



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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https://diabetesonthenet.com/journals/

Diabetes on the net.

News





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: Statin heart benefits outweigh diabetes risks

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

22 Apr 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

2 Apr 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?

Diabetes Distilled: Type 2 diabetes remission associated with renal and cardiovascular benefits

33-55% lower rates of CKD and 40-49% lower rates of CVD observed in Look AHEAD... participants who achieved 6 Mar 2024

Diabetes Distilled: Reaching a XENITH in cardiorenal protection

Phase 2b study demonstrates significant reductions in uACR with developmental drug... zibotentan plus dapagliflozin,

10 Jan 2024

Diabetes Distilled: MACE risk higher in newly diagnosed type 2 diabetes treated with lifestyle alone

Foregoing therapies to reduce glucose, lipids and BP immediately after diagnosis... increases MACE risk even if

10 Jan 2024

Diabetes Distilled: Metformin does not increase risk of GI side effects during **GLP-1 RA initiation and** titration

No benefit to pausing metformin therapy during GLP-1 RA initiation.

Diabetes Distilled: Calcium supplementation in people with diabetes – is caution needed?

Increased cardiovascular risk observed in people with diabetes taking regular calciu... supplements.

6 Mar 2024

Diabetes Distilled: Physical activity - how much is needed to optimise glycaemic control?

Do people with type 2 diabetes need more physical activity than is recommended for the... general population?

6 Mar 2024

18 Mar 2024

Diabetes Distilled: DELIVERing reassurance that early eGFR reductions with SGLT2 inhibitors should not prompt drug discontinuation

Initial eGFR reductions of >10% when starting SGLT2 inhibitors are not associated with advers... cardiovascular or renal

10 Jan 2024

Diabetes Distilled: "Twincretin" tirzepatide

significantly SURPASSes comparator effects on glucose, weight and quality of life

Will this highly effective new agent change current treatment guidelines, especiall... with regard to glycaemic and

10 Jan 2024

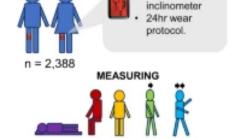
6 Mar 2024

What's new in lifestyle

What is the perfect activity mix for cardiometabolic risk? The Maastricht Study

Associations of 24hr sitting, standing, physical activity, and sleeping time-use compositions with optimal cardiometabolic risk and glycaemic control: The Maastricht Study

COHORT AND MEASURES IDENTIFYING OPTIMAL ASSOCIATIONS OPTIMAL 24HR TIME USE



LPA: light-intensity physical activity MVPA: Moderate-to-vigorous-intensity physical activity

ASSOCIATIONS WITH



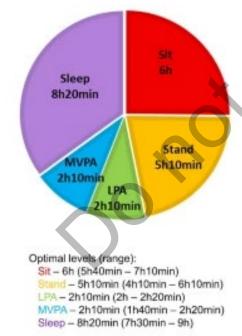
Waist circumference (WC)



Fasting glucose (FPG), 2h post-load glucose, Matsuda index, HbA_i,



Clustered cardiometabolic risk score



Brakenridge, C.J., Koster, A., de Galan, B.E. *et al.* Associations of 24 h time-use compositions of sitting, standing, physical activity and sleeping with optimal cardiometabolic risk and glycaemic control: The Maastricht Study. *Diabetologia* (2024).

Open access.

Sleep 7.5 - 9 hrs

Sit 6 -7hrs

Stand 4 - 6 hrs

Light activity 2-2.5hrs

✓ Even small changes will help

No surprises but clarifies goals to share:

Moderate to vigorous activity 1.5-2.5hrs

Start discussions. Many people have wearable technology – let's help them use it to gather baseline data and make changes to optimise cardiometabolic risk

How much sitting is bad and how can we counteract it?

