analyzed 40 studies conducted between 1966 and 2005 that included 250,152 patients.

They found that, compared with patients with a BMI in the normal range (20–24.9 kg/m^2), those with a low BMI (<20 kg/m^2) had a higher risk of cardiovascular mortality and overall mortality; those with a high BMI (25–29.9) had a lower risk of cardiovascular mortality and overall mortality. Obese patients (BMI 30–34.9 kg/m^2) were no more at risk of cardiovascular mortality or overall mortality than normal-BMI patients were. Severely obese patients (BMI ≥35 kg/m^2) did not have an elevated risk of overall mortality, but did have an increased risk of cardiovascular mortality. The results were unaffected by factors such as age, sex, and tobacco use.

The authors caution that these findings should be interpreted with care, as they might be the result of several factors. A high BMI does not necessarily signal obesity: it is possible that, in some patients, slightly elevated BMI values might represent increases in lean mass rather than increases in body fat, as BMI cannot distinguish between the two. Increases in lean mass have been associated with higher levels of fitness and the ability to exercise, and would presumably decrease the risk of cardiovascular events and death.

Original article Romero-Corral A *et al.* (2006) Association of bodyweight with total mortality and with cardiovascular events in coronary artery disease: a systematic review of cohort studies. *Lancet* **368:** 666–678

Treatment of early signs of diabetes might not delay progression

A common early sign of type 2 diabetes is postprandial hyperglycemia. As it has been proposed that the consequent glucose toxicity might cause β-cell failure, it is possible that treatment of postprandial hyperglycemia in early diabetes could prevent disease progression (which is characterized by fasting hyperglycemia). The results of a new US study, however, indicate that such treatment might not prevent progression.

In total, 196 patients with early diabetes were included in the intention-to-treat analysis. Patients had been randomly allocated to receive either acarbose 25–100 mg daily (a drug proven to reduce postprandial glucose levels without affecting β-cell function, insulin resistance or fasting glucose levels) or placebo until disease progression or the end of the 5-year study period. Disease progression was defined as the development of frank fasting hyperglycemia (two consecutive quarterly fasting-plasma-glucose measurements of ≥140 mg/dl).

Acarbose reduced the incidence of postprandial hyperglycemia over the first 2 years of treatment, but there was no difference in the number of patients who developed frank fasting hyperglycemia between the acarbose and placebo groups; β-cell function was also unaffected.

Kirkman and colleagues propose that, even in early disease, β-cell failure might already be too far advanced for treatment to have any effect. Alternatively, it is possible that postprandial hyperglycemia is not the primary cause of β-cell failure in diabetes.

Original article Kirkman MS *et al.* (2006) Treating postprandial hyperglycemia does not appear to delay progression of early type 2 diabetes. The early diabetes intervention program. *Diabetes Care* **29:** 2095–2101

Pubertal boys treated with aromatase inhibitors require serum lipid monitoring

Aromatase inhibitors such as letrozole are used to treat some growth disorders. Since aromatase inhibitors suppress estrogen biosynthesis and stimulate secretion of gonadal androgens, these drugs could also affect lipid metabolism and insulin sensitivity in peripubertal males with growth disorders.

In a prospective, double-blinded trial, 31 boys aged between 9.0 and 14.5 years with idiopathic short statue were randomly treated with placebo or 2.5 mg letrozole daily for 2 years. At baseline, there was no difference in BMI, percentage of fat mass, age or pubertal maturation stage between the groups. Pubertal boys who received letrozole showed a decrease in HDL cholesterol compared with those who received placebo. The decrease in HDL cholesterol correlated with the decrease in adiponectin levels, and there was an inverse correlation between the decrease in HDL cholesterol and rise in serum testosterone. Relative fat mass decreased during the 2-year study, which inversely correlated with increased testosterone levels in letrozole-treated boys, compared with placebo-treated boys. Insulin sensitivity, in addition to concentrations of LDL cholesterol, apolipoprotein B and triglycerides, did not alter in either group.

