Diabetes Distilled

PCDO Society

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Putting it all together:
Treatment of the whole person

Leonardo Hotel, Cardiff | 22 May 2025

16TH Welsh Conference | PCDO Society

My disclosures

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OmniaMed, RCGP, Innovate, Sherborne Gibbs

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diabetesdistilled
the latest developments filtered for you

Diabetes Distilled

Diabetes distilled is an e-newsletter from the Primary Care Diabetes and Obesity Society designed to share the latest developments in diabetes and obesity for primary care teams. We summarise the latest papers that matter.

Sign up to receive the Diabetes Distilled newsletter at the link below

Diabetes Distilled: Heart and SOUL – oral semaglutide demonstrates cardiovascular benefit in high-risk people with type 2 diabetes

Results of SOUL trial suggest oral semaglutide offers similar cardiovascular benefits to the... injectable formulation.

22 Apr 2025

Diabetes Distilled: Time to intensify blood pressure treatment in people with type 2 diabetes?

BPROAD study: Reducing systolic blood pressure to <120 mmHg versus <140 mmHg in... people with type 2 diabetes

3 Apr 2025

Diabetes Distilled: Preserving muscle is important when using incretin mimetics for weight loss

How to minimise loss of muscle mass when using GLP-1-based therapies for weight loss.

26 Mar 2025

Diabetes Distilled: Finerenone reduces new diabetes and improves heart failure outcomes in the FINEARTS-HF trial

Some of the known excess risk of type 2 diabetes in people with heart failure attenuated,... and outcomes improved.

3 Mar 2025

Diabetes Distilled: Reframing the definition and diagnosis of clinical obesity

Consensus report advises definitions of clinical and pre-clinical obesity, according to... the presence of obesity-related

3 Mar 2025

Diabetes Distilled: The 4S Pathway – realigning management for older people with diabetes

Practical guidance from the International Geriatric Diabetes Society on the management o... diabetes in older people.

3 Mar 2025

What’s new in obesity?

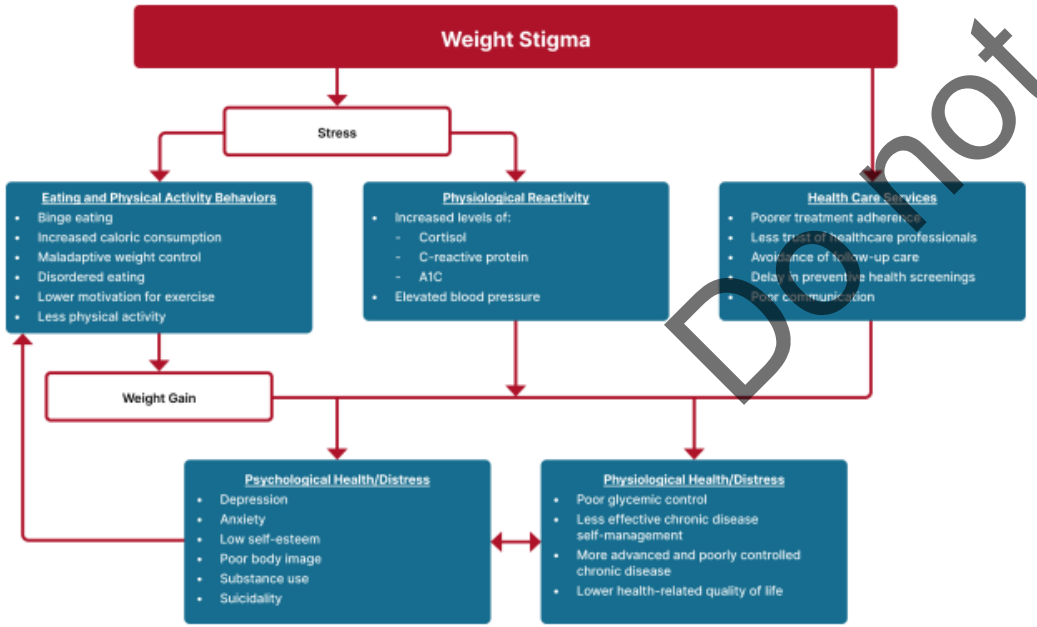
BMJ Open Diabetes Research & Care

Weight stigma and bias: standards of care in overweight and obesity—2025

Raveendhara R Bannuru, Professional Practice Committee

ADA 2025 May:13:e004962

- ✓ Weight bias – negative attitudes, blame. Explicit or implicit
- ✓ Weight stigma – social devaluation and mistreatment based on size
- ✓ 3 crucial areas: education and training, clinical environment and practice, communication and collaboration (person-centred language, ask first, shared decision-making)



Recent obesity–related resources from our journals

NICE overweight and obesity guidelines – what's new?

Erskine S (2025) At a glance factsheet: *Diabetes and Primary Care* 27: 51-3

Intermittent fasting for the management of weight and diabetes

Harvie M, McDiarmid S (2024) At a glance factsheet: *Diabetes & Primary Care* 26: 81–4

Diabetes Distilled

Tirzepatide SURMOUNTs semaglutide for weight loss

Preserving muscle is important when using incretin mimetics for weight loss

NICE guidance on tirzepatide for weight management

How carefully have we assessed our own weight bias? How often do we really consider impact of weight stigma?
Is our practice obesity-friendly?

Lancet Diabetes and Endocrinology Commission
Definition and diagnostic criteria of clinical obesity

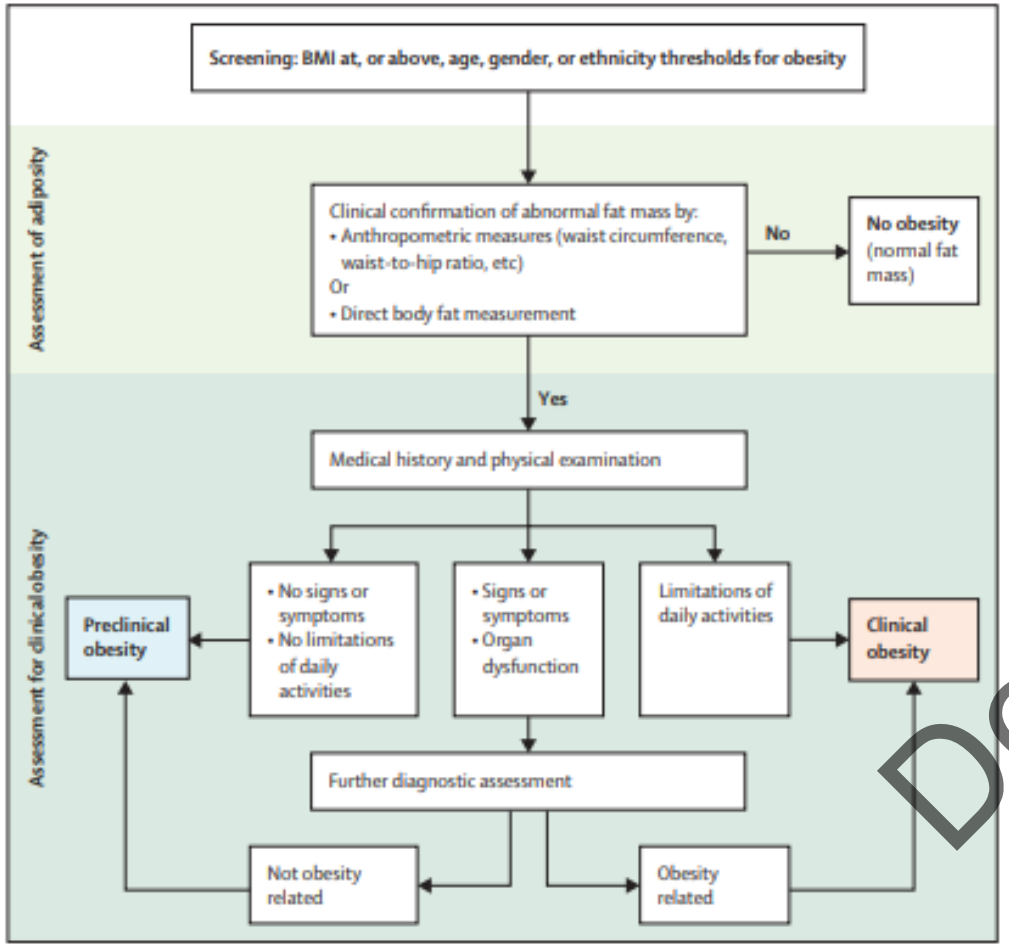
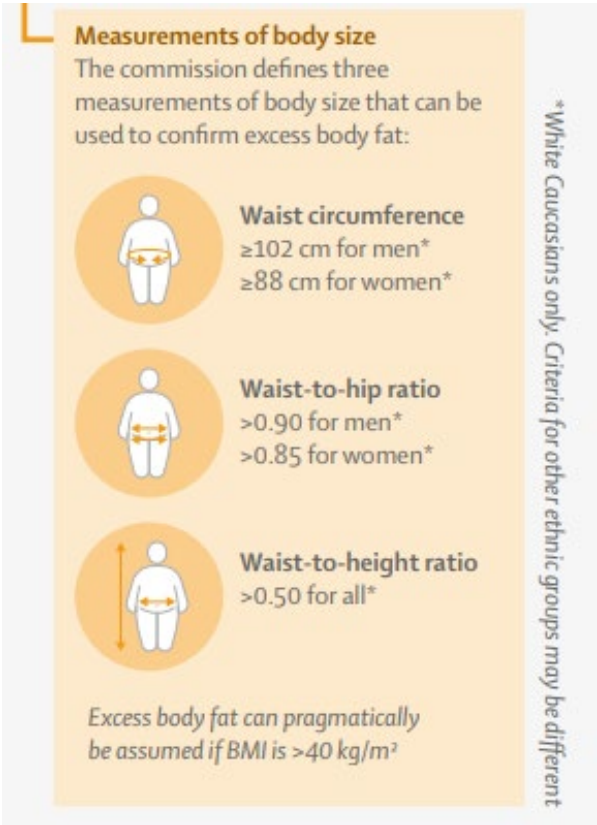


Figure 8: Clinical assessment of obesity

Coming soon from PCDOS – Obesity and weight management modules



Most guidelines measurement body size/distribution not just BMI
Do we consider functional impairment and whether due to obesity or not?

