

United Kingdom Prospective Diabetes Study 24: a 6-year, randomized, controlled trial comparing sulfonylurea, insulin, and metformin therapy in patients with newly diagnosed type 2 diabetes that could not be controlled with diet therapy.

United Kingdom Prospective Diabetes Study Group.

Ann Intern Med. 1998 Feb 1; 128(3): 165-75.

BACKGROUND: Uncertainty exists about the suitability of oral hypoglycemic drugs and insulin therapy for patients with newly diagnosed type 2 diabetes. **OBJECTIVE:** To assess and compare response to sulfonylurea, insulin, or metformin over 6 years in patients with newly diagnosed type 2 diabetes in whom disease could and could not be controlled with diet therapy alone. **DESIGN:** Multicenter, randomized, controlled trial. **SETTING:** Outpatient diabetes clinics of 15 hospitals in the United Kingdom. **INTERVENTION:** Sulfonylurea (chlorpropamide or glyburide), insulin, or metformin (if patients were obese). **PATIENTS:** 458 patients with newly diagnosed type 2 diabetes that could not be controlled with diet and had hyperglycemic symptoms or fasting plasma glucose levels greater than 15 mmol/L during the initial 3 months of diet therapy (primary diet failure group) and 1620 patients in whom disease was controlled by diet therapy and who had fasting plasma glucose levels of 6 to 15 mmol/L and no hyperglycemic symptoms while receiving diet therapy alone. **MEASUREMENTS:** Fasting plasma levels of glucose and insulin, hemoglobin A1c concentrations, body weight, and therapy required. **RESULTS:** Compared with the diet-controlled group, the primary diet failure group was younger and less obese and had more retinopathy, lower fasting plasma insulin levels, and reduced beta-cell function. At 6 years, patients allocated to insulin had lower fasting plasma glucose levels than did patients allocated to oral agents, but hemoglobin A1c concentrations were similar. Forty-eight percent (95% CI, 37% to 58%) of patients in the primary diet failure group maintained hemoglobin A1c concentrations less than 0.08. By 6 years, 51% of patients (CI, 42% to 62%) allocated to ultralente insulin required additional short-acting insulin and 66% of patients (CI, 58% to 73%) allocated to sulfonylurea required additional therapy with metformin or insulin to control symptoms and maintain fasting plasma glucose levels less than 15 mmol/L. Patients allocated to insulin gained more weight and had more hypoglycemic attacks than did patients

allocated to sulfonylurea. Obese patients allocated to metformin gained the least weight and had the fewest hypoglycemic attacks. For all therapies, control achieved at 6 years was worse in the primary diet failure group than in the diet-controlled group. **CONCLUSIONS:** Because initial insulin therapy induced more hypoglycemic reactions and weight gain without necessarily providing better control, it may be reasonable to start with oral agents and change to insulin if goals for glycemic levels are not achieved.