

In Brief

This is an abridged reprint of a technical review on exercise and type 2 diabetes, which was originally published in the journal *Diabetes Care* in October 2004. Full text of this article, as well as its accompanying references, is available on the American Diabetes Association website at <http://care.diabetesjournals.org/cgi/content/full/27/10/2518>. Reprinted with permission from *Diabetes Care* 27:2518–2539, 2004.

Physical Activity/Exercise and Type 2 Diabetes

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For decades, exercise has been considered a cornerstone of diabetes management, along with diet and medication. However, high-quality evidence on the importance of exercise and fitness in diabetes was lacking until recent years. The last American Diabetes Association (ADA) technical review of exercise and type 2 diabetes (formerly known as non-insulin dependent diabetes) was published in 1990. The present work emphasizes the advances that have occurred since the last technical review was published.

Major developments since the 1990 technical review include:

- Advances in basic science, increasing our understanding of the effects of exercise on glucoregulation.
- Large clinical trials demonstrating that lifestyle interventions (diet and exercise) reduce incidence of type 2 diabetes in people with impaired glucose tolerance (IGT).
- Meta-analyses of structured exercise interventions in type 2 diabetes showing: 1) effectiveness of exercise in reducing HbA_{1c}, independent of body weight; and 2) association between exercise training intensity and change in HbA_{1c}.

- Large cohort studies showing that low aerobic fitness and low physical activity level predict increased risk of overall and cardiovascular disease (CVD) mortality in people with diabetes.
- Clinical trials showing effectiveness of resistance training (such as weight lifting) for improving glycemic control in type 2 diabetes.
- New data on safety of resistance training in populations at high risk for CVD.

Based on this new evidence, we have refined the recommendations on the desired types, amounts, and intensities of aerobic physical activity for people with diabetes. Resistance training will now be recommended in a broader group of patients and at a broader range of intensity than done previously. There are other areas in which new evidence is lacking, but we feel that previous recommendations may have been more conservative than necessary. These areas include indications for exercise stress test before beginning an exercise program and precautions regarding exercise in the presence of some specific complications or suboptimal metabolic control. The levels of evidence used are defined by the ADA (See Ref.1).

A new *Handbook of Exercise* was published in 2002 by the ADA, including 40 articles by leading experts on specific topics related to exercise and diabetes. Space limitations do not allow the present work to be comprehensive, and where appropriate we refer the reader to chapters in the *Handbook of Exercise* and other review articles for additional details. The present review focuses on type 2 diabetes. Issues primarily germane to type 1 diabetes will be covered in a subsequent technical review.

Definitions

The following definitions are based on those outlined in "Physical Activity and Health," the 1996 report of the Surgeon General.²

Physical activity. Bodily movement produced by the contraction of skeletal muscle that requires energy expenditure in excess of resting energy expenditure.

Exercise. A subset of physical activity: planned, structured, and repetitive bodily movement performed to improve or maintain one or more components of physical fitness. In the present review, the terms "physical activity" and "exercise" will be used interchangeably.

Physical fitness. This includes cardiorespiratory fitness, muscular fitness, and flexibility.

Cardiorespiratory fitness (also known as cardiorespiratory endurance or aerobic fitness). The ability of the circulatory and respiratory systems to supply oxygen during sustained physical activity. The gold standard for measurement of cardiorespiratory fitness is a test of maximal oxygen uptake ($\dot{V}O_{2max}$), typically performed using indirect calorimetry on a treadmill or bicycle ergometer. Cardiorespiratory fitness can be estimated accurately using graded maximal exercise testing on standard treadmill or bicycle ergometer protocols without indirect calorimetry.³

Aerobic exercise. This consists of rhythmic, repeated, and continuous movements of the same large muscle groups for at least 10 min at a time. Examples include walking, bicycling, jogging, continuous swimming, water aerobics, and many sports. When performed at sufficient intensity and fre-

quency, this type of exercise increases cardiorespiratory fitness.

Intensity of aerobic exercise. This will be described as "moderate" when it is at 40–60% of $\dot{V}O_{2max}$ (~50–70% of maximum heart rate) and "vigorous" when it is at > 0% of $\dot{V}O_{2max}$ (> 70% of maximum heart rate).

Muscular fitness. This refers to strength (the amount of force a muscle can exert) and muscular endurance (the ability of the muscle to continue to perform without fatigue).

Resistance exercise. Activities that use muscular strength to move a weight or work against a resistive load. Examples include weight lifting and exercises using weight machines. When performed with regularity and moderate to high intensity, resistance exercise increases muscular fitness.

Intensity of resistance exercise. This will be described as "high" if the resistance is $\geq 75\%$ of the maximum that can be lifted a single time ($\geq 75\%$ of 1-RM [repetition maximum]) and "moderate" if resistance is 50–74% of 1-RM.

Flexibility. This term refers to the range of motion available at joints.

Flexibility exercise. This is exercise (typically stretching) aimed at increasing or maintaining range of motion at joints.

MET (metabolic equivalent). A MET is a unit of intensity equal to energy expenditure at rest. Physical activity at 3 METs uses three times as much energy as stationary sitting. MET-hours are units of exercise volume, in which intensity in METs is multiplied by duration of the activity in hours.

PHYSIOLOGY OF FUEL METABOLISM DURING EXERCISE

Carbohydrate ingestion and exercise
Glucose feeding has been shown⁷ to improve exercise endurance. The underlying mechanism for this improvement is probably related to increased glucose availability to working muscle. The amount, form, and timing of an oral carbohydrate load, along with the duration and intensity of exercise, will determine how effective glucose ingestion is at sustaining

glucose availability to the working muscle.

Carbohydrate ingestion slows the mobilization of endogenous fuels during prolonged exercise. It also slows the rate of fall of circulating glucose that would otherwise occur or leads to an overt increase in circulating glucose.⁷ At least two important endocrine changes accompany the increase in glucose availability. The exercise-induced fall in insulin and rise in glucagon are attenuated or eliminated altogether. The absence of the fall in insulin attenuates the increases in lipolysis and EGP, whereas a reduction in glucagon will reduce the latter.⁷ Although insulin acts to suppress glycogen breakdown, multiple signals are present in working muscle, and glycogen is generally not spared by carbohydrate ingestion.⁵⁹

The metabolic availability of ingested carbohydrate depends on the composition and quantity of the substrate load. In addition, exercise parameters (i.e., work intensity, duration, and modality) also determine the availability of ingested glucose. As a consequence, it is difficult to ascribe an exact metabolic efficiency of ingested glucose. In any case, a reasonable estimate might be that ~40% of a 50-g glucose load, ingested at the start of moderate exercise, is metabolized during the first hour.⁶⁰ There is probably little difficulty in delivering adequate amounts of ingested glucose to the muscle during light exercise. Because glucose oxidation by muscle increases at higher work rates, it may no longer be possible to absorb adequate amounts of ingested glucose. As a consequence, limitations to the oxidation of ingested glucose may shift at different work intensities: low muscle demand limits glucose oxidation at light work rates, whereas absorption from the gastrointestinal tract limits it at high work rates.⁶¹ In humans, the maximum absorption rate of carbohydrate in the gut during exercise is about 1 g/min.⁶²

EVALUATION OF THE DIABETIC PATIENT BEFORE RECOMMENDING AN EXERCISE PROGRAM

For a more detailed review on this subject, see Ref. 92.