Lancet Diabetes and Endocrinology Commission
Definition and diagnostic criteria of clinical obesity

Reframing the definition and diagnosis of clinical obesity

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Brown P (2025) Diabetes Distilled
Diabetes & Primary Care 27: 25–8

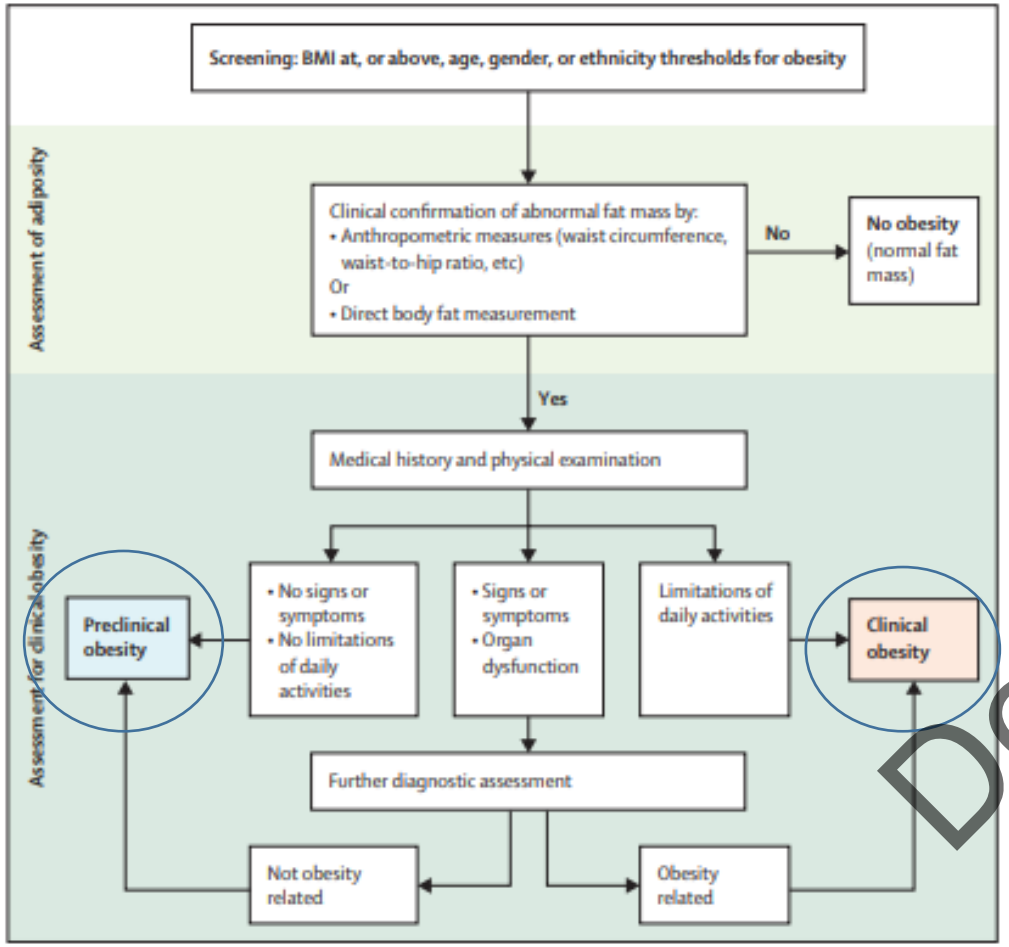


Figure 8: Clinical assessment of obesity

Preclinical obesity

A condition of excess body fat associated with variable level of health risk, but no ongoing illness

People living with preclinical obesity:

- Have no evidence of reduced organ or tissue function due to obesity
- Can complete day-to-day activities unhindered
- Are generally at a higher risk of developing diseases, such as:
  - Clinical obesity
  - Cardiovascular disease
  - Some cancers
  - Type 2 diabetes

Clinical obesity

A chronic disease due to obesity alone, and characterised by signs and symptoms of ongoing organ dysfunction and/or reduced ability to conduct daily activities

People living with clinical obesity have reduced tissue or organ function due to obesity, such as:

- Breathlessness caused by effects of obesity on the heart or lungs
- Knee or hip pain with joint stifness and reduced range of motion
- A cluster of metabolic abnormalities
- Dysfunction of other organs including kidneys, upper airways, nervous, urinary, and reproductive systems.

Consider the distribution, function and biochemical impact of the excess body fat not just the BMI

Lancet Diabetes and Endocrinology Commission
Definition and diagnostic criteria of clinical obesity

Some aspects of the guidance is controversial!

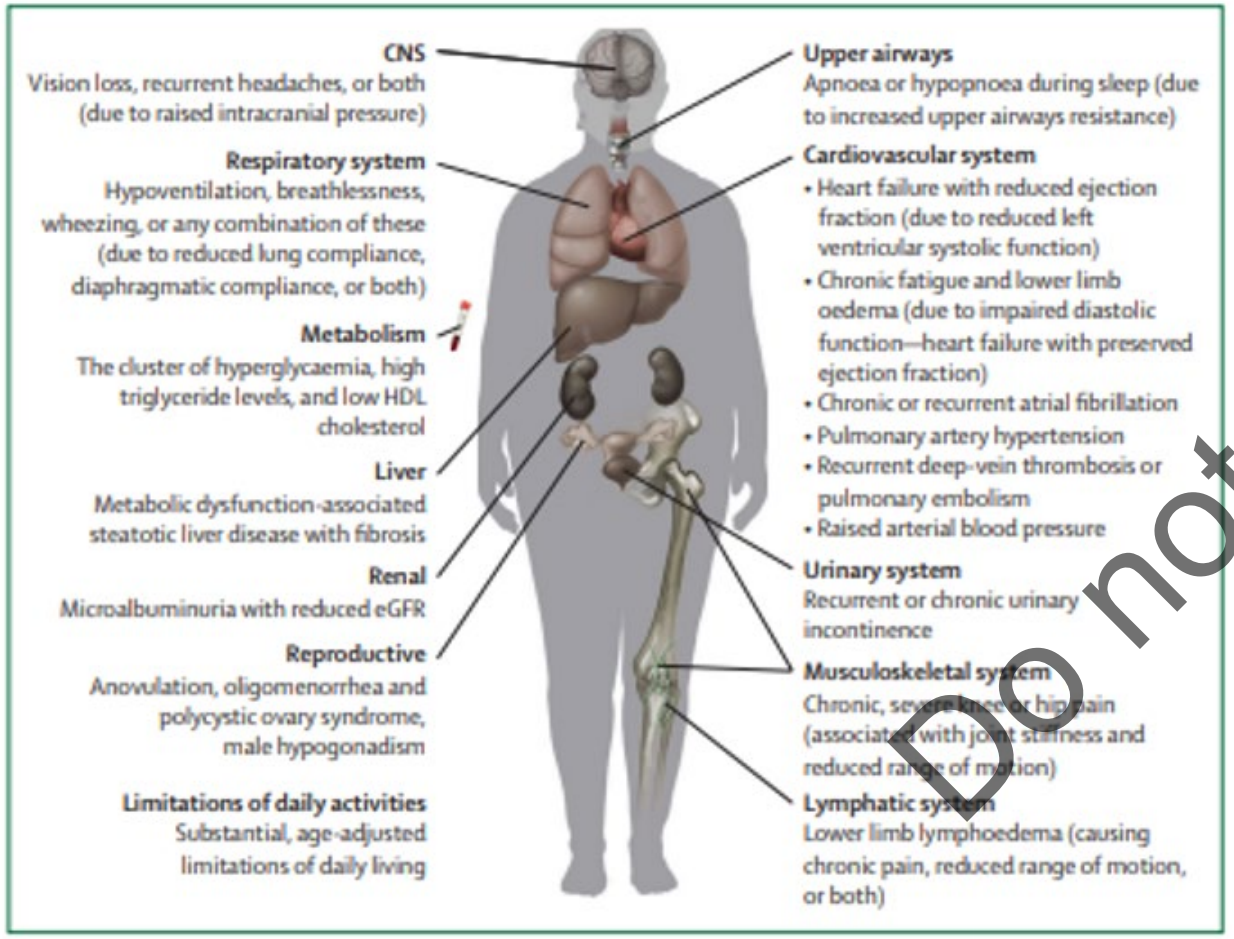


Figure 6: **Diagnostic criteria for clinical obesity in adults**
eGFR=estimated glomerular filtration rate.

Box 2. Diagnostic criteria for clinical obesity in adults.

Central nervous system
Signs of raised intracranial pressure, such as:
- Vision loss
- Recurrent headaches

Upper airways
- Apnoea/hypopnoea during sleep (due to increased upper airway resistance)

Respiratory
Signs of reduced lung compliance or diaphragmatic compliance, such as:
- Hypoventilation
- Breathlessness
- Wheezing

Cardiovascular
- Reduced left ventricular systolic function – heart failure with reduced ejection fraction (HFrEF)
- Chronic fatigue
- Lower limb oedema due to impaired diastolic dysfunction – heart failure with preserved ejection fraction (HFpEF)
- Chronic/recurrent atrial fibrillation
- Pulmonary artery hypertension
- Recurrent deep vein thrombosis
- Pulmonary thromboembolic disease
- Raised arterial blood pressure

Metabolism
- The cluster of hyperglycaemia, high triglyceride levels and low HDL-cholesterol levels

Liver
- NAFLD with hepatic fibrosis

Renal
- Microalbuminuria with reduced eGFR

Urinary
- Recurrent/chronic urinary incontinence

Reproductive (female)
- Anovulation
- Oligomenorrhoea
- Polycystic ovary syndrome

Reproductive (male)
- Male hypogonadism

Musculoskeletal
- Chronic, severe knee or hip pain associated with joint stiffness and reduced range of joint motion

Lymphatic
- Lower limb lymphedema causing chronic pain and/or reduced range of motion

Limitations of day-to-day activities
Significant, age-adjusted limitations of mobility and/or other basic activities of daily living, such as:
- Bathing
- Dressing
- Toileting
- Continence
- Eating

Note: Be aware some of these conditions may have other causes than obesity.

