

Obesity

A landmark for type 2 diabetes: 1-year results of the look AHEAD trial



Jonathan Pinkney,
Consultant Physician,
Royal Cornwall
Hospital, Truro, and
Senior Lecturer,
Peninsula Medical
School

It is often still taught that type 2 diabetes is an irreversible and progressive disease, that early pharmacological intervention with oral hypoglycaemic agents is required, and when the individual fails to reach arbitrary glycaemic targets then early treatment with insulin is required. But is this really true?

For me, the reality has always been rather more complex than this. Both the disease and human beings are so heterogeneous and, additionally, the unfolding epidemic of obesity and diabetes argues that weight loss should be a higher priority.

While studies of new pharmaceutical products are backed by industrial sponsorship, vital studies of non-pharmaceutical interventions have not benefited from such support and we have been left waiting for many years for essential studies to be undertaken. Therefore, the look AHEAD trial, currently under way in North America, is the first large-scale study of an intensive lifestyle behavioural intervention in the control of established type 2 diabetes and will complement

recent major diabetes prevention trials and work on the role of bariatric surgery in treating type 2 diabetes.

These exciting 12-month results of a trial that is planned to run for 11 years are abstracted alongside. The characteristics of the participants, such as age, BMI and existing treatment requirements including insulin, are typical of those often seen as an utterly lost cause for lifestyle intervention. The significant weight loss achieved here, even in insulin-treated individuals, strikes at the heart of diabetes, improving all aspects of the metabolic syndrome without necessarily needing escalating pharmacotherapy or indeed insulin.

While longer-term data are now awaited eagerly, the look AHEAD trial has the potential to redefine the treatment of type 2 diabetes, reinforcing the view that unhealthy lifestyles should be the main focus of attention in all those with type 2 diabetes. No doubt a different clinical emphasis would be needed if a lifestyle-centred approach were adopted routinely in the treatment for type 2 diabetes. Look AHEAD challenges us all to consider whether or not rapid escalation of drug therapy to meet glycaemic targets is necessarily the right approach to treating type 2 diabetes.

DIABETES CARE

Intensive lifestyle intervention reduces weight and CVD risk at 1 year

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

- The Look AHEAD trial intends to follow participants for 11.5 years to investigate the long-term impact of an intensive lifestyle intervention in overweight or obese individuals with type 2 diabetes. This paper reports the 1-year data.
- Recruited to the study were 5 145 adults aged 45–74 years with type 2 diabetes and a BMI >25 kg/m². The average BMI was around 35 kg/m².
- Participants were assigned either intensive lifestyle intervention (ILI; n=2 570), aimed to reduce their body weight by at least 7% via diet modification and an increase in physical activity, or standard diabetes support and education (n=2 575).
- Over the course of the first year, those receiving ILI decreased their body weight by, on average, 8.6%, significantly more than the support and education group, who lost 0.7% ($P<0.001$).

- ILI reduced mean HbA_{1c} from 7.3 to 6.6% and there were significant improvements in blood pressure, lipid profile and urinary albumin excretion compared with the standard treatment arm.
- Average weight was 8.6% with ILI compared with just 0.7% with standard treatments. Even insulin users achieved 7.6% average weight loss.
- The authors anticipate that the long-term data from this study will elucidate whether or not the improved diabetes control and CVD risk reduction is sustained beyond 1 year.

Look AHEAD Research Group, Pi-Sunyer X, Blackburn G et al (2007) Reduction in weight and cardiovascular disease risk factors in individuals with type 2 diabetes: one-year results of the look AHEAD trial. *Diabetes Care* 30: 1374–83

DIABETES CARE

Obesity: A strong risk factor for gestational diabetes

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

- Previous studies have suggested an increased risk of gestational diabetes as maternal body weight rises. This paper reports on a meta-analysis aiming to provide better risk estimates for gestational diabetes in overweight and obese women compared to lean or normal weight women.
- Twenty studies conducted between 1980 and 2006 that reported pregnancy body mass, used a normal weight comparison group and whose data

allowed a quantitative measurement of risk were included in the meta-analysis.

- A Bayesian model was used to perform a meta-analysis and meta-regression on data collected.
- Compared with women of normal weight, overweight women had an unadjusted OR of developing gestational diabetes during pregnancy of 2.14 (95% CI: 1.82–2.53). In obese women, this OR was 3.56 (95% CI: 3.05–4.21) and in the severely obese 8.56 (95% CI: 5.07–16.04).
- The authors state that these findings have important public health ramifications due to the adverse events associated with obesity during pregnancy and gestational diabetes, such as risk of adverse infant outcomes and risk of future diabetes in the child and mother.

