

Beyond the numbers:  
Addressing what matters most  
to the person with diabetes

Hilton Templepatrick, Belfast | 19 September 2024

14<sup>th</sup> NORTHERN IRELAND  
CONFERENCE  
OF THE PCDS  
Primary Care  
Diabetes Society



diabetes**distilled**  
the latest developments filtered for you

## Pam Brown

GP with an interest in diabetes, obesity and lifestyle medicine  
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I have received funding from the following companies for  
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Abbott, Boehringer Ingelheim, Astra Zeneca, Eli Lilly,  
Janssen, MSD, Napp and Novo Nordisk  
OmniaMed, RCGP and Sherborne Gibbs



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Staying up to date



**Diabetes-busting 'soup-and-shake' diet works, claim experts... but just one in ten are able to stick to brutal 800 calorie a day plan**

**The Telegraph**

**HEALTH**

Doctors told me I was heading for diabetes – here's what I did

**I wore a glucose tracker for two weeks – it's bad news for my favourite breakfast**

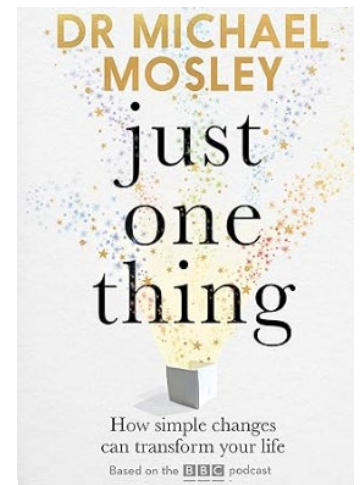
**Move over, Ozempic! New 'anti-diet' crafted by top expert Professor Tim Spector helps slimmers lose more than two inches off their waist**

• Participants who stuck to the strategy saw their weight fall by 4.7 per cent

**Making six simple lifestyle tweaks can cut your dementia risk, say experts - as diagnoses hit record high of almost 500,000**

**Kidney disease: How to protect yourself and the symptoms the NHS may not spot**

Pay tribute to Michael Mosley by looking after ourselves better and sharing his evidence-based advice



**Scientists discover new 'supercharged' probiotic said to burn fat faster than Ozempic... and it's half the price**

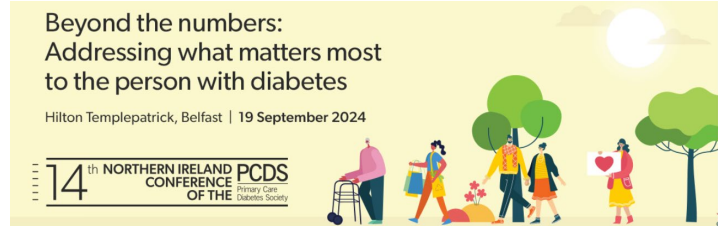
**EXPRESS**



Doctor says start taking 2p pill from today to stop getting dementia in the future

Excessive light pollution may increase risk of Alzheimer's, one study warns

# Useful reading and updates



## PRACTICAL PRESCRIBING

### Insulin for people with type 2 diabetes mellitus

Natalie Vanderpant,<sup>1</sup> Emily Ward,<sup>2</sup> Edward Farrell,<sup>3</sup> Aikaterini Theodoraki<sup>4</sup>

Cite this as: *BMJ* 2024;386:e078015

<http://dx.doi.org/10.1136/bmj-2023-078015>

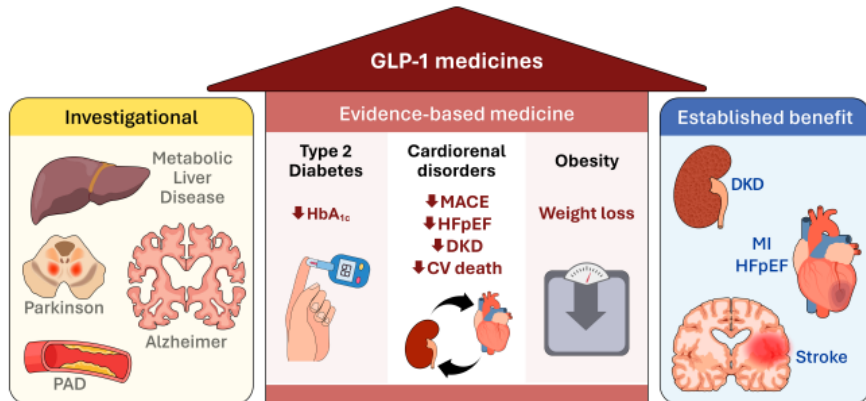
Published: 17 July 2024

### Efficacy and Safety of GLP-1 Medicines for Type 2 Diabetes and Obesity

Daniel J. Drucker

*Diabetes care* 2024 open access

<https://doi.org/10.2337/dci24-0003>



### New advances in type 1 diabetes

Savitha Subramanian, Farah Khan, Irl B Hirsch

Cite this as: *BMJ* 2024;384:e075681

<http://dx.doi.org/10.1136/bmj-2023-075681>

#### STATE OF THE ART REVIEW

- ✓ Diagnosis
- ✓ CGM interpretation
- ✓ Closed loop systems

Table 4 | Pharmacokinetics of commonly used insulin preparations

	Half life*	Effective peak	Duration of action <sup>†</sup>	Notes
<b>Basal insulin type</b>				
NPH	~4 h	2-8 h	14-24 h	-
Insulin glargine U-100	12 h	No pronounced peak	20-24 h	-
Insulin glargine U-300	19 h	No pronounced peak	30-34 h	Higher doses by 10-20% compared with U-100 glargine will be needed
Detemir	5-7 h	3-9 h	8-24 h	-
Degludec	25 h	No pronounced peak	42 h	-
<b>Prandial insulin type</b>				
Human regular	30 min	2-4 h	5-8 h	Times vary depending on site of injection
Insulin lispro and aspart	15-30 min	1-3 h	4-7 h	-
Fast acting aspart	16-20 min	1-1.5 h	4-5 h	-
Lispro-aabc	15-17 min	1-1.5 h	4-5 h	More infusion site skin reactions than lispro
Inhaled insulin	12 min	0.5-0.9 h	1.5-3 h	Often requires postprandial dosing

NPH=neutral protamine Hagedorn.  
 \*In general, four half lives are needed to reach steady state.  
 †In general, the larger the dose, the longer the duration of action.

Early morning walk. Exercise less but more often.



