Diabetes Distilled

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I have received funding from the following companies for education, writing, speaking and attending advisory boards and conferences:

Abbott, Boehringer Ingelheim, Astra Zeneca, Eli Lilly, Janssen, MSD, Napp and Novo Nordisk, OmniaMed, RCGP and Sherborne Gibbs

Complex needs, Clear priorities:

MASLD (NAFLD)

Early onset T2DM (EOT2D)

What's new in drugs

Diabetes on the net.

News Journals

Diabetes & Primary Care

The journal for healthcare professionals with an interest in primary care diabetes

RESOURCES

- Interactive case studies
- At-a-glance factsheets
- How to series
- Need to know series
- Prescribing pearls
- Diabetes Distilled

Diabetes Distilled

Diabetes Distilled: Cardiovascular disease risk in type 1 versus type 2 diabetes – interactions with age and sex

Risk of CVD and cardiovascular mortality differ between people with type 1 and type 2 diabetes... and between men and women.

2 Oct 2025

Diabetes Distilled: New oral GLP-1 RA, orforglipron, achieves up to 11.2% mean weight loss

Daily oral GLP-1 receptor agonist in development results in significant weight loss but... with no dosing restrictions.

24 Sep 2025

Diabetes Distilled: Weight loss – is it quantity or quality that matters?

Consider outcomes beyond the degree of weight loss to prioritise when discussing... weight management options.

10 Sep 2025

Diabetes Distilled: Tirzepatide treatment associated with increased proliferative retinopathy but possible reduced new retinopathy

It is crucial that we review retinal screening reports prior to prescribing GLP-1 or GIP/GLP-1... receptor agonists.

10 Sep 2025

Diabetes Distilled: Increased heart failure risk in older people with pregabalin versus gabapentin

Increased risk of new-onset heart failure in over-65s suggests caution is required... before prescribing pregabalin

10 Sep 2025

Diabetes Distilled: Potatoes and new type 2 diabetes risk

Higher intake of French fries, but not baked, boiled or mashed potatoes, associated with... increased risk of developing

10 Sep 2025

2 new papers summarised monthly – 30 second read; more in depth read including primary care implications

Meet Amy

Stock free access photograph
Name changed; composite of cases

Age 42, 2 children
BMI 40
Gestational diabetes and then T2DM
Presented 3 years ago with vague R upper quadrant pain
Liver palpable and irregular
CT scan showed cirrhosis
Prior ultrasound scan for gallstones showed fatty liver 10 years earlier

Fully investigated – no cause found apart from MASH/severe fibrosis related to obesity
T2DM believed to have hastened progression

People are dying from CVD and cirrhosis because they do not know they have high risk MASLD/fibrosis

