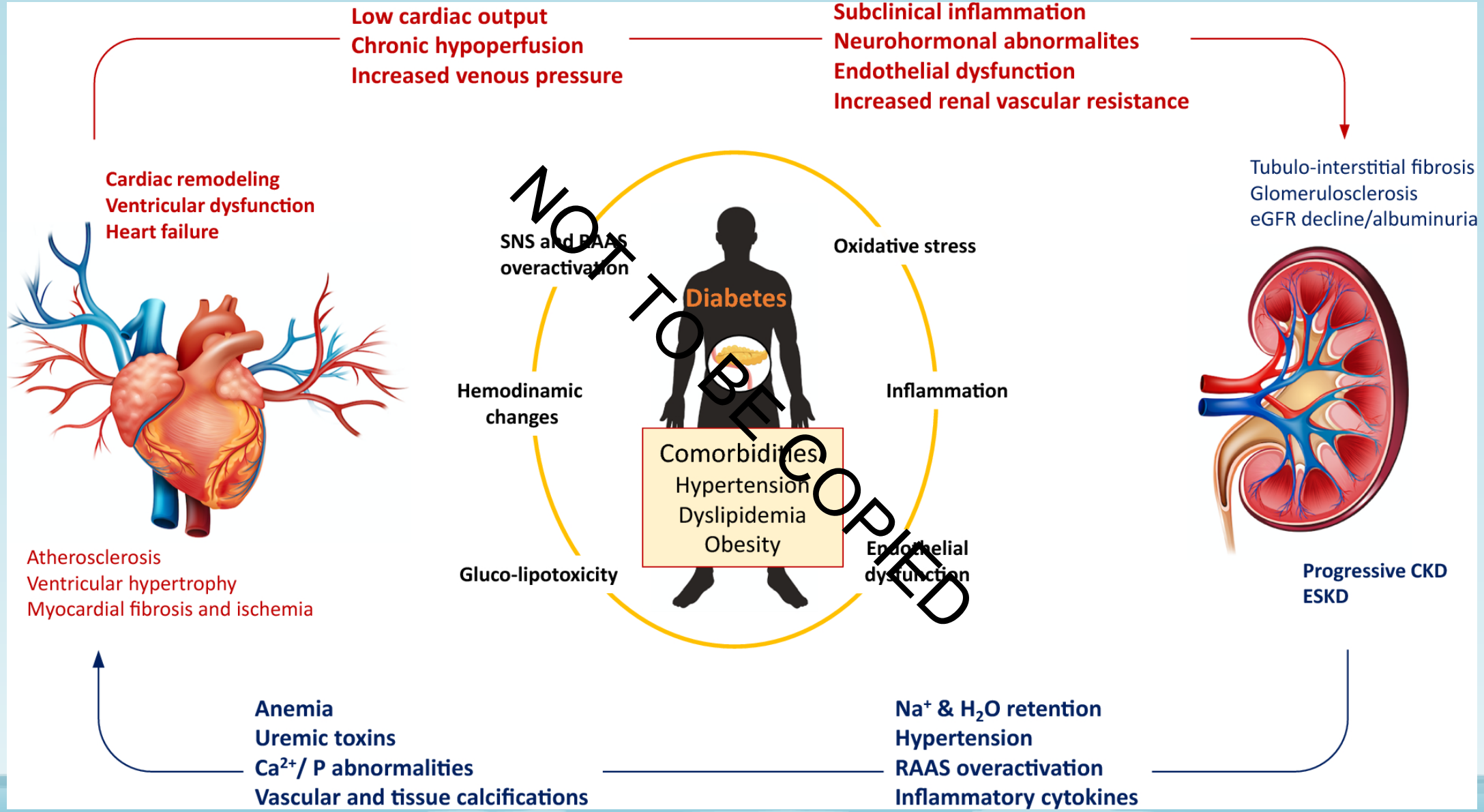
Beyond Glycaemia in the Management of T2DM

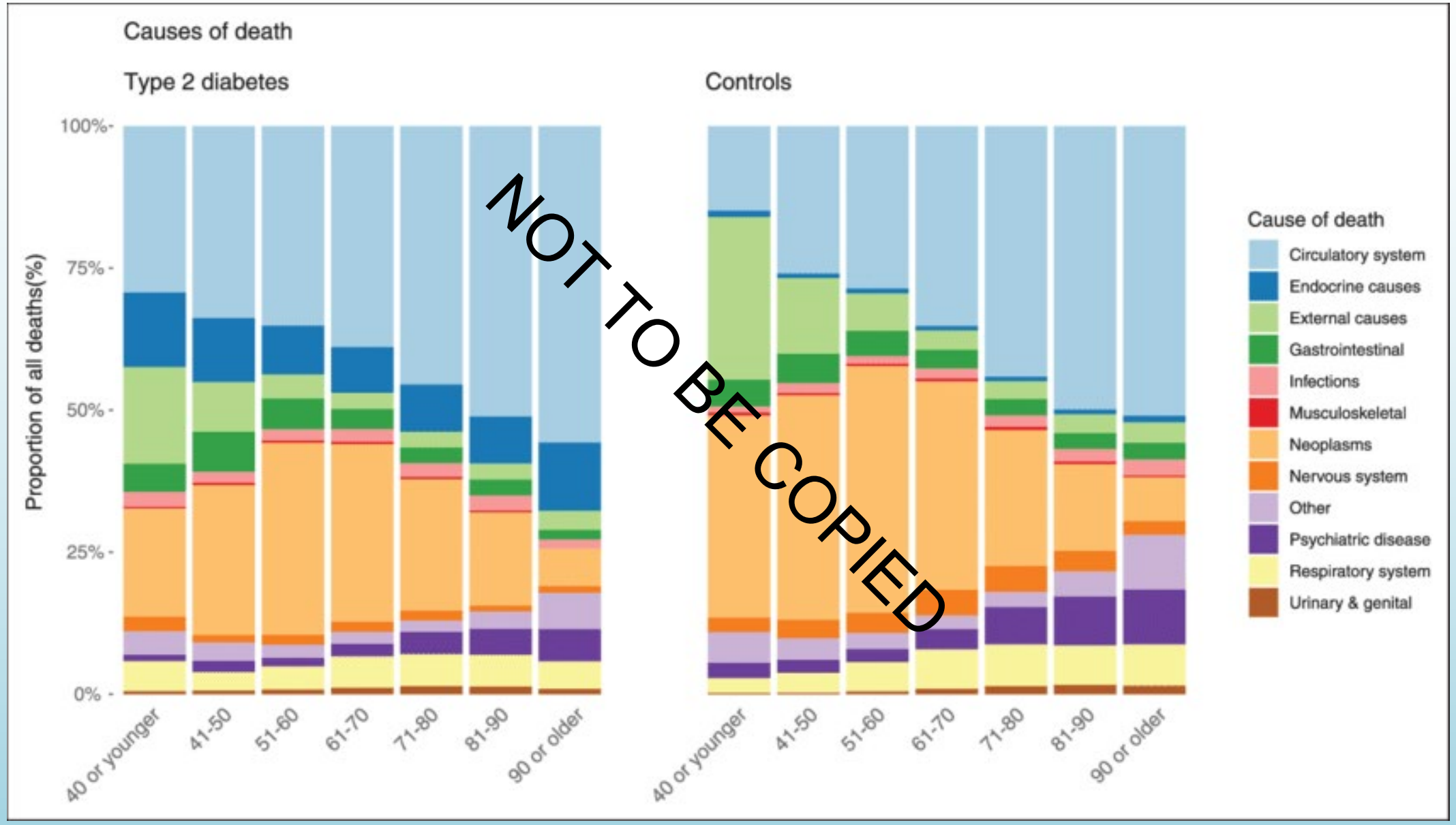
KASHIF ALI
GP , GLASGOW
PRIMARY CARE LEAD DIABETES MCN, NHS GGC

The Cardio-Renal-Metabolic Connection



Marassi, M., Fadini, G.P. The cardio-renal-metabolic connection: a review of the evidence. *Cardiovasc Diabetol* **22**, 195 (2023)**https://rdcu.be/dWqP1**

