Management & prevention of type 2 diabetes

Bend it, stretch it: Achieving exercise benefits at home

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Engaging in exercise helps individuals stay fit and helps prevent weight gain. A large amount of exercise can also promote weight loss, but evidence suggests reducing caloric intake is an "easier" route to weight loss (Logue et al, 2010). Several large trials have shown lifestyle changes incorporating a reduction in calories and an increase in exercise can help prevent type 2 diabetes in those at increased risk (Gillies et al, 2007). However, there are few well-controlled trials addressing the metabolic benefits of such interventions among people with type 2 diabetes, in particular testing the value of different forms of exercise (i.e. aerobic vs resistance).

With this in mind, Church et al (2010; summarised alongside) compared changes in HbA_{1c} levels over 9 months among people with type 2 diabetes randomised to aerobic training alone, resistance training alone, or a combination of both. Baseline characteristics of the participants (average age, 56 years; average BMI, 35 kg/m^2) and baseline medication history was not too different from that which could be expected in the average type 2 diabetes clinic.

Resistance training included upper (e.g. bench presses) and lower (e.g. leg presses, extension and flexion) body exercises, as well as abdominal crunches and back exercises. Of note, all exercises were supervised and intervention groups were broadly equivalent in energy expended.

The group randomised to both aerobic and resistance training fared best, achieving a modest but significant reduction in HbA_{1c} (–0.34% overall) compared with a comparator non-exercise control group. Changes in HbA_{1c} were more impressive in those with baseline HbA_{1c} level >7% (>53 mmol/mol), where HbA_{1c} fell by around 0.5% in both the aerobic exercise alone group and in the combined exercise group. There were accompanying small, albeit significant, reductions in weight, improved fitness and increase in lean body mass in the combined exercise group. Furthermore, such interventions seemed to be generally safe. Overall, the study supports the use of resistance training by people with type 2 diabetes as part of their regular exercise regimen.

But what do the results mean for real-life clinical practice where resources to conduct supervised exercise are very limited? Of course, getting our patients to sustain any form of exercise is difficult and we appreciate that only a motivated minority undertake recommended levels of exercise. Nevertheless, the results of this study suggest that resistance training – some forms of which can be adapted and undertaken by most people in the safety of their homes – could be emphasised along with aerobic exercise. Indeed, for reasons of convenience, it may be that resistance training has the potential to be sustained for longer than aerobic exercise (although, ideally, a combination of both is best).

> *"... for reasons of convenience, it may be that resistance training has the potential to be sustained for longer than aerobic exercise."*

Two interesting follow-ups to Church et al's study would be to: (i) develop a chart that details simple resistance exercises that can be done at home; and (ii) determine to what extent resistance training can lower the risk of developing type 2 diabetes beyond established lifestyle interventions in those at risk.

Logue J, Thompson L, Romanes F et al (2010) Management of obesity: summary of SIGN guideline. *BMJ* **340**: c154

Gillies CL, Abrams KR, Lambert PC et al (2007) Pharmacological and lifestyle interventions to prevent or delay type 2 diabetes in people with impaired glucose tolerance: systematic review and meta-analysis. *BMJ* **334**: 299

JAMA

Aerobic exercise with resistance training improves HbA_{1c}

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 It is well known that regular exercise improves glycaemic control in people with T2D.

2 The authors examined the benefits of aerobic exercise alone, resistance training alone and both in combination on HbA_{1c} in 262 sedentary people with T2D (mean age of 55.8 years; mean baseline HbA_{1c} level 7.7% [61 mmol/mol]).

3 Participants were randomised to receive aerobic exercise expending 12 kcal/kg per week (n=72), resistance training 3 days per week (n=73), a combination of aerobic exercise expending 10 kcal/kg per week and resistance training 2 days per week (n=76) or to a control group undertaking no exercise (n=41) for 9 months.

4 The primary outcome measure was change in HbA_{1c}.

5 Compared with the control group, the mean change in HbA_{1c} level in the aerobic exercise group was –0.24% (95% confidence interval [CI], –0.55% to 0.07%; P=0.14) and in the resistance training group was –0.16%, (95% CI, –0.46% to 0.15%; P=0.32), which were both nonsignificant.

6 Compared with the control group, the mean change in HbA_{1c} in the combination exercise group was –0.34% (95% CI, –0.64% to –0.03%; P=0.03), which was a significant improvement.

7 The authors concluded that both aerobic exercise and resistance training provide health benefits to people with T2D, but only a combination of these exercises reduces HbA_{1c} levels.

