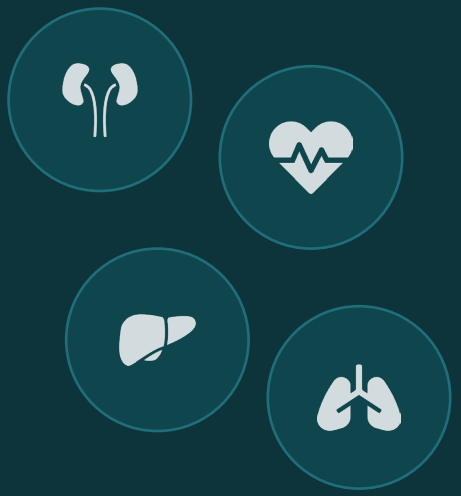
CLINICAL EDUCATION SESSION

Diabetes & Obesity Management in Complexity

The physical-health dimension — managing the connected cluster of organ disease



- Chronic kidney disease
- Cardiovascular disease
- MASLD / MASH
- Obstructive sleep apnoea
- Slowing progression & secondary prevention

PRESENTED BY

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ROADMAP

What we'll cover …

Framing the problem

Why diabetes & obesity drive a connected, multi-organ cluster (CKM syndrome).

The pharmacotherapy toolkit

The agents that now cross organ boundaries — and the evidence behind them.

Five organ domains

CKD, CVD, MASLD/MASH, OSA, and secondary prevention — each with trial evidence.

Landmark trial deep-dives

Design, populations and key outcomes from the practice-changing studies.

Five worked cases

Applying the evidence to real, increasingly complex patients.

Evidence into practice

Sequencing, monitoring, deprescribing, limitations and the pipeline.

WHY THIS MATTERS

Multimorbidity is the rule, not the exception

The cardiovascular–kidney–metabolic (CKM) cluster

- Adiposity and insulin resistance are shared upstream drivers of CKD, atherosclerotic CVD, steatotic liver disease and obstructive sleep apnoea.
- The American Heart Association formalised this as CKM syndrome (2023) — a continuum from risk factors to organ damage.
- Patients accumulate diagnoses across organ systems, yet are too often managed in single-disease silos.
- The therapeutic opportunity: several modern agents now modify outcomes across more than one organ simultaneously.
- Implication for prescribers — treat the driver, sequence foundational protection early, and choose agents that earn their place across multiple domains.

~40%

of people with type 2 diabetes have chronic kidney disease

up to 70%

prevalence of MASLD in type 2 diabetes

2–4×

cardiovascular mortality risk conferred by diabetes

>2 in 3

of people with obesity have some degree of sleep-disordered breathing

Ndumele et al. (2023) Circulation; ElSayed et al. / ADA Standards of Care (2024). Figures are representative population estimates.

SHARED MECHANISM

One driver, four trajectories of organ damage

Chronic kidney disease

Glomerular hyperfiltration, albuminuria, progressive eGFR loss

Cardiovascular disease

Accelerated atherosclerosis, heart failure, arrhythmia

Visceral adiposity & insulin resistance

inflammation · RAAS / SNS · ectopic fat · endothelial dysfunction

MASLD → MASH

Hepatic steatosis to steatohepatitis, fibrosis, cirrhosis

Obstructive sleep apnoea

Upper-airway fat loading, reduced lung volumes, hypoxic burden

Conceptual schema after the AHA CKM framework (Ndumele et al., 2023). For illustration of shared drivers, not a quantitative model.

THE TOOLKIT

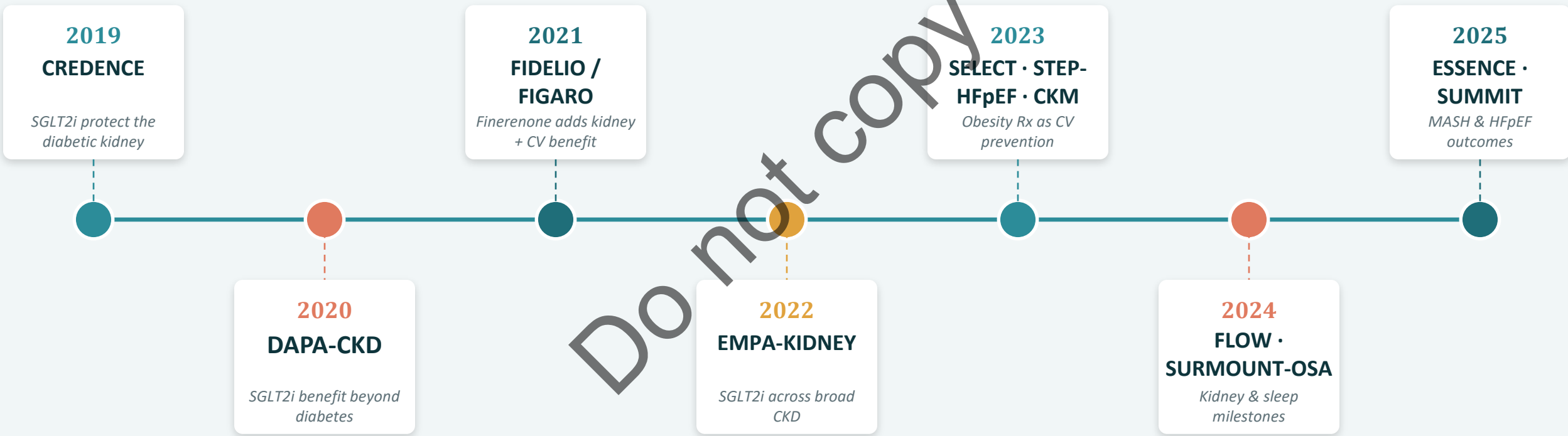
Pharmacotherapy that crosses organ boundaries

Drug class	Representative agents	Multi-organ benefit (key trial)	UK / NICE positioning
GLP-1 receptor agonist	Semaglutide, dulaglutide, liraglutide	Weight & glycaemia; CVD (SELECT); CKD (FLOW); MASH (ESSENCE)	TA875 (obesity); NG28; CV & MASH indications emerging
Dual GIP / GLP-1 agonist	Tirzepatide	Weight & glycaemia; OSA (SURMOUNT-OSA); HFpEF (SUMMIT)	TA1026 (obesity); Mounjaro in T2D
SGLT2 inhibitor	Dapagliflozin, empagliflozin	CKD progression (DAPA-CKD, EMPA-KIDNEY); HF; CVD	TA775 (CKD); NG28; HF guidance — foundational
Non-steroidal MRA	Finerenone	Kidney + CV outcomes in T2D CKD (FIDELIO, FIGARO), HF	TA877 — add-on to RAAS ± SGLT2i
Foundational protection	ACEi/ARB, statin ± ezetimibe/ PCSK9 target medicines, antiplatelet	BP, albuminuria, LDL-C, atherothrombotic risk	NG28, NG203, CG181 — treat to target

TA = NICE technology appraisal; NG = NICE guideline. Indications and access evolve — verify against current SPC and local formulary.