Stock free access photograph
Name changed; composite of cases

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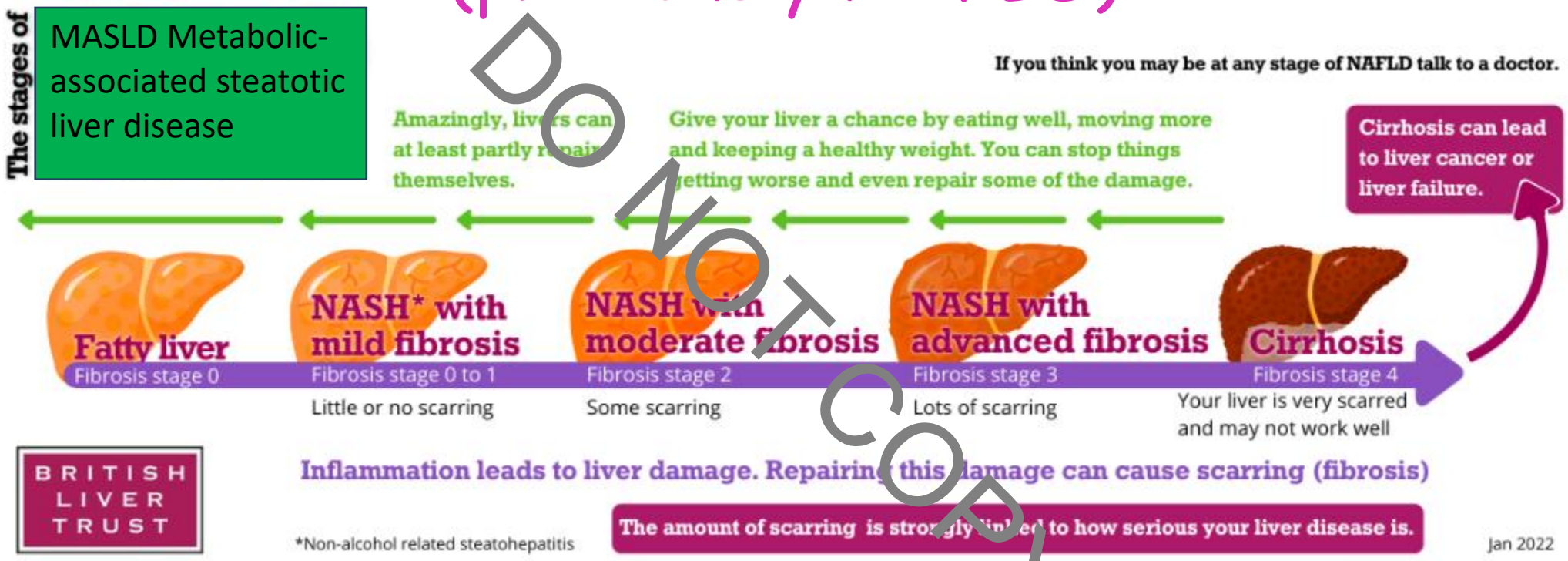
Let me share with you a simple way we can change this

MASLD Metabolic-associated steatotic liver disease (previously NAFLD)



MASLD to MASH
7-35% per year

MASH to CIRRHOSIS
1-10% per year

MASLD – increased fat; MASH – inflammation and fibrosis

MASLD what we need to know and do

MASLD is a multisystem disease

Increased risk new onset clinical conditions with MASLD

- ✓ T2DM if not present at diagnosis x 2.2
- ✓ Fatal/non-fatal CVD event x 1.5
- ✓ Atrial fibrillation x 1.2
- ✓ CKD 3 or more x 1.5
- ✓ Extrahepatic cancers x 1.5

(oesophagus, stomach, pancreas, colorectal, thyroid, lung, breast, prostate, haematological)

- ✓ Cirrhosis or Hepatocellular Carcinoma x 2-10

The time is right to tackle MASLD

- ✓ MASLD, MASH and cirrhosis increasing
- ✓ Commonest cause of liver transplant
- ✓ Drugs soon to gain licences

Metabolic Dysfunction–Associated Steatotic Liver Disease

G. Targher, L. Valenti, and C.D. Byrne | N Engl J Med 2025;393:683-698

An effortless way to identify more high risk MASLD and reduce cirrhosis, CVD and mortality

People with T2DM

- ✓ meet the metabolic MASLD criteria
- ✓ ↑ risk of high risk MASLD and progression

- ✓ Add AST, ALT and platelets to annual diabetes blood tests; calculate Fib-4
- ✓ Identify those with Fib-4 ≥ 1.3, provide urgent weight loss guidance and investigate
  - ✓ ELF blood test; refer if ≥10.51 OR
  - ✓ Refer for fibroscan/elastography
  - ✓ Keep note of referrals/monitor results and Mx
- ✓ Fib-4 <1.3, weight loss, repeat in 1-3 years
- ✓ Continue to check Fib-4:
  - ✓ Abnormal LFTs - if wait until abnormal will miss many with fibrosis
  - ✓ Excess liver fat on imaging

