

# 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

This joint position statement is written by the American College of Sports Medicine and the American Diabetes Association; approved by Executive Committee of the American Diabetes Association in July 2010. This statement is published concurrently in *Medicine & Science in Sports & Exercise*® and *Diabetes Care*. Individual name recognition is stated in the acknowledgments at the end of the statement.

0195-9131/10/4212-2282/0

MEDICINE & SCIENCE IN SPORTS & EXERCISE®

Copyright © 2010 by the American College of Sports Medicine and the American Diabetes Association

DOI: 10.1249/MSS.0b013e3181eeb61c

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	● 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.	A/*
	● 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.	A/*
	● 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.	C/*
	● 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.	C/*
	● 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.	B/*
	● Milder forms of exercise (e.g., tai chi, yoga) have shown mixed results.	C/*
	● PA can result in acute improvements in systemic insulin action lasting from 2 to 72 h.	A/*
Chronic effects of exercise training	● Both aerobic and resistance training improve insulin action, BG control, and fat oxidation and storage in muscle.	B/*
	● Resistance exercise enhances skeletal muscle mass.	A/*
	● 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.	C/*
	● Aerobic training may slightly reduce systolic BP, but reductions in diastolic BP are less common, in individuals with T2DM.	C/*
	● Observational studies suggest that greater PA and fitness are associated with a lower risk of all-cause and CV mortality.	C/*
	● 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.	C/*
	● Individuals with T2DM engaged in supervised training exhibit greater compliance and BG control than those undertaking exercise training without supervision.	B/*
PA and prevention of type 2 diabetes	● Increased PA and physical fitness can reduce symptoms of depression and improve health-related QOL in those with T2DM.	B/*
	● 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.	A/A
PA in prevention and control of gestational diabetes	● Epidemiologic studies suggest that higher levels of PA may reduce risk of developing GDM during pregnancy.	C/*
	● RCTs suggest that moderate exercise may lower maternal BG levels in GDM.	B/*
Preexercise evaluation	● 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.	C/C
	● 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.	B/B
Recommended PA participation for persons with type 2 diabetes	● In addition to aerobic training, persons with T2DM should undertake moderate to vigorous resistance training at least 2–3 d·wk <sup>-1</sup> .	B/B
	● 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.	B/C
	● 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.	C/E
Exercise with nonoptimal BG control	● 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.	C/C
	● 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.	C/C

(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).

ACSM: Sheri R. Colberg, Ph.D., FACSM (Chair); Ann L. Albright, Ph.D., RD; Bryan J. Blissmer, Ph.D.; Barry Braun, Ph.D., FACSM; Lisa Chasan-Taber, Sc.D., FACSM; and Bo Fernhall, Ph.D., FACSM.

ADA: Judith G. Regensteiner, Ph.D.; Richard R. Rubin, Ph.D.; and Ronald J. Sigal, M.D., M.P.H., FRCPC.

The authors have no financial support or professional conflicts of interest to disclose related to its content. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

This pronouncement was reviewed by the American College of Sports Medicine Pronouncements Committee, American Diabetes Association Professional Practice Committee, and by Gregory D. Cartee, Ph.D., FACSM; Peter A. Farrell, Ph.D., FACSM; Laurie J. Goodyear, Ph.D., FACSM; and Andrea M. Kriska, Ph.D., FACSM.

This joint position statement replaces the 2000 ACSM Position Stand "Exercise and Type 2 Diabetes" [*Med Sci Sports Exerc.* 2000; 32(7):1345–60].

## REFERENCES

- Albright A, Franz M, Hornsby G, et al. American College of Sports Medicine. Position Stand: exercise and type 2 diabetes. *Med Sci Sports Exerc.* 2000;32(7):1345–60.
- Aljassam LI, Peyrot M, Wissow L, Rubin RR. The impact of barriers and self-efficacy on self-care behaviors in type 2 diabetes. *Diabetes Educ.* 2001;27(3):393–404.
- American Diabetes Association. Physical activity/exercise and diabetes. *Diabetes Care.* 2004;27(90001):S58–62.
- American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care.* 2010;33(1 suppl):S62–9.
- American Diabetes Association. Standards of medical care in diabetes 2010. *Diabetes Care.* 2010;33(1 suppl):S11–61.
- Araiza P, Hewes H, Gashetewa C, Vella CA, Burge MR. Efficacy of a pedometer-based physical activity program on parameters of diabetes control in type 2 diabetes mellitus. *Metabolism.* 2006;55(10):1382–7.
- Armit CM, Brown WJ, Marshall AL, et al. Randomized trial of three strategies to promote physical activity in general practice. *Prev Med.* 2009;48(2):156–63.
- Bahr DB, Browning RC, Wyatt HR, Hill JO. Exploiting social networks to mitigate the obesity epidemic. *Obesity.* 2009;17(4):723–8.
- Bajpeyi S, Tanner CJ, Slentz CA, et al. Effect of exercise intensity and volume on persistence of insulin sensitivity during training cessation. *J Appl Physiol.* 2009;106(4):1079–85.
- Balducci S, Iacobellis G, Parisi L, et al. Exercise training can modify the natural history of diabetic peripheral neuropathy. *J Diabetes Complications.* 2006;20(4):216–23.
- Balducci S, Zanuso S, Nicolucci A, et al. Effect of an intensive exercise intervention strategy on modifiable cardiovascular risk factors in type 2 diabetic subjects. A randomized controlled trial: The Italian Diabetes and Exercise Study (IDES). *Arch Intern Med.* In press.
- Barnard RJ, Lattimore L, Holly RG, Cherny S, Pritikin N. Response of non-insulin-dependent diabetic patients to an intensive program of diet and exercise. *Diabetes Care.* 1982;5(4):370–4.
- Barnard RJ, Ugianskis EJ, Martin DA. The effects of an intensive diet and exercise program on patients with non-insulin-dependent diabetes mellitus. *J Cardiopulm Rehabil.* 1992;12:194–201.
- Baynard T, Franklin RM, Goulopoulou S, Carhart R Jr, Kanaley JA. Effect of a single vs multiple bouts of exercise on glucose control in women with type 2 diabetes. *Metabolism.* 2005;54(8):989–94.

