

Obesity

Obesity and heart disease in women with diabetes



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One of the major aims of treating diabetes is to reduce the patient's risk of coronary heart disease (CHD). To this end, much energy of diabetes clinics is channelled into treating hypertension and dyslipidaemia – interventions that are now supported by substantial evidence. Aspirin and smoking cessation also reduce the risks of CHD. By contrast, obesity has received little attention as a risk factor for CHD and mortality in people with diabetes.

The study of Cho et al highlights the implications of obesity for people with type 2 diabetes. After adjustment for other risk factors, current body mass index (BMI) was strongly related to the risks of CHD in women with diabetes. The risk is of the same order of magnitude as that seen in non-diabetic subjects. In the context of the approximate CHD risk reductions achieved by people with diabetes from lowering cholesterol, optimising blood pressure, achieving good glycaemic control using metformin (all between 20% and 40%) and taking aspirin (about 15%), it is worth noting that for people with type 2 diabetes the theoretical CHD risk reduction at BMI <23 compared with BMI >30 is about 70%. Of course, it is unclear whether this risk is reversible in practice. Interestingly, weight gain before (but not

after) the diagnosis of diabetes seemed to be associated with CHD risk. As a possible explanation for this finding the authors postulated that further weight gain might not result in further deterioration of insulin sensitivity.

What are the clinical implications of these findings? These data provide important prospective confirmation of the everyday clinical impression that obesity is harmful for people with diabetes. Although there was no measurable effect of intentional weight loss on CHD risk, the study was not designed, or able, to examine this key question. However, on the basis of other data (Lean et al, 1990; Williamson et al, 2000) it is tempting to speculate that weight loss in overweight patients with established diabetes reduces mortality by reducing the risk of CHD. We are led back to the perennial problem of weight control in the diabetic clinic! Current treatment for obesity is not yet effective enough to make this a realistic option for the majority of people with diabetes (Pinkney, 2002). It is likely, however, that weight loss responders would begin to enjoy reduced CHD risk if they could realise weight reductions of around 5–10%.

Lean ME, Powrie JK, Anderson AS, Garthwaite PH (1990) Obesity, weight loss and prognosis in type 2 diabetes. *Diabetic Medicine* 7: 228–33

Pinkney J (2002) Prevention and cure of type 2 diabetes. *British Medical Journal* 325: 232–3

Williamson DF, Thompson TJ, Thun M, Flanders D et al (2000) Intentional weight loss and mortality among overweight individuals with diabetes. *Diabetes Care* 23: 1499–504

DIABETES CARE



Obesity and CHD in the diabetic clinic

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

- This study examined the relationship of obesity and weight change to incidence of coronary heart disease (CHD) in women with diabetes.
- Follow-up was ≤20 years for 5897 women with type 2 diabetes who had no history of cardiovascular disease or cancer at the start of follow-up. Body weight was assessed every 2 years during the study period.
- A total of 418 incident cases of CHD were documented.
- Current body mass index (BMI) was strongly associated with an increased risk of CHD in diabetic women. Increasing BMI values from age 18, before diagnosis of diabetes, were also positively associated with risk of CHD.
- Weight gain before the diagnosis of diabetes was related to increased risk of CHD in women with type 2 diabetes. By contrast, weight change after diagnosis of diabetes was not associated with risk of CHD.

Cho E, Manson JE, Stampfer MJ, Solomon CG et al (2002) A prospective study of obesity and risk of coronary heart disease among diabetic women. *Diabetes Care* 25 (7): 1142–8

OBESITY RESEARCH



Orlistat in obese adolescents

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

- Obesity is now becoming common in children, yet there are few data on anti-obesity drugs in this group.
- This study investigated the safety, tolerability and potential efficacy of orlistat in adolescents with obesity.

A total of 20 adolescents took orlistat (120 mg, three times daily) and a multivitamin for 3 months. They were simultaneously enrolled in a 12-week programme emphasising strategies for behaviour change.

Orlistat treatment significantly decreased weight, body mass index, total cholesterol, low-density lipoprotein cholesterol, fasting insulin and fasting glucose. Insulin sensitivity also improved significantly.

Side-effects were generally mild, limited to gastrointestinal effects that decreased with time.

Because no subjects were enrolled in the behavioural programme without receiving orlistat, definitive evidence for orlistat's effects on body weight cannot be produced.

The study concludes that short-term treatment with orlistat, in combination with a behavioural programme, is well tolerated in adolescents, although the treatment still needs to be compared with conventional therapy in placebo-controlled trials.

McDuffie JR, Calis KA, Uwaifo GI, Sebring NG et al (2002) Three-month tolerability of orlistat in adolescents with obesity-related comorbid conditions. *Obesity Research* 10 (7): 642–50



Initial results from a lifestyle clinic

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

- 1 Obese patients with higher morbidity risk who had been referred to dietitians were invited to attend a new lifestyle clinic.
- 2 Treatment included more time with the dietitian and pharmacotherapy if appropriate; emphasis was placed on achieving a realistic weight loss of 10% within a 6-month period.
- 3 So far, out of the 103 patients that enrolled, 26 have completed the lifestyle clinic: 18 started on orlistat

Does orlistat impair fat-soluble vitamin absorption?

