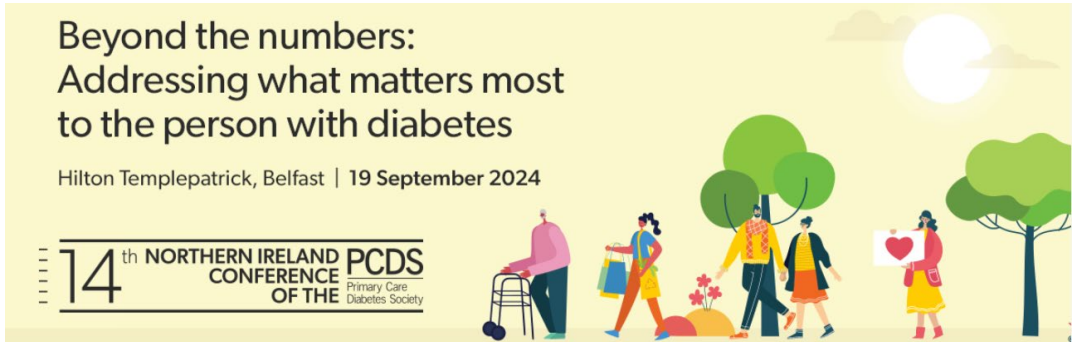

diabetesdistilled
the latest developments filtered for you

Pam Brown

GP with an interest in diabetes, obesity and lifestyle medicine
SA1 Medical Practice, Beacon Centre for Health, Swansea
Editor-in-Chief *Diabetes Distilled*
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I have received funding from the following companies for providing educational sessions, writing documents, and for attending advisory boards and conferences:

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

Staying up to date

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Diabetes

health

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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

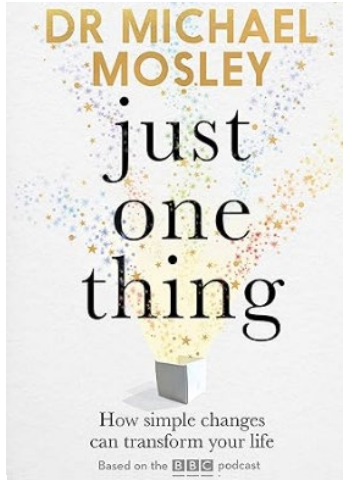
Making six simple lifestyle tweaks can cut your dementia risk, say experts - as diagnoses hit record high of almost 500,000

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

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

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



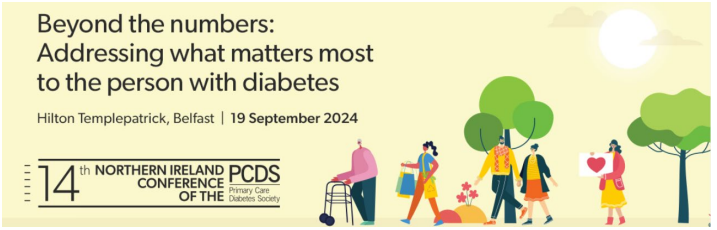
Scientists discover new 'supercharged' probiotic said to burn fat faster than Ozempic... and it's half the price

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,[1] Emily Ward,[2] Edward Farrell,[3] Aikaterini Theodoraki[4]

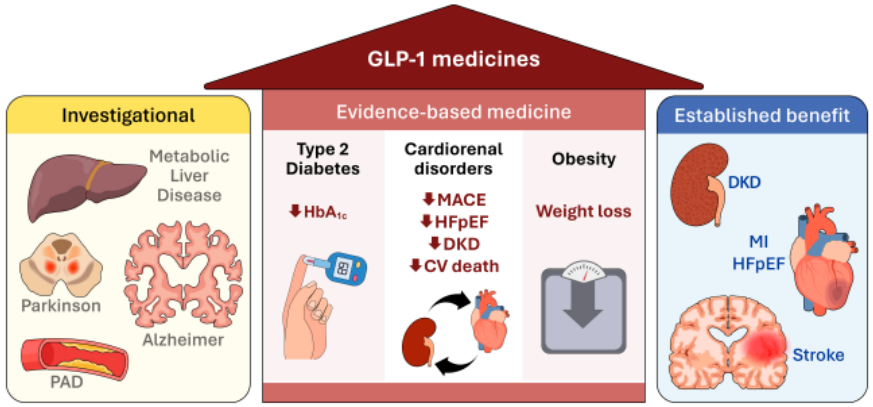
Cite this as: *BMJ* 2024;386:e078015
http://dx.doi.org/10.1136/bmj-2023-078015
Published: 17 July 2024

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

Daniel J. Drucker

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

Diabetes care 2024 open access



New advances in type 1 diabetes

STATE OF THE ART REVIEW

Savitha Subramanian, Farah Khan, Irl B Hirsch

Cite this as: *BMJ* 2024;384:e075681
http://dx.doi.org/10.1136/bmj-2023-075681

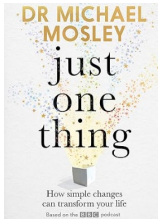
- ✓ Diagnosis
- ✓ CGM interpretation
- ✓ Closed loop systems

Table 4 | Pharmacokinetics of commonly used insulin preparations

	Half life*	Effective peak	Duration of action†	Notes
Basal insulin type				
NPH	4-4 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	-
Prandial insulin type				
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.

