Available online at www.sciencedirect.com

ScienceDirect

Journal of Science and Medicine in Sport 15 (2012) 25–31

Journal of Science and Medicine in Sport

www.elsevier.com/locate/jsams

Review

Exercise prescription for patients with type 2 diabetes and pre-diabetes: A position statement from Exercise and Sport Science Australia

Matthew D. Hordern[a,b,c], David W. Dunstan[g], Johannes B. Prins[a,b], Michael K. Baker[d,e,h], Maria A. Fiatarone Singh[e,f,h], Jeff S. Coombes[b,c,*]

[a] School of Medicine, The University of Queensland, Australia
[b] Centre of Clinical Research Excellence in Cardiovascular Disease and Metabolic Disorders, The University of Queensland, Princess Alexandra Hospital, Australia
[c] School of Human Movement Studies, The University of Queensland, Australia
[d] School of Exercise, Biomedical and Health Sciences, Edith Cowan University, Australia
[e] Exercise, Health & Performance Faculty Research Group, Faculty of Health Sciences, University of Sydney, Australia
[f] Hebrew SeniorLife and Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University, Boston, MA, USA
[g] Baker IDI Heart and Diabetes Institute, Australia
[h] Boden Institute of Obesity, Nutrition and Exercise, University of Sydney, Australia

Received 5 March 2011; received in revised form 28 April 2011; accepted 29 April 2011

Abstract

Type 2 diabetes mellitus (T2DM) and pre-diabetic conditions such as impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT) are rapidly increasing in prevalence. There is compelling evidence that T2DM is more likely to develop in individuals who are insufficiently active. Exercise training, often in combination with other lifestyle strategies, has beneficial effects on preventing the onset of T2DM and improving glycaemic control in those with pre-diabetes. In addition, exercise training improves cardiovascular risk profile, body composition and cardiorespiratory fitness, all strongly related to better health outcomes. Based on the evidence, it is recommended that patients with T2DM or pre-diabetes accumulate a minimum of 210 min per week of moderate-intensity exercise or 125 min per week of vigorous intensity exercise with no more than two consecutive days without training. Vigorous intensity exercise is more time efficient and may also result in greater benefits in appropriate individuals with consideration of complications and contraindications. It is further recommended that two or more resistance training sessions per week (2–4 sets of 8–10 repetitions) should be included in the total 210 or 125 min of moderate or vigorous exercise, respectively. It is also recommended that, due to the high prevalence and incidence of comorbid conditions in patients with T2DM, exercise training programs should be written and delivered by individuals with appropriate qualifications and experience to recognise and accommodate comorbidities and complications.

Keywords: Exercise; Impaired fasting glucose; Impaired glucose tolerance; Pre-diabetes; Resistance training; Type 2 diabetes mellitus

1. Background

Impaired glucose tolerance (IGT), impaired fasting glucose (IFG) and type 2 diabetes (T2DM) are conditions characterised by varying levels of insulin resistance causing hyperglycaemia on the background of an insulin secretion defect. Patients with IGT and/or IFG do not have as severe insulin resistance and hyperglycaemia as those with T2DM and they are often regarded as having pre-diabetes. Rising levels of obesity, insufficient physical activity and high levels of uninterrupted sedentary time are independent risk factors for insulin resistance/diabetes.[1,2] Already, these have resulted in a high prevalence of IGT (16.4% in Australia in 2002[3]) and T2DM (7.4% in Australia in 2002,[3] 10.7% in the US in 2007[4]). Recent data from Australia indicate that a further 0.7–0.8% of Australians are diagnosed with T2DM every year.[5] In the US, the incidence of T2DM has doubled over

* Corresponding author.
E-mail address: jcoombes@uq.edu.au (J.S. Coombes).

1440-2440/$ – see front matter © 2011 Sports Medicine Australia. Published by Elsevier Ltd. All rights reserved.
doi:10.1016/j.jsams.2011.04.005

the last 30 years.[6] It is also estimated that approximately quarter of people with T2DM are undiagnosed.[7] In 2002 it was calculated that $10,900 is spent on every T2DM patient each year in Australia and this can increase to over $15,000 for each individual with additional micro and macro vascular complications.[8] In total this is over $3 billion per year. In the US it was estimated that $172 billion was spent on T2DM in 2007.[4]

Exercise training, is a recognised, although relatively underutilised strategy that is central to the prevention, care and management of T2DM and pre-diabetes.[9,10] The purpose of this statement is to provide practical exercise guidelines and recommendations for individuals with T2DM and pre-diabetes, while examining the benefits and specific considerations for these conditions.