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

- 1 The effect of orlistat on the absorption of fat-soluble vitamins was studied in 17 adolescents with body mass index above the 95th percentile for age, race and sex, and presence of at least one obesity-related comorbid condition.
- 2 Before starting on orlistat, the subjects were prescribed a 500 kcal/day deficit diet containing less than 30% fat. Subjects then attended a psychoeducational programme.

Orlistat-metformin combination therapy

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

- 1 This study examined the efficacy and safety of orlistat in terms of body weight, glycaemic control and cardiovascular risk factors in overweight and obese metformin-treated type 2 diabetic patients.
- 2 Patients were given either 120mg orlistat or placebo, combined with

and 8 stayed on lifestyle advice alone.

- 4 These 26 subjects achieved clinically significant benefits with regard to exercise tolerance, waist measurement and total cholesterol.
- 5 Weight loss was greater in this group than in patients treated at general dietetic clinics (data from historical records), and in patients receiving orlistat compared with those receiving lifestyle intervention alone.
- 6 Lifestyle clinics might facilitate beneficial lifestyle changes, which impact positively on morbidity. It remains to be determined whether this approach is sufficiently cost-effective to be implemented more widely in the NHS.

Frost G, Lyons F, Bovill-Taylor C, Carter L et al (2002) Intensive lifestyle intervention combined with the choice of pharmacotherapy improves weight loss and cardiac risk factors in the obese. *Journal of Human Nutrition and Dietetics* 15: 287-95

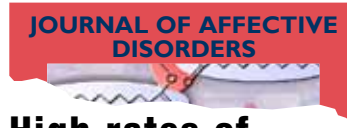


- 3 Subjects were given 120 mg orlistat three times daily, and a daily multivitamin supplement for 6 months.
- 4 Retinol absorption was not significantly affected, although alpha-tocopherol absorption was reduced. Serum vitamin D decreased, but changes in levels of vitamins A, E and K were not statistically significant.
- 5 It may be prudent to monitor vitamin D levels even during multivitamin therapy in patients on long-term orlistat.

McDuffie JR, Calis KA, Booth SL, Uwaifo GI, Yanovski JA (2002) Effects of orlistat on fat-soluble vitamins in obese adolescents. *Pharmacotherapy* 22 (7): 814-22

a reduced calorie diet, for 1 year.

- 3 Compared with the placebo group, those on orlistat had greater mean weight loss, bigger improvements in glycaemic control, and greater decreases in total cholesterol, LDL cholesterol and systolic blood pressure.
- 4 These benefits were observed within 2 weeks of initiation of treatment, before significant difference in weight loss.
- 5 Gastrointestinal side-effects increased with orlistat treatment,



High rates of diabetes in psychiatric patients

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

- 1 Diabetes is common in psychiatric patients but it is unclear whether this is related to antipsychotic drugs or to lifestyle and obesity.
- 2 The aim of this study was to investigate whether there is a link between abnormal glucose metabolism and psychiatric disorders. Medical records of 243 inpatients with major depression, bipolar I disorder, schizoaffective disorder, schizophrenia and dementia were reviewed.
- 3 Diabetic patients had a higher body mass index (BMI) but not a significantly higher use of psychotropic medications. Psychiatric diagnosis and BMI were the only significant and independent predictors of diabetes.
- 4 Rates of type 2 diabetes were significantly elevated in bipolar I affective and schizoaffective patients.
- 5 Drug use was not the most important factor determining the risk of type 2 diabetes. Rather, body mass and psychiatric diagnosis were the most important determinants.

Regenold WT, Thapar RK, Marano C, Gavimani S, Kondapavuluru PV (2002) Increased prevalence of type 2 diabetes mellitus among psychiatric inpatients with bipolar I affective and schizoaffective disorders independent of psychotropic drug use. *Journal of Affective Disorders* 70: 19-26



but this did not lead to a greater drop-out rate.

- 6 The study concludes that orlistat is a useful adjunctive treatment for weight loss in obese patients with type 2 diabetes who are being treated with metformin.

Miles JM, Leiter L, Hollander P, Wadden T et al (2002) Effect of orlistat in overweight and obese patients with type 2 diabetes treated with metformin. *Diabetes Care* 25 (7): 1123-8

‘Rates of type 2 diabetes were significantly elevated in only bipolar I affective and schizoaffective patients.’

‘Lifestyle clinics facilitate beneficial lifestyle changes, which impact positively on morbidity risk factors.’

‘Orlistat is a useful adjunctive treatment for weight loss in obese patients with type 2 diabetes who are being treated with metformin.’