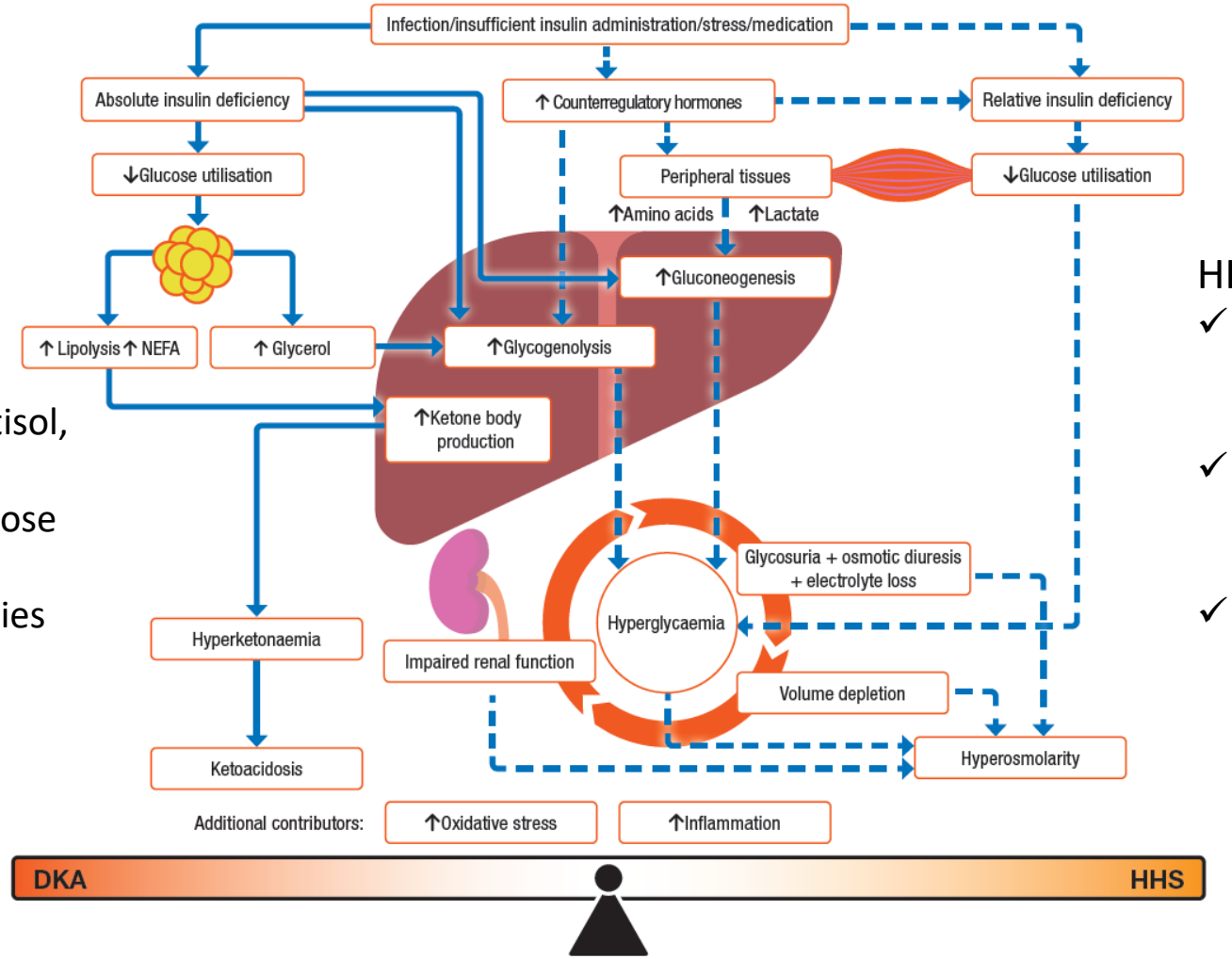


Pathogenesis of DKA and HHS

Hyperglycemic Crises in Adults With Diabetes: A Consensus Report

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

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

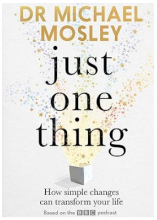


HHS
- ✓ Enough insulin to prevent ketonaemia but not hyperglycaemia
- ✓ Hyperglycaemia causes osmotic diuresis, volume depletion
- ✓ If inadequate fluid intake, hyperosmolar state, renal impairment and decline cognitive function

Early diagnosis and urgent admission for management - insulin and hydration

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

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

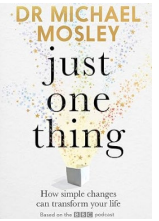
Both

- ✓ 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

Stand on one leg – improve balance



What’s new in remission?

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

Lancet Diabetes Endocrinol
2024; 12: 653–63

Valabhji et al

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[1], Hilda O. Hounkpatin[1]*, Beth Stuart[1¤], Andrew Farmer[2], Simon Griffin[3,4]

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, [1] Brendan Deeney, [1] Laura Swaithes, [1] Hilda Hounkpatin, [2] Hajira Dambha-Miller[2]

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

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

diabetesdistilled
the latest developments filtered for you

Remission is achievable at scale
Remission also available with low carb diet, bariatric surgery

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 Schwartzenberg 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