Many people we support will fit clinical obesity criteria and should be managed as having a chronic disease

Guidelines in practice

What Do Primary Care Practitioners Need to Know About Weight-loss Medications?

Use of Liraglutide, Semaglutide, and Tirzepatide for Adults Living With Overweight and Obesity

Medscape UK X Guidelines Primary Care Hacks

NHS prescribing

- ✓ Wales - only via specialist weight management services except for NICE-recommended use in T2DM

Private prescribing

- ✓ *Help keep people safe*
  - ✓ Raise awareness counterfeit products
  - ✓ If consult for other reasons educate regarding diet and physical activity/lifestyle change benefits
  - ✓ Contraception – non-hormonal 4 weeks at initiation/dose change tirzepatide in obese women
  - ✓ Ensure women know to discontinue prior to planning pregnancy – 2/12 sema, 1/12 tirzepatide

Take special care:

- ✓ Acute pancreatitis risk (uncommon ≤1%)
  - ✓ avoid if history of pancreatitis
  - ✓ Care if high risk eg very high triglycerides
- ✓ Gallbladder disease (uncommon ≤1%)
  - ✓ Rapid or significant weight loss increases risk gallstones

Milne N 2023 How to use GLP-1 receptor agonist therapy safely and effectively *Diabetes & Primary Care* 25: 11–13

Diabetes Distilled

Preserving muscle is important when using incretin mimetics for weight loss

Brown P (2025) Diabetes Distilled: *Diabetes & Primary Care* 27: 69–71

Tirzepatide and muscle composition changes in people with type 2 diabetes (SURPASS-3 MRI): a post-hoc analysis of a randomised, open-label, parallel-group, phase 3 trial Sattar et al 2025 Lancet diabetes endocrinol

Muscle loss and malnutrition – real concerns or not – follow the ongoing debate

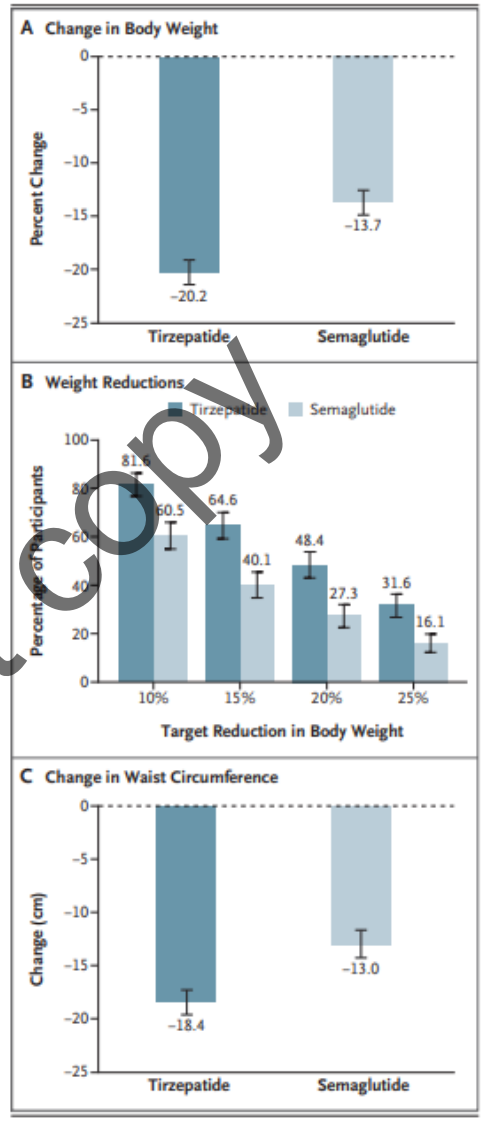
How are we coding people who are receiving non-NHS weight loss injections so we can search for them?

What's new from European Congress on Obesity 2025

Tirzepatide as Compared with Semaglutide for the Treatment of Obesity

Aronne et al for SURMOUNT-5 trial investigators
NEJM 2025

- ✓ Open label RCT, obesity without T2DM; n=751
- ✓ Tirzepatide 10 or 15mg, semaglutide 1.7 or 2.4mg + behaviour change support
- ✓ % weight change baseline to 72 weeks
- ✓ WC change, % achieving 10%, 15%, 20%, 25%
- ✓ Results
  - ✓ Mean% change in weight -20.2% tirzepatide -13.7% semaglutide
  - ✓ 31.6% achieved 25%+ with tirzepatide v 16.1% semaglutide
  - ✓ Mean change WC 18.4cm tirzepatide v 13cm semaglutide
- ✓ Beneficial changes BP, glycemia, fasting insulin, TGs; no change in LDL or non-HDL cholesterol
- ✓ Safety profiles consistent with previous studies



SURMOUNT-OSA
Malhotra et al 2024
Licensed for OSA in US

SURMOUNT-MMO
ongoing

Diabetes Distilled

Tirzepatide SURMOUNTs semaglutide for weight loss

Semaglutide and tirzepatide both very effective drugs for weight loss. We should individualise our drug choice depending on clinical need – weight loss needed, CVD, renal, OSA, MASLD.

Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes

SELECT trial NEJM 2023; 389

- ✓ 17,604, obesity, established CVD, 45yrs+
- ✓ Semaglutide to 2.4mg v placebo + CV standard of care

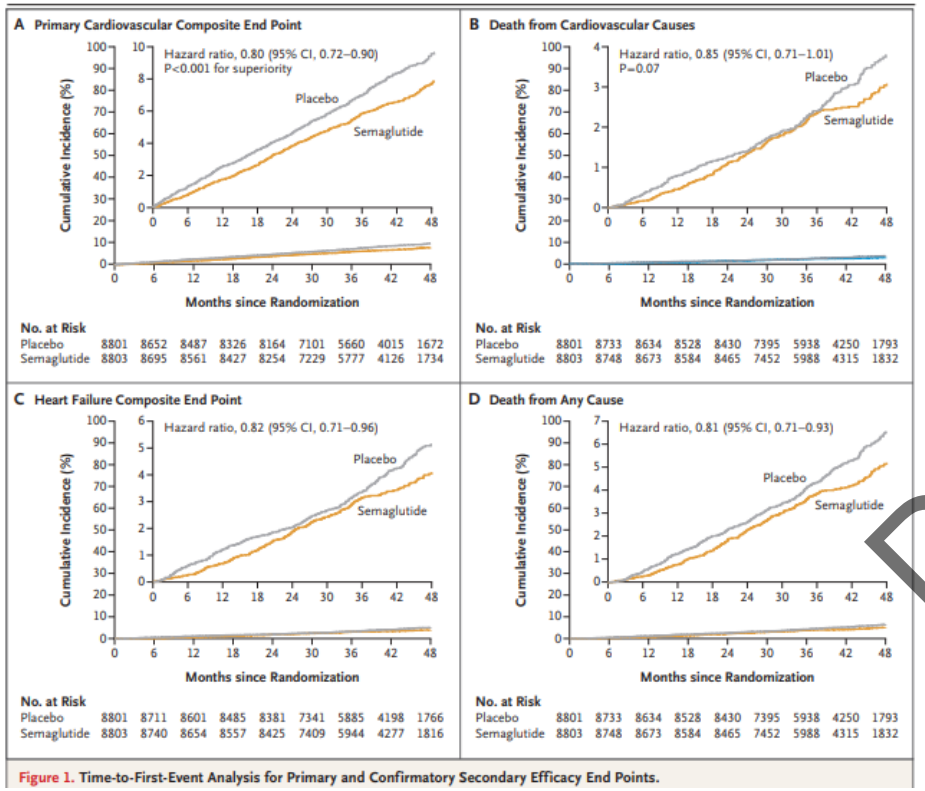


Figure 1. Time-to-First-Event Analysis for Primary and Confirmatory Secondary Efficacy End Points.

Exploring the early semaglutide benefits in adults with overweight or obesity and cardiovascular disease: a secondary analysis of the SELECT trial

- ✓ 1255 3 point MACE endpoints - 20% reduction on top of good CVD standard of care
- ✓ All 3 MACE components contributed to the risk reduction – CVD death, non-fatal MI or stroke
- ✓ In the first 3 months HR 0.62 MACE (38% reduction)
- ✓ In the first 6 months
  - ✓ HR 0.59 3 point MACE (41% reduction)
  - ✓ HR 0.27 CV deaths (53% reduction)
  - ✓ HR 0.57 MI (43% reduction)

  Stroke numerically fewer but not statistically significant

Rapidly improves disease trajectory

- ✓ Before clinically meaningful weight loss
- ✓ Not yet titrated to maximum tolerated dose

Suggests other actions beyond weight loss which impact very early

The effect of GLP-1RAs on mental health and psychotropics-induced metabolic disorders: A systematic review

Sigrid Breit *, Daniela Hubl

Psychoneuroendocrinology 176 (2025) 107415

Translational Research Center, University Hospital of Psychiatry and Psychotherapy, University of Bern, Bern, Switzerland

Comprehensive review – GLP-1RAs safe and effective for obesity treatment in adults with mental illness

- ✓ People with severe mental health problems 3X more likely to be living with obesity (60%)
- ✓ Weight gain and elevated glucose common with antidepressants and antipsychotics

GLP-1RA data from 36 studies, 25,677 adults; liraglutide, semaglutide, exenatide and dulaglutide

- ✓ Weight and glycaemic reductions
- ✓ Beneficial effects on mood, well-being, QoL
- ✓ No worsening of mental state, suicidal risk or admissions but continue to monitor closely

Efficacy and safety of semaglutide 2.4 mg according to antidepressant use at baseline: A post hoc subgroup analysis

Robert F. Kushner[1] | Anders Fink-Jensen[2] | Ofir Frenkel[3] | Barbara McGowan[4] | Bryan Goldman[3] | Maria Overvad[3] | Thomas Wadden[5]

Obesity (Silver Spring). 2024;32:273–280.

