Clinical **DIGEST 3**

Obesity

Obesity, diabetes and CVD: Time for Activity?



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besity and accompanying T2D are complex disorders that have a strong genetic basis but have been increasing in prevalence due to various environmental factors. While energy homeostasis is clearly dependent on energy

intake and energy expenditure, to tackle the enormous problems of obesity and diabetes, there is a need for greater understanding of factors that impact on energy intake and expenditure. There has been a great focus on the energy intake side of the equation with increased availability and overconsumption of cheap energy-dense foods being repeatedly highlighted. On the energy expenditure side, great interest has been generated recently regarding the role of brown adipose tissue (Cypress et al, 2009). Emphasis has been placed on moderate-to-vigorous physical activity to improve cardiovascular (CV) health (World Health Organization, 2010; Garber et al, 2011; Lee et al, 2012). Given that the environment has changed with people using their cars more, having greater dependence on technology, and becoming increasingly more inactive in their daily lives, it is important to gauge whether this sedentariness, that is greater sitting time or greater time being inactive (Sedentary Behaviour Research Network, 2012), is contributing to the pandemics of obesity and diabetes, and ensuing CV disease (CVD).

Wilmot and colleagues (2012; summarised alongside) have carried out a systematic review and meta-analysis of the association between sedentary behaviour and diabetes and CVD. They examined both prospective and cross-sectional studies. Although the studies varied in quality, they found that sedentary time was associated with increased risk of diabetes and CVD. Importantly, sedentary time was associated with increased CV and all-cause mortality. The findings were most robust for diabetes. In a recent report by the Early ACTID (Activity in Diabetes) study carried out in Southwest England, Cooper and colleagues (2012) reported that greater sedentary time, measured objectively by accelerometry, was associated with lower high-density lipoprotein cholesterol and greater insulin resistance (measured through the HOMA-IR [Homeostasis Model of Assessment

- Insulin Resistance]). Thus, there is a need to consider sedentary behavior as an important problem to tackle in reducing diabetes and CVD. There are, however, several issues with the available evidence. Mainly, the majority of the data available to Wilmot and colleagues employed self-reported data with most studies using television viewing as the measure of sedentary behaviour — television viewing may be a surrogate marker for other deleterious factors or behaviours that may predispose to diabetes and CVD. In another recent review, television viewing was associated with lower levels of education, unemployment or lower working hours, and greater BMI; reported sitting behaviour, however, was not associated with age, sex or education level (Rhodes et al, 2012).

There is now a need for more studies to use objective measures of activity/sedentariness. Also, given that there is now a greater reliance on new technologies such as mobile telephones and tablet computers with multiple functions, the impact of these devices on health and activity needs further examination. If sedentariness does indeed predispose to the development of diabetes and CVD, then a better understanding of factors that determine sedentary behaviour is also required such that effective approaches can be recommended. It may be that while older technologies may have promoted sedentariness, the answer to increasing activity (and reducing sedentariness) may surprisingly come from novel technologies and associated applications that allow the individual to objectively determine and alter their activity levels.

Cooper AR, Sebire S, Montgomery AA et al (2012) Sedentary time, breaks in sedentary time and metabolic variables in people with newly diagnosed type 2 diabetes. *Diabetologia* **55**: 589–99 Cypess AM, Lehman S, Williams G et al (2009) Identification and importance of brown adipose tissue in adult humans. *N Engl J*

Med 360: 1509–17
Garber CE, Blissmer B, Deschenes MR et al (2011) 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
43: 1334–59

Lee IM, Shiroma EJ, Lobelo F et al (2012) Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. Lancet 380:

219–9
Rhodes RE, Mark RS, Temmel CP (2012) Adult sedentary behavior:
a systematic review. *Am J Prev Med* **42**: e3–28

Sedentary Behaviour Research Network (2012) Letter to the Editor: Standardized use of the terms "sedentary" and "sedentary behaviours". *Appl Physiol Nutr Metab* **37**: 540–2

World Health Organization (2010) Global recommendations on physical activity for health. WHO, Geneva. Available at: http://bit.ly/cfzCdN (accessed 26.11.12)



Sedentary time and the link to diabetes, cardiovascular disease and death

Readability	////
Applicability to practice	1111
WOW! factor	1111

Everyday activities that characterise modern life, such as watching the television, using a computer, or driving a car promote sedentary behaviour.

The aim of this study was to assess the relationship between the length of time a person spends sitting and diabetes, cardiovascular disease (CVD) and cardiovascular (CV) and all-cause mortality.

The authors reviewed findings from Medline, Embase and Cochrane Library database searches, focusing on sedentary time and its effect on health; this yielded 18 studies involving 794 577 people.

The study showed that sedentary behaviour time was associated with an increase in the relative risk (RR) of developing diabetes, CVD and CV and all-cause mortality (RR increased by 112%, 147%, 90%, 49%, respectively) The relationship to time spent sitting was strongest for diabetes than for mortality outcomes.

The largest insulin-sensitive organ in the body is skeletal muscle and explains 80% of insulinstimulated glucose disposal. Insulin sensitivity in these muscles is dynamic, and findings from rodent studies showed that immobility soon leads to peripheral resistance.