Fib-4 score is an easy to calculate risk marker

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

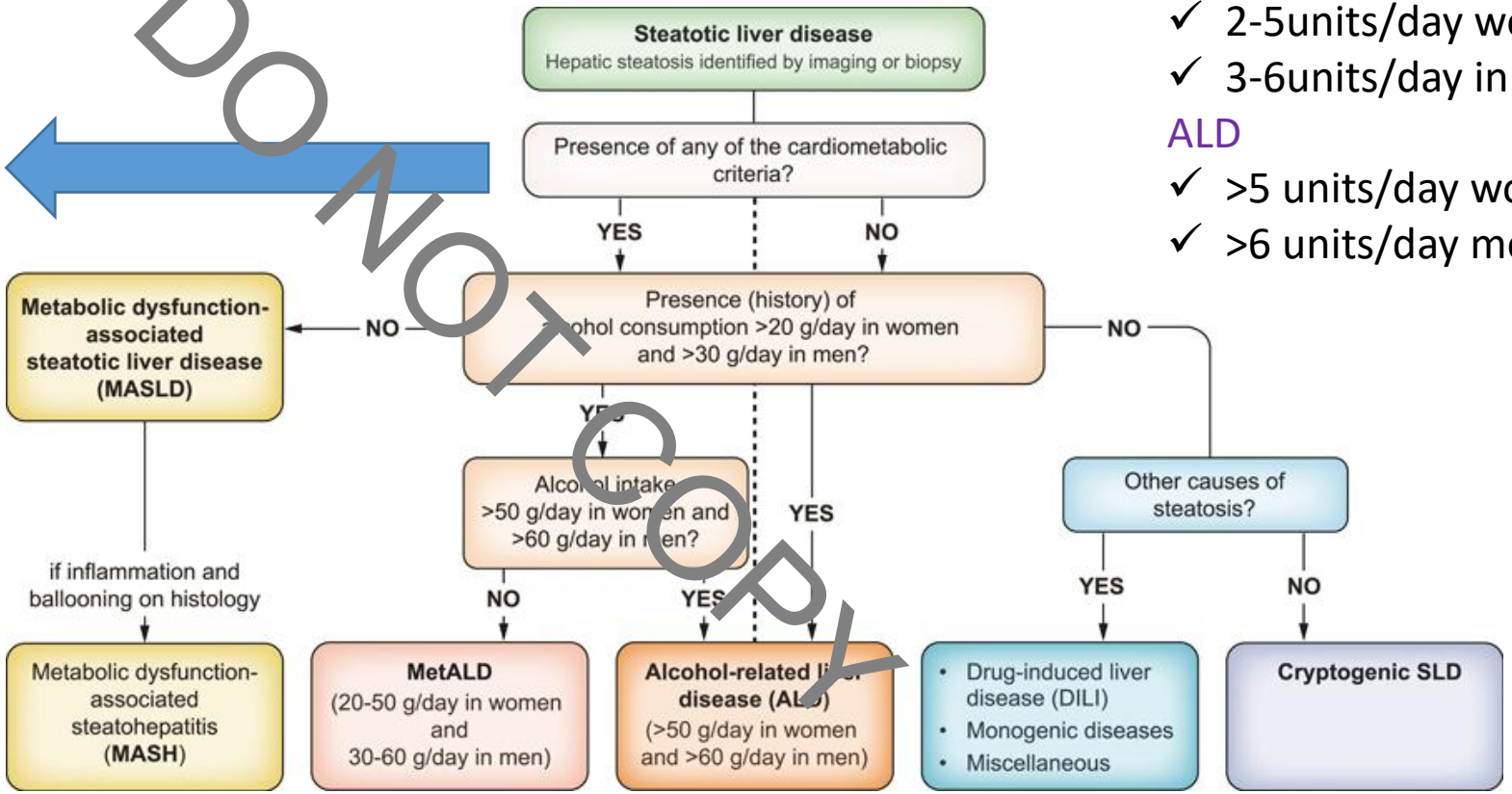
Obes Facts. 2024;17(4):374-444. doi:10.1159/000539371

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

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

- ✓ 2-5units/day women
- ✓ 3-6units/day in men

ALD

- ✓ >5 units/day women
- ✓ >6 units/day men

- ✓ 99% concordance between NAFLD and MASLD

Fib-4 score is the key risk marker

Simple MASLD management

Practical Lifestyle Management of Nonalcoholic Fatty Liver Disease for Busy Clinicians