Before beginning a program of physical activity more vigorous than brisk walking, people with diabetes should be assessed for conditions that might contraindicate certain types of

exercise or predispose to injury (e.g., severe autonomic neuropathy, severe peripheral neuropathy, or preproliferative or proliferative retinopathy), which require treatment before beginning vigorous exercise, or that may be associated with increased likelihood of CVD. The patient's age and previous physical activity level should be considered.

One potential area of controversy is the circumstances under which a graded exercise electrocardiogram (ECG) stress test should be considered medically indicated. We unfortunately did not find any randomized trials or large cohort studies evaluating the utility of exercise stress testing specifically in people with diabetes; the lack of such studies is an important gap in the literature. Previous ADA guidelines⁹³ have suggested that before beginning a vigorous or moderate exercise program, an exercise ECG stress test should be done in all diabetic individuals aged > 35 years and in all individuals aged > 25 years in the presence of even one additional CVD risk factor (diabetes duration > 10 years for type 2 diabetes or > 15 years for type 1 diabetes, hypertension, dyslipidemia, smoking, proliferative retinopathy, nephropathy including microalbuminuria, peripheral vascular disease, or autonomic neuropathy). If this previous recommendation were followed strictly, the great majority of people with diabetes, including a large number of younger individuals with very low absolute risk of CVD, would require formal exercise stress testing before beginning even a moderate-intensity exercise program. The costs of such widespread stress testing might be prohibitive.⁹² The prevalence of both symptomatic and asymptomatic coronary artery disease (CAD) is higher in both type 1 and type 2 diabetic individuals compared with nondiabetic individuals of the same age-group. However, many younger diabetic patients have relatively low absolute risk for a coronary event. For example, a 38-year-old Caucasian nonsmoking man with diabetes for 5 years, HbA_{1c} 7.5%, systolic blood pressure 130 mmHg, total cholesterol 5.2 mmol/l, and HDL cholesterol 1.1 mmol/l would have a 10-year CAD risk of only 7.3% or ~0.7% per year, calculated using the U.K. Prospective Diabetes Study (UKPDS) Risk Engine⁹⁴ (<http://www.dtu.ox.ac.uk>). The lower the absolute CAD risk, the higher the likelihood of a false-positive

test. A recent systematic review for the U.S. Preventive Services Task Force came to the conclusion that stress tests should usually not be recommended to detect ischemia in asymptomatic individuals at low CAD risk (< 10% risk of a cardiac event over 10 years) because the risks of subsequent invasive testing triggered by false-positive tests outweighed the expected benefits from the detection of previously unsuspected ischemia.^{95,96}

There is, however, some value to performing a maximal aerobic exercise test in a broader range of individuals. In addition to screening for exercise-induced ischemia, a maximal exercise test can provide useful information regarding maximal heart rate, and blood pressure responses to different exercise levels, initial performance status, and prognosis, and therefore is potentially of some benefit to any individual, diabetic or otherwise. Without a maximal exercise test, one cannot know a given individual's maximum heart rate or the heart rate associated with a given percentage of the maximum. Use of the Borg scale (Rating of Perceived Exertion,⁹⁷ with target perceived intensities of "moderate," "somewhat hard," or "hard") is sometimes recommended as a possible alternative to heart-rate-based targets based on maximal exercise testing. A large long-term cohort study found that exercising habitually at perceived intensity of "moderate," "somewhat strong," "strong," or more intense than "strong" were associated with adjusted relative risks for coronary heart disease of 0.86, 0.69, and 0.72, respectively, compared with exercising at perceived intensity of "weak" or less intense.⁹⁸ However, there is a great deal of variability among individuals in terms of the perceived exertion associated with performing the same exercise at the same objectively defined exercise intensities.⁹⁹ Likewise, the same individuals often have different ratings of perceived exertion when performing different exercises at the same intensities (e.g., running or bicycling at the same percentage of heart rate reserve) and even at equivalent stages of different treadmill protocols (Bruce versus Balke).¹⁰⁰

Therefore, available clinical evidence does not support any specific definitive recommendations regarding which individuals should undergo stress testing. Potential benefits must be weighed against risks and costs.

Our recommendations should be considered in this context.

A stress test is most useful in terms of positive predictive value for coronary ischemia when the probability of CAD is at least moderate. When the probability of CAD is low (e.g., < 10% over 10 years), the number of false-positive tests is likely to be substantially greater than the number of true-positive tests.

Therefore, we propose the following revised criteria for deciding when a stress test is indicated for detection of ischemia. These criteria would encompass virtually all people with diabetes with a 10-year CAD risk of at least 10% (1% per year).

Recommendations: indications for graded exercise test with ECG monitoring

In the absence of contraindications,^{101,102} maximal exercise testing could be considered in all diabetic individuals in order to assess maximal heart rate, set exercise intensity targets, and assess functional capacity and prognosis. A graded exercise test with ECG monitoring should be seriously considered before undertaking aerobic physical activity with an intensity exceeding the demands of everyday living (more intense than brisk walking) in previously sedentary diabetic individuals whose 10-year risk of a coronary event is $\geq 10\%$. This risk could be estimated directly using the UKPDS Risk Engine (<http://www.dtu.ox.ac.uk>)⁹⁴ and would correspond approximately to meeting any of the following criteria:

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

The above should not be construed as a recommendation against stress testing for individuals without the above risk factors or for those who are planning less-intense exercise.
Level of evidence: E.

AEROBIC FITNESS AND AEROBIC EXERCISE IN TYPE 2 DIABETES

Effects of structured exercise interventions on glycemic control and body weight in type 2 diabetes

For details of the individual aerobic exercise clinical trials, see Ref. 119.

Most clinical trials on the effects of physical activity interventions in type 2 diabetes have had small sample sizes and therefore inadequate statistical power to determine the effects of exercise on glycemic control and body weight. Boulé et al.¹¹⁹ undertook a systematic review and meta-analysis on the effects of structured exercise interventions in clinical trials of duration ≥ 8 weeks on HbA_{1c} and body mass in people with type 2 diabetes. Twelve aerobic training studies and two resistance training studies were included (totaling 504 subjects), and the results were pooled using standard meta-analytic statistical methods. The exercise and control groups did not differ at baseline in HbA_{1c} or body weight. Postintervention HbA_{1c} was significantly lower in exercise than control groups (7.65 vs. 8.31%, weighted mean difference -0.66% ; $P < 0.001$). In contrast, postintervention body weight did not differ between exercise and control groups. Meta-regression confirmed that the beneficial effect of exercise on HbA_{1c} was independent of any effect on body weight. Therefore, structured exercise programs had a statistically and clinically significant beneficial effect on glycemic control, and this effect was not mediated primarily by weight loss.

Although the significant effect of exercise on HbA_{1c} in these studies is encouraging, the lack of overall effect of exercise on body weight in these studies is disappointing but not surprising. The exercise volumes and program durations (mean 53 min/session, mean 3.4 sessions/week, mean duration 15 weeks) may have been insufficient to achieve the energy deficit necessary for major weight loss. Most of these studies did not examine body composition, and loss of fat might have been partially offset by increased lean body mass.^{119a}

Boulé et al.¹²⁰ later undertook a meta-analysis of the interrelationships among exercise intensity, exercise volume, change in cardiorespiratory fitness, and change in HbA_{1c}. This analysis was restricted to aerobic exercise studies in which $\dot{V}O_{2max}$ was either directly measured or estimated from a maximal exercise test using a validated equation. Exercise intensities during training ranged from $\sim 50\%$ of $\dot{V}O_{2max}$ to $> 75\%$ of $\dot{V}O_{2max}$, exercise volume 8.75–24.75 MET-hours/week. Meta-analysis revealed a clinically significant 11.8% increase in $\dot{V}O_{2max}$ in exercising groups, compared with a 1% decrease in control groups. Exercise intensity predicted postintervention weighted mean difference in HbA_{1c} ($r = -0.91$, $P = 0.002$) to a larger extent than exercise volume ($r = -0.46$, $P = 0.26$).