2. Role of exercise in the prevention and treatment of type 2 diabetes

The benefits of exercise in preventing and treating T2DM are widely recognised.[11] Exercise training improves glycaemic control, body composition, cardiorespiratory fitness, cardiovascular risk, physical functioning and well-being in patients with T2DM or pre-diabetes.[10,12]

Low levels of physical activity and physical fitness (both cardiovascular and musculoskeletal) are prominent, independent and modifiable risk factors for the development of T2DM.[3,5,13,14] Furthermore, lifestyle modification, including exercise training now represents a central strategy in diabetes prevention. A number of large-scale randomised controlled trials (RCTs) of lifestyle modification in pre-diabetic populations have been conducted.[15–21] The aim of these trials has been to reduce incident T2DM, as well as ameliorate risk factors associated with both T2DM and cardiovascular morbidity and mortality. These lifestyle interventions, that in most cases targeted physical activity and nutritional goals simultaneously, have been highly successful in preventing the onset of T2DM. The largest of these, the U.S. Diabetes Prevention Program reported a 58% reduction in the incidence of T2DM from a four-year lifestyle intervention that prescribed 150 min/week of moderate activity exercise and dietary change program designed to induce a 7% weight loss. Importantly, the patients actually completed on average approximately 300 min/week at this intensity.[17] A similar risk reduction of 58% was reported in the Finish Diabetes Prevention Study that prescribed 210 min/week of moderate to strenuous intensity exercise (including resistance training) and dietary intervention to reduce fat and increase fibre intake, with patients completing an average of 204 min/week of exercise.[16] In Asian Indians with IGT, lifestyle advice to undertake 210 min/week of brisk walking resulted in a 28.5% risk reduction of incident diabetes[18] and the Da Qing Study from China reported a 46% risk reduction when moderate intensity activity was prescribed at 140 min/week and 280 min/week for persons ≥50 years and <50 years, respectively.[21] Patients in this study actually completed on average 560 min/week of exercise at moderate intensity. Finally, the Japanese Diabetes Prevention Program prescribed 210–280 min/week of moderate intensity exercise reported a risk reduction of 67%.[19]

Poor glycaemic control leads to accelerated cardiovascular, renal and ophthalmic diseases resulting in elevated morbidity and mortality. Therefore, glycaemic control has traditionally been the primary focus of exercise training studies in patients at risk or with T2DM. Beneficial effects have been shown with both aerobic,[22,23] resistance[22,24] or a combination of both modes of training, in which case they have shown to be synergistic[22] and may yield greater results than each mode of exercise alone.[25] These improvements in glycaemic control commonly result in reductions in T2DM medications.[26] Further, there is data to suggest that the greatest benefits occur in patients with the poorest metabolic control.[27,28] Importantly, studies that failed to show improvements in glycaemic control have commonly reported poor exercise compliance[29] or prescribed low exercise volume[30] and/or intensity.[31] The mechanisms responsible for these exercise training-induced benefits are complex and include improvements in insulin sensitivity,[32] and insulin dependent glucose uptake[33] from increases in muscle GLUT4 number and function,[34] increases in muscle capillarisation and blood flow.[35] These adaptations are strongly influenced by energy expenditure.[36] Further, given the close association of aging and diabetes, efforts to reduce the effect of sarcopenia are likely to transfer not only to improvements in glycaemic control, but also physical function and independence.[37]

Exercise training has been shown to be beneficial in decreasing body fat and improving lean mass in patients with T2DM,[22,38] although, these improvements may not be necessary to induce improvements in glycaemic control.[39] It has been suggested however, that metabolic improvements appear to be more closely related to a loss of visceral adiposity rather than weight loss in general.[40,41] In addition, it is widely accepted that anabolic resistance exercise is the only antidote to the loss of lean tissue accompanying hypocaloric diets to reduce weight in this cohort.

