training if the frequency of hypoglycemia increases (161,230).

Diabetic individuals are often prescribed a variety of medications for comorbid conditions, including diuretics,  $\beta$ -blockers, angiotensin-converting enzyme (ACE) inhibitors, aspirin, lipid-lowering agents, and more. These medications generally do not affect exercise responses, with some notable exceptions.  $\beta$ -blockers are known to blunt HR responses to exercise and lower maximal exercise capacity to  $\sim 87\%$  of expected via negative inotropic and chronotropic effects (241). They may also block adrenergic symptoms of hypoglycemia, increasing the risk of undetected hypoglycemia during exercise. However,  $\beta$ -blockers may increase exercise capacity in those with CAD, rather than lowering it, by reducing coronary ischemia during activity (53). Diuretics, however, may lower overall blood and fluid volumes resulting in dehydration and electrolyte imbalances, particularly during exercise in the heat. Statin use has been associated with an elevated risk of myopathies (myalgia and myositis), particularly when combined with use of fibrates and niacin (203). An extended discussion on medications can be found in the *Handbook of Exercise in Diabetes* (2002) (84).

**Evidence statement.** Medication dosage adjustments to prevent exercise-associated hypoglycemia may be required by individuals using insulin or certain insulin secretagogues. Most other medications prescribed for concomitant health problems do not affect exercise, with the exception of  $\beta$ -blockers, some diuretics, and statins. *ACSM evidence category C. ADA C level recommendation.*

## EXERCISE WITH LONG-TERM COMPLICATIONS OF DIABETES

**Vascular disease.** Individuals with angina and T2DM classified as moderate or high risk should preferably exercise in a supervised cardiac rehabilitation program, at least initially (245). Diabetes accelerates the development of atherosclerosis and is a major risk factor for CVD and PAD. Individuals with T2DM have a lifetime risk of CAD that includes 67% of women and 78% of men and is exacerbated by obesity (22,80,165). Moreover, some individuals who have an acute myocardial infarction may not experience chest pain, and up to a third may have silent myocardial ischemia (45,180).

For individuals with PAD, with and without intermittent claudication and pain in the extremities during PA, low-to-moderate walking, arm-crank, and cycling exercise have all been shown to enhance mobility, functional capacity, exercise pain tolerance, and QOL (214,295). Lower extremity resistance training also improves functional performance measured by treadmill walking, stair climbing ability, and QOL measures (187).

Vascular alterations are common in diabetes, even in the absence of overt vascular disease. Endothelial dysfunction may be an underlying cause of many associated vascular problems (45,54). In addition to traditional risk factors, hyperglycemia, hyperinsulinemia, and oxidative stress contribute to endothelial damage, leading to poor arterial function and greater susceptibility to atherogenesis (45,82,289). Both aerobic and resistance training can improve endothelial function (46,294), but not all studies have shown posttraining improvement (283).

**Evidence statement.** Known CVD is not an absolute contraindication to exercise. Individuals with angina classified as moderate or high risk should likely begin exercise in a supervised cardiac rehabilitation program. PA is advised for anyone with PAD. *ACSM evidence category C. ADA C level recommendation.*

**Peripheral neuropathy.** Mild to moderate exercise may help prevent the onset of peripheral neuropathy (10). Individuals without acute foot ulcers can undertake moderate weight-bearing exercise, although anyone with a foot injury or open sore or ulcer should be restricted to non-weight-bearing PA. All individuals should closely examine their feet on a daily basis to prevent detect sores or ulcers early and follow recommendations for use of proper footwear. Previous guidelines stated that persons with severe peripheral neuropathy should avoid weight-bearing activities to reduce risk of foot ulcerations (102,264). However, recent studies indicated that moderate walking does not increase risk of foot ulcers or reulceration in those with peripheral neuropathy (166,167).

Peripheral neuropathy affects the extremities, particularly the lower legs and feet. Hyperglycemia causes nerve toxicity, leading to nerve damage and apoptosis (242,244), which causes microvascular damage and loss of perfusion. Symptoms manifest as neuropathic pain and/or loss of sensation that, coupled with poor blood flow, increase the risk of foot injuries and ulcerations (45,244). Up to 40% of diabetic individuals may experience peripheral neuropathy, and 60% of lower extremity amputations in Americans are related to diabetes (166,199,216).