Church TS, Blair SN, Cocreham S et al (2010) Effects of aerobic and resistance training on haemoglobin A_{1c} levels in patients with type 2 diabetes. *JAMA* **304**: 2253–62

DIABETES CARE

Excess liver fat common in women with history of GD

Readability	✓✓✓
Applicability to practice	✓✓
WOW! factor	✓✓✓

1 It is known that women with a history of gestational diabetes (GD) have elevated ectopic lipids and diabetes risk.

2 This study investigated whether deteriorated energy metabolism contributed to these abnormalities in a group of 23 glucose-tolerant non-obese women with a history of GD (hGD) and eight women with normal glucose metabolism during pregnancy of similar age, BMI and activity levels.

3 Participants underwent oral glucose tolerance tests (OGTT; <463 mL/min(–1)/m^2 indicative of insulin resistance) and intravenous glucose tolerance tests at 4–5 years after delivery. hGD participants were further stratified into insulin-resistant (hGD-IR) and insulin-sensitive (hGD-IS) groups.

4 hGD women had 36% higher fat mass and 12% lower insulin sensitivity than non-hGD women.

5 Intramyocellular lipids were 61% and 69% higher in hGD-IR (P<0.05 vs hGD-IS) and insulin resistant women (P<0.003 vs insulin sensitive), respectively. Hepatocellular lipids were doubled (P<0.05) in hGD and insulin resistant women, and correlated positively with body fat mass (r=0.50; P<0.01) and inversely with insulin sensitivity (r=–0.46; P<0.05).

6 The authors concluded that the alteration of hepatic lipid storage in women with hGD represents an early and predominant abnormality in this cohort.

Prikoszovich T, Winzer C, Schmid AI et al (2011) Body and liver fat mass rather than muscle mitochondrial function determines glucose metabolism in women with a history of gestational diabetes. *Diabetes Care* [Epub ahead of print]

DIABETES CARE

Improved diabetes risk prediction using 40 SNPs, but only in people <50 years

Readability	✓✓✓✓
Applicability to practice	✓✓
WOW! factor	✓✓

1 Predicted risk of T2D was ascertained using an updated genetic risk score comprising 40 common diabetes-associated single nucleotide polymorphisms (SNPs).

2 Data from the Framingham Offspring Study included 3471 people with available genetic data who were followed over 34 years; the mean genetic risk score was compared for those who did versus those who did not develop T2D, stratified by age (< and ≥50 years).

3 The mean age of the study sample was 36±9 years at baseline; 446 people were diagnosed with T2D during follow-up (144 were <50 years; 302 were ≥50 years).

4 Prediction of diabetes was improved using the 40 diabetes-associated SNPs in those <50 years; the authors concluded that genetic information has the potential to improve prediction of T2D beyond classic risk factors in younger individuals.

de Miguel-Yanes JM, Shrader P, Pencina MJ et al (2011) Genetic risk reclassification for type 2 diabetes by age below or above 50 years using 40 type 2 diabtes risk single nucleotide polymorphisms. *Diabetes Care* **34**: 121–5

DIABETOLOGIA

Mean glycaemia and HbA$_{1c}$ best correlates to CVD risk factors

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓✓

1 The place of postprandial hyperglycaemia and glucose variability in relation to the risk of cardiovascular disease (CVD) and mortality is uncertain in diabetes.

2 The authors examined the association between indices of glycaemia measured during daily activities and metabolic CVD risk factors.

3 In total, 268 people with T1D and 159 people with T2D underwent intensive continuous glucose monitoring and self-monitoring of blood glucose for 16 weeks; associations between glycaemic indices and known CVD risk factors were determined.

4 In both T1D and T2D, average glycaemia showed the strongest association with CVD risk factors. By contrast, fasting glucose levels, postprandial glucose levels and glucose variability were found to be weaker correlates to CVD risk factors.

Borg R, Kuenen JC, Carstensen B et al (2011) HbA$_{1c}$ and mean blood glucose show stronger associations with cardiovascular disease risk factors than do postprandial glycaemia or glucose variability in persons with diabetes. *Diabetologia* **54**: 69–72

DIABETES CARE

High systolic but low diastolic BP associated with greater CVD risk

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓✓

1 The study aim was to determine whether blood pressure (BP; systolic BP [SBP], diastolic BP [DBP], or both) could predict cardiovascular disease (CVD) events in 1791 people with T2D and hypertension as part of the VADT.

2 Participants received either standard or intensive glycaemic therapy with stepped treatment to maintain BP <130/80 mmHg; results were analysed to determine associations with CVD risk.

3 The risk of CVD was significantly increased with a SBP ≥140 mmHg and increased with a DBP <70 mmHg.

4 The authors concluded that there is a need to focus more on reducing systolic hypertension in T2D.

Anderson RJ, Bahn GD, Moritz TE et al (2011) Blood pressure and cardiovascular disease risk in the Veterans Affairs Diabetes Trial. *Diabetes Care* **34**: 34–8 [Epub November 2010]

"The risk of cardiovascular disease was significantly increased with a systolic blood pressure ≥140 mmHg and increased with a diastolic blood pressure <70 mmHg."