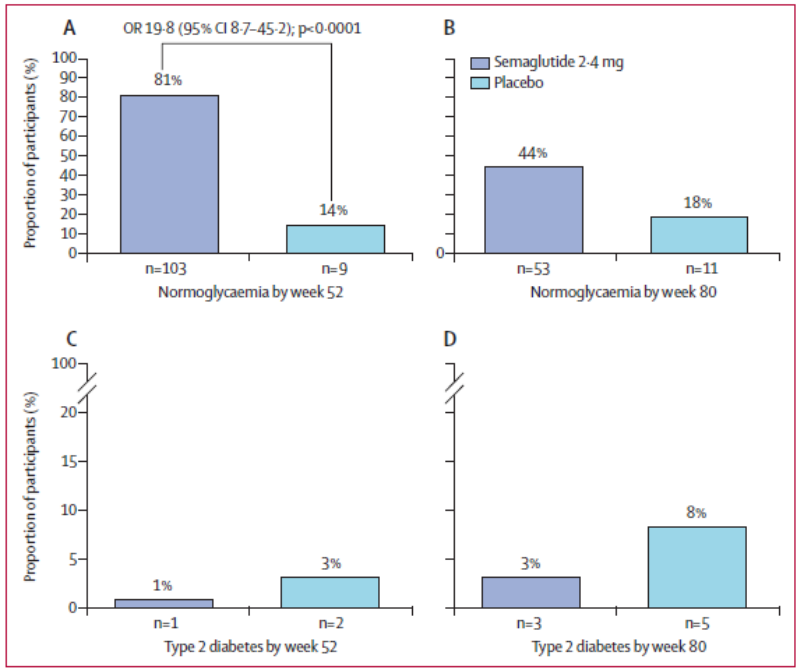


Figure 3: **Proportion of participants who reverted to normoglycaemia or progressed to type 2 diabetes with semaglutide 2·4 mg versus placebo in the full analysis set during the in-trial observation period**

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?

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

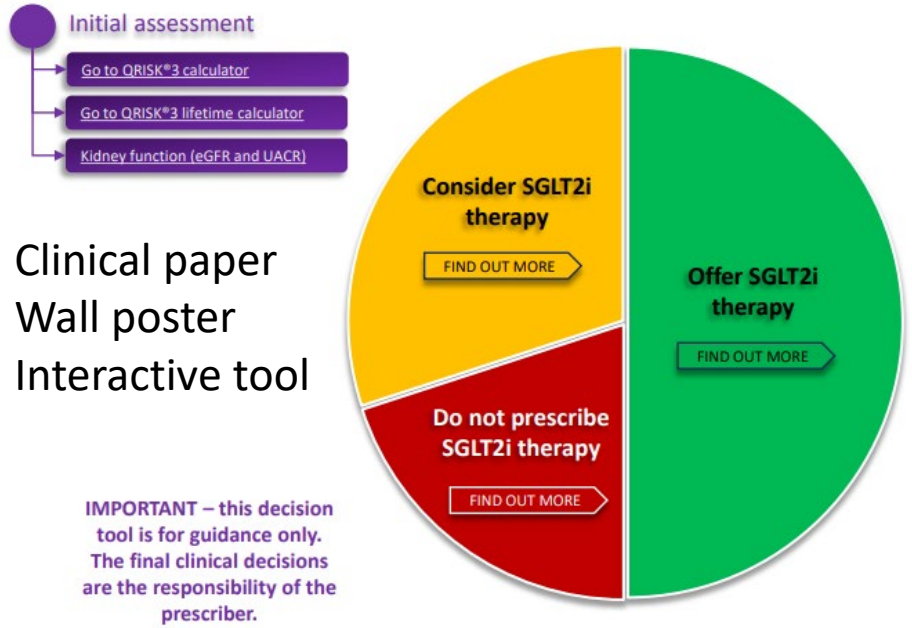
UKPDS 91 Adler et al Lancet 2024; 404:145-155

Diabetes Ther (2024) 15:1099–1124
https://doi.org/10.1007/s13300-024-01550-5

Seidu et al

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

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

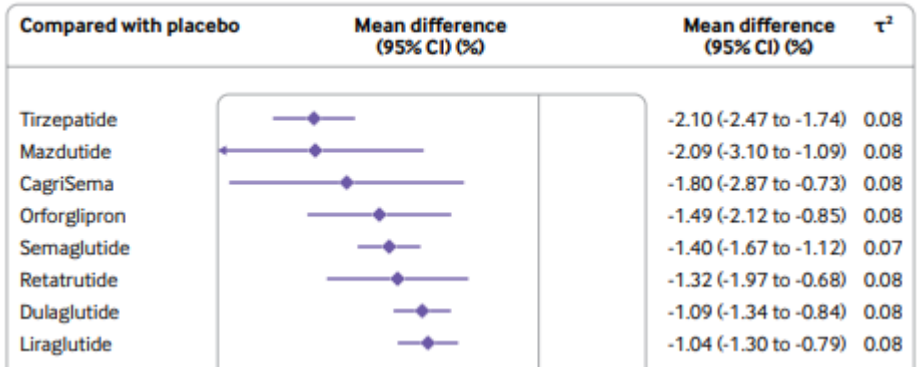
Comparative effectiveness of GLP-1 receptor agonists on glycaemic control, body weight, and lipid profile for type 2 diabetes: systematic review and network meta-analysis

Haiqiang Yao,[1,2] Anqi Zhang,[2] Delong Li,[1,2] Yuqi Wu,[1,2] Chong-Zhi Wang,[3,4] Jin-Yi Wan,[1,2] Chun-Su Yuan[3,4]