**Evidence statement.** Individuals with peripheral neuropathy and without acute ulceration may participate in moderate weight-bearing exercise. Comprehensive foot care including daily inspection of feet and use of proper footwear is recommended for prevention and early detection of sores or ulcers. Moderate walking likely does not increase risk of foot ulcers or reulceration with peripheral neuropathy. *ACSM evidence category B. ADA B level recommendation.*

**Autonomic neuropathy.** Moderate-intensity aerobic training can improve autonomic function in individuals with and without CV autonomic neuropathy (CAN) (112,176,208); however, improvements may only be evident after an acute submaximal exercise (78). Screening for CAN should include a battery of autonomic tests (including HR variability) that evaluate both branches of the autonomic nervous system. Given the likelihood of silent ischemia, HR, and BP



abnormalities, individuals with CAN should have physician approval and possibly undergo stress testing to screen for CV abnormalities before commencing exercise (265). Exercise intensity may be accurately prescribed using the HR reserve method (a percentage of the difference between maximal and resting HR, added to the resting value) to approximate oxygen consumption during submaximal exercise with maximal HR directly measured, rather than estimated, for better accuracy (48,265).

Approximately 22% of those with T2DM have CAN, but most exhibit alterations in autonomic function (292). The presence of CAN doubles the risk of mortality (48,265) and indicates more frequency of silent myocardial ischemia (265), orthostatic hypotension, or resting tachycardia (76,177). CAN also impairs exercise tolerance and lowers maximal HR (131,265). Although both sympathetic and parasympathetic dysfunctions can be present, vagal dysfunction usually occurs earlier. Slower HR recovery after PA is associated with mortality risk (38,265).

**Evidence statement.** Individuals with CAN should be screened and receive physician approval and possibly an exercise stress test before exercise initiation. Exercise intensity is best prescribed using the HR reserve method with direct measurement of maximal HR. *ACSM evidence category C. ADA C level recommendation.*

**Retinopathy.** In diabetic individuals with proliferative or preproliferative retinopathy or macular degeneration, careful screening and physician approval are recommended before initiating an exercise program. Activities that greatly increase intraocular pressure, such as high-intensity aerobic or resistance training (with large increases in systolic BP) and head-down activities, are not advised with uncontrolled proliferative disease, nor are jumping or jarring activities, all of which increase hemorrhage risk (1). Diabetic retinopathy is the main cause of blindness in developed countries and is associated with increased CV mortality (129,147). Individuals with retinopathy may receive some benefits, such as improved work capacity, after low- to moderate-intensity exercise training (16,17). While PA has been shown to be protective against development of age-related macular degeneration (150), very little research exists in T2DM.

**Evidence statement.** Individuals with uncontrolled proliferative retinopathy should avoid activities that greatly increase intraocular pressure and hemorrhage risk. *ACSM evidence category D. ADA E level recommendation.*

**Nephropathy and microalbuminuria.** Both aerobic and resistance training improve physical function and QOL in individuals with kidney disease (126,209,210), although BP increases during PA may transiently elevate levels of microalbumin in urine. Resistance exercise training is especially effective in improving muscle function and activities of daily living, which are normally severely affected by later-stage kidney disease (126). Before initiation of PA, individuals with overt nephropathy should be carefully screened, have physician approval, and possibly undergo stress testing to detect CAD and abnormal HR and BP

responses (1,27). Exercise should be begun at a low intensity and volume because aerobic capacity and muscle function are substantially reduced, and avoidance of the Valsalva maneuver or high-intensity exercise to prevent excessive increases in BP is advised (1). Supervised, moderate aerobic exercise undertaken during dialysis sessions, however, has been shown to be effective as home-based exercise and may improve compliance (126,151).

Diabetic nephropathy develops in approximately 30% of individuals with diabetes and is a major risk factor for death in those with diabetes (20,45). Microalbuminuria, or minute amounts of albumin in the urine, is common and a risk factor for overt nephropathy (45) and CV mortality (91). Tight BG and BP control may delay progression of microalbuminuria (127,148), along with exercise and dietary changes (81,162). Exercise training delays the progression of diabetic nephropathy in animals (89,259), but few evidence is available in humans.