32nd EUROPEAN CONGRESS ON OBESITY
11-14 MAY, 2025 | MALAGA, SPAIN

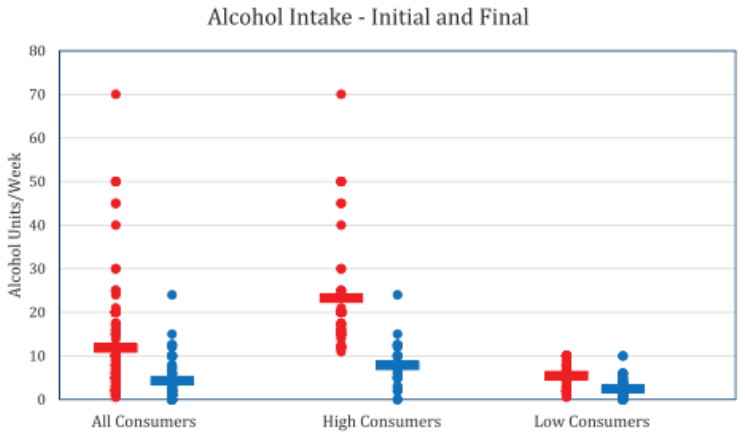
Glucagon-like peptide-1 analogues reduce alcohol intake

Maurice O'Farrell MBBS[1] | Faisal I. Almohaileb MBBS[2] | Carel W. le Roux MD[3]

Diabetes Obes Metab. 2025;1–4.

Small study 262 people being treated for obesity

- ✓ 188 followed for 4 months; none increased intake
- ✓ Average alcohol intake ↓ - 11.3 units/wk to 4.3
- ✓ Regular drinkers intake ↓ - 23.2 units/wk to 7.8 – 68% decrease
- ✓ Exact mechanism not known
  - ✓ may curb cravings arising in subcortical areas not under conscious control – 'effortless'



When we do mental health reviews, do we consider weight and cardiometabolic impact of drugs?

Glucagon-like peptide-1 receptor agonists compared with bariatric metabolic surgery and the risk of obesity-related cancer: an observational, retrospective cohort study

Yael Wolff Sagy,[a,i,*] Noga Ramot,[a,i] Erez Battat,[a] Ronen Arbel,[b,c] Orna Reges,[a,d,j] Dror Dicker,[e,f,j] and Gil Lavie[a,g,j]

eClinicalMedicine
2025;■: 103213

Obesity and diabetes associated with increased cancer risk

- ✓ How do first generation GLP-1RAs and bariatric/metabolic surgery compare for obesity related cancer rates (ORCs)
- ✓ Observational, retrospective cohort study, 7-12 yrs F/U
- ✓ Wt loss lower with GLP-1RAs but similar ORC rates
- ✓ Possible increased risks for thyroid and pancreatic cancer with these drugs never confirmed in humans
- ✓ Suggests additional mechanism(s) for ORC reduction with drugs eg anti-inflammatory, immune modulating

Estimating direct tissue effects versus weight loss effects of incretin-based drugs for obesity on various chronic conditions

Lancet Diabetes Endocrinol. 2025 Apr;13(4):347-354.

Naveed Sattar, Matthew M Y Lee

Personal view

- ✓ MACE – mainly direct tissue effects
- ✓ T2DM – weight loss and direct tissue effects
- ✓ CKD – weight loss and tissue effects; less clear
- ✓ Hypertension – mainly weight loss
- ✓ HFpEF – mainly weight loss
- ✓ MASH – mainly weight loss
- ✓ OSA – all weight loss
- ✓ OA knee all weight loss

Many of the mechanisms by which newer drugs achieve their effects still to be identified

What’s new on MASLD

Metabolic dysfunction-associated steatotic liver disease (MASLD) and metabolic dysfunction-associated steatohepatitis (MASH)

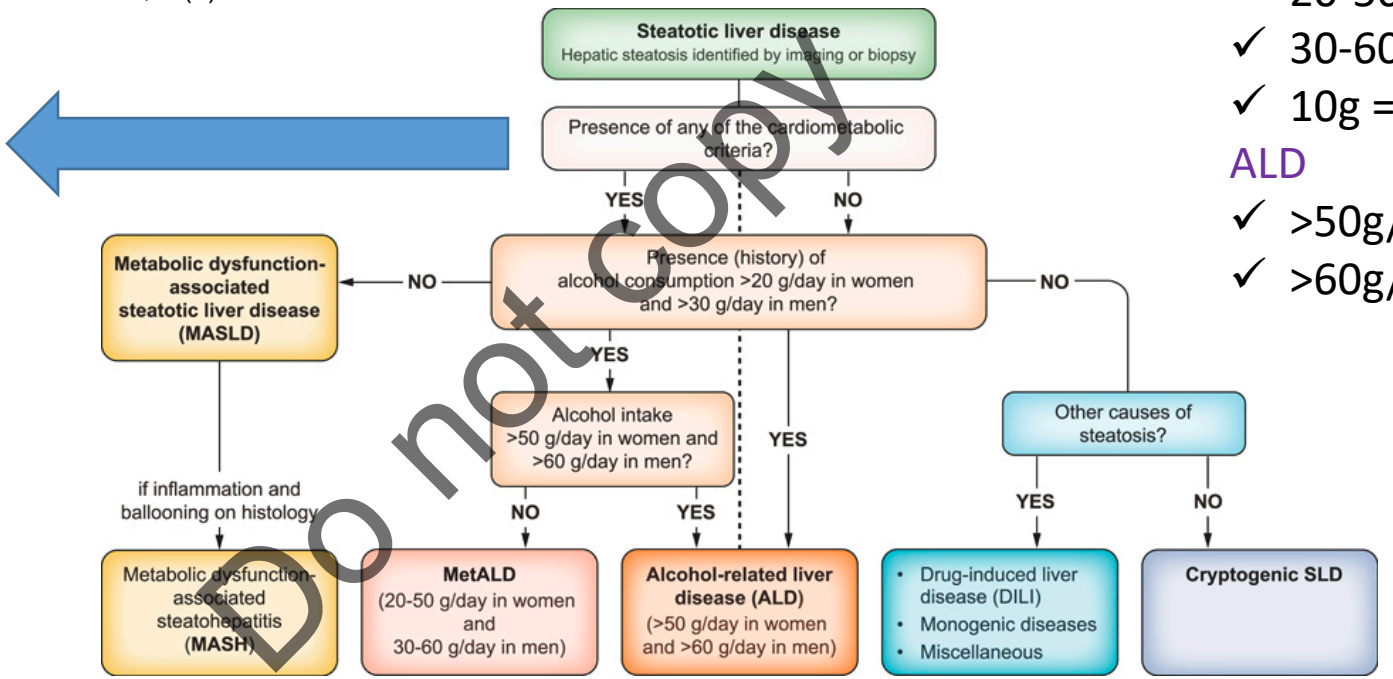
From: **EASL-EASD-EASO Clinical Practice Guidelines on the Management of Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)**

Obes Facts. 2024;17(4):374-444. doi:10.1159/000539371

Adult criteria

At least 1 out of 5:

- ☐ BMI ≥25 kg/m² [23 Asia] **OR** WC >94 cm (M) 80 cm (F) **OR** ethnicity adjusted equivalent
- ☐ Fasting serum glucose ≥5.6 mmol/L [100 mg/dl] **OR** 2-hour post-load glucose levels ≥7.8 mmol/L [≥140 mg/dl] **OR** HbA1c ≥5.7% [39 mmol/L] **OR** type 2 diabetes **OR** treatment for type 2 diabetes
- ☐ Blood pressure ≥130/85 mmHg **OR** specific antihypertensive drug treatment
- ☐ Plasma triglycerides ≥1.70 mmol/L [150 mg/dl] **OR** lipid lowering treatment
- ☐ Plasma HDL-cholesterol ≤1.0 mmol/L [40 mg/dl] (M) and ≤1.3 mmol/L [50 mg/dl] (F) **OR** lipid lowering treatment



Self-reported alcohol intake

MetALD

- ✓ 20-50g/day women
- ✓ 30-60g/day in men
- ✓ 10g = 1 unit

ALD

- ✓ >50g/day women
- ✓ >60g/day men

- ✓ 99% concordance between NAFLD and MASLD

Fatty liver on imaging – identify 1 MASLD criteria – alcohol intake – diagnosis

Fib-4 fibrosis score to assess need for further investigation

Why is it important to tackle MASLD in practice?

Metabolic dysfunction-associated steatotic liver disease (MASLD)

MASLD: a systemic metabolic disorder with cardiovascular and malignant complications

Giovanni Targher [1], Christopher D Byrne [2], Herbert Tilg [3] Gut 2024; 74:691-702

Fatty liver – inflammation – increasing fibrosis – cirrhosis

- ✓ Multisystem disease due to insulin resistance/metabolic dysfunction
  - ✓ Liver – fibrosis, cirrhosis, liver failure, hepatocellular carcinoma
  - ✓ CVD including ASCVD, AF and heart failure, T2DM, CKD
  - ✓ Cancers – oesophagus, stomach, pancreas, colorectal, thyroid, lung, breast, prostate, haematological

Where does the fat come from?