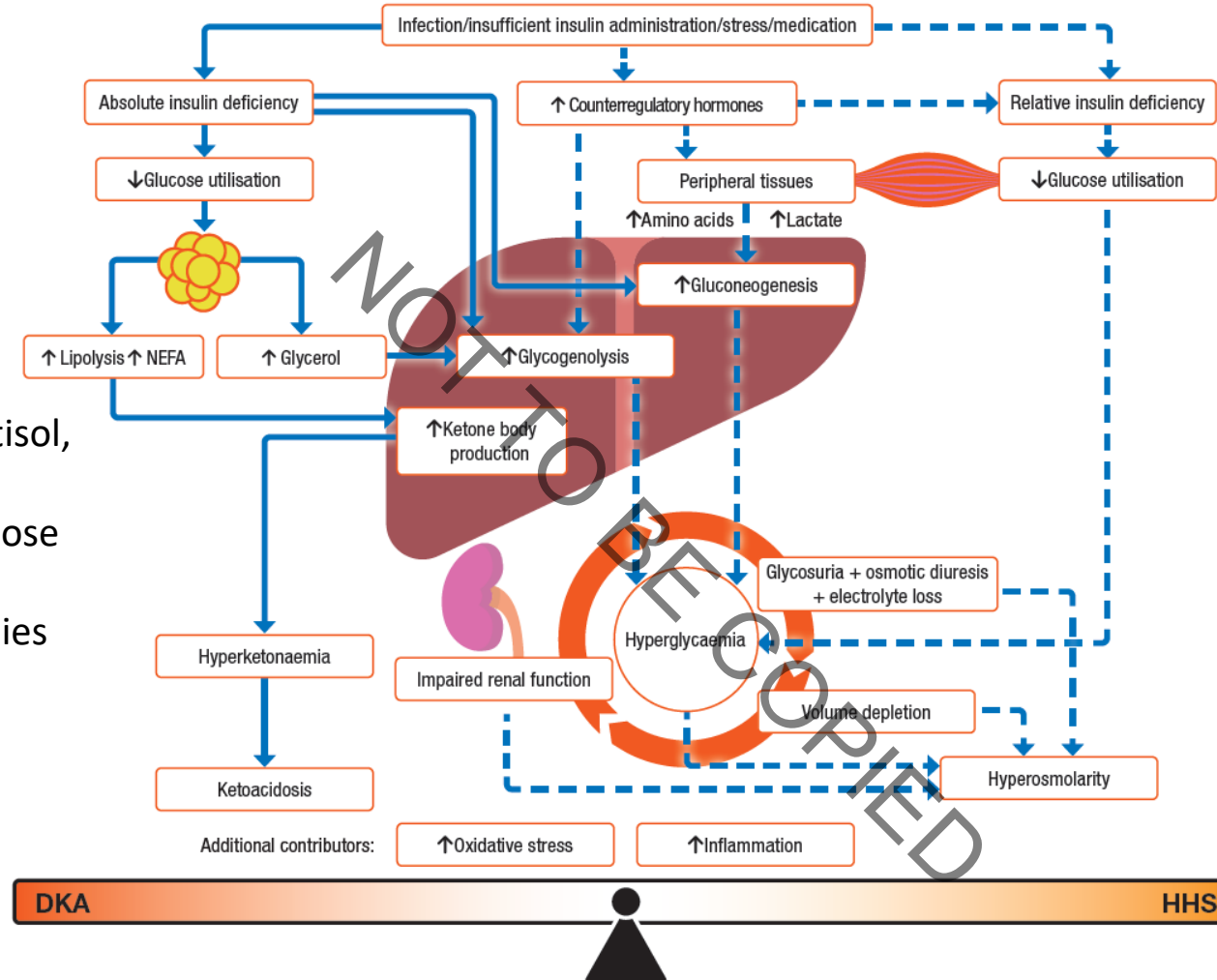
# Hyperglycemic Crises in Adults With Diabetes: A Consensus Report

Diabetes Care 2024;47:1257–1275 | <https://doi.org/10.2337/dci24-0032>

## Pathogenesis of DKA and HHS

### DKA

- ✓ Severe insulin deficiency
- ✓ ↑ counterregulatory hormones (glucagon, cortisol, epinephrine)
- ✓ Free fatty acids from adipose tissue, liver fatty acid oxidation and ketone bodies formed
- ✓ Ketoacidosis develops



### HHS

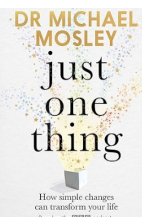
- ✓ Enough insulin to prevent ketonaemia but not hyperglycaemia
- ✓ Hyperglycaemia causes osmotic diuresis, volume depletion
- ✓ If inadequate fluid intake, hyperosmolar state, renal impairment and decline cognitive function

**Early diagnosis and urgent admission for management - insulin and hydration**

Umpierrez et al (2024) Diabetologia DOI 10.1007/s00125-024-06183-8

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Drink water – weight loss, cognitive function





# Hyperglycaemic crises in adults with diabetes: A consensus report

DKA	HHS
Develops over hours to days	Develops over days to a week
Usually alert	Change in cognitive state common
Polyuria, polydipsia, weight loss and dehydration	
Nausea, vomiting and abdominal pain	Often co-presenting with other acute illness
Kussmaul respiration	
1/3 of hyperglycaemic emergencies have a hybrid DKA/HHS presentation	

## Triggers – DKA

- ✓ New T1DM; infections, insufficient insulin, psychological stress, SGLT2is, **checkpoint inhibitors** nivolumab (Opdivo) pembrolizumab (Keytruda), ipilimumab (Yervoy)

## Triggers – HHS

- ✓ Volume depletion, dehydration, infections, CVD events, surgery, pancreatitis

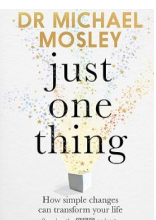
## Both

- ✓ Steroid, antipsychotics
- ✓ Educate team members about the small DKA risk with SGLT2 inhibitors (0.6-4.9/1000 pt-yrs); test blood ketones
- ✓ Share sick day rules at every consultation
- ✓ Ask about ketogenic diet
- ✓ Pause SGLT2is prior to elective surgery guided by local policy

Umpierrez et al (2024) Diabetologia DOI 10.1007/s00125-024-06183-8

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Stand on one leg – improve balance



What's new in remission?

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## Early findings from the NHS Type 2 Diabetes Path to Remission Programme: a prospective evaluation of real-world implementation

Valabhji et al

Lancet Diabetes Endocrinol  
2024; 12: 653-63

Early data from September 2020-December 2022  
12-20 weeks total diet replacement; 20 support sessions over 12 months

- ✓ 7540 referred
  - ✓ 68% attended initial assessment
  - ✓ 58% started the total diet replacement (TDR)
- ✓ 1710 able to complete 12 months' programme by December 2022
  - ✓ Completers 55%; mean weight loss 10.3kg
- ✓ 2 HbA1c measurements and remission
  - ✓ 190/710 (27%) including non-completers mean wt loss 14.8kg
  - ✓ 145/450 (32%) completers achieved remission; mean wt loss 15.9kg
  - ✓ 60 had 2 readings <48mmol/mol but were on metformin

## Type 2 diabetes remission trajectories and variation in risk of diabetes complications: A population-based cohort study

Hajira Dambha-Miller<sup>1</sup>, Hilda O. Hounkpatin<sup>1\*</sup>, Beth Stuart<sup>1\*</sup>, Andrew Farmer<sup>2</sup>, Simon Griffin<sup>3,4</sup>