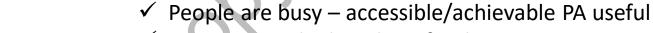
Diabetologia (2024) 67:1051–1065 https://doi.org/10.1007/s00125-024-06090-y

Ahmadi et al

ARTICLE

Relationship of device-measured physical activity type and posture with cardiometabolic health markers: pooled dose-response associations from the Prospective Physical Activity, Sitting and Sleep Consortium

Prospective Physical Activity, Sitting and Sleep (ProPASS) consortium: 6 cohorts including British Cohort Study and Maastricht n= 15,168



- ✓ 5 min+ stair climbing beneficial 350 steps,70 steps/min
- ✓ Each additional minute to 12 mins, similar rate improvement to running same duration
- √ 13:1 minute/day ratio walking to stair-climbing
- √ 7-15:1 ratio moderate intensity (walking) activity to high intensity
- ✓ Women greater protection than men

5 min/day of stair climbing was associated with favourable overall cardiometabolic health



64 min/day of walking was associated with favourable overall cardiometabolic health

Adverse association of sitting increased linearly at >10 h/day, and >12 h/day was associated with unfavourable cardiometabolic health

>90 min/day of walking or 3–8 min/day of stair climbing eliminated the adverse associations of sitting



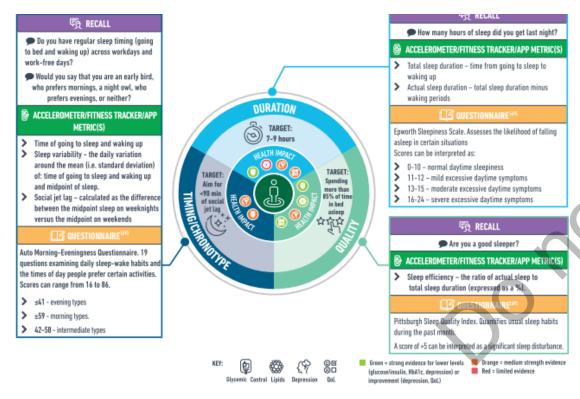
-BMI
-Waist circumference
-Total cholesterol
-Triglycerides
-HDL-cholesterol
-HbA_{1c}

Real world data to share to help shape lifestyle guidance and recommendations

Waking Up to the Importance of Sleep in Type 2 Diabetes Management: A Narrative Review

Joseph Henson, Alix Covenant, Andrew P. Hall, Louisa Herring, Alex V. Rowlands, Thomas Yates, and Melanie J. Davies

Diabetes Care 2024;47(3):331-343 | https://doi.org/10.2337/dci23-0037



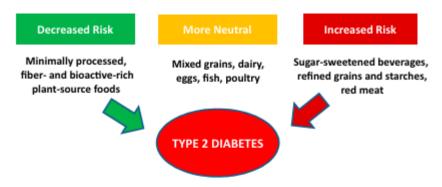
Sleep: a neglected public health issue Lancet Diab Endocr May 2024

Habitual short sleep duration, diet and development T2DM in adults Noga et al JAMA Network Open 2024; 7(3)

- ✓ Monitoring technology common
- ✓ Help people understand sleep quantity/quality/timing impact
- ✓ Simple questions:
 - ✓ How many hrs/night?
 - ✓ Regular sleep timing?
 - ✓ Are you a good sleeper?
- ✓ Clear goals:
 - ✓ 7-9hrs
 - √ <90 minutes social jetlag
 </p>
 - √ 85% time in bed asleep
- ✓ Treat sleep disrupters if possible
- ✓ Refer for OSA evaluation

Ask about sleep, encourage to avoid social jetlag, help minimise sleep disrupters, identify OSA Plant-Based Diets and Diabetes Risk: Which Foods, What Mechanisms?