THE EVIDENCE BASE

An avalanche of practice-changing trials, 2019–2025



Within six years, every domain in this talk gained at least one landmark randomised outcome trial — the pace is the point.

Selected pivotal trials; see references. Year reflects primary publication / topline read-out.

PILLAR 1 — CHRONIC KIDNEY DISEASE

Layered cardio-renal protection

Management framework

- Foundation — RAAS blockade (ACEi or ARB) to maximum tolerated dose; BP <130/80; glycaemic and lifestyle optimisation.
- SGLT2 inhibitor — now foundational in albuminuric CKD, diabetic or not. DAPA-CKD: 39% lower kidney/CV composite; corroborated by EMPA-KIDNEY and CREDENCE.
- Finerenone (ns-MRA) — add-on to RAAS ± SGLT2i in T2D CKD. FIDELIO/FIGARO: ~13–18% reduction in composites. NICE TA877.
- GLP-1 RA — FLOW: semaglutide cut major kidney events by 24% in T2D + CKD, with CV and mortality benefit.
- Direction of travel — combination ('pillars') therapy; CONFIDENCE showed additive albuminuria reduction with finerenone + empagliflozin.
- Expect an initial 'dip' in eGFR after starting RAAS / SGLT2i / finerenone — haemodynamic, not a reason to stop.

24%

RRR major kidney events — semaglutide, FLOW

39%

RRR kidney/CV composite — dapagliflozin, DAPA-CKD

TA877

Finerenone: add-on once SGLT2i established & K^+ ≤4.8

Perkovic et al. (2024); Heerspink et al. (2020); EMPA-KIDNEY Group (2023); Bakris et al. (2020); Pitt et al. (2021); NICE TA877; TA775.

EVIDENCE — CKD (1 OF 2)

SGLT2 inhibitors: a reproducible class effect

TRIAL

DAPA-CKD · EMPA-KIDNEY · CREDENCE

DESIGN

Three large double-blind RCTs of dapagliflozin, empagliflozin and canagliflozin vs placebo on a background of RAAS blockade

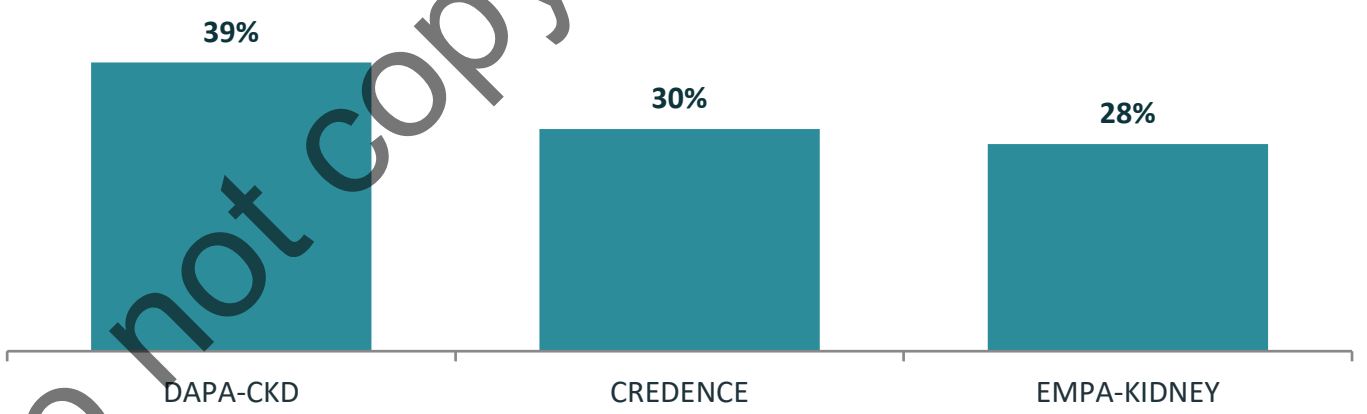
POPULATION

Albuminuric CKD with and (for DAPA-CKD / EMPA-KIDNEY) without diabetes; ~4,300–6,600 each

PRIMARY ENDPOINT

Composite kidney-disease progression ± cardiovascular / renal death

Relative risk reduction — primary composite endpoint (%)



HR 0.61
DAPA-CKD primary composite

–50%
slower eGFR decline (EMPA-KIDNEY)

Class
effect across all three agents

SGLT2 inhibitors are now standard of care in albuminuric CKD — initiate early, regardless of diabetes status.

Heerspink et al. (2020); EMPA-KIDNEY Collaborative Group (2023); Perkovic et al. (2019) CREDENCE.

EVIDENCE — CKD (2 OF 2)

Finerenone and semaglutide extend protection

TRIAL

FIDELIO / FIGARO-DKD · FLOW

DESIGN

ns-MRA finerenone (FIDELIO/FIGARO) and GLP-1 RA semaglutide (FLOW) vs placebo, added to optimised RAAS ± SGLT2i

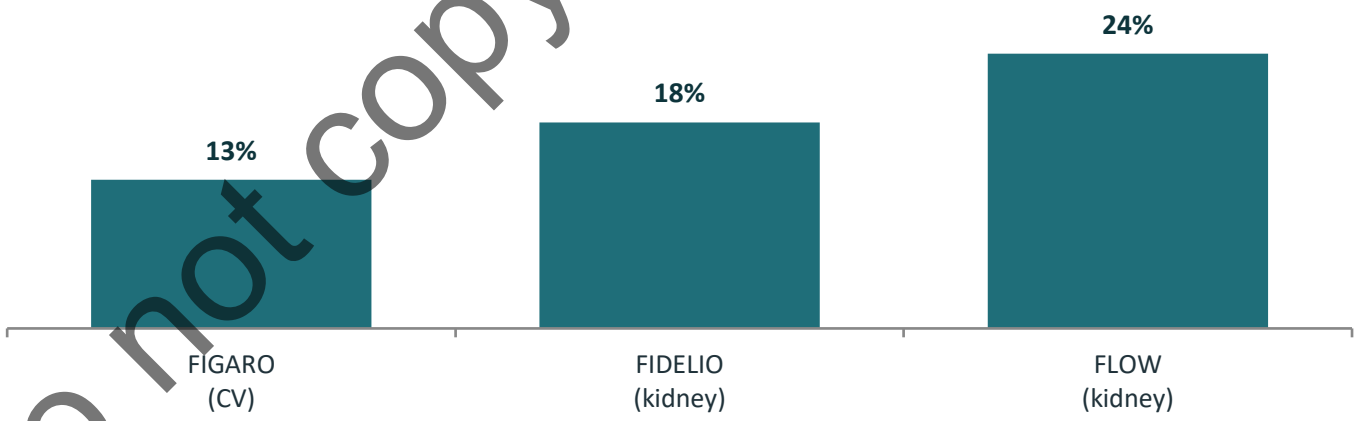
POPULATION

T2D with albuminuric CKD; FLOW eGFR 25–75 with raised UACR (n=3,533)

PRIMARY ENDPOINT

Kidney / CV composite (finerenone); major kidney-disease events (FLOW)

Relative risk reduction on each trial's primary endpoint (%)



24%
FLOW major kidney events

20%
FLOW all-cause mortality

+CV
finerenone CV composite benefit

Finerenone and semaglutide each add protection on top of RAAS and SGLT2i — building the four-pillar CKD stack.