PLOS ONE | <https://doi.org/10.1371/journal.pone.0290791>

Cite this as: *BMJ* 2024;384:q516

<http://dx.doi.org/10.1136/bmj.q516>

### NIHR ALERTS

### Even short periods of diabetes remission are linked to lower risk of heart attack and stroke

Helen Saul,<sup>1</sup> Brendan Deeney,<sup>1</sup> Laura Swaithe,<sup>1</sup> Hilda Hounkpatin,<sup>2</sup> Hajira Dambha-Miller<sup>2</sup>

Remission by lifestyle changes, over 7 years:  
Those who achieved remission v high glucose:

- ✓ ↓ CVD
- ✓ ↓ macrovascular and microvascular complications
- ✓ Any remission ↓ mortality



# Pre-diabetes remission – a new goal

HbA1c < 42mmol/mol (US <39mmol/mol) FBG <5.5mmol/L

Previous goal T2DM prevention

Guideline goal ≥7% weight loss

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

- ✓ Pre-diabetes/intermediate hyperglycaemia associated with microvascular complications and CVD
- ✓ Secondary analysis Diabetes Prevention Programme data, 480 achieved ≥7% weight loss by 1 year; 114 of them achieved normoglycaemia at 12 months (US criteria) – ‘responders’
- ✓ At 4 years, 42/366 (11.5%) who did not achieve normoglycaemia developed T2DM v 1/114 (0.9%) ‘responders’; RR T2DM ↓ 72% within 6 years

Jumpertz von Schwartzberg et al Diabetologia 2024 67: 1714-1718

Bergman Lancet Diab Endocr 2024 12: 603-605

Drink 1-3 cups of coffee



## Efficacy and safety of once-weekly semaglutide 2.4 mg versus placebo in people with obesity and prediabetes (STEP 10): a randomised, double-blind, placebo-controlled, multicentre phase 3 trial

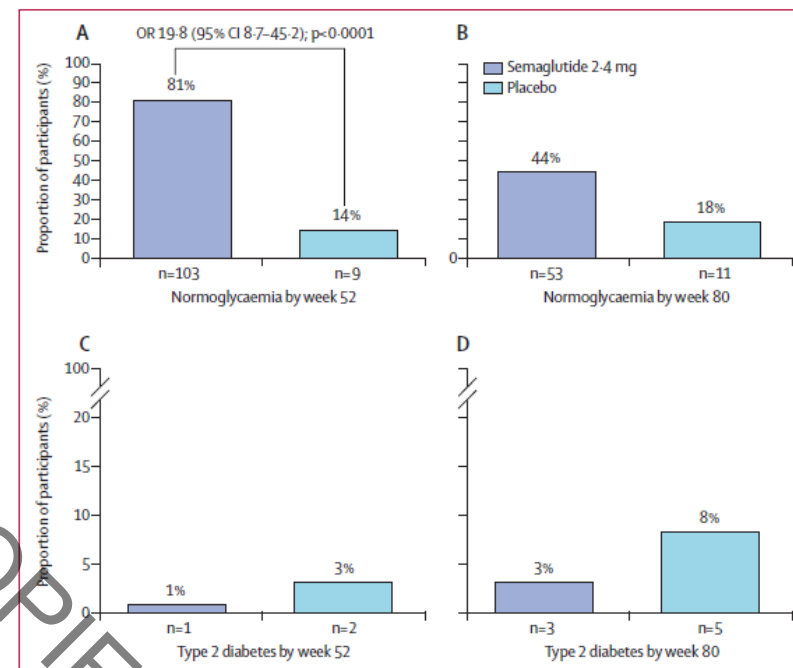


Figure 3: Proportion of participants who reverted to normoglycaemia or progressed to type 2 diabetes with semaglutide 2.4 mg versus placebo in the full analysis set during the in-trial observation period

Weight loss 13.9% v 2.7% week 52

Weight loss 7.9% v 1.3% week 80

Remission 81% week 52, 44% week 80

Treatment discontinuation 6% v 1%

McGowan et al Lancet Diabetes Endocrinol 2024 12: 631-42

What's new in drugs?

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# Glycaemic control still an important goal

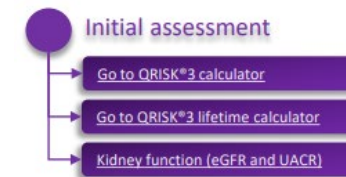
Khunti et al Diabetologia 2024

- ✓ 2 pronged approach to optimise T2DM outcomes:
  - ✓ Intensive, early control of blood glucose, ideally before complications
  - ✓ Optimal management of cardiorenal complications
- ✓ Depending on criteria, around 50% of people with T2DM don't meet criteria for SGLT2i or GLP-1RA
  - ✓ People at lower risk of complications – lower absolute risk reduction/benefit
  - ✓ Some of benefits newer drugs due to glucose lowering
- ✓ UKPDS 44 years – early 8.7mmol/mol ↓ glucose compared to controls translated to:
  - ✓ 10% ↓ diabetes-related endpoints
  - ✓ 17% ↓ MI
  - ✓ 26% ↓ microvascular complications
  - ✓ 10% ↓ mortality

UKPDS 91 Adler et al Lancet 2024; 404:145-155

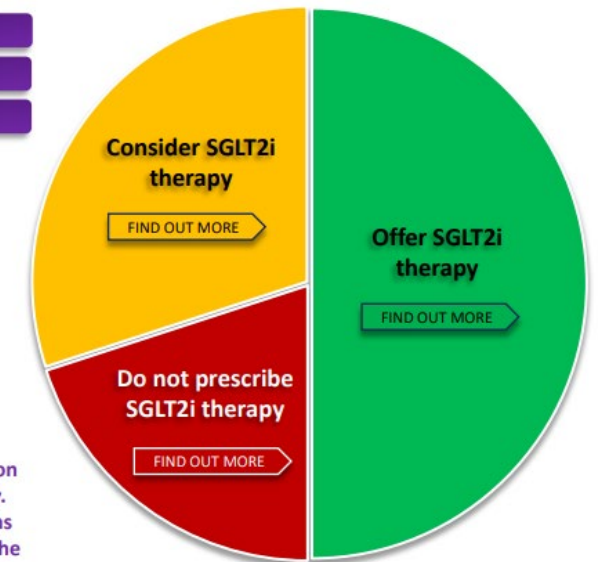
REVIEW

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



- ✓ Clinical paper
- ✓ Wall poster
- ✓ Interactive tool

IMPORTANT – this decision tool is for guidance only. The final clinical decisions are the responsibility of the prescriber.