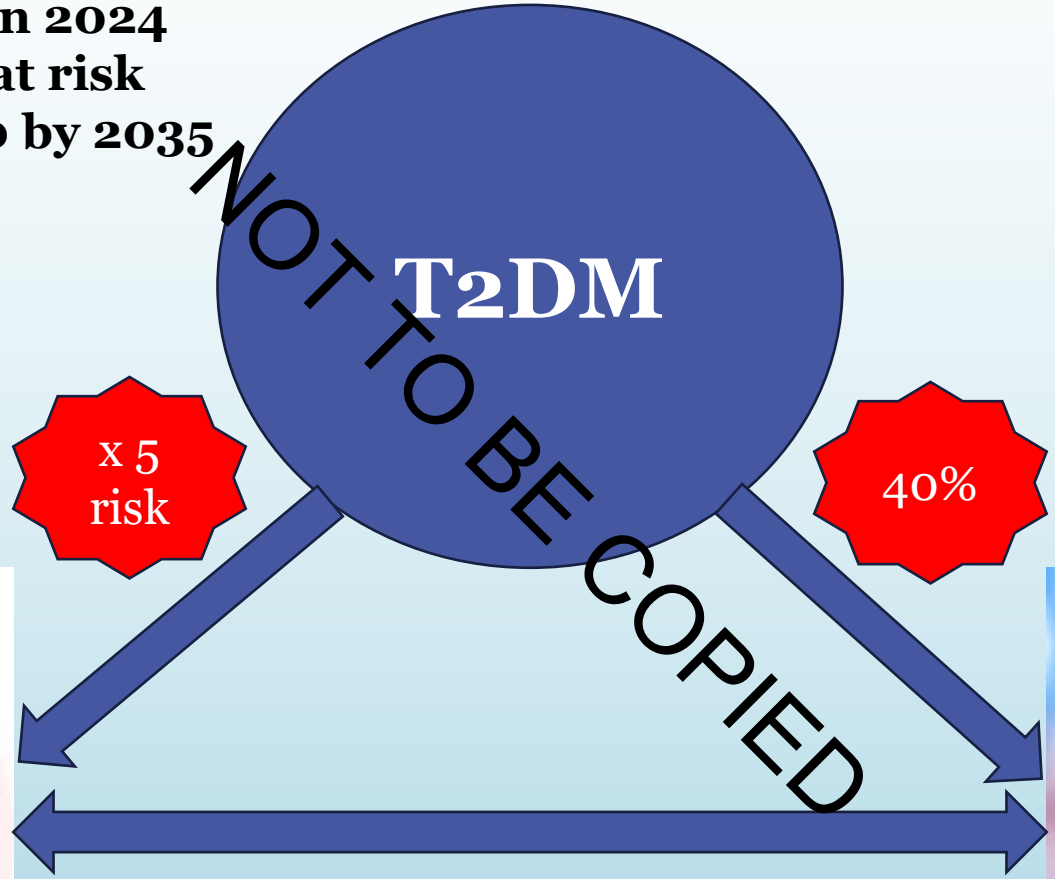
Causes of death in relation to age at onset of T2D diagnosis v controls



Sattar, Naveed & Rawshani et al. (2019). Age at Diagnosis of Type 2 Diabetes Mellitus and Associations With Cardiovascular and Mortality Risks Findings From the Swedish National Diabetes Registry. Circulation. 139. 10.1161.

T2D, HEART FAILURE AND CKD ARE INTERLINKED

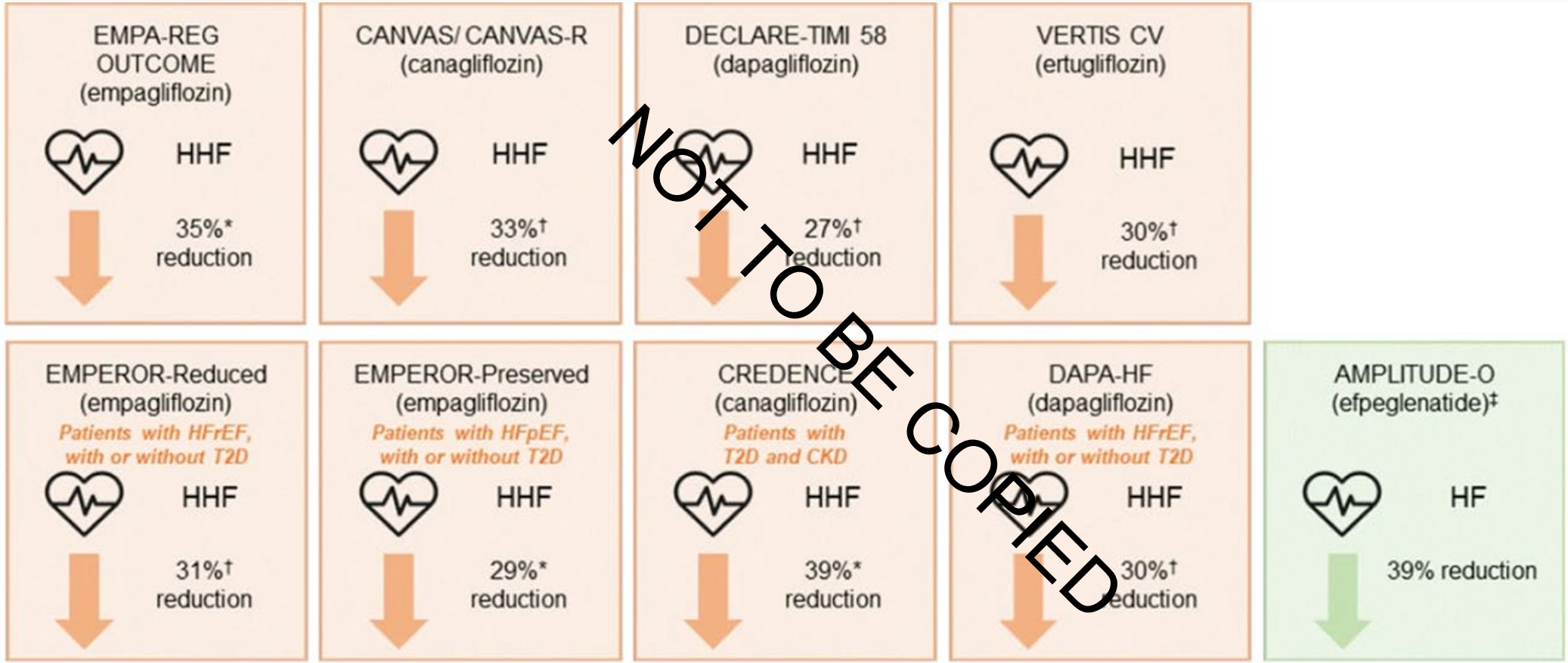
- 323,000 in 2024
- 500,000 at risk
- >480,000 by 2035