Bakris et al. (2020) FIDELIO-DKD; Pitt et al. (2021) FIGARO-DKD; Perkovic et al. (2024) FLOW.

CASE 1 — CHRONIC KIDNEY DISEASE

Albuminuric diabetic kidney disease with residual risk

PATIENT

62-year-old man

Background
Type 2 diabetes 9 years; BMI 34 kg/m²; ex-smoker

Bloods
HbA1c 64 mmol/mol; eGFR 48; uACR 62 mg/mmol

Obs
BP 148/88 mmHg; K^+ 4.4 mmol/L

Current Rx
Ramipril 5 mg; metformin 1 g BD; atorvastatin 20 mg

CLINICAL PROBLEM
Sub-maximal RAAS, persistent albuminuria, BP and lipids above target, no organ-protective add-on.

Pharmacotherapy & management plan

1. **Up-titrate ramipril to maximum tolerated dose; recheck eGFR/K^+ at 2–4 weeks.**
2. **Add dapagliflozin 10 mg — renal + CV protection (DAPA-CKD); counsel on sick-day rules.**
3. **Add finerenone 10–20 mg once SGLT2i established and K^+ ≤4.8 (TA877); monitor potassium.**
4. Consider semaglutide for weight, glycaemia and kidney benefit (FLOW) given BMI and albuminuria.
5. Switch to high-intensity statin; target BP <130/80 mmHg.

Outcome: a four-agent cardio-renal package built in sequence — each step monitored for eGFR and potassium.

Perkovic et al. (2024); Heerspink et al. (2020); NICE TA877; KDIGO (2024).

PILLAR 2 — CARDIOVASCULAR DISEASE

Weight management as cardiovascular therapy

Management framework

- Secondary-prevention backbone — high-intensity statin ± ezetimibe / bempedoic acid/Inclisiran/ PCSK9i, antiplatelet, ACEi/ARB, BP control, cardiac rehab.
- LDL-C targets — <1.8 mmol/L at high risk; <1.4 mmol/L very-high risk; consider <1.0 mmol/L at extreme risk (ESC/EAS).
- SGLT2i and GLP-1 RA confer cardiovascular benefit independent of glucose lowering.
- SELECT — semaglutide 2.4 mg reduced MACE by 20% in obesity + established CVD without diabetes; benefit largely independent of weight lost.
- Tirzepatide — SUMMIT: lower CV death / worsening-HF events in obesity-related HFpEF.
- Reframe — obesity is a modifiable cardiovascular risk factor, and its pharmacotherapy is secondary prevention.

20%

RRR in MACE — semaglutide, SELECT

<1.4

mmol/L LDL-C target, very-high risk (ESC/EAS)

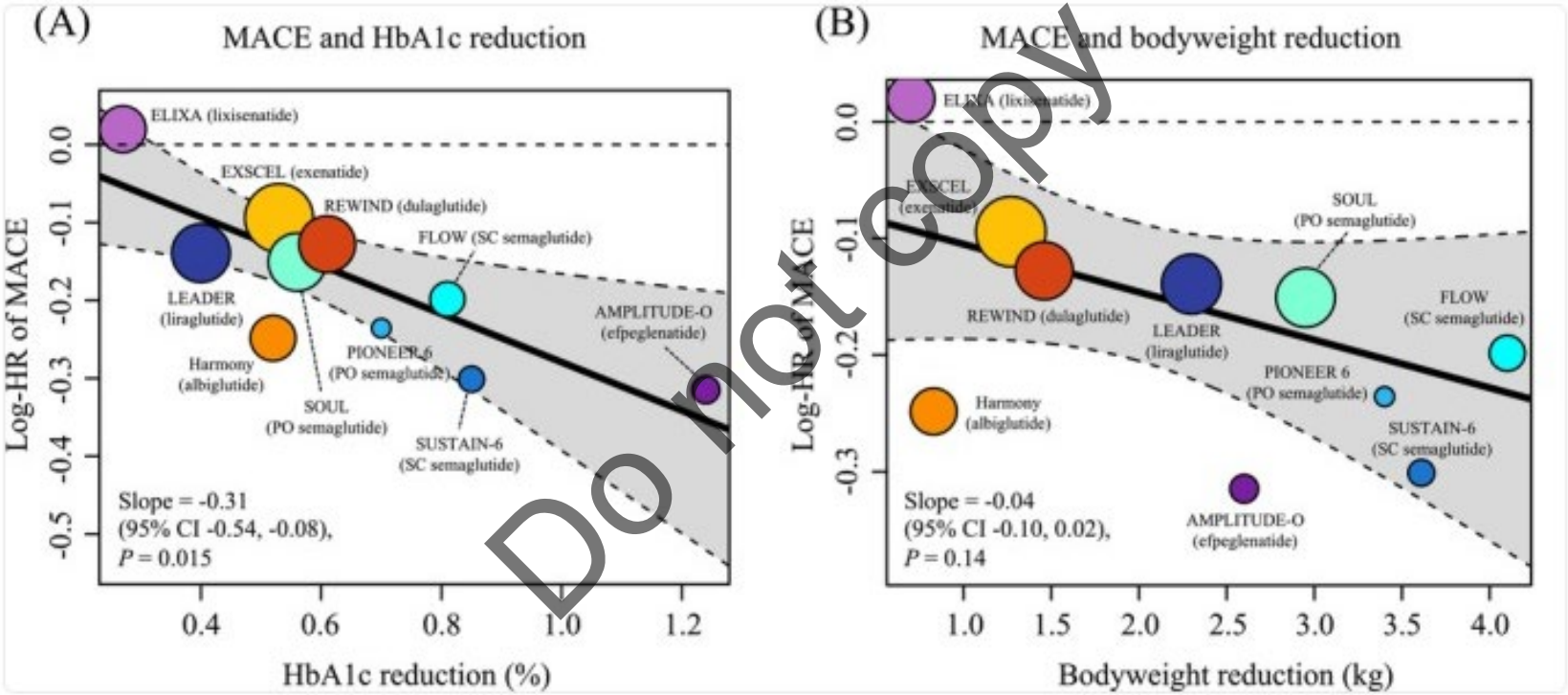
SUMMIT

Tirzepatide: fewer CV death / HF events in HFpEF + obesity

Lincoff et al. (2023); Deanfield et al. (2025) Lancet; Packer et al. (2025); Marx et al. (2023) ESC Guidelines.