<https://resources.gpnotebook.com/bridging-the-gap-between-type-2-diabetes-guidelines-and-prescribing-practices/>

Multifactorial risk factor management, informed self care and avoidance of clinical inertia all important

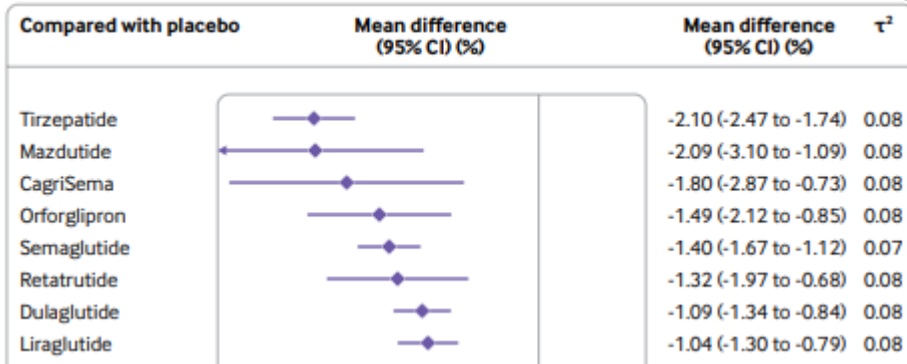
# Comparative effectiveness of GLP-1 receptor agonists on glycaemic control, body weight, and lipid profile for type 2 diabetes: systematic review and network meta-analysis

Haiqiang Yao,<sup>1,2</sup> Anqi Zhang,<sup>2</sup> Delong Li,<sup>1,2</sup> Yuqi Wu,<sup>1,2</sup> Chong-Zhi Wang,<sup>3,4</sup> Jin-Yi Wan,<sup>1,2</sup> Chun-Su Yuan<sup>3,4</sup>

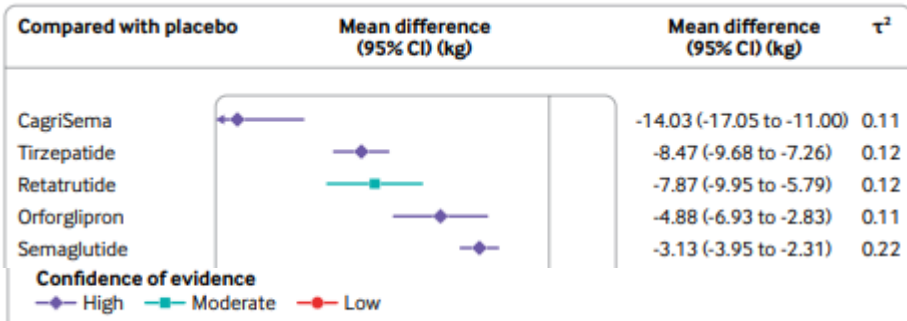
Cite this as: *BMJ* 2024;384:e076410  
<http://dx.doi.org/10.1136/bmj-2023-076410>

76 RCTs, n=39,246

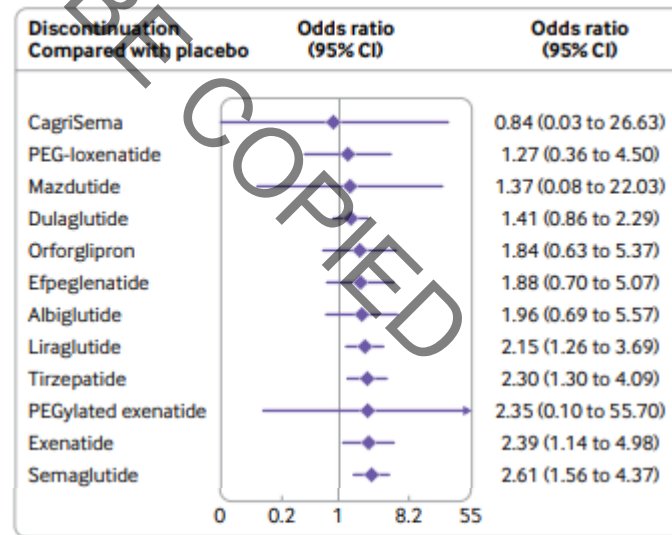
HbA1c reduction in %



Weight reduction in kg



GI adverse events – dose dependent increases



Enjoy oily fish  
 Eat beetroot  
 Eat an apple a day

Cochrane risk of bias for RCTs; Confidence in Network Meta-Analysis



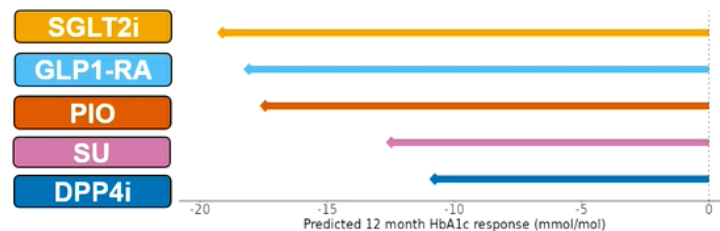
## Will seeing T2DM in HD improve treatment choice?

New 5-drug predictive model will help drug decision-making for optimal outcomes – MASTERMIND consortium - John Dennis

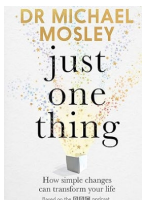
- ✓ Routine clinical features – age, sex, diabetes duration, HbA1c, BMI, eGFR, ALT, TC, HDL, Ethnicity, deprivation quintile, number previous and current therapies, smoking
- ✓ Differences reflect the underlying drug mechanisms of action
- ✓ Expected HbA1c reduction over 12 months
- ✓ Best treatment reduced and delayed intensification by 40% and delayed this by 2.7 years
- ✓ Could reduce MACE, renal progression; reduction retinopathy
- ✓ Take home message – this may encourage personalised treatment and discourage inertia

A validated & practical approach to selecting the best T2D treatment

Routine clinical feature based 5-drug treatment selection for glycaemia



<https://pm-cardoso.shinyapps.io/t2dst/>



Stand up more

What's new in CKD?

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# Top 10 Takeaways on Management for Primary Care Physicians from the KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease



## Primary Care in CKD Video Series: Insights from the KDIGO 2024 CKD Guideline

In this six-part video series, KDIGO CKD Guideline Work Group Member, Michael Shlipak, MD (United States) shares key insights for primary care physicians from the guideline. The series includes:

- Part 1: The Burden of CKD
- Part 2: Detection of CKD
- Part 3: Staging of CKD
- Part 4: Risk Assessment
- Part 5: Statins, BP Control, and RAS Inhibitors
- Part 6: SGLT2 Inhibitors