The authors concluded that replacing sedentary behaviour with standing or light physical activity (PA) could lower the risk of chronic disease and mortality, and have a significant role in diabetes prevention. This substitution was found to be independent of the amount of moderate-to-vigorous PA carried out.

Wilmot EG, Edwardson CL, Achana FA et al (2012) Sedentary time in adults and the association with diabetes, cardiovascular disease and death: systematic review and meta-analysis. *Diabetologia* **55**: 2895–905

DIABETES CARE

CV event incidence after bariatric surgery in obese people with T2D

Readability	111
Applicability to practice	///
WOW! factor	111

- People with T2D who are obese are more likely to develop cardiovascular disease (CVD). Bariatric surgery is recommended in people with T2D and BMI ≥35 kg/m².
- The aim of this study was to analyse the effect of bariatric surgery on cardiovascular (CV) events in people with T2D, and to compare this with conventional obesity treatment.
- The SOS (Swedish Obese Subjects) study was a prospective, non-randomised controlled intervention trial involving 4047 obese participants, 2010 of whom underwent bariatric surgery.
- The current report is based on a subset of people from the SOS study (*n*=607; 345 underwent bariatric surgery and 262 received standard treatment). Individuals were assessed at baseline and follow-up intervals over 20 years.
- Bariatric surgery was associated with a lower incidence of myocardial infarction (adjusted hazard ratio [HR], 0.56; 95% confidence interval [CI], 0.34–0.93; *P*=0.025); this relationship was stronger in people with higher baseline serum total cholesterol and triglyceride levels (*P*=0.02 for both).
- Stroke incidence did not appear to be affected by weight-loss surgery. There was no correlation between BMI and surgery outcome.
- The authors concluded that in obese people with T2D, bariatric surgery lowers the occurrence of myocardial infarction. They suggested that BMI should be incorporated into metabolic guidelines to increase the benefits associated with bariatric surgery.

Romeo S, Maglio C, Burza MA et al (2012) Cardiovascular events after bariatric surgery in obese subjects with type 2 diabetes. *Diabetes Care* 1 Aug [Epub ahead of print]

DIABETES CARE

Ethnic differences in the progress of diabetes and the effect of obesity

Readability	111
Applicability to practice	111
WOW! factor	1111

- It has been hypothesised that factors associated with racial/ ethnic differences in diabetes incidence act before the development of impaired glucose tolerance (IGT).
- The authors of the South American Heart Study set out to compare IGT, impaired fasting glucose (IFG) and obesity as effect modifiers among Mexican Americans and non-Hispanic white people in San Antonio, Texas.
- Of 4429 people who did not have diabetes at baseline, 3228 developed diabetes, of whom 3015 were included in the study analysis; the group was followed up for a median of 7.8 years.
- During follow-up, 5.7% of non-Hispanic white people (67 of 1168) and 11.3% of Mexican Americans (208 of 1847) developed diabetes. Of people who did not develop diabetes and who had normal baseline 2-hour glucose levels, 11.2% of non-Hispanic white people (116 of 1039) and 14.1% of Mexican Americans (216 of 1533) developed IGT.
- Compared with non-Hispanic white people, Mexican Americans had an excess risk of incident IGT (odds ratio [OR], 1.48; 95% confidence interval [CI], 1.16–1.89) and incident IFG (OR, 1.71; 95% CI, 1.31–2.23).
- Obesity significantly affected the relationship between ethnicity and progression to IGT or diabetes (P=0.034), which was stronger in leaner people.
- The authors concluded that ethnic differences are noticeable in the early and later phases of diabetes, yet non-Hispanic whites lose most of their ethnic advantage if they become obese. Lorenzo C, Lee R, Haffner SM (2012) Impaired glucose tolerance and obesity as effect modifiers of ethnic disparities of the progression to diabetes: the San Antonio heart study. Diabetes Care 24 Aug [Epub

OBESITY SURGERY

Bariatric surgery: Clinical and costeffectiveness for people with T2D

Readability \(\sqrt{sqrt} \ \sqrt{sqrt} \)

Applicability to practice \(\sqrt{sqrt} \ \sqrt{sqrt} \ \sqrt{sqrt} \)

WOW! factor \(\sqrt{sqrt} \ \sqrt{sqrt} \ \sqrt{sqrt} \ \sqrt{sqrt} \)

This authors set out to assess the cost-effectiveness and relative benefits and risks of carrying out bariatric surgery in people with T2D who are mildly (class I; BMI 30–34.99 kg/m²) or moderately (class II; BMI 35–39.99 kg/m²) obese.

Searches of 17 electronic databases and other literature sources identified two RCTs meeting the study inclusion criteria; both compared laparoscopic adjustment gastric banding (LAGB) with a non-surgical treatment option.

At 2 years, compared with nonsurgical treatment, LAGB was associated with significantly greater weight loss and remission of T2D (*P*>0.001 for both comparisons). Adverse events were reported in both trial arms of the two studies.

One study assessed quality of life outcomes using the short-form health survey (SF-36). At 2 years, LAGB significantly improved scores for five or the eight SF-36 domains compared with non-surgical treatment (*P*<0.05 for each of the five domains).