PILLAR 2 — CARDIOVASCULAR DISEASE

Type 2 Diabetes and CV risk reduction



Hasebe M, Su CY, Keidai Y, Minamino H, Yabe D, Inagaki N, Yoshiji S. Cardiovascular risk reduction with glucagon-like peptide-1 receptor agonists is proportional to HbA1c lowering in type 2 diabetes: An updated meta-regression analysis incorporating FLOW and SOUL trials. Diabetes Obes Metab. 2025 Dec;27(12):7210-7220. doi: 10.1111/dom.70121. Epub 2025 Sep 9. PMID: 40926380; PMCID: PMC12587236.

SELECT: obesity treatment as secondary prevention

TRIAL

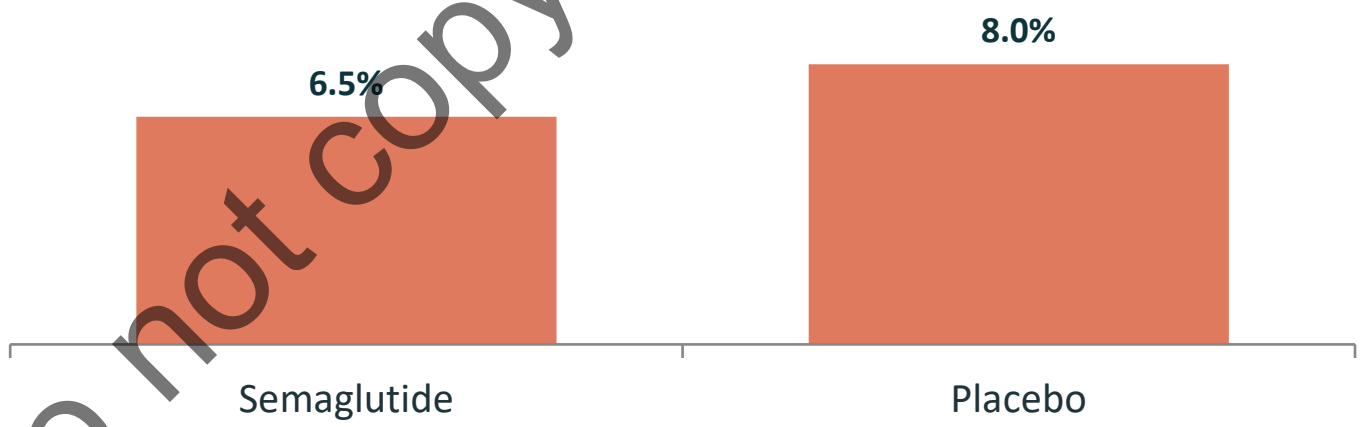
SELECT

DESIGN
Double-blind RCT, semaglutide 2.4 mg vs placebo; 804 sites, ~40 months' follow-up

POPULATION
17,604 adults, BMI ≥27, established CVD, no diabetes

PRIMARY ENDPOINT
3-point MACE — CV death, non-fatal MI or non-fatal stroke

Primary MACE event rate (%) over ~40 months



20%
RRR in MACE (HR 0.80)

–9.4%
mean body-weight reduction

Weight-
independent benefit (Lancet 2025)

Semaglutide reduces hard cardiovascular events in obesity without diabetes — irrespective of how much weight is lost.

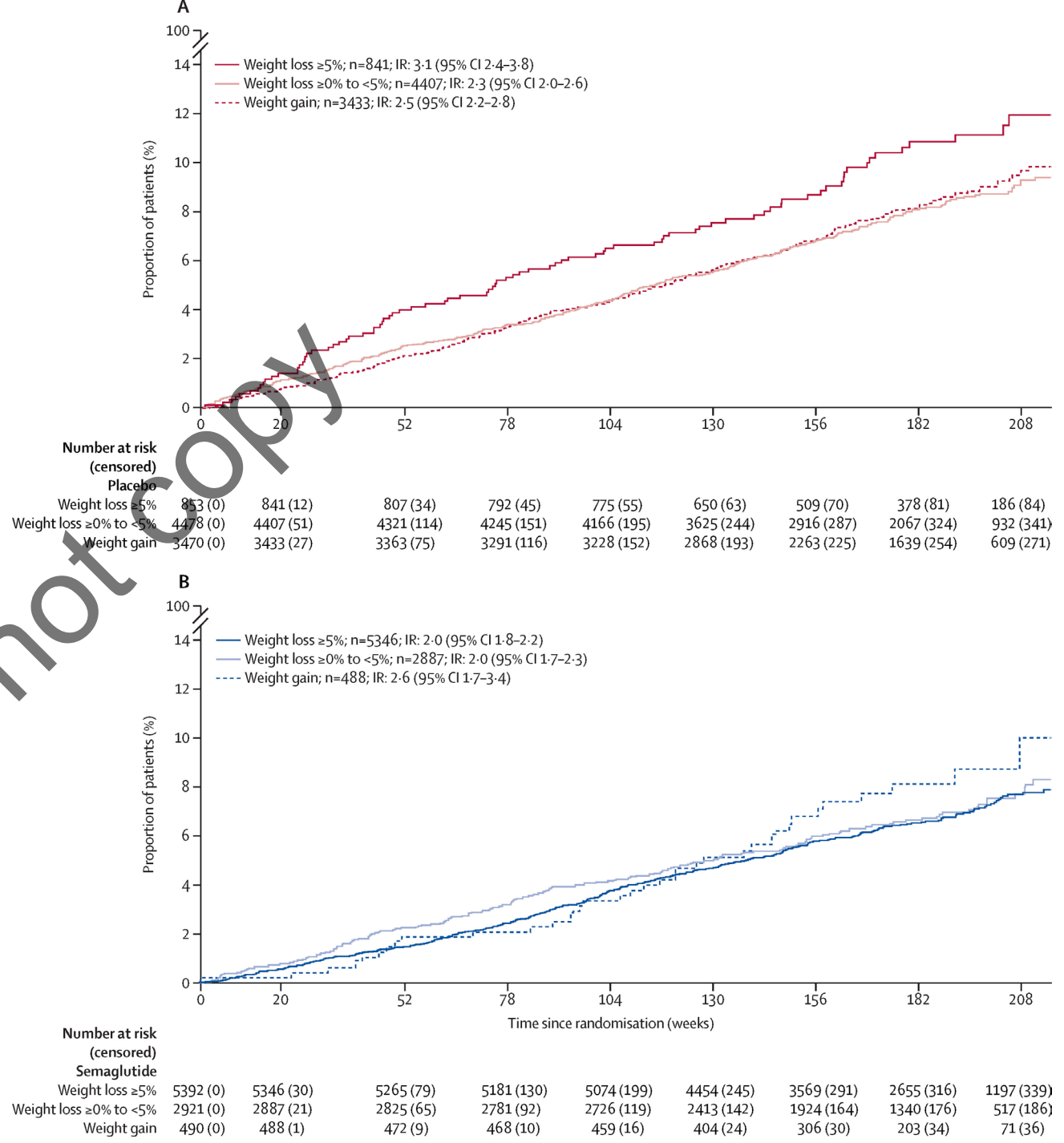
Lincoff et al. (2023) NEJM; Deanfield et al. (2025) Lancet.