#1 cause of hospital > 65yrs
>50% die within 5 yrs

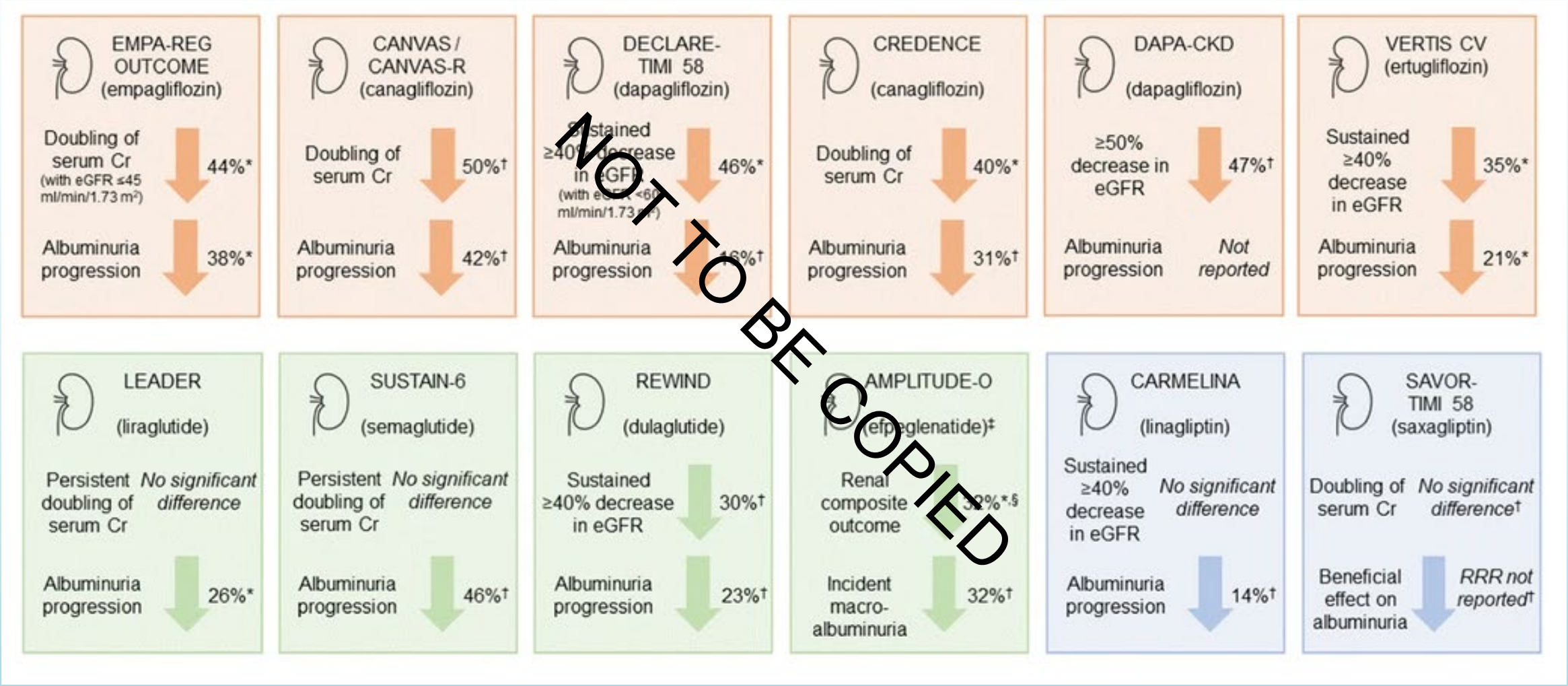
>10,000 Dialysis within 10yrs
Cost £1bn to Scottish economy

SGLT2-Is and Heart Failure



Davies, M.J., Drexel, H., Jornayvaz, F.R. *et al.* Cardiovascular outcomes trials: a paradigm shift in the current management of type 2 diabetes. *Cardiovasc Diabetol* **21**, 144 (2022). https://doi.org/10.1186/s12933-022-01575-9

Newer treatments and CKD

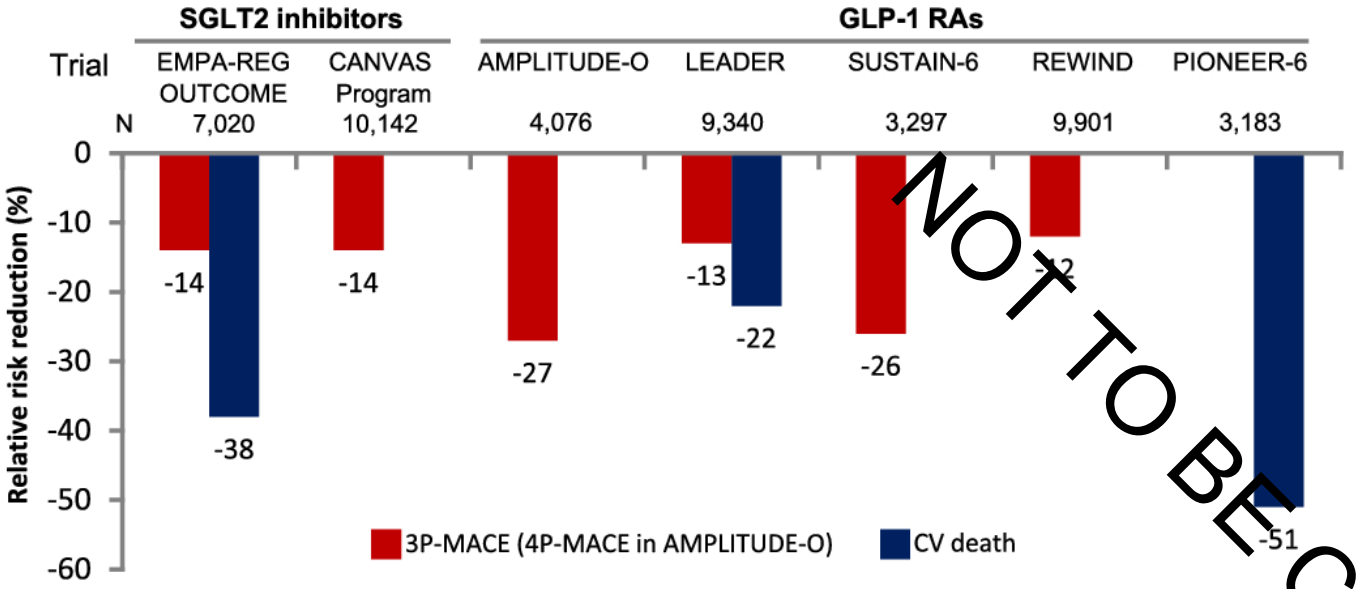


Davies, M.J., Drexel, H., Jornayvaz, F.R. *et al.* Cardiovascular outcomes trials: a paradigm shift in the current management of type 2 diabetes. *Cardiovasc Diabetol* **21**, 144 (2022). https://doi.org/10.1186/s12933-022-01575-9