Consistent with the above, the greatest effect of exercise on HbA_{1c} (mean absolute postintervention HbA_{1c} difference of 1.5% between exercise and control groups) was seen in the single study with the highest exercise intensity.¹²¹ In this study, subjects exercised at 75% of $\dot{V}O_{2max}$ with intervals at even higher intensity, for 55 min three times a week, including 5 min of warm-up and 5 min of cool down. $\dot{V}O_{2max}$ increased 41% in the exercising subjects versus 1% in control subjects. Abdominal visceral fat assessed by magnetic resonance imaging was reported to decline by 48% and abdominal subcutaneous fat by 18% in the exercising group in this study, which are much larger fat losses than seen in most exercise studies and surprising in light of the relatively moderate total energy expenditure on exercise.

This meta-analysis provides support for higher-intensity aerobic exercise in people with type 2 diabetes as a means of improving HbA_{1c}. The analysis, however, is limited by the fact that only one study¹²¹ featured an unequivocally high-intensity exercise program at 75% of $\dot{V}O_{2max}$. This intensity might be difficult to sustain or even hazardous for many previously sedentary people with type 2 diabetes. Nevertheless, there was a strong dose-response relationship between exercise intensity across studies and both cardiorespiratory fitness and HbA_{1c} change. These results would provide support for encouraging type 2 diabetic individuals who are already exercising at moderate intensity to consider increasing the intensity of their exercise to obtain additional

benefits in both aerobic fitness and glycemic control.

Physical activity, aerobic fitness, and risk of cardiovascular and overall mortality

The effects of exercise on glycemic control, while statistically and clinically significant, might be perceived as modest in relation to the time and effort involved. After all, a similar degree of glucose lowering could be achieved in many cases by adding a single oral hypoglycemic medication. The effects of aerobic exercise on lipids and blood pressure are also relatively modest. However, large cohort studies have found that higher levels of habitual aerobic fitness and/or physical activity are associated with significantly lower subsequent cardiovascular and overall mortality, to a much greater extent than could be explained by glucose lowering alone.

Wei et al.¹²² reported on 1,263 type 2 diabetic men, a subsample of $> 20,000$ men in the Aerobics Center Longitudinal Study who underwent a detailed examination, including a maximal treadmill exercise test with ECG monitoring, physical exam, blood tests, and extensive health and lifestyle questionnaires between 1970 and 1993 and followed for mortality through 31 December 1994 using the National Death Index. Cardiorespiratory fitness was classified as low when treadmill time was at the bottom 20% of the overall cohort (including nondiabetic subjects) for the subject's age-group (30–39 years, 40–49 years, etc.), moderate if performance was in the 21st to 60th percentile for age-group, and high if in the highest 40% for age-group. Among the diabetic subjects, 42% were classified as “low fit” and 58% as “moderate” or “high-fit.” The 50% of diabetic subjects who reported any participation in walking, jogging, or other aerobic exercise programs in the previous 3 months were classified as “active,” and the other 50% were classified as “inactive.” After a mean of 11.7 years of follow-up, there were 180 deaths. Mortality in the moderate-fit men was $\sim 60\%$ lower than in low-fit men. Even after adjustment for age, examination year, baseline CVD, hypercholesterolemia, hypertriglyceridemia, BMI, hypertension, parental CVD, smoking, and baseline fasting glucose levels, low-fit diabetic men had a 2.2-fold greater mortality risk compared with men with moderate or high fitness (95% CI 1.6–3.2). Similarly,

after adjusting for the same list of confounders, mortality in diabetic men reporting no physical activity participation in the previous 3 months was 1.8-fold higher than in those reporting any participation in such activity (95% CI 1.3-2.5). Low cardiorespiratory fitness was at least as strong a risk factor for mortality as smoking, hypertension, hypercholesterolemia, and any of the other listed risk factors. The same research team has now published an updated study¹²³ with more subjects and longer follow-up. This later analysis found that moderate or high cardiorespiratory fitness was associated with lower mortality than low fitness independently of body composition and that essentially all of the association between higher BMI and higher mortality was explained by confounding with cardiorespiratory fitness.

Because moderate fitness was associated with vastly lower mortality than low fitness, it is of interest to know the activity levels associated with moderate fitness. Over 17,000 mainly nondiabetic participants in the Aerobic Center Longitudinal Study completed detailed physical activity logs and a maximal exercise test. Among moderately fit subjects (21st to 60th percentile for age) whose only exercise was walking, the mean time spent per week on exercise was 130 min for men and 148 min/week for women. These times are consistent with recommendations from the U.S. Surgeon General¹²⁴ and other respected bodies¹²⁵⁻¹²⁷ to accumulate about 150 min/week of moderate-intensity exercise. Moderately fit subjects whose only exercise was jogging or running reported a mean of 90 min/week for men and 92 min/week for women. These times are consistent with an alternative and equally valid recommendation for vigorous activity 30 min three times a week.

Hu et al.¹²⁸ reported on 5,125 female nurses with type 2 diabetes who completed detailed health questionnaires every 2 years, of whom 323 developed new CVD events over 14 years of follow-up. Age-adjusted relative risks according to average hours per week of moderate or vigorous activity were 1.0 for < 1 h (reference group), 0.93 for 1-1.9 h, 0.82 for 2-3.9 h, 0.54 for 4-6.9 h, and 0.52 for \geq 7 h. There was little change with adjustment for BMI, smoking, and other CVD risk factors (relative risks 1.0, 1.02, 0.87, 0.61, and 0.55 for < 1, 1-1.9, 2-3.9, 4-6.9, and \geq 7

h/week, respectively). Faster usual walking pace was associated with reduced CVD risk, independently of total physical activity score. Therefore, there was some cardioprotection associated with 2-3.9 h/week of physical activity, but a greater degree of cardioprotection associated with at least 4 h/week of such activity.

Myers et al.¹²⁹ reported on 6,213 consecutive men referred for treadmill exercise testing for clinical reasons, including ~500 with diabetes (J. Myers, e-mail communication, August 2003). They found that in people with and in those without baseline CVD, absolute exercise capacity was a better predictor of mortality risk than percentage of age-predicted exercise capacity. Every 1-MET increment in treadmill performance was associated with 12% greater probability of survival.