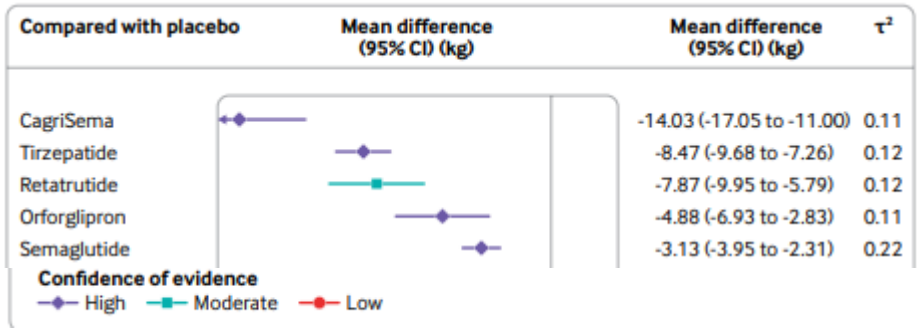
Cite this as: BMJ 2024;384:e076410
http://dx.doi.org/10.1136/bmj-2023-076410

76 RCTs, n=39,246

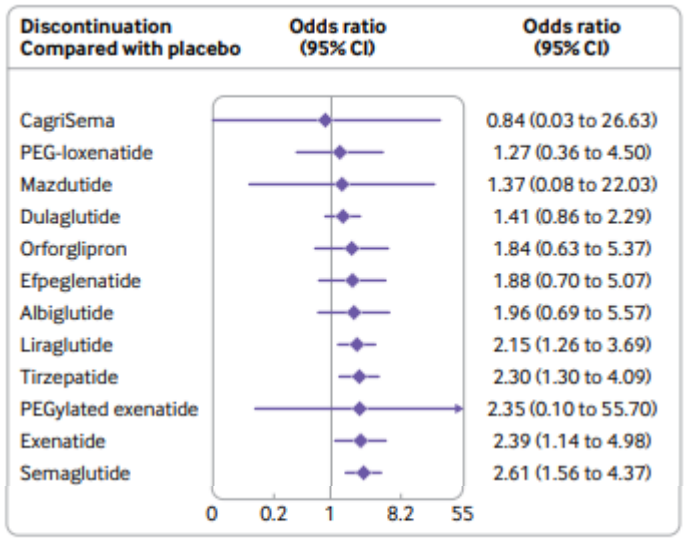
HbA1c reduction in %



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

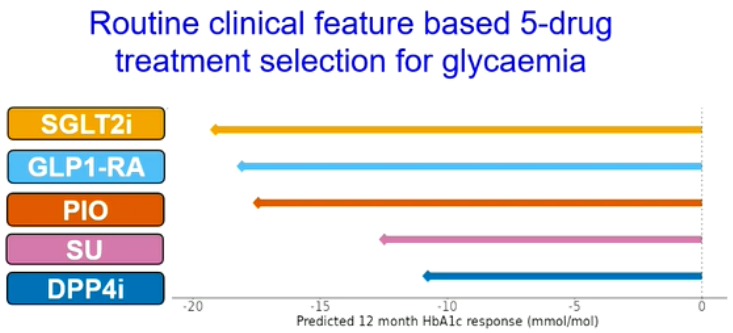
Will seeing T2DM in HD improve treatment choice?

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

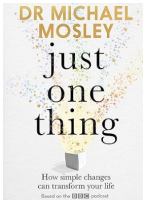
- ✓ Routine clinical features – age, sex, diabetes duration, HbA1c, BMI, eGFR, ALT, TC, HDL, Ethnicity, deprivation quintile, number previous and current therapies, smoking
- ✓ Differences reflect the underlying drug mechanisms of action
- ✓ Expected HbA1c reduction over 12 months
- ✓ Best treatment 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