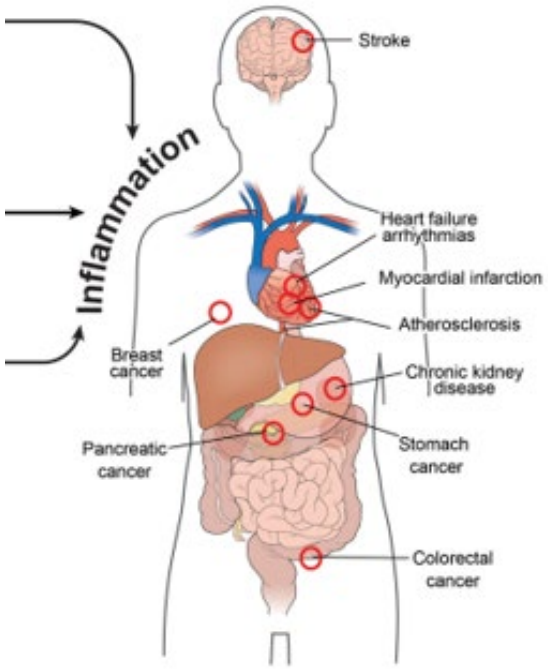
- ✓ Excess sugar and fat in the diet
- ✓ Fat spilling over from other body sites

Management:

- ✓ Weight loss – 5-7% steatosis; 10% if fibrosis; 3-5% if lean
- ✓ Mediterranean diet or similar; ↓ UPF/sugar/fizzy drinks
- ✓ Aerobic and resistance physical activity
- ✓ Drugs not yet licensed – TZDs, GLP-1RAs, tirzepatide, resmetirom (thyroid homone receptor –β agonist)

Aostee et al Lancet Regional Health; 2024:36

Fib-4 <1.3 – repeat 1-3 years
≥1.3 – refer for fibroscan
Uses age, AST, ALT and platelets



70% of people we see with T2DM will also have MASLD

Do we share new diagnoses fatty liver, calculate Fib-4 and support weight loss? Motivated when new diagnosis

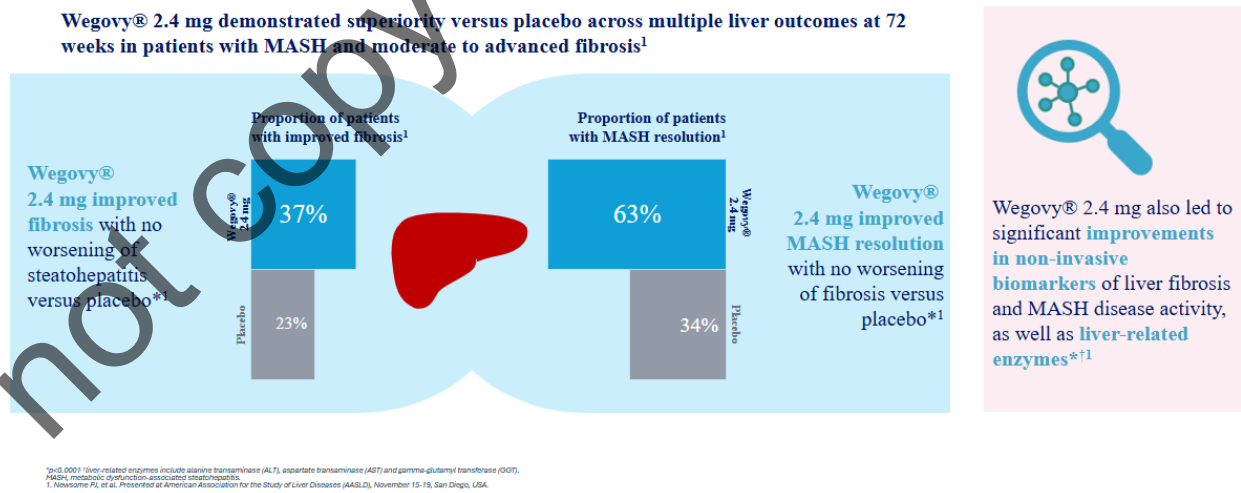
ESSENCE – Semaglutide in metabolic dysfunction-associated steatohepatitis

Sanyal et al NEJM 2025

1200 with histological evidence MASH and fibrosis 2 or 3
Wegovy 2.4mg v Placebo

- ✓ Part 1 - improves liver histology at 72 weeks
  - ✓ Steatohepatitis resolution) and combined
  - ✓ Improvement liver fibrosis)
  - ✓ Changes in body weight, SF 36 bodily pain
- ✓ Part 2 - lowers risk liver-related events at End of Trial – Time to first event:
  - ✓ Histological progression to cirrhosis
  - ✓ Death any cause, MELD score >/=15
  - ✓ Liver transplant
  - ✓ Hepatic decompensation

Wegovy® 2.4 mg : Significant improvements in liver fibrosis and histological resolution



Tirzepatide for metabolic dysfunction-associated steatohepatitis with liver fibrosis
Phase 2 dose-finding
MASH resolution no fibrosis worsening- 62% tirzepatide 15mg v 10% placebo
Fibrosis improved ≥1 stage no NASH worsening 51% tirzepatide 15mg v 30% placebo

Loomba et al for SYNERGY-NASH investigators
N Engl J Med 2024;391:299-310

Survodutide – GLP-1RA and glucagon receptor agonist

Sanyal et al N Engl J Med 2024; 391:311-319

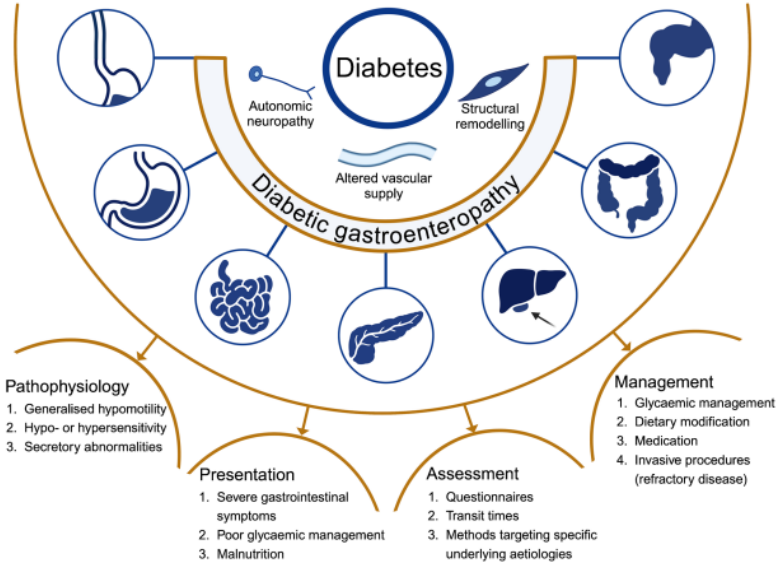
Wegovy and Mounjaro are not approved for the treatment of MASLD or MASH and Survodutide not yet licensed in UK

What’s new in diabetes?

Do not miss

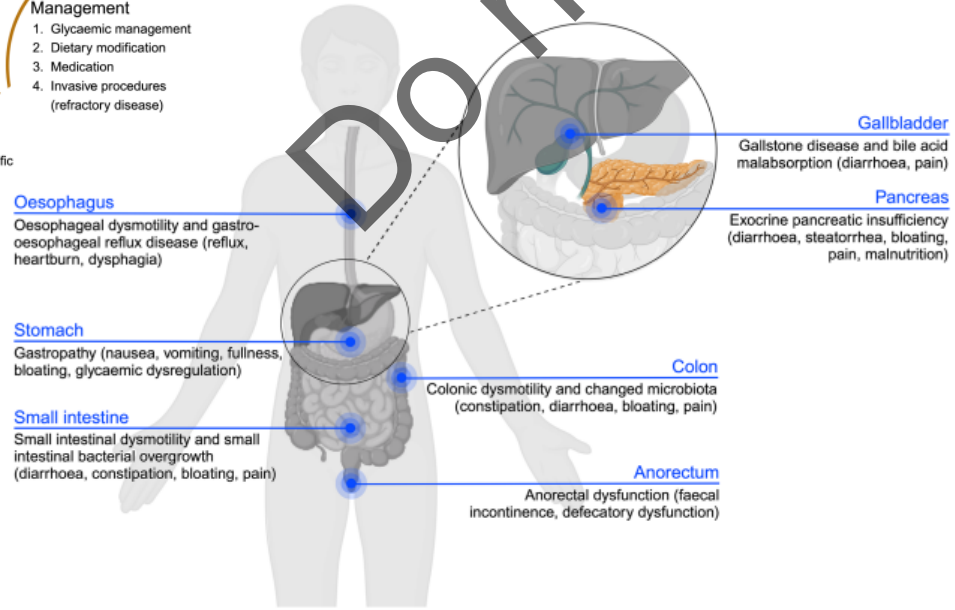
Diabetic gastroenteropathy: a pan-alimentary complication