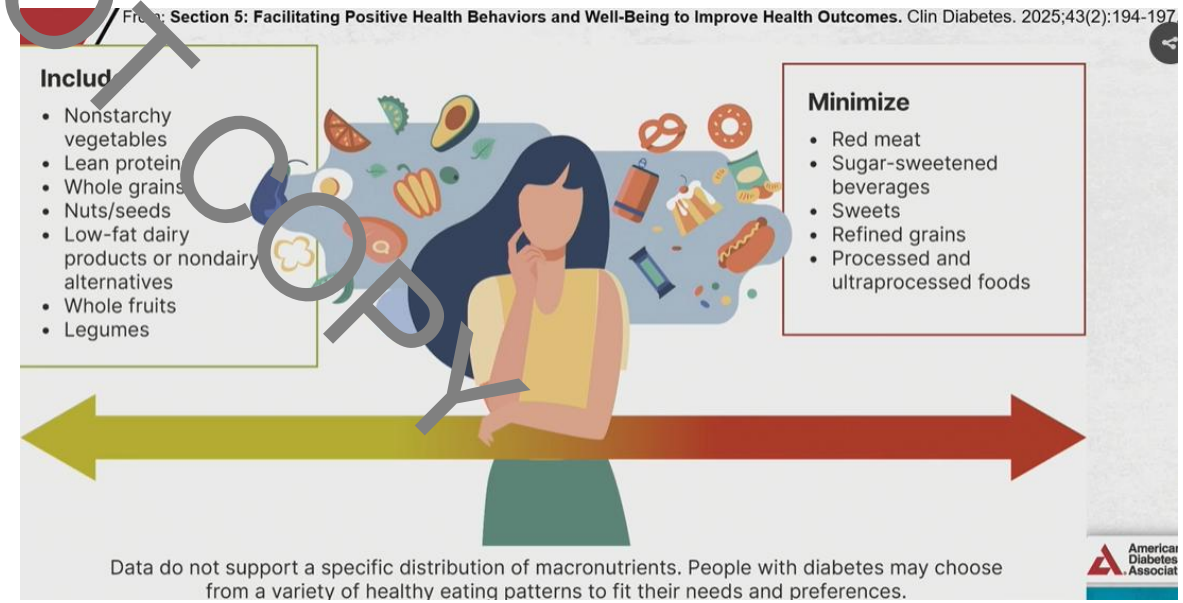
Shira Zelber-Sagi[1] and J. Bernadette Moore[2]

TABLE 1 Lifestyle Checklist for Health Care Practitioners

Liu et al 2025 Special correlation between diet and MASLD Cell & Bioscience 15, 44

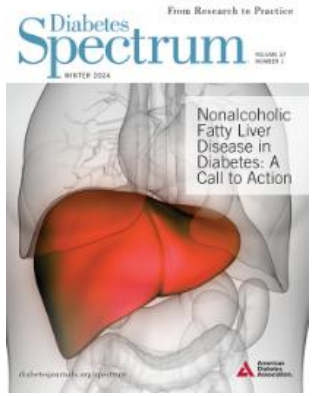
Lifestyle recommendations for MASLD

- ✓ Stop smoking
- ✓ Minimise/avoid alcohol
- ✓ Aerobic and resistance physical activity
- ✓ Weight loss 5-7% steatosis; 10% fibrosis; 3-5% if lean
  - ✓ Intermittent fasting/TRE
  - ✓ ↓ UPF/high fat/sugar/fizzy drinks
  - ✓ ↑ fruit, veg, Mediterranean diet
  - ✓ 3+ cups coffee daily
- ✓ Behavioural support to achieve and maintain weight loss



Diet and T2DM ADA Standards of Care 2025

Diabetes Spectrum February 2024, Vol.37, 39-47. doi:https://doi.org/10.2337/dsi23-0009



Pharmacological Approaches to Nonalcoholic Fatty Liver Disease: Current and Future Therapies