To our knowledge, no meta-analysis of the effects of exercise training on lipids or blood pressure in people with diabetes has been published. In the general, predominantly nondiabetic population, the effects of exercise training on blood pressure and lipids are relatively modest. A meta-analysis of the effects of aerobic exercise training on blood pressure¹³⁰ (54 trials, total 2,419 participants) found a weighted mean blood pressure change through exercise interventions of -3.84 mmHg systolic and -2.58 mmHg diastolic. A review of the effects of supervised, structured aerobic exercise training on lipids (51 trials of duration \geq 12 weeks, ~ 4,700 subjects)¹³¹ found a mean increase in HDL cholesterol of 4.6% ($P < 0.05$), and reductions in plasma triglycerides and LDL and total cholesterol of 3.7% ($P < 0.05$), 5.0% ($P < 0.05$), and 1.0% (NS), respectively. Greater increases in HDL cholesterol and decreases in plasma triglycerides have been seen with exercise programs that are more rigorous in terms of both volume and intensity than those that have been evaluated in diabetic subjects.¹³² Aerobic exercise training increases lipoprotein lipase activity and reduces the number of apolipoprotein B-containing particles.¹³³⁻¹³⁶

Potential mechanisms through which exercise could improve cardiovascular health were reviewed recently by Stewart.¹³⁷ These include decreased systemic inflammation, improved early diastolic filling (reduced diastolic dysfunction), improved endothelial vasodilator function, and decreased abdominal visceral fat accumulation.

Frequency of exercise

The U.S. Surgeon General's report recommended that most people accumulate \geq 30 min of moderate intensity activity on most, ideally all, days of the week. However, most clinical trials evaluating exercise interventions in people with type 2 diabetes have used a three times per week frequency,¹¹⁹ and many people find it easier to schedule fewer longer sessions rather than five or more weekly shorter sessions. The effect on insulin sensitivity of a single bout of aerobic exercise lasts 24-72 h, depending on the duration and intensity of the activity.¹³⁸ Because the duration of increased insulin sensitivity is generally not > 72 h, we recommend that the time between successive sessions of physical activity be no more than 72 h (i.e., there should not be more than 2 consecutive days without aerobic physical activity). There is some evidence that the effect of resistance exercise training on insulin sensitivity is somewhat longer,¹³⁹ perhaps because some of its effects are mediated by increases in muscle mass.

Exercise for weight loss and weight maintenance

The most successful programs for long-term weight control have involved combinations of diet, exercise, and behavior modification.¹⁴⁰ University-based obesity research programs using combinations of diet, exercise, and behavior modification have typically produced weight losses of 9-13.6 kg after 20 weeks, and ~ 60% of this weight loss is maintained over 1 year of follow-up.¹⁴⁰ Exercise alone, without concomitant dietary caloric restriction and behavior modification, tends to produce only modest weight loss of ~2 kg. Weight loss is typically this small primarily because obese people often have difficulty performing sufficient exercise to create a large energy deficit, and it is relatively easy to counterbalance increased energy expenditure through exercise by eating more or becoming less active outside of exercise sessions.¹⁴⁰ However, in a randomized trial, high-volume aerobic exercise (700 kcal/day, about 1 h/day of moderate-intensity aerobic exercise) produced at least as much fat loss as the equivalent degree of caloric restriction.¹⁴¹ Furthermore, exercise-induced weight loss resulted in greater improvements in insulin sensitivity than diet-induced weight loss.¹⁴¹

The optimal volume of exercise to achieve sustained major weight loss is probably much larger than that needed to achieve improved glycemic control and cardiovascular health. In the National Weight Control Registry,¹⁴² a study of individuals who lost at least 13.6 kg (mean 30 kg) and maintained the weight loss for at least 1 year (mean 5 years), the average self-reported energy expenditure on exercise was 2,545 kcal/week among women and 3,293 kcal/week among men. These amounts would correspond to ~7 h/week of moderate-intensity exercise. Similarly large amounts of exercise have been associated with long-term maintenance of weight loss in other studies.^{143–146}

Recommendations: aerobic exercise

The amount and intensity recommended for aerobic exercise vary according to goals.

- To improve glycemic control, assist with weight maintenance, and reduce risk of CVD, we recommend at least 150 min/week of moderate-intensity aerobic physical activity (40–60% of $\dot{V}O_{2max}$ or 50–70% of maximum heart rate) and/or at least 90 min/week of vigorous aerobic exercise (> 60% of $\dot{V}O_{2max}$ or > 70% of maximum heart rate). The physical activity should be distributed over at least 3 days/week and with no more than 2 consecutive days without physical activity.
- Performing ≥ 4 h/week of moderate to vigorous aerobic and/or resistance exercise is associated with greater CVD risk reduction compared with lower volumes of activity.¹²⁸
- For long-term maintenance of major weight loss (≥ 13.6 kg [30 lb]), larger volumes of exercise (7 h/week of moderate or vigorous aerobic physical activity per week) may be helpful.

Levels of evidence: A, for improved glycemic control;^{119,147} B, for CVD prevention;^{122,128} and B, for long-term maintenance of major weight loss.^{142–146}

RESISTANCE EXERCISE

For more detailed reviews on this topic, see Refs. 148 and 149.

The proven value of aerobic exercise notwithstanding, it does have some limitations. Some find aerobic

exercise monotonous. Most forms of aerobic exercise would not be advisable with advanced peripheral neuropathy and are challenging in people with severe obesity. Resistance exercise training, by increasing muscle mass and endurance, often causes more rapid changes in functional status and body composition than aerobic training and might therefore be more immediately rewarding. Because each session involves many different resistance exercises, some find it less monotonous than aerobic exercise. Resistance exercise improves insulin sensitivity to about the same extent as aerobic exercise.¹⁵⁰

Because of the increased evidence for health benefits from resistance training during the past 10–15 years, the American College of Sports Medicine (ACSM) now recommends resistance training be included in fitness programs for healthy young and middle-aged adults,¹²⁵ older adults,¹⁵¹ and adults with type 2 diabetes.¹²⁷ With increased age, there is a tendency to progressive declines in muscle mass, leading to “sarcopenia,” decreased functional capacity, decreased resting metabolic rate, increased adiposity, and increased insulin resistance, and resistance training can have a major positive impact on each of these.¹⁵¹

Studies of resistance exercise in type 2 diabetes

Notwithstanding the above, the previous ADA Position Statement on physical activity and exercise took a conservative view on resistance exercise, stating that high-intensity resistance training with weights might be appropriate for younger diabetic patients but not for older patients or those with longstanding disease; instead lower-intensity resistance exercise with light weights was endorsed.⁹³ This was due to a lack of published studies on high-intensity resistance exercise in older diabetic individuals and concerns about the safety of this type of exercise in the absence of published data (Table 1).

Before 1997 there were no published studies of resistance exercise in type 2 diabetic subjects. The first such published experiment was by Eriksson et al.,¹⁵² who studied eight moderately obese type 2 diabetic patients aged 55 ± 9 years (\pm SD) before and after a 3-month program of moderate-intensity weight training. Muscle endurance increased by 32%. HbA_{1c} decreased from 8.8 to 8.2% ($P < 0.05$), and