Diabetes CVOTs

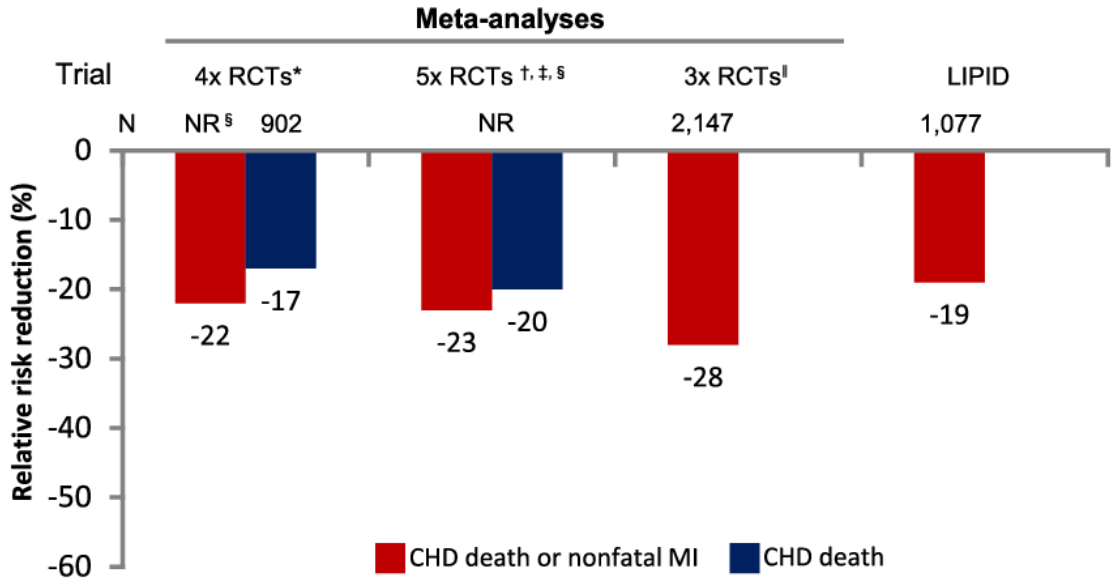
A

Relative risk reduction in **3P-MACE** and **CV death** with GLDs



Reductions only shown for diabetes CVOTs with statistically significant benefit

Secondary prevention with **statins** in patients with diabetes



B

NNT with GLDs

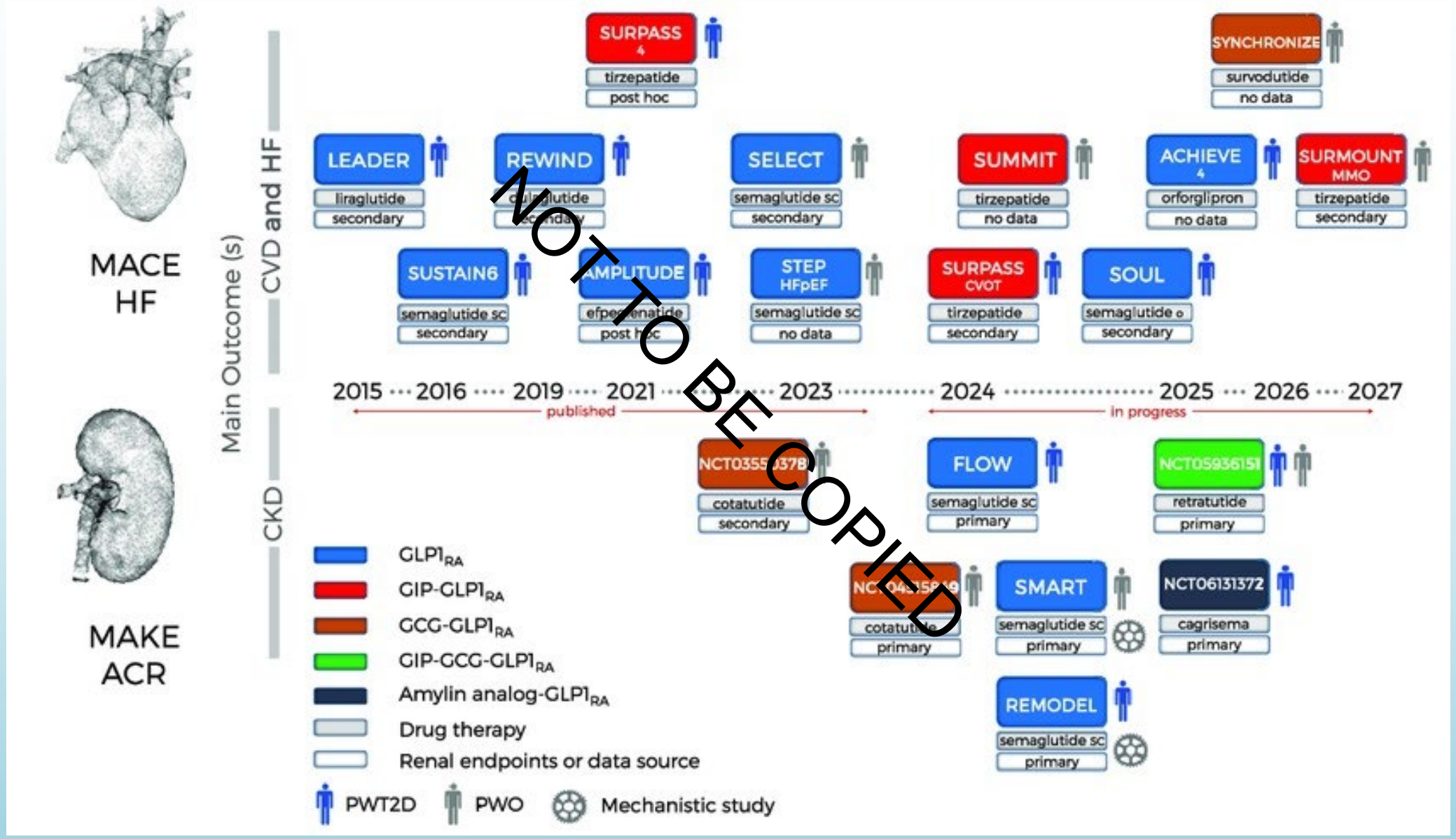
Empagliflozin EMPA-REG OUTCOME	Liraglutide LEADER	Semaglutide SUSTAIN-6	Empagliflozin EMPA-REG OUTCOME
63 NNT	53 NNT	44 NNT	39 NNT
in **3.1 years** to prevent one **3P-MACE**	in **3.8 years** to prevent one **3P-MACE**	in **2 years** to prevent one **3P-MACE**	in **3.1 years** to prevent one **death**

NNT with cardiorenal therapies

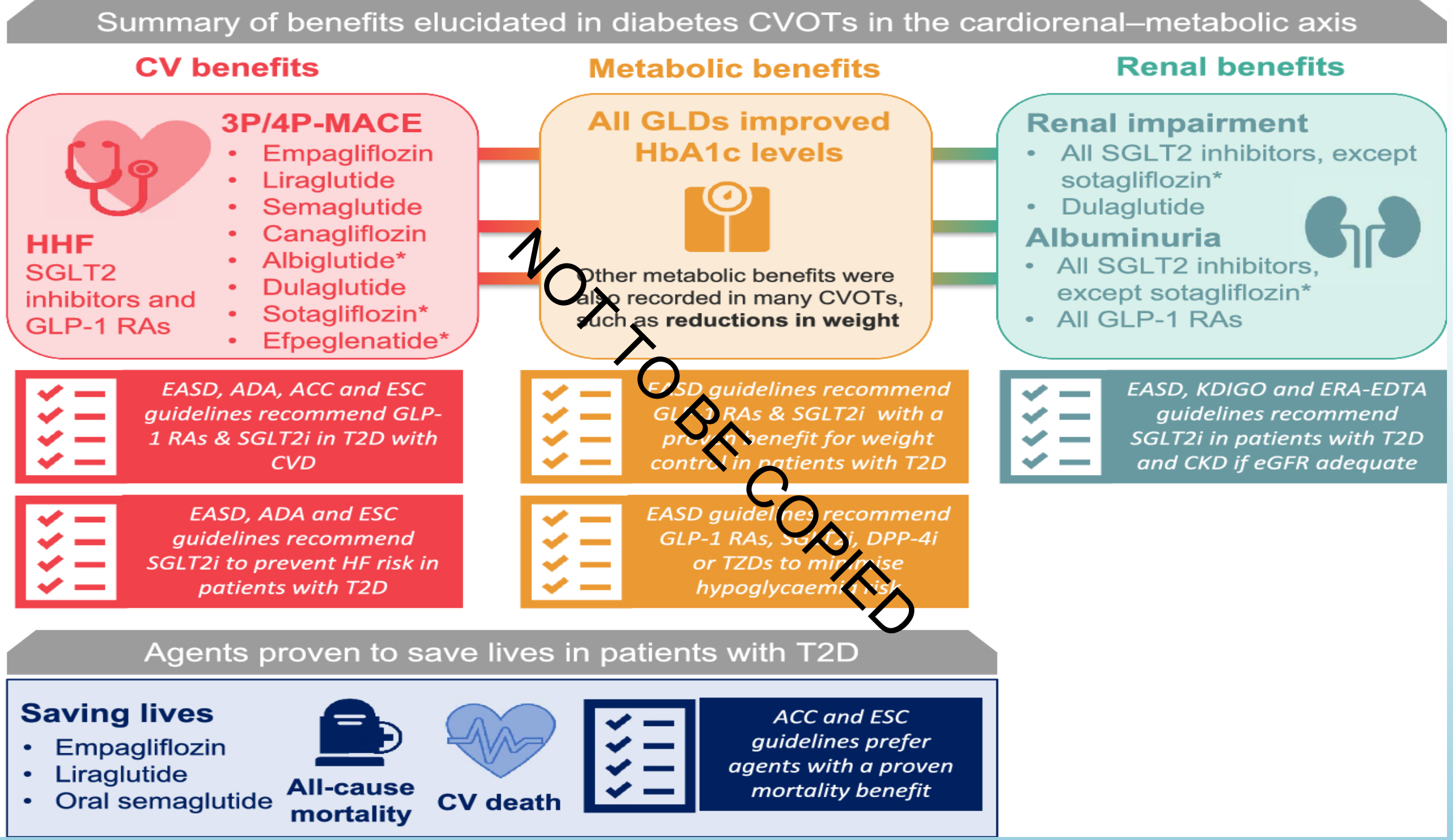
Aspirin in prior MI or stroke	Statins in known CAD or stroke	Antihypertensive therapy
50 NNT	83 NNT	125 NNT
in **2 years** to prevent one **3P-MACE**	in **5 years** to prevent one **death**	in **5 years** to prevent one **death**

