# High-Intensity Exercise Training for the Prevention of Type 2 Diabetes Mellitus

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**Abstract:** Aerobic exercise training and diet are recommended for the primary prevention of type 2 diabetes mellitus and cardiovascular disease. The American Diabetes Association (ADA) recommends that adults with prediabetes engage in ≥ 150 minutes per week of moderate activity and target a 7% weight loss. However, traditional moderate-intensity (MI) exercise training programs are often difficult to sustain for prediabetic adults; a commonly cited barrier to physical activity in this population is the "lack of time" to exercise. When matched for total energy expenditure, high-intensity (HI) exercise training has a lower overall time commitment compared with traditional low-intensity (LI) or MI exercise training. Several recent studies comparing HI exercise training with LI and MI exercise training reported that HI exercise training improves skeletal muscle metabolic control and cardiovascular function in a comparable and/or superior way relative to LI and MI exercise training. Although patients can accrue all exercise benefits by performing LI or MI activities such as walking, HI activities represent a time-efficient alternative to meeting physical activity guidelines. High-intensity exercise training is a potent tool for improving cardiometabolic risk for prediabetic patients with limited time and may be prescribed when appropriate.

**Keywords:** prediabetes; metabolic syndrome; exercise intensity; interval training

## Introduction

Lifestyle intervention, including aerobic exercise training and diet, is essential for the prevention of type 2 diabetes mellitus (T2DM). In particular, the preventative role of exercise training is supported by several well-conducted RCTs, including the US Diabetes Prevention Program (DPP), Finnish Diabetes Prevention Study, the Chinese Da Qing IGT and Diabetes Study, and the Swedish Malmo study, which clearly demonstrate that exercise reduces the progression of prediabetes to T2DM by approximately 28.5% to 58% (prediabetes is defined as impaired glucose tolerance [IGT], impaired fasting glucose, or a glycated hemoglobin [$HbA_{1c}$] level of 5.7%–6.4%).[1–6] Consequently, an expert consensus statement from the American Diabetes Association (ADA) recommends that adults with prediabetes should engage in ≥ 150 minutes per week of moderate activity, such as walking, and target a weight loss of 7% of body mass in order to prevent the development of T2DM.[7] Importantly, data from the DPP and the US Diabetes Prevention Program Outcomes Study (DPPOS) provide strong evidence to suggest that the rate of T2DM development is lower after lifestyle intervention compared with metformin therapy[1,8–11]; follow-up cost analyses of the DPP and DPPOS show that lifestyle intervention is highly cost effective as well.[1,8–11]

Despite being an important and cost-saving component of the DPP, many patients with prediabetes find it difficult to maintain lifestyle interventions, such as exercise training. Sedentary prediabetic adults report many barriers to physical activity, but

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the most common reason given is having a "lack of time" to exercise.[12–14] However, there is a growing body of literature that compares cardiometabolic risk reduction effects from traditional aerobic/endurance training programs with reductions of risk from novel exercise interventions that present a minimal time burden to patients. High-intensity (HI) exercise training has emerged as a primary alternative to traditional exercise programs because they present a reduced overall time commitment to patients. Additionally, a number of recent studies of previously sedentary and prediabetic adults reported comparable or superior improvements to skeletal muscle metabolic control and cardiovascular function with HI exercise training compared with traditional low-intensity (LI) and moderate-intensity (MI) exercise training.[15–23] A common misconception is that patients with prediabetes or other conditions cannot tolerate HI exercise. However, when HI exercise is individually prescribed to patients as a function of peak oxygen consumption ($VO_{2peak}$), it may be associated with an absolute exercise intensity that is considered moderate in other groups (eg, HI activity for adults with T2DM might be a brisk walking pace, which is an LI or MI activity for healthy young adults). High-intensity exercise training interventions were safely employed and well tolerated by a wide range of patient populations, including both healthy patients and patients who experienced heart failure[18,19]; there is also data suggesting that HI exercise training is more enjoyable to perform than prolonged endurance training.[24]

This review provides physicians and other clinicians with a comparison of the metabolic effects of HI exercise training versus traditional LI to MI exercise training in adults with prediabetes. In addition, we briefly examine the physiologic rationale for using HI exercise to improve metabolic control and cardiovascular function in prediabetic adults. Our review of the HI exercise training approach to improve cardiometabolic outcomes in prediabetes is not meant to overshadow the benefits of traditional exercise training programs, nor is it meant to be a "one size fits all" method to improve cardiometabolic risk in T2DM. However, HI exercise training represents a time-efficient alternative to meeting physical activity guidelines for many patients and may be used as a potent resource for prescribing exercise when appropriate.

## High-Intensity Exercise Training Defined

High-intensity or *vigorous* exercise is individually prescribed as percent maximum oxygen consumption ($VO_{2\,max}$), percent oxygen consumption reserve ($VO_2R$), and/or maximum heart rate ($HR_{max}$). Vigorous exercise may also be individually prescribed at a rating of perceived exertion (RPE) that is considered "hard" to "very hard" (eg, 15–17 on the Borg 6–20 scale). The American College of Sports Medicine (ASCM) considers any intensity $\geq 60\%$ of $VO_2R$ ($> 77\%$ of $HR_{max}$) to be vigorous exercise[25]; however, training intensities near the upper ranges of $VO_{2\,max}$ likely confer greater overall benefits to patients, which we discuss in a later section.[23,26] High-intensity exercise may be performed as a single continuous effort or as interval training. Interval exercise is defined as brief intermittent bouts of HI exercise (usually $> 90\%$ $HR_{max}$) followed by LI recovery periods.