SELECT Trial: Semaglutide for cardiovascular risk reduction

17,604 patients with CVD and obesity. Semaglutide cuts MACE by 20%: Benefit had almost nothing to do with weight loss.

SELECT followed patients for 3.3 years:

- 20% ⬇️ in MACE (stroke, MI, CV death)
- 8.5% average weight loss with semaglutide
- BUT: Patients who lost <5% had SAME benefit as those losing >5%
- Waist circumference changes explained only 33% of CV benefit



1.Semaglutide and cardiovascular outcomes by baseline and changes in adiposity measurements: a prespecified analysis of the SELECT trial. Deanfield, John et al. The Lancet, Volume 406, Issue 10516, 2257 - 2268

Conclusions: Weight loss and CV disease

- Weight loss is a heterogeneous outcome.
- Surrogate markers for central adiposity and visceral fat is associated with MACE reduction
- GLP-1 RA in Type 2 with modest or no weight loss still showed CV benefit
- Pioglitazone had favourable effect on CVD and caused weight gain (changed fat distribution from visceral to s/c)
- Not all weight loss is the same metabolically, however weight loss in general has wider implications that metabolic conditions

CASE 2 — CARDIOVASCULAR DISEASE

Residual risk after myocardial infarction in obesity

PATIENT

58-year-old woman

Background
MI with PCI 18 months ago; BMI 28 kg/m²; no diabetes

Bloods
HbA1c 41 mmol/mol; LDL-C 2.6 mmol/L

Obs
BP 134/82 mmHg

Current Rx
Aspirin; atorvastatin 80 mg; bisoprolol; ramipril

CLINICAL PROBLEM

LDL-C above very-high-risk target; obesity driving residual atherothrombotic risk despite optimal background therapy.

Pharmacotherapy & management plan

1. **Add inclisiran; escalate if LDL-C remains ≥1.4 mmol/L.**
2. **Initiate semaglutide 2.4 mg for weight reduction and 20% MACE reduction (SELECT) — applies without diabetes.**
3. Reinforce cardiac rehabilitation, diet, activity and smoking-cessation support.
4. Confirm BP at target; continue dual secondary-prevention therapy.
5. Frame the conversation as cardiovascular risk reduction, not cosmetic weight loss.

Outcome: lipid target reached and an evidence-based MACE-lowering agent added — obesity treated as secondary prevention.

Lincoff et al. (2023); Marx et al. (2023); NICE NG238 / CG181.

PILLAR 3 — MASLD / MASH

From silent steatosis to fibrosis — now treatable

Identify, stratify, treat

- MASLD affects up to 70% of people with T2D; fibrosis stage drives liver outcomes — and cardiovascular disease is the leading cause of death.
- Risk-stratify non-invasively — FIB-4 first, then ELF or transient elastography to identify clinically significant fibrosis (F≥2).
- **Weight loss is disease-modifying and dose-dependent — ≥10% body-weight loss resolves steatohepatitis in ~90% and regresses fibrosis in ~45% (Vilar-Gomez).**
- Statins are safe and indicated; optimise glycaemia, BP and lipids in parallel.
- **Semaglutide 2.4 mg — ESSENCE: 62.9% steatohepatitis resolution vs 34.3% placebo, with fibrosis benefit (NEJM 2025).**
- Pioglitazone / vitamin E have limited, selective roles and are not first-line in this multimorbid context.

62.9%

steatohepatitis resolution — semaglutide, ESSENCE (vs 34.3%)

≥10%

weight loss → ~90% NASH resolution, ~45% fibrosis regression

FIB-4

first-line non-invasive fibrosis triage

Vilar-Gomez et al. (2015); Sanyal et al. (2025); Rinella et al. (2023) AASLD; NICE NG49.

EVIDENCE — MASH (1 OF 2)

Weight loss is dose-dependent, disease-modifying therapy

TRIAL

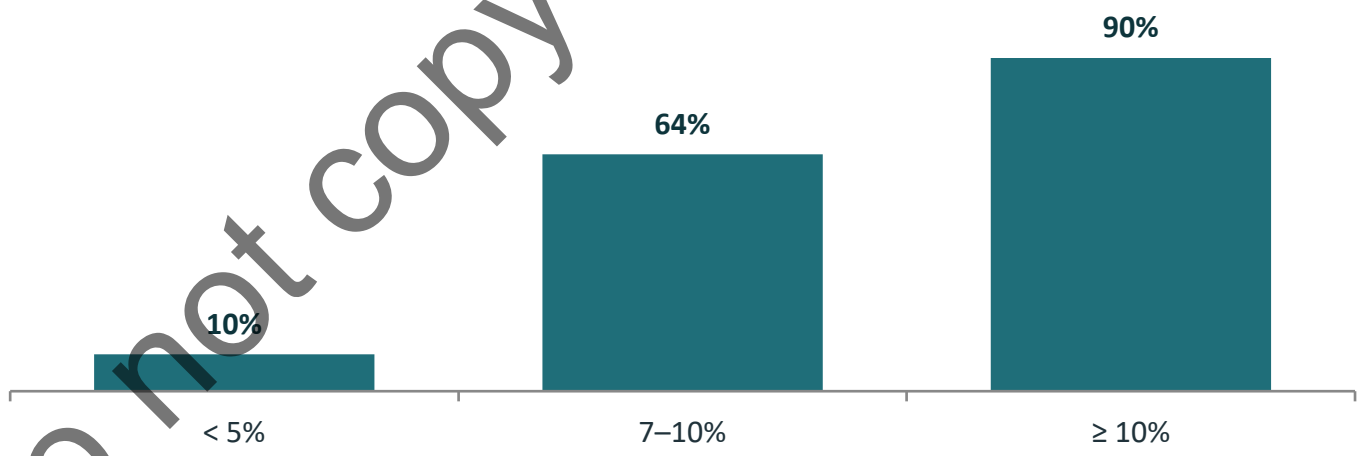
Lifestyle weight-loss cohort (Vilar-Gomez)

DESIGN
Prospective study with paired liver biopsy at baseline and 52 weeks of structured lifestyle intervention

POPULATION
293 adults with biopsy-proven steatohepatitis (NASH); response by weight-loss achieved

PRIMARY ENDPOINT
Steatohepatitis resolution and ≥1-stage fibrosis regression on histology

Steatohepatitis resolution by weight loss achieved (%)



90%
NASH resolution at ≥10% weight loss

45%
fibrosis regression at ≥10%

≥10%
the therapeutic threshold

The greater the weight loss, the greater the histological benefit — ≥10% is the target modern pharmacotherapy now makes reachable.