Davies, M.J., Drexel, H., Jornayvaz, F.R. *et al.* Cardiovascular outcomes trials: a paradigm shift in the current management of type 2 diabetes. *Cardiovasc Diabetol* **21**, 144 (2022). https://doi.org/10.1186/s12933-022-01575-9

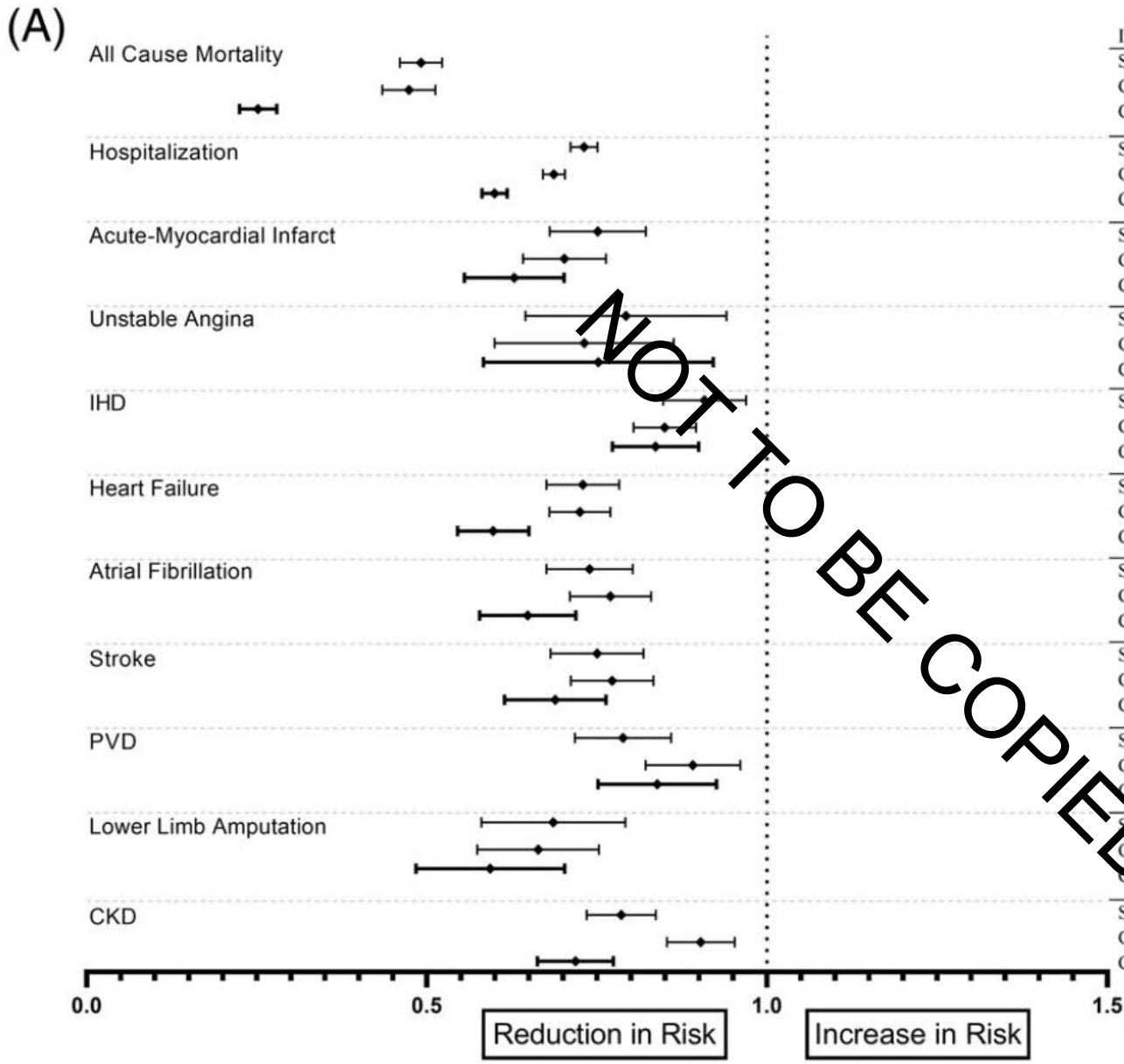
INCRETIN-BASED RX AND TIMELINE OF KIDNEY, METABOLIC AND CV OUTCOMES



Moreno-Perez et al. Are we ready for an adipocentric approach in people living with T2D and CKD. Clinical Kidney Journal. 2024, vol 17, no.4



Davies, M.J., Drexel, H., Jornayvaz, F.R. *et al.* Cardiovascular outcomes trials: a paradigm shift in the current management of type 2 diabetes. *Cardiovasc Diabetol* **21**, 144 (2022).