Dariush Mozaffarian



Mechanisms

Reduced body weight, body fat, and insulin resistance from soluble fiber

Beneficial effects of unsaturated fats on glucose, insulin, insulin resistance, and insulin secretion

Metabolic benefits of trace bioactives like menaquinones

Positive diet-microbiome interactions from prebiotics (fermentable fibers, polyphenols), probiotics (active cultures), and synbiotics (their combination) Postprandial spikes in blood sugar and insulin from rapidly digested grains, starches, and sugars

Hepatic de novo lipogenesis from excess dietary fructose (and perhaps protein)

Oxidant and cellular harms of heme iron and lipid oxidation products in red meat

Microbiome dysbiosis with reduced microbial diversity, increased proinflammatory species, and insulin resistance

Figure 1-Diet patterns and type 2 diabetes risk.

Diabetes Care 2024;47:787-789 | https://doi.org/10.2337/dci24-0011

Food additive emulsifiers and the risk of type 2 diabetes: analysis of data from the NutriNet-Santé prospective cohort study Lancet Diabetes Endocrinol 2024: 12: 339-49

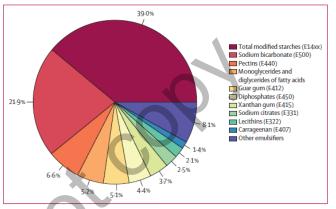


Figure 2: Contribution of individual emulsifiers to total emulsifier intakes (%) among study participants from the NutriNet-Santé cohort, 2009-23 (n=104139)

Artificial sweeteners and T2DM

Diabetes Care 2023;46(9):1681-1690 | https://doi.org/10.2337/dc23-0206

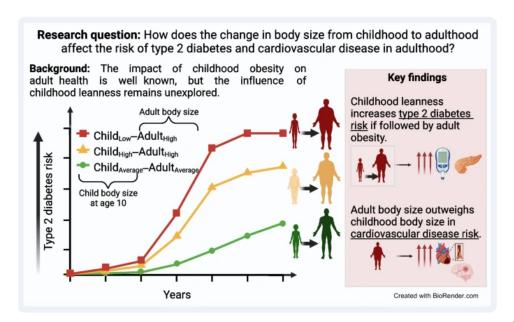
- ✓ Population cohort, N= 104,139, 80% female; 2009-2023
- ✓ Increased risk Carrageenan gum E407, Sodium citrate E331, Guar gum E412, Xanthan gum E415, E340, E414, E472e
- ✓ Quantified increased risk per cumulative intake
- ✓ Mainly UPF fruits and veg, cakes and biscuits, dairy products
- ✓ Gut microbial dysbiosis, inflammation, metabolic dysregulation

Recommend simple changes most likely to make a difference – 'eat more plants and fibre', 'decrease ultraprocessed food', 'artificial sweeteners short term only'

What's new in weight

Child to adult body size change and T2DM risk

Carrasquilla et al Diabetologia 2024



Previous focus on obesity in children and adult risk T2DM

- ✓ UK Biobank 364,695 participants median follow up 12.8 yrs
- ✓ Self-reported size age 10 'thinner', 'average' or 'plumper'
- ✓ Similar sized adult groups adult BMI means 35.3, 27.6, 22.8
- ✓ Highest T2DM risk if low child size and high adult size (HR4.73 compared to average/average group) Women same as men
- ✓ Low childhood size higher T2DM risk at each adult size

Low birthweight and overweight during childhood and young adulthood and the risk of type 2 diabetes in men: a population-based cohort study Celind et al Diabetologia 2024

BEST cohort study Gothenberg – males

- ✓ Birthweight (≤ 2.5kg) and BMI >25 aged 20yrs:
 - √ risk early T2DM ≤ 59.4yrs 10 times higher
 v those normal birth and age 20 weights
 - ✓ 27% absolute risk T2DM ≤ 59.4yrs v 6% risk normal birth and aged 20 weight

Do we record birth weights? Are we aware of children with low body size? Do we weigh young adults or identify weight gain?

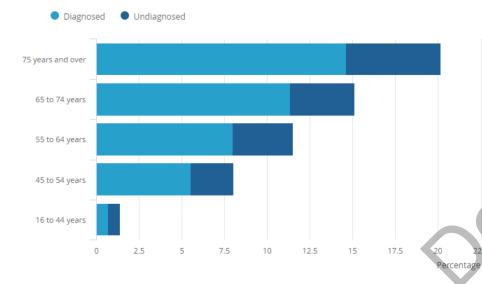
What's new in management?

