Metformin: in for the long haul

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This study underlines the central importance of metformin in the ongoing management of type 2 diabetes. For the same degree of blood glucose lowering, metformin is associated with less weight gain, less hypoglycaemia and potentially more cardiovascular (CV) protection than either sulphonylurea or insulin-based therapy. The drug of first choice when more than lifestyle treatment is required is thus metformin: but for how long should metformin be continued?

This study suggests that with the need for progressive intensification of treatments, insulin should be added to metformin. Continuing metformin after initiation of insulin is associated with improved glycaemic control, less weight gain and lower small dense LDL cholesterol, suggesting that metformin may have important advantages in type 2 diabetes intensively treated with insulin. This moderately large clinical study was performed in the district general hospitals (not academic teaching centres) and therefore has a widely applicable message.

An intriguing finding is that despite the freedom to increase insulin to reach defined glycaemic targets in both groups, a difference in overall glucose control was found. This may reflect the fundamental difference in effects between metformin and exogenous insulin, with, for example, metformin's ability to suppress hepatic glucose output more effectively.

This study forms the interim report of a planned 4.3 year study: 'Hyperinsulinemia: the outcome of its metabolic effects" (HOME). We await the long-term data that will confirm whether or not the benefits translate into a long-term reduction in CV morbidity/ mortality, but early omens are good. Meanwhile, the weight benefit and the potential metabolic advantages are likely to appeal to patients and professionals. We clearly need to adjust our sales pitch, and promote insulin in the management of type 2 diabetes as an addition rather than an alternative to tablets. An honest debate with our patients is required as concordance remains a major issue.

The list of indications for metformin continues to grow: diabetes prevention; polycystic ovarian syndrome; monotherapy for type 2 diabetes; combination therapy with other oral agents; and combination with insulin. Unlike other new drugs it has one other major advantage: it is cheap!

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Implementing the UKPDS findings will cost £100.5m

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

1 This study set out to estimate the total incremental cost of implementing the policies of intensive control of blood glucose concentrations and blood pressure recommended by the UKPDS for all patients with diagnosed type 2 diabetes in England.

2 The study population comprised 5102 people with newly diagnosed diabetes recruited between 1977 and 1991, aged 25–65 years, who had a fasting plasma glucose level of >6 mmol/l on two occasions.

3 Total costs based on use of healthcare resources, including costs of management, treatment and hospitalisation, were measured.

4 Implementing the main findings of the UKPDS to all people diagnosed with type 2 diabetes in England would cost £100.5m. This equates to 1% of the planned increase in expenditure on the NHS over 2001–2005.

5 Approximately 720 additional staff would be needed to implement these policies, particularly DSNs and practice nurses.

6 Policies to improve control of blood pressure and blood glucose are effective in reducing the complications associated with diabetes, as well as being cost-effective.

Gray A, Clarke P, Farmer A, Holman R, on behalf of UKPDS (2002) Implementing intensive control of blood glucose concentration and blood pressure in type 2 diabetes in England (UKPDS 63) *British Medical Journal* **325**: 860–3

DIABETES CARE

Adding metformin to insulin therapy improves glycaemic control

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

1 Some people with type 2 diabetes cannot achieve tight glycaemic control with oral agents and need to be treated with insulin, either as a single agent or added to an oral regimen.

2 There have been few studies on combination therapy with metformin and insulin. This study investigated the metabolic effects of metformin in people with type 2 diabetes intensively treated with insulin.

3 In this randomised controlled double-blind trial, the investigators took 390 people with type 2 diabetes who were taking insulin and randomly assigned them to the placebo or metformin group.

4 Intensive glucose monitoring with immediate insulin adjustments was conducted, and indexes of glycaemic control, insulin requirements, body weight, blood pressure, plasma lipids, hypoglycaemic events and other adverse events were measured.

5 In those who completed 16 weeks of treatment, metformin use was associated with improved glycaemic control, reduced insulin requirements, reduced weight gain and decreased LDL cholesterol.

6 People with type 2 diabetes who are treated with a combination of insulin and metformin have superior glycaemic control compared with insulin therapy alone, and reduced insulin requirements and weight gain.

Wulffelé MG, Kooy A, Lehert P et al (2002) Combination of insulin and metformin in the treatment of type 2 diabetes. *Diabetes Care* **25**(12): 2133–40