Beyond glycaemic control: Cardiovascular Benefits

Supported by an educational grant from Novo Nordisk A/S

Radcliffe Medical Education

Cardiovascular Outcome Trial Evidence

CVOTs using GLP-1 RAs have shown **significant reductions in 3-point MACE** – *MI, stroke and CV death*

LEADER[2]

Liraglutide superior to t for time to 3-point MACE in T2D with established CVD, CRF or aged ≥60 with CV risk

SUSTAIN-6[3]

Semaglutide superior to placebo for time to 3-point MACE in T2DM with established CVD, CRF or aged ≥60 with CV risk

HARMONY[4]

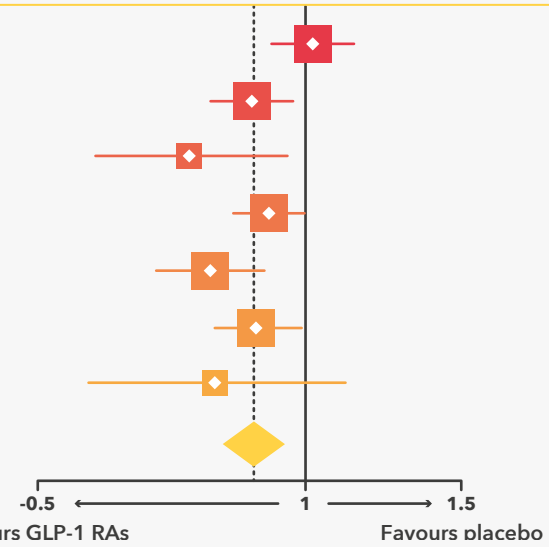
Albiglutide superior to placebo for time to 3-point MACE in T2DM with established CVD, aged ≥40

REWIND[5]

Dulaglutide superior to placebo for time to 3-point MACE in T2DM with low CV risk

Meta-analysis of CVOTs[6] showed that despite various patient populations and drug formulations, there was a clinically meaningful and statistically **significant benefit in 3-point MACE**

	3-point MACE %				
	GLP-1RAs	Placebo	Hazard ratio	NNT	p value
ELIXA	13%	13%	1.02		0.78
LEADER	13%	15%	0.87		0.015
SUSTAIN-6	7%	9%	0.74		0.016
EXSCEL	11%	12%	0.91		0.061
Harmony Outcomes	7%	9%	0.78		<0.0001
REWIND	12%	13%	0.88		0.026
PIONEER	4%	5%	0.79		0.17
Overall	11%	12%	0.88	75	<0.0001



Adapted from Kristensen SL et al. 2019

Additional benefits include reductions in risk of HF hospitalization, composite kidney outcomes, and favourable trends towards reduced hard kidney events

How can we optimise outcomes in high CV risk patients?

Despite the compelling data and universal adoption in guidelines, **most patients do not receive these therapies**

In a large US-based registry, **less than 10%** of patients received SGLT-2is or GLP-1 RAs and **less than 7%** received optimal guideline directed medical therapy[7]

Patient-centred, comprehensive risk-reduction, delivered by multidisciplinary teams, leads to optimal therapy and better patient outcomes

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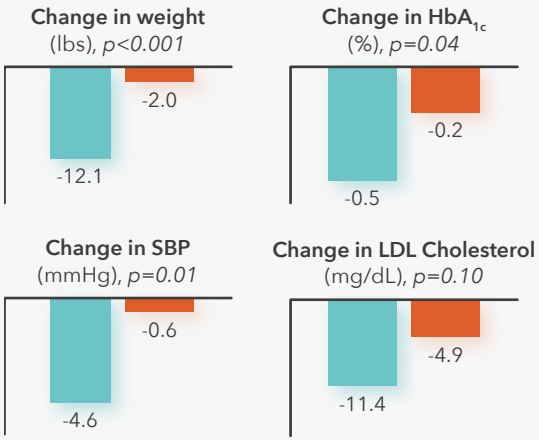
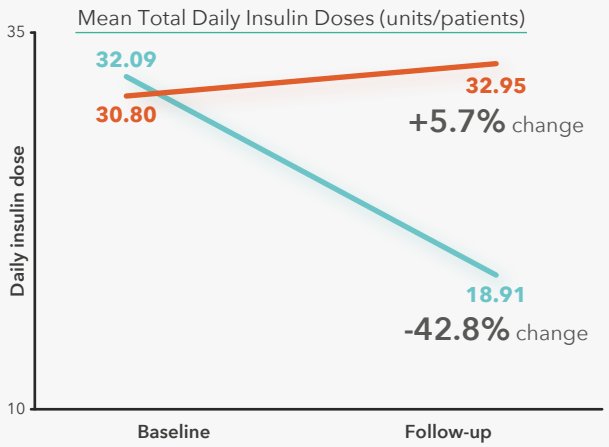
How does collaborative care impact outcomes?