there was a strong negative correlation between HbA_{1c} and muscle cross-sectional area ($r = -0.73$). There was no control group. Ishii et al.¹⁵³ studied nine nonobese middle-aged type 2 diabetic subjects before and after 4–6 weeks of high-volume, moderate-intensity weight training. They were compared with control subjects unable to exercise because of orthopedic disorders. Insulin sensitivity rose 48% in exercisers but remained unchanged in control subjects. HbA_{1c} declined from 9.6 to 7.6% in the weight training group, but also inexplicably declined from 8.8 to 7.6% in the sedentary subjects. In a nonrandomized trial,¹⁵⁴ 18 subjects with type 2 diabetes (12 men and 6 women; mean age 62 years) underwent 5 months of moderate-intensity resistance training and were compared with 5 men and 15 women (mean age 67 years) with type 2 diabetes who did not exercise during this time. HbA_{1c} in the exercise group was 7.5% at baseline and 7.4% at 20 weeks, whereas HbA_{1c} in control subjects increased from 7.7 to 8.1% ($P < 0.05$ between groups). Interpretation of this study is complicated by a lack of randomization and imbalances at baseline in age and sex between the exercisers and control subjects. The first randomized controlled trial evaluating resistance training on glycemic control in type 2 diabetic patients was done by Dunstan et al.¹⁵⁵ in which 27 type 2 diabetic patients were randomized to nonexercise control or 8 weeks of circuit training in which subjects alternated between 30 s at a time of moderate-intensity weight lifting and 30 s at a time of light stationary cycling following each 30 s of weight lifting.¹⁵⁵ In the exercising subjects, both the insulin and glucose areas under the oral glucose tolerance test curve decreased nonsignificantly, and there was no significant effect on HbA_{1c}. In a similar study, Maiorana et al.¹⁵⁶ randomized 16 subjects in a crossover design to nonexercise control, followed by 8 weeks of three times per week circuit training or vice versa. During each circuit training session, subjects alternated 45 s of aerobic exercise at a moderate-intensity stationary cycling station with 45 s of moderate-intensity weight lifting. Mean HbA_{1c} was 8.5% following sedentary periods and 7.9% following exercise periods. This study and the 1998 Dunstan et al. study¹⁵⁵ shared two limitations. First, duration of the

Table 1. Clinical Trials of Resistance Exercise With People With Diabetes

Source	Sessions per week	Duration	No. of exercises	No. of sets, rest interval, and intensity of exercise	HbA _{1c} (mean ± SD)
Eriksson et al., 1997 ¹⁵²	2	13 weeks	11 (including both upper and lower body, performed at stations arranged in a circuit)	1 set, maximum 30-s rest interval between each exercise, 15–20 repetitions performed at > 50% of maximal exertion.	No control group. Intervention: 8.8 ± 1.4 to 8.2 ± 1.4%*
Honkola et al., 1998 ¹⁵⁴	2	5 months	8–10 (including both upper and lower body)	2 sets, total of 16–20 sets performed, rest interval between sets was < 60 s, 12–15 repetitions performed at a moderate intensity.	Control (type 2 diabetes): 7.7 ± 0.3 to 8.1 ± 0.3%.† Intervention group (type 2 diabetes): 7.5 ± 0.3 to 7.4 ± 0.3%.
Ishii et al., 1998 ¹⁵³	5	4–6 weeks	4 (lower body) and 5 (upper body)	2 sets, rest interval between sets of < 1 min, 10 and 20 repetitions for upper and lower body exercises, respectively, performed at 40–50% of 1-RM.	Control (type 2 diabetes): 8.8 ± 2.1 to 7.6 ± 1.9%. Intervention group (type 2 diabetes): 9.6 ± 2.8 to 7.6 ± 1.3%. (All subjects were hospitalized.)
Dunstan et al., 1998 ¹⁵⁵	3	8 weeks	3 (lower body) and 7 (upper body)	3 sets; rest interval between sets 30 s, with active recovery on cycle ergometer; 10–15 repetitions performed at 50–55% of 1-RM.	Control group (type 2 diabetes): 8.1 ± 0.6 to 8.3 ± 0.7%. Intervention group: 8.2 ± 0.5 to 8.0 ± 0.8%
Maiorana et al., 2002 ¹⁵⁶	3	8 weeks	7 (lower and upper body exercises)	Number of sets was increased from 1 to 3; rest interval between sets of 45 s, with active recovery on a cycle ergometer or treadmill; resistance training intensity commenced at 55% of 1-RM and increased to 65% of 1-RM by week 4. Aerobic exercise was performed at 70% of peak heart rate, increasing to 85% by week 6.	Control group (type 2 diabetes): 8.0 ± 0.5 to 8.4 ± 0.6%. Intervention group (type 2 diabetes): 8.5 ± 0.4 to 7.9 ± 0.3%.
Dunstan et al., 2002 ¹⁵⁹	3	26 weeks	8–10 (including both upper and lower body)	Intervention group: Initial 3 sessions involved 2 sets, 8–10 repetitions performed at 50–60% of 1-RM and increased to 3 sets in the subsequent 3 sessions. 3 sets, 8–10 repetitions performed at 75–85% of 1-RM was performed for the duration of the intervention. Control group: placebo exercise training program for 3 days/week, incorporating 18 different stretching/flexibility exercises.	Control group (type 2 diabetes, placebo exercise): 7.5 ± 1.1 to 7.1 to 0.8%. Intervention group (type 2 diabetes): 8.1 ± 0.9 to 6.9 ± 0.9%. (All subjects followed a moderate energy-restriction diet.)
Castaneda et al., 2002 ¹⁶⁰	3	16 weeks	3 (lower body) and 2 (upper body)	3 sets of 8–10 repetitions, progression to 75% of 1-RM, 2–3 min of rest between sets.	Control group (type 2 diabetes): increased 0.4 ± 1.2%. Intervention group (type 2 diabetes) decreased 1.0 ± 1.1%.‡ (All subjects were Hispanic.)
Cuff et al., 2003 ¹⁵⁸	3	16 weeks	Control group: no exercise, usual care. Combined aerobic and resistance group: warm up, aerobic phase (continuous aerobic activity), resistance phase (three lower body and two upper body exercises), and cool down. Aerobic-only group: warm up, aerobic phase (continuous aerobic activity), warm down.	Control group: usual care. Combined aerobic and resistance group: total duration of sessions, 75 min. Strength component comprised 2 sets, 12 repetitions, light initial intensity that increased thereafter, technique permitting. Aerobic component comprised 60–75% heart rate reserve (progression not defined). Aerobic-only group: total duration of sessions was 75 min. Aerobic component comprised 60–75% heart rate reserve progression not defined). Low-impact, low-intensity aerobic activity was used during the time period allocated for the resistance phase in the combined treatment group.	Control group (type 2 diabetes): decreased 0.03 ± 0.43%. Combined group (type 2 diabetes): decreased 0.1 ± 1.4%. Aerobic-only group (type 2 diabetes): decreased 0.1 ± 1.6%.

*P < 0.05 vs. baseline; †P < 0.001 vs. baseline; ‡P = 0.0001 vs. control group. This is a corrected version of the table that ran in *Diabetes Care*.

intervention was insufficient to significantly affect body composition through resistance training because 3–6 months of training are required for clinically significant muscle hypertrophy.¹⁵⁷ Second, the mixed resistance and aerobic training design precluded distinguishing the independent effects of each modality.

In recent trial, Cuff et al.¹⁵⁸ randomized 28 well-controlled, obese, postmenopausal type 2 diabetic women to combined aerobic and resistance training, aerobic training alone, or a nonexercising control group. Subjects in the exercising groups participated in three 75-min gym sessions per week for 16 weeks. The aerobic exercise was at 60–75% of heart rate reserve, whereas the resistance training program included two sets of 12 repetitions of five exercises. The aerobic-only group spent additional time on very-low-intensity warm-up and cool-down activity that was not expected to affect glucose metabolism. HbA_{1c} was excellent in all groups before training (6.3–6.9%) and did not change with exercise training. However, insulin sensitivity assessed with glucose clamp was increased significantly more in the combined aerobic and resistance exercise group than in the aerobic exercise only or control groups. Body fat declined significantly and similarly in both exercise groups, but muscle mass increased significantly only in the combined aerobic and resistance exercise group.