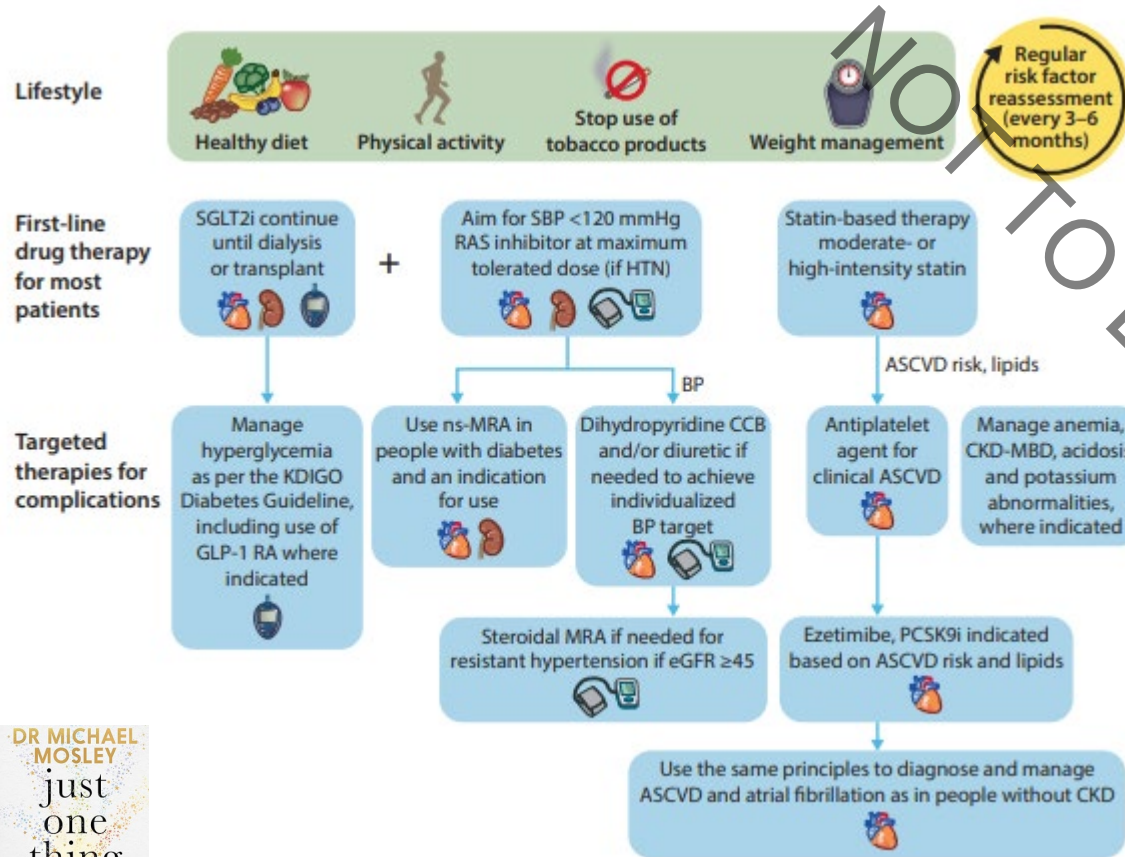
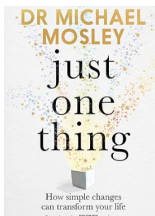
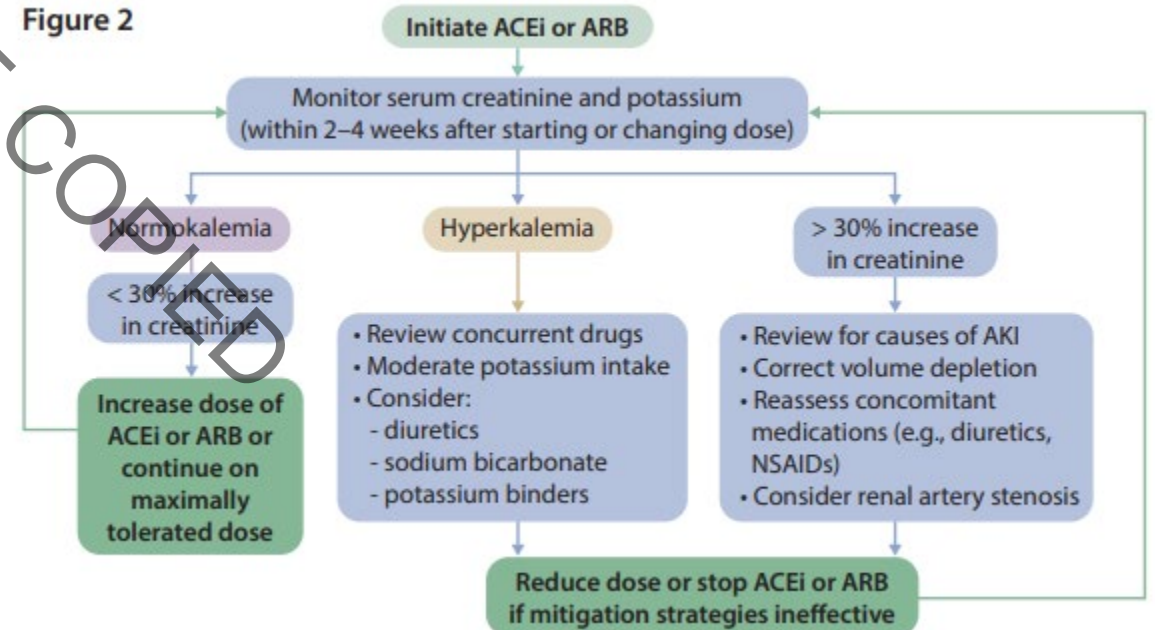


Figure 2



Soak in a hot bath. Read

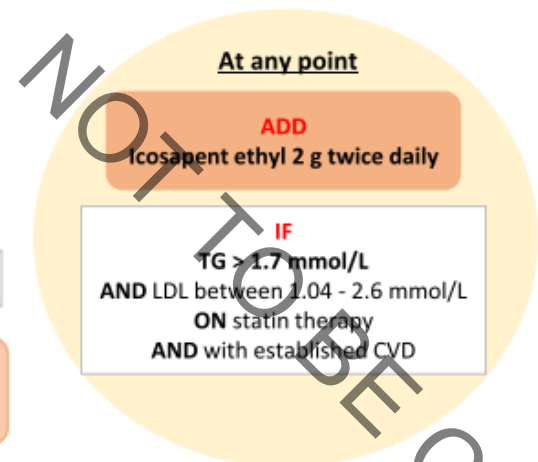
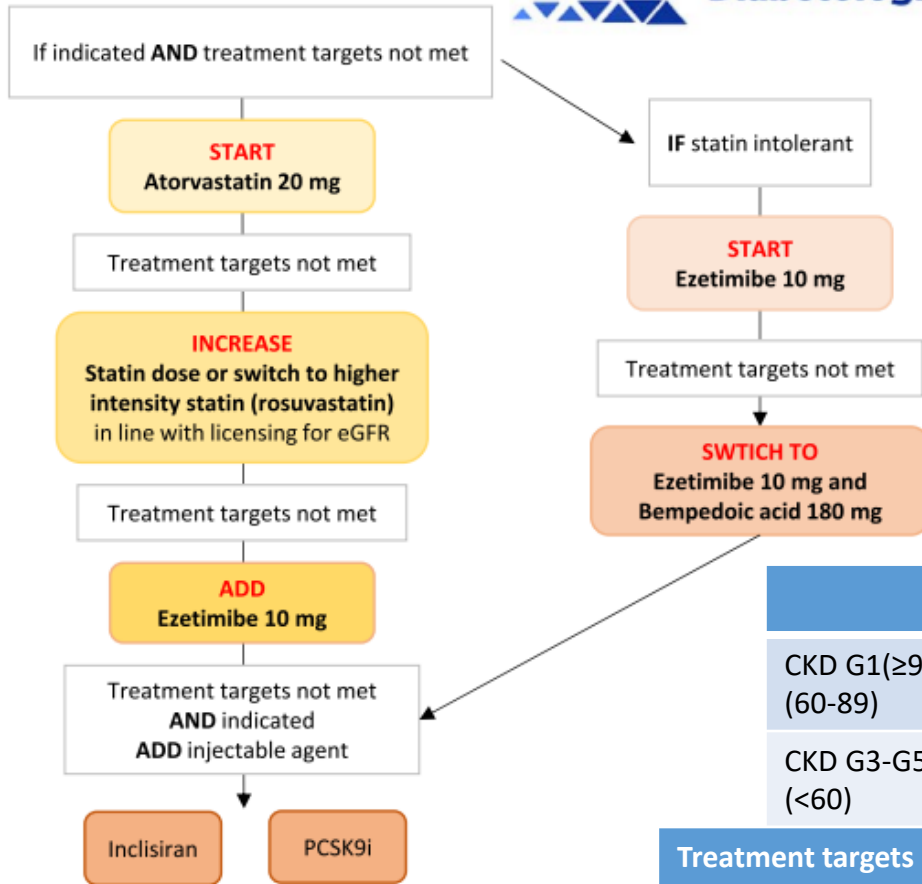
# Clinical practice guideline for the management of lipids in adults with diabetic kidney disease: 2024