Vilar-Gomez et al. (2015) Gastroenterology 149(2):367–378.

EVIDENCE — MASH (2 OF 2)

ESSENCE: the metabolic-axis approach to MASH

TRIAL

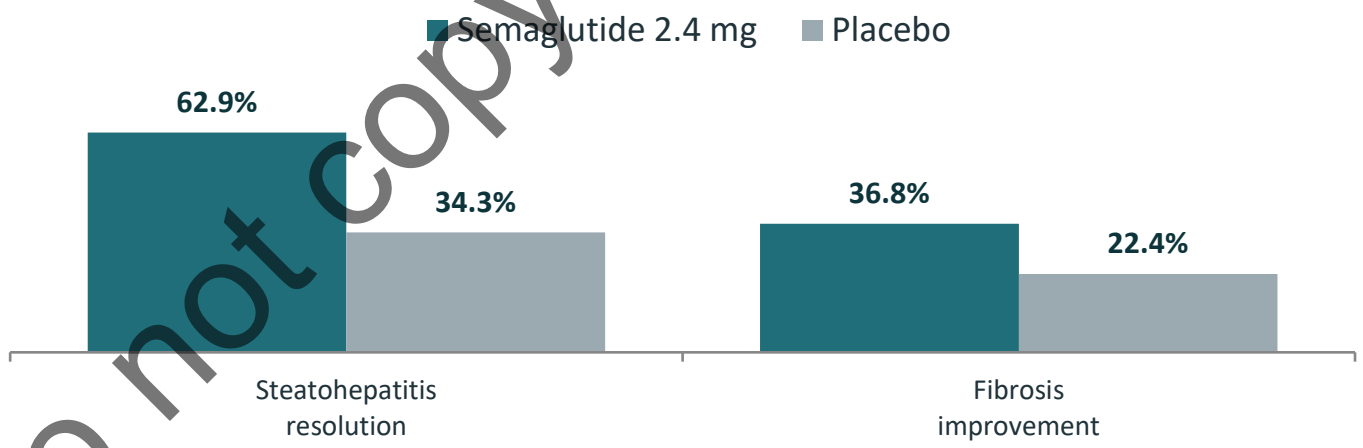
ESSENCE

DESIGN
Phase 3 RCT, semaglutide 2.4 mg vs placebo; 72-week interim histology (part 1)

POPULATION
800 of 1,197 adults, biopsy-confirmed MASH with F2–F3 fibrosis

PRIMARY ENDPOINT
Steatohepatitis resolution without worsening fibrosis; fibrosis improvement

Histological response at week 72 (% of patients)



62.9%
resolution vs 34.3% placebo

+28.7%
absolute difference, resolution

Multi-
organ metabolic benefit

Semaglutide resolves steatohepatitis in ~2 in 3 — while also acting on weight, glycaemia, CV and kidney risk.

Sanyal et al. (2025) NEJM 392:2089–2099.

CASE 3 — MASLD / MASH

Steatohepatitis with significant fibrosis

PATIENT

49-year-old man

Background
Type 2 diabetes; BMI 36 kg/m²; metabolic syndrome

Bloods
ALT 78 U/L; FIB-4 2.1; HbA1c 69 mmol/mol

Imaging
Transient elastography → F3 fibrosis

Alcohol
Within low-risk limits; other liver disease excluded

CLINICAL PROBLEM

Confirmed advanced fibrosis (F3) in MASH with active cardiometabolic risk — at risk of cirrhosis and CV events.

Pharmacotherapy & management plan

1. **Confirm staging and exclude competing aetiology; structured weight-loss target ≥10% body weight.**
2. **Initiate semaglutide 2.4 mg (ESSENCE) — addresses MASH, weight, glycaemia and CV risk together.**
3. Refer to hepatology for F3 disease — co-ordinate surveillance and specialist follow-up.
4. Continue statin (safe in MASLD); optimise glycaemia and blood pressure; avoid hepatotoxins.
5. Monitor LFTs and repeat non-invasive fibrosis markers to track response.

Outcome: one incretin therapy targets the liver and the wider metabolic milieu, anchored by a ≥10% weight-loss goal.

Sanyal et al. (2025); Vilar-Gomez et al. (2015); Rinella et al. (2023).

PILLAR 4 — OBSTRUCTIVE SLEEP APNOEA

A new pharmacological lever in obesity-related OSA

Management framework

- OSA and obesity are bidirectionally linked; untreated OSA worsens hypertension, atrial fibrillation, insulin resistance and CV risk.
- Screen actively in obesity and diabetes clinics — STOP-Bang and Epworth, with referral for sleep study where indicated.
- CPAP remains first-line for moderate-to-severe disease, but real-world adherence is limited.
- Weight loss reduces apnoea severity; bariatric surgery and now pharmacotherapy expand the options.
- **Tirzepatide — SURMOUNT-OSA: AHI reduced by ~50–63%, up to ~50% met disease-resolution criteria, with falls in BP and hsCRP.**
- FDA-approved (Dec 2024) for moderate-to-severe OSA with obesity; UK access evolving — drug therapy as adjunct or alternative. *NICE guidance for OSA was last updated 2021 (prior to evidence evolving).

–50 to –63%

reduction in apnoea–hypopnoea index — tirzepatide

~50%

of participants met OSA disease-resolution criteria

+CV

lower systolic BP and hsCRP alongside AHI

Malhotra et al. (2024) NEJM SURMOUNT-OSA. AHI = apnoea–hypopnoea index. Confirm current UK licensing and access.