15. Bergman BC, Butterfield GE, Wolfel EE, Casazza GA, Lopaschuk GD, Brooks GA. Evaluation of exercise and training on muscle lipid metabolism. *Am J Physiol*. 1999;276(1 Pt 1):E106–17.
16. Bernbaum M, Albert SG, Cohen JD. Exercise training in individuals with diabetic retinopathy and blindness. *Arch Phys Med Rehabil*. 1989;70(8):605–11.
17. Bernbaum M, Albert SG, Cohen JD, Drimmer A. Cardiovascular conditioning in individuals with diabetic retinopathy. *Diabetes Care*. 1989;12(10):740–2.
18. Black LE, Swan PD, Alvar BA. Effects of intensity and volume on insulin sensitivity during acute bouts of resistance training. *J Strength Cond Res*. 2010;24(4):1109–16.
19. Blair SN, Kohl HW 3rd, Barlow CE, Paffenbarger RS Jr, Gibbons LW, Macera CA. Changes in physical fitness and all-cause mortality. A prospective study of healthy and unhealthy men. *JAMA*. 1995;273(14):1093–8.
20. Bo S, Ciccone G, Rosato R, et al. Renal damage in patients with type 2 diabetes: a strong predictor of mortality. *Diabet Med*. 2005;22(3):258–65.
21. Boon H, Blaak EE, Saris WH, Keizer HA, Wagenmakers AJ, van Loon LJ. Substrate source utilisation in long-term diagnosed type 2 diabetes patients at rest and during exercise and subsequent recovery. *Diabetologia*. 2007;50(1):103–12.
22. Booth GL, Kapral MK, Fung K, Tu JV. Recent trends in cardiovascular complications among men and women with and without diabetes. *Diabetes Care*. 2006;29(1):32–7.
23. Borghouts LB, Wagenmakers AJ, Goyens PL, Keizer HA. Substrate utilization in non-obese Type II diabetic patients at rest and during exercise. *Clin Sci (Lond)*. 2002;103(6):559–66.
24. Boulé NG, Haddad E, Kenny GP, Wells GA, Sigal RJ. Effects of exercise on glycemic control and body mass in type 2 diabetes mellitus: a meta-analysis of controlled clinical trials. *JAMA*. 2001;286(10):1218–27.
25. Boulé NG, Kenny GP, Haddad E, Wells GA, Sigal RJ. Meta-analysis of the effect of structured exercise training on cardiorespiratory fitness in type 2 diabetes mellitus. *Diabetologia*. 2003;46(8):1071–81.
26. Boulé NG, Weisnagel SJ, Lakka TA, et al. Effects of exercise training on glucose homeostasis: the HERITAGE family study. *Diabetes Care*. 2005;28(1):108–14.
27. Braden C. Nephropathy: advanced. In: *The Health Professional's Guide to Diabetes and Exercise*. Alexandria (VA): American Diabetes Association; 1995. p. 177–80.
28. Braun B, Sharoff C, Chipkin SR, Beaudoin F. Effects of insulin resistance on substrate utilization during exercise in overweight women. *J Appl Physiol*. 2004;97(3):991–7.
29. Braun B, Zimmermann MB, Kretchmer N. Effects of exercise intensity on insulin sensitivity in women with non-insulin-dependent diabetes mellitus. *J Appl Physiol*. 1995;78(1):300–6.
30. Bravata DM, Smith-Spangler C, Sundaram V, et al. Using pedometers to increase physical activity and improve health: a systematic review. *JAMA*. 2007;298(19):2296–304.
31. Burke LM, Hawley JA. Carbohydrate and exercise. *Curr Opin Clin Nutr Metab Care*. 1999;2(6):515–20.
32. Bweir S, Al-Jarrah M, Almalaty AM, et al. Resistance exercise training lowers HbA<sub>1c</sub> more than aerobic training in adults with type 2 diabetes. *Diabetol Metab Syndr*. 2009;1:27.
33. Cartee GD, Young DA, Sleeper MD, Zierath J, Wallberg-Henriksson H, Holloszy JO. Prolonged increase in insulin-stimulated glucose transport in muscle after exercise. *Am J Physiol*. 1989;256(4 Pt 1):E494–9.
34. Castaneda C, Layne JE, Munoz-Orians L, et al. A randomized controlled trial of resistance exercise training to improve glycemic control in older adults with type 2 diabetes. *Diabetes Care*. 2002;25(12):2335–41.
35. Cauza E, Hanusch-Enserer U, Strasser B, et al. The relative benefits of endurance and strength training on the metabolic factors and muscle function of people with type 2 diabetes mellitus. *Arch Phys Med Rehabil*. 2005;86(8):1527–33.
36. Ceysens G, Rouiller D, Boulvain M. Exercise for diabetic pregnant women. *Cochrane Database Syst Rev*. 2006;3:CD004225.
37. Chasan-Taber L, Schmidt MD, Pekow P, et al. Physical activity and gestational diabetes mellitus among Hispanic women. *J Womens Health (Larchmt)*. 2008;17(6):999–1008.
38. Cheng YJ, Lauer MS, Earnest CP, et al. Heart rate recovery following maximal exercise testing as a predictor of cardiovascular disease and all-cause mortality in men with diabetes. *Diabetes Care*. 2003;26(7):2052–7.
39. Christ-Roberts CY, Pratipanawatr T, Pratipanawatr W, et al. Exercise training increases glycogen synthase activity and GLUT4 expression but not insulin signaling in overweight non-diabetic and type 2 diabetic subjects. *Metabolism*. 2004;53(9):1233–42.
40. Christ-Roberts CY, Pratipanawatr T, Pratipanawatr W, Berria R, Belfort R, Mandarino LJ. Increased insulin receptor signaling and glycogen synthase activity contribute to the synergistic effect of exercise on insulin action. *J Appl Physiol*. 2003;95(6):2519–29.
41. Christakis NA, Fowler JH. The spread of obesity in a large social network over 32 years. *N Engl J Med*. 2007;357(4):370–9.
42. Church TS, Cheng YJ, Earnest CP, et al. Exercise capacity and body composition as predictors of mortality among men with diabetes. *Diabetes Care*. 2004;27(1):83–8.
43. Church TS, LaMonte MJ, Barlow CE, Blair SN. Cardiorespiratory fitness and body mass index as predictors of cardiovascular disease mortality among men with diabetes. *Arch Intern Med*. 2005;165(18):2114–20.
44. Clark M, Hampson SE, Avery L, Simpson R. Effects of a tailored lifestyle self-management intervention in patients with type 2 diabetes. *Br J Health Psychol*. 2004;9(Pt 3):365–79.
45. Coccheri S. Approaches to prevention of cardiovascular complications and events in diabetes mellitus. *Drugs*. 2007;67(7):997–1026.
46. Cohen ND, Dunstan DW, Robinson C, Vulikh E, Zimmet PZ, Shaw JE. Improved endothelial function following a 14-month resistance exercise training program in adults with type 2 diabetes. *Diabetes Res Clin Pract*. 2008;79(3):405–11.
47. Colberg SR, Hagberg JM, McCole SD, Zmuda JM, Thompson PD, Kelley DE. Utilization of glycogen but not plasma glucose is reduced in individuals with NIDDM during mild-intensity exercise. *J Appl Physiol*. 1996;81(5):2027–33.
48. Colberg SR, Swain DP, Vinik AI. Use of heart rate reserve and rating of perceived exertion to prescribe exercise intensity in diabetic autonomic neuropathy. *Diabetes Care*. 2003;26(4):986–90.
49. Cornelissen VA, Fagard RH. Effect of resistance training on resting blood pressure: a meta-analysis of randomized controlled trials. *J Hypertens*. 2005;23(2):251–9.
50. Craft LL, Perna FM. The benefits of exercise for the clinically depressed. *Prim Care Companion J Clin Psychiatry*. 2004;6(3):104–11.
51. Cuff DJ, Meneilly GS, Martin A, Ignaszewski A, Tildesley HD, Frohlich JJ. Effective exercise modality to reduce insulin resistance in women with type 2 diabetes. *Diabetes Care*. 2003;26(11):2977–82.
52. Curtis JM, Horton ES, Bahnson J, et al. Prevalence and predictors of abnormal cardiovascular responses to exercise testing among individuals with type 2 diabetes: the Look AHEAD (Action for Health in Diabetes) study. *Diabetes Care*. 2010;33(4):901–7.
53. de Muinck ED, Lie KI. Safety and efficacy of beta-blockers in the treatment of stable angina pectoris. *J Cardiovasc Pharmacol*. 1990;16(5 suppl):S123–8.
54. Deckert T, Feldt-Rasmussen B, Borch-Johnsen K, Jensen T, Kofoed-Enevoldsen A. Albuminuria reflects widespread