Few studies in the literature compare the metabolic effects of calorically matched continuous or interval-based HI exercise training programs to traditional LI to MI programs consistent with the ACSM/ADA exercise guidelines for T2DM prevention (~1000/kcal/week).[15,16,25–31] This is problematic because independent contributions of exercise volume versus intensity cannot be examined. We limited our review to studies which compare exercise training intensity when total exercise volume is equated. We also considered several recent studies which compare traditional endurance training to novel HI interval training programs consisting of very low weekly volumes (eg, 15–30 minutes HI interval work per week) because these types of programs fit our time efficiency paradigm.

## Exercise Training Intensity and Metabolic Control

### Postprandial Glycemic Control

Impaired glucose tolerance is the hallmark characteristic of prediabetes and describes the exaggerated glycemic response to a standard 75-g 2-hour oral glucose tolerance test (OGTT). Impaired glucose tolerance is defined as having 2-hour plasma glucose concentrations between 140 to 200 mg/dL during the OGTT and is associated with both hepatic and skeletal muscle insulin resistance.[32] Adults with IGT have an approximately 2-fold higher risk for cardiovascular events compared with euglycemic adults.[33–35] Impaired glucose tolerance is a proxy for the frequent postprandial hyperglycemic excursions most prediabetic adults experience after mixed meals consumed in daily life. Postprandial hyperglycemia is the most significant contributor to elevated $HbA_{1c}$ levels in patients at risk for T2DM and precedes deteriorations in fasting blood glucose.[36] Objectively measured continuous 24-hour glucose data suggest that prediabetic adults spend approximately 9% of waking hours in a hyperglycemic state, which is a percentage that is approximately 3-fold higher than euglycemic adults.[37] Ceriello and colleagues[36] clearly


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demonstrated that fluctuations in blood glucose occurring as a result of consuming meals during the course of a day are more deleterious to skeletal muscle homeostasis than chronic sustained hyperglycemia.

The beneficial effects of exercise on postprandial glucose (PPG) disposal may be due to transient changes in insulin action and glucose transporter-4 protein content instead of more profound chronic adaptations to skeletal muscle (eg, mitochondrial biogenesis). Acute muscle contraction independent of insulin improves glucose disposal and lowers patient blood glucose levels for 2 to 72 hours into the recovery period.[38,39]

We recently compared the effects of acute isocaloric bouts of HI and MI exercise (~30% peak power output vs 80% peak power output) on PPG disposal in a sample of middle-aged sedentary adults with prediabetes.[40] Patients experienced an improved late phase PPG response to an OGTT with HI, but not MI exercise or compared with a no-exercise control group (late phase glucose area under the curve was 13% lower after HI exercise [$P = 0.002$]).[40] In contrast to our findings, Manders et al[41] reported that the prevalence of 24-hour episodes of hyperglycemia (measured by continuous glucose monitoring) was similarly improved after isocaloric acute bouts of HI and MI cycle ergometer exercise (70% vs 35% peak power) in a sample of patients with T2DM.

Studies incorporating 30-second Wingate anaerobic bicycle sprints in which patients were encouraged to go "all out" reported that the low-volume HI interval training rapidly improved carbohydrate metabolism in healthy adults.[19] However, the Wingate protocols used in these studies may not be tolerable or practical for use in prediabetic adults. A recent pilot study examining the effects of a 2-week practical model of low-volume HI interval training in adults with T2DM (10 repetitions at 1-minute intervals performed at 90% $VO_{2\ max}$ with 1-minute recovery) reported that patients experienced significant reductions in 24-hour glycemia and PPG levels after breakfast, lunch, and dinner.[20] Although the patients performed only 6 sessions of interval training during the 2 weeks of the study, the authors observed an increase of approximately 260% in glucose transporter-4 muscle content.[22] Importantly, total training volume in this study was much lower than current ADA recommendations. Currently, these practical models of low-volume interval training have not been compared with traditional endurance training in large scale studies.

## Insulin

Exercise exerts its beneficial effects on T2DM prevention in patients via improvements in skeletal muscle insulin sensitivity. Insulin sensitivity generally improves for $\leq$ 24 to 48 hours after the last bout of exercise[42] and the sensitivity tends to wane over time.[43,44] Because of the transient effects of exercise, the ADA recommends that patients with T2DM should undertake $\geq$ 150 minutes per week of moderate to vigorous aerobic exercise; patients should exercise 3 days per week and the space between bouts of exercise should not be $>$ 2 consecutive days.[45]

Dube et al[46] recently reported that a graded dose-response relationship exists between exercise intensity and improvements in insulin sensitivity. When matched for caloric expenditure, HI exercise appears to be at least as effective as MI exercise for improving insulin sensitivity.[47] DiPietro et al[47] reported a 21% improvement in insulin action for older men and women after patients participated in a 9-month, HI aerobic exercise program (80% of $VO_{2\ max}$) compared with 16% and 8% in the MI and LI intensity groups, respectively. We recently reported that acute HI exercise lowered the late phase postprandial insulin response of patients with prediabetes (~29% lower during a 3-hour OGTT), whereas the reductive effects of MI exercise upon late phase insulin were less pronounced and more variable.[40] Additionally, when compared with a no-exercise control condition, patient insulin sensitivity improved by 51% ($P = 0.02$) and 85% ($P < 0.001$) after acute MI and HI exercise, respectively, when assessed using the oral minimal model.