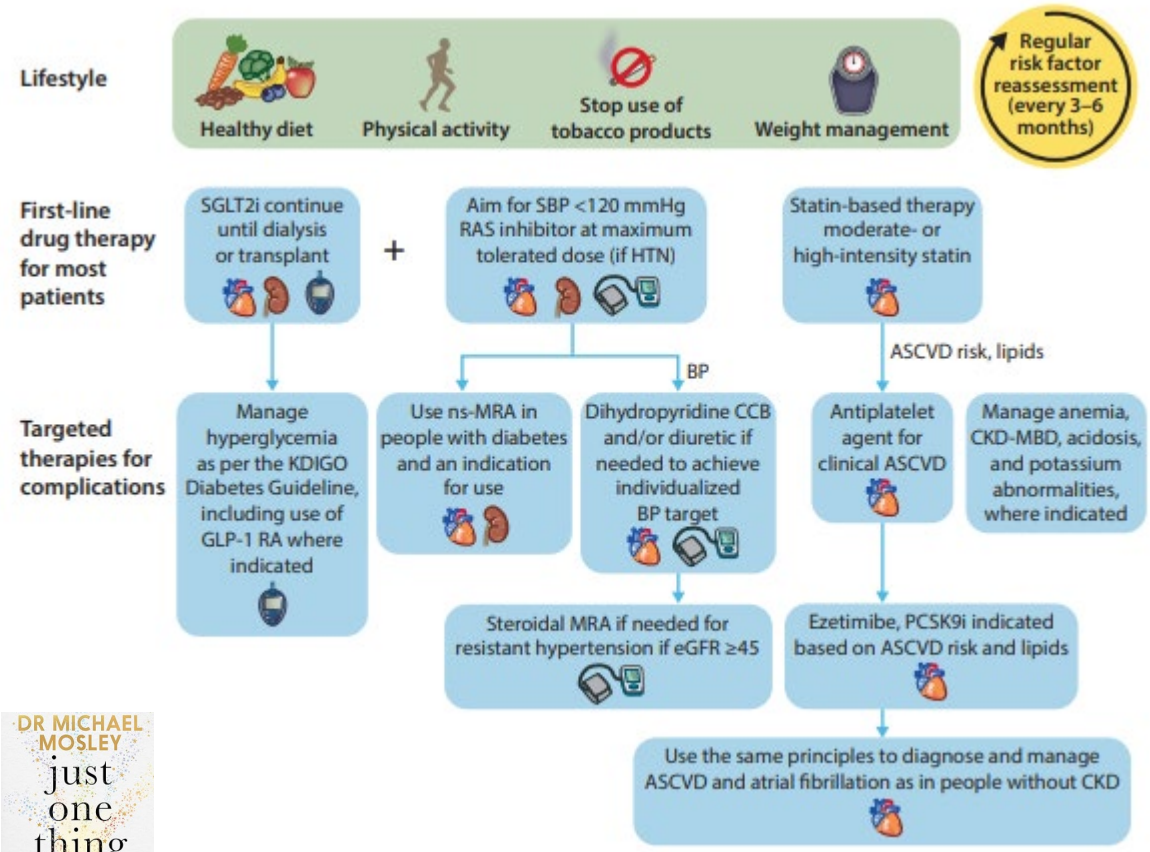
https://pm-cardoso.shinyapps.io/t2dtst/



Stand up more

What’s new in CKD?