The benefits of exercise training on cardiorespiratory fitness are well reported, with studies typically showing approximately 12% improvement.[42] Not surprisingly, greater improvements in cardiorespiratory fitness have been associated with higher intensities of aerobic training or interval training, although data on interval training in T2DM is lacking.[43,44] Improvement in cardiorespiratory fitness is also very pertinent given its association with cardiovascular risk factors,[45] cardiovascular-related mortality and all cause mortality.[46]

Other co-morbidities prevalent in older adults with T2DM include osteoarthritis, peripheral vascular disease, mobility impairment, peripheral neuropathy and elevated fall risk, depression, and cognitive impairment. In all of these conditions, targeted exercise prescriptions (aerobic, resistance,

Table 1
Minimum exercise prescription recommendations for patients with type 2 diabetes or pre-diabetes.

Type of exercise	Intensity	Duration, week	Frequency
Aerobic (large muscle activities) e.g. walking, running, cycling and swimming.	Moderate: 40–59% VO_2R or HRR, 55–69% HR_{max}, RPE 12–13	210 min total	No more than two consecutive days without exercising
	OR		
	Vigorous: 60–84% VO_2R or HRR, 70–89% HR_{max}, RPE 14–16	125 min total	
Resistance (multi joint exercises, progressive, large muscle groups)	Moderate to vigorous: 8–10 exercises, 2–4 sets, 8–10 repetitions[a], 1–2 min rest intervals	60 min (included in totals above)	2 or more times/week

$VO_2R = VO_2$ reserve, HRR = heart rate reserve.
[a] Resistance training repetitions should be performed at a weight that cannot be lifted more than 8–10 times (70–84% of 1 RM).

or balance training and multi-modal exercise programs) have been shown to provide significant clinical benefits in terms of symptom relief.[47] Therefore, using exercise in the prevention and treatment of T2DM is likely to have even wider ranging benefits for this cohort.

3. Exercise guidelines

The exercise recommendations for patients with T2DM or pre-diabetes are shown in Table 1 and are similar to those advocated for the apparently healthy/lower risk population.[11] Patients should aim to accumulate a minimum of 210 min of moderate intensity or 125 min of vigorous intensity exercise each week. This total amount of exercise should consist of a combination of aerobic and resistance training. It is recommended that resistance training (2–4 sets of 8–10 repetitions) should make up two or more sessions each week. Aerobic and resistance training can be combined in the one session. Exercise should be performed on at least 3 days each week with no more than two consecutive days without training. The exercise recommendation can be achieved with a combination of moderate and vigorous intensity exercise, if desired and clinically feasible. When using a combination, we suggest that the vigorous intensity exercise can be multiplied by 1.7 to allow this to be added to the moderate intensity time. For example, in one week a person could exercise on four days for 40 min at a moderate intensity and on another day for 30 min at a vigorous intensity. The 1.7 multiplication factor was derived from recommendations that 150 min of moderate intensity is equivalent to 90 min of vigorous physical activity (a ratio of 1:1.7).[10,48] Our recommendation is consistent with the recent position statement from the American College of Sports Medicine and American Diabetes Association[46] with the exceptions that we are providing more guidance regarding the amount of vigorous intensity exercise and our 210 min/week incorporates both aerobic and resistance exercise. We are recommending that at least 60 min of resistance exercise be completed per week (e.g. two 30 min sessions).

If the recommended levels of exercise cannot be achieved, patients should still be encouraged to achieve what they can. This will still result in health benefits. Given the close association with T2DM and obesity, the accumulation of ≥250 min per week is recommended for overweight patients if weight loss is also a goal as this volume of exercise is considered necessary for significant weight reduction.[49]

Outside of the prescription for weight loss, the frequency of exercise for patients with T2DM or pre-diabetes should be designed to maximise the acute benefits of an exercise bout. Given that increases in insulin sensitivity declines markedly by 48 h post exercise,[50] scheduling sessions at this interval will maintain this increase over time. It is therefore recommended that there be no more than 2 consecutive days without training.