- vascular damage. The Steno hypothesis. *Diabetologia*. 1989;32(4): 219–26.
55. Delahanty LM, Conroy MB, Nathan DM. Psychological predictors of physical activity in the Diabetes Prevention Program. *J Am Diet Assoc*. 2006;106(5):698–705.
  56. Delahanty LM, Nathan DM. Implications of the Diabetes Prevention Program and Look AHEAD clinical trials for lifestyle interventions. *J Am Diet Assoc*. 2008;108(4 suppl 1):S66–72.
  57. Dempsey JC, Butler CL, Sorensen TK, et al. A case-control study of maternal recreational physical activity and risk of gestational diabetes mellitus. *Diabetes Res Clin Pract*. 2004;66(2): 203–15.
  58. Dempsey JC, Sorensen TK, Williams MA, et al. Prospective study of gestational diabetes mellitus risk in relation to maternal recreational physical activity before and during pregnancy. *Am J Epidemiol*. 2004;159(7):663–70.
  59. Deshpande AD, Baker EA, Lovegreen SL, Brownson RC. Environmental correlates of physical activity among individuals with diabetes in the rural midwest. *Diabetes Care*. 2005;28(5): 1012–8.
  60. Diabetes Prevention Program (DPP) Research Group. The Diabetes Prevention Program (DPP): description of lifestyle intervention. *Diabetes Care*. 2002;25(12):2165–71.
  61. Dishman RK, Renner KJ, Youngstedt SD, et al. Activity wheel running reduces escape latency and alters brain monoamine levels after footshock. *Brain Res Bull*. 1997;42(5):399–406.
  62. Donnelly JE, Blair SN, Jakicic JM, Manore MM, Rankin JW, Smith BK, American College of Sports Medicine. Position Stand: appropriate physical activity intervention strategies for weight loss and prevention of weight regain for adults. *Med Sci Sports Exerc*. 2009;41(2):459–71.
  63. Droste SK, Gesing A, Ulbricht S, Muller MB, Linthorst AC, Reul JM. Effects of long-term voluntary exercise on the mouse hypothalamic-pituitary-adrenocortical axis. *Endocrinology*. 2003; 144(7):3012–23.
  64. Duncan GE, Perri MG, Theriaque DW, Hutson AD, Eckel RH, Stacpoole PW. Exercise training, without weight loss, increases insulin sensitivity and postheparin plasma lipase activity in previously sedentary adults. *Diabetes Care*. 2003;26(3):557–62.
  65. Dunstan DW, Daly RM, Owen N, et al. High-intensity resistance training improves glycemic control in older patients with type 2 diabetes. *Diabetes Care*. 2002;25(10):1729–36.
  66. Dunstan DW, Daly RM, Owen N, et al. Home-based resistance training is not sufficient to maintain improved glycemic control following supervised training in older individuals with type 2 diabetes. *Diabetes Care*. 2005;28(1):3–9.
  67. Dutton GR, Provost BC, Tan F, Smith D. A tailored print-based physical activity intervention for patients with type 2 diabetes. *Preventive Medicine*. 2008;47(4):409–11.
  68. Dutton GR, Tan F, Provost BC, Sorenson JL, Allen B, Smith D. Relationship between self-efficacy and physical activity among patients with type 2 diabetes. *J Behav Med*. 2009;32(3):270–7.
  69. Dyck R, Klomp H, Tan LK, Turnell RW, Boctor MA. A comparison of rates, risk factors, and outcomes of gestational diabetes between aboriginal and non-aboriginal women in the Saskatoon health district. *Diabetes Care*. 2002;25(3):487–93.
  70. Dyck RF, Sheppard MS, Cassidy H, Chad K, Tan L, Van Vliet SH. Preventing NIDDM among aboriginal people: is exercise the answer? Description of a pilot project using exercise to prevent gestational diabetes. *Int J Circumpolar Health*. 1998;57(1 suppl): 375–8.
  71. Eakin EG, Reeves MM, Lawler SP, et al. The Logan Healthy Living Program: a cluster randomized trial of a telephone-delivered physical activity and dietary behavior intervention for primary care patients with type 2 diabetes or hypertension from a socially disadvantaged community—rationale, design and recruitment. *Contemp Clin Trials*. 2008;29(3):439–54.
  72. Eddy DM, Schlessinger L, Heikes K. The metabolic syndrome and cardiovascular risk: implications for clinical practice. *Int J Obes (Lond)*. 2008;32(2 suppl):S5–10.
  73. Egede LE, Zheng D. Independent factors associated with major depressive disorder in a national sample of individuals with diabetes. *Diabetes Care*. 2003;26(1):104–11.
  74. Eriksson J, Lindstrom J, Valle T, et al. Prevention of type II diabetes in subjects with impaired glucose tolerance: the Diabetes Prevention Study (DPS) in Finland. Study design and 1-year interim report on the feasibility of the lifestyle intervention programme. *Diabetologia*. 1999;42(7):793–801.
  75. Evans EM, Racette SB, Peterson LR, Villareal DT, Greiwe JS, Holloszy JO. Aerobic power and insulin action improve in response to endurance exercise training in healthy 77–87 yr olds. *J Appl Physiol*. 2005;98(1):40–5.
  76. Ewing DJ, Clarke BF. Diabetic autonomic neuropathy: present insights and future prospects. *Diabetes Care*. 1986;9(6):648–65.
  77. Featherstone JF, Holly RG, Amsterdam EA. Physiologic responses to weight lifting in coronary artery disease. *Am J Cardiol*. 1993;71(4):287–92.
  78. Figueroa A, Baynard T, Fernhall B, Carhart R, Kanaley JA. Endurance training improves post-exercise cardiac autonomic modulation in obese women with and without type 2 diabetes. *Eur J Appl Physiol*. 2007;100(4):437–44.
  79. Fowler-Brown A, Pignone M, Pletcher M, Tice JA, Sutton SF, Lohr KN. Exercise tolerance testing to screen for coronary heart disease: a systematic review for the technical support for the U.S. Preventive Services Task Force. *Ann Intern Med*. 2004;140(7): W9–24.
  80. Fox CS, Pencina MJ, Wilson PW, Paynter NP, Vasan RS, D'Agostino RB Sr. Lifetime risk of cardiovascular disease among individuals with and without diabetes stratified by obesity status in the Framingham heart study. *Diabetes Care*. 2008;31(8):1582–4.
  81. Fredrickson SK, Ferro TJ, Schuttrumpf AC. Disappearance of microalbuminuria in a patient with type 2 diabetes and the metabolic syndrome in the setting of an intense exercise and dietary program with sustained weight reduction. *Diabetes Care*. 2004;27(7):1754–5.
  82. Gaede P, Vedel P, Larsen N, Jensen GV, Parving HH, Pedersen O. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. *N Engl J Med*. 2003;348(5):383–93.
  83. Galbo H, Tobin L, van Loon LJ. Responses to acute exercise in type 2 diabetes, with an emphasis on metabolism and interaction with oral hypoglycemic agents and food intake. *Appl Physiol Nutr Metab*. 2007;32(3):567–75.
  84. Ganda O. Patients on various drug therapies. In: Ruderman N DJ, Schenider SH, Kriska A, editors. *Handbook of Exercise in Diabetes*. Alexandria (VA): American Diabetes Association; 2002. p. 587–99.
  85. Garcia-Roves PM, Han DH, Song Z, Jones TE, Hucker KA, Holloszy JO. Prevention of glycogen supercompensation prolongs the increase in muscle GLUT4 after exercise. *Am J Physiol Endocrinol Metab*. 2003;285(4):E729–36.
  86. Garetto LP, Richter EA, Goodman MN, Ruderman NB. Enhanced muscle glucose metabolism after exercise in the rat: the two phases. *Am J Physiol*. 1984;246(6 Pt 1):E471–5.
  87. Ghanassia E, Brun JF, Fedou C, Raynaud E, Mercier J. Substrate oxidation during exercise: type 2 diabetes is associated with a decrease in lipid oxidation and an earlier shift towards carbohydrate utilization. *Diabetes Metab*. 2006;32(6): 604–10.
  88. Ghilarducci LE, Holly RG, Amsterdam EA. Effects of high resistance training in coronary artery disease. *Am J Cardiol*. 1989; 64(14):866–70.
  89. Ghosh S, Khazaei M, Moien-Afshari F, et al. Moderate exercise attenuates caspase-3 activity, oxidative stress, and inhibits