"HDL-cholesterol <1.0 mmol/L was associated with an increased risk of cancer in people not taking metformin, but this was not significant in people treated with metformin."

DIABETES CARE

Metformin reduces cancer risk in T2D and low HDL-cholesterol

Readability	✓✓✓
Applicability to practice	✓✓
WOW! factor	✓✓✓✓

1 People with T2D are at increased risk of cancer, possibly associated with low HDL-cholesterol; however, treatment with metformin may reduce cancer risk.

2 HDL-cholesterol and metformin activate the adenosine monophosphate-activated protein kinase pathway, which plays an important role in regulating energy metabolism.

3 The study hypothesis was that the anti-cancer effects of metformin would be most evident in people with T2D and low HDL-cholesterol.

4 Participants comprised 2658 people (median age 56 years) with T2D from the Hong Kong Diabetes Registry; none had cancer or were treated with metformin at study entry.

5 The outcome measure was incident cancer during follow-up (13 808 person-years; median follow-up, 5.51 years).

6 During follow up, 129 people developed cancer.

7 HDL-cholesterol <1.0 mmol/L was associated with an increased risk of cancer in people not taking metformin, but this was not significant in people treated with metformin; analyses showed an interactive effect of not using metformin and HDL-cholesterol <1.0 mmol/L on the risk of cancer.

8 The authors concluded that the anti-cancer effect of metformin was most evident in people with T2D and low HDL-cholesterol.

Yang X, So WY, Ma RCW et al (2010) Low HDL cholesterol, metformin use and cancer risk in type 2 diabetes: the Hong Kong Diabetes Registry. *Diabetes Care* [epub ahead of print]

DIABETES

Accurate prediction of GD possible in first trimester

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 Predicting which women will develop gestational diabetes (GD) is currently based on maternal history (approximately 60% detection rate for a 40% false-positive rate).

2 The authors sought to improve current GD predictive ability using routinly collected demographic and clinical variables and novel parameters.

3 This nested case-control study comprised women in their first trimester who developed GD (n=124) and those who did not (n=248).

4 Data obtained included age, BMI, ethnicity, smoking, previous GD, family history of diabetes and blood pressure; biochemical measures included routine tests (lipids, high-sensitivity C-reactive protein, gamma-glutamyltransferase) and novel parameters (adiponectin, E-selectin and tissue plasminogen activator [t-PA]).

5 Compared with controls, women who developed GD were older, had higher BMIs, were more likely to be of Asian origin, had a family history of GD or T2D and had higher systolic blood pressure (P<0.05).

6 Receiver operator area under the curve for simple clinical measure was 0.824 improving to 0.861 with the addition of blood tests.

7 The authors were able to predict GD with high levels of accuracy using simple maternal demographic and clinical characteristics. They also found that beyond the panel of routinely collected clinical data, inclusion of lipid (HDL-cholesterol) and t-PA markers improved GD prediction.

Savvidou M, Nelson SM, Makgoba M et al (2010) First-trimester prediction of gestational diabetes mellitus: examining the potential of combining maternal characteristics and laboratory measures. *Diabetes* **59**: 3017–22

DIABETOLOGIA

Diet rich in low-GI fruit reduces HbA_{1c}, blood pressure and CHD risk

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓✓

1 Fruit containing natural sugar has a low glycaemic index (GI) and in the present study the authors examined the benefits of low-GI fruit (e.g. apples, pears, citrus fruit, berries) consumption on glycaemic control and CHD risk factors in people with T2D.

2 In total, 201 people with T2D (men and postmenopausal women; on oral agents stable for the previous 3 months) were randomised to a low-GI diet or high-cereal fibre diet for 6 months; the main outcome measure was HbA_{1c} level, with CHD risk as a secondary measure. Study and dietary records for both pretreatment and study end were available for 152 participants, who were the analysis group.

3 By study end, participants on the low-GI diet increased their low-GI fruit intake from 0.7 to 1.3 servings per day; people on the high-cereal fibre diet ate less low-GI fruit (0.8 to 0.3 servings per day).

4 Reductions in HbA_{1c} levels were significantly associated with increased low-GI fruit intake (P=0.011), as were reductions in systolic blood pressure (P=0.024) and CHD risk (P=0.008).

5 Low-GI fruit intake significantly reduced HbA_{1c}, systolic blood pressure and CHD risk in the present study and the authors called for further research to determine optimal levels of fruit consumption to improve glycaemic control among people with T2D.

Jenkins DJA, Srichaikul K, Kendall CWC et al (2010) The relation of low glycaemic index fruit consumption to glycaemic control and risk factors for coronary heart disease in type 2 diabetes. *Diabetologia* [epub ahead of print]