Major journals

Does increased physical activity reduce cardiovascular risk in people with impaired glucose tolerance?

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Clinical trials have previously shown that lifestyle interventions can effectively reduce the risk of high-risk individuals with impaired glucose tolerance (IGT) developing type 2 diabetes. In addition, lifestyle interventions in such a setting have also been shown to be cost effective (Tuomilehto et al, 2001; Knowler et al, 2002); consequently, lifestyle modifications have become a cornerstone of any diabetes prevention programme.

However, whether lifestyle modifications affect the risk of cardiovascular disease (CVD) in individuals with IGT is unclear since previous diabetes prevention trials were not designed to assess this outcome.

Observational studies (e.g. Li and Siegrist, 2012) have, however, consistently shown that higher levels of physical activity or cardiorespiratory fitness are associated with a lower risk of cardiovascular events. Unfortunately though, such data are plagued by limitations; for example, the measurement of physical activity is usually achieved by self-reporting (which has poor validity, particularly when assessing habitual or total physical activity levels). Furthermore, cardiorespiratory fitness, even when measured objectively, is affected by factors beyond physical activity, such as genetic makeup, which also affect the cardiovascular risk of an individual. Along with practical limitations around the measurement of physical activity, the extent to which change in physical activity can act to ameliorate the risk of CVD in individuals already displaying IGT and other cardiovascular risk factors is also unknown.

The study by Yates et al (summarised alongside) analysed prospective data from the NAVIGATOR (Nateglinide and Valsartan in Impaired Glucose Tolerance Outcomes Research) trial to evaluate the association between (1) baseline levels of daily ambulatory activity and (2) change in ambulatory activity over time with subsequent cardiovascular risk in individuals with IGT and either pre-existing CVD or at least one additional cardiovascular risk factor. In total, over 9300 individuals with IGT were recruited in 40 countries over 2 years.

The authors found that baseline ambulatory activity and change in ambulatory activity over 12 months were both independently associated with the risk of a cardiovascular event in the ensuing 5 years. Specifically, every 2000 step per day increment in ambulatory activity at baseline was associated with a 10% lower risk of a cardiovascular event. Furthermore, each 2000 step per day change from baseline to 12 months was associated with an additional 8% difference in the cardiovascular event rate. This difference was unaffected when further adjusted for change in BMI and other potential confounding factors at 12 months. Results were not modified by sex, age, level of baseline activity, or pre-existing CVD.

This is the first study to fully assess the relationship between daily ambulatory activity and cardiovascular events in a high-risk group. As such, it has several strengths. First, the analysis was adjusted for a comprehensive list of possible confounding variables, both at baseline and 12 months. Second, the trial recruited a study population from 40 countries, and, as such, the data can represent a truly global perspective. Third, the large study cohort was recruited over a relatively short time-frame, thus, minimising the possibility of temporal factors affecting the results.

The main limitation of this study was the large amount of missing pedometer data at baseline and 12 months, which the authors addressed by using rigorous multiple imputation techniques. Sensitivity analysis revealed no meaningful difference between the modelled estimates and the complete data sets. Anecdotally, since walking is the most popular form of increased physical activity expressed by many patients in the clinic, the results of this analysis provide evidence that even small amounts of increased daily walking can result in significant cardiovascular health benefits. ■

Knowler WC, Barrett-Connor E, Fowler SE et al (2002) *N Engl J Med* **346**: 393–403
Li J and Siegrist J (2012) *Int J Environ Res Public Health* **9**: 391–407
Tuomilehto J, Lindström J, Eriksson JG et al (2001) *N Engl J Med* **344**: 1343–50

The Lancet

Daily ambulatory activity reduces cardiovascular risk in people with IGT

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓✓

1 Data from the NAVIGATOR (Nateglinide and Valsartan in Impaired Glucose Tolerance Outcomes Research) trial were used to explore the relationship between daily ambulatory activity and cardiovascular (CV) events in people with high CV risk and impaired glucose tolerance (IGT).

2 In total, 9306 individuals over 50 years of age were recruited from 40 countries between January 2002 and January 2004. Participants were followed for an average of 6 years and the primary end-point was a CV event (defined as cardiovascular mortality, non-fatal stroke, or myocardial infarction).

3 Ambulatory activity was measured by a pedometer for 7 days, and participants also completed a log book of steps taken each day.

4 During 45 211 person-years, 531 CV events occurred. Baseline ambulatory activity and the change in activity over a year were both associated with a reduced risk of CV events.

5 Every 2000 step-per-day (equivalent to 20 minutes a day of moderately paced walking) increment in ambulatory activity at baseline was associated with a 10% lower risk of a CV event.

6 Also, each 2000 step-per-day change from baseline to 1 year was associated with an additional 8% reduction in the CV event rate.