- progression of diabetic renal disease in *db/db* mice. *Am J Physiol Renal Physiol*. 2009;296(4):F700–8.
90. Gillison FB, Skevington SM, Sato A, Standage M, Evangelidou S. The effects of exercise interventions on quality of life in clinical and healthy populations; a meta-analysis. *Soc Sci Med*. 2009;68(9):1700–10.
  91. Gimeno Orna JA, Boned Juliani B, Lou Arnal LM, Castro Alonso FJ. Microalbuminuria and clinical proteinuria as the main predictive factors of cardiovascular morbidity and mortality in patients with type 2 diabetes [in Spanish]. *Rev Clin Esp*. 2003;203(11):526–31.
  92. Glasgow RE, Nutting PA, King DK, et al. Randomized effectiveness trial of a computer-assisted intervention to improve diabetes care. *Diabetes Care*. 2005;28(1):33–9.
  93. Gleeson-Kreig J. Social support and physical activity in type 2 diabetes: a social-ecologic approach. *Diabetes Educ*. 2008;34(6):1037–44.
  94. Goldsmith JR, Lidtke RH, Shott S. The effects of range-of-motion therapy on the plantar pressures of patients with diabetes mellitus. *J Am Podiatr Med Assoc*. 2002;92(9):483–90.
  95. Goodpaster BH, Katsiaras A, Kelley DE. Enhanced fat oxidation through physical activity is associated with improvements in insulin sensitivity in obesity. *Diabetes*. 2003;52(9):2191–7.
  96. Goodyear LJ, Kahn BB. Exercise, glucose transport, and insulin sensitivity. *Annu Rev Med*. 1998;49:235–61.
  97. Gordon BA, Benson AC, Bird SR, Fraser SF. Resistance training improves metabolic health in type 2 diabetes: a systematic review. *Diabetes Res Clin Pract*. 2009;83(2):157–75.
  98. Gordon LA, Morrison EY, McGrowder DA, et al. Effect of exercise therapy on lipid profile and oxidative stress indicators in patients with type 2 diabetes. *BMC Complement Altern Med*. 2008;8:21.
  99. Gorin AA, Wing RR, Fava JL, et al. Weight loss treatment influences untreated spouses and the home environment: evidence of a ripple effect. *Int J Obes*. 2008;32(11):1678–84.
  100. Goulet ED, Melancon MO, Aubertin-Leheudre M, Dionne IJ. Aerobic training improves insulin sensitivity 72–120 h after the last exercise session in younger but not in older women. *Eur J Appl Physiol*. 2005;95(2–3):146–52.
  101. Goulet ED, Melancon MO, Dionne IJ, Aubertin-Leheudre M. No sustained effect of aerobic or resistance training on insulin sensitivity in nonobese, healthy older women. *J Aging Phys Act*. 2005;13(3):314–26.
  102. Graham C, Lasko-McCarthy P. Exercise options for persons with diabetic complications. *Diabetes Educ*. 1990;16(3):212–20.
  103. Grossman E, Messerli FH, Goldbourt U. High blood pressure and diabetes mellitus: are all antihypertensive drugs created equal? *Arch Intern Med*. 2000;160(16):2447–52.
  104. Hamman RF, Wing RR, Edelstein SL, et al. Effect of weight loss with lifestyle intervention on risk of diabetes. *Diabetes Care*. 2006;29(9):2102–7.
  105. Haskell WL, Lee IM, Pate RR, et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Med Sci Sports Exerc*. 2007;39(8):1423–34.
  106. Healy GN, Dunstan DW, Salmon J, et al. Breaks in sedentary time: beneficial associations with metabolic risk. *Diabetes Care*. 2008;31(4):661–6.
  107. Healy GN, Wijndaele K, Dunstan DW, et al. Objectively measured sedentary time, physical activity, and metabolic risk: the Australian Diabetes, Obesity and Lifestyle Study (AusDiab). *Diabetes Care*. 2008;31(2):369–71.
  108. Helmrich SP, Ragland DR, Leung RW, Paffenbarger RS Jr. Physical activity and reduced occurrence of non-insulin-dependent diabetes mellitus. *N Engl J Med*. 1991;325(3):147–52.
  109. Herriott MT, Colberg SR, Parson HK, Nunnold T, Vinik AI. Effects of 8 weeks of flexibility and resistance training in older adults with type 2 diabetes. *Diabetes Care*. 2004;27(12):2988–9.
  110. Holten MK, Zacho M, Gaster M, Juel C, Wojtaszewski JF, Dela F. Strength training increases insulin-mediated glucose uptake, GLUT4 content, and insulin signaling in skeletal muscle in patients with type 2 diabetes. *Diabetes*. 2004;53(2):294–305.
  111. Houmard JA, Tanner CJ, Slentz CA, Duscha BD, McCartney JS, Kraus WE. Effect of the volume and intensity of exercise training on insulin sensitivity. *J Appl Physiol*. 2004;96(1):101–6.
  112. Howorka K, Pumpura J, Haber P, Koller-Strametz J, Mondrzyk J, Schabmann A. Effects of physical training on heart rate variability in diabetic patients with various degrees of cardiovascular autonomic neuropathy. *Cardiovasc Res*. 1997;34(1):206–14.
  113. Hu FB, Sigal RJ, Rich-Edwards JW, et al. Walking compared with vigorous physical activity and risk of type 2 diabetes in women: a prospective study. *JAMA*. 1999;282(15):1433–9.
  114. Hu FB, Stampfer MJ, Solomon C, et al. Physical activity and risk for cardiovascular events in diabetic women. *Ann Intern Med*. 2001;134(2):96–105.
  115. Ibanez J, Gorostiaga EM, Alonso AM, et al. Lower muscle strength gains in older men with type 2 diabetes after resistance training. *J Diabetes Complications*. 2008;22(2):112–8.
  116. Ibanez J, Izquierdo M, Arguelles I, et al. Twice-weekly progressive resistance training decreases abdominal fat and improves insulin sensitivity in older men with type 2 diabetes. *Diabetes Care*. 2005;28(3):662–7.
  117. Innes KE, Vincent HK. The influence of yoga-based programs on risk profiles in adults with type 2 diabetes mellitus: a systematic review. *Evid Based Complement Alternat Med*. 2007;4(4):469–86.
  118. Ishii T, Yamakita T, Sato T, Tanaka S, Fujii S. Resistance training improves insulin sensitivity in NIDDM subjects without altering maximal oxygen uptake. *Diabetes Care*. 1998;21(8):1353–5.
  119. Ivy JL, Holloszy JO. Persistent increase in glucose uptake by rat skeletal muscle following exercise. *Am J Physiol*. 1981;241(5):C200–3.
  120. Jackson R, Asimakopoulou K, Scammell A. Assessment of the transtheoretical model as used by dietitians in promoting physical activity in people with type 2 diabetes. *J Hum Nutr Diet*. 2007;20(1):27–36.
  121. Jacobs-van der Bruggen MA, Bos G, Bemelmans WJ, Hoogenveen RT, Vijgen SM, Baan CA. Lifestyle interventions are cost-effective in people with different levels of diabetes risk: results from a modeling study. *Diabetes Care*. 2007;30(1):128–34.
  122. Jacobs-van der Bruggen MA, van Baal PH, Hoogenveen RT, et al. Cost-effectiveness of lifestyle modification in diabetes patients. *Diabetes Care*. 2009;32(8):1453–8.
  123. Jakicic JM, Marcus BH, Gallagher KI, Napolitano M, Lang W. Effect of exercise duration and intensity on weight loss in overweight, sedentary women: a randomized trial. *JAMA*. 2003;290(10):1323–30.
  124. Jeffery RW, Wing RR, Sherwood NE, Tate DF. Physical activity and weight loss: does prescribing higher physical activity goals improve outcome? *Am J Clin Nutr*. 2003;78(4):684–9.
  125. Jeon CY, Lokken RP, Hu FB, van Dam RM. Physical activity of moderate intensity and risk of type 2 diabetes: a systematic review. *Diabetes Care*. 2007;30(3):744–52.
  126. Johansen KL. Exercise and chronic kidney disease: current recommendations. *Sports Med*. 2005;35(6):485–99.
  127. John L, Rao PS, Kanagasabapathy AS. Rate of progression of albuminuria in type II diabetes. Five-year prospective study from south India. *Diabetes Care*. 1994;17(8):888–90.
  128. Johnson NA, Sachinwalla T, Walton DW, et al. Aerobic exercise training reduces hepatic and visceral lipids in obese individuals without weight loss. *Hepatology*. 2009;50(4):1105–12.