Recently, low-volume HI interval training was shown to improve insulin action in healthy subjects. Babraj et al[31] showed that a minimal amount of HI exercise protocol (only ~250 kcal of work each week) resulted in improved insulin action in sedentary subjects. Richards et al[48] found that 16 minutes of HI sprint interval exercise during a period of 14 days was sufficient to augment insulin sensitivity in healthy adults. Limited data from 2 small 2-week training interventions suggest that the beneficial effects of insulin sensitivity from low-volume HI interval protocols (eg, repeats of 30-second Wingate anaerobic sprints) also occur in overweight and obese sedentary men.[49,50] Larger sample sizes and longer trials involving prediabetic adults are necessary before Wingate sprint interval programs can be clinically recommended.

Importantly, some studies demonstrate that LI to MI exercise is equally or more effective than HI exercise at improving insulin sensitivity in patients. For example, in the Studies of a Targeted Risk Reduction Intervention Through Defined Exercise (STRRIDE) trial, a low-volume MI training program (≈12 miles of jogging per week) was significantly better at improving insulin sensitivity than a calorically equivalent HI exercise training program in obese and overweight men and women (~85% vs ~40% improvement in insulin sensitivity).[51,52] Interestingly, in the STRRIDE study, a high-volume HI training program approximately equal to 20 miles of jogging per week was only slightly better at improving insulin sensitivity in patients than the low-volume MI training program.[52] The STRRIDE findings support current ACSM/ADA exercise recommendations for diabetes mellitus prevention and suggest that the insulin sensitizing benefits of exercise may be achieved by walking approximately 12 miles per week at an MI level.

## β-cell Function

Several recent studies demonstrated that by the time a patient with prediabetes meets the diagnostic criteria for T2DM, they are near maximally insulin resistant and present with severe β-cell dysfunction (80% less function compared with healthy controls).[53–57] One study suggests that interventions aimed at preventing the progression of IGT to T2DM also demonstrate the efficacy of the programs in preserving β-cell insulin secretory function.[32]

The influence of exercise intensity on β-cell function was studied by Slentz et al,[58] who reported greater improvements in β-cell function; results were modeled from an intravenous glucose tolerance test after 8 weeks of low-volume MI exercise training (14 kcal/kg/week; 40%–55% $VO_{2peak}$) compared with high-volume HI exercise training (23 kcal/kg/week; 65%–80% $VO_{2peak}$) in a sample of sedentary adults. Data from our group suggest that HI exercise acutely improves the disposition index (a marker of β-cell function) to a greater extent than MI exercise in prediabetic adults.[59]

## Lipids

Dietary fat intake acutely augments glucose-stimulated insulin secretion in order to facilitate the storage of fat in adipocytes. Chronic exposure to fat results in impaired glucose-stimulated insulin secretion, most likely due to interference with β-cell glucose metabolism, insulin synthesis, β-cell loss, or defects in calcium channel function.[60] There is a strong correlation between fat deposition around the pancreas and impaired glucose-stimulated insulin secretion and glucose tolerance. For example, Lim et al[61] demonstrated a restoration of first phase insulin secretion that correlated with decreased pancreatic and liver triglyceride stores in a sample of T2DM subjects placed on an ultra-low–calorie diet (600 kcal/day) for 8 weeks.

Independent of patient diet, exercise training has beneficial effects on lipoprotein sub-fractions and triglycerides in patients. Exercise training appears to be most beneficial for treating dyslipidemia in patients with the most atherogenic lipid profiles. In a study of overweight men and women with mild to moderate dyslipidemia, 8 months of exercise training reduced total cholesterol and low-density lipoprotein cholesterol and resulted in an increased high-density lipoprotein cholesterol/total cholesterol ratio.[62] In this study, patients performing the highest amount of HI weekly exercise experienced more beneficial lipoprotein profile effects than other patients.[62] Acute HI exercise has also shown favorable benefits for improving postprandial lipemia in patients. When equated for exercise energy expenditure, Trombold et al[63] reported that HI exercise was more effective than MI exercise (50% vs 90% $VO_{2\,max}$) at lowering postprandial triglycerides and increasing postprandial fat oxidation. However, data in the literature conflicts regarding the effects of the intensity of exercise upon postprandial reductions in lipemia and chronic reductions in lipid sub-fractions.[64–66] It is likely that discrepancies in the various studies are related to prior exercise and dietary control, meal timing, and the energy expended by patients during the exercise bout.

# Exercise Training Intensity and Cardiovascular Adaptations

## Fitness and $VO_{2max}$

Maximal oxygen consumption is the criterion measure of cardiorespiratory fitness and is an independent predictor of mortality.[67] Every increase in fitness of 1 metabolic unit (3.5 ml/kg/min increase in $VO_2$) is associated with high improvements (10%–25%) in patient survival.[68] Regardless of the sample studied, HI exercise has the greatest impact on improving cardiorespiratory fitness in patients.[26,29,30] A review by Swain and Franklin[26] concluded that greater improvements in $VO_{2\,max}$ are observed with HI exercise training compared with MI exercise training when exercise volume is held constant.

A recent meta-analysis that included 10 studies with 273 patients (patients had coronary artery disease, heart failure, hypertension, metabolic syndrome, and obesity) concluded that there was a significantly higher increase in patient $VO_{2peak}$ after HI interval training compared with traditional endurance training (~9.1% increase in fitness, or approximately double the effects typically seen with MI exercise).[69] The studies examined by the meta-analysis included training protocols of HI intervals of 4 minutes with 3-minute active recovery periods, 5 repetitions of 3-minute intervals with 3-minute recovery periods, and 30-second intervals with 60-second recovery periods.