Diabetologia (2025) 68:905–919



Pathophysiology

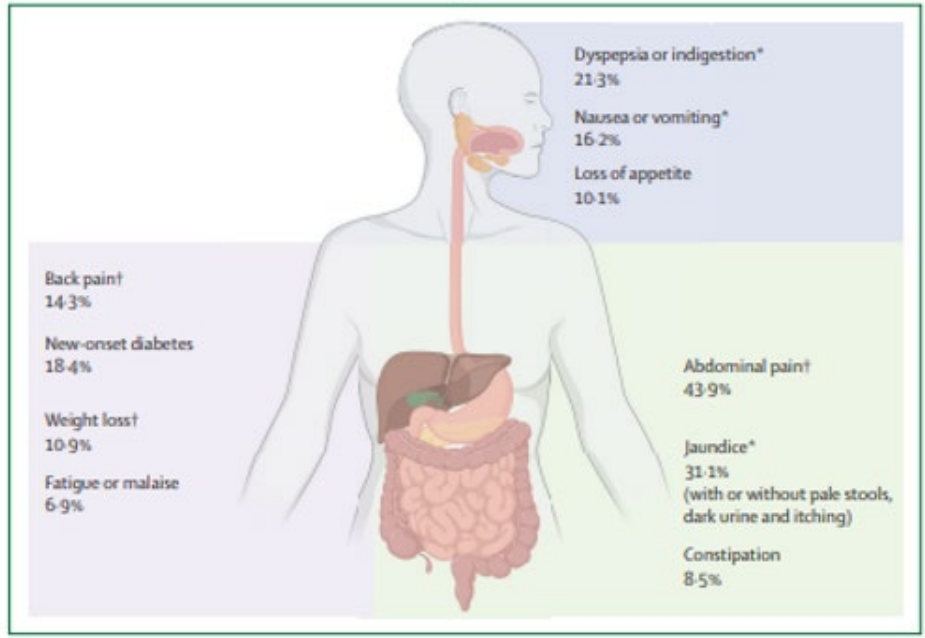
- ✓ Generalised hypomotility
- ✓ Hypo or hypersentivity
- ✓ Secretory abnormalities



Pancreatic cancer

Lancet 2025; 405: 1182–202

Thomas F Stoop, Ammar A Javed, Atsushi Oba, Bas Groot Koerkamp, Thomas Seufferlein, Johanna W Wilmink, Marc G Besselink



Diabetes and cancer

Chowdhury TA (2025) At a glance factsheet Diabetes and Cancer *Diabetes and Primary Care* 27:47-9

Remission

Impact of bodyweight loss on type 2 diabetes remission: a systematic review and meta-regression analysis of randomised controlled trials

Sarah Kanbour, Rwedah A Ageeb, Rayaz A Malik, Laith J Abu-Raddad

Lancet Diabetes Endocrinol
2025; 13: 294–306

- ✓ Every 1% weight loss = 2.17% ↑ complete remission (HbA1c <42) and 2.74% ↑ partial remission (HbA1c<48)
- ✓ Robust dose-response relationship independent of (age), T2DM duration, HbA1c, BMI, intervention type

Consensus report: definition and interpretation of remission in type 2 diabetes

Diabetologia (2021) 64:2359–2366
https://doi.org/10.1007/s00125-021-05542-z

- ✓ HbA1c<48mmol/mol, no DM medication ≥ 3 months
- ✓ Don't pursue if high HbA1c and worse than background retinopathy
- ✓ Not achievable if SGLT2i needed for CVD, CKD or HF

Does remission of type 2 diabetes matter? A qualitative study of healthcare professionals' perspectives and views about supporting remission in primary care

Diabetic Medicine. 2025;00:e15515.
https://doi.org/10.1111/dme.15515

Small Scottish study, remission 'not a clinical priority'; people in remission 'self-motivated' so don't need support

- ✓ PCPs report:
  - ✓ Remission 'positive and empowering' but not sustainable
  - ✓ Reluctance to code in case 'lost to follow up'
  - ✓ Reluctance to pursue in case not achieved

Pre-diabetes remission v T2DM prevention

Role of weight loss-induced prediabetes remission in the prevention of type 2 diabetes: time to improve diabetes prevention

Diabetologia (2024) 67:1714–1718
https://doi.org/10.1007/s00125-024-06178-5

- ✓ Remission rates correlate with weight loss
- ✓ >5% weight loss in pre-diabetes – 43% pre-diabetes remission (<39mmol/mol)
- ✓ If achieve pre-diabetes remission – 73% lower risk of future T2DM

Pre-diabetes remission the new goal – not just T2DM prevention. Early T2DM diagnosis important.
Do we discuss remission when new diagnosis? Do we give clear guidance on weight loss required?

Diabetes and surgery

Elective peri-operative management of adults taking glucagon-like peptide-1 receptor agonists, glucose-dependent insulinotropic peptide agonists and sodium-glucose cotransporter-2 inhibitors: a multidisciplinary consensus statement

Volume 80, Issue 4
April 2025
Pages 412-424

GLP-1RAs/GIP RAs

- ✓ Discuss risk of pulmonary aspiration
- ✓ Do not withhold GLP-1RAs; adhere to fasting recommendations, regional anaesthesia preferred
- ✓ Consider gastric USS immediately prior to surgery

SGLT2 inhibitors

- ✓ Discuss DKA risk, stop 24 hours prior to surgery
- ✓ Adhere to fasting times but not excess
- ✓ Restart 24-48 hours post op when eating and drinking normally

Is There a Safe Glycemic Threshold for Cataract Surgery?

American Journal of Ophthalmology

Post-operative endophthalmitis – no increased risk with high HbA1c

Hussain et al 2025

Centre for Perioperative Care
Academy of Medical Royal Colleges

Guideline for Perioperative Care for People with Diabetes Mellitus Undergoing Elective and Emergency Surgery

March 2021

Determining the Threshold for HbA1c as a Predictor for Adverse Outcomes After Total Joint Arthroplasty: A Multicenter, Retrospective Study

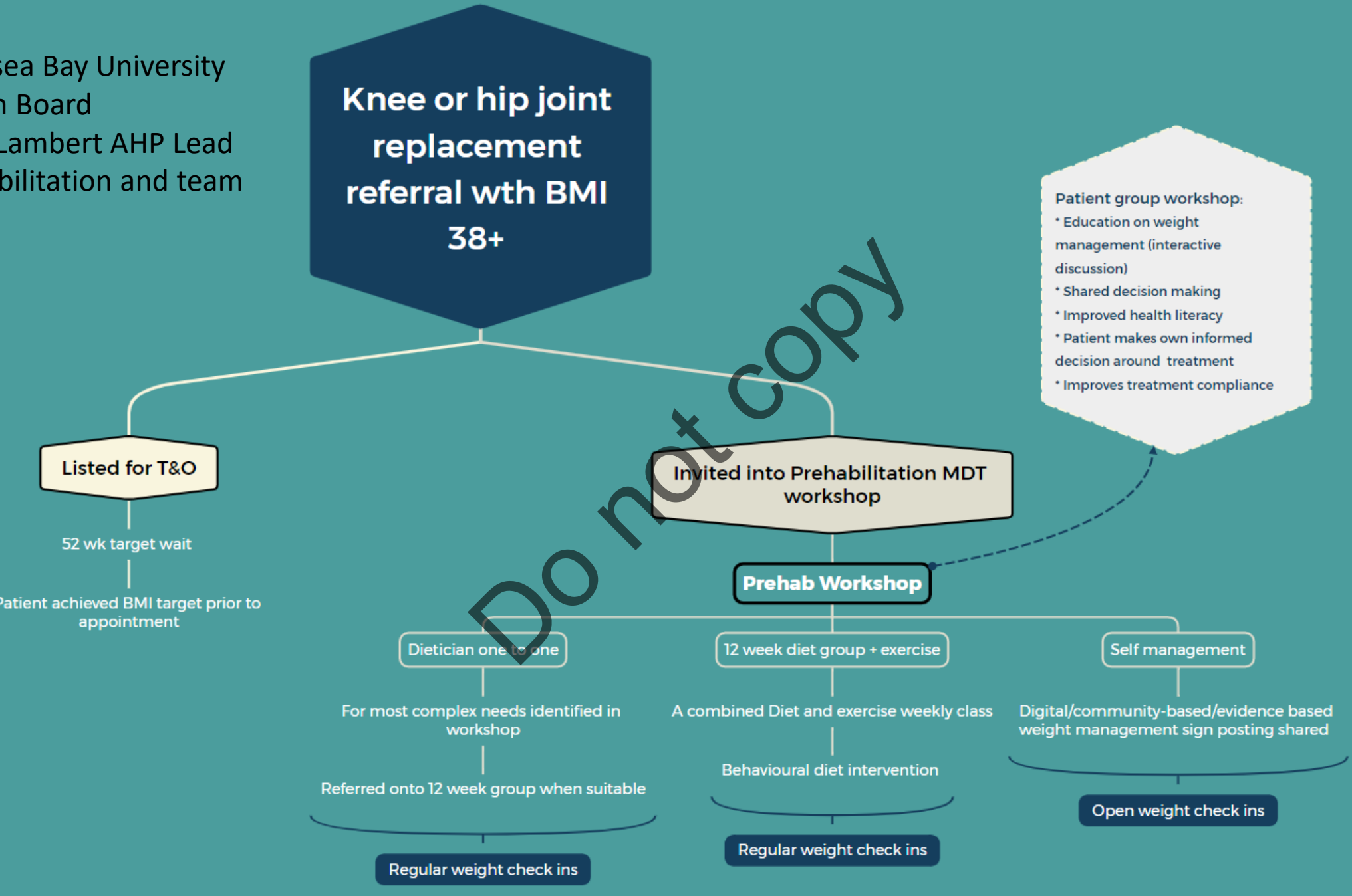
Tarabachi The journal of arthroplasty 2017

- ✓ HbA1c <69mmol/mol for all elective surgery
- ✓ HbA1c <60 or 61mmol/mol for joint replacement

Shared decision making and individualisation important - not always safe to achieve these targets with SU/insulin

Do we remember to include recent HbA1c in referral letters?

Swansea Bay University
Health Board
Chris Lambert AHP Lead
Prehabilitation and team



Diabetes and pregnancy

Association between maternal diabetes and neurodevelopmental outcomes in children: a systematic review and meta-analysis of 202 observational studies comprising 56·1 million pregnancies

T2DM ↑ women of child-bearing age and gestational diabetes ↑.
Maternal diabetes may alter fetal brain development.

