Editor's Comment

What are we treating?

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An editorial by John Yudkin, Bernd Richter and Edwin Gale in a recent *Lancet* caught my eye. The title is 'Intensified glucose control in type 2 diabetes – whose agenda?' Those of you who follow my editorials will know that my father is an elderly type 2 diabetic and I have a particular interest in the subject.

The question asked by the three authors is 'How solid is the evidence for glucose lowering in people with diabetes?' They point out that the Diabetes Control and Complications Trial showed that glucose control slows progression of microvascular complications in type 1 diabetes and the UK Prospective Diabetes Study (UKPDS) showed the same for type 2 diabetes. The main difference between the two studies was the high incidence of arterial disease in type 2 diabetes – 22% of UKPDS participants had a coronary or stroke event within 10 years of enrolment. Judkin *et al.* say that what is needed is an unequivocal demonstration that macrovascular disease would respond to tight glucose control in type 2 diabetes. However, combined analysis of four major trials, which included around 27 000 patients, suggested that lowering HbA_{1C} by 1% had a minor effect on heart disease, and no effect on stroke, cardiovascular mortality, total mortality, blindness or renal failure. At this stage, the authors suggest, policy makers might have reconsidered the role of aggressive blood-glucose lowering in type 2 diabetes – but this has not happened.

Given the above results, should we be screening the population for type 2 diabetes? A recent analysis from the American Diabetes Association (ADA), supported by an educational grant from three drug companies involved in diabetes care, found that between 138 and 208 people would need screening to prevent one myocardial infarction over 50 years of follow-up, with similar numbers required to prevent one person becoming blind. The conclusion of the study was that screening would be cost effective when started between 30 and 45 years of age and repeated every 3 - 5 years, assuming that all those diagnosed would be treated to a target HbA_{1C} below 7%. One additional result would be a diagnosis of diabetes in an additional 10 - 12% of older people in the USA.

Judkin *et al.* point out that the model assumes that pharmacological glucose lowering fully reverses the impact of hyperglycaemia on complications and that there is no affect on quality of life. The first assumption has been challenged by recent studies; the second is unlikely because tight glucose control involves multiple injection regimens along with blood glucose monitoring within 15 years of diagnosis. We know that intensified therapy is associated with weight gain and hypoglycaemia. People who actually have to live with diabetes report that intensified regimens impair quality of life by one-third – equivalent to a diagnosis of angina. But the ADA continues to recommend regular screening from the age of 30 - 45 years.

We also know from recent studies (Steno-2) that the most effective way to lower cardiovascular risk in type 2 diabetics is to combine treatment of blood pressure, lipids and glucose. This is not surprising because blood pressure and lipids have stronger epidemiological associations than hyperglycaemia does with cardiovascular events, greater effect of risk factor lowering on outcomes and simpler regimens to achieve target levels. So, the big questions these authors pose is 'Why then has there been so much focus on glucose management?'

They do point out that glucose prevention does have undoubted benefit in the prevention of microvascular disease, but, that said, there are diminishing returns for such a policy in older patients, those who have had diabetes for a long time, or those who already have advanced complications. However, there is still a blanket recommendation of aggressive glucose lowering.

'The most entrenched conflict of interest in medicine is a disinclination to reverse a previous opinion.' Judkin *et al.* suggest that there may be a synergy between the interests of professional societies and the drug industry when it comes to aggressive glucose lowering in treatment guidelines, in patients with myocardial infarction or in such 'dubious' categories as 'dysglycaemia' and 'pre-diabetes'. There are also problems when there is corporate sponsorship of guideline committees or when experts have financial ties to relevant companies. The increasing prevalence of diabetes, stricter treatment targets and proposals for population screening 'provide fertile areas for the drug industry'.

Judkin *et al.* conclude that current guidelines put too much emphasis on intensified glucose control in the routine management of diabetes in older patients. They suggest that it is time to move away from the simplistic 'one size fits all' to a more careful debate as to how, when and why aggressive glucose lowering should be used.

Judkin JS, Richter B, Gale EAM. *Lancet* 2011;377:1220-1222.

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