Pioneering studies by the Gibala laboratory[70,71] demonstrated significant increases in markers of mitochondrial biogenesis following acute and chronic HI interval training. A key regulator of oxidative capacity is the peroxisome proliferator-activated receptor-γ coactivator 1α, which plays a role in reducing oxidative stress and inflammation in patients, as well as improving glucose uptake.

## Blood Pressure

Aerobic exercise training reduces resting and daytime ambulatory blood pressure (BP) by approximately 2.4 to 3.0 mm Hg in systolic blood pressure (SBP) and decreases diastolic BP by approximately 3.3 to 3.5 mm Hg.[72] Exercise training reductions in SBP tend to be most pronounced in hypertensive subjects (a decrease of 6.9 mm Hg in SBP and 4.9 mm Hg in diastolic BP).[72] The effects of differing training intensities on BP are equivocal. Cornelissen et al[28] did not find a relationship between BP changes and training intensity in a recent meta-analysis; the authors concluded that HI and MI exercise were equally effective. Additionally, both acute HI and MI exercise demonstrate sufficient reduction in patient BP after exercise (an effect known as post-exercise hypotension). However, a study of 16 stage 1 and 2 non-medicated hypertensive adults by Quinn et al[73] measured BP for a 24-hour period and demonstrated that patients sustained SBP reductions for 13 hours after acute HI exercise (75% of $VO_{2\,max}$) compared with only 4 hours following acute MI exercise (50% of $VO_{2\,max}$).

Limited data suggest that low-volume HI interval exercise may be more beneficial for reducing patient BP compared with traditional endurance training. Molmen-Hansen et al[74] demonstrated an intensity-dependent decrease of 12 mm Hg in 24-hour ambulatory SBP in an interval training group of patients with essential hypertension compared with a decrease of 4.5 mm Hg in an MI training group. In this study, $VO_{2\,max}$ also improved by 15% in the interval training group compared with 5% in the MI training group.

## Endothelial Function

Vascular endothelial dysfunction is a key early event in the process of atherosclerosis. Studies demonstrate that endothelial dysfunction presents at all levels of the arterial tree in prediabetic adults; studies also report that experimental manipulations (eg, free fatty acid or glucose IV infusions) rapidly worsens vascular function.[75–78] Several lines of research support the notion that postprandial dysmetabolism contributes to the pathogenesis of atherosclerosis.[79] Even in healthy people, a single high carbohydrate meal increases the production of reactive oxygen species and nuclear factor κB activation in circulating mononuclear cells in ≤ 2 hours. The deleterious effects associated with the consumption of meals high in carbohydrates or fats are exacerbated in obese, insulin-resistant subjects.[80]

In adults with metabolic syndrome, exercise training improves endothelium dependent vasodilation (FMD) of the brachial artery; results are dependent on the intensity of the exercise.[16,81,82] Tjonna et al[81]studied patients with metabolic syndrome and reported a 9% improvement in brachial artery FMD after 16 weeks of HI exercise compared with a 5% improvement in FMD after isocaloric MI exercise training. The same authors recently demonstrated a sustained improvement in FMD for 72 hours post-exercise in a group of patients who underwent a 16-week aerobic HI interval training intervention compared with 24-hour post-exercise improvement in an MI training group.[16,81]

# Exercise Training Intensity and Weight Loss

Weight loss is poorly maintained long-term when achieved through lifestyle intervention.[83] An important review of the literature by Gaesser et al[84] concluded that lifestyle intervention independent of weight loss resulted in improved cardiometabolic risk for overweight and obese adults at risk for T2DM and cardiovascular disease.

Although exercise training has a variable impact on patient weight loss, studies show that it is a powerful strategy for the loss of abdominal visceral fat.[29,84] Moreover, HI exercise appears to be superior to MI exercise for reducing abdominal visceral fat. For example, in the STRRIDE study, patients in the high-volume HI exercise training group (≈20 miles/week of activity with 1 mile of jogging) had significantly higher reductions in abdominal visceral fat compared with patients in the low-volume MI or low-volume HI exercise training groups.[85] In a sample of obese women with metabolic syndrome, Irving et al[29] showed that 16 weeks of HI exercise training significantly reduced abdominal visceral fat; no significant changes abdominal visceral fat were observed in patients in the LI exercise training or non-exercise control groups.

One advantage to continuous HI exercise training programs that are calorically equivalent to ACSM/ADA guidelines is the potential for patient weight loss. For example, Irving et al[29] reported significant reductions in total abdominal fat, abdominal subcutaneous fat, body mass, and waist circumference in addition to abdominal visceral fat loss. These parameters were not reduced post-training in the control or LI training groups. High-intensity exercise training is a potent stimulator of lipolytic hormones such as growth hormone and epinephrine; these hormones may augment post-exercise energy expenditure, fat oxidation, and lead to a larger energy deficit, all of which favors greater weight loss. It is unlikely that most low-volume minimal HI

**Table 1.** Exercise Training Intensity and Cardiometabolic Risk Reduction in Prediabetic Adults

| Variable | MI Training[a] | HI Training[a] |
|---|---|---|
| Fitness ($VO_{2\ max}$) | ↑ [26,29,30] | ↑↑ [26,29,30,69] |
| Endurance Capacity (Lactate Threshold) | ↑ [29] | ↑↑ [29,70,71] |
| Postprandial Metabolic Control | ↑ [40,41] | ↑ [19,20,40] |
| Insulin Sensitivity | ↑ [40,51,52] | ↑↑ [31,40,46–50] |
| β-Cell Function | ↑/– [58,59] | ↑/– [58,59] |
| Lipid Profile | ↑ [62–66] | ↑ [63] |
| Blood Pressure | ↑ [28,72] | ↑↑ [73,74] |
| Endothelial Function | ↑ [16,81,82] | ↑/– [16,81,82] |
| Weight Loss | ↑ [29,85] | ↑↑ [29,85] |
| Visceral Fat Loss | ↑ [29,85] | ↑↑ [29,85] |

[a]↑, Improved with aerobic exercise training and similar improvements observed with MI training vs HI training; ↑↑, improvements with HI training > MI training; –, no change with training or limited data comparing intensities.
**Abbreviations:** HI, high-intensity; MI, moderate-intensity; $VO_{2\ max}$, maximum oxygen consumption.

exercise protocols would induce significant fat loss due to the low total caloric expenditure; however, this hypothesis has not been tested yet.