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



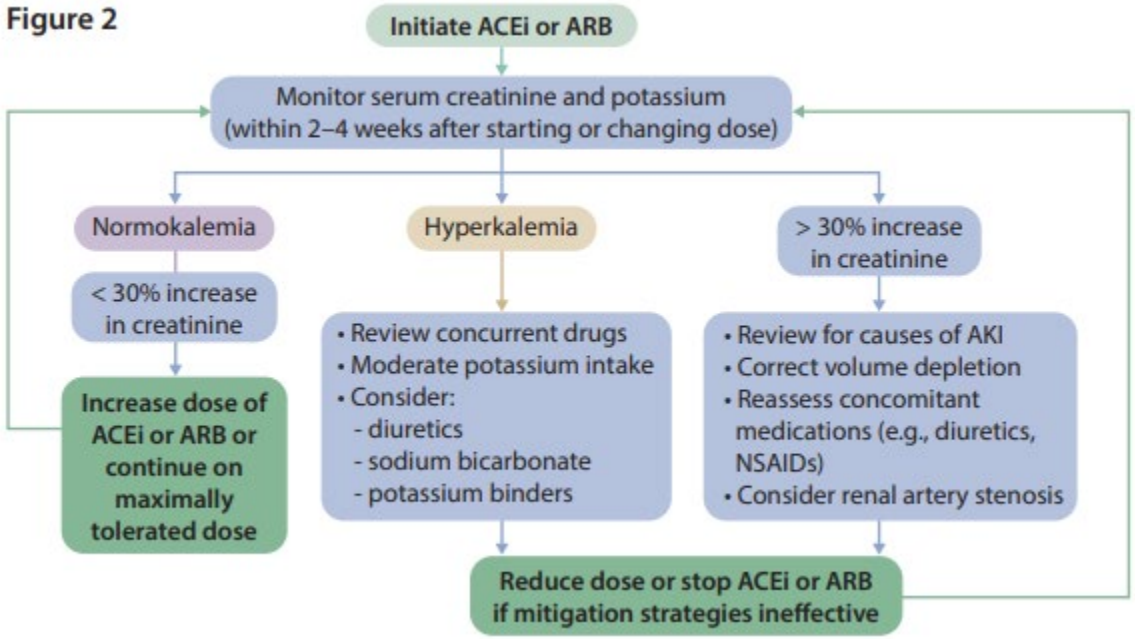
Soak in a hot bath. Read

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**

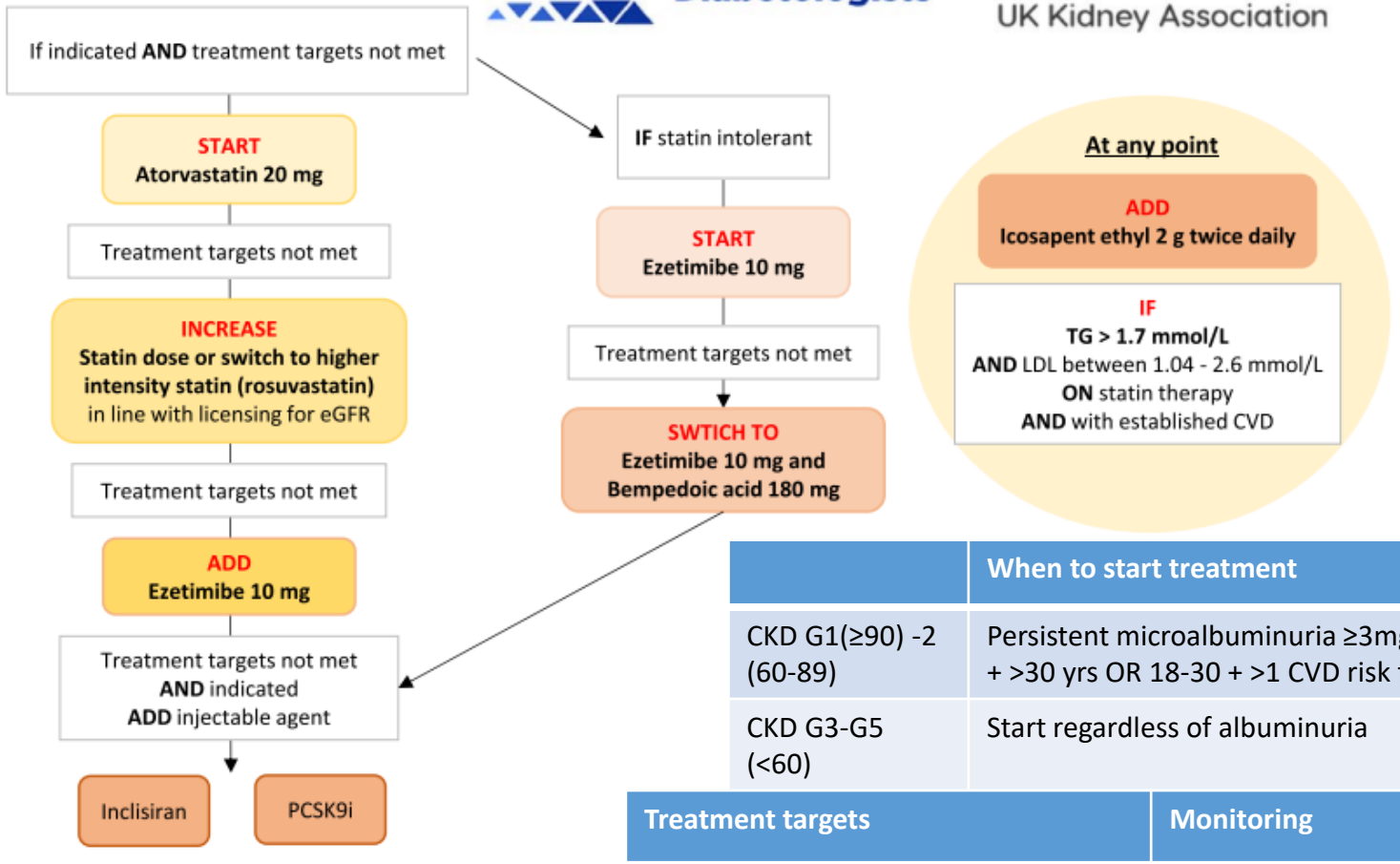
Figure 2



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

Association of British Clinical Diabetologists

UKKA 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	With CVD	
		High risk[1]	Very high risk[2]
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

[1]ACS, CHD, PVD, ischaemic stroke, revascularisation
[2]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

Zac-Varghese *et al. BMC Nephrology* (2024) 25:216
https://doi.org/10.1186/s12882-024-03664-1

What’s new in NAFLD/MASLD?

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

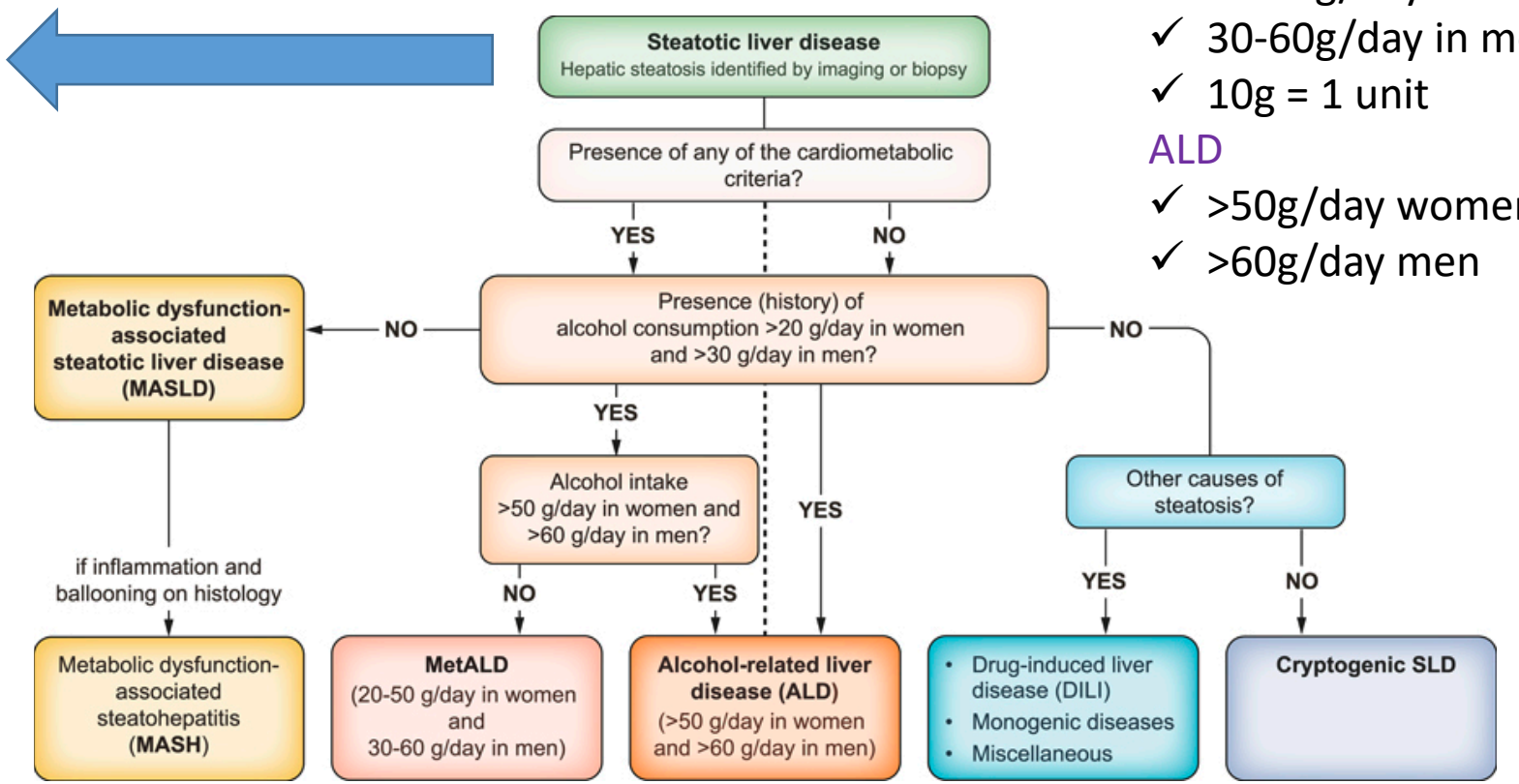
Metabolic dysfunction-associated steatotic liver disease (MASLD) and metabolic dysfunction-associated steatohepatitis (MASH)

