diabetesdistilled
the latest developments filtered for you

Pam Brown

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I have received funding from the following companies for providing educational sessions, documents, and for attending advisory boards and conferences:

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

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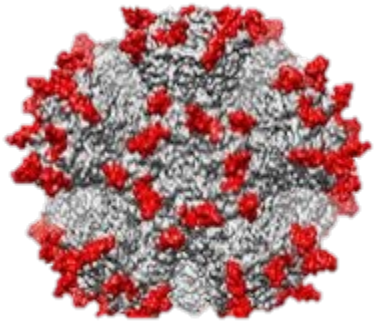
CKD: ADA/KDIGO consensus

Diabetes remission: ReTUNE

Guidelines
ADA/EASD physical activity



What might we do differently?

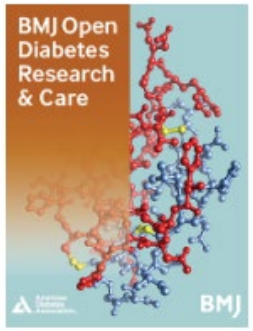
UKPDS
44 year follow up

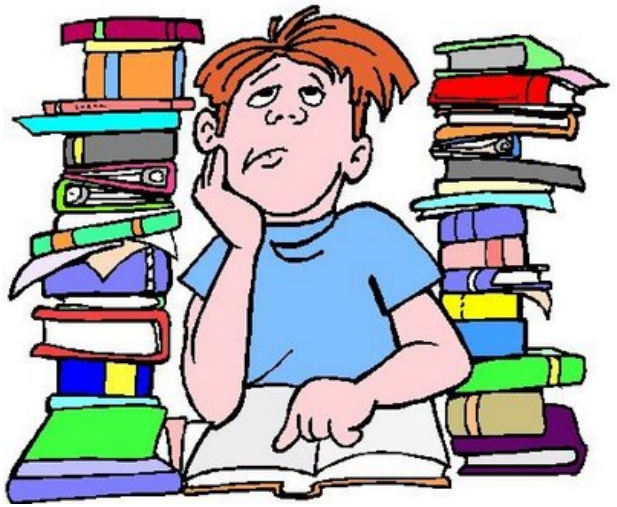
GLP-1 shortages

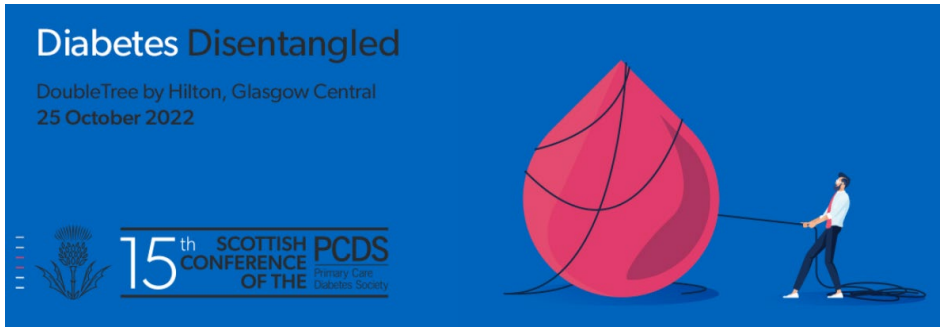
EASD

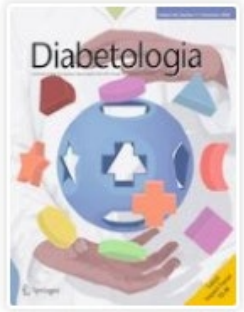
What's new in sleep?

Staying up to date









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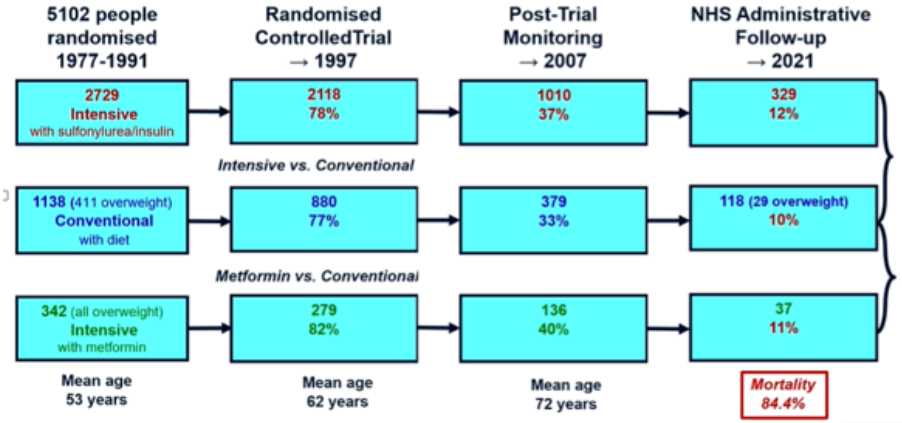
NICE National Institute for Health and Care Excellence

Management of hyperglycaemia in type 2 diabetes, 2022.
A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

Glycosmedia DIABETES NEWS SERVICE

What’s new from EASD?