## Safety Considerations

Currently, the literature reports no adverse effects of continuous or interval-based HI exercise training. However, most HI exercise training studies are < 6 months in duration; longer trials must be performed to evaluate intervention safety and durability. Early studies using Wingate interval training used extremely strenuous protocols and may not be safe for or well-tolerated by prediabetic adults. Practical models of HI interval training, such as the program with 10 repetitions of 60-second intervals (90% $HR_{max}$) proposed by Little et al[21] or the program of 4 repetitions of 4-minute intervals (90% $HR_{max}$) used by Wisloff et al,[15] have a broader application for treating cardiometabolic risk factors in prediabetes and may be a more tolerable alternative to continuous HI exercise training programs.

## Conclusion

When matched for total energy expenditure, HI exercise is associated with equal or superior improvements in patient metabolic and cardiovascular health compared with LI or MI exercise. Improvements in metabolic control, cardiovascular function, and visceral fat loss resulting from HI exercise also appear to be supported in the literature. Although the vast majority of the cardiometabolic benefits described in our review can be achieved with MI walking, traditional exercise training requires a considerable time commitment from patients. Patients may accrue similar benefits with HI exercise training, which represents a significant decrease in total weekly energy expenditure and may only require patients to exert approximately 250 kcal/week.

Many clinicians have previously discouraged HI exercise based on the premise that patients who are older, obese, or have cardiometabolic risk are unable to exercise at high intensities. However, with the advent of individual parameters of HI exercise, recent studies demonstrated that HI exercise is tolerable in a number of clinical patient populations, such as patients with T2DM, prediabetes, heart failure, and old age.[28,86]

The majority of HI exercise training interventions are short in duration, which represents a significant gap in the literature; short interventions are especially prevalent in studies comparing traditional endurance training with low-volume interval training programs. Long-term studies are warranted to address unknown issues related to the sustainability of HI training programs and whether the long-term adaptations to HI exercise training programs remain superior to MI exercise training over time. Additionally, no studies demonstrate a reduced conversion of prediabetes to T2DM after HI exercise training interventions compared with LI exercise programs or metformin. Although these important studies must be undertaken in the future, the literature contains sufficient data to support HI exercise as a potent and time efficient tool in reducing metabolic risk for patients with prediabetes, particularly for patients with limited time to commit to exercise.

## Conflict of Interest Statement

Corey A. Rynders, PhD, and Arthur Weltman, PhD, disclose no conflicts of interest.

## References

1. Knowler WC, Barrett-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med*. 2002;346(6):393–403.
2. Laaksonen DE, Lindstrom J, Lakka TA, et al. Physical activity in the prevention of type 2 diabetes: the Finnish diabetes prevention study. *Diabetes*. 2005;54(1):158–165.
3. Li GW, Zhang P, Wang JP, et al. The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study. *Lancet*. 2008;371(9626):1783–1789.
4. Tuomilehto J, Lindstrom J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med*. 2001;344(18):1343–1350.
5. Pan XR, Li GW, Hu YH, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. *Diabetes Care*. 1997;20(4):537–544.
6. Eriksson KF, Saltin B, Lindgarde F. Increased skeletal muscle capillary density precedes diabetes development in men with impaired glucose tolerance. A 15-year follow-up. *Diabetes*. 1994;43(6):805–808.
7. American Diabetes Association. Standards of medical care in diabetes–2012. *Diabetes Care*. 2012;35(Suppl 1):S11–S63.
8. Ackermann RT, Finch EA, Brizendine E, Zhou H, Marrero DG. Translating the Diabetes Prevention Program into the community. The DEPLOY Pilot Study. *Am J Prev Med*. 2008;35(4):357–363.