Two clinical trials published in late 2002^{159,160} provided much stronger evidence for the value of resistance training in type 2 diabetes. Dunstan et al.¹⁵⁹ randomized 36 Australian sedentary, overweight, type 2 diabetic subjects aged 60–80 years to 6 months of moderate weight loss plus high-intensity resistance training (RT/WL group; progressing to three sets of 8–10 repetitions of 8–10 exercises three times per week at 75–80% of maximum) or moderate weight loss plus flexibility exercise (control/WL group). Absolute HbA_{1c} declined 1.2% in the RT/WL group compared with just 0.4% in the control/WL group ($P < 0.05$ between groups). Mean weight loss and fat loss were similar in both groups, but mean lean body mass increased by 0.5 kg in RT/WL subjects while decreasing 0.4 kg in control/WL subjects ($P < 0.05$ between groups). Castaneda et al.¹⁶⁰ randomized 62

older sedentary Hispanic adults (40 women and 22 men; mean age 66 years) to 16 weeks of individually supervised high-intensity resistance exercise (RT group, progressing to three sets of eight repetitions of five exercises three times per week at 70–80% of maximum) or sedentary control. Mean HbA_{1c} declined from 8.7 to 7.6% in RT but did not change in control subjects ($P = 0.01$ between groups), even though 72% of RT subjects (versus 3% of control subjects) had hypoglycemic medications reduced and 42% of control subjects (versus 7% of RT subjects) had hypoglycemic medications increased. Mean systolic blood pressure declined 9.7 mmHg in RT subjects and rose 7.7 mmHg in control subjects ($P = 0.05$ between groups). Free fatty acid concentrations declined significantly by 27% in the RT group compared with control subjects, in whom circulating free fatty acids increased by 10%.¹⁶¹ There was a significant positive correlation between the changes in glycosylated hemoglobin and plasma free fatty acid concentrations in the groups combined. The interventions in these two studies involved higher exercise intensity (70–85% of maximum versus 40–60% of maximum) and more sets of each exercise (three sets vs. one to two sets) than the other studies described above. Both studies enrolled only older subjects, with mean age of ~66 years in both.

Resistance exercise improves bone density, muscle mass, strength, balance, and overall capacity for physical activity and therefore is potentially important for prevention of osteoporotic fractures in the elderly.^{162,163}

The ACSM recommends a resistance training regimen for type 2 diabetic individuals whenever possible. It recommends “a minimum of 8–10 exercises involving the major muscle groups...with a minimum of one set of 10–15 repetitions to near fatigue. Increased intensity of exercise, additional sets, or combinations of volume and intensity may produce greater benefits and may be appropriate for certain individuals.” These recommendations were published in 2000, before the 2002 Dunstan et al.¹⁵⁹ and Castaneda et al.¹⁶⁰ results were known. Given the superiority of Castaneda et al. and Dunstan et al.’s results in programs requiring three sets of each exercise compared with the other trials evaluating programs

requiring just one to two sets of each exercise, we advocate a resistance program similar to theirs: progressing to three sets of 8–10 repetitions of the heaviest weight that can be lifted 8–10 times to near fatigue. Although one set of each exercise may be sufficient to increase muscle strength,¹⁶⁴ it appears that three sets of each exercise produce the greater metabolic benefit in type 2 diabetes.

A conservative approach is to begin with one set of 10–15 repetitions two to three times per week at moderate intensity for several weeks, then two sets of 10–15 repetitions two to three times per week for several weeks, and then progress to three sets of 8–10 repetitions at a weight that cannot be lifted more than 8–10 times (8–10 RM). In the studies by Dunstan et al.¹⁶⁵ and Castaneda et al.,¹⁶⁰ intensity of resistance exercise was increased more rapidly than this. Each workout should be preceded by 5 min of warm up and followed by 5 min of cool down, each consisting of light aerobic activity with or without flexibility exercises. Initial supervision and periodic reassessment by a qualified exercise specialist is recommended to optimize benefits while minimizing risk of injury; such supervision was included in all of the above published studies.

Safety of resistance training

Some medical practitioners have concerns about the safety of higher-intensity resistance exercise in middle-aged and older people who are at risk of CVD. The main concern is often that the acute rises in blood pressure associated with higher-intensity resistance exercise might be harmful, possibly provoking stroke, myocardial ischemia, or retinal hemorrhage. We have found no evidence that resistance training actually increases these risks. No serious adverse events have been reported in any research study of resistance training in patients with type 2 diabetes, although the total number of subjects enrolled in these studies^{152–155,159,160} was small. A review of 12 resistance exercise studies in a total of 246 male cardiac rehabilitation patients¹⁶⁶ found no angina, ST depression, abnormal hemodynamics, ventricular dysrhythmias, or other cardiovascular complications. A study of 12 men with known coronary ischemia and ECG changes inducible by moderate aerobic exercise found that even maximal-intensity resistance

exercise did not induce ECG changes.¹⁶⁷ Therefore, moderate- to high-intensity resistance training was found to be safe even in men at significant risk of cardiac events. Lombardi et al.¹⁶⁸ analyzed data from the National Electronic Injury Surveillance System (NEISS, a nationwide representative sample of hospital emergency departments), the National Death Index, the U.S. Consumer Products Safety Commission, and two other databases in an effort to determine the morbidity and mortality associated with resistance training in the U.S. Between 1999 and 2001 there were 20 deaths in the U.S. associated with weight lifting. All of them were related to weights or barbells falling and causing injury. Fourteen of the deaths were due to asphyxia, primarily from dropping a barbell on the chest and neck. Most of these occurred in subjects' homes. There were no cases of death from myocardial infarction or stroke associated with resistance exercise.

The reason why resistance exercise appears less likely to induce ischemia than aerobic exercise has not been clearly demonstrated. A number of reasons seem plausible. First, in resistance exercise at least as much time is spent resting between sets as is spent lifting, lifting generally does not last > 60 s at a time. In contrast, with aerobic exercise, there is generally no rest during the exercise session. Second, during resistance exercise, systolic and diastolic blood pressure rise in parallel, possibly helping to maintain coronary perfusion, whereas in aerobic exercise systolic pressure rises significantly more than diastolic pressure.¹⁶⁹ Third, the rise in cardiac output with high-intensity resistance exercise is significantly less than that associated with high-intensity aerobic exercise.¹⁷⁰

Although it is well known that blood pressure rises while lifting a heavy weight, it is often not appreciated that blood pressure can also rise considerably in healthy older people performing aerobic exercise. Benn et al.¹⁷¹ studied the responses to aerobic and resistance exercise in 17 healthy men aged 64 ± 6 years. Subjects performed each of the following exercises with continuous monitoring of heart rate and intra-arterial blood pressure: one-arm military press, one-arm curl at 70% of 1-RM (moderate intensity), single- and double-leg press at 80% of 1-RM (high intensity), horizontal

walking for 20 min at 2.5 mph carrying 20 lbs in minutes 4–6 then 30 lbs in minutes 8–10, 4-min treadmill walk at 3 mph up an 8% incline, and 192 steps on a Stairmaster in ~3 min. The highest peak systolic blood pressures occurred in stair climbing (271 mmHg) and military press (261 mmHg), whereas the lowest peaks were in the single-arm curl (224 mmHg) and carrying a 20-lb weight (220 mmHg). Peak diastolic pressures were 128–151 mmHg in the resistance exercises, 121 mmHg in stair climbing, and 101–118 mmHg in the various treadmill exercises. Rate-pressure product, which is significantly correlated with myocardial oxygen demand, was highest at 41,000 for stair climbing; it was 22,000–30,000 for resistance exercises and 23,000–28,000 for treadmill exercises. Therefore, the myocardial demands of high-intensity resistance exercise are not out of line with those occasionally needed for activities of daily living, such as climbing stairs, walking up a hill, or carrying 20–30 lbs of groceries.