**Evidence statement.** Exercise training increases physical function and QOL in individuals with kidney disease and may even be undertaken during dialysis sessions. The presence of microalbuminuria per se does not necessitate exercise restrictions. *ACSM evidence category C. ADA C level recommendation.*

## ADOPTION AND MAINTENANCE OF EXERCISE BY PERSONS WITH DIABETES

Most American adults with T2DM or at highest risk for developing it do not engage in regular PA; their rate of participation is significantly below national norms (193). Additional strategies are needed to increase the adoption and maintenance of PA.

One of the most consistent predictors of greater levels of activity has been higher levels of self-efficacy (2,55,68), which reflect confidence in the ability to exercise (185). Social support has also been associated with greater levels of PA (93,190,215), supporting the role of social networks in the spread of obesity (41). Fortunately, those same social dynamics may be exploited to increase the effects of interventions beyond the “target” individual (8,99) and potentially can help spread PA behavior. Counseling delivered by health care professionals may be a meaningful source of support and effective source for delivery (7,144). Physicians vary in counseling their patients to exercise: on average, advice or referral related to exercise occurred at 18% of office visits among diabetic patients (213), and 73% of patients reported receiving advice at some point to exercise more (192). The availability of facilities or pleasant and safe places to walk may also be important predictors of regular PA (59).

When prescribing PA for the prevention or control of T2DM, the effects of the dose of the prescription on adherence are small (225). Therefore, practitioners are encouraged to use factors such as choice and enjoyment in helping determine specifically how an individual would meet recommended

participation. Affective responses to exercise may be important predictors of adoption and maintenance, and encouraging activity at intensities below the ventilatory threshold may be most beneficial (172,277,278). Many individuals with, or at risk of developing, T2DM prefer walking as an aerobic activity (190), and pedometer-based interventions can be effective for increasing aerobic activity (30,205,258). Finally, the emerging importance of sedentary behaviors in determining metabolic risk (106,107) suggests that future interventions may also benefit from attempting to decrease sitting time and periods of extended sedentary activity.

Large-scale trials like the DPP and Look AHEAD provide some insight into successful lifestyle interventions that help promote PA by incorporating goal setting, self-monitoring, frequent contact, and stepped-care protocols (56,60,71,266). Delivering these programs requires extensive access to resources, staff, and space, although they are cost-effective overall (121,122).

These large studies are multifactorial, targeting several behaviors that include PA, but include multiple behavior interventions that also require changes in diet and focusing on weight loss or management (179). Therefore, strategies for PA intervention in weight management are highly relevant to this population (62). Fewer RCTs solely targeted PA behavior in individuals with or at risk of developing T2DM (279,284,285). The results have been mixed, with some showing increased PA (67,120,145,171) and others showing no effect (142,143,189). Effective short-term programs have used print (67), phone (44,144,233), in-person (120,139), or Internet (92,171) delivery. Long-term effectiveness of such interventions has not been assessed (197).

**Evidence statement.** Efforts to promote PA should focus on developing self-efficacy and fostering social support from family, friends, and health care providers. Encouraging mild or moderate PA may be most beneficial to adoption and

maintenance of regular PA participation. Lifestyle interventions may have some efficacy in promoting PA behavior. *ACSM evidence category B. ADA B level recommendation.*

## CONCLUSIONS

Exercise plays a major role in the prevention and control of insulin resistance, prediabetes, GDM, T2DM, and diabetes-related health complications. Both aerobic and resistance training improve insulin action, at least acutely, and can assist with the management of BG levels, lipids, BP, CV risk, mortality, and QOL, but exercise must be undertaken regularly to have continued benefits and likely include regular training of varying types. Most persons with T2DM can perform exercise safely as long as certain precautions are taken. The inclusion of an exercise program or other means of increasing overall PA is critical for optimal health in individuals with T2DM.

This joint position statement is written by the American College of Sports Medicine (ACSM) and the American Diabetes Association (ADA).

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