Idoia Genua[1] and Kenneth Cusi[2]

Diabetes Spectr 2024;37(1):48–58
https://doi.org/10.2337/dsi23-0012

Drugs not yet licensed in UK; resmetirom/Rezdiffra EMEA conditional marketing authorisation, thyroid hormone receptor (THR-β) agonist in the liver, decreases fat, inflammation, fibrosis and beneficial on lipid profile

Pioglitazone, Vitamin E, or Placebo for Nonalcoholic Steatohepatitis N Engl J Med 2010;362:1675-1685

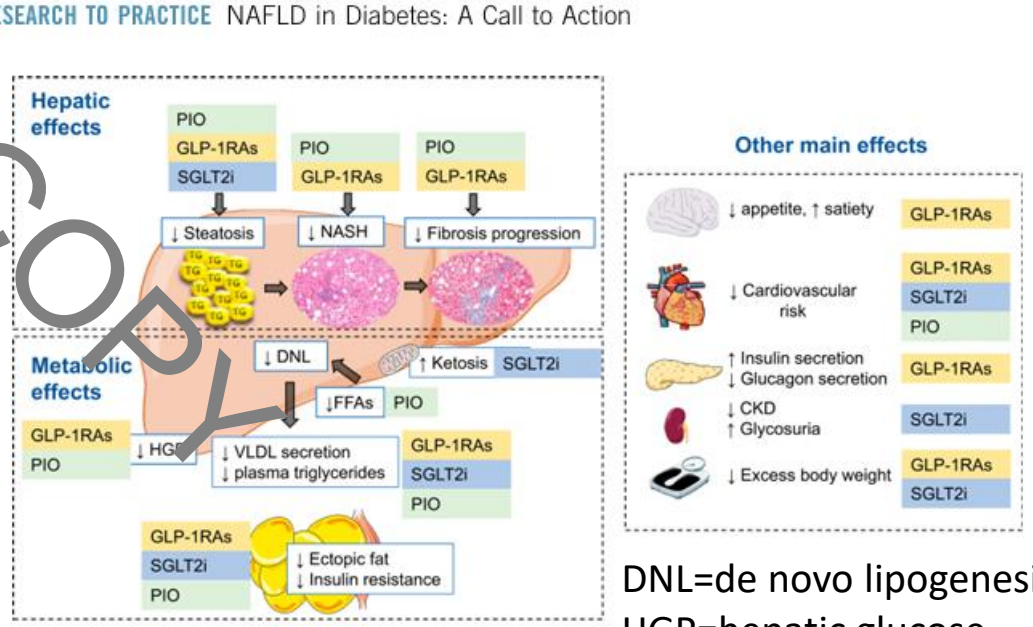
A Phase 3, Randomized, Controlled Trial of Resmetirom in NASH with Liver Fibrosis

February 8, 2024 | DOI: 10.1056/NEJMdo007386

Phase 3 Trial of Semaglutide in Metabolic Dysfunction–Associated Steatohepatitis

A.J. Sanyal and Others | N Engl J Med 2025;392:2089-2099

Tirzepatide for Metabolic Dysfunction–Associated Steatohepatitis with Liver Fibrosis Loomba et al N Engl J Med 2024;391:299-310



We can find high risk people like Amy and refer before it is too late

DNL=de novo lipogenesis
HGP=hepatic glucose production

Early onset T2DM
Age <40

Early onset T2DM – 3 key papers

Early-Onset Type 2 Diabetes 1

Early-onset type 2 diabetes: the next major diabetes transition *The Lancet*, Vol. 405, No. 10497, p2313-2326

Andrea Luk, Sarah H Wild, Sophie Jones, Ranjit Mohan Anjana, Marie-France Hivert, John McCaffrey, Edward W[illegible]egg, Shivani Misra

- ✓ Early obesity
- ✓ Rapid early weight gain
- ✓ Genetics
- ✓ Prenatal exposure - epigenetics
- ✓ Socioeconomic status
- ✓ Social determinants of health
- ✓ Ethnicity – ↑ectopic fat, diet transitions, *in-utero* undernutrition, ↓lean muscle mass, ↓ beta cell mass

Diabetes on the net.