There is little or no evidence to guide practitioners in terms of whether stress testing before undertaking resistance training is necessary. One might ask whether such testing should use resistance exercise, rather than the usual aerobic exercise, during a stress test in such circumstances. Very few test centers would currently be equipped for such testing, and such tests have not been standardized. In contrast, aerobic exercise stress testing is widely available, standardized, and of proven prognostic value.

Recommendations: resistance exercise

In the absence of contraindications, people with type 2 diabetes should be encouraged to perform resistance exercise three times a week, including all major muscle groups, progressing to three sets of 8–10 repetitions at a weight that cannot be lifted more than 8–10 times (8–10 RM).

Level of evidence. A.^{159,160} In order to ensure resistance exercises are performed correctly, maximize health benefits, and minimize the risk of injury, we recommend initial supervision and periodic reassessments by a qualified exercise specialist, as was done in the clinical trials.

FLEXIBILITY EXERCISE

Flexibility exercise (stretching) has frequently been recommended as a

means of increasing range of motion and hopefully reducing risk of injury. However, two systematic reviews^{172,173} have found that flexibility exercise does not reduce risk of exercise-induced injury. It should be noted that most studies included in these systematic reviews evaluated younger subjects undertaking very vigorous activity programs, such as those in military basic training; these results may not be generalizable to older subjects. Flexibility exercise has been successfully used in clinical trials as a “placebo” exercise,^{159,174} since there is no evidence that flexibility exercise affects metabolic control or quality of life. We found two small studies providing indirect support for flexibility exercise in reducing risk of foot ulceration. In a case-control study,¹⁷⁵ 25 diabetic patients with a history of neuropathic foot ulceration had higher pressure on the planar aspect of the foot and lower ankle joint flexibility than 50 control subjects without neuropathy or foot ulceration. In a small randomized trial, 19 diabetic subjects were randomized to unsupervised active and passive range of motion exercises of the joints in feet or an inactive control group. After 1 month, the nine who performed range of motion exercises had a 4.2% decrease in peak plantar pressures compared with a 4.4% increase in peak plantar pressures in the control group. We found no studies that directly evaluated whether flexibility training reduced the risk of ulceration or injury in people with diabetes. Therefore, we feel that there is insufficient evidence to recommend for or against flexibility exercise as a routine part of the exercise prescription.

EXERCISE IN THE PRESENCE OF NONOPTIMAL GLYCEMIC CONTROL

Hyperglycemia

When people with type 1 diabetes are deprived of insulin for 12–48 h and ketotic, exercise can worsen the hyperglycemia and ketosis.¹⁷⁶ Previous ADA exercise position statements have suggested that physical activity be avoided if fasting glucose levels are > 250 mg/dl and ketosis is present and performed with caution if glucose levels are > 300 mg/dl even if no ketosis is present.⁹³ We agree that vigorous activity should probably be avoided in the presence of ketosis.

However, the recommendation to avoid physical activity if plasma glucose is > 300 mg/dl, even in the absence of ketosis, is probably more cautious than necessary for a person with type 2 diabetes, especially in a postprandial state. In the absence of very severe insulin deficiency, light- or moderate-intensity exercise would tend to decrease plasma glucose. Therefore, provided the patient feels well and urine and/or blood ketones are negative, it is not necessary to postpone exercise based simply on hyperglycemia.

Hypoglycemia

In individuals taking insulin and/or insulin secretagogues, physical activity can cause hypoglycemia if medication dose or carbohydrate consumption is not altered. This is particularly so at times when exogenous insulin levels are at their peaks and if physical activity is prolonged. Hypoglycemia would be rare in diabetic individuals who are not treated with insulin or insulin secretagogues. Previous ADA guidelines suggest that added carbohydrate should be ingested if pre-exercise glucose levels are < 100 mg/dl.⁹³ We agree with this recommendation for individuals on insulin and/or an insulin secretagogue. However, the revised guidelines clarify that supplementary carbohydrate is generally not necessary for individuals treated only with diet, metformin, α -glucosidase inhibitors, and/or thiazolidinediones without insulin or a secretagogue. Those who take insulin or secretagogues should check capillary blood glucose before, after, and several hours after completing a session of physical activity, at least until they know their usual glycemic responses to such activity. For those who show a tendency toward hypoglycemia during or after exercise, several strategies can be used. Doses of insulin or secretagogues can be reduced before sessions of physical activity, extra carbohydrate can be consumed before or during physical activity, or both. For a detailed discussion of medication adjustments to reduce risk of hypoglycemia, see Ref. 177.

Concomitant medications

Diabetic patients frequently take diuretics, β -blockers, ACE inhibitors, aspirin, and lipid-lowering agents. In most type 2 diabetic individuals, medications will not interfere with the

physical activities they choose to perform, but patients and health care personnel should be aware of potential problems to minimize their impact. Diuretics, especially in higher doses, can interfere with fluid and electrolyte balance. β -Blockers can blunt the adrenergic symptoms of hypoglycemia, possibly increasing risk of hypoglycemia unawareness. They can reduce maximal exercise capacity to $\sim 87\%$ of what it would be without β -blockade¹¹ through their negative inotropic and chronotropic effects. However, most people with type 2 diabetes do not choose to exercise at very high intensity, so this reduction of maximum capacity is generally not problematic. In people with CAD, β -blockade actually increases exercise capacity by reducing coronary ischemia. ACE inhibitors may modestly increase insulin sensitivity, and both ACE inhibitors and aspirin (especially in high doses [4–6 g/day]) may increase risk of hypoglycemia in some individuals through unclear mechanisms. In rare cases, statins, especially in combination with fibrates, can produce myositis. For additional discussion of the impact of concomitant medications on physical activity, see Ref. 92.

EXERCISE IN THE PRESENCE OF SPECIFIC LONG-TERM COMPLICATIONS OF DIABETES

There is a paucity of research on risks and benefits of exercise in the presence of diabetes complications. Therefore, recommendations in this section are based largely on “expert opinion.”

Retinopathy

Exercise and physical activity are not known to have any adverse effects on vision or the progression of nonproliferative diabetic retinopathy or macular edema.¹⁷⁸ This applies to resistance training as well as aerobic training. However, in the presence of proliferative or severe nonproliferative diabetic retinopathy, vigorous aerobic or resistance exercise may be contraindicated because of the risk of triggering vitreous hemorrhage or retinal detachment.¹⁷⁸ We found no research studies that would provide guidance as to an appropriate time interval between successful laser photocoagulation and initiation or resumption of resistance exercise. Ophthalmologists with whom one of us (C.C.-S.) consulted suggested wait-

ing 3–6 months after laser photocoagulation before initiating or resuming this type of exercise.