The authors conclude that in pubertal boys with idiopathic short statue who are treated with letrozole, levels of HDL cholesterol and relative fat mass decline. The authors, therefore, recommend a careful follow-up of lipid profile in pubertal boys with short statue who are treated with an aromatase inhibitor.

Original article Hero M *et al.* (2006) Blockage of oestrogen biosynthesis in peripubertal boys: effects on lipid metabolism, insulin sensitivity, and body composition. *Eur J Endocrinol* **155:** 453–460

Chromogranin A identifies patients with pheochromocytoma with high sensitivity

Chromogranin A is an accurate general marker for neuroendocrine tumors—most patients with pheochromocytomas or paragangliomas have high plasma concentrations of this marker. Grossrubatscher and colleagues, therefore, evaluated the diagnostic value of chromogranin A compared with that of urinary levels of catecholamines and their metabolites in patients with pheochromocytomas. The role of chromogranin A in the assessment of surgical cure of pheochromocytoma was also investigated.

The authors observed 21 consecutive patients who had pheochromocytomas at initial presentation or who had experienced postsurgical relapse, plus one patient who was followed up for malignant pheochromocytoma. A control group of 20 patients in whom pheochromocytoma was suspected, but not subsequently diagnosed, was also evaluated.

No patient with pheochromocytoma had normal urinary levels of both metanephrine and normetanephrines. Measurement of both metanephrine and normetanephrine, therefore, had a sensitivity of 100% in identifying pheochromocytoma. Overall, 17 patients were assessed before and after surgery; postoperatively, 14 of these patients had normal metanephrine and normetanephrine levels, and 12 had normal chromogranin A levels. At initial presentation, 20 patients with pheochromocytomas had high chromogranin A levels. The two patients with normal chromogranin A levels had high levels of catecholamines and their metabolites.

Chromogranin A has a sensitivity of 91% in identifying patients with pheochromocytomas; measurement of both chromogranin A and catecholamines increases the sensitivity to 100%. A decrease in chromogranin A levels might also help to demonstrate cure after surgery.

Original article Grossrubatscher E *et al.* (2006) The role of chromogranin A in the management of patients with phaeochromocytoma. *Clin Endocrinol (Oxf)* **65:** 287–293

Baseline FSH levels could identify men with impaired testicular functioning

Testicular varicocele can result in impaired functioning of the hypothalamic–pituitary–gonadal axis, indicative of latent hypogonadism. Many patients with varicocele are asymptomatic, but untreated lesions cause progressive testicular damage. Men with impaired hormonal functioning secondary to varicocele could benefit from surgery: this condition is usually diagnosed by an exaggerated response to gonadotropin-releasing hormone (GnRH) stimulation, but the test is expensive and labor-intensive, and might be less useful for men with unilateral (rather than bilateral) varicocele.

Bach *et al*. evaluated 102 men (all Tanner stage 5; aged 15–37 years) with unilateral varicocele. Baseline, peripheral-venous levels of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) were determined. LH and FSH levels were measured again 30 min and 60 min after GnRH stimulation: an exaggerated response was defined as FSH >8.2 U/l at either time point, or LH >51.7 U/l at 30 min and >44.1 U/l at 60 min. Baseline FSH levels >5.6 U/l were associated with reduced testicular volume, and predicted an exaggerated GnRH test response. In total, 50 men had an exaggerated GnRH response, which indicated impaired Sertoli-cell functioning; of these, 44 had an exaggerated FSH response only, while the remainder had both exaggerated LH and FSH responses. Leydig-cell functioning was predominantly unaffected.

FSH levels experience little diurnal variation compared with GnRH levels; Bach *et al*. suggest that a validated FSH test could give clearer results than the GnRH stimulation test in diagnosis of impaired spermatogenesis.

Original article Bach T *et al.* (2006) Baseline follicle-stimulating hormone is a strong predictor for the outcome of the gonadotrophin-releasing hormone test in young men with unilateral medium- or high-grade varicocele. *BJU Int* **98:** 619–622