Importance of Early Intensive Glycaemic Control

Supported by an educational grant from Novo Nordisk A/S

Radcliffe Medical Education

The Legacy Benefit

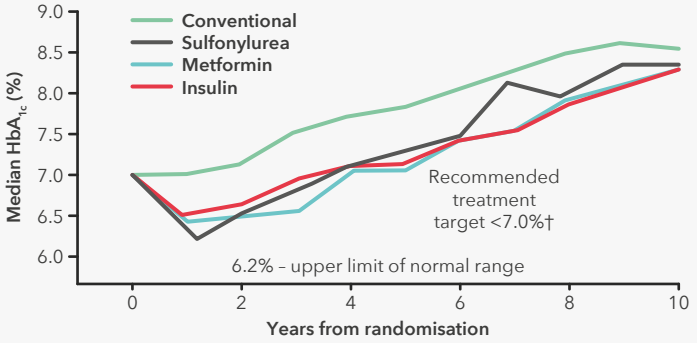
- T2DM is a progressive disease due to deteriorating β-cell dysfunction and increasing insulin resistance, hence **early intensive therapies are needed** to prevent/ slow progressive β-cells failure[1]
- Several studies have shown that early tight glycaemic control is associated with reduced microvascular, macrovascular and mortality outcomes– the so-called "**legacy benefit**"[2-7]

Study	Microvascular		CVD		Mortality	
UKPDS	↓	↓	↔	↓	↔	↓
DCCT/EDIC[a]	↓	↓	↔	↓	↔	↔
ACCORD	↓		↔		↑	
ADVANCE	↓		↔		↔	
VADT	↓		↔	↓	↔	

UKPDS

A multicentre, prospective RCT of **newly diagnosed** patients with T2DM, aimed to determine whether early, intensive glucose lowering would reduce long-term morbidity and mortality complications

- >4000 were randomly assigned to conventional therapy (dietary restriction) or intensive therapy (sulfonylurea, insulin or, in overweight subjects, metformin) and followed for 10 years
- Even though between group differences in glucose control were lost after Year 1, intensive control achieved a median HbA_{1c} of **7.0%** (vs **7.9%** with conventional therapy) over 10 years
- The lower average HbA_{1c} achieved with intensive lowering was coupled with a **24%** reduction in **microvascular disease**[2]

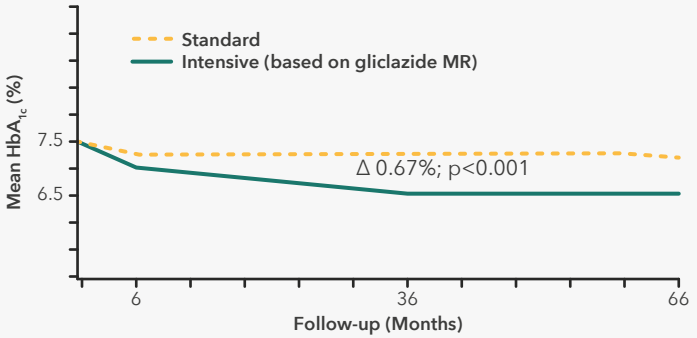


Adapted from Holman R, et al. 2008

ADVANCE study

A multicentre, 2X2 factorial RCT of **>10,000** adults with T2DM for >10 years, at elevated risk of vascular disease. The study aimed to examine whether intensive glucose control reduces the incidence of macrovascular and microvascular disease

- Intensive therapies lowered HbA_{1c} from **7.3%** to **6.5%** and yielded a **10%** relative reduction in the combined outcome of major macrovascular and microvascular events, primarily as a consequence of a **21%** relative reduction in nephropathy[3]



Adapted from ADVANCE Collaborative Group. 2008

Takeaway Message

Guidelines have emphasised the importance of **avoiding clinical inertia** in T2DM management and recommend various early intensive therapies based on the **individual patient profile** with **regular follow-ups every 3-6 months**[8]

Despite strong evidence and guidelines recommendations, there is considerable delay in initiating early, intensive glucose control into clinical practice[9]

Abbreviations: ACCORD, Action to Control Cardiovascular Risk in Diabetes; ADVANCE, Action in Diabetes and Vascular Disease: Preterax and Diamicron - MR Controlled Evaluation; CVD, cardiovascular disease; DCCT, Diabetes Control and Complications Trial; DM, diabetes mellitus; DPP-4i, dipeptidyl peptidase-4 inhibitor; EDIC, The Epidemiology of Diabetes Interventions and Complications; GLP-1, glucagon-like peptide-1; GLP-1 RAs, glucagon-like peptide-1 receptor agonists; HbA_{1c}, Hemoglobin A_{1c}; MR, modified release; RCT, randomised controlled trial; SGLT2i, sodium-glucose co-transporter-2 inhibitors; T2DM, type 2 diabetes mellitus; UKPDS, The UK Prospective Diabetes Study; VADT, Veterans Affairs Diabetes Trial

References: **1.** Kathleen A et al. *Curr Diab Rep*. 2013; 13(2):252-260. **2.** Holman R et al. *N Engl J Med*. 2008; 359:1577-1589. **3.** ADVANCE Collaborative Group. *N Engl J Med*. 2008; 358:2560-72. **4.** Hayward RA et al *N Engl J Med*. 2015; 372:2197-206. **5.** Laiteerapong et al. *Diabetes Care* 2019; 42(3):416-426. **6.** ACCORD Study Group. *N Engl J Med*. 2008; 358: 2545-2559. **7.** DCCT/EDIC Study Group. *N Engl J Med*. 2005; 353:2643-2653. **8.** Davies MJ et al. *Diabetes Care* 2018; Sep:dci180033. **9.** Khunti K. Lancet *Diab & Endoc*. 2017; 11:105-106.