7 The authors conclude by highlighting the importance of maintaining physical activity levels.

Yates T, Haffner SM, Schulte PJ et al (2014) Association between change in daily ambulatory activity and cardiovascular events in people with impaired glucose tolerance (NAVIGATOR trial): a cohort analysis. *Lancet* **383**: 1059–66

The Lancet

Comparison of acute coronary survival in Sweden and the UK

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓✓

1 Researchers assessed the differences in care, management and outcomes for acute coronary syndrome between Sweden and the UK.

2 The primary outcome was all-cause mortality 30 days after hospital admission for acute myocardial infarction.

3 Data for 119 786 Swedish and 391 077 UK participants who were admitted between 2004 and 2010 were used. The 30-day mortality was 7.6% (95% confidence interval [CI], 7.4–7.7%) in Sweden and 10.5% (95% CI, 10.4–10.6%) in the UK.

4 After analysis, the proportion of people with ST-segment-elevation myocardial infarction (STEMI) was lower in Sweden than in the UK (32% vs 40%). However, total reperfusion for STEMI and fibrinolysis treatment were both more common in the UK.

5 In Sweden, there was earlier and more extensive uptake of primary percutaneous coronary interventions (PCI) compared to the UK (59% vs 22%). There was also a lag over time in the uptake of primary PCI in the UK.

6 Specifically, there was more frequent use of beta-blockers at discharge in Sweden compared to the UK (89% vs 78%).

7 After casemix standardisation, the 30-day mortality ratio for UK versus Sweden was 1.37 (95% CI, 1.30–1.45), which corresponds to 11 263 excess deaths in the UK. However, this did decline over time.

8 These are clinically important differences that highlight where the UK can improve the delivery of acute coronary syndrome care and prevent avoidable deaths.

Chung SC, Gedeborg R, Nicholas O et al (2014) Acute myocardial infarction: a comparison of short-term survival in national outcome registries in Sweden and the UK. *Lancet* **383**: 1305–12

BMJ

Cardiovascular drugs may increase risk of new-onset diabetes

Readability	✓✓✓✓
Applicability to practice	✓✓✓
WOW! Factor	✓✓✓✓

1 In a reanalysis of data from the NAVIGATOR (Nateglinide and Valsartan in Impaired Glucose Tolerance Outcomes Research) trial, the authors examined the degree to which beta-blockers, statins and thiazide diuretics in people with impaired glucose tolerance are associated with new-onset diabetes (NOD).

2 Participants were selected if they were not receiving any of these treatments at baseline (calcium blockers were a metabolically neutral control).

3 During the median 5 years of follow-up, some participants started the drug treatments.

4 After adjusting for baseline characteristics, diuretics and statins were both significantly associated with an increased risk of NOD. Beta-blockers and calcium channel blockers were not associated with NOD.

Shen L, Shah BR, Reyes EM (2013) Role of diuretics, beta blockers, and statins in increasing the risk of diabetes in patients with impaired glucose tolerance. *BMJ* **347**: f6745

N Engl J Med

Terminated early: Bardoxolene methyl for stage 4 CKD

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓✓

1 This clinical trial investigated the efficacy of bardoxolone methyl to reduce the progression of stage 4 chronic kidney disease (CKD) to end-stage renal disease (ESRD).

2 As part of a Phase III, double-blind placebo-controlled trial, bardoxolone methyl was prescribed at 20 mg/day.

3 Among 2185 randomly assigned participants, 6% of participants from each group reached the primary composite outcome (ESRD or death from cardiovascular causes).

4 Ninety-six people in the bardoxolone methyl group were hospitalised for heart failure or died from heart failure compared with 55 in the placebo group (hazard ratio, 1.83; 95% confidence interval, 1.32–2.55; $P<0.001$).

5 Due to a higher rate of cardiovascular events in the bardoxolone methyl group compared to the placebo group, the study was terminated after 9 months of follow-up.

de Zeeuw D, Akizawa T, Audhya P et al (2013) Bardoxolone methyl in type 2 diabetes and stage 4 chronic kidney disease. *N Engl J Med* **369**: 2492–503

JAMA

Guidelines for high blood pressure care

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! Factor	✓✓✓✓

1 The panel from the 8th Joint National Committee (USA) released guidelines for the management of hypertension in adults. They used an evidence-based approach to draw guidelines from randomised controlled trials collected from a systematic review.

2 Among other recommendations, the panel propose a blood pressure of less than 140/90 mmHg for people under the age of 60 and for people under the age of 30 who have hypertension.

3 The same guideline is also recommended for people with diabetes and hypertension.

4 These recommendations are not a substitute for clinical judgement.

James PA, Oparil S, Carter BL et al (2014) Evidence-based guideline for the management of high blood pressure in adults. *JAMA* **311**: 507–20

> *"After adjusting for baseline characteristics, diuretics and statins were both significantly associated with an increased risk of new-onset diabetes. Beta-blockers and calcium channel blockers were not associated with an increased risk of new-onset diabetes."*