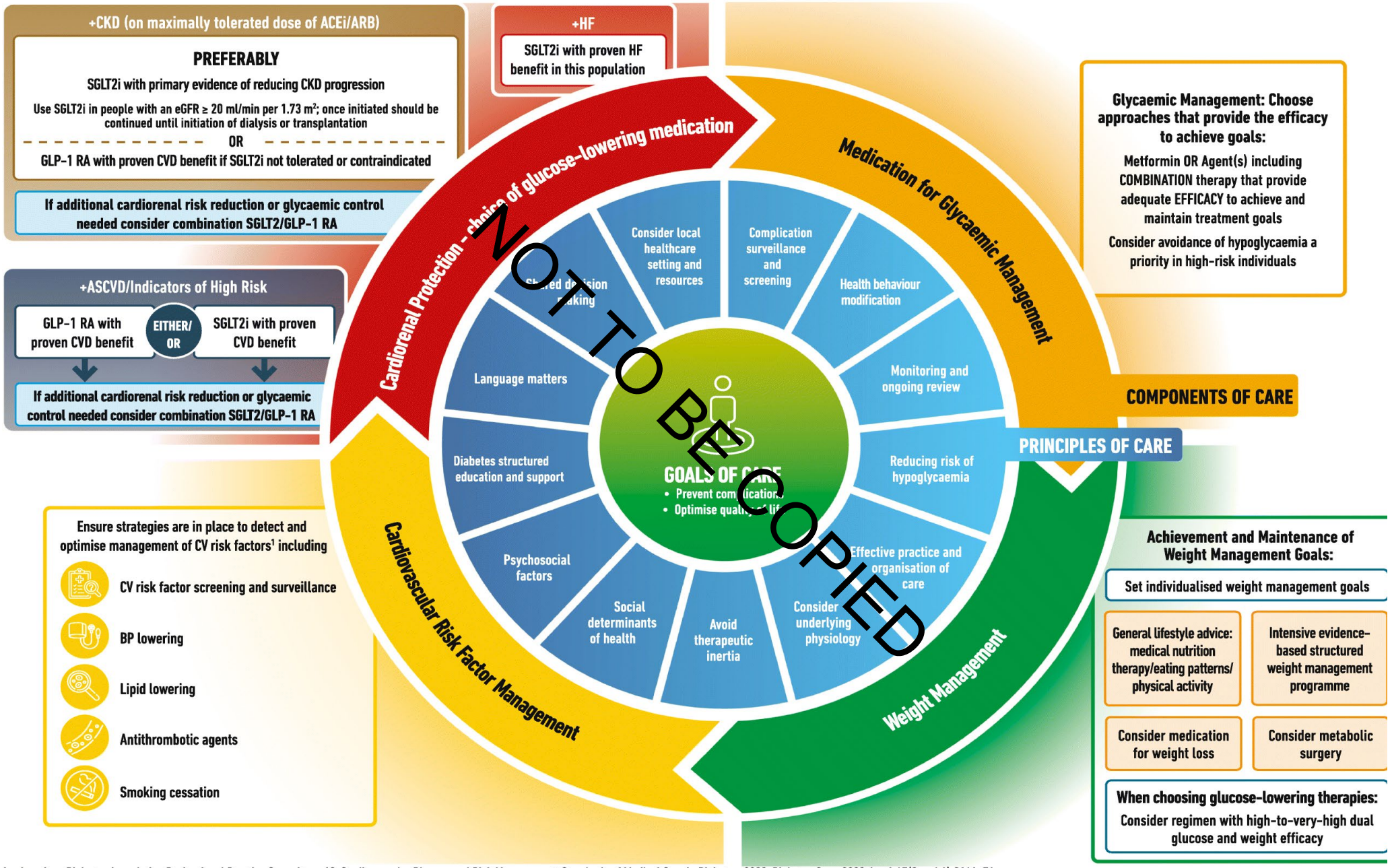


Intervention Cohort	Hazard Ratio (95% CI)	P value
SGLT2i	0.49 (0.48, 0.50)	<0.001
GLP-1RA	0.47 (0.46, 0.48)	<0.001
Combination	0.25 (0.24, 0.26)	<0.001
SGLT2i	0.73 (0.72, 0.74)	<0.001
GLP-1RA	0.69 (0.68, 0.69)	<0.001
Combination	0.60 (0.59, 0.61)	<0.001
SGLT2i	0.75 (0.72, 0.78)	<0.001
GLP-1RA	0.70 (0.68, 0.73)	<0.001
Combination	0.63 (0.60, 0.66)	<0.001
SGLT2i	0.79 (0.73, 0.85)	<0.001
GLP-1RA	0.73 (0.68, 0.79)	<0.001
Combination	0.75 (0.69, 0.82)	<0.001
SGLT2i	0.91 (0.88, 0.93)	<0.001
GLP-1RA	0.85 (0.83, 0.87)	<0.001
Combination	0.84 (0.81, 0.86)	<0.001
SGLT2i	0.73 (0.71, 0.75)	<0.001
GLP-1RA	0.73 (0.71, 0.74)	<0.001
Combination	0.60 (0.58, 0.62)	<0.001
SGLT2i	0.74 (0.71, 0.77)	<0.001
GLP-1RA	0.77 (0.75, 0.79)	<0.001
Combination	0.65 (0.62, 0.68)	<0.001
SGLT2i	0.75 (0.72, 0.78)	<0.001
GLP-1RA	0.77 (0.75, 0.80)	<0.001
Combination	0.69 (0.66, 0.72)	<0.001
SGLT2i	0.79 (0.76, 0.82)	<0.001
GLP-1RA	0.89 (0.86, 0.92)	<0.001
Combination	0.84 (0.80, 0.87)	<0.001
SGLT2i	0.69 (0.64, 0.73)	<0.001
GLP-1RA	0.66 (0.63, 0.70)	<0.001
Combination	0.59 (0.55, 0.64)	<0.001
SGLT2i	0.79 (0.77, 0.81)	<0.001
GLP-1RA	0.90 (0.88, 0.92)	<0.001
Combination	0.72 (0.70, 0.74)	<0.001

Riley et. Al "All-cause mortality and cardiovascular outcomes with sodium-glucose Co-transporter 2 inhibitors, glucagon-like peptide-1 receptor agonists and with combination therapy in people with type 2 diabetes. Diabetes, Obesity and Metabolism. June 2023

Retrospective cohort analysis of 2.2 million people with type 2 diabetes receiving insulin across 85 health care organisations using a global federated health research network.

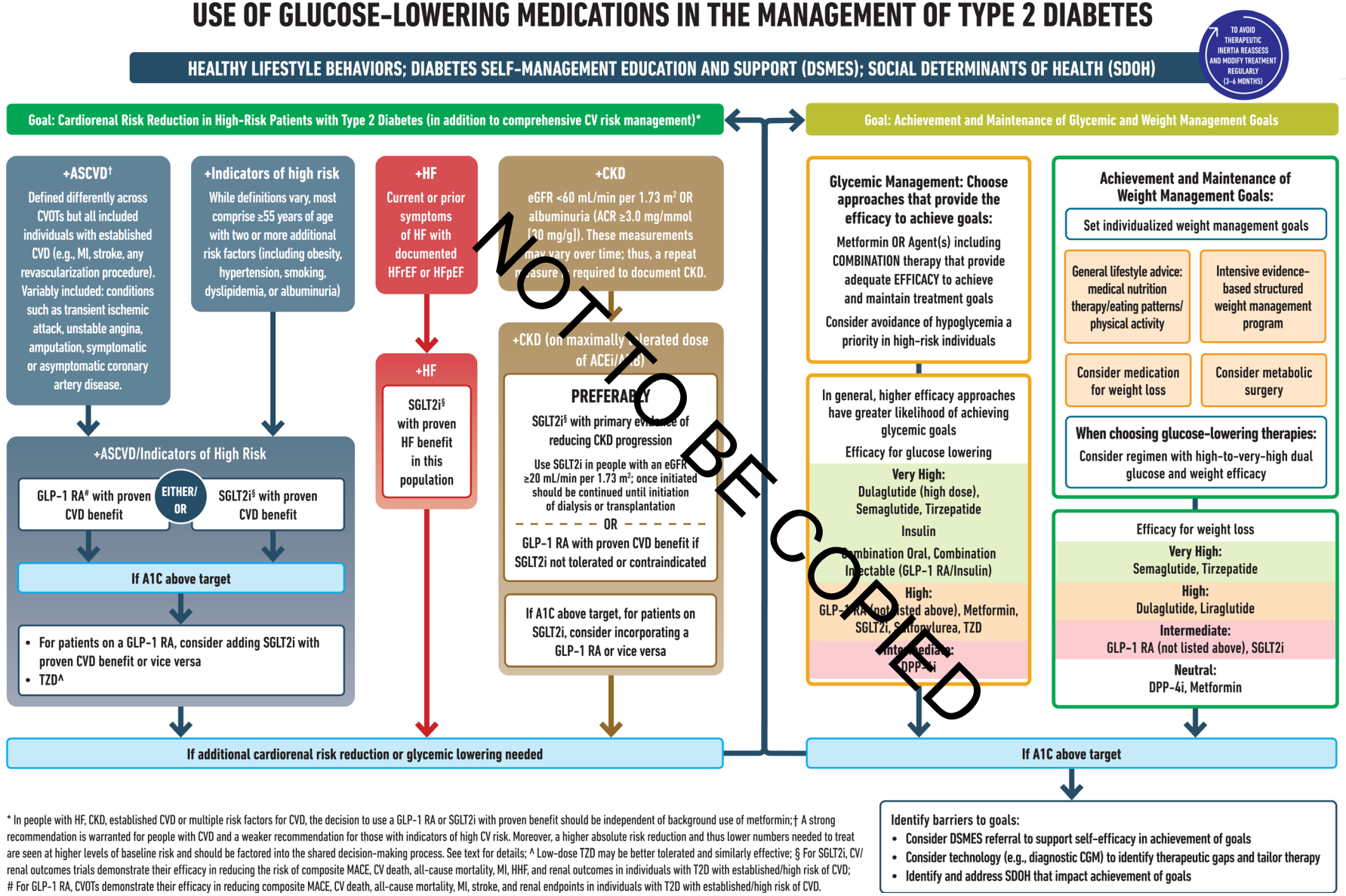
HOLISTIC PERSON-CENTRED APPROACH TO T2DM MANAGEMENT



1 = American Diabetes Association Professional Practice Committee. 10. Cardiovascular Disease and Risk Management: Standards of Medical Care in Diabetes-2022. Diabetes Care. 2022 Jan 1;45(Suppl 1):S144–74.