Diabetes & Primary Care

HOW TO UNDERTAKE A MULTIPLE LONG-TERM CONDITIONS REVIEW

Early-Onset Type 2 Diabetes 2

Understanding the drivers and consequences of early-onset type 2 diabetes *The Lancet*, Vol. 405, No. 10497, p2327-2340

Lee-Ling Lim, Sophie Jones, Justin Cirhuza Cikomola, Marie-France Hivert, Shivani Misra

Typical complications:

- ✓ CVD, CKD, microvascular complications
- ✓ Additional metabolic long-term conditions:
  - ✓ Obesity, hypertension and dyslipidemia
- ✓ Other associated long-term conditions:
  - ✓ Asthma, physical disability, learning disability, OA/chronic pain, depression, anxiety, severe mental illness, chronic liver disease

- ✓ Multiple LTCs
- ✓ Increased hospitalisation and mortality
- ✓ Increased microvascular complications at diagnosis
- ✓ Faster progression microvascular complications
- ✓ Broader range of complications (cancer, MASLD, mental health, pregnancy-related)

Early-Onset Type 2 Diabetes 3

Managing early-onset type 2 diabetes in the individual and at the population level

Shivani Misra, Kamlesh Khunti, Alpesh Goyal, David Gable, Benedetta Armocida, Nikhil Tandon, Pooja Sachdev, Sarah H Wild, Marie-France Hivert, David Beran

Lancet 2025; 405: 2341–54

Tasks – Our role

- Prevention high risk groups (eg previous gestational diabetes)
- Confirm T2DM not other types
- Aggressive CVD risk reduction, tight glycaemic control
- Weight management
- Psychosocial care
- Early and aggressive complication management
- Good communication
- Overcome clinical inertia

Reproductive healthcare summary

- ✓ Not planning pregnancy
  - ✓ contraception
  - ✓ education about preconception care
- ✓ Pre-conception care
  - ✓ Optimise HbA1c 6.5% (48mmol/mol)
  - ✓ Stop potential teratogens
  - ✓ Folate 5mg
  - ✓ Lifestyle advice, smoking cessation
- ✓ Postpartum
  - ✓ Breastfeeding support
  - ✓ Restart medications when appropriate
  - ✓ Screen for PP depression
  - ✓ Encourage contraception
  - ✓ Interpregnancy weight loss

Assertive, person-centred, holistic, individualised care

Behaviour change and intensifying drug therapy

Diabetes on the net.