Where appropriate, both moderate and vigorous intensity exercise can be used to meet the exercise recommendations and higher intensities of aerobic exercise may also prove to be more time efficient. Indeed, a meta-analysis found that exercise intensity is more important in improving insulin sensitivity than duration[42] and individuals performing higher intensity exercise were more likely to achieve greater improvements in metabolic control and myocardial function.[27] Indeed, a recent study has shown that uphill walking (4× 4 min at 90–95% HR_{peak} with 3 min active recovery in between bouts) was more effective in reversing the risk factors of the metabolic syndrome than moderate intensity exercise.[51] Furthermore, two recent studies reported that short-term sprint interval training increases insulin sensitivity in healthy sedentary adults.[52,53] In contrast, Hansen et al. reported that low to moderate intensity exercise (50%HR_{max}) was not significantly different than moderate to vigorous intensity exercise (75%HR_{max}) for improving glycaemic control.[54] However, in this study the moderate to vigorous intensity group had a greater (0.5%) absolute reduction in

HbA_{1c} compared to a smaller reduction (0.2%) in the low to moderate intensity group. While vigorous intensities of exercise (both aerobic and resistance) may be a preferable option for some patients, for a large majority of people at risk or with T2DM, moderate intensities of exercise may be more appropriate, better tolerated and result in greater exercise adherence.[55]

For resistance training, high intensity exercise is generally possible even in the face of cardiovascular disease, peripheral vascular disease, or osteoarthritis, the most common co-morbidities influencing exercise prescription. In the case of aerobic exercise, exercise intensity is far more likely to be limited by these co-morbidities, making vigorous or sustained aerobic exercise difficult or impossible in such individuals. Consideration needs to be given to strategies for achieving beneficial exercise intensity when angina, claudication, or arthritis pain preclude activities such as jogging or prolonged brisk walking. Alternative choices may include short bouts of stair climbing, hills, upper body exercise, or water-based exercise for example.

Similar to the intensity of exercise, the optimal duration of exercise in patients with T2DM or pre-diabetes remains undefined. The majority of studies in patients with pre-diabetes have shown improvements in glycaemic control and/or reduction in the incidence of T2DM from around 210 min/week or more of exercise.[15–21] Furthermore, two of these studies showed a dose-response relationship.[16,17] In T2DM patients, the studies have been more varied. One of the large scale studies failed to show improvements in glycaemic control, rather prevented a decline seen in the control group.[27] The authors suggested that exercise in excess of 150 min may be required. However, another found improvements in glycaemic control with 150–270 min/week.[22] It is possible to achieve similar benefits in glycaemic control by accumulating short 10 min bouts or single longer sessions.[56] There may be both behavioural, physical and psychological reasons for promoting multiple short bouts in this cohort.

Theoretically, both aerobic and resistance training should be combined in the exercise prescription for T2DM and prediabetes, as they have complementary effects on metabolic, body composition and fitness outcomes. Studies comparing these two types of training show similar improvements in glycaemic control, despite producing different outcomes in body composition.[22] The addition of both types of training have also been shown to be synergistic for glycaemic control. Further, in some, but not all studies, resistance training has been shown to be superior to aerobic training.[57] Importantly, recent research has identified that combining both forms of exercise to achieve the same dose of exercise may lead to greater glycaemic control benefits.[25] The exact contributions of both forms of training to the overall exercise prescription will vary based on comorbidities, complications, patient preference and availability of equipment and/or facilities.

Aerobic training may maximise caloric expenditure and improvements in cardiorespiratory fitness,[42] whereas resistance training has been related to improvements in insulin sensitivity and GLUT4 number and function.[34,58] The addition of resistance training to aerobic training in the DARE study had additive effects on glycaemic control, although this may have been due to the larger volume of exercise in the combined treatment arm.[22] However, a recent study included combined training that was isocaloric and showed an advantage of the combined that was not found in either type of training alone.[25] Vigorous intensity exercise is contraindicated in poorly controlled hypertensive IGT and T2DM patients (and those with proliferative retinopathy or unstable cardiovascular disease), but it is well tolerated even in older T2DM patients who have controlled blood pressure and other chronic conditions.[24] Improvement in glycaemic control appears to be associated with the amount of muscle mass used during exercise[59] and this principle should be applied to both types of training.

Elevated volumes and uninterrupted durations of sedentary behaviour (those behaviours that involve sitting and low levels of energy expenditure) have shown to be predictive of poor glycaemic control, independent of moderate to vigorous-intensity activity in people at risk of developing T2DM.[60,61] Further, light-intensity (incidental) activity may also play an important protective role,[60] although this activity should be seen as additional to, and not a substitute for, moderate or vigorous intensity activity. It is recommended that patients with T2DM or pre-diabetes minimise sedentary behaviour by breaking these periods with frequent bouts of light-intensity activity or incorporating regular breaks that involve standing up from a seated position.[62]

4. Special considerations and contraindications

When initiating an exercise program for patients with T2DM or pre-diabetes it is necessary to consider the associated risks and contraindications. However, it is important to note that in the majority of circumstances, these risks should not prevent patients from exercising. The following is a discussion on the more common risks and contraindications associated with T2DM.