129. Juutilainen A, Lehto S, Ronnema T, Pyorala K, Laakso M. Retinopathy predicts cardiovascular mortality in type 2 diabetic men and women. *Diabetes Care*. 2007;30(2):292–9.
130. Kadooglou NP, Iliadis F, Angelopoulou N, et al. The anti-inflammatory effects of exercise training in patients with type 2 diabetes mellitus. *Eur J Cardiovasc Prev Rehabil*. 2007;14(6):837–43.
131. Kahn JK, Zola B, Juni JE, Vinik AI. Decreased exercise heart rate and blood pressure response in diabetic subjects with cardiac autonomic neuropathy. *Diabetes Care*. 1986;9(4):389–94.
132. Kang J, Kelley DE, Robertson RJ, et al. Substrate utilization and glucose turnover during exercise of varying intensities in individuals with NIDDM. *Med Sci Sports Exerc*. 1999;31(1):82–9.
133. Kang J, Robertson RJ, Hagberg JM, et al. Effect of exercise intensity on glucose and insulin metabolism in obese individuals and obese NIDDM patients. *Diabetes Care*. 1996;19(4):341–9.
134. Kelley GA, Kelley KA, Tran ZV. Aerobic exercise and resting blood pressure: a meta-analytic review of randomized, controlled trials. *Prev Cardiol*. 2001;4(2):73–80.
135. Kelley GA, Kelley KS. Progressive resistance exercise and resting blood pressure: a meta-analysis of randomized controlled trials. *Hypertension*. 2000;35(3):838–43.
136. Kelley GA, Kelley KS. Effects of aerobic exercise on lipids and lipoproteins in adults with type 2 diabetes: a meta-analysis of randomized-controlled trials. *Public Health*. 2007;121(9):643–55.
137. Kelley GA, Sharpe Kelley K. Aerobic exercise and resting blood pressure in older adults: a meta-analytic review of randomized controlled trials. *J Gerontol A Biol Sci Med Sci*. 2001;56(5):M298–303.
138. Kennedy JW, Hirshman MF, Gervino EV, et al. Acute exercise induces GLUT4 translocation in skeletal muscle of normal human subjects and subjects with type 2 diabetes. *Diabetes*. 1999;48(5):1192–7.
139. Keyserling TC, Samuel-Hodge CD, Ammerman AS, et al. A randomized trial of an intervention to improve self-care behaviors of African-American women with type 2 diabetes: impact on physical activity. *Diabetes Care*. 2002;25(9):1576–83.
140. Kim SH, Lee SJ, Kang ES, et al. Effects of lifestyle modification on metabolic parameters and carotid intima-media thickness in patients with type 2 diabetes mellitus. *Metabolism*. 2006;55(8):1053–9.
141. King DS, Baldus PJ, Sharp RL, Kesl LD, Feltmeyer TL, Riddle MS. Time course for exercise-induced alterations in insulin action and glucose tolerance in middle-aged people. *J Appl Physiol*. 1995;78(1):17–22.
142. Kinmonth AL, Wareham NJ, Hardeman W, et al. Efficacy of a theory-based behavioural intervention to increase physical activity in an at-risk group in primary care (ProActive UK): a randomised trial. *Lancet*. 2008;371(9606):41–8.
143. Kirk A, Barnett J, Leese G, Mutrie N. A randomized trial investigating the 12-month changes in physical activity and health outcomes following a physical activity consultation delivered by a person or in written form in type 2 diabetes: Time2Act. *Diabet Med*. 2009;26(3):293–301.
144. Kirk A, Mutrie N, MacIntyre P, Fisher M. Effects of a 12-month physical activity counselling intervention on glycaemic control and on the status of cardiovascular risk factors in people with type 2 diabetes. *Diabetologia*. 2004;47(5):821–32.
145. Kirk AF, Mutrie N, Macintyre PD, Fisher MB. Promoting and maintaining physical activity in people with type 2 diabetes. *Am J Prev Med*. 2004;27(4):289–96.
146. Kirwan JP, Solomon TP, Wojta DM, Staten MA, Holloszy JO. Effects of 7 days of exercise training on insulin sensitivity and responsiveness in type 2 diabetes mellitus. *Am J Physiol Endocrinol Metab*. 2009;297(1):E151–6.
147. Klein R, Klein BE, Moss SE. Epidemiology of proliferative diabetic retinopathy. *Diabetes Care*. 1992;15(12):1875–91.
148. Klein R, Klein BE, Moss SE. Prevalence of microalbuminuria in older-onset diabetes. *Diabetes Care*. 1993;16(10):1325–30.
149. Knowler WC, Barrett-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med*. 2002;346(6):393–403.
150. Knudtson MD, Klein R, Klein BE. Physical activity and the 15-year cumulative incidence of age-related macular degeneration: the Beaver Dam Eye study. *Br J Ophthalmol*. 2006;90(12):1461–3.
151. Koh KP, Fassett RG, Sharman JE, Coombes JS, Williams AD. Effect of intradialytic versus home-based aerobic exercise training on physical function and vascular parameters in hemodialysis patients: a randomized pilot study. *Am J Kidney Dis*. 2010;55(1):88–99.
152. Koivisto V, DeFronzo R. Exercise in the treatment of type II diabetes. *Acta Endocrinol (Copenh)*. 1984;262(suppl):107–16.
153. Kokkinos P, Myers J, Nylen E, et al. Exercise capacity and all-cause mortality in African American and Caucasian men with type 2 diabetes. *Diabetes Care*. 2009;32(4):623–8.
154. Kosaka K, Noda M, Kuzuya T. Prevention of type 2 diabetes by lifestyle intervention: a Japanese trial in IGT males. *Diabetes Res Clin Pract*. 2005;67(2):152–62.
155. Kothari V, Stevens RJ, Adler AI, et al. UKPDS 60: risk of stroke in type 2 diabetes estimated by the UK Prospective Diabetes Study risk engine. *Stroke*. 2002;33(7):1776–81.
156. Kreisman SH, Halter JB, Vranic M, Marliss EB. Combined infusion of epinephrine and norepinephrine during moderate exercise reproduces the glucoregulatory response of intense exercise. *Diabetes*. 2003;52(6):1347–54.
157. Kwon HR, Han KA, Ku YH, et al. The effects of resistance training on muscle and body fat mass and muscle strength in type 2 diabetic women. *Korean Diabetes J*. 34(2):101–10.
158. Laaksonen DE, Lindstrom J, Lakka TA, et al. Physical activity in the prevention of type 2 diabetes: the Finnish diabetes prevention study. *Diabetes*. 2005;54(1):158–65.
159. Lam P, Dennis SM, Diamond TH, Zwar N. Improving glycaemic and BP control in type 2 diabetes: The effectiveness of tai chi. *Aust Fam Physician*. 2008;37(10):884–7.
160. Larsen JJ, Dela F, Madsbad S, Galbo H. The effect of intense exercise on postprandial glucose homeostasis in type II diabetic patients. *Diabetologia*. 1999;42(11):1282–92.
161. Larsen JJ, Dela F, Madsbad S, Vibe-Petersen J, Galbo H. Interaction of sulfonylureas and exercise on glucose homeostasis in type 2 diabetic patients. *Diabetes Care*. 1999;22(10):1647–54.
162. Lazarevic G, Antic S, Vlahovic P, Djordjevic V, Zvezdanovic L, Stefanovic V. Effects of aerobic exercise on microalbuminuria and enzymuria in type 2 diabetic patients. *Ren Fail*. 2007;29(2):199–205.
163. Lee DC, Sui X, Church TS, Lee IM, Blair SN. Associations of cardiorespiratory fitness and obesity with risks of impaired fasting glucose and type 2 diabetes in men. *Diabetes Care*. 2009;32(2):257–62.
164. Lee IM, Skerrett PJ. Physical activity and all-cause mortality: what is the dose-response relation? *Med Sci Sports Exerc*. 2001;33(6 suppl):S459–71; discussion S93–4.
165. Legato MJ, Gelzer A, Goland R, et al. Gender-specific care of the patient with diabetes: review and recommendations. *Gend Med*. 2006;3(2):131–58.
166. Lemaster JW, Mueller MJ, Reiber GE, Mehr DR, Madsen RW, Conn VS. Effect of weight-bearing activity on foot ulcer incidence in people with diabetic peripheral neuropathy: feet first randomized controlled trial. *Phys Ther*. 2008;88(11):1385–98.
167. Lemaster JW, Reiber GE, Smith DG, Heagerty PJ, Wallace C. Daily weight-bearing activity does not increase the risk of diabetic foot ulcers. *Med Sci Sports Exerc*. 2003;35(7):1093–9.
168. Levine JA, Lanningham-Foster LM, McCrady SK, et al. Interindividual variation in posture allocation: possible role in human obesity. *Science*. 2005;307(5709):584–6.