EVIDENCE — OSA

SURMOUNT-OSA: drug therapy that moves the AHI

TRIAL

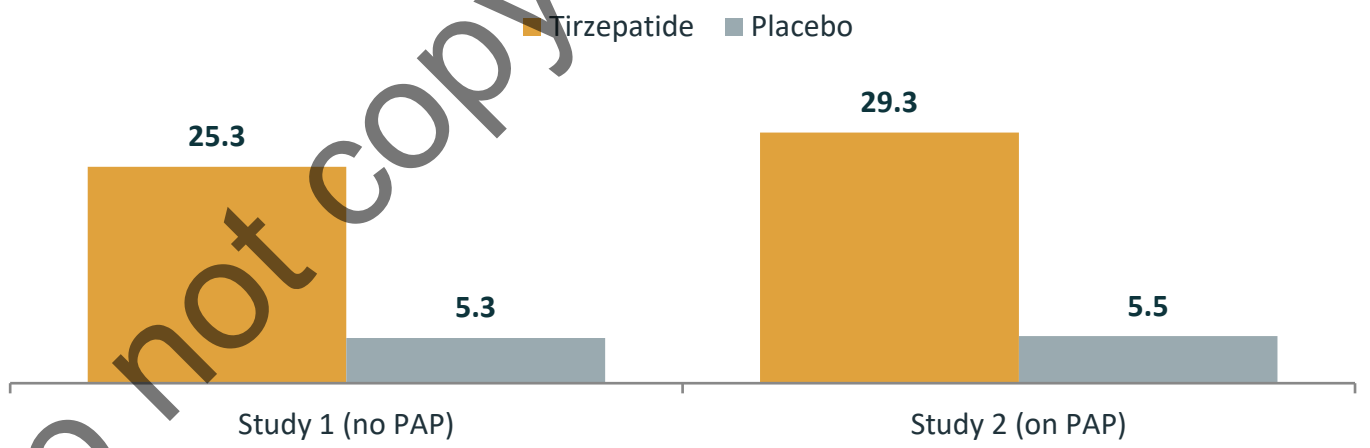
SURMOUNT-OSA

DESIGN
Two phase 3 RCTs of tirzepatide (10/15 mg) vs placebo over 52 weeks — Study 1 (no PAP), Study 2 (on PAP)

POPULATION
Adults with moderate-to-severe OSA and obesity (baseline AHI ~50/h)

PRIMARY ENDPOINT
Change in apnoea–hypopnoea index (events/hour) at week 52

Reduction in AHI at week 52 (events/hour)



~50–63%
reduction in AHI vs placebo

43–51%
met disease-resolution criteria

↓BP
and ↓hsCRP alongside

Tirzepatide meaningfully lowers apnoea severity — an option alongside or beyond CPAP in obesity-related OSA.

Malhotra et al. (2024) NEJM 391:1193–1205.

CASE 4 — OBSTRUCTIVE SLEEP APNOEA

CPAP-intolerant moderate-to-severe OSA in obesity

PATIENT

54-year-old man

Background
BMI 39 kg/m²; type 2 diabetes; hypertension

Sleep study
Moderate–severe OSA, AHI 42 events/hour

Therapy
CPAP trialled — poor tolerance and adherence

Symptoms
Daytime somnolence; Epworth 14

CLINICAL PROBLEM

Symptomatic OSA with failed CPAP, compounding poorly controlled blood pressure and glycaemia.

Pharmacotherapy & management plan

1. **Re-engage the sleep service — mask/interface review and CPAP optimisation; positional and lifestyle measures.**
2. **Initiate tirzepatide, titrated to maximum tolerated dose (10–15 mg) — SURMOUNT-OSA addresses AHI, weight, BP and glycaemia.**
3. Re-assess AHI and Epworth after weight response; PAP need reviewed by the sleep team if resolution criteria are met.
4. Treat hypertension and diabetes concurrently — expect synergistic improvement.
5. Counsel on gradual GI titration and tolerability.

Outcome: a single agent attacks the airway, the weight and two comorbidities at once — within a sleep-service MDT.

Malhotra et al. (2024); NICE NG202 (OSA).

PILLAR 5 — THE UNIFYING GOAL

Slowing progression & secondary prevention

Five principles that hold across every organ domain

Treat the driver

Sustained weight loss and cardiometabolic control modify all four trajectories at once.

Foundation first, early

RAAS blockade, SGLT2i, statin and BP control before organ failure — not after it.

Layer by residual risk

Add disease-modifying agents (GLP-1 / dual agonist, SGLT2i, finerenone) to indication and risk.

Treat to target

Drive albuminuria, LDL-C, BP, HbA1c and weight to goal — not merely to tolerance.

Think absolute risk

Act on the whole-patient risk picture, not a single isolated number.

Own the follow-through

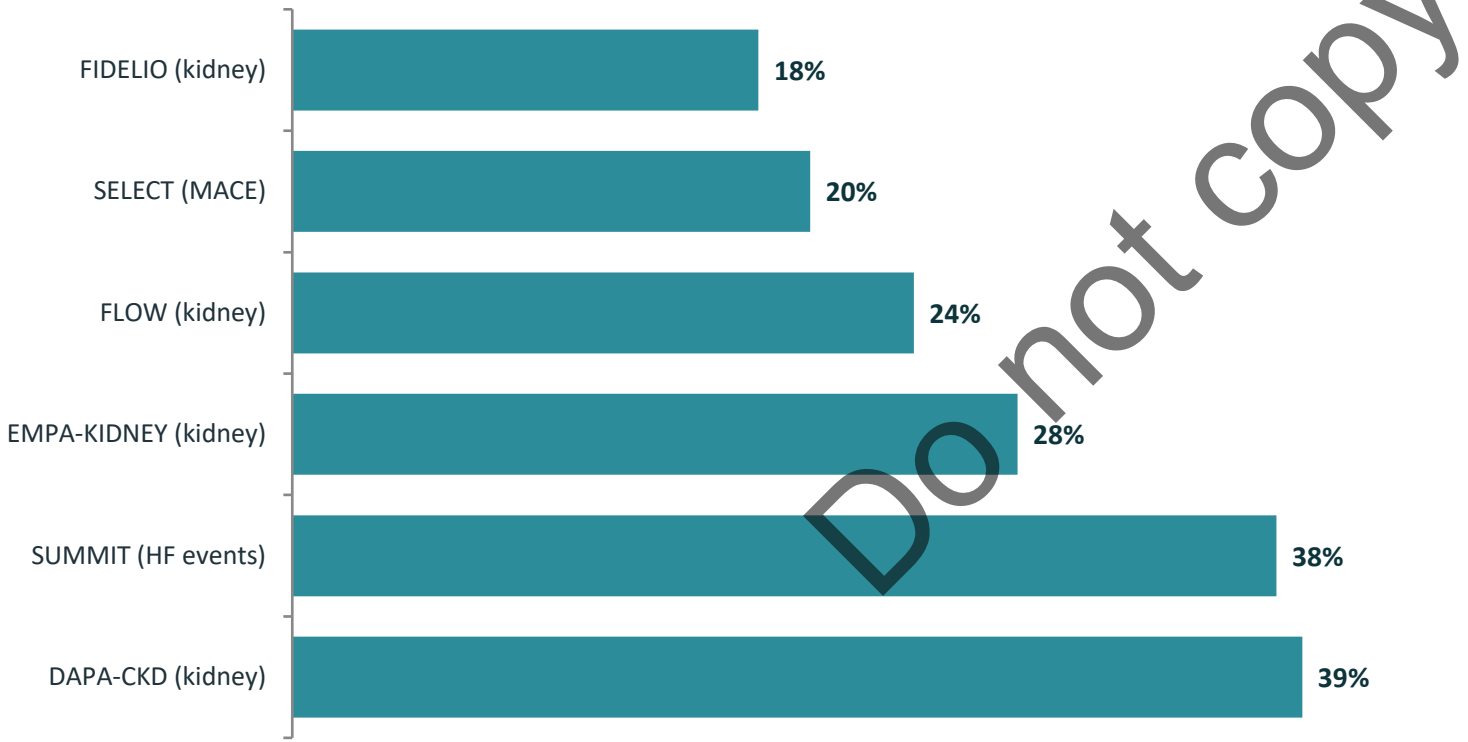
Monitoring, titration and deprescribing are where outcomes are won or lost.