44-Year Follow-up Symposium



UKPDS 33 Lancet 1998;352:837-853. UKPDS 80. N Engl J Med 2008;359:1577-89. Unpublished ukpds

- SU/insulin – 0.9% (10mmol/mol) difference
- Metformin – 0.6% (6mmol/mol) difference

Summary of Legacy Effects

- The *glycaemic legacy effect*, first identified in the UKPDS 30-year analyses, remains virtually unchanged after up to 44 years follow-up
- Early intensive blood glucose control with sulfonylurea or insulin led to:
  – 11% fewer deaths
  – 26% fewer microvascular complications
- The *metformin legacy effect*, first identified in the UKPDS 30-year analyses, also remains virtually unchanged after up to 44 years follow-up
- Early intensive blood glucose control with metformin led to:
  – 31% fewer heart attacks
  – 25% fewer deaths
- These landmark findings emphasise the critical importance of detecting and treating type 2 diabetes intensively at the earliest possible opportunity

Unpublished Data ukpds

Impact of Intensive Glucose Control with Sulfonylurea/Insulin

		Median Follow-up 10.0y	16.9y	17.4y
Aggregate Endpoint		**1997**	**2007**	**2021**
Any diabetes-related endpoint	*RRR:*	12%	9%	10%
	P:	0.029	0.040	0.016
Myocardial infarction	*RRR:*	16%	15%	15%
	P:	0.052	0.014	0.0074
Microvascular disease	*RRR:*	25%	24%	26%
	P:	0.0099	0.001	<0.0001
All-cause mortality	*RRR:*	6%	13%	11%
	P:	0.44	0.007	0.0093

RRR = Relative Risk Reduction, P = Log Rank

UKPDS 33 Lancet 1998;352:837-853. UKPDS 80. N Engl J Med 2008;359:1577-89. Unpublished data ukpds

Impact of Intensive Glucose Control with Metformin

		Median Follow-up 10.7y	17.7y	18.0y
Aggregate Endpoint		**1997**	**2007**	**2021**
Any diabetes-related endpoint	*RRR:*	32%	21%	19%
	P:	0.0023	0.013	0.015
Myocardial infarction	*RRR:*	39%	33%	31%
	P:	0.010	0.005	0.0037
Microvascular disease	*RRR:*	29%	16%	10%
	P:	0.19	0.31	0.49
All-cause mortality	*RRR:*	36%	27%	25%
	P:	0.011	0.002	0.002

RRR = Relative Risk Reduction, P = Log Rank

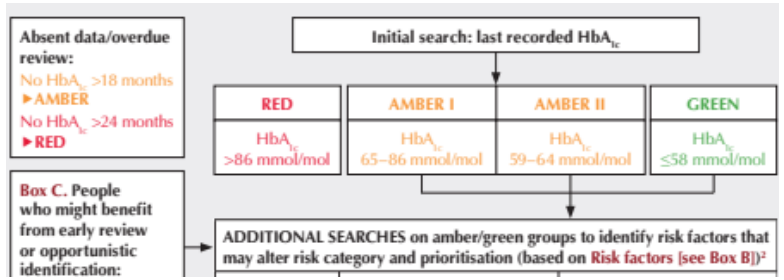
UKPDS 33 Lancet 1998;352:837-853. UKPDS 80. N Engl J Med 2008;359:1577-89. Unpublished data ukpds

Take Home Messages

- The *glycaemic legacy effect* in reality is the *hyperglycaemic legacy effect*
- Inadequate control of hyperglycaemia appears to induce irreversible pathophysiological changes, permanently increasing the risk of diabetic complications and of premature death
- Establishing and maintaining near-normoglycaemia from day 1 can minimise the risk of complications and prolong life
- Early metformin therapy appears to further reduce the risk of complications and further increase life expectancy
- Whilst newer glucose-lowering agents also reduce the risk of some diabetic complications, maintaining near-normoglycaemia is essential if the risk of complications is to be reduced to the greatest extent possible

Unpublished Data ukpds

How to prioritise primary care diabetes services during and post COVID-19 pandemic



How to manage high HbA_{1c} in people with type 2 diabetes

Before the consultation – review electronic record

	Clinical characteristic	
C	**During the consultation**	
	Action	
S	Share and discuss results, including self-monitoring blood glucose where relevant (is this compatible with HbA_{1c}?).	
O U N T R O L	Uncover reasons for high HbA_{1c}: • Medication – ask about adherence, administration, new medications, side effects. • Illness, including infections. • Lifestyle – diet, snacking, smoking, sleep, physical activity, relationships.	• Emotions and mental health problems – depression, anxiety, stress, loneliness, boredom, bereavement and break-ups. • Socioeconomic impact of COVID-19 – furloughed, long hours, job loss or change, food banks, family support. (See Resources 3)
G	Gather missing data (weight, BMI, waist circumference, blood pressure, foot exam, injection technique, injection sites). Glucose and ketone point-of-care tests, if at risk DKA/HHS. Ask about osmotic symptoms. New underlying disease or complications, comorbidities? (See Resources 4)	
A	Agree goals, management plan and further investigations needed. (See Resources 5)	
R	Resistance – are there barriers to new intervention(s)? (See Resources 6) Referrals – are further investigations appropriate (e.g. to exclude malignancy [see Box D overleaf] or to other specialist services, such as foot-care team, retinal screening, health coaching). Review date for bloods and follow-up.	