169. Levine JA, McCrady SK, Lanningham-Foster LM, Kane PH, Foster RC, Manohar CU. The role of free-living daily walking in human weight gain and obesity. *Diabetes*. 2008;57(3):548–54.
170. Li G, Zhang P, Wang J, et al. The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study. *Lancet*. 2008;371(9626):1783–9.
171. Liebreich T, Plotnikoff RC, Courneya KS, Boule N. Diabetes NetPLAY: a physical activity website and linked email counseling randomized intervention for individuals with type 2 diabetes. *Int J Behav Nutr Phys Act*. 2009;6:18.
172. Lind E, Ekkekakis P, Vazou S. The affective impact of exercise intensity that slightly exceeds the preferred level: ‘pain’ for no additional ‘gain’. *J Health Psychol*. 2008;13(4):464–8.
173. Lindstrom J, Ilanne-Parikka P, Peltonen M, et al. Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the Finnish Diabetes Prevention Study. *Lancet*. 2006;368(9548):1673–9.
174. Liu J, Laditka JN, Mayer-Davis EJ, Pate RR. Does physical activity during pregnancy reduce the risk of gestational diabetes among previously inactive women? *Birth*. 2008;35(3):188–95.
175. Loimaala A, Groundstroem K, Rinne M, et al. Effect of long-term endurance and strength training on metabolic control and arterial elasticity in patients with type 2 diabetes mellitus. *Am J Cardiol*. 2009;103(7):972–7.
176. Loimaala A, Huikuri HV, Koobi T, Rinne M, Nenonen A, Vuori I. Exercise training improves baroreflex sensitivity in type 2 diabetes. *Diabetes*. 2003;52(7):1837–42.
177. Low PA, Walsh JC, Huang CY, McLeod JG. The sympathetic nervous system in diabetic neuropathy. A clinical and pathological study. *Brain*. 1975;98(3):341–56.
178. Maiorana A, O’Driscoll G, Goodman C, Taylor R, Green D. Combined aerobic and resistance exercise improves glycemic control and fitness in type 2 diabetes. *Diabetes Res Clin Pract*. 2002;56(2):115–23.
179. Malpass A, Andrews R, Turner KM. Patients with type 2 diabetes experiences of making multiple lifestyle changes: a qualitative study. *Patient Educ Couns*. 2009;74(2):258–63.
180. Mamcarz A, Chmielewski M, Braksator W, et al. Factors influencing cardiac complications in patients with type-2 diabetes mellitus and silent myocardial ischaemia: five-year follow-up [in Polish]. *Pol Arch Med Wewn*. 2004;112(6):1433–43.
181. Manetta J, Brun JF, Perez-Martin A, Callis A, Prefaut C, Mercier J. Fuel oxidation during exercise in middle-aged men: role of training and glucose disposal. *Med Sci Sports Exerc*. 2002;34(3):423–9.
182. Manson JE, Rimm EB, Stampfer MJ, et al. Physical activity and incidence of non-insulin-dependent diabetes mellitus in women. *Lancet*. 1991;338(8770):774–8.
183. Marcus RL, Smith S, Morrell G, et al. Comparison of combined aerobic and high-force eccentric resistance exercise with aerobic exercise only for people with type 2 diabetes mellitus. *Phys Ther*. 2008;88(11):1345–54.
184. Marliss EB, Vranic M. Intense exercise has unique effects on both insulin release and its roles in glucoregulation: implications for diabetes. *Diabetes*. 2002;51(1 suppl):S271–83.
185. McAuley E, Blissmer B. Self-efficacy determinants and consequences of physical activity. *Exerc Sport Sci Rev*. 2000;28(2):85–8.
186. McAuley PA, Myers JN, Abella JP, Tan SY, Froelicher VF. Exercise capacity and body mass as predictors of mortality among male veterans with type 2 diabetes. *Diabetes Care*. 2007;30(6):1539–43.
187. McDermott MM, Ades P, Guralnik JM, et al. Treadmill exercise and resistance training in patients with peripheral arterial disease with and without intermittent claudication: a randomized controlled trial. *JAMA*. 2009;301(2):165–74.
188. McGavock J, Sellers E, Dean H. Physical activity for the prevention and management of youth-onset type 2 diabetes mellitus: focus on cardiovascular complications. *Diab Vasc Dis Res*. 2007;4(4):305–10.
189. McKay HG, King D, Eakin EG, Seeley JR, Glasgow RE. The diabetes network Internet-based physical activity intervention: a randomized pilot study. *Diabetes Care*. 2001;24(8):1328–34.
190. Mier N, Medina AA, Ory MG. Mexican Americans with type 2 diabetes: perspectives on definitions, motivators, and programs of physical activity. *Prev Chronic Dis*. 2007;4(2):A24.
191. Minuk HL, Vranic M, Hanna AK, Albisser AM, Zinman B. Glucoregulatory and metabolic response to exercise in obese non-insulin-dependent diabetes. *Am J Physiol*. 1981;240:E458–64.
192. Morroto EH, Hill JO, Wyatt HR, Ghushchyan V, Sullivan PW. Are health care professionals advising patients with diabetes or at risk for developing diabetes to exercise more? *Diabetes Care*. 2006;29(3):543–8.
193. Morroto EH, Hill JO, Wyatt HR, Ghushchyan V, Sullivan PW. Physical activity in U.S. adults with diabetes and at risk for developing diabetes, 2003. *Diabetes Care*. 2007;30(2):203–9.
194. Morrison S, Colberg SR, Mariano M, Parson HK, Vinik AI. Balance training reduces falls risk in older individuals with type 2 diabetes. *Diabetes Care*. 2003;26(4):748–50.
195. Mourad JJ, Le Jeune S. Blood pressure control, risk factors and cardiovascular prognosis in patients with diabetes: 30 years of progress. *J Hypertens Suppl*. 2008;26(3):S7–13.
196. Mourier A, Gautier JF, De Kerviler E, et al. Mobilization of visceral adipose tissue related to the improvement in insulin sensitivity in response to physical training in NIDDM. Effects of branched-chain amino acid supplements. *Diabetes Care*. 1997;20(3):385–91.
197. Muller-Riemenschneider F, Reinhold T, Nocon M, Willich SN. Long-term effectiveness of interventions promoting physical activity: a systematic review. *Prev Med*. 2008;47(4):354–68.
198. Musi N, Fujii N, Hirshman MF, et al. AMP-activated protein kinase (AMPK) is activated in muscle of subjects with type 2 diabetes during exercise. *Diabetes*. 2001;50(5):921–7.
199. Narayan KM, Boyle JP, Geiss LS, Saaddine JB, Thompson TJ. Impact of recent increase in incidence on future diabetes burden: U.S., 2005–2050. *Diabetes Care*. 2006;29(9):2114–6.
200. Narayan KM, Boyle JP, Thompson TJ, Sorensen SW, Williamson DF. Lifetime risk for diabetes mellitus in the United States. *JAMA*. 2003;290(14):1884–90.
201. National High Blood Pressure Education Program Working Group. National High Blood Pressure Education Program Working Group report on hypertension in diabetes. *Hypertension*. 1994;23(2):145–58; discussion 59–60.
202. Nelson ME, Rejeski WJ, Blair SN, et al. Physical activity and public health in older adults: recommendation from the American College of Sports Medicine and the American Heart Association. *Med Sci Sports Exerc*. 2007;39(8):1435–45.
203. Nichols GA, Koro CE. Does statin therapy initiation increase the risk for myopathy? An observational study of 32,225 diabetic and nondiabetic patients. *Clin Ther*. 2007;29(8):1761–70.
204. O’Gorman DJ, Karlsson HK, McQuaid S, et al. Exercise training increases insulin-stimulated glucose disposal and GLUT4 (SLC2A4) protein content in patients with type 2 diabetes. *Diabetologia*. 2006;49(12):2983–92.
205. Ogilvie D, Foster CE, Rothnie H, et al. Interventions to promote walking: systematic review [see comment]. *BMJ*. 2007;334(7605):1204.
206. Oken E, Ning Y, Rifas-Shiman SL, Radesky JS, Rich-Edwards JW, Gillman MW. Associations of physical activity and inactivity before and during pregnancy with glucose tolerance. *Obstet Gynecol*. 2006;108(5):1200–7.
207. Paffenbarger RS Jr, Hyde RT, Wing AL, Lee IM, Jung DL, Kampert JB. The association of changes in physical-activity level