Association of  
**British Clinical Diabetologists**



UK Kidney Association



Inclisiran indications	LDL cholesterol	AND co-existing
NHS England	≥ 2.6 mmol/L	established CVD
NHS Wales	≥ 4.0 mmol/L	established CVD
	≥ 3.5 mmol/L	Recurrent/ polyvascular disease
	≥ 5.0 mmol/L	heterozygous familial hypercholesterolaemia for primary prevention

PCSK9i indications	Without CVD	High risk <sup>1</sup>	Very high risk <sup>2</sup>
Primary non-familial hypercholesterolaemia or mixed dyslipidaemia		LDL ≥ 4.0 mmol/L	LDL ≥ 3.5 mmol/L
Primary heterozygous-familial hypercholesterolaemia	LDL ≥ 5.0 mmol/L	LDL ≥ 3.5 mmol/L	LDL ≥ 3.5 mmol/L

<sup>1</sup>ACS, CHD, PVD, ischaemic stroke, revascularisation

<sup>2</sup>Recurrent events in more than 1 vascular bed

	When to start treatment
CKD G1(≥90) -2 (60-89)	Persistent microalbuminuria ≥3mg/mmol) + >30 yrs OR 18-30 + >1 CVD risk factor
CKD G3-G5 (<60)	Start regardless of albuminuria

Treatment targets	Monitoring
TC ≤4.0mmol/L	Full non-fasted lipid profile and LFTs:
LDL cholesterol ≤ 1.8mmol/L	Baseline, 3 months after initiation/change, Annually
Non-HDL cholesterol ≤ 2.5mmol/L	Measure CK if myalgia

**Caution with all lipid-lowering treatments in women of child-bearing age, pregnant or lactating**

What's new in  
NAFLD/MASLD?

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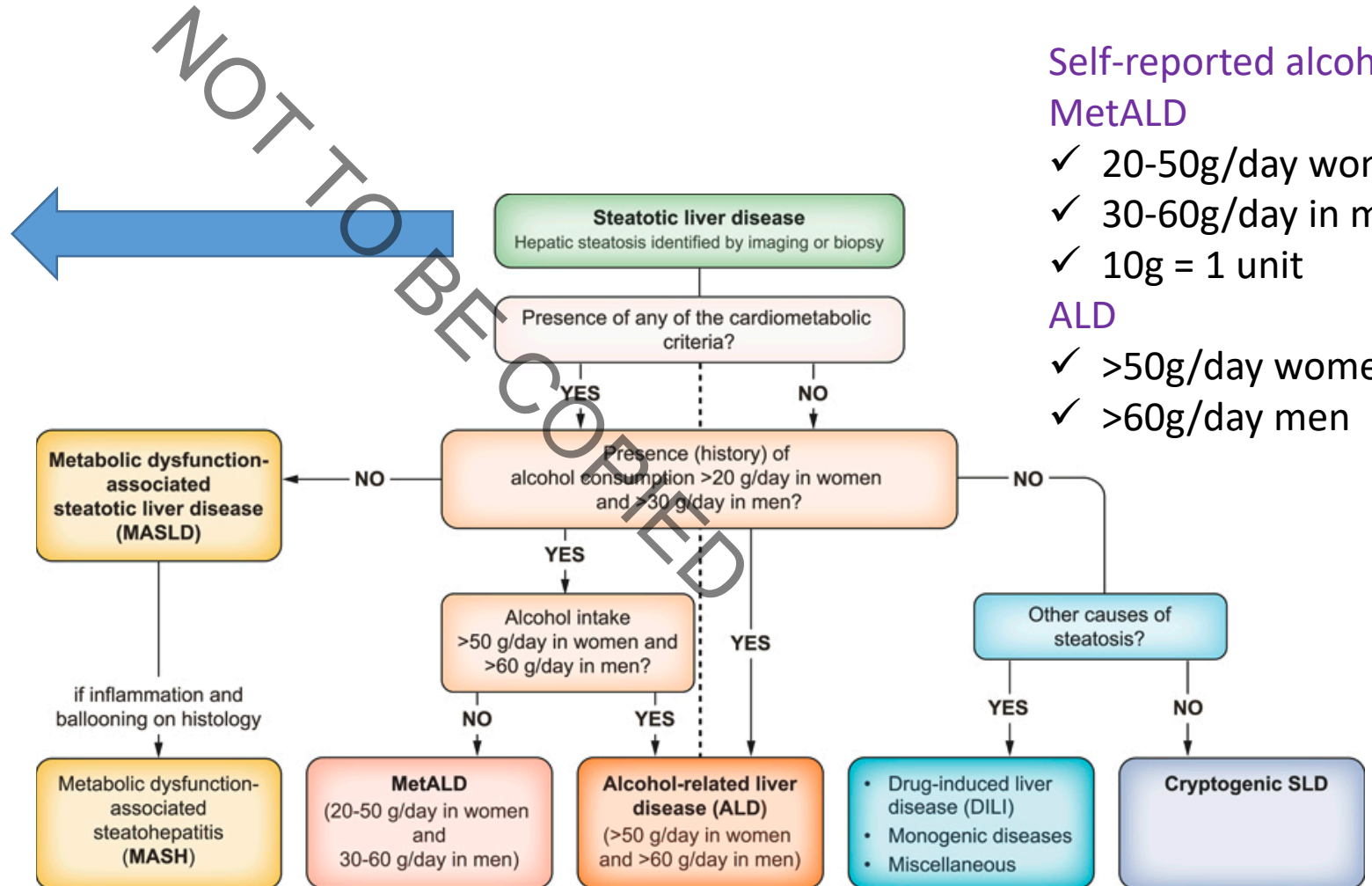
## Metabolic dysfunction-associated steatotic liver disease (MASLD) and metabolic dysfunction-associated steatohepatitis (MASH)