The occurrence of hypoglycaemia in patients with T2DM is relatively rare, although is higher in poorly controlled patients, especially in older patients with a longer history of the disease and those on multiple oral hypoglycaemic agents and long acting insulin[63,64] While specific thresholds for hypoglycaemia vary depending on individual symptoms, 4.0 mmol/L has been suggested as a reasonable lower limit.[65] Prevention of hypoglycaemia centres around self monitoring of blood glucose levels and consultation with the patient's doctor. Important considerations are timing of medications, meals, and exercise. Given the risk of post-prandial hyperglycemia,[66] a good strategy is to take advantage of the acute glucose-lowering effect of exercise by timing the session for approximately one hour after a meal (to coincide with peak post-prandial rise in glucose). Exercise may need to be temporarily modified or suspended during acute illnesses or fevers, when metabolic control is sometimes unpredictable.

While the risk of a cardiac event during exercise cannot be ignored, the cardiac risk of patients with T2DM or pre-diabetes remaining inactive is greater.[67] Cardiac screening, including a stress test is recommended for previously sedentary patients with additional CV risk factors, especially for those attempting to undergo more than brisk walking, although clinical judgement should prevail.[10,47] Stress test screening, while providing valuable exercise prescription information, is not necessary in all patients with T2DM or pre-diabetes.[68]

Peripheral neuropathy reduces sensation in the hands and feet of patients with T2DM, exposing patients to a reduced awareness of painful sores that can result from impact-related activities (walking or running). Appropriate footwear, regular foot inspection and low impact exercises are essential for patients with peripheral neuropathy and are highly advised in all patients with T2DM. However, patients who are active (even with weight bearing exercise) do not seem to increase their risk of ulcers.[69]

Hypertension is a common comorbidity in patients with T2DM. Specific guidelines relating to the management of hypertension in T2DM are provided elsewhere.[9] Exercise has shown to be beneficial in reducing and managing hypertension in these populations. Poorly controlled hypertensive patients should avoid vigorous intensity training, particularly vigorous intensity resistance training and the Valsalva manoeuvre.

Obesity is closely associated with T2DM.[70] Obese T2DM patients may experience a higher rate of joint pain and discomfort, further contributing to the large list of potential barriers to exercise in this population. While weight loss may or may not be necessary to improve glycaemic control,[39] improvements in body composition may have particular importance for long-term adherence.

Peripheral vascular disease is common in T2DM, particularly those with hypertension, obesity and smoking histories, and may present with pain in the calves or buttocks with exercise.[71] Exercise is highly recommended as treatment for claudication,[72] but some patients may be unable to undertake vigorous aerobic exercise if symptoms are severe. Caution regarding high impact or traumatic foot injuries due to exercise is most critical. Resistance training is a viable alternative which may be used even in individuals who experience claudication after very short distances of walking.

Patients with OA may have particular difficulty exercising, especially using modes of exercise than increase the load of the affected joints (e.g. walking, running).[73] While a commonly held perception is that exercise may be deleterious and cause OA, low impact exercise has been shown to not accelerate the condition. Further, low impact exercise can increase joint motility and decrease body mass, both of which can have a dramatic effect on a patient's ability to exercise. Low impact exercise includes cycling, swimming and resistance training.

5. Summary

Exercise training is a well-established prevention strategy, treatment and management therapy for patients with T2DM and pre-diabetes. It is recommended that individuals with these conditions accumulate a minimum of 210 min of moderate intensity or 125 min of vigorous intensity exercise each week using a combination of both aerobic and resistance training. Ideally the total amount of exercise should consist of some aerobic and some resistance training, however, if only one modality can be performed due to comorbidities, behavioural considerations or other constraints, then either modality alone has been shown to be effective. The risks associated with exercise are considered less than those of inactivity, even in older adults with multiple chronic diseases. Therefore, exercise training should be an essential component of any treatment plan for all patients at risk of or with T2DM. Due to the potential risks and likelihood of the presence of comorbidities, programs should be designed and delivered by qualified personnel who are trained and experienced to deal with the likely additional considerations. In Australia, when these services are delivered by an accredited exercise physiologist patients are able to get a financial rebate via the national health program: Medicare.