- and other lifestyle characteristics with mortality among men. *N Engl J Med*. 1993;328(8):538–45.
208. Pagkalos M, Koutlianos N, Kouidi E, Pagkalos E, Mandroukas K, Deligiannis A. Heart rate variability modifications following exercise training in type 2 diabetic patients with definite cardiac autonomic neuropathy. *Br J Sports Med*. 2008;42(1):47–54.
  209. Painter P, Carlson L, Carey S, Paul SM, Myll J. Low-functioning hemodialysis patients improve with exercise training. *Am J Kidney Dis*. 2000;36(3):600–8.
  210. Painter P, Carlson L, Carey S, Paul SM, Myll J. Physical functioning and health-related quality-of-life changes with exercise training in hemodialysis patients. *Am J Kidney Dis*. 2000;35(3):482–92.
  211. Pan XR, Li GW, Hu YH, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. *Diabetes Care*. 1997;20(4):537–44.
  212. Pavlou KN, Krey S, Steffee WP. Exercise as an adjunct to weight loss and maintenance in moderately obese subjects. *Am J Clin Nutr*. 1989;49(5 suppl):1115–23.
  213. Peek ME, Tang H, Alexander GC, Chin MH. National prevalence of lifestyle counseling or referral among African-Americans and whites with diabetes. *J Gen Intern Med*. 2008;23(11):1858–64.
  214. Pena KE, Stopka CB, Barak S, Gertner HR Jr, Carmeli E. Effects of low-intensity exercise on patients with peripheral artery disease. *Phys Sportsmed*. 2009;37(1):106–10.
  215. Penn L, Moffatt SM, White M. Participants' perspective on maintaining behaviour change: a qualitative study within the European Diabetes Prevention Study. *BMC Public Health*. 2008;8:235.
  216. Pham H, Armstrong DG, Harvey C, Harkless LB, Giurini JM, Veves A. Screening techniques to identify people at high risk for diabetic foot ulceration: a prospective multicenter trial. *Diabetes Care*. 2000;23(5):606–11.
  217. Physical Activity Guidelines Advisory Committee. *Physical Activity Guidelines Advisory Committee Report*. 2008. Washington (DC); US Department of Health and Human Services; 2008. 683 p.
  218. Pi-Sunyer X, Blackburn G, Brancati FL, et al. Reduction in weight and cardiovascular disease risk factors in individuals with type 2 diabetes: one-year results of the look AHEAD trial. *Diabetes Care*. 2007;30(6):1374–83.
  219. Plockinger U, Topuz M, Riese B, Reuter T. Risk of exercise-induced hypoglycaemia in patients with type 2 diabetes on intensive insulin therapy: comparison of insulin glargine with NPH insulin as basal insulin supplement. *Diabetes Res Clin Pract*. 2008;81(3):290–5.
  220. Ploug T, Galbo H, Richter EA. Increased muscle glucose uptake during contractions: no need for insulin. *Am J Physiol*. 1984;247(6 Pt 1):E726–31.
  221. Poirier P, Mawhinney S, Grondin L, et al. Prior meal enhances the plasma glucose lowering effect of exercise in type 2 diabetes. *Med Sci Sports Exerc*. 2001;33(8):1259–64.
  222. Practice ACO. ACOG Committee opinion. Number 267, January 2002: exercise during pregnancy and the postpartum period. *Obstet Gynecol*. 2002;99(1):171–3.
  223. Pruchnic R, Katsiaras A, He J, Kelley DE, Winters C, Goodpaster BH. Exercise training increases intramyocellular lipid and oxidative capacity in older adults. *Am J Physiol Endocrinol Metab*. 2004;287(5):E857–62.
  224. Ramachandran A, Snehalatha C, Mary S, et al. The Indian Diabetes Prevention Programme shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1). *Diabetologia*. 2006;49(2):289–97.
  225. Rhodes RE, Warburton DE, Murray H. Characteristics of physical activity guidelines and their effect on adherence: a review of randomized trials. *Sports Med*. 2009;39(5):355–75.
  226. Richter EA, Garetto LP, Goodman MN, Ruderman NB. Muscle glucose metabolism following exercise in the rat: increased sensitivity to insulin. *J Clin Invest*. 1982;69(4):785–93.
  227. Richter EA, Ploug T, Galbo H. Increased muscle glucose uptake after exercise. No need for insulin during exercise. *Diabetes*. 1985;34(10):1041–8.
  228. Rimbert V, Boirie Y, Bedu M, Hocquette JF, Ritz P, Morio B. Muscle fat oxidative capacity is not impaired by age but by physical inactivity: association with insulin sensitivity. *FASEB J*. 2004;18(6):737–9.
  229. Ronnema T, Marniemi J, Puukka P, Kuusi T. Effects of long-term physical exercise on serum lipids, lipoproteins and lipid metabolizing enzymes in type 2 (non-insulin-dependent) diabetic patients. *Diabetes Res*. 1988;7(2):79–84.
  230. Rosenstock J, Hassman DR, Maddar RD, et al. Repaglinide versus nateglinide monotherapy: a randomized, multicenter study. *Diabetes Care*. 2004;27(6):1265–70.
  231. Ross R, Dagnone D, Jones PJ, et al. Reduction in obesity and related comorbid conditions after diet-induced weight loss or exercise-induced weight loss in men. A randomized, controlled trial. *Ann Intern Med*. 2000;133(2):92–103.
  232. Ross R, Janssen I, Dawson J, et al. Exercise-induced reduction in obesity and insulin resistance in women: a randomized controlled trial. *Obes Res*. 2004;12(5):789–98.
  233. Sacco WP, Malone JJ, Morrison AD, Friedman A, Wells K. Effect of a brief, regular telephone intervention by paraprofessionals for type 2 diabetes. *J Behav Med*. 2009;32(4):349–59.
  234. Saris WH, Blair SN, van Baak MA, et al. How much physical activity is enough to prevent unhealthy weight gain? Outcome of the IASO 1st Stock Conference and consensus statement. *Obes Rev*. 2003;4(2):101–14.
  235. Schoeller DA, Shay K, Kushner RF. How much physical activity is needed to minimize weight gain in previously obese women? *Am J Clin Nutr*. 1997;66(3):551–6.
  236. Sharples L, Hughes V, Crean A, et al. Cost-effectiveness of functional cardiac testing in the diagnosis and management of coronary artery disease: a randomised controlled trial. The CECaT trial. *Health Technol Assess*. 2007;11(49):iii–iv, ix–115.
  237. Shrier I. Stretching before exercise does not reduce the risk of local muscle injury: a critical review of the clinical and basic science literature. *Clin J Sport Med*. 1999;9(4):221–7.
  238. Sigal RJ, Kenny GP, Boulé NG, et al. Effects of aerobic training, resistance training, or both on glycemic control in type 2 diabetes: a randomized trial. *Ann Intern Med*. 2007;147:357–69.
  239. Sigal RJ, Kenny GP, Wasserman DH, Castaneda-Sceppa C. Physical activity/exercise and type 2 diabetes. *Diabetes Care*. 2004;27(10):2518–39.
  240. Sigal RJ, Kenny GP, Wasserman DH, Castaneda-Sceppa C, White RD. Physical activity/exercise and type 2 diabetes: a consensus statement from the American Diabetes Association. *Diabetes Care*. 2006;29(6):1433–8.
  241. Sigal RJ, Purdon C, Bilinski D, Vranic M, Halter JB, Marliss EB. Glucoregulation during and after intense exercise: effects of beta-blockade. *J Clin Endocrinol Metab*. 1994;78(2):359–66.
  242. Singleton JR, Smith AG, Russell JW, Feldman EL. Microvascular complications of impaired glucose tolerance. *Diabetes*. 2003;52(12):2867–73.
  243. Sjosten N, Kivela SL. The effects of physical exercise on depressive symptoms among the aged: a systematic review. *Int J Geriatr Psychiatry*. 2006;21(5):410–8.
  244. Smith AG, Singleton JR. Impaired glucose tolerance and neuropathy. *Neurologist*. 2008;14(1):23–9.
  245. Smith SC Jr, Allen J, Blair SN, et al. AHA/ACC guidelines for secondary prevention for patients with coronary and other atherosclerotic vascular disease: 2006 update: endorsed by the National Heart, Lung, and Blood Institute. *Circulation*. 2006;113(19):2363–72.