**Adult criteria**

At least 1 out of 5:

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

✓ 99% concordance between NAFLD and MASLD



Self-reported alcohol intake  
**MetALD**

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

**ALD**

- ✓ >50g/day women
- ✓ >60g/day men



# From NAFLD to MASLD – 2024 update

- ✓ Fib-4 is non-invasive test to identify who needs further investigations
  - ✓ Use age, ALT, AST, platelets to calculate
  - ✓ <1.3 OK; 1.3-2.67 refer fibrosis possible; >2.67 fibrosis likely
- ✓ 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

## Management:

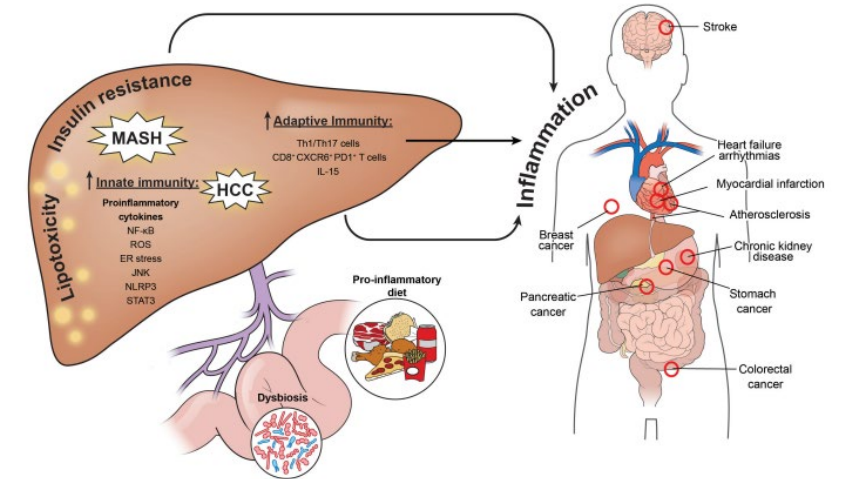
- ✓ Weight loss – 5-7% steatosis; 10% if fibrosis; 3-5% if lean
- ✓ Mediterranean diet or similar; ↓ UPF/sugar/fizzy drinks
- ✓ Aerobic and resistance physical activity
- ✓ Drug not yet licensed – TZDs, GLP-1RAs

Aostee et al Lancet Regional Health; 2024:36

MASLD: a systemic metabolic disorder with cardiovascular and malignant complications

Giovanni Targher <sup>1</sup>, Christopher D Byrne <sup>2</sup>, Herbert Tilg <sup>3</sup>

Gut 2024; 74:691-702



GLP-1RA associated with reduced cirrhosis (1.12 events/1000 pt years) and reduced mortality (2.66 events/1000 pt years)

Kanwal et al JAMA Int Med 16.9.24



Eat some bacteria – sauerkraut, kimchi, kefir, live yoghurt for physical and mental health

What's new in dementia?

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# Dementia prevention, intervention and care: 2024 report of the Lancet standing Commission

Livingston et al  
Lancet 2024;  
404: 572-628

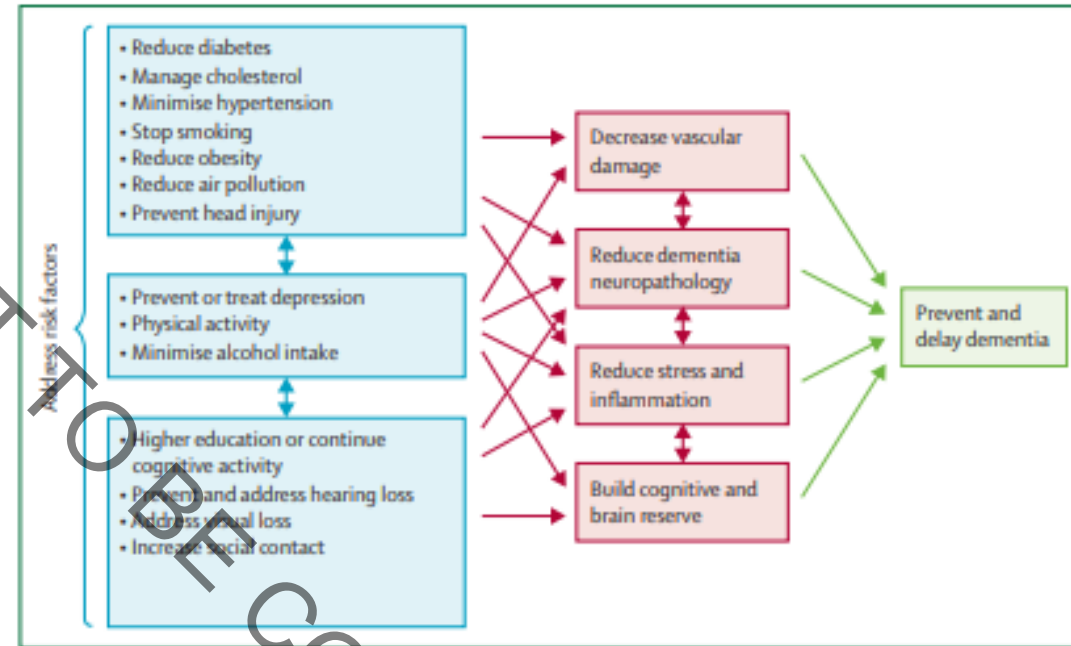
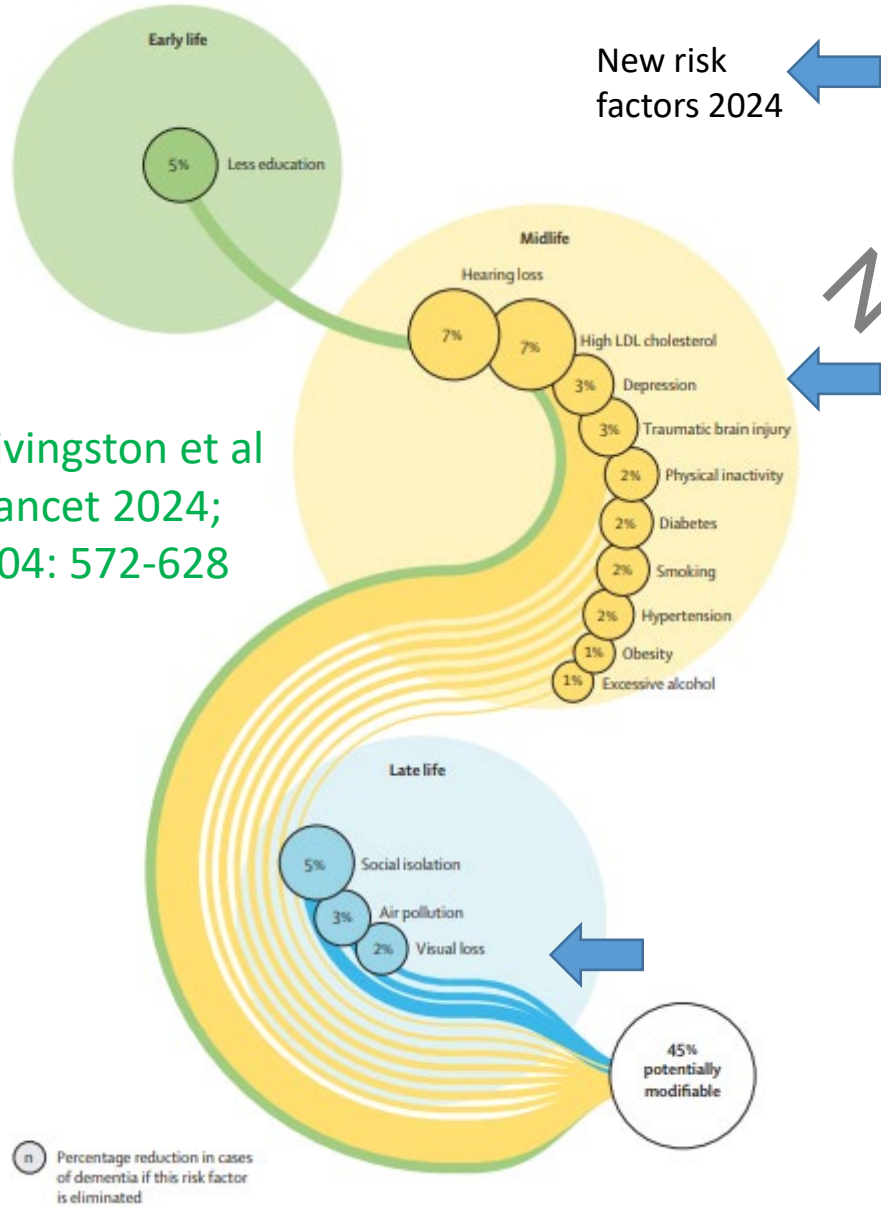