Jane and I have a Masterclass at PCDS National

We have lost time during the pandemic – late diagnoses, high HbA1c values
This too is likely to leave a (detrimental) legacy effect
Time to take action now!

B12 deficiency with metformin

The efficacy of vitamin B_{12} supplementation for treating vitamin B_{12} deficiency and peripheral neuropathy in metformin-treated type 2 diabetes mellitus patients: A systematic review

Samuel Pratama [a,*], Brigitta Cindy Lauren [a], Wismandari Wisnu [a,b]

Diabetes & Metabolic Syndrome: Clinical Research & Reviews 16 (2022) 102634

Metformin-induced vitamin B12 deficiency can cause or worsen distal symmetrical, autonomic and cardiac neuropathy in the patient with diabetes

David S. H. Bell MB

Diabetes Obes Metab. 2022;24:1423–1428.

Potential mechanisms:

- Decreased absorption
  - Altered intrinsic factor level, bacterial overgrowth
- Increased liver accumulation B12
- Altered bile acid enterohepatic circulation

Presentations

- Megaloblastic anaemia, glossitis
- Peripheral neuropathy, proprioception ↓
- Central neurological symptoms – poor memory, cognitive impairment, depression

- MHRA alert June 2022 – known risk, common (6-50%)
- Depletion begins early but presents 5-10 years
- Risk factors – Long term, high dose treatment, elderly, IBS, vegan diets, PPI or colchicine treatment
- Neurological involvement – urgent specialist support
- Consider oral therapy and recheck levels at 8-12 weeks
  - Cyanocobalamin 50-150mcg daily
  - If FBC and B12 not normalised, switch to IM

Has everyone on long term metformin had B12 checked?
Has everyone with diabetic neuropathy symptoms had a B12 level?
Have people given trial of oral therapy continued and been rechecked?
Has anyone on B12 injections been lost to follow up post-pandemic?

Metformin use and vitamin B12 deficiency: New MHRA guidance Sarah Davies

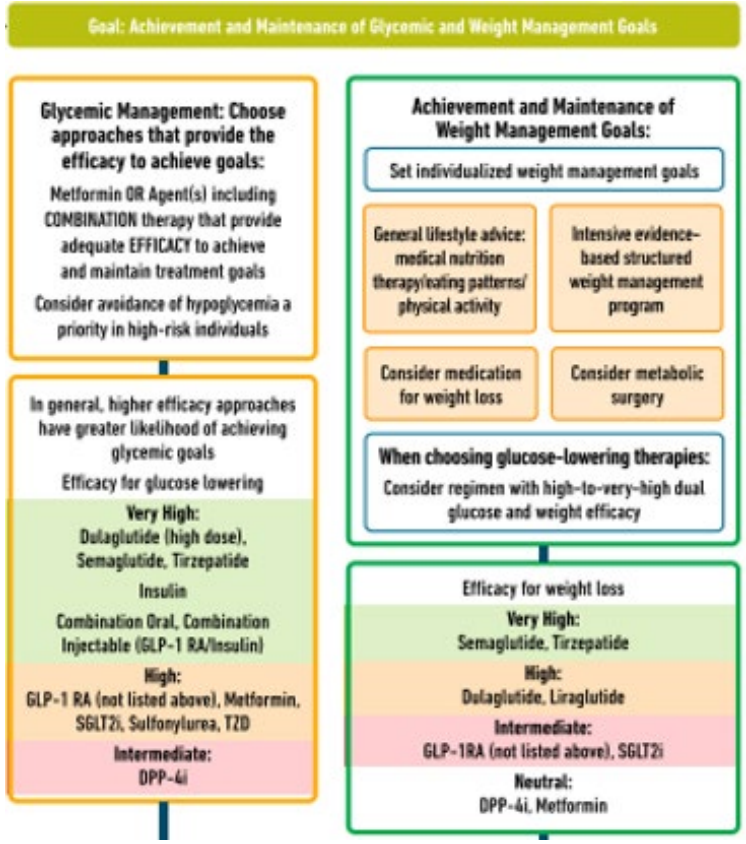
Journal of Diabetes Nursing Volume 26 No 5 2022

What’s new in guidelines?

