

Glycemic control with diet, sulfonylurea, metformin, or insulin in patients with type 2 diabetes mellitus: progressive requirement for multiple therapies (UKPDS 49). UK Prospective Diabetes Study (UKPDS) Group.

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CONTEXT: Treatment with diet alone, insulin, sulfonylurea, or metformin is known to improve glycemia in patients with type 2 diabetes mellitus, but which treatment most frequently attains target fasting plasma glucose (FPG) concentration of less than 7.8 mmol/L (140 mg/dL) or glycosylated hemoglobin A1c (HbA1c) below 7% is unknown. **OBJECTIVE:** To assess how often each therapy can achieve the glycemic control target levels set by the American Diabetes Association. **DESIGN:** Randomized controlled trial conducted between 1977 and 1997. Patients were recruited between 1977 and 1991 and were followed up every 3 months for 3, 6, and 9 years after enrollment. **SETTING:** Outpatient diabetes clinics in 15 UK hospitals. **PATIENTS:** A total of 4075 patients newly diagnosed as having type 2 diabetes ranged in age between 25 and 65 years and had a median (interquartile range) FPG concentration of 11.5 (9.0–14.4) mmol/L [207 (162–259) mg/dL], HbA1c levels of 9.1% (7.5%–10.7%), and a mean (SD) body mass index of 29 (6) kg/m². **INTERVENTIONS:** After 3 months on a low-fat, high-carbohydrate, high-fiber diet, patients were randomized to therapy with diet alone, insulin, sulfonylurea, or metformin. **MAIN OUTCOME MEASURES:** Fasting plasma glucose and HbA1c levels, and the proportion of patients who achieved target levels below 7% HbA1c or less than 7.8 mmol/L (140 mg/dL) FPG at 3, 6, or 9 years following diagnosis. **RESULTS:** The proportion of patients who maintained target glycemic levels declined markedly over 9 years of follow-up. After 9 years of monotherapy with diet, insulin, or sulfonylurea, 8%, 42%, and 24%, respectively, achieved FPG levels of less than 7.8 mmol/L (140 mg/dL) and 9%, 28%, and 24% achieved HbA1c levels below 7%. In obese patients randomized to metformin, 18% attained FPG levels of less than 7.8 mmol/L (140 mg/dL) and 13% attained HbA1c levels below 7%. Patients less likely to achieve target levels were younger, more obese, or more hyperglycemic than other patients. **CONCLUSIONS:** Each therapeutic agent, as monotherapy, increased 2- to 3-fold the proportion of patients who

attained HbA1c below 7% compared with diet alone. However, the progressive deterioration of diabetes control was such that after 3 years approximately 50% of patients could attain this goal with monotherapy, and by 9 years this declined to approximately 25%. The majority of patients need multiple therapies to attain these glycemic target levels in the longer term.