Practical implications

- Exercise training should be an essential component of any treatment plan for all patients at risk of or with T2DM.
- Individuals with these conditions should accumulate a minimum of 210 min of moderate intensity or 125 min of vigorous intensity exercise each week using a combination of both aerobic and resistance training.
- Exercise programs patients at risk of or with T2DM should be designed and delivered by appropriately trained and qualified personnel.

Acknowledgement

We thank Exercise and Sport Science Australia for financial support to produce this statement.

References

1. Chen L, Magliano DJ, Balkau B, et al. Ausdrisk: an Australian type 2 diabetes risk assessment tool based on demographic, lifestyle and simple anthropometric measures. *Med J Aust* 2010;**192**:197–202.

2. Venables MC, Jeukendrup AE. Physical inactivity and obesity: links with insulin resistance and type 2 diabetes mellitus. *Diabetes Metab Res Rev* 2009;**25**(Suppl. 1):S18–23.
3. Dunstan DW, Zimmet PZ, Welborn TA, et al. The rising prevalence of diabetes and impaired glucose tolerance: the Australian diabetes, obesity and lifestyle study. *Diabetes Care* 2002;**25**:829–834.
4. Centers for disease control and prevention. National diabetes fact sheet: general information and national estimates of diabetes in the United States, 2007. 2008.
5. Magliano DJ, Barr EL, Zimmet PZ, et al. Glucose indices, health behaviors, and incidence of diabetes in australia: the Australian diabetes, obesity and lifestyle study. *Diabetes Care* 2008;**31**:267–272.
6. Fox CS, Pencina MJ, Meigs JB, et al. Trends in the incidence of type 2 diabetes mellitus from the 1970s to the 1990s: the Framingham heart study. *Circulation* 2006;**113**:2914–2918.
7. Centers for Disease Control and Prevention. *National diabetes fact sheet: national estimates and general information on diabetes and prediabetes in the United States, 2011*. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention; 2011.
8. Colagiuri S, Colagiuri R, Conway B, et al. *Diabcost Australia: assessing the burden of type 2 diabetes in Australia* 2003.
9. Standards of medical care in diabetes—2008. *Diabetes Care* 2008;**31**(Suppl. 1):S12–54.
10. Marwick TH, Hordern MD, Miller T, et al. Exercise training for type 2 diabetes mellitus: impact on cardiovascular risk: a scientific statement from the American heart association. *Circulation* 2009;**119**:3244–3262.
11. 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. *Circulation* 2007;**116**:1081–1093.
12. 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**:2518–2527.
13. Barr ELM, Magliano DJ, Zimmet PZ, et al. The Australian diabetes, obesity and lifestyle study. *Ausdiab Report* 2005.
14. Meisinger C, Lowel H, Thorand B, et al. Leisure time physical activity and the risk of type 2 diabetes in men and women from the general population, the Monica/Kora Augsburg cohort study. *Diabetologia* 2005;**48**:27–34.
15. 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**:537–544.
16. 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**:1343–1350.
17. 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**:393–403.
18. 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**:289–297.
19. 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**:152–162.
20. 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**:1673–1679.
21. 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**:1783–1789.
22. Sigal RJ, Kenny GP, Boule 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**:357–369.