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

✓ 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

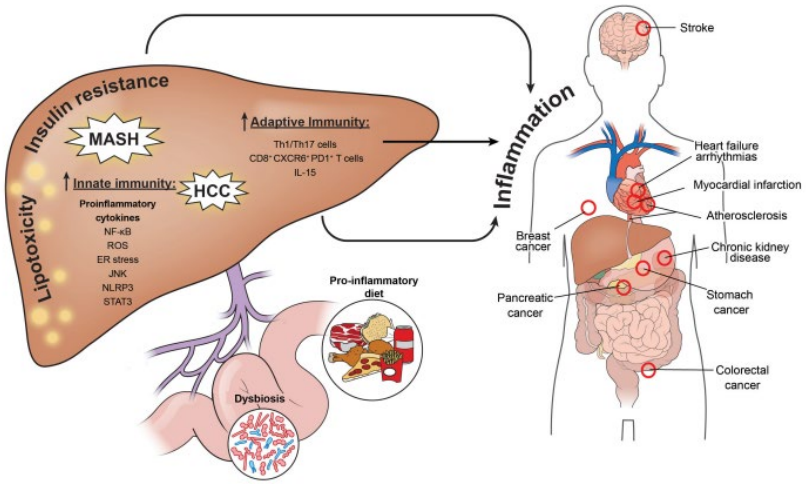
MASLD: a systemic metabolic disorder with cardiovascular and malignant complications

Giovanni Targher [1], Christopher D Byrne [2], Herbert Tilg [3]

Gut 2024; 74:691-702

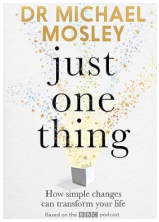
- ✓ Fib-4 is non-invasive test to identify who needs further investigations
  - ✓ Use age, ALT, AST, platelets to calculate
  - ✓ <1.3 OK; 1.3-2.67 refer fibrosis possible; >2.67 fibrosis likely

- ✓ 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

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



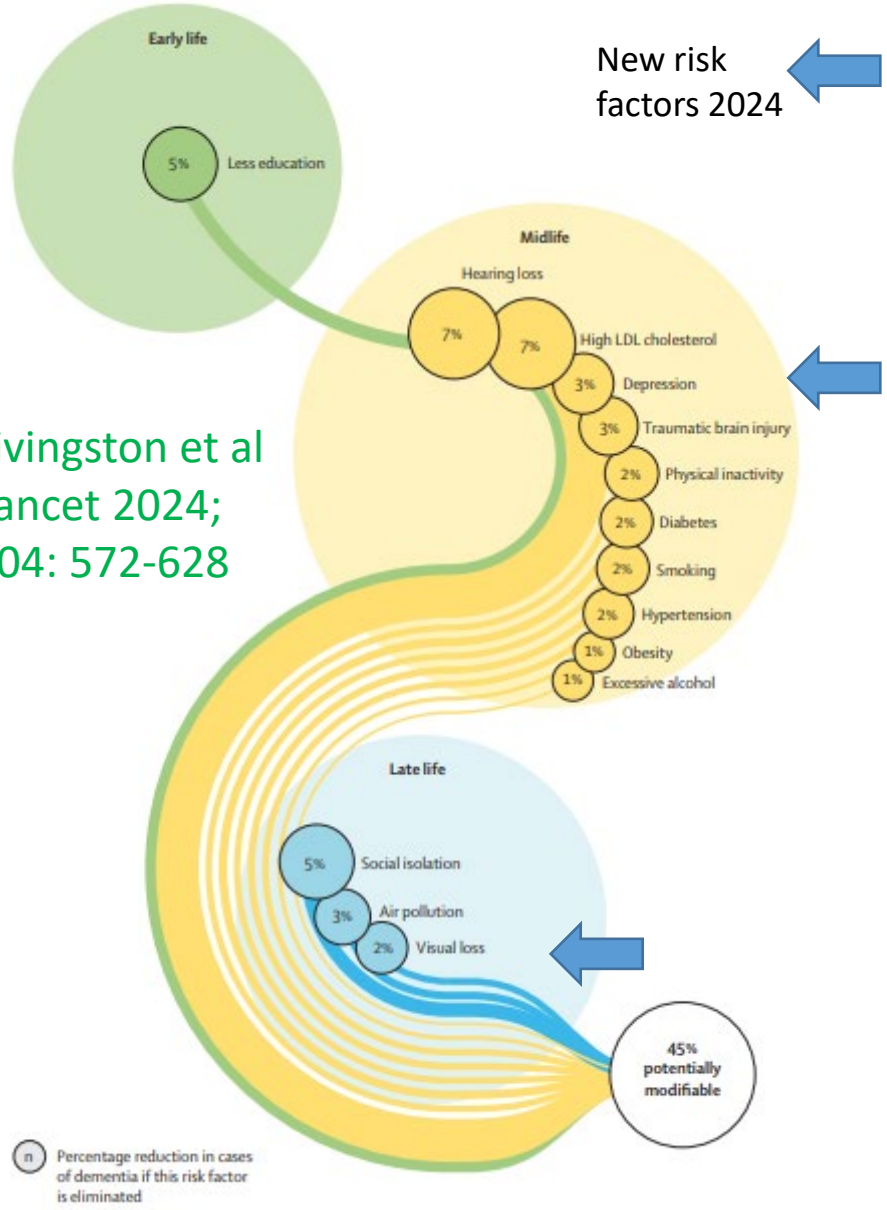
Eat some bacteria – sauerkraut, kimchi, kefir, live yoghurt for physical and mental health