Figure 2: Possible brain mechanisms for enhancing or maintaining cognitive reserve and risk reduction of potentially modifiable risk factors in dementia

We can influence/discuss: (17%)  
 Diabetes – 2%  
 High LDL – 7% 1mmol/L ↑ - 8% ↑  
 PA  
 Smoking – cessation ↓risk  
 Hypertension - ≤ 130mm Hg  
 Obesity  
 Excess alcohol intake

We may be aware of: (17%)  
 Hearing loss – 4-24% ↑ risk/10dB loss  
 Vision loss  
 Depression - bidirectional  
 Social isolation

Potential risk factors – sleep, diet, infections, bipolar, psychosis, anxiety, PTSD, early menopause, HRT

n Percentage reduction in cases of dementia if this risk factor is eliminated

# Dementia prevention, intervention and care: 2024 report of the Lancet standing Commission

## Diabetes specific contribution:

- ✓ Midlife (<65 yrs) impact
- ✓ Increased risk:
  - ✓ Midlife obesity, higher WC ↑ risk >65 years
  - ✓ every 5 year earlier onset HR 1.24 up to age 70 yrs
  - ✓ Long duration and less than optimal control ↑ risk
  - ✓ SU treatment
- ✓ Improved risk:
  - ✓ Even 2kg weight loss by diet/PA improves cognition
  - ✓ SGLT2i, GLP-1RAs, DPP4is associated lower risk; metformin some studies
- ✓ Effective diabetes treatment may not decrease dementia
- ✓ Some obesity effects may be due to diabetes or ↓ PA

## Other key messages:

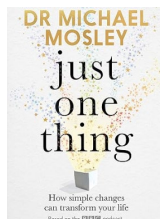
- ✓ Remain cognitively, socially and physically active in midlife and later life (>65 years)
- ✓ Target risk factors as early as possible and keep them low throughout life
- ✓ Risk modifiable even in APOE4
- ✓ Improved cognitive reserve can mean no signs or symptoms despite neuropathology

Meta-analysis 8M with diabetes – some heterogeneity

- ✓ Diabetes overall relative risk 1.59
  - ✓ Impact may begin early after diagnosis
  - ✓ Hypoglycaemia significantly increased risk
- Cao et al 2024 Diabet Metab Syndr 16

Dance. Sing. Learn a new skill.

Get some sun



**Target risk factors early to make most difference**  
**It is never too early or too late to reduce dementia risk**

<https://diabetesonthenet.com/journals/>

## 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

diabetesdistilled  
the latest developments filtered for you



billy

#### Diabetes Distilled: Deep dive into diabetes and infection

The increased risk of, and impaired response to, infection in people with diabetes, and... how we can help in primary

8 Jul 2024

#### Diabetes Distilled: Keeping kidneys FLOWing – semaglutide improves renal outcomes

First dedicated randomised controlled trial of kidney outcomes with a GLP-1 receptor agonist shows significant renal

8 Jul 2024

#### Diabetes Distilled: Fib-4 – A diagnostic and prognostic marker for liver and cardiovascular events and mortality

Should sequential Fib-4 testing now be made part of ongoing care in people with obesity... and/or type 2 diabetes?

20 May 2024

#### Diabetes Distilled: Diabetes remission in the real world

Early data from the NHS Type 2 Diabetes Path to Remission programme show it is effective... in achieving remission at scale

3 Sep 2024

#### Diabetes Distilled: Smoking cessation cuts excess mortality rates after as little as 3 years

The mortality benefits of smoking cessation may be greater and accrue more... rapidly than previously

20 May 2024

#### Diabetes Distilled: Statin heart benefits outweigh diabetes risks

Quantifying the risk of worsening glycaemia, and how should healthcare professional... respond?

20 May 2024

#### Diabetes Distilled: Predicting risk of kidney failure and mortality – a new tool

KDpredict algorithm accurately estimates risk of renal failure and mortality over 1–5 years.

20 May 2024

#### Diabetes Distilled: Pneumonia hospitalisation associated with long- and short-term risk of cardiovascular mortality

More than a 4-fold increased risk of cardiovascular death in the long term (>30 days post-... infection) following pneumonia

15 Jul 2024

#### Diabetes Distilled: Impact of metformin timing on glucose and GLP-1 response

Administering standard-release metformin 30–60 minutes before meals may lead to... improved postprandial

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#### Diabetes Distilled: Diabetes-related foot ulcers – detailed advice for primary care

Review and guidelines highlight opportunities for primary care to really make a difference.

25 Jul 2024

#### Diabetes Distilled: Optimising sleep – simple questions and goals

The importance of sleep in type 2 diabetes management.

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#### Diabetes Distilled: UKPDS at 44 years

Persistent benefits reinforce the need to aim for tight glycaemic control as early as possible... after type 2 diabetes diagnosis.

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