23. 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**:1374–1383.
24. 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**:1729–1736.
25. Church TS, Blair SN, Cocreham S, et al. Effects of aerobic resistance training on hemoglobin a1c levels in patients with type 2 diabetes: a randomized controlled trial. *JAMA* 2010;**304**:2253–2262.
26. Dunstan DW, Puddey IB, Beilin LJ, et al. Effects of a short-term circuit weight training program on glycaemic control in niddm. *Diabetes Res Clin Pract* 1998;**40**:53–61.
27. Hordern MD, Coombes JS, Cooney LM, et al. Effects of exercise intervention on myocardial function in type 2 diabetes. *Heart* 2009;**95**:1343–1349.
28. Hordern MD, Cooney LM, Beller EM, et al. Determinants of changes in blood glucose response to short-term exercise training in patients with type 2 diabetes. *Clin Sci (Lond)* 2008;**115**:273–281.
29. Krousel-Wood MA, Berger L, Jiang X, et al. Does home-based exercise improve body mass index in patients with type 2 diabetes? Results of a feasibility trial. *Diabetes Res Clin Pract* 2008;**79**:230–236.
30. Brun JF, Bordenave S, Mercier J, et al. Cost-sparing effect of twice-weekly targeted endurance training in type 2 diabetics: a one-year controlled randomized trial. *Diabetes Metab* 2008;**34**:258–265.
31. Khan S, Rupp J. The effect of exercise conditioning, diet, and drug therapy on glycosylated hemoglobin levels in type 2 (NIDDM) diabetics. *J Sports Med Phys Fitness* 1995;**35**:281–288.
32. 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**:771–778.
33. Santos JM, Ribeiro SB, Gaya AR, et al. Skeletal muscle pathways of contraction-enhanced glucose uptake. *Int J Sports Med* 2008;**29**:785–794.
34. Holten MK, Zacho M, Gaster M, et al. Strength training increases insulin-mediated glucose uptake, glut4 content, and insulin signaling in skeletal muscle in patients with type 2 diabetes. *Diabetes* 2004;**53**:294–305.
35. Ishii T, Yamakita T, Sato T, et al. Resistance training improves insulin sensitivity in niddm subjects without altering maximal oxygen uptake. *Diabetes Care* 1998;**21**:1353–1355.
36. Larsen JJ, Dela F, Madsbad S, et al. The effect of intense exercise on post-prandial glucose homeostasis in type II diabetic patients. *Diabetologia* 1999;**42**:1282–1292.
37. Park SW, Goodpaster BH, Lee JS, et al. Excessive loss of skeletal muscle mass in older adults with type 2 diabetes. *Diabetes Care* 2009.
38. Boule NG, Haddad E, Kenny GP, et al. Effects of exercise on glycemic control and body mass in type 2 diabetes mellitus: a meta-analysis of controlled clinical trials. *JAMA* 2001;**286**:1218–1227.
39. Klein S, Fontana L, Young VL, et al. Absence of an effect of liposuction on insulin action and risk factors for coronary heart disease. *N Engl J Med* 2004;**350**:2549–2557.
40. 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**:385–391.
41. Giannopoulou I, Ploutz-Snyder LL, Carhart R, et al. Exercise is required for visceral fat loss in postmenopausal women with type 2 diabetes. *J Clin Endocrinol Metab* 2005;**90**:1511–1518.
42. Boule NG, Kenny GP, Haddad E, et al. Meta-analysis of the effect of structured exercise training on cardiorespiratory fitness in type 2 diabetes mellitus. *Diabetologia* 2003;**46**:1071–1081.
43. Boudou P, De Kerviler E, Vexiau P, et al. Effects of a single bout of exercise and exercise training on steroid levels in middle-aged type 2 diabetic men: relationship to abdominal adipose tissue distribution and metabolic status. *Diabetes Metab* 2000;**26**:450–457.