ACEi, Angiotensin-Converting Enzyme Inhibitor; ARB, Angiotensin Receptor Blockers; ASCVD, Atherosclerotic Cardiovascular Disease; BP, Blood Pressure; CKD, Chronic Kidney Disease; CV, Cardiovascular; eGFR, Estimated Glomerular Filtration Rate; GLP-1 RA, Glucagon-Like Peptide-1 Receptor Agoni Failure; SGLT2i, Sodium-Glucose Cotransporter-2 Inhibitor; T2D, Type 2 Diabetes.

From: **Standards of Care in Diabetes—2023 Abridged for Primary Care Providers**



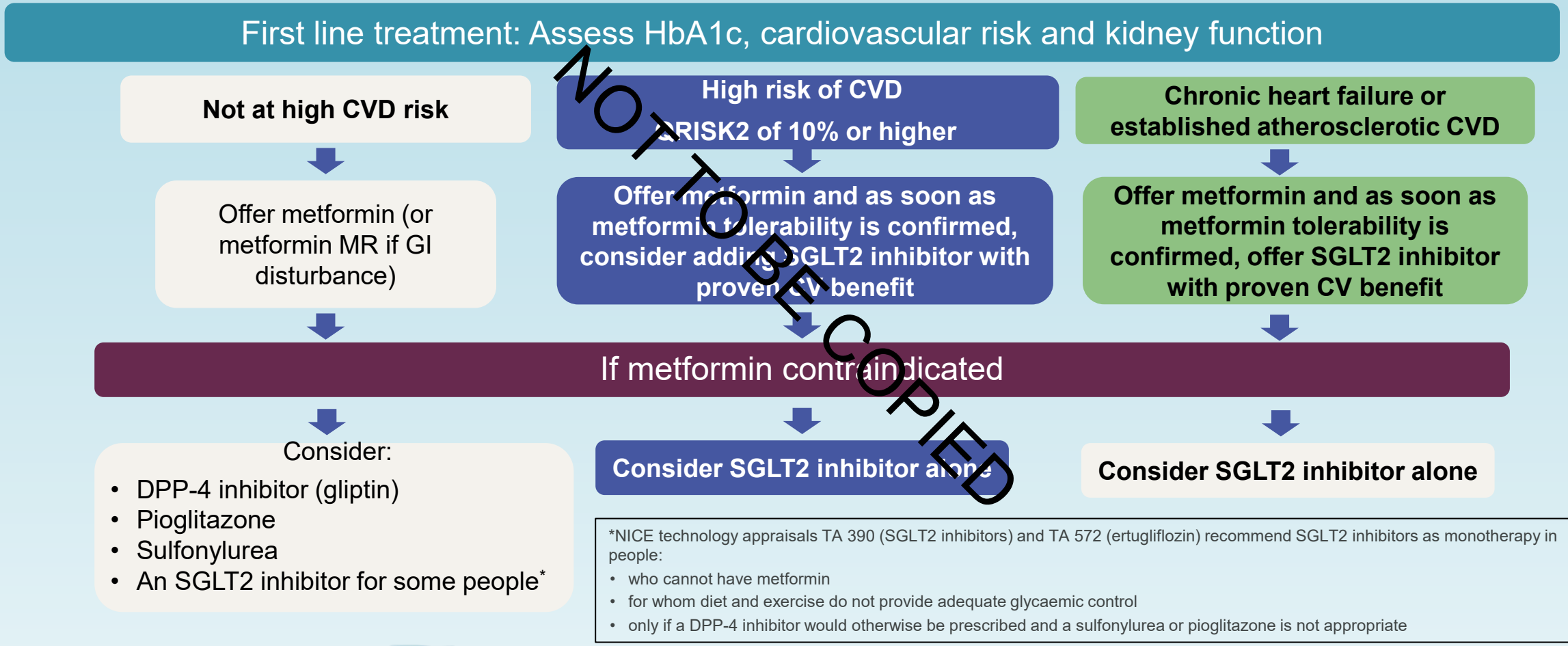
Please refer to the individual SmPCs for full prescribing information.

•Use of glucose-lowering medications in the management of type 2 diabetes.; T2D, type 2 diabetes. Adapted from ADA, Diabetes care 2024;47(Supplement_1):S158-S178

•https://diabetesjournals.org/care/article/47/Supplement_1/S158/153955/9-Pharmacologic-Approaches-to-Glycemic-Treatment

.

NICE recommends SGLT2i's as a first-line treatment with metformin for type 2 diabetes patients at high-risk of CVD



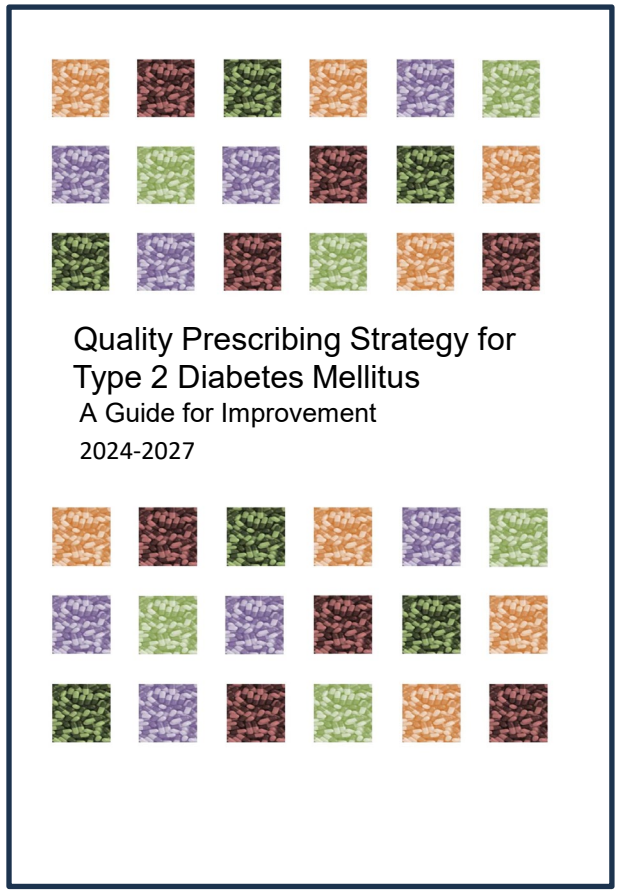
*NICE technology appraisals TA 390 (SGLT2 inhibitors) and TA 572 (ertugliflozin) recommend SGLT2 inhibitors as monotherapy in people:

- who cannot have metformin
- for whom diet and exercise do not provide adequate glycaemic control
- only if a DPP-4 inhibitor would otherwise be prescribed and a sulfonylurea or pioglitazone is not appropriate