Diabetes & Primary Care

2024 webinar on demand

Interactive case studies

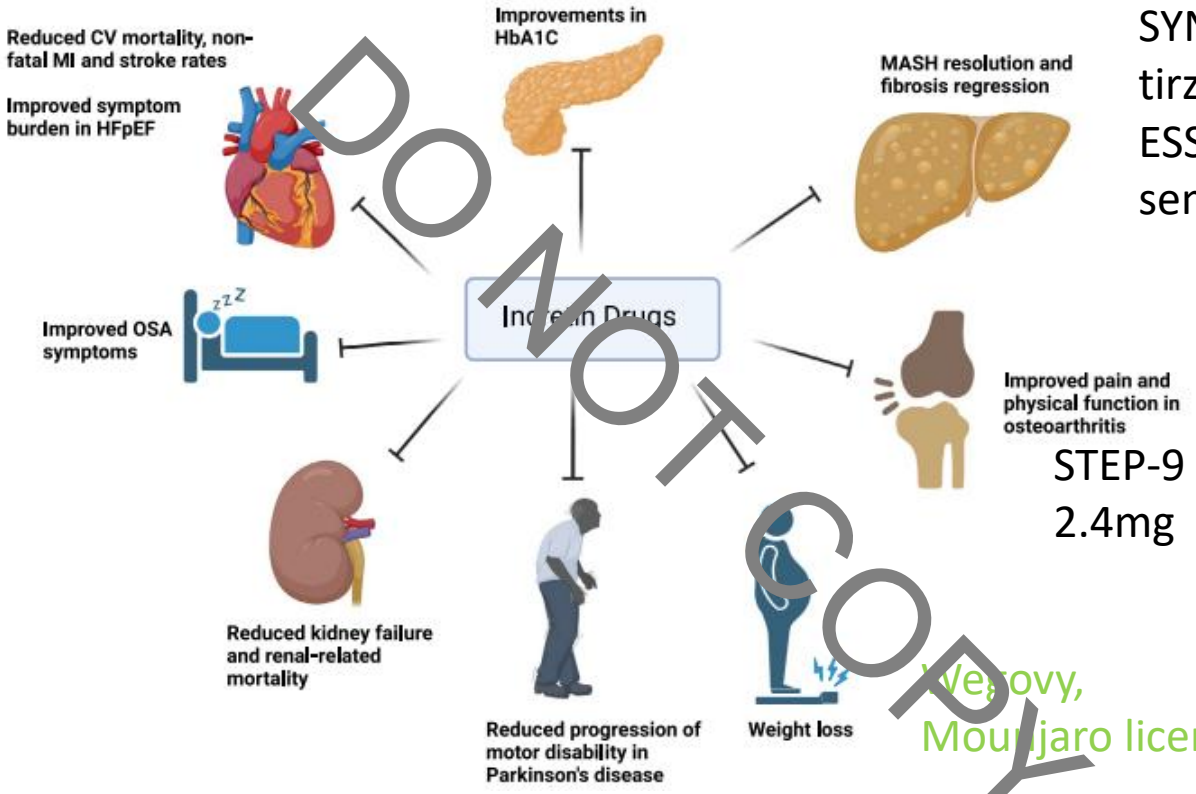
HOW TO CONDUCT AN EXTENDED REVIEW FOR PEOPLE WITH EARLY-ONSET TYPE 2 DIABETES

What’s new in drugs

Expanding evidence base for incretin-based drugs

All incretins licensed for inadequately controlled T2DM

STEP HFpEF
SUSTAIN-7 with semaglutide



SYNERGY-NASH tirzepatide; ESSENCE semaglutide

↓ obesity related cancers

↓ Alcohol intake/food noise

Improved mental health

STEP-9 semaglutide 2.4mg

FLOW study semaglutide

Peripheral arterial disease
STRIDE semaglutide 2.4mg

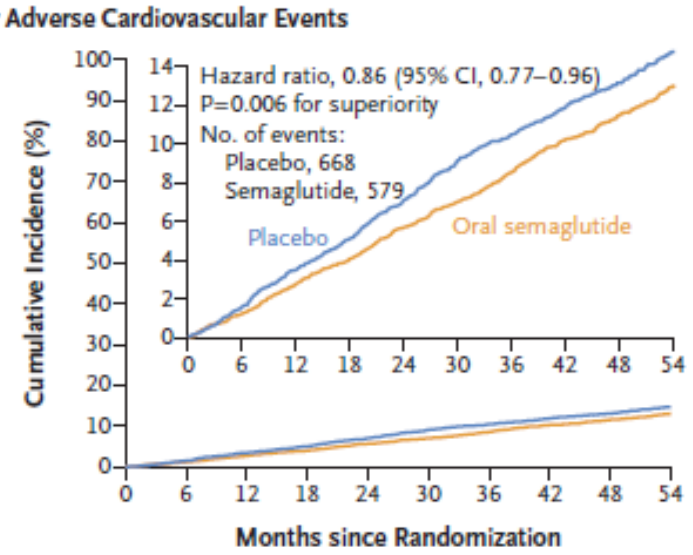
Wegovy, Mounjaro licensed

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

Useful to know all the areas where evidence is developing

Oral semaglutide and CVD

Oral Semaglutide and Cardiovascular Outcomes in High-Risk Type 2 Diabetes N Engl J Med 2025;392:2001-2012