LAGB is more expensive than nonsurgical management of obesity; the incremental cost-effectiveness ratio (ICER) fell from £20 159 at 2 years to £1634 at 20 years for people with class I and II obesity and T2D (largely driven by T2D resolution). LAGB management for people with class I obesity was much less cost-effective.

The authors concluded that bariatric surgery is an effective treatment for people with class I or II obesity and T2D, although it was less cost-effective for those with class I obesity.

Picot J, Jones J, Colquitt JL et al (2012) Weight loss surgery for mild to moderate obesity: a systematic review and economic evaluation. *Obes Surg* 22: 1496–506

Ethnic differences are noticeable in the early and later phases of diabetes, yet, non-Hispanic whites lose most of their ethnic advantage if they become obese."

Were to be reduced by 25%, over 1.3 million deaths could be avoided each year worldwide. These findings are comparable to the established risk factors of smoking and obesity."

LANCET

Physical inactivity has a major impact on health wordwide

Readability	1111
Applicability to practice	1111
WOW! factor	1111

Physical inactivity has been linked to several health conditions, including heart disease, T2D and breast and colon cancer. The aim of this study was to assess the effect of inactivity on these diseases by calculating to what extent the disease could be avoided if inactive participants were to become active. The authors also sought to predict the change to life expectancy in active individuals.

The authors were able to measure the effect of physical inactivity using conservative assumptions for each disease to calculate population attributable fractions. They estimated

that physical inactivity led to, on average, 6% of the burden of illness from coronary heart disease. In addition, it was found to be the cause of 7% of T2D, 10% of breast cancer and 10% of colon cancer.

The authors calculated that inactivity was responsible for over 5.3 million out of 57 million deaths worldwide in 2008. Their data also showed that, if inactivity were to be reduced by 25%, over 1.3 million deaths could be avoided each year worldwide. These findings are comparable to the established risk factors of smoking and obesity.

The authors concluded that physical inactivity has a substantial effect on health on a wordwide scale, and that increased activity leads to significantly improved health outcomes. They also estimated that if physical inactivity were to be eliminated, the life expectancy of the global population would rise by 0.68 years.

Lee I-M, Shiroma EJ, Lobelo F et al (2012) Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. *Lancet* **380**: 219–9

DIABETES CARE

Impact of OSA on insulin sensitivity and secretion in healthy men

Readability	111
Applicability to practice	111
WOW! factor	111

Obstructive sleep apnoea (OSA) is widespread among people who are overweight and obese.

The authors assessed whether OSA affects glucose metabolism in young (aged 18–30 years), lean (BMI 18–25 kg/m²), healthy men who did not have cardiometabolic disease (n=52). All individuals were stratified by diabetes risk.

All participants underwent overnight laboratory polysonography followed by a morning oral glucose tolerance test (following an overnight fast).

Frequency matching resulted in data from 12 men with OSA being compared with data from 20 men without OSA (control group). The groups were similar in terms of age, BMI, ethnicity-based diabetes risk, family history of diabetes and physical activity levels.

On average, men with OSA had a notably higher arousal index and the amount of time spent in deep sleep tended to be lower when compared with control subjects. This is consistent with interrupted sleep and poor sleep quality linked to OSA.

After ingestion of a glucose load, insulin sensitivity was 27% lower and insulin secretion 37% higher in men with OSA compared with controls.

The authors concluded that in young, lean and healthy men, OSA is linked to insulin resistance and higher insulin secretion, which acts to control glucose tolerance.

Pamidi S, Wroblewski K, Broussard J et al (2012) Obstructive sleep apnea in young lean men: impact on insulin sensitivity and secretion. *Diabetes Care* **35**: 2384–9 COCHRANE DATABASE SYST REV

Computer-based interventions are effective for weight management

Readability	///
Applicability to practice	111
WOW! factor	111

The study authors set out to examine the effect computer-based interventions have on weight loss or weight management in people who are overweight or obese.

According to the Word Health
Organization, the number of
overweight people globally will rise to
1.5 billion by 2015; obesity is linked to
diseases such as diabetes, heart disease
and stroke.

The authors reviewed RCTs and quasi-randomised controlled trials, which assessed interactive computer-based weight loss or weight management in overweight or obese people. They carried out literature searches in a number of electronic databases, including Central, Medline and Embase, and also reviewed clinical trials registries.

Literature searches identified 14 weight-loss studies (with data from 2537 participants), and four weightmanagement studies (with data from 1603 participants).

The treatment time was between 4 weeks and 30 months. The authors found that, after 6 months of therapy, computer-based interventions prompted increased weight loss compared with minimal interventions (mean difference -1.5 kg; 95% confidence interval, -2.1 -0.9; two trials) but the weight loss was not as great as that achieved with in-person treatment.

The authors concluded that computer-based interventions were effective for weight loss and weight maintenance, compared with minimal or no intervention.

Wieland LS, Falzon L, Sciamanna CN et al (2012) Interactive computer-based interventions for weight loss or weight. *Cochrane Database Syst Rev* 8: CD007675