44. Maiorana A, O'Driscoll G, Goodman C, et al. Combined aerobic and resistance exercise improves glycemic control and fitness in type 2 diabetes. *Diabetes Res Clin Pract* 2002;**56**:115–123.
45. Wing RR, Jakicic J, Neiberg R, et al. Fitness, fatness, and cardiovascular risk factors in type 2 diabetes: look ahead study. *Med Sci Sports Exerc* 2007;**39**:2107–2116.
46. Blair SN, Kohl 3rd HW, Barlow CE, et al. Changes in physical fitness and all-cause mortality. A prospective study of healthy and unhealthy men. *JAMA* 1995;**273**:1093–1098.
47. Exercise and type 2 diabetes: American college of sports medicine and the American diabetes association: joint position statement. Exercise and type 2 diabetes. *Med Sci Sports Exerc* 2010;**42**:2282–2303.
48. Sigal RJ, Kenny GP, Wasserman DH, et al. Physical activity/exercise and type 2 diabetes: a consensus statement from the american diabetes association. *Diabetes Care* 2006;**29**:1433–1438.
49. Donnelly JE, Blair SN, Jakicic JM, et al. 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**:459–471.
50. Borghouts LB, Keizer HA. Exercise insulin sensitivity: a review. *Int J Sports Med* 2000;**21**:1–12.
51. Tjonna AE, Lee SJ, Rognmo O, et al. Aerobic interval training versus continuous moderate exercise as a treatment for the metabolic syndrome: a pilot study. *Circulation* 2008;**118**:346–354.
52. Richards JC, Johnson TK, Kuzma JN, et al. Short-term sprint interval training increases insulin sensitivity in healthy adults but does not affect the thermogenic response to beta-adrenergic stimulation. *J Physiol* 2010;**588**:2961–2972.
53. Babraj JA, Vollaard NB, Keast C, et al. Extremely short duration high intensity interval training substantially improves insulin action in young healthy males. *BMC Endocr Disord* 2009;**9**:3.
54. Hansen D, Dendale P, Jonkers RA, et al. Continuous low- to moderate-intensity exercise training is as effective as moderate- to high-intensity exercise training at lowering blood hba(1c) in obese type 2 diabetes patients. *Diabetologia* 2009.
55. Perri MG, Anton SD, Durning PE, et al. Adherence to exercise prescriptions: effects of prescribing moderate versus higher levels of intensity and frequency. *Health Psychol* 2002;**21**:452–458.
56. Eriksen L, Dahl-Petersen I, Haugaard SB, et al. Comparison of the effect of multiple short-duration with single long-duration exercise sessions on glucose homeostasis in type 2 diabetes mellitus. *Diabetologia* 2007;**50**:2245–2253.
57. 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**:1527–1533.
58. Tabata I, Suzuki Y, Fukunaga T, et al. Resistance training affects glut-4 content in skeletal muscle of humans after 19 days of head-down bed rest. *J Appl Physiol* 1999;**86**:909–914.
59. Park SW, Goodpaster BH, Strotmeyer ES, et al. Decreased muscle strength and quality in older adults with type 2 diabetes: the health, aging, and body composition study. *Diabetes* 2006;**55**:1813–1818.
60. Healy GN, Dunstan DW, Salmon J, et al. Objectively measured light-intensity physical activity is independently associated with 2-h plasma glucose. *Diabetes Care* 2007;**30**:1384–1389.
61. Dunstan DW, Salmon J, Healy GN, et al. Association of television viewing with fasting and 2-h postchallenge plasma glucose levels in adults without diagnosed diabetes. *Diabetes Care* 2007;**30**:516–522.
62. Owen N, Healy GN, Matthews CE, et al. Too much sitting: the population health science of sedentary behavior. *Exerc Sport Sci Rev* 2010;**38**:105–113.
63. U.K. prospective diabetes study 16. Overview of 6 years' therapy of type ii diabetes: a progressive disease. U.K. Prospective diabetes study group. *Diabetes* 1995;**44**:1249–1258.
64. Bremer JP, Jauch-Chara K, Hallschmid M, et al. Hypoglycemia unawareness in older compared to middle-aged patients with type 2 diabetes. *Diabetes Care* 2009.
65. Cryer PE, Davis SN, Shamoon H. Hypoglycemia in diabetes. *Diabetes Care* 2003;**26**:1902–1912.
66. Praet SF, Manders RJ, Lieverse AG, et al. Influence of acute exercise on hyperglycemia in insulin-treated type 2 diabetes. *Med Sci Sports Exerc* 2006;**38**:2037–2044.
67. Smart N, Marwick TH. Exercise training for patients with heart failure: a systematic review of factors that improve mortality and morbidity. *Am J Med* 2004;**116**:693–706.
68. Sigal RJ, Kenny GP, Wasserman DH, et al. Physical activity/exercise and type 2 diabetes. *Diabetes Care* 2004;**27**:2518–2539.
69. Lemaster JW, Mueller MJ, Reiber GE, et al. Effect of weight-bearing activity on foot ulcer incidence in people with diabetic peripheral neuropathy: feet first randomized controlled trial. *Phys Ther* 2008;**88**:1385–1398.
70. Wannamethee SG, Shaper AG. Weight change and duration of overweight and obesity in the incidence of type 2 diabetes. *Diabetes Care* 1999;**22**:1266–1272.
71. Adler AI, Stevens RJ, Neil A, et al. UKPDS 59: hyperglycemia and other potentially modifiable risk factors for peripheral vascular disease in type 2 diabetes. *Diabetes Care* 2002;**25**:894–899.
72. Armen J, Smith BW. Exercise considerations in coronary artery disease, peripheral vascular disease, and diabetes mellitus. *Clin Sports Med* 2003;**22**:123–133, viii.
73. Hunter DJ, Eckstein F. Exercise and osteoarthritis. *J Anat* 2009;**214**:197–207.