- ✓ N=9650
- ✓ CVD, CKD or both
- ✓ Median follow up 48 months
- ✓ 14% reduction MACE in those treated with semaglutide
- ✓ No CKD benefit unlike in FLOW

New formulation of Rybelsus to improve absorption (2026); same dosing guidance 1.5mg, 4mg and 9mg

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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

SOUL not yet on SPC

Tirzepatide and CVD
SURPASS CVOT

Early data

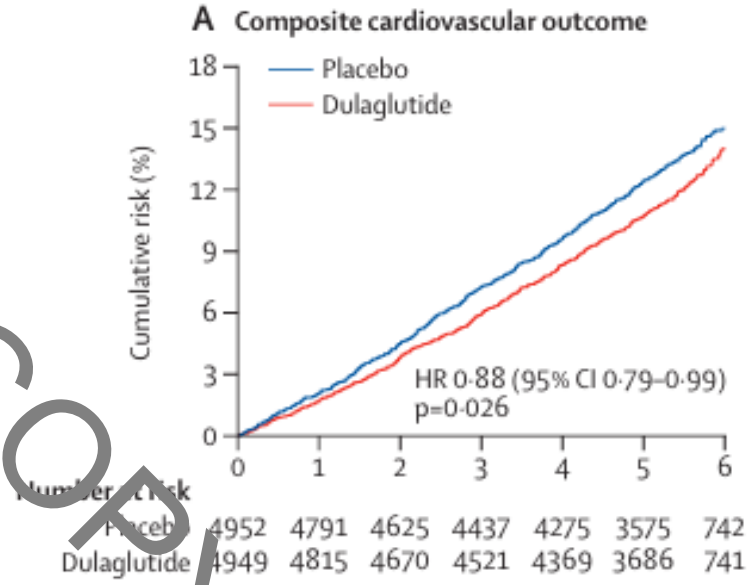
- ✓ Active comparator CVOT aiming to demonstrate non-inferiority tirzepatide up to 15mg v dulaglutide 1.5mg (REWIND study dose)
- ✓ N=13,165 median follow up 4 years
- ✓ Primary outcome non-inferiority 3-point MACE (CV death, non fatal MI or stroke) v REWIND
- ✓ Non-inferiority to dulaglutide 1.5mg confirmed
- ✓ Tirzepatide significantly greater reduction in HbA1c and weight at 36 months v dulaglutide

- ✓ Ongoing evaluation regarding cardiac deaths, revascularisation and other data

Unpublished data presented at EASD

Dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND): a double-blind, randomised placebo-controlled trial

Gerstein et al Lancet 2019; 394: 121-30



- ✓ 9901 people, 31.5% CVD; age 50+
- ✓ 12% reduction MACE over 5.4 years v placebo

American Diabetes Association 2025

Diabetes Distilled

Conference over coffee: New obesity standards of care and pharmacotherapies in development

Highlights from the 85th Scientific Sessions of the American Diabetes… Association, held in Chicago

10 Sep 2025

Diabetes & Primary Care

Weight loss: Is it quantity or quality that matters?

REDEFINE studies – Cagrilintide and semaglutide - CagriSema
BELIEVE study – Bimagrumab and muscle loss with incretins
MariTide – maridebart cafraglutide monthly

CATALYST trial – hypercortisolism in T2DM

New oral GLP-1 RA, orforglipron, achieves up to 11.2% mean weight loss

Obesity Association
A division of the **American Diabetes Association®**

STANDARDS OF CARE

Setting the Standards of Care in Overweight and Obesity

Building upon ADA's process and expertise in developing trusted, evidence-based guidelines, the *Standards of Care in Overweight and Obesity* offer comprehensive standards to reduce weight stigma and improve care for people living with overweight and obesity.

Open access Review

BMJ Open Diabetes Research & Care

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

Raveendhara R Bannuru, Professional Practice Committee

Weight stigma and bias: New standards of care from the ADA

https://diabetesonthenet.com/wp-content/uploads/107.-Conf-coffee_ADA-2025.pdf

Knowledge, if combined with action, really can change lives

Thank you