Undiagnosed T2DM – a significant risk factor

Figure 1: Older adults had higher prevalence of type 2 diabetes, but younger adults were more likely to be undiagnosed if they did have type 2 diabetes

Percentage of adults with type 2 diabetes by age group, 2013 to 2019,

England



Source: Health Survey for England (HSE) from NHS Digital

Cholesterol Treatment Trialists' Collaboration (2024). "Effects of statin therapy on diagnoses of new-onset diabetes and worsening glycaemia in large-scale randomised blinded statin trials: an individual participant data meta-analysis." <u>Lancet Diab and Endocr.</u>

Analysis reveals extent of undiagnosed type 2 diabetes

3 Apr 2024

- ✓ 50% of those with T2DM aged 16-44 years undiagnosed v 27% of those over 75 years
- ✓ Black and Asian pre-diabetes/NDH 22%
- ✓ Wales highest rate of diabetes in UK 8% adults
- ✓ 200,000 cases with diabetes with 65,000 cases T2DM undiagnosed
- ✓ Cholesterol Treatment Trialists Collaboration study demonstrated 24% proportional increase glycaemia with high intensity statin therapy/small increased T2DM risk

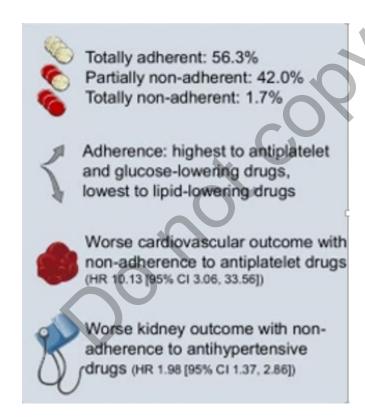
How can we find people with undiagnosed T2DM and non-diabetic hyperglycaemia? Has everyone on a statin had an HbA1c?

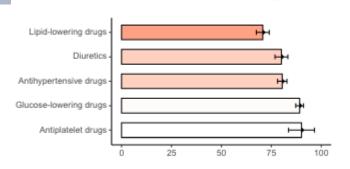
Non-adherence to cardiometabolic medication as assessed by LC-MS/MS in urine and its association with kidney and cardiovascular outcomes in type 2 diabetes mellitus

Denicolo et al 2024 Diabetologia

PROVALID study – n=1125

- ✓ Baseline urine samples for 79 cardiometabolic drugs
- ✓ CV endpoint 3 point MACE
- ✓ Kidney endpoint: eGFR decline, albuminuria progression, ESKD, kidney death
- ✓ GLP-1 RA not detectable cleaved; no one on SGLT2i

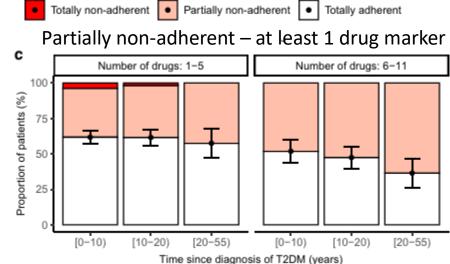




Totally adherent patients (%)

80

Fig. 2 Adherence by drug class. Adherence was found to be highest to antiplatelet and glucose-lowering drugs and lowest to lipid-lowering drugs. Bars represent sample averages and whiskers 95% CIs



Non-adherence difficult to evaluate from prescribing records; most people happy to share if we ask