- ✓ Pre-gestational T1DM and T2DM and gestational diabetes
- ✓ Studies adjusted for single confounders:
  - ✓ Maternal diabetes associated with all neurodevelopmental disorders, lower IQ and psychomotor scores
- ✓ Studies adjusted for multiple confounders – exposed children
  - ✓ 1.28 risk ratio any neurodevelopmental disorder
  - ✓ 1.25 risk ratio autism spectrum disorder
  - ✓ 1.3 risk ratio ADHD
  - ✓ 1.32 risk ratio intellectual disability
- ✓ Pre-existing diabetes associated with higher risk than gestational 1.39 v 1.18

Early and more severe gestational diabetes stronger associations – duration of exposure may be important

Epigenetic intrauterine programming increases cardiometabolic disease and obesity in offspring

Diabetes in Pregnancy for Mothers and Offspring: Reflection on 30 Years of Clinical and Translational Research: The 2022 Norbert Freinkel Award Lecture

Anny H. Xiang

Diabetes Care 2023;46:482–489 | https://doi.org/10.2337/dci22-0055

Diabetologia (2023) 66:1961–1970
https://doi.org/10.1007/s00125-023-05965-w

REVIEW

An unwelcome inheritance: childhood obesity after diabetes in pregnancy

Claire L. Meek[1,2]

Increase awareness of possible neurodevelopmental concerns in at risk children
Be more alert to parental concerns in such children ensuring early referral for further assessment?

Physical activity and incident T2DM

Accelerometer-derived "weekend warrior" and regularly active physical activity and incident diabetes

Obesity (Silver Spring). 2025;1–11.

Moderate to vigorous physical activity and new T2DM
86000 people from UK Biobank wearing accelerometer
Retrospective cohort study

- ✓ Guideline threshold 150 min+ MVPA per week; mean 230min per week
  - ✓ Weekend warrior - achieve MVPA threshold but over 1-2 days/week
  - ✓ Regularly active – achieve threshold but more days per week
  - ✓ Inactive – below the MVPA threshold
- ✓ Results
  - ✓ 43.7% 'Weekend Warrior' pattern
  - ✓ 24%-36% lower risk v inactive (150min/week)
  - ✓ Same reduction T2DM in Weekend Warrior and regular active

Neuroprotective mechanisms of exercise and importance of fitness for healthy brain ageing
Tari et al Lancet 2025; 405:1093-118

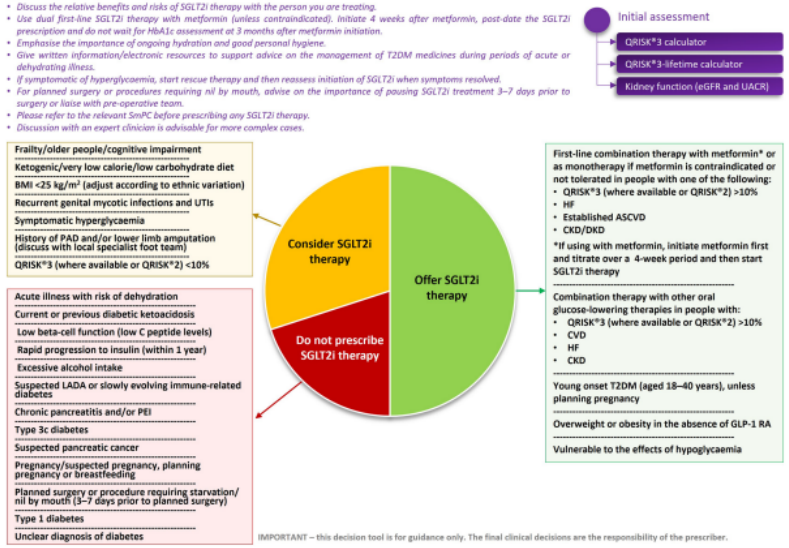
Physical activity can prevent T2DM, slow its progression, reduce CVD and multiple other benefits in diabetes

What have we done today to protect our own health – sleep, stress, physical activity, nutrition?

Expanding evidence-base for SGLT2 inhibitors

SGLT2 Inhibitors – The New Standard of Care for Cardiovascular, Renal and Metabolic Protection in Type 2 Diabetes: A Narrative Review

Diabetes Ther (2024) 15:1099–1124 1111

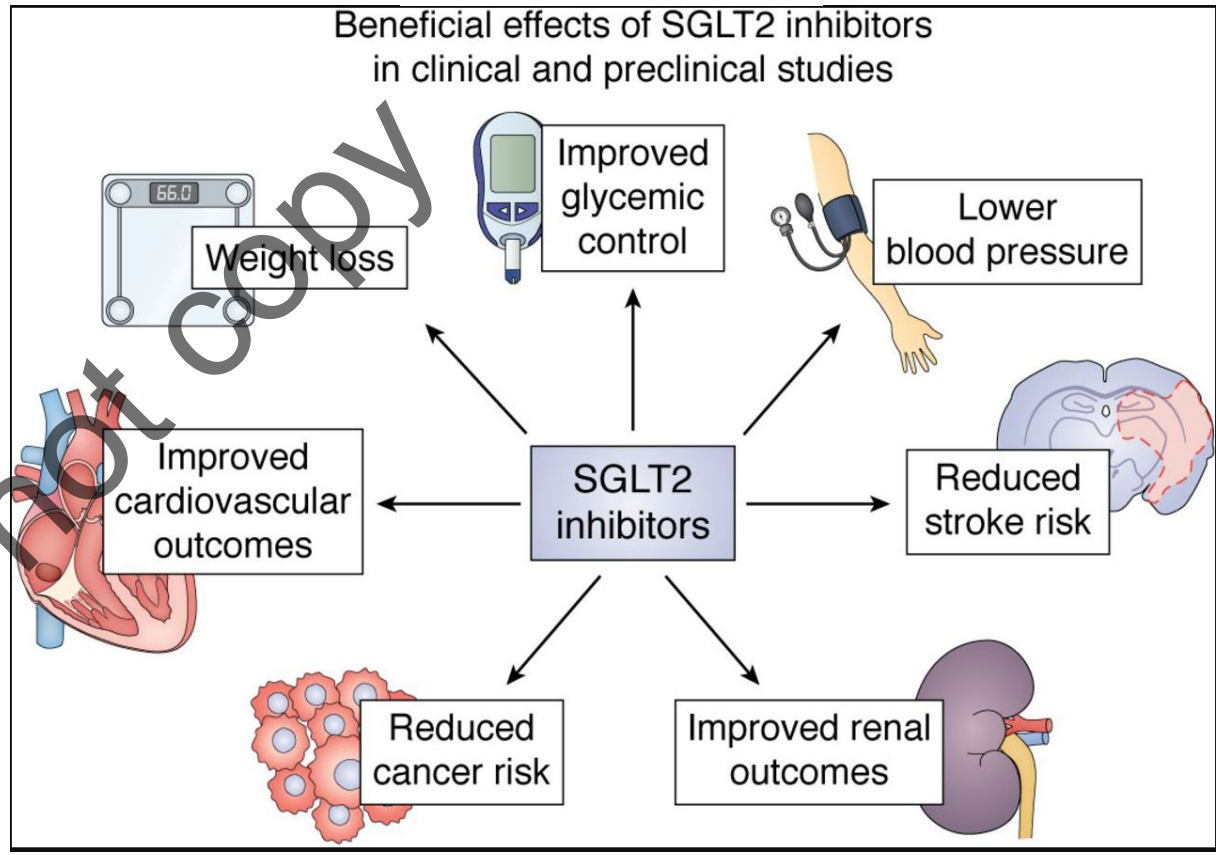


Interactive on-line resource

Decreased hyperkalemia on RAAS inhibitors
Wing et al JAMA Int Med 2025

Sodium-glucose cotransporter-2 inhibitors: Understanding the mechanisms for therapeutic promise and persisting risks

J. Biol. Chem. (2020) 295(42) 14379–14390



MASLD effects, cognitive effects, colitis, bone benefits

How do we stay up to date with new studies? How do we individualise our choice within class?
Be aware of different eGFRs for initiation and stopping of individual SGLT2is

Expanding evidence base for incretin-based drugs

Diabetes Distilled

Heart and SOUL – oral semaglutide demonstrates cardiovascular benefit in high-risk people with type 2 diabetes