Chu SY, Callaghan WM, Kim SY et al (2007) Maternal obesity and risk of gestational diabetes mellitus. *Diabetes Care* 30: 2070–6

‘The odds of diabetes associated with obesity defined by BMI increased from 1.62 to 2.62 in women between 1993 and 2003, and from 1.24 to 2.10 in men.’

‘While survival of the kidney graft did not vary between the two groups of patients, overall mortality was greater in the overweight individuals.’

TRANSPLANTATION PROCEEDINGS

Improved survival in lean kidney transplant recipients

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

- This study investigated graft and patient survival in overweight people undergoing kidney transplant.
- In total, 134 people who were overweight (BMI >25 and <30 kg/m²) and 160 with a BMI <25 kg/m² who underwent a renal allograft were followed for, on average, 53.4 ± 30.6 months.
- Overall, overweight participants were significantly older than the controls and had significantly greater levels of hypertension ($P=0.028$), left ventricular hypertrophy ($P=0.014$) and dyslipidaemia ($P=0.001$). In addition, average age of their donor kidneys was significantly greater ($P=0.019$) and post-surgery rates of acute tubular necrosis were higher ($P=0.006$).
- Diabetes diagnosed after transplant surgery was more common in those who were overweight ($P<0.001$). Systolic blood pressure, total cholesterol levels and triglycerides were all significantly elevated compared with the normal weight group ($P<0.05$ in all cases).
- While survival of the kidney graft did not vary between the two groups of patients, overall mortality was greater in the overweight individuals ($P=0.02$).
- Following a logistic regression, the authors found that recipient age and whether or not they were overweight were independent prognostic factors in predicting patient mortality (RR: 5.2 and 1.1, respectively).
- The authors highlight the prevalence of high BMIs in people undergoing renal transplants and emphasise the need to avoid weight gain in this group.

Sancho A, Avila A, Gavela E (2007) Effect of overweight on kidney transplantation outcome. *Transplantation Proceedings* **39**: 2202–4

PUBLIC HEALTH NUTRITION

England-specific data confirm link between waist circumference and risk of diabetes

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

- The authors of this study set out to investigate the trends in BMI and abdominal obesity in England between 1993 and 2003 and identify any association with diabetes, hypertension and hypertension–diabetes comorbidity.
- The study analysed nationally representative cross-sectional population surveys of people aged ≥35 years that were carried out by the Health Survey for England. Most variables were collected via a questionnaire, with waist circumference and blood pressure collected by a nurse.
- The rates of obesity, defined as a BMI ≥30 kg/m² increased linearly from 15.8% to 26.3% in men and 19.3% to 25.8% in women.
- Rates of abdominal obesity assessed via waist circumference (>102 cm for men; >88 cm in women) increased linearly by 12.8% in men and 14.6% in women.
- The odds of diabetes associated with obesity defined by BMI increased from 1.62 to 2.62 in women between 1993 and 2003, and from 1.24 to 2.10 in men. Even in those with a BMI <30 kg/m², raised waist circumference was a similar predictor of diabetes.
- This study highlights the importance of obesity as a risk factor for diabetes and supports the use of waist circumference measures in risk stratification in people with a BMI <30 kg/m².

Hirani V, Zaninotto P, Primatesta P (2007) Generalised and abdominal obesity and risk of diabetes, hypertension and hypertension–diabetes co-morbidity in England. *Public Health Nutrition* doi: 10.1017/S136898007000845

APPLIED PHYSIOLOGY, NUTRITION AND METABOLISM

Diet and exercise reduce macrosomia in gestational diabetes

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

- This study investigated the effects of a programme of diet and exercise on weight gain, glycaemic control and pregnancy outcome in women with gestational diabetes.
- Participants were asked to follow a eucaloric or hypocaloric meal plan alone (n=57) or the meal plan plus an exercise regimen (n=39). Treatment allocations was self-selected.
- Both study groups had a similar BMI at baseline: 35.2 ± 5.7 kg/m² in the exercise plus diet group versus 33.5 ± 9.2 kg/m² in the diet alone group.
- Weight gain, assessed on a weekly basis, was significantly lower in the diet plus exercise group than the diet alone group (0.1 versus 0.4 kg, respectively, $P<0.05$).
- The study was unable to demonstrate significant benefits to the child. However, the neonate was less likely to be macrosomic.
- Rates of complications and Caesarean delivery were similar between groups, as was gestational age at delivery.
- The study suggests that dietary restriction and exercise can limit weight gain in women with gestational diabetes and decrease the frequency of macrosomic newborn babies without a significant increase in adverse outcomes.

Artal R, Catanzaro RB, Gavard JA et al (2007) A lifestyle intervention of weight-gain restriction: diet and exercise in obese women with gestational diabetes mellitus. *Applied Physiology, Nutrition, and Metabolism* **32**: 596–601