United Kingdom Prospective Diabetes Study 17: a 9-year update of a randomized, controlled trial on the effect of improved metabolic control on complications in non-insulin-dependent diabetes mellitus.

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Ann Intern Med. 1996 Jan 1; 124(1 Pt 2): 136-45.

PURPOSE: To report the progress (after 9-year follow-up) of a study designed to determine whether improved glucose control in patients with newly diagnosed non-insulin-dependent diabetes mellitus (NIDDM) is effective in reducing the incidence of clinical complications. DATA SOURCE: A multicenter, randomized, controlled trial of different therapies for NIDDM. After initial diet therapy, 4209 asymptomatic patients who remained hyperglycemic (fasting plasma glucose levels, 6.0 to 15.0 mmol/L) were assigned to either a conventional therapy policy, primarily with diet alone, or to an intensive therapy policy, aiming for fasting plasma glucose levels of less than 6.0 mmol/L, with assignment to primary therapy with sulfonylurea or insulin (which increased insulin supply) or metformin (which enhanced insulin sensitivity). RESULTS: All three modes of pharmacologic therapy in the intensively treated group-sulfonylurea, insulin, and metformin-had similar efficacy in reducing the fasting plasma glucose and glycated hemoglobin levels. Over 9 years, patients assigned to intensive therapy with sulfonylurea or insulin had lower fasting plasma glucose levels (median, 7.3 and 9.0 mmol/L, respectively) than patients assigned to conventional therapy. Regardless of the assigned therapy, however, the fasting plasma glucose and hemoglobin A1c levels increased, and maintaining near-normal glycemia was, in general, not feasible. Even insulin therapy did not achieve the therapeutic goal of near-normal glycemia because of the difficulty in treating marked hyperglycemia and the risk for hypoglycemic episodes. Nine years after the diagnosis of diabetes, 29% of the patients had had a diabetes-related clinical end point, 20% had had a macrovascular complication, and 9% had had a microvascular complication. CONCLUSIONS: A report will be published in 1998 after a median duration from randomization of 11 years (range, 6 to 20 years) with an 81% power at a 1% level of significance of detecting whether the obtained improvement in glucose control causes a 15% decrease or

increase in the incidence of major complications and whether any specific therapy is advantageous or disadvantageous.