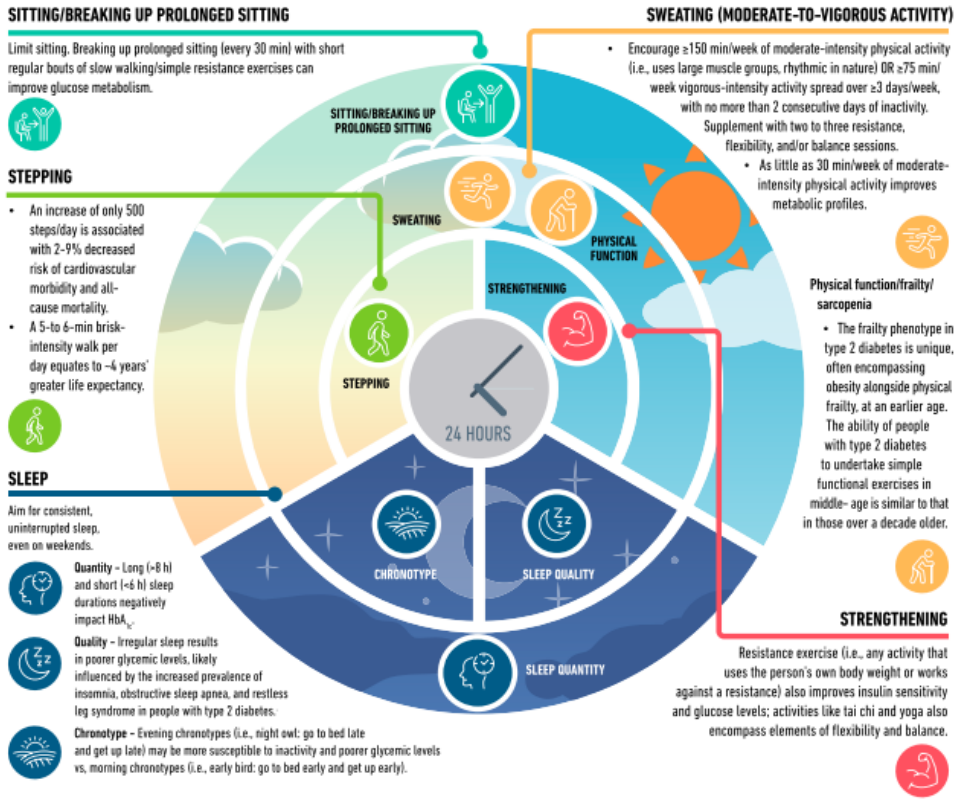
Management of Hyperglycemia in Type 2 Diabetes, 2022. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

Melanie J. Davies,[1,2] Vanita R. Aroda,[3] Billy S. Collins,[4] Robert A. Gabbay,[5] Jennifer Green,[6] Nisa M. Maruthur,[7] Sylvia E. Rosas,[8] Stefano Del Prato,[9] Chantal Mathieu,[10] Geltrude Mingrone,[11,12,13] Peter Rossing,[14,15] Tsvetalina Tankova,[16] Apostolos Tsapas,[17,18] and John B. Buse[19]

https://doi.org/10.2337/dci22-0034



IMPORTANCE OF 24-HOUR PHYSICAL BEHAVIORS FOR TYPE 2 DIABETES



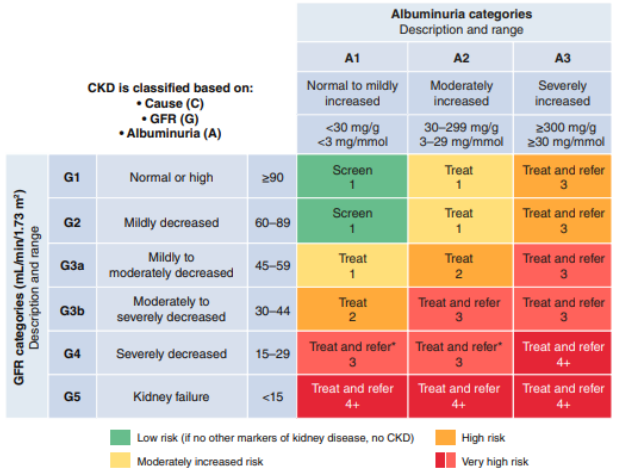
	Glucose/insulin	Blood pressure	HbA_{1c}	Lipids	Physical function	Depression	Quality of life
SITTING/BREAKING UP PROLONGED SITTING	↓	↓	↓	↓	↑	↓	↑
STEPPING	↓	↓	↓	↓	↑	↓	↑
SWEATING (MODERATE-TO-VIGOROUS ACTIVITY)	↓	↓	↓	↓	↑	↓	↑
STRENGTHENING	↓	↓	↓	↓	↑	↓	↑
ADEQUATE SLEEP DURATION	↓	↓	↓	↓	?	↓	↑
GOOD SLEEP QUALITY	↓	↓	↓	↓	?	↓	↑
CHRONOTYPE/CONSISTENT TIMING	↓	?	↓	?	?	↓	?