Continuous glucose monitoring for the routine care of type 2 diabetes mellitus

Ajjan R et al

nature reviews endocrinology

https://doi.org/10.1038/s41574-024-00973-1

Table 2 | Proposed use of CGM throughout the natural history of T2DM

Group	At diagnosis and early disease	Management of stable disease	Long duration of disease*
All people with T2DM	Utilize CGM for 14 days after T2DM diagnosis Establish a baseline glucometric	Predict risk of microvascular complications Adjust therapy Manage glycaemic goals for time in range, time below range, time above range, glycaemic variability and glucose management indicator (CGM-defined HbA _{5c} correlate)	Facilitate T2DM therapy de-escalation in older and/or frail people with T2DM
	profile		Prevent hypoglycaemia
	Provide education on the glycaemic response to diet and exercise in T2DM		Reduce risk of cardiorenal complications (for example, chronic kidney disease)
	Decide on the initial treatment plan and therapy		Reduce incidence and progression of microvascular disease
	Evaluate the patient's early (14-day) response to T2DM treatment		Allow care workers to more effectively manage the care of
People with T2DM on: Multiple daily injections Basal insulin Premixed insulin Insulinotropic drugs ^h	Continuous access to CGM for daily	use	people with T2DM
	Prevent hypoglycaemia	Prevention of hypoglycaemia	
	Manage hyperglycaemia	Manage hyperglycaemia	
	Support self-management	Facilitate periods of therapy escalation or de-escalation	
		Support self-management	
People with T2DM on non-insulin therapy ^c	Intermittent use of CGM at least eve	ery 3 months, with HCP review	
	Reinforce education on glucose	Can be combined with a coincident HbA _{1c} test	
	profiles, diet, physical activity and the effects of medication	HCP can make decisions on whether to change therapy or not	
		Predict changes in risk of microvascular complications	
		People with T2DM can re-establish the behaviours of good self-management with support from CGM	

CGM, continuous glucose monitoring; HCP, health-care professional; T2DM, type 2 diabetes mellitus. People with long-standing T2DM, with risk of consequent comorbid microvascular and macrovascular disease. People with T2DM at increased risk of frequent hypoglycaemia confirmed during a CGM-led medical review. Can include people on insulmotropic oral drugs with low risk of hypoglycaemia confirmed during a CGM-led medical review.

Not on insulin

- ✓ At diagnosis and early disease
 - ✓ Impact of diet and PA, early Rx
- ✓ Management stable disease
 - ✓ Adjust therapy, assess variability
- ✓ Long duration disease
 - ✓ De-escalation therapies
 - ✓ Prevent hypos
 - ✓ Reduce microvascular disease
 - ✓ Empower carers/care workers
- ✓ Intermittent every 3 months
 - ✓ HCP therapy review



HEALTH TECHNOLOGY WALES (HTW) GUIDANCE 004-2 (July 2021)

HTW Guidance:

The evidence supports the routine adoption of Freestyle Libre flash glucose monitoring to guide blood glucose regulation in people with diabetes who require treatment with insulin.

The use of Freestyle Libre flash glucose monitoring in these people improves the proportion of time that the blood glucose is in target range and reduces time in hypo and hyperglycaemia.



Order a free FreeStyle Libre 2 sensor sample

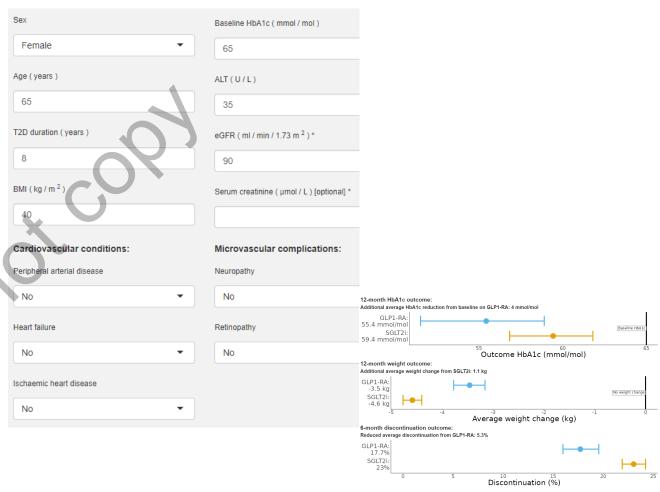
Get first-hand experience of how the FreeStyle Libre 2 system works

How should we choose between SGLT2i and GLP-1RA?