9. Herman WH, Hoerger TJ, Brandle M, et al. The cost-effectiveness of lifestyle modification or metformin in preventing type 2 diabetes in adults with impaired glucose tolerance. *Ann Intern Med*. 2005; 142(5):323–332.
10. Diabetes Prevention Program Research Group. The 10-year cost-effectiveness of lifestyle intervention or metformin for diabetes prevention: an intent-to-treat analysis of the DPP/DPPOS. *Diabetes Care*. 2012;35(4):723–730.
11. Diabetes Prevention Program Research Group, Knowler WC, Fowler SE, et al. 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. *Lancet*. 2009;374(9702):1677–1686.
12. Kimm SY, Glynn NW, McMahon RP, Voorhees CC, Striegel-Moore RH, Daniels SR. Self-perceived barriers to activity participation among sedentary adolescent girls. *Med Sci Sports Exerc*. 2006;38(3):534–540.
13. Trost SG, Owen N, Bauman AE, Sallis JF, Brown W. Correlates of adults' participation in physical activity: review and update. *Med Sci Sports Exerc*. 2002;34(12):1996–2001.
14. Stutts WC. Physical activity determinants in adults. Perceived benefits, barriers, and self efficacy. *AAOHN J*. 2002;50(11):499–507.
15. 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(4):346–354.
16. Tjonna AE, Rognmo O, Bye A, Stolen TO, Wisloff U. Time course of endothelial adaptation after acute and chronic exercise in patients with metabolic syndrome. *J Strength Cond Res*. 2011;25(9):2552–2558.
17. Tjonna AE, Stolen TO, Bye A, et al. Aerobic interval training reduces cardiovascular risk factors more than a multitreatment approach in overweight adolescents. *Clin Sci*. 2009;116(3–4):317–326.
18. Wisloff U, Stoylen A, Loennechen JP, et al. Superior cardiovascular effect of aerobic interval training versus moderate continuous training in heart failure patients: A randomized study. *Circulation*. 2007;115(24):3086–3094.
19. Gibala MJ, McGee SL, Garnham AP, Howlett KF, Snow RJ, Hargreaves M. Brief intense interval exercise activates AMPK and p38 MAPK signaling and increases the expression of PGC-1 alpha in human skeletal muscle. *J Appl Physiol*. 2009;106(3):929–934.
20. Hood MS, Little JP, Tarnopolsky MA, Myslik F, Gibala MJ. Low-volume interval training improves muscle oxidative capacity in sedentary adults. *Med Sci Sports Exerc*. 2011;43(10):1849–1856.
21. Little JP, Safdar A, Wilkin GP, Tarnopolsky MA, Gibala MJ. A practical model of low-volume high-intensity interval training induces mitochondrial biogenesis in human skeletal muscle: potential mechanisms. *J Physiol*. 2010;588(Pt 6):1011–1022.
22. Little JP, Gillen JB, Percival ME, et al. Low-volume high-intensity interval training reduces hyperglycemia and increases muscle mitochondrial capacity in patients with type 2 diabetes. *J Appl Physiol*. 2011;111(6):1554–1560.
23. Boule NG, Kenny GP, Haddad E, Wells GA, Sigal RJ. Meta-analysis of the effect of structured exercise training on cardiorespiratory fitness in Type 2 diabetes mellitus. *Diabetologia*. 2003;46(8):1071–1081.
24. Bartlett JD, Close GL, MacLaren DP, Gregson W, Drust B, Morton JP. High-intensity interval running is perceived to be more enjoyable than moderate-intensity continuous exercise: implications for exercise adherence. *J Sports Sci*. 2011;29(6):547–553.
25. Garber CE, Blissmer B, Deschenes MR, et al; American College of Sports Medicine. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: Guidance for prescribing exercise. *Med Sci Sports Exerc*. 2011;43(7):1334–1359.
26. Swain DP, Franklin BA. Comparison of cardioprotective benefits of vigorous versus moderate intensity aerobic exercise. *Am J Cardiol*. 2006;97(1):141–147.
27. Tyldum GA, Schjerve IE, Tjonna AE, et al. Endothelial dysfunction induced by post-prandial lipemia: Complete protection afforded by high-intensity aerobic interval exercise. *J Am Coll Cardiol*. 2009;53(2): 200–206.
28. Molmen-Hansen HE, Stolen T, Tjonna AE, et al. Aerobic interval training reduces blood pressure and improves myocardial function in hypertensive patients. *Eur J Cardiovasc Prev Rehabil*. 2012;19(2):151–160.
29. Irving BA, Davis CK, Brock DW, et al. Effect of exercise training intensity on abdominal visceral fat and body composition. *Med Sci Sports Exerc*. 2008;40(11):1863–1872.
30. Gormley SE, Swain DP, High R, et al. Effect of intensity of aerobic training on VO2 max. *Med Sci Sports Exerc*. 2008;40(7):1336–1343.
31. Babraj JA, Vollaard NB, Keast C, Guppy FM, Cottrell G, Timmons JA. Extremely short duration high intensity interval training substantially improves insulin action in young healthy males. *BMC Endocr Disord*. 2009;9:8.
32. DeFronzo RA, Abdul-Ghani MA. Preservation of beta-cell function: the key to diabetes prevention. *J Clin Endocrinol Metab*. 2011; 96(8):2354–2366.
33. Coutinho M, Gerstein HC, Wang Y, Yusuf S. The relationship between glucose and incident cardiovascular events. A metaregression analysis of published data from 20 studies of 95,783 individuals followed for 12.4 years. *Diabetes Care*. 1999;22(2):233–240.
34. No authors listed. Glucose tolerance and mortality: comparison of WHO and American Diabetes Association diagnostic criteria. The DECODE study group. European Diabetes Epidemiology Group. Diabetes epidemiology: Collaborative analysis of diagnostic criteria in Europe. *Lancet*. 1999;354(9179):617–621.
35. Decode Study Group, European Diabetes Epidemiology Group. Glucose tolerance and cardiovascular mortality: Comparison of fasting and 2-hour diagnostic criteria. *Arch Intern Med*. 2001;161(3):397–405.
36. Monnier L, Colette C, Dunseath GJ, Owens DR. The loss of postprandial glycemic control precedes stepwise deterioration of fasting with worsening diabetes. *Diabetes Care*. 2007;30(2):263–269.
37. Manders RJF, Pennings B, Beckers CPG, Aipassa TI, van Loon LJC. Prevalence of daily hyperglycemia in obese type 2 diabetic men compared with that in lean and obese normoglycemic men: effect of consumption of a sucrose-containing beverage. *Am J Clin Nutr*. 2009;90(3):511–518.
38. King DS, Baldus PJ, Sharp RL, Kesl LD, Feltmeyer TL, Riddle MS. Time course for exercise-induced alterations in insulin action and glucose tolerance in middle-aged people. *J Appl Physiol*. 1995;78(1):17–22.
39. O'Gorman DJ, Del Aguila LF, Williamson DL, Krishnan RK, Kirwan JP. Insulin and exercise differentially regulate PI3-kinase and glycogen synthase in human skeletal muscle. *J Appl Physiol*. 2000;89(4):1412–1419.
40. Rynders CA, Weltman JY, Jiang B, et al. Effects of exercise intensity on postprandial improvement in glucose disposal and insulin sensitivity in prediabetic adults [published online ahead of print November 15, 2013]. *J Clin Endocrinol Metab*. doi:10.1210/jc.2013–2687.
41. Manders RJ, Van Dijk JW, van Loon LJ. Low-intensity exercise reduces the prevalence of hyperglycemia in type 2 diabetes. *Med Sci Sports Exerc*. 2010;42(2):219–225.
42. Mikines KJ, Sonne B, Farrell PA, Tronier B, Galbo H. Effect of physical exercise on sensitivity and responsiveness to insulin in humans. *Am J Physiol*. 1988;254(3):E248–E259.
43. Perseghin G, Price TB, Petersen KF, et al. Increased glucose transport-phosphorylation and muscle glycogen synthesis after exercise training in insulin-resistant subjects. *N Engl J Med*. 1996;335(18):1357–1362.
44. Larsen JJ, Dela F, Kjaer M, Galbo H. The effect of moderate exercise on postprandial glucose homeostasis in NIDDM patients. *Diabetologia*. 1997;40(4):447–453.
45. Colberg SR, Albright AL, Blissmer BJ, et al; American College of Sports Medicine; American Diabetes Association. 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(12):2282–2303.
46. Dube JJ, Allison KF, Rousson V, Goodpaster BH, Amati F. Exercise dose and insulin sensitivity: relevance for diabetes prevention. *Med Sci Sports Exerc*. 2012;44(5):793–799.
47. DiPietro L, Dziura J, Yeckel CW, Neufer PD. Exercise and improved insulin sensitivity in older women: evidence of the enduring benefits of higher intensity training. *J Appl Physiol*. 2006;100(1):142–149.