Peripheral neuropathy

We are unaware of research studies assessing the risk of exercise-induced injury in people with peripheral sensory neuropathy. Common sense, however, would indicate that decreased pain sensation in the extremities would result in increased risk of skin breakdown and infection and of Charcot joint destruction. Therefore, in the presence of severe peripheral neuropathy, it may be best to encourage non-weight-bearing activities such as swimming, bicycling, or arm exercises.^{179,180}

Autonomic neuropathy

Autonomic neuropathy can increase the risk of exercise-induced injury by decreasing cardiac responsiveness to exercise, postural hypotension, impaired thermoregulation due to impaired skin blood flow and sweating, impaired night vision due to impaired papillary reaction, impaired thirst increasing risk of dehydration, and gastroparesis with unpredictable food delivery.¹⁷⁹ Autonomic neuropathy is also strongly associated with CVD in people with diabetes.¹⁸¹ People with diabetic autonomic neuropathy should definitely undergo cardiac investigation before beginning physical activity more intense than that to which they are accustomed. Some experts advocate thallium scintigraphy as the preferred screening technique for CVD in this high-risk population.¹⁷⁹

Microalbuminuria and nephropathy

Physical activity can acutely increase urinary protein excretion. The magnitude of this increase is in proportion to the acute increase in blood pressure. This finding has led some experts to recommend¹⁸² that people with diabetic kidney disease perform only light or moderate exercise, such that blood pressure during exercise would not rise to > 200 mmHg. However, there is no evidence from clinical trials or cohort studies demonstrating that vigorous exercise increases the rate of progression of diabetic kidney disease. Several randomized trials in animals with diabetes and proteinuria showed that aerobic exercise training decreased urine protein excretion,^{183,184} possibly in part due to

Table 2. The positions of other major professional associations on the recommended types and amounts of physical activity

Reference	Aerobic training			Resistance training		
	Frequency	Intensity	Duration/mode	Frequency	No. of exercises	Sets/repetitions
Healthy adults						
1995 CDC/ACSM Public Health Statement ¹²⁶	Daily	Moderate	Accumulate 30 min/day continuous physical activity	—	Addressed but not specified	—
1996 U.S. Surgeon General's Report ²	Near daily	Moderate/intense	Accumulate ≥ 30 min	2 days/week	8–10 exercises involving major muscle groups	1–2 sets, 8–12 reps
1998 Health Canada ¹⁸⁶	Daily	Light/moderate	Accumulate 60 min/day with light physical activity, can decrease to 30 min with moderate intensity	2–4 days/week	Involve all major muscle groups	2–4 sets, 10–15 reps
2000 ACSM Position Stand ¹²⁷	3–5 days/week	65–90% HR_{max} or 50–85% $\dot{V}O_{2max}$ or HR_{max} reserve; start at lower intensity if initially unfit or sedentary	20–60 min continuous aerobic activities; 20–30 min minimum	2 days/week	8–10 exercises involving major muscle groups	1 set, 8–12 reps
Elderly people (aged ≥ 65 years)						
1998 ACSM Position Stand ¹⁵¹	3–5 days/week	50–85% $\dot{V}O_{2max}$ or 40–80% HR_{max} reserve	30–60 min continuous aerobic activity	2 days/week	8–10 exercises involving major muscle groups	1 set, 10–15 reps
Cardiac patients						
1995 AHA Exercise Standards ¹⁸⁷	Minimum of 3 days/week	50–60% $\dot{V}O_{2max}$ or HR_{max} reserve	Minimum of 30 min continuous physical activity	2–3 days/week	8–10 exercises involving major muscle groups	1 set, 10–15 reps
1999 AACVPR ¹⁸⁸	3–5 days/week	50–60% $\dot{V}O_{2max}$ or HR_{max} reserve	30–45 min of continuous or intermittent aerobic activity	2–3 days/week	Incorporate all major muscle groups	1 set, 10–15 reps
Individuals with type 2 diabetes						
2003 Canadian Diabetes Association ^{189*}	At least 3 nonconsecutive days/week	Moderate or intense	Accumulate at least 150 min/week (≥ 4 h/week, if willing)	3 days/week	~8 exercises involving major muscle groups	Initially 1 set, 10–15 reps. Progress to 3 sets, 8–12 reps
2000 ACSM Position Stand ¹²⁷	At least 3 nonconsecutive days/week	40–70% $\dot{V}O_{2max}$	10–15 min continuous physical activity in early stages, gradually increased to 30 min. Sessions can be divided into three 10-min sessions	At least 2 days/week	Minimum of 8–10 exercises involving major muscle groups	Minimum of 1 set, 10–15 reps
Previous ADA guidelines ¹⁹⁰	3–5 days/week	55–79% of HR_{max} or 40–74% HR_{max} reserve	20–60 min continuous or intermittent aerobic activity (min of 10-min bouts)		High resistance exercise using weights may be acceptable for young individuals or those with longstanding diabetes. Moderate weight training programs that utilize light weights and high repetitions can be used for maintaining or enhancing upper body strength in nearly all patients with diabetes	

*The 2003 Canadian Diabetes Association Clinical Practice Guidelines, published in December 2003, were drafted by two of the authors of the present technical review and reviewed by the Canadian Diabetes Association Expert Committee. The Canadian Diabetes Association guidelines are based on some of the same authors examining the same updated evidence reviewed in the present work, and therefore the recommendations are similar to the new proposed ADA recommendations. AHA, American Heart Association; AACVPR, American Association of Cardiovascular and Pulmonary Rehabilitation; CDC, U.S. Centers for Disease Control and Prevention; HR, heart rate.

This is a corrected version of the table that ran in *Diabetes Care*.

improved glycemic control, blood pressure, and insulin sensitivity. Resistance training also may be of benefit. In one clinical trial,¹⁸⁵ 26 older people with renal disease treated with a low-protein diet, including 10 with diabetic nephropathy, were randomized to 12 weeks of high-intensity resistance training or an inactive control group. Those allocated to resistance training had significant improvements in muscle mass, nutritional status, functional capacity, and even glomerular filtration rate compared with control subjects. Because of these encouraging findings, we believe there may be no need for any specific exercise restrictions for people with diabetic kidney disease. However, because microalbuminuria and proteinuria are associated with increased risk for CVD, it is important to perform an exercise ECG stress test before beginning exercise significantly more intense than the demands of everyday living.

COMPARISON BETWEEN THE PROPOSED NEW ADA GUIDELINES AND THE 2000 ACSM POSITION STAND ON TYPE 2 DIABETES AND EXERCISE
There is substantial agreement between our recommendations and those of the 2000 ACSM Position Stand. Our position on the recommended frequency, duration, and intensity of aerobic exercise is similar to the ACSM recommendations. The ACSM document was written before the publication of most resistance exercise trials in type 2 diabetes, but nevertheless endorsed resistance training. Our new recommendations for three sets of 8–10 repetitions of a range of resistance exercises are based on trials published in 2002^{159,160} in which results were superior with this type of regimen compared with other trials evaluating less-intense regimens. The ACSM Position Stand is similar to ours in firmly recommending aerobic and resistance exercise, but not explicitly recommending for or against flexibility exercise. See Table 2 for descrip-

tions of the positions of other major professional associations on the recommended types and amounts of physical activity.

Our position on which individuals should undergo stress testing is based on a re-evaluation of the evidence rather than on new evidence. The ACSM Position Stand, similarly to the previous ADA position, advocates stress testing for all diabetic individuals aged ≥ 35 years before participating in most physical activity. Our position advocates stress testing for those age > 30 years with additional risk factors, and age > 40 years regardless of additional risk factors, who wish to undertake vigorous exercise. We see stress testing as less essential for detection of ischemia in younger individuals because of their relatively low absolute risks of CVD. However, we continue to recognize the potential value of maximal exercise testing for the purposes of setting appropriate exercise intensities and assessing physical capacity and prognosis.