Synthesis of KDIGO (2024), ESC (2023), AASLD (2023) and NICE NG28 / NG203 principles.

SYNTHESIS

Putting the magnitude of benefit in one view

Relative risk reduction on each trial's primary endpoint (%)



How to read this

- Each bar is a different trial, population and endpoint — this is not a head-to-head comparison.
- It shows that effect sizes across the cardio-renal-metabolic field are large and clinically meaningful.
- Several sit alongside the benefit we expect from statins or RAAS blockade.
- **The clinical art is choosing agents whose benefits stack for a given patient.**

Composite of primary-endpoint RRRs from the cited pivotal trials. Endpoints differ; presented for scale, not direct comparison.

CASE 5 — THE COMPLEX MULTIMORBID PATIENT

When every pillar is in play at once

60-year-old woman

Diabetes T2D 12 years; HbA1c 71 mmol/mol

Obesity BMI 41 kg/m²

Cardiac Established CAD, prior PCI

Renal eGFR 38; uACR 90 mg/mmol; K^+ 4.6

Liver MASLD, F2 fibrosis

Sleep OSA, established on CPAP

Lipids/BP LDL-C 2.6 mmol/L; BP 150/90

Current Rx Metformin, gliclazide, ramipril, atorvastatin 40, aspirin

Integrated, sequenced plan

1 Foundation
Maximise RAAS; high-intensity statin + ezetimibe to LDL-C <1.4; drive BP to target.

2 SGLT2 inhibitor
Dapagliflozin/empagliflozin early — kidney, heart-failure and CV protection.

3 Incretin therapy
GLP-1 RA or tirzepatide — one agent touching weight, glycaemia, CV, MASH, OSA & kidney.

4 Finerenone
Add for residual albuminuria once SGLT2i stable and potassium permits (TA877).

5 Deprescribe
Withdraw gliclazide as incretin/SGLT2i optimise — reduce hypoglycaemia and weight gain.

6 Monitor & MDT
eGFR/K^+, LFTs, weight, BP, HbA1c, lipids; sick-day rules; primary care + specialties + pharmacy.

Key message: one well-chosen incretin therapy plus foundational protection addresses the whole cluster — and pharmacist-led sequencing, monitoring and deprescribing is central to delivering it safely.

Lincoff et al. (2023); Perkovic et al. (2024); Sanyal et al. (2025); Malhotra et al. (2024); NICE TA877.

PRACTICAL PRESCRIBING

Safety, monitoring & deprescribing

SGLT2 inhibitors

- Euglycaemic DKA risk — counsel sick-day rules; withhold in acute illness, dehydration and around surgery.
- Genital mycotic infection; volume depletion. Expect an initial eGFR dip.
- Not a weight-loss agent in isolation — prescribe for the protective indication.

Finerenone

- Hyperkalaemia is the key risk — baseline and ~4-weekly potassium monitoring.
- Initiate if eGFR ≥25 and K^+ ≤5.0; caution with other potassium-raising drugs.
- Sequence after SGLT2i, which mitigates hyperkalaemia risk.

GLP-1 RA & tirzepatide

- GI intolerance — titrate slowly; counsel on nausea and hydration.
- Pancreatitis caution; avoid in pregnancy. Withhold around sedation/anaesthesia per current guidance.
- Manage supply constraints via formulary prioritisation and equity-aware allocation.

Polypharmacy & equity

- De-escalate sulfonylureas/insulin as incretins and SGLT2i optimise — reduce hypoglycaemia.
- Structured medication review; align with shared decision-making.
- Apply an equality lens (EIA) to access and uptake.

MHRA/SPC guidance; NICE NG28; KDIGO (2024); local formulary and shortage protocols apply.

FROM EVIDENCE TO PRACTICE

Monitoring blueprint

Agent	Before starting	Ongoing monitoring	Key safety action
SGLT2 inhibitor	eGFR, volume status, foot review	eGFR at 2–4 wks (accept initial dip), then routine	Sick-day rules; hold if acutely unwell / peri-operative
Finerenone	K^+ and eGFR (need K^+ ≤5.0, eGFR ≥25)	K^+ at 4 weeks, after dose changes, then periodically	Withhold if K^+ >5.5; review K^+-raising co-meds
GLP-1 RA / tirzepatide	Weight, HbA1c, pregnancy status, GI history, retinal screening	Weight/HbA1c response; tolerability; injection technique	Slow titration; withhold around anaesthesia per guidance
Foundational (statin, RAAS)	LFTs/CK if indicated; LDL-C, BP baselines	LDL-C and BP to target; adherence review	Escalate to ezetimibe/PCSK9i if LDL-C above goal

The trials only deliver their outcomes if the monitoring happens — this is where pharmacists convert evidence into benefit.

Operationalised from SPCs, NICE NG28, KDIGO (2024) and trial protocols; adapt to local pathways.

CAVEATS & HORIZON

Limitations, evidence gaps & the pipeline

Surrogate vs hard endpoints

AHI (OSA) and histology (MASH) are surrogates; long-term cardiovascular and liver-outcome data are still maturing.

Trial vs real-world populations

Selected, adherent trial cohorts may overstate real-world effect; frailty, multimorbidity and deprivation are under-represented.

Access, cost & equity

Cost, supply constraints and uneven uptake risk widening inequalities — an active equity lens is essential.

What's coming

ESSENCE part 2 (liver outcomes ~2029); combination/quadruple CKD therapy (CONFIDENCE); oral incretins (oral semaglutide, orforglipron); triple agonists (retatrutide).

Forward-looking; pipeline timelines are indicative and subject to regulatory and trial outcomes.

Key takeaways

1. Obesity and type 2 diabetes drive a connected cluster — CKD, CVD, MASLD/MASH and OSA share one metabolic root.
2. Modern pharmacotherapy is increasingly multi-organ: GLP-1 and dual GIP/GLP-1 agonists, SGLT2 inhibitors and finerenone.
3. The evidence base is large and recent — most domains now offer statin-sized benefits from randomised outcome trials.
4. Treat the driver, lay foundational protection early, then layer disease-modifying agents by indication and residual risk.
5. Sequencing, monitoring and deprescribing are core pharmacist roles — and where trial benefit becomes real-world benefit.

Questions & discussion

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Questions

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