246. Snowling NJ, Hopkins WG. Effects of different modes of exercise training on glucose control and risk factors for complications in type 2 diabetic patients: a meta-analysis. *Diabetes Care*. 2006; 29(11):2518–27.
247. Stellingwerff T, Boon H, Gijzen AP, Stegen JH, Kuipers H, van Loon LJ. Carbohydrate supplementation during prolonged cycling exercise spares muscle glycogen but does not affect intramyocellular lipid use. *Pflugers Arch*. 2007;454(4): 635–47.
248. Stevens RJ, Kothari V, Adler AI, Stratton IM. The UKPDS risk engine: a model for the risk of coronary heart disease in Type II diabetes (UKPDS 56). *Clin Sci (Lond)*. 2001;101(6):671–9.
249. Stewart KJ. Role of exercise training on cardiovascular disease in persons who have type 2 diabetes and hypertension. *Cardiol Clin*. 2004;22(4):569–86.
250. Suh SH, Paik IY, Jacobs K. Regulation of blood glucose homeostasis during prolonged exercise. *Mol Cells*. 2007;23(3):272–9.
251. Sui X, Hooker SP, Lee IM, et al. A prospective study of cardiorespiratory fitness and risk of type 2 diabetes in women. *Diabetes Care*. 2008;31(3):550–5.
252. Szewieczek J, Dulawa J, Strzalkowska D, Batko-Szwaczka A, Hornik B. Normal insulin response to short-term intense exercise is abolished in type 2 diabetic patients treated with gliclazide. *J Diabetes Complications*. 2009;23(6):380–6.
253. Szewieczek J, Dulawa J, Strzalkowska D, Hornik B, Kawecki G. Impact of the short-term, intense exercise on postprandial glycemia in type 2 diabetic patients treated with gliclazide. *J Diabetes Complications*. 2007;21(2):101–7.
254. The Today Study Group, Zeitler P, Epstein L, et al. Treatment options for type 2 diabetes in adolescents and youth: a study of the comparative efficacy of metformin alone or in combination with rosiglitazone or lifestyle intervention in adolescents with type 2 diabetes. *Pediatr Diabetes*. 2007;8(2):74–87.
255. Thomas DE, Elliott EJ, Naughton GA. Exercise for type 2 diabetes mellitus. *Cochrane Database Syst Rev*. 2006;3:CD002968.
256. Tomas E, Sevilla L, Palacin M, Zorzano A. The insulin-sensitive GLUT4 storage compartment is a postendocytic and heterogeneous population recruited by acute exercise. *Biochem Biophys Res Commun*. 2001;284(2):490–5.
257. Tsang T, Orr R, Lam P, Comino E, Singh MF. Effects of tai chi on glucose homeostasis and insulin sensitivity in older adults with type 2 diabetes: a randomised double-blind sham-exercise-controlled trial. *Age Ageing*. 2008;37(1):64–71.
258. Tudor-Locke C, Bell RC, Myers AM, et al. Controlled outcome evaluation of the First Step Program: a daily physical activity intervention for individuals with type II diabetes. *Int J Obes Relat Metab Disord*. 2004;28(1):113–9.
259. Tufescu A, Kanazawa M, Ishida A, et al. Combination of exercise and losartan enhances renoprotective and peripheral effects in spontaneously type 2 diabetes mellitus rats with nephropathy. *J Hypertens*. 2008;26(2):312–21.
260. Tuomilehto J, Lindstrom J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med*. 2001;344(18): 1343–50.
261. US Department of Health and Human Services Centers for Disease Control and Prevention. *National Diabetes Fact Sheet: General Information and National Estimates on Diabetes in the United States, 2007*. Atlanta (GA): US Department of Health and Human Services Centers for Disease Control and Prevention; 2008.
262. US Preventive Services Task Force. Screening for coronary heart disease: recommendation statement. *Ann Intern Med*. 2004; 140(7):569–72.
263. Vincent KR, Braith RW, Feldman RA, et al. Resistance exercise and physical performance in adults aged 60 to 83. *J Am Geriatr Soc*. 2002;50(6):1100–7.
264. Vinik AI. Neuropathy. In: *The Health Professional's Guide to Diabetes and Exercise*. Alexandria (VA): American Diabetes Association; 1995. p. 183–97.
265. Vinik AI, Ziegler D. Diabetic cardiovascular autonomic neuropathy. *Circulation*. 2007;115(3):387–97.
266. Wadden TA, West DS, Delahanty L, et al. The Look AHEAD study: a description of the lifestyle intervention and the evidence supporting it. *Obesity*. 2006;14(5):737–52.
267. Wagner H, Degerblad M, Thorell A, et al. Combined treatment with exercise training and acarbose improves metabolic control and cardiovascular risk factor profile in subjects with mild type 2 diabetes. *Diabetes Care*. 2006;29(7):1471–7.
268. Wahren J, Ekberg K. Splanchnic regulation of glucose production. *Annu Rev Nutr*. 2007;27:329–45.
269. Wang JH. Effects of tai chi exercise on patients with type 2 diabetes. *Med Sport Sci*. 2008;52:230–8.
270. Wang Y, Simar D, Fiatarone Singh MA. Adaptations to exercise training within skeletal muscle in adults with type 2 diabetes or impaired glucose tolerance: a systematic review. *Diabetes Metab Res Rev*. 2009;25(1):13–40.
271. Watt MJ, Heigenhauser GJ, Dyck DJ, Spriet LL. Intramuscular triacylglycerol, glycogen and acetyl group metabolism during 4 h of moderate exercise in man. *J Physiol*. 2002;541(Pt 3):969–78.
272. Wei M, Gibbons LW, Kampert JB, Nichaman MZ, Blair SN. Low cardiorespiratory fitness and physical inactivity as predictors of mortality in men with type 2 diabetes. *Ann Intern Med*. 2000; 132(8):605–11.
273. Wei M, Gibbons LW, Mitchell TL, Kampert JB, Lee CD, Blair SN. The association between cardiorespiratory fitness and impaired fasting glucose and type 2 diabetes mellitus in men. *Ann Intern Med*. 1999;130(2):89–96.
274. Weinsier RL, Hunter GR, Desmond RA, Byrne NM, Zuckerman PA, Darnell BE. Free-living activity energy expenditure in women successful and unsuccessful at maintaining a normal body weight. *Am J Clin Nutr*. 2002;75(3):499–504.
275. Wenger NK, Froelicher ES, Smith LK, et al. Cardiac rehabilitation as secondary prevention. Agency for Health Care Policy and Research and National Heart, Lung, and Blood Institute. *Clin Pract Guidel Quick Ref Guide Clin*. 1995;17:1–23.
276. Willey KA, Singh MA. Battling insulin resistance in elderly obese people with type 2 diabetes: bring on the heavy weights. *Diabetes Care*. 2003;26(5):1580–8.
277. Williams DM. Exercise, affect, and adherence: an integrated model and a case for self-paced exercise. *J Sport Exerc Psychol*. 2008;30(5):471–96.
278. Williams DM, Dunsiger S, Ciccolo JT, Lewis BA, Albrecht AE, Marcus BH. Acute affective response to a moderate-intensity exercise stimulus predicts physical activity participation 6 and 12 months later. *Psychol Sport Exerc*. 2008;9(3):231–45.
279. Williams K, Prevost AT, Griffin S, et al. The ProActive trial protocol—a randomised controlled trial of the efficacy of a family-based, domiciliary intervention programme to increase physical activity among individuals at high risk of diabetes [ISRCTN61323766]. *BMC Public Health*. 2004;4:48.
280. Williamson DA, Rejeski J, Lang W, et al. Impact of a weight management program on health-related quality of life in overweight adults with type 2 diabetes. *Arch Intern Med*. 2009; 169(2):163–71.
281. Wing RR. Exercise and weight control. In: Ruderman N, Devlin JT, Schneider SH, Kriska A, editors. *Handbook of Exercise in Diabetes*. Alexandria (VA): American Diabetes Association; 2002. p. 355–64.
282. Winnick JJ, Sherman WM, Habash DL, et al. Short-term aerobic exercise training in obese humans with type 2 diabetes mellitus improves whole-body insulin sensitivity through gains in peripheral, not hepatic insulin sensitivity. *J Clin Endocrinol Metab*. 2008;93(3):771–8.

283. Wycherley TP, Brinkworth GD, Noakes M, Buckley JD, Clifton PM. Effect of caloric restriction with and without exercise training on oxidative stress and endothelial function in obese subjects with type 2 diabetes. *Diabetes Obes Metab*. 2008;10(11):1062–73.
284. Yates T, Davies M, Gorely T, Bull F, Khunti K. Rationale, design and baseline data from the Pre-diabetes Risk Education and Physical Activity Recommendation and Encouragement (PRE-PARE) programme study: a randomized controlled trial. *Patient Educ Couns*. 2008;73(2):264–71.
285. Yates T, Khunti K, Bull F, Gorely T, Davies MJ. The role of physical activity in the management of impaired glucose tolerance: a systematic review. *Diabetologia*. 2007;50(6):1116–26.
286. Yeh SH, Chuang H, Lin LW, Hsiao CY, Wang PW, Yang KD. Tai chi chuan exercise decreases A<sub>1c</sub> levels along with increase of regulatory T-cells and decrease of cytotoxic T-cell population in type 2 diabetic patients. *Diabetes Care*. 2007;30(3):716–8.
287. Yeung EW, Yeung SS. Interventions for preventing lower limb soft-tissue injuries in runners. *Cochrane Database Syst Rev*. 2001;3:CD001256.
288. Young LH, Wackers FJ, Chyun DA, et al. Cardiac outcomes after screening for asymptomatic coronary artery disease in patients with type 2 diabetes: the DIAD study: a randomized controlled trial. *JAMA*. 2009;301(15):1547–55.
289. Zee RY, Romero JR, Gould JL, Ricupero DA, Ridker PM. Polymorphisms in the advanced glycosylation end product-specific receptor gene and risk of incident myocardial infarction or ischemic stroke. *Stroke*. 2006;37(7):1686–90.
290. Zhang C, Solomon CG, Manson JE, Hu FB. A prospective study of pregravid physical activity and sedentary behaviors in relation to the risk for gestational diabetes mellitus. *Arch Intern Med*. 2006;166(5):543–8.
291. Zhang Y, Fu FH. Effects of 14-week tai ji quan exercise on metabolic control in women with type 2 diabetes. *Am J Chin Med*. 2008;36(4):647–54.
292. Ziegler D, Gries FA, Spuler M, Lessmann F. The epidemiology of diabetic neuropathy. Diabetic Cardiovascular Autonomic Neuropathy Multicenter Study Group. *J Diabetes Complications*. 1992;6(1):49–57.
293. Zierath JR, He L, Guma A, Odegaard Wahlstrom E, Klip A, Wallberg-Henriksson H. Insulin action on glucose transport and plasma membrane GLUT4 content in skeletal muscle from patients with NIDDM. *Diabetologia*. 1996;39(10):1180–9.
294. Zoppini G, Targher G, Zamboni C, et al. Effects of moderate-intensity exercise training on plasma biomarkers of inflammation and endothelial dysfunction in older patients with type 2 diabetes. *Nutr Metab Cardiovasc Dis*. 2006;16(8):543–9.
295. Zwierska I, Walker RD, Choksy SA, Male JS, Pockley AG, Saxton JM. Upper- vs lower-limb aerobic exercise rehabilitation in patients with symptomatic peripheral arterial disease: a randomized controlled trial. *J Vasc Surg*. 2005;42(6):1122–30.