Diabetologia (2024) 67:822-836 Cardoso et al https://doi.org/10.1007/s00125-024-06099-3 ARTICLE

Phenotype-based targeted treatment of SGLT2 inhibitors and GLP-1 receptor agonists in type 2 diabetes

- ✓ HF, CKD/DKD SGLT2i
- ✓ ASCVD/high risk ASCVD GLP-1RA or SGLT2i None of these conditions?
- ✓ Precision medicine approach predict differential glucose-lowering, microvascular complications, weight loss
- ✓ Predictive algorithm developed/validated using UK Clinical Practice Research Datalink; external validation SCI-Diabetes Tayside and Fife
- ✓ Glycaemic control: Mean ↓ SGLT2i = GLP-1RA
- ✓ GLP-1RA better in females, older, lower baseline eGFR and BMI
- ✓ SGLT2i better in 32% HbA1c <64 mmol/mol and 67% HbA1c >86mmol/mol; higher number of Rx



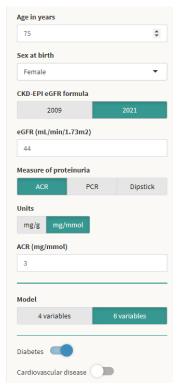
https://pm-cardoso.shinyapps.io/SGLT2 GLP1 calculator/ Prototype treatment selection calculator in development

What's new in CKD?

KDPredict – predicting kidney failure and death in moderate/severe CKD Developed with Machine Learning Liu et al Citethis as: BM/2024;385:e078063

- ✓ Developed using Canadian, Danish and Scottish data
- ✓ More accurate 1 to 5 year renal failure risk than current KFRE + predicts 1 to 5 year all cause mortality risk
- ✓ 4 and 6 variable scores similar for renal failure risk, 6 variable more accurate for mortality

http://kdpredict.com





- ✓ Older population (77-80 yrs) v 69-70 yrs
- ✓ eGFR 15-44 (CKD 3b-4) v eGFr <59 (CKD 3a)
- ✓ May make it less clear who to refer
- ✓ Competing mortality risk may help decision-making.
- In an environment where sharing the diagnosis is not universal, will this make it even harder?

THE KIDNEY FAILURE RISK EQUATION Age (Yrs) Sex Select Select Urine Albumin: Creatinine Ratio mg/mmol •

NICE recommends 5% 5yr risk threshold for referral using KFRE

Are we using a kidney failure risk equation to assist in referral decisions?

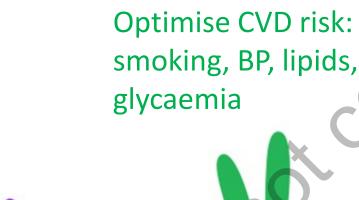
5 FINGER PROMPT FOR CKD MANAGEMENT

Code, calculate risk, share the diagnosis, involve in decisions, refer if appropriate

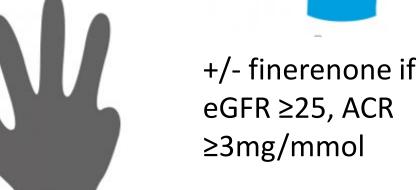
Adapted from an unknown original source



Slow CKD progression/ monitor: smoking, BP, glycaemia, ACEI/ARB







Screen, diagnose early, code; refer appropriately

What's new in guidelines?

Cardiovascular disease: risk assessment and reduction, including lipid modification NG238

NICE guideline

www.nice.org.uk/guidance/ng238

December 2023 update

Summary of National Guidance for Lipid Management for Primary and Secondary Prevention of CVD

Authors: Dr Rani Khatib & Dr Dermot Neely on behalf of the AAC Clinical Subgroup. Updated by NHSE Cholesterol Expert Advisory Group.

March 2024. Review date: March 2026.

