function, tumor suppression, and increased insulin sensitivity. The negative effects of insulin were attributed to it being proatherogenic, its effect on the insulin-like growth factor-1 axis, survival and proliferation of malignant cells, and hypoglycemia.

ADDITION Shows No Increased Benefit Of Early Multifactorial Intensive Therapy

The issue of intensive diabetes therapy became a bit more perplexing after the latest results of the ADDITION (Anglo-Danish-Dutch Study of Intensive Treatment. In People with Screen Detected Diabetes in Primary Care; NCT00237549) trial found no significant differences in overall cardiovascular (CV) events between such care and the routine management of patients with screen-detected diabetes.

Simon J. Griffin, DM, Medical Research Council Epidemiology Unit, Cambridge, UK, presented the latest findings of the 3000-patient multifactorial trial. The trial was designed to evaluate various stepped screening programs to identify diabetes in at-risk individuals; determine whether primary care practices could provide intensive therapy; and assess the differences between intensive and routine management of diabetes over 5 years, based on continually updated clinical guidelines.

The trial was conducted in three countries: The Netherlands, the UK, and Denmark. Most participants were obese and had high blood pressure (>120/80 mm Hg) and a median HbA1C of 6.6% upon entry. The primary endpoint was a composite of the first CV event, including CV mortality and morbidity (nonfatal myocardial infarction or nonfatal stroke), revascularization, and nontraumatic amputation.

General practitioners in the intensive intervention arm were encouraged to provide education on lifestyle changes that were designed to reduce their patients' CV risk and improve glycemic levels, and treatment started once HbA1C levels reached ≥6.5%, blood pressure was >120/80 mm Hg, and/or total cholesterol was >3.5 mmol/L. Physicians in this arm also received practice-based education.

Routine care was based on national guidelines. Over time, it is important to note that the national guidelines changed and became more similar to the intensive treatment guidelines, with more intensive goals for blood pressure, cholesterol, and HbA1C levels. In fact, Prof. Griffin noted that this congruence of treatment goals was a possible reason for the lack of significant effects that were associated with intensive treatment.

Both groups demonstrated improvements in CV risk factors during the study, with the intensive treatment arm demonstrating significant, albeit modest, greater improvements in risk factors and achievement of treatment targets. Rates of CV events in both groups over 5 years were lower than expected (7.2% [intensive] vs 8.5% [control]; HR, 0.83; 95% CI, 0.65 to 1.05; p=0.12). An analysis from William Herman, MD, University of Michigan, Ann Arbor, Michigan, USA, postulated that had the patients in the trial not been screened, diagnosed with diabetes, and treated, the composite endpoint would have doubled, regardless of the type of care that was provided.

There was no increased mortality in the intensive treatment arm, though such increases were seen in other large diabetes trials that assessed the role of intensive treatment in CV risk.

Early Treatment With Olmesartan Delays Progression of Nephropathy in Patients With Type 2 Diabetes

Preventing the progression of normal albumin excretion to microalbuminuria should be a goal in the management of patients with type 2 diabetes mellitus (T2DM), since microalbuminuria is an early sign of diabetic nephropathy and elevated cardiovascular (CV) risk. The Randomized Olmesartan And Diabetes MicroAlbuminuria Prevention (ROADMAP; NCT00185159) study investigated whether early administration of an angiotensin receptor blocker (ARB) to diabetic patients with normal albumin excretion could delay or prevent the first occurrence of microalbuminuria and whether it could affect the incidence of CV and renal events.

This multinational European trial randomly assigned 4447 patients (aged 18 to 75 years) with T2DM and at least one additional CV risk factor and normoalbuminuria to olmesartan 40 mg (n=2232) or placebo (n=2215). Patients could also receive other antihypertensive medication that did not act on the renin-angiotensin system but could not have been treated with an angiotensin-converting enzyme inhibitor or ARB in the previous 6 months. The groups were well matched at baseline for gender, age (58 years), body mass index (31 kg/m^2), glycated hemoglobin (7.65%