The expanding evidence base - what have we added to our understanding of diabetes disease modification?

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The UKPDS demonstrated that type 2 diabetes is a progressive condition, showing that HbA1c levels continue to rise over time despite monotherapy with any of the therapeutic agents it compared in its head-to-head trial design. Additional UKPDS data analyses suggested that this increasing hyperglycaemia was probably secondary to the year-on-year decline observed in beta-cell function, measured as HOMA %B, with no substantive changes in insulin sensitivity (HOMA %S). Although none of the traditional therapeutic modalities evaluated by the UKPDS appeared to alter disease progression, data from the later DPP and TRIPOD studies suggested that a newer class of agents, the thiazolidenediones, might maintain or enhance beta-cell function over time. More recently the DREAM trial has shown that in people with impaired glucose tolerance and/or impaired fasting glucose, a 60% reduction in new-onset diabetes can be achieved with rosiglitazone therapy, albeit at the expense of increased adiposity and an increased risk of congestive heart failure. In people with recent onset type 2 diabetes, the ADOPT study has demonstrated that rosiglitazone can slow progression to monotherapy failure to a greater extent than metformin or glibenclamide, with not only a corresponding decrease in the rate of loss of beta-cell function, but improved insulin sensitivity. This demonstration that progressive hyperglycaemia may not be inexorable is welcome and offers new insights into how type 2 diabetes might best be treated, and increases interest in newly emerging antidiabetic agents such as cannabinoid 1 receptor blockers, incretin mimetics and dipeptidyl peptidase IV (DPP-IV) inhibitors.