Aostee et al Lancet Regional Health; 2024:36

diabetesdistilled
the latest developments filtered for you

What’s new in dementia?

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



New risk factors 2024

Livingston et al Lancet 2024; 404: 572-628

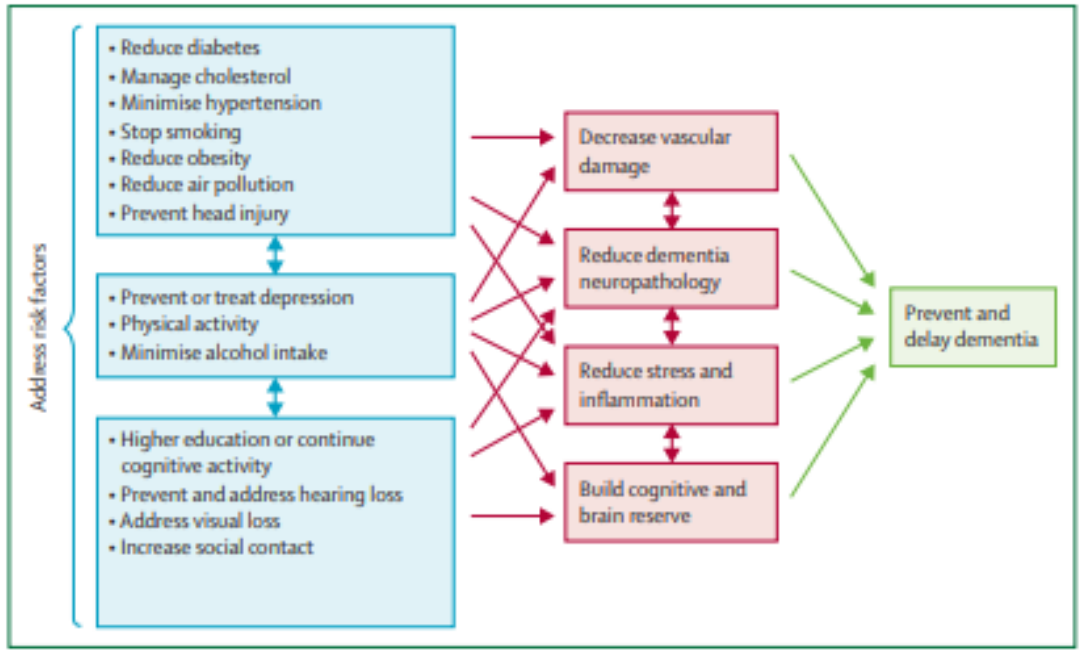


Figure 2: **Possible brain mechanisms for enhancing or maintaining cognitive reserve and risk reduction of potentially modifiable risk factors in dementia**

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

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

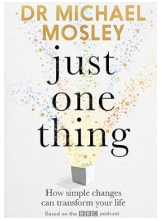
Meta-analysis 8M with diabetes – some heterogeneity

- ✓ Diabetes overall relative risk 1.59
- ✓ Impact may begin early after diagnosis
- ✓ Hypoglycaemia significantly increased risk

Cao et al 2024 Diabet Metab Synd 16

Dance. Sing. Learn a new skill.

Get some sun

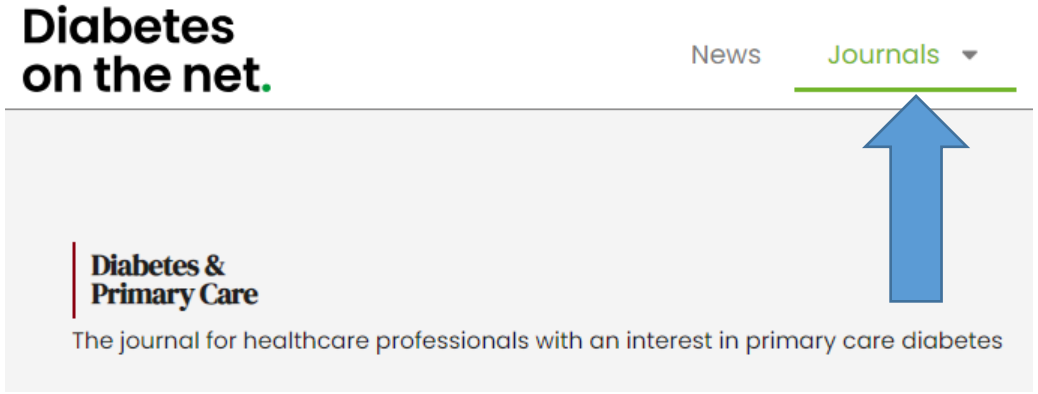


Target risk factors early to make most difference

It is never too early or too late to reduce dementia risk

Livingston et al Lancet 2024; 404: 572-628

https://diabetesonthenet.com/journals/



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Thank you for your attention!