48. 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(Pt 15):2961–2972.
49. Hood MS, Little JP, Tarnopolsky MA, Myslik F, Gibala MJ. Low-volume interval training improves muscle oxidative capacity in sedentary adults. *Med Sci Sports Exerc*. 2011;43(10):1849–1856.
50. Whyte LJ, Gill JM, Cathcart AJ. Effect of 2 weeks of sprint interval training on health-related outcomes in sedentary overweight/obese men. *Metabolism*. 2010;59(10):1421–1428.
51. Johnson JL, Slentz CA, Houmard JA, et al. Exercise training amount and intensity effects on metabolic syndrome (from Studies of a Targeted Risk Reduction Intervention through Defined Exercise). *Am J Cardiol*. 2007;100(12):1759–1766.
52. Houmard JA, Tanner CJ, Slentz CA, Duscha BD, McCartney JS, Kraus WE. Effect of the volume and intensity of exercise training on insulin sensitivity. *J Appl Physiol*. 2004;96(1):101–106.
53. Abdul-Ghani MA, Jenkinson CP, Richardson DK, Tripathy D, DeFronzo RA. Insulin secretion and action in subjects with impaired fasting glucose and impaired glucose tolerance: Results from the Veterans Administration Genetic Epidemiology Study. *Diabetes*. 2006;55(5):1430–1435.
54. Abdul-Ghani MA, Lyssenko V, Tuomi T, DeFronzo RA, Groop L. The shape of plasma glucose concentration curve during OGTT predicts future risk of type 2 diabetes. *Diabetes Metab Res Rev*. 2010;26(4):280–286.
55. Abdul-Ghani MA, Tripathy D, DeFronzo RA. Contributions of beta-cell dysfunction and insulin resistance to the pathogenesis of impaired glucose tolerance and impaired fasting glucose. *Diabetes Care*. 2006;29(5):1130–1139.
56. Ferrannini E, Gastaldelli A, Miyazaki Y, Matsuda M, Mari A, DeFronzo RA. Beta-cell function in subjects spanning the range from normal glucose tolerance to overt diabetes: A new analysis. *J Clin Endocrinol Metab*. 2005;90(1):493–500.
57. DeFronzo RA. From the triumvirate to the ominous octet: A new paradigm for the treatment of type 2 diabetes mellitus. *Diabetes*. 2009;58(4):773–795.
58. Slentz CA, Tanner CJ, Bateman LA, et al. Effects of exercise training intensity on pancreatic beta-cell function. *Diabetes Care*. 2009;32(10):1807–1811.
59. Rynders CA, Chan A, Weltman JY, Barrett EJ, Weltman A. Effects of isocaloric moderate- and high intensity exercise on glucose disposal and beta-cell function. Abstract presented at: Experimental Biology Meeting; April 21–25, 2012; San Diego, CA.
60. Ashcroft Frances M, Rorsman P. Diabetes mellitus and the beta-cell: The last ten years. *Cell*. 2012;148(6):1160–1171.
61. Lim EL, Hollingsworth KG, Aribisala BS, Chen MJ, Mathers JC, Taylor R. Reversal of type 2 diabetes: normalisation of beta cell function in association with decreased pancreas and liver triacylglycerol. *Diabetologia*. 2011;54(10):2506–2514.
62. Kraus WE, Houmard JA, Duscha BD, et al. Effects of the amount and intensity of exercise on plasma lipoproteins. *N Engl J Med*. 2002;347(19):1483–1492.
63. Trombold JR, Christmas KM, Machin DR, Kim IY, Coyle EF. Acute high-intensity endurance exercise is more effective than moderate-intensity exercise for attenuation of postprandial triglyceride elevation. *J Appl Physiol*. 2013;114(6):792–800.
64. Altena TS, Michaelson JL, Ball SD, Guilford BL, Thomas TR. Lipoprotein subfraction changes after continuous or intermittent exercise training. *Med Sci Sports Exerc*. 2006;38(2):367–372.
65. Altena TS, Michaelson JL, Ball SD, Thomas TR. Single sessions of intermittent and continuous exercise and postprandial lipemia. *Med Sci Sports Exerc*. 2004;36(8):1364–1371.
66. Paton CM, Brandauer J, Weiss EP, et al. Hemostatic response to postprandial lipemia before and after exercise training. *J Appl Physiol*. 2006;101(1):316–321.
67. Blair SN, Morris JN. Healthy hearts—and the universal benefits of being physically active: physical activity and health. *Ann Epidemiol*. 2009;19(4):253–256.