"This summary accurately reflects NICE guidance and JBS3 recommendations", NICE March 2024







Welcome to the QRISK®3-2018 risk calculator https://qrisk.org



Welcome to QRISK® 3-lifetime cardiovascular risk calculator: https://qrisk.org/lifetime

Optimise statin use/targets; find those defaulted; increase use other lipid lowering drugs

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The 2024 ADA Standards of Care: What's new?

- ✓ Language changes 'person first', empowering
- ✓ Screening recommendations second generation anti-psychotic drugs, asymptomatic HF, peripheral arterial disease, psychosocial screening protocols, those at high risk of T1DM for treatment to delay onset
- ✓ Increased focus on bone health, fracture risk, liver disease
- ✓ CGM metrics added to glycaemic goals
- ✓ Focus on treatment deintensification and hypoglycaemia
- ✓ Focus on weight management lifestyle, drugs, surgery importance of weight maintenance programmes
- ✓ Early combination drug therapy to achieve goals for weight and glycaemic control in T2DM
- ✓ GIP/GLP-1 RAs as options alongside GLP-1RAs; insulin at any stage but alter other drugs to avoid hypos
- ✓ New statin intolerance section, bempedoic acid, PCSK9 inhibitors and inclisiran
- ✓ Stronger ACEI/ARB recommendations
- ✓ Older people individualised glycaemic goals, offer drugs with cardiorenal benefits, care with hypos

The annual update section useful for flagging up what has changed significantly in the last year – published December

https://diabetesonthenet.com/wp-content/uploads/229.-Factsheet_ADA-standards-2024.pdf

New advances in type 1 diabetes

Savitha Subramanian, Farah Khan, Irl B Hirsch

thebmj | BMJ 2024;384:e075681 | doi: 10.1136/bmj-2023-075681

- ✓ Risk prediction and slowing progression to symptomatic disease with disease modifying Rx
- ✓ 50% in adults risk of misclassification
- ✓ Increased CGM use
- ✓ Insulin advances ultra-long-acting and ultra-rapid
- ✓ Insulin pumps to 'hybrid' closed loop systems/automated insulin delivery technologies
- ✓ B cell replacement therapies pancreas transplant, islet transplantation
- ✓ Adjunctive therapies metformin, GLP-1RAs
- ✓ Improved management DKA
- ✓ Hypoglycaemia CGM to reduce burden, easier to use glucagon
- ✓ Coming soon weekly basal insulins
- ✓ ADA/EASD management guidelines 2021

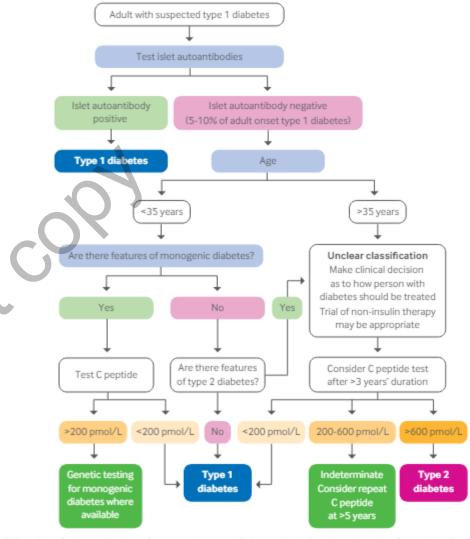


Fig 2 | Flowchart for investigation of suspected type 1 diabetes in adults, based on data from white European populations. No single clinical feature in isolation confirms type 1 diabetes. The most discriminative feature is younger age at diagnosis (<35 years), with lower body mass index (<25), unintentional weight loss, ketoacidosis, and glucose >360 mg/dL at presentation. Adapted with permission from Holt RIG, et al. Diabetes Care 2021;44:2589-625¹

Diolch!





To read the latest summaries and sign up for Diabetes Distilled, visit https://www.pcdsociety.org/diabetes-distilled or scan the QR code