Brown P (2025) Diabetes Distilled: *Diabetes & Primary Care* 27: 59–61

Semaglutide oral and injectable, dulaglutide, liraglutide

STEP HFpEF
SUSTAIN-7 with semaglutide

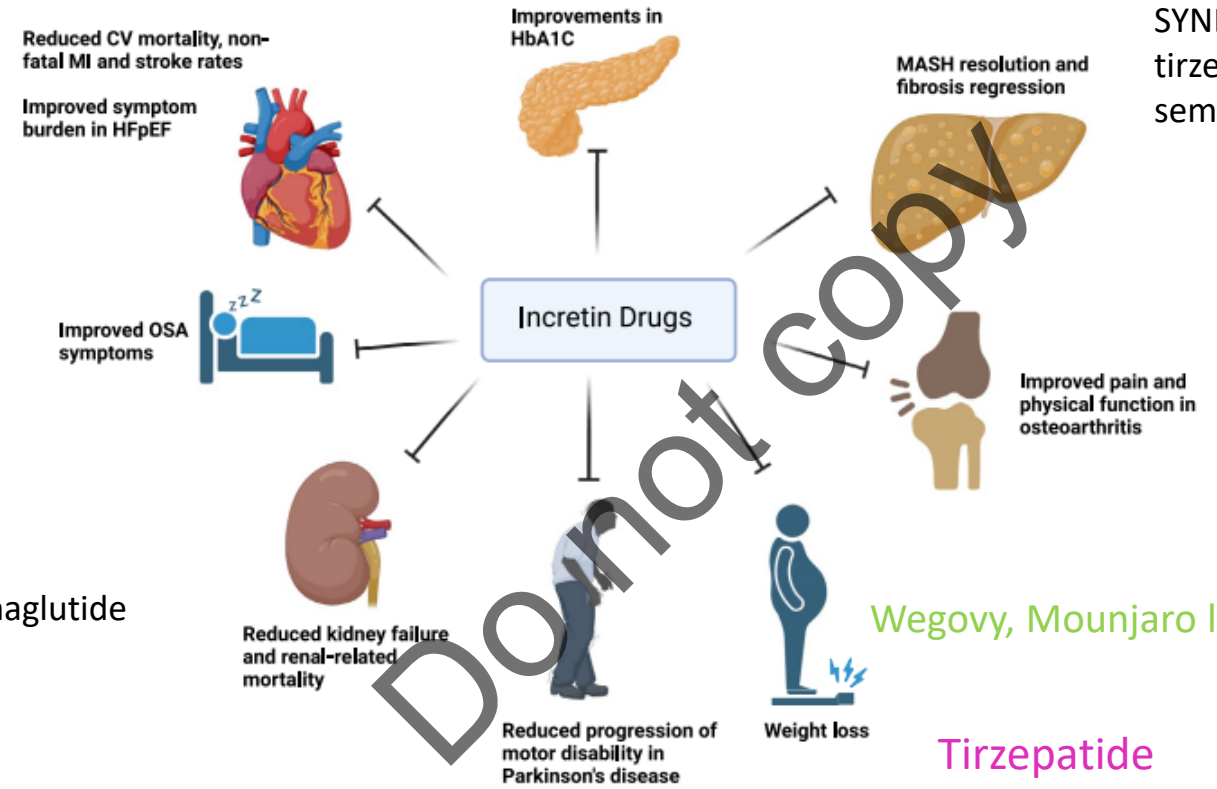


Diagram from: Elangovan et al Hepatology International (2025) 19:337-348

FLOW study semaglutide

SYNERGY-NASH tirzepatide; ESSENCE semaglutide

↓ obesity related cancers

↓ Alcohol intake

Improved mental health and safety

STEP-9 semaglutide

Peripheral arterial disease STRIDE semaglutide

Wegovy, Mounjaro licensed

Semaglutide

- ✓ SUSTAIN trials for T2DM
- ✓ STEP trials obesity
- ✓ PIONEER and SOUL rybelsus oral

Tirzepatide

- ✓ SURPASS trials T2DM
- ✓ SURMOUNT trials obesity

Increasingly difficult to stay on top of the evidence – focus on licensed indications

Please be aware that only the indications or drugs in green are licensed indications in the UK

T2DM

Semaglutide and walking capacity in people with symptomatic peripheral artery disease and type 2 diabetes (STRIDE): a phase 3b, double-blind, randomised, placebo-controlled trial

Bonaca et al Lancet 2025: 405;1580-93

- ✓ 52 week placebo controlled RCT 1mg semaglutide
- ✓ Peripheral arterial disease with ABPI ≤ 0.90, or toe brachial index ≤ 0.70, able to walk at least 200m; T2DM; N=792
- ✓ Ratio week 52 walking distance to baseline, on fixed load treadmill 12% incline, 3.2km/h
- ✓ Significantly greater walking distance with semaglutide – treatment ratio 1.13 (26.4m median and 39.9m mean); beneficial from 6 months
- ✓ Also improved pain free walking distance and QoL
- ✓ 6 serious adverse events (1%) with semaglutide and 9 in placebo group (2%)

Semaglutide – also general CVD benefits

No major adverse limb event data from this study

Will benefits extend to people with PAD but no T2DM?

Obesity

Once-Weekly Semaglutide in Persons with Obesity and Knee Osteoarthritis

Bliddal et al for STEP 9 Study Group NEJM 2024:391;1573-83

- ✓ 68 week double blind, randomised, placebo controlled trial; BMI ≥30; mean BMI 40+; no T2DM; xray OA knee, at least moderate pain. N=407
- ✓ % weight change, change in WOMAC score (0-100); physical function score on SF-36 questionnaire
- ✓ Weight change -13.7% v -3.2%; improved WOMAC score -41 v -27.5; greater improvement in SF-36 physical function score
- ✓ Decreased analgesics, greater in semaglutide group
- ✓ Discontinuation AEs 6.0% semaglutide v 3.0% PBO

Will benefits extend to those without obesity?

Glucagon-Like Peptide-1 Receptor Agonists and Osteoarthritis

David T. Felson, M.D., M.P.H.

Obesity ↑ knee OA - increasing stress across the joint; adipocytokine production from visceral fat increases pain; inflammatory processes. GLP-1RAs ↑ weight loss, anti-inflammatory and immunomodulation effects.

People with OA using NSAIDs - risk of kidney, CVD and GI problems, GLP-1s safer and added weight loss

Do we specifically ask about and assess problems with walking or any calf pain when assessing PLWD?

We have all the drugs we need and many more coming soon

The challenges are:

- ✓ T2DM – how do we support people to choose the right drug and stick with long-term treatment?
- ✓ Obesity – how do we help people gain access to drug treatment, help change behaviour and keep people safe

When we support either of these processes we should congratulate ourselves

A five-drug class model using routinely available clinical features to optimise prescribing in type 2 diabetes: a prediction model development and validation study

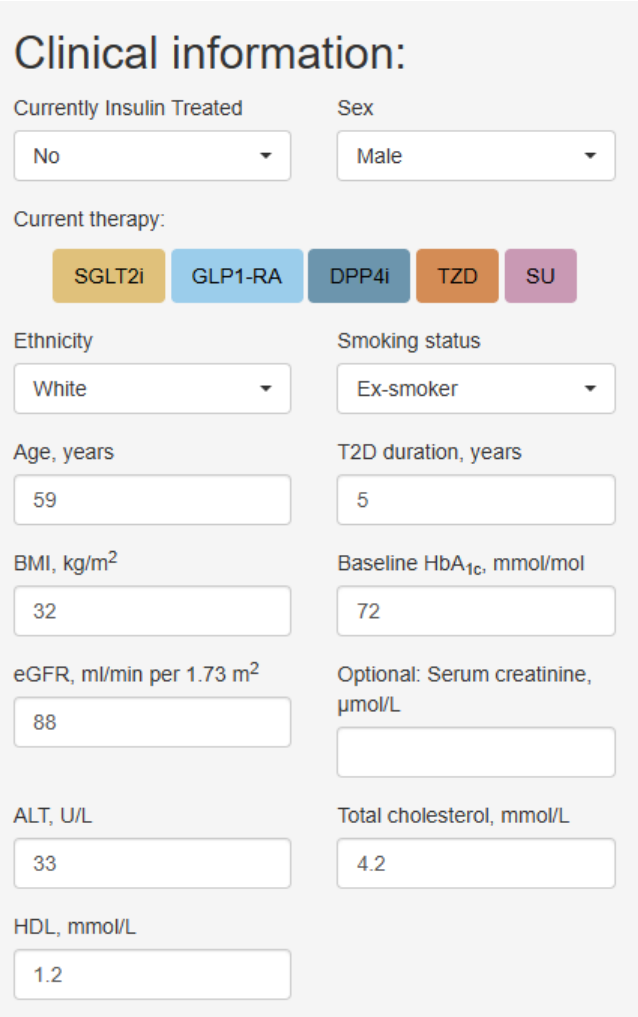
Dennis et al for Mastermind Consortium Lancet 2025; 405: 701–14

Predicting optimal drug choice for glucose lowering in type 2 diabetes

Diabetes Distilled

Development/validation prediction model across 5 treatment classes using CPRD UK data

- ✓ Model predicted optimal treatment v model discordant drug choices:
  - ✓ HbA1c >5 mmol/mol lower at 12 months
  - ✓ Less likely to need additional therapies
  - ✓ Adjusted 5 year risk glycaemic failure 38% lower
  - ✓ Similar 5 year all cause mortality
  - ✓ Adjusted MACE-HF risk 15% lower, renal progression 29% lower, microvascular complications 34% lower (HbA1c/SGLT2i use)
- ✓ Since 2018 in England >18% of drug initiations were model concordant
- ✓ Recommendations - GLP-1RAs 33.4%, 28.9% SGLT2is, 27.6% SUs,10% TZDs, <0.01% DPP4-is
- ✓ Sex influenced recommendations – GLP-1RAs recommended for 71.9% females and <10% males, with SGLT2is and SUs more likely for men



https://www.diabetesgenes.org/t2-treatment/

As with all models and guidelines, continue to use clinical judgement

Remember to request ALT if planning to use this tool. Request ALT, AST and platelets to calculate Fib-4

Diolch!

diabetesdistilled
the latest developments filtered for you

Diabetes Distilled

Diabetes distilled is an e-newsletter from the Primary Care Diabetes and Obesity Society designed to share the latest developments in diabetes and obesity for primary care teams. We summarise the latest papers that matter.

Sign up to receive the Diabetes Distilled newsletter at the link below

Diabetes Distilled: Heart and SOUL – oral semaglutide demonstrates cardiovascular benefit in high-risk people with type 2 diabetes

Results of SOUL trial suggest oral semaglutide offers similar cardiovascular benefits to the... injectable formulation.

22 Apr 2025

Diabetes Distilled: Time to intensify blood pressure treatment in people with type 2 diabetes?

BPROAD study: Reducing systolic blood pressure to <120 mmHg versus <140 mmHg in... people with type 2 diabetes

3 Apr 2025

Diabetes Distilled: Preserving muscle is important when using incretin mimetics for weight loss

How to minimise loss of muscle mass when using GLP-1-based therapies for weight loss.

26 Mar 2025

Diabetes Distilled: Finerenone reduces new diabetes and improves heart failure outcomes in the FINEARTS-HF trial

Some of the known excess risk of type 2 diabetes in people with heart failure attenuated,... and outcomes improved.

3 Mar 2025

Diabetes Distilled: Reframing the definition and diagnosis of clinical obesity

Consensus report advises definitions of clinical and pre-clinical obesity, according to... the presence of obesity-related

3 Mar 2025

Diabetes Distilled: The 4S Pathway – realigning management for older people with diabetes

Practical guidance from the International Geriatric Diabetes Society on the management o... diabetes in older people.

3 Mar 2025