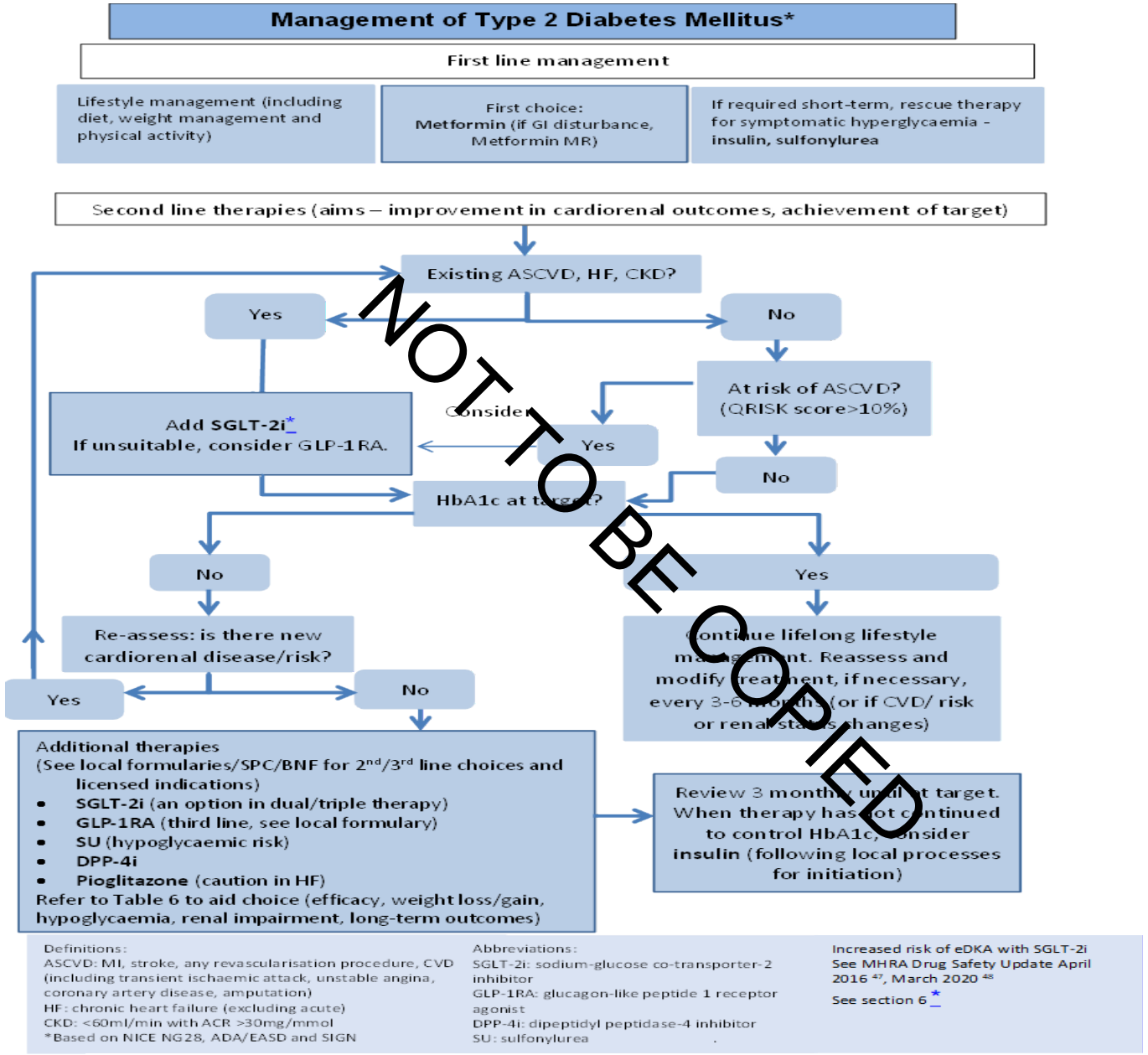
CVD, cardiovascular disease.
*Tolerability of Metformin should be assessed before considering/offering an SGLT2i
NICE. NG28. Available at: https://www.nice.org.uk/guidance/ng28/chapter/Recommendations (accessed August 2024).

Quality Prescribing for Type 2 Diabetes Mellitus 2024-2027

A toolkit to support improvements in prescribing



https://www.gov.scot/publications/quality-prescribing-strategy-type-2-diabetes-mellitus-guide-improvement-2024-2027/documents/



https://www.therapeutics.scot.nhs.uk/wp-content/uploads/2022/12/Diabetes-Draft-for-Consultation.pdf

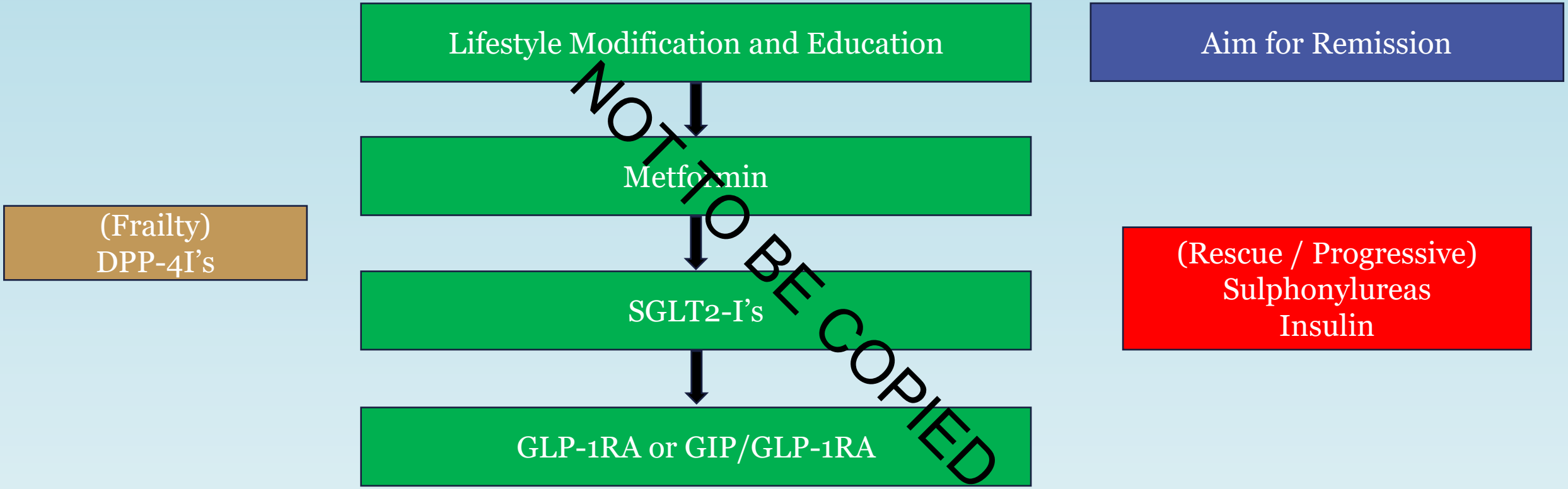
Please refer to the individual SmPCs for full prescribing information.

Management of T2DM in frailty. Adapted from Quality Prescribing for Type 2 Diabetes Mellitus: A Guide for Improvement 2022-2025 (https://www.therapeutics.scot.nhs.uk/diabetes/)

	Treatment target		De-escalation threshold	
	Levels	Therapy considerations	Levels	Suggested interventions
Not frail (CFS scale 1-3)	**53 mmol/mol (7.0%)**	Treat as usual considering co-morbidities.	**Not applicable**	As required, e.g. to minimise side effects, Dose adjustments for renal impairment
Mild frailty (CFS scale 4-5)	**58 mmol/mol (7.5%)**	•Avoid initiating new agents that may cause •hypoglycaemia (e.g., SUs) •exaggerate weight loss (e.g., GLP-1RA) •Consider co-morbidities, e.g., ASCVD, HF, CKD.	**53 mmol/mol (7.0%)**	•Discontinue sulfonylurea (unless required for symptomatic hyperglycaemia). •Review insulin therapy that may cause hypoglycaemia. •Consider appropriate dosage dependent on renal function
Moderate frailty (CFS scale 6)	**64 mmol/mol (8.0%)**	•SGLT-2i* have positive long-term outcomes in people with ASCVD, HF, CKD •Pioglitazone may increase risk of heart failure (avoid). •DPP-4i and longer-acting insulins have demonstrated safety	**58 mmol/mol (7.5%)**	•Discontinue any sulfonylurea (as above) •Discontinue pioglitazone because of risk of heart failure. •Cautious use of insulin •Consider appropriate dosage dependent on renal function
Severe to very severe frailty (CFS scale 7-8)	**70 mmol/mol (8.5%)**	• As moderate frailty •Although additional long-term benefits for SGLT-2i* and GLP-1RA, consider if long-term benefits will be realised. •Consider once-daily morning NPH insulin or analogue alternatives if symptomatic nocturnal hyperglycaemia. •Educate carers and relatives regarding risk of hypoglycaemia	**64 mmol/mol (8.0%)**	• As moderate frailty • Insulins: -withdraw short-acting insulins because of risk of hypoglycaemia. -review timings and suitability of NPH insulin with regard to risk of hypoglycaemia. •Avoid therapies that promote weight loss & may exacerbate sarcopenia, e.g., SGLT-2i, GLP-1RA

PP-IN-UK-1167 / Date of prep Jan 2024

Kash's cheat slide



Speaker's opinion/summary of existing Guidelines

▶ Announcements and latest updates

Type 2 diabetes prescribing

Scottish Government Effective Prescribing & Therapeutics Division

Quick reference guide

Key messages

Implementation toolkit