Over a period of 3 – 4 months, a collaborative approach at a specialist CMC resulted in[8]

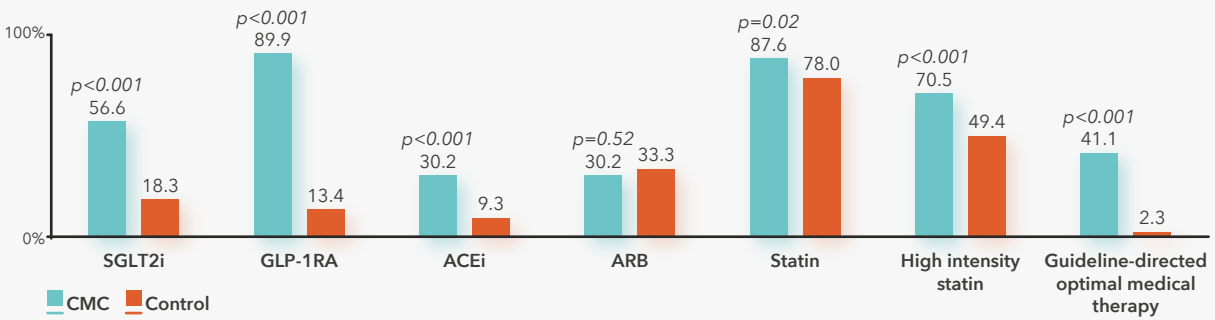
- **significant reductions in key risk factors**



- **significant reduction in insulin requirements**



- **greater adherence to guideline-directed medical therapies**
  - Nearly **20-fold** improvement in composite metric of optimal medical therapy according to the guidelines



Adapted from Thomas et al. 2020

What is comprehensive, collaborative care?

Key support staff & personnel

- Driven by preventive cardiology in collaboration with endocrinology and primary care
- Support staff including advance practice providers, nurse navigators and others cross-trained in both CVD and T2DM
- Key support personnel includes certified DM educator, dietician, and pharmacist with plan to include others over time

Comprehensive treatment plans

- Both CV and DM-related aspects of care addressed at each visit
- Comprehensive treatment plan developed and tailored to individual patients with chief objective of aggressive secondary risk reduction

Abbreviations: ACEi, Angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; CMC, Cardiometabolic Center; CRF, chronic renal failure; CV, cardiovascular; CVD, cardiovascular disease; CVOT, cardiovascular outcomes trial; DM, diabetes mellitus; GLP-1RA, glucagon-like peptide 1 receptor agonist; HbA_{1c}, haemoglobin A_{1c}; HF, heart failure; LDL-C, low density lipoprotein cholesterol; MACE, major adverse cardiovascular events; MI, myocardial infarction; NNT, number needed to treat; SBP, systolic blood pressure; SGLT2i, sodium-glucose cotransporter 2 inhibitor; T2DM, type 2 diabetes mellitus.

References: **1.** Drucker DJ. *Cell Metab* 2016;24:15–30. **2.** Marso SP et al. *N Engl J Med* 2016;375:311–322. **3.** Marso SP et al. *N Engl J Med* 2016;375:1834–1844. **4.** Hernandez AF et al. *Lancet* 2018;392:1519–1529. **5.** Gerstein HC et al. *Lancet* 2019; S0140-6736:31149-31153. **6.** Kristensen SL et al. *Lancet Diabetes* Endocrinol, 2019;10:776-785. **7.** Arnold SV et al. *Circulation*. 2019;140:618-620. **8.** Thomas et al. *Circ Cardiovasc Qual Outcomes*. 2021;14:e007682.