68. Kaminsky LA, Arena R, Beckie TM, et al; American Heart Association Advocacy Coordinating Committee; Council on Clinical Cardiology; Council on Nutrition, Physical Activity and Metabolism. The importance of cardiorespiratory fitness in the United States: the need for a national registry: a policy statement from the American Heart Association. *Circulation*. 2013;127(5):652–662.
69. Weston KS, Wisloff U, Coombes JS. High-intensity interval training in patients with lifestyle-induced cardiometabolic disease: a systematic review and meta-analysis [published online ahead of print October 21, 2013]. *Br J Sports Med*. doi:10.1136/bjsports-2013–092576.
70. Gibala M. Molecular responses to high-intensity interval exercise. *Appl Physiol Nutr Metab*. 2009;34(3):428–432.
71. Gibala MJ, McGee SL. Metabolic adaptations to short-term high-intensity interval training: a little pain for a lot of gain? *Exerc Sport Sci Rev*. 2008;36(2):58–63.
72. Cornelissen VA, Fagard RH. Effects of endurance training on blood pressure, blood pressure-regulating mechanisms, and cardiovascular risk factors. *Hypertension*. 2005;46(4):667–675.
73. Quinn TJ. Twenty-four hour, ambulatory blood pressure responses following acute exercise: impact of exercise intensity. *J Hum Hypertens*. 2000;14(9):547–553.
74. Molmen-Hansen HE, Stolen T, Tjonna AE, et al. Aerobic interval training reduces blood pressure and improves myocardial function in hypertensive patients. *Eur J Cardiovasc Prev Rehabil*. 2012;19(2):151–160.
75. Steinberg HO, Paradisi G, Hook G, Crowder K, Cronin J, Baron AD. Free fatty acid elevation impairs insulin-mediated vasodilation and nitric oxide production. *Diabetes*. 2000;49(7):1231–1238.
76. Tripathy D, Mohanty P, Dhindsa S, et al. Elevation of free fatty acids induces inflammation and impairs vascular reactivity in healthy subjects. *Diabetes*. 2003;52(12):2882–2887.
77. de Jongh RT, Serne EH, Ijzerman RG, de Vries G, Stehouwer CD. Free fatty acid levels modulate microvascular function: relevance for obesity-associated insulin resistance, hypertension, and microangiopathy. *Diabetes*. 2004;53(11):2873–2882.
78. Liu Z, Liu J, Jahn LA, Fowler DE, Barrett EJ. Infusing lipid raises plasma free fatty acids and induces insulin resistance in muscle microvasculature. *J Clin Endocrinol Metab*. 2009;94(9):3543–3549.
79. Ceriello A, Esposito K, Piconi L, et al. Oscillating glucose is more deleterious to endothelial function and oxidative stress than mean glucose in normal and type 2 diabetic patients. *Diabetes*. 2008;57(5):1349–1354.
80. Patel C, Ghanim H, Ravishankar S, et al. Prolonged reactive oxygen species generation and nuclear factor-kappaB activation after a high-fat, high-carbohydrate meal in the obese. *J Clin Endocrinol Metab*. 2007;92(11):4476–4479.
81. Tjonna AE, Rognmo O, Bye A, Stolen TO, Wisloff U. Time course of endothelial adaptation after acute and chronic exercise in patients with metabolic syndrome. *J Strength Cond Res*. 2011;25(9):2552–2558.
82. Walsh JH, Bilsborough W, Maiorana A, et al. Exercise training improves conduit vessel function in patients with coronary artery disease. *J Appl Physiol*. 2003;95(1):20–25.
83. Anderson JW, Konz EC, Frederich RC, Wood CL. Long-term weight-loss maintenance: a meta-analysis of US studies. *Am J Clin Nutr*. 2001;74(5):579–584.
84. Gaesser GA, Angadi SS, Sawyer BJ. Exercise and diet, independent of weight loss, improve cardiometabolic risk profile in overweight and obese individuals. *Phys Sportsmed*. 2011;39(2):87–97.
85. Bateman LA, Slentz CA, Willis LH, et al. Comparison of aerobic versus resistance exercise training effects on metabolic syndrome (from the Studies of a Targeted Risk Reduction Intervention Through Defined Exercise—STRRIDE-AT/RT). *Am J Cardiol*. 2011;108(6):838–844.
86. Wisloff U, Ellingsen O, Kemi OJ. High-Intensity Interval Training to Maximize Cardiac Benefits of Exercise Training? *Exerc Sport Sci Rev*. 2009;37(3):139–146.