IMPACT OF PHYSICAL BEHAVIORS ON CARDIOMETABOLIC HEALTH IN PEOPLE WITH TYPE 2 DIABETES

CONSENSUS REPORT | OCTOBER 03 2022

Diabetes Management in Chronic Kidney Disease: A Consensus Report by the American Diabetes Association (ADA) and Kidney Disease: Improving Global Outcomes (KDIGO) FREE

Ian H. de Boer; Kamlesh Khunti; Tami Sadusky; Katherine R. Tuttle; Joshua J. Neumiller; Connie M. Rhee; Sylvia E. Rosas; Peter Rossing; George Bakris



CKD is classified based on: • Cause (C) • GFR (G) • Albuminuria (A)				Albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–299 mg/g 3–29 mg/mmol	≥300 mg/g ≥30 mg/mmol
GFR categories (mL/min/1.73 m²) Description and range	G1	Normal or high	≥90	Screen 1	Treat 1	Treat and refer 3
	G2	Mildly decreased	60–89	Screen 1	Treat 1	Treat and refer 3
	G3a	Mildly to moderately decreased	45–59	Treat 1	Treat 2	Treat and refer 3
	G3b	Moderately to severely decreased	30–44	Treat 2	Treat and refer 3	Treat and refer 3
	G4	Severely decreased	15–29	Treat and refer* 3	Treat and refer* 3	Treat and refer 4+
	G5	Kidney failure	<15	Treat and refer 4+	Treat and refer 4+	Treat and refer 4+

Low risk (if no other markers of kidney disease, no CKD) · Moderately increased risk · High risk · Very high risk

Risk, monitoring frequency, when to treat and refer

Do we share CKD diagnosis and education?

Without ACR, impossible to understand risk and agree treatments

Chronic kidney disease: assessment and management

NICE guideline
Published: 25 August 2021
www.nice.org.uk/guidance/ng203

Dapagliflozin for treating chronic kidney disease

Technology appraisal guidance
Published: 9 March 2022
www.nice.org.uk/guidance/ta775

- Test more people

- diabetes
- hypertension
- previous episode of acute kidney injury
- cardiovascular disease
- structural renal tract disease, recurrent renal calculi or prostatic hypertrophy
- multisystem diseases with potential kidney involvement
- gout
- family history of end-stage renal disease or hereditary kidney disease
- incidental haematuria or proteinuria

- Use age, sex, ACR, eGFR to calculate 5 year failure risk https://kidneyfailurerisk.co.uk/

- Referral clarity:
  - >5% 5 year risk kidney failure
  - eGFR ↓ >25% and change in category in 12 months; sustained ↓ 15% in 12 months;
  - ACR >70mg/mmol, ACR >30mg/mmol and haematuria; poorly controlled BP on 4 drugs

SGLT2 inhibitors: Indications, doses and licences in adults

Indications, doses and licences of SGLT2 inhibitors, by indication.

Indication	Drug and dose	Initiate	Stop/reduce	Notes
Insufficiently controlled type 2 diabetes (as an adjunct to diet and exercise)	**Canagliflozin 100 mg** Increase to **300 mg** if required	eGFR ≥30* eGFR ≥60	Stop if eGFR persistently <30 and ACR <30 mg/mmol.* Can continue to dialysis/transplant if ACR ≥30 mg/mmol.* Reduce to 100 mg if eGFR <60	*All four SGLT2 inhibitors are licensed for use at eGFR <45; however, due to their mode of action, they have **reduced glucose-lowering effects at eGFR <45. Add another glucose-lowering drug if HbA_{1c} is above the agreed, individualised, target** †Empagliflozin is licensed for initiation to eGFR ≥30 in those with established CVD and can be continued down to eGFR 30
	Dapagliflozin 10 mg	eGFR ≥15*	No lower eGFR limit for continuation.* Specialist discussion as dialysis/transplant approaches	
	Empagliflozin 10 mg Increase to **25 mg** if required	eGFR ≥60† eGFR ≥60	Reduce to 10 mg if eGFR <60 Stop if eGFR <45 (T2D alone) or <30* (T2D and CVD)	
	Ertugliflozin 5 mg Increase to **15 mg** if required	eGFR ≥45 eGFR ≥45	Stop if eGFR persistently <30*	
Diabetic kidney disease/chronic kidney disease (DKD/CKD)	**Dapagliflozin 10 mg**	eGFR ≥15‡	No lower eGFR limit for continuation. Specialist discussion as dialysis/transplant approaches	Use with other CKD therapies With or without type 2 diabetes ‡NICE TA775 and SMC2428 advise initiation in people with eGFR 25–75 and type 2 diabetes or ACR ≥22.6 mg/mmol (≥23 mg/mmol in SMC2428)
Diabetic kidney disease (DKD)	**Canagliflozin 100 mg**	eGFR ≥30	Stop if eGFR persistently <30 and ACR <30 mg/mmol. Can continue to dialysis/transplant if ACR ≥30 mg/mmol	Add on to standard of care (e.g. ACEi or ARB) for DKD
Symptomatic chronic HF	**Empagliflozin 10 mg**	eGFR ≥20	Stop if eGFR <20; should not be used in those with end-stage renal disease or on dialysis	With or without type 2 diabetes
Symptomatic chronic HFrEF	**Dapagliflozin 10 mg**	eGFR ≥15	No lower eGFR limit for continuation. Specialist discussion as dialysis/transplant approaches	With or without type 2 diabetes

eGFR presented in mL/min/1.73 m^2.
ACEi=angiotensin-converting enzyme inhibitor; ACR=albumin:creatinine ratio; ARB=angiotensin receptor blocker; CVD=cardiovascular disease; eGFR=estimated glomerular filtration rate; HF=heart failure; HFrEF=heart failure with reduced ejection fraction.

Information correct on 6th July 2022. **Licence amendments frequent – view most recent version.**
Always consult the electronic BNF or the Summaries of Product Characteristics (SPCs) prior to prescribing any drug.
SPCs: Canagliflozin | Dapagliflozin | Empagliflozin | Ertugliflozin

Author: Pam Brown, GP, Swansea
Citation: Brown P (2022) SGLT2 inhibitors: Indications, doses and licences in adults. Updated July 2022. *Diabetes & Primary Care* **24**: 111–12

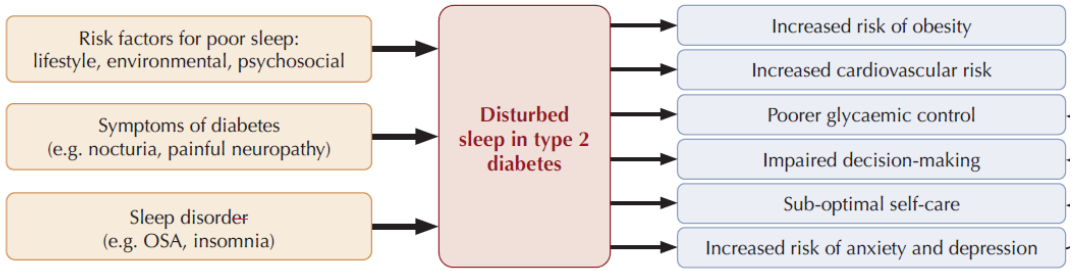
What’s new in sleep?

Lifestyle discussions: At a glance factsheet
Sleep and type 2 diabetes

Sarah Steven and Martin Rutter

- Shift workers with T2DM: ↑ HbA1c, poorer mental health, ↑ microvascular complications
- Frequent insomnia: ↑ HbA1c, obesity, CVD

Causes and consequences of sleep disturbance in people with type 2 diabetes



REVIEW ARTICLE

Sleep, circadian rhythms, and type 2 diabetes mellitus

Gokul Parameswaran[1,2] | David W. Ray[1,2]

- Sleep deprivation and circadian misalignment interact
- Average 1 hour less sleep/night – 7-8 hrs optimal
- Sleep deprivation ↑ calories (385kcals) and carb snacks evenings
- 'Living against the clock' - social jet lag 70% people
- 20% workforce work shifts
- Circadian misalignment ↑ insulin resistance

Open access revie *Clinical Endocrinology*. 2022;96:12–20.

Do we ask about sleep?
Do we know who works shifts?
Do we identify sleep disorders?

What’s new in remission?

The Reversal of Type 2 diabetes upon normalisation of energy intake in the Non-Obese – The ReTUNE study

- ReTUNE: Average BMI 24.8; average age 59 years
- Aim 10-15% loss – average 7.7kg, 10.7%; stable 6-12 months
- Up to 3 weight loss cycles:
  - 2-4 weeks low calorie 800kcal/day meal replacement
  - 4-6 weeks weight maintenance – 5% aim each cycle
- 20 people with T2DM and 20 controls; 12 month
- Remission 10 after cycle 1 , 3 after cycle 2, 1 after cycle 3 – 14/20, 70% achieved remission
- BMI decreased from 24.8 to 22.4
- Imaging:
  - Liver fat 4.1% and decreased to 1.4%; baseline 3x liver fat v controls
  - Pancreas fat decreased from 5.8% to 4.3%
- Supports Personal Fat Threshold - exceed and develop T2DM; same mechanism for remission as in heavier people with T2DM

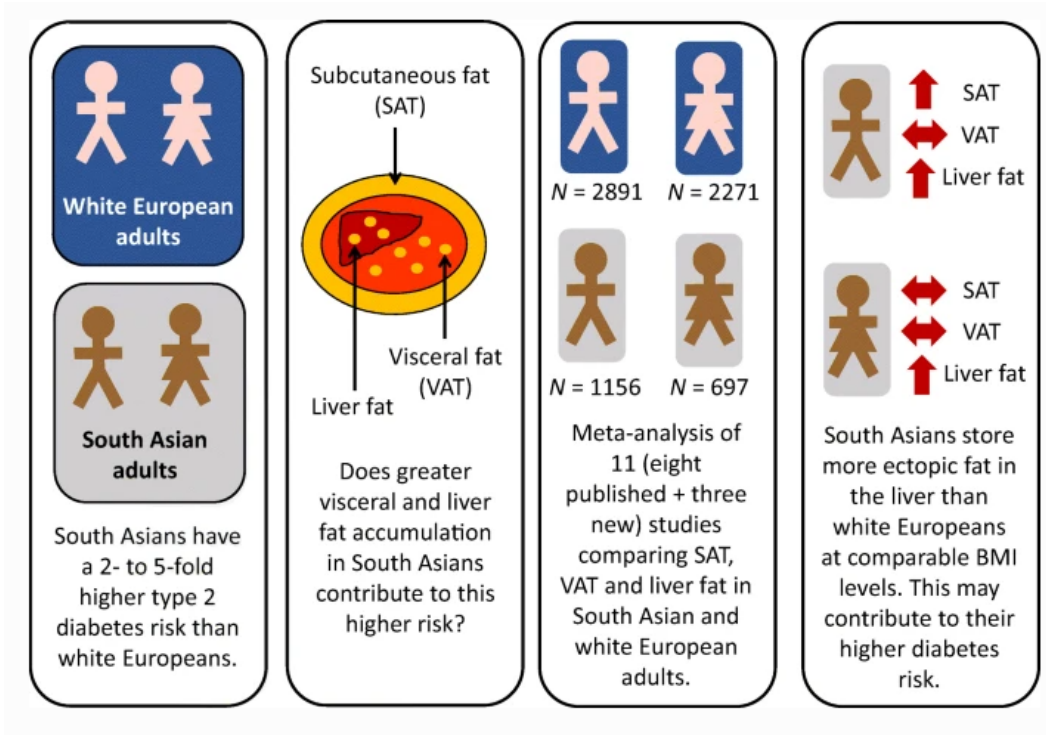
Do we remember to discuss remission as an option?
Do we discuss weight loss with people with T2DM?

Diabetologia
https://doi.org/10.1007/s00125-022-05803-5

ARTICLE

Liver, visceral and subcutaneous fat in men and women of South Asian and white European descent: a systematic review and meta-analysis of new and published data

Stamatina Iliodromiti[1,2] · James McLaren[3] · Nazim Ghouri[3] · Melissa R. Miller[4] · Olof Dahlqvist Leinhard · Jennifer Linge[5] · Stuart Ballantyne[7] · Jonathan Platt[7] · John Foster[8] · Scott Hanvey[9] · Unjali P. Gujral[10] · Alka Kanaya[11] · Naveed Sattar[3] · Mary Ann Lumsden[2] · Jason M. R. Gill[3]



What’s new in dementia?

biobank uk
Improving the health of future generations

JAMA Neurology | Brief Report

Association of Daily Step Count and Intensity With Incident Dementia in 78 430 Adults Living in the UK

Borja del Pozo Cruz, PhD; Matthew Ahmadi, PhD; Sharon L. Naismith, PhD; Emmanuel Stamatakis, PhD

JAMA Neurol. 2022;79(10):1059-1063. doi:10.1001/jamaneurol.2022.2672
Published online September 6, 2022. Corrected on September 9, 2022.

- N= 78,430 median follow up 6.9 years
- Incidental and purposeful steps based on cadence
- Optimal risk reduction all cause dementia HR 0.49 - 9,826 steps
- Minimum dose 25% reduction with 3,826 steps
- Higher intensity stepping stronger associations
- Limitations – observational data; age/lack of formal assessment may have limited cases
- 4400 steps associated with ↓ mortality previously [1]

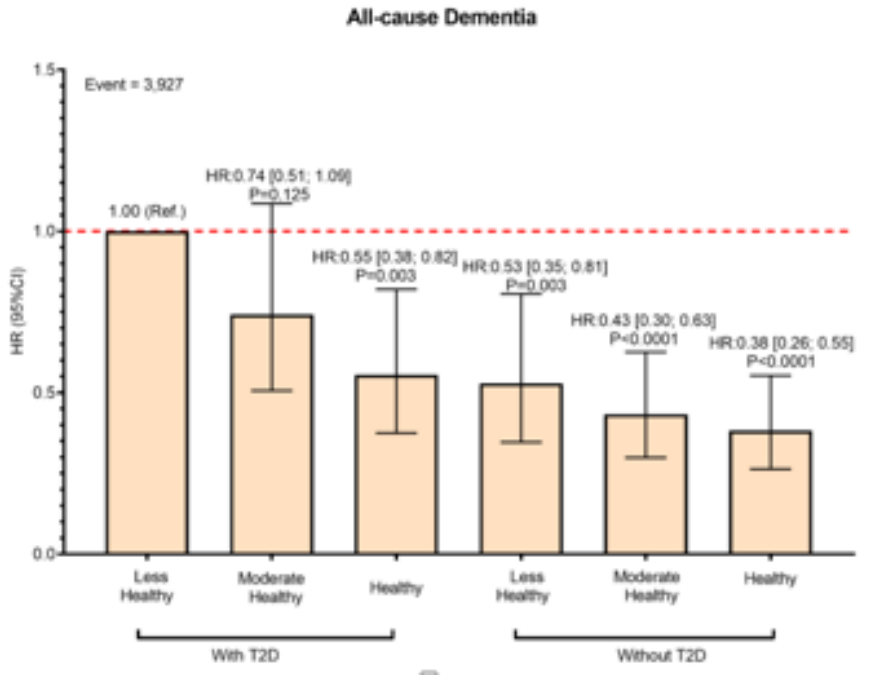
1. Saint-Maurice et al JAMA 2022: 323; 151-160

Does health-related lifestyle modify association between T2DM and dementia. UK Biobank

Boonpor, Glasgow

- N= 445,364 mean age 55.6; median 9 years (after excluding years 1-2)
- TV time, sleep duration, PA, alcohol, smoking, processed/red meat, fruit, egg and oily fish
- T2DM associated with 33% increase dementia
- Healthy lifestyle almost halves dementia risk in T2DM

Abstract 319 EASD



How should we manage GLP-1RA shortages?

PCDS consensus statement: A strategy for managing the supply shortage of the GLP-1 RAs Ozempic and Trulicity

Hannah Beba
Consultant Pharmacist, Diabetes Leeds Health and Care Partnership

Clair Ranns
Senior Pharmacist, Diabetes Leeds Health and Care Partnership

Clare Hambling
GP, Norfolk, and Chair of PCDS

Jane Diggle
Specialist Diabetes Nurse Practitioner, West Yorkshire, and co-Vice Chair of PCDS

Pam Brown
GP, Swansea

Proactive approach – write to warn people of potential shortages OR
Reactive approach – deal with supply problems as they occur
Close liaison with local pharmacies
New demo pens?

- Based on guidance from Department Health and Social Care re supply shortages
- DO NOT INITIATE new people on dulaglutide or semaglutide
- Dose increases dulaglutide can continue; semaglutide intermittent shortages 0.5/1mg
- DO NOT RECOMMEND DOUBLE DOSES OF SEMAGLUTIDE ie 2 x 0.5mg instead of 1mg

Alternative GLP-1 RAs until shortages resolve

Table 1. Options for initiating GLP-1 receptor agonists or switching from Ozempic (subcutaneous semaglutide) to an alternative GLP-1 receptor agonist owing to supply issues.

	Option 1: Rybelsus (oral semaglutide)	Option 2: Victoza (liraglutide)	Option 3: Byetta or Bydureon (exenatide)
Drug description	Once daily oral tablet Available in three doses: 3 mg (starter dose), 7 mg and 14 mg (maintenance doses)	Once daily subcutaneous injection Prefilled, multi-use, disposable pen containing 18 mg liraglutide, allowing delivery of three dose strengths: 0.6 mg, 1.2 mg and 1.8 mg	**Byetta:** Twice daily subcutaneous injection Prefilled, multi-use disposable pens (available in 5 µg and 10 µg doses) **Bydureon:** Once weekly subcutaneous injection Prefilled, single-use, disposable pen: dose 2 mg
How to initiate if naïve to GLP-1 RA therapy or switch if on Ozempic 0.25 mg	Start at a dose of 3 mg once daily for 1 month, then increase to 7 mg once daily for at least 1 month if tolerated. Based on individual need, dose may be increased to 14 mg once daily	Start at 0.6 mg once daily and increase to 1.2 mg once daily after 1 week	**Byetta:** Initiate at 5 µg twice daily for at least 1 month. Dose can then be increased to 10 µg twice daily **Bydureon:** 2 mg once weekly (no dose titration needed)
How to if already on Ozempic 0.5 mg or 1.0 mg	Start at a dose of 7 mg once daily, titrating up to 14 mg once daily after 1 month if tolerated. To cut down on general practice workload, consider issuing an acute prescription for the 7 mg tablets and a repeat prescription for the 14 mg (14 mg is equivalent in HbA_{1c}-lowering efficacy to Ozempic 0.5 mg). Some people may wish to start on 14 mg straight away.	Start at a dose of 1.2 mg once daily for at least 1 week (note the 1.8 mg dose is not usually recommended due to cost)	**Byetta:** Start at 10 µg twice daily, to be taken within 1 hour before two main meals (at least 6 hours apart) **Bydureon:** start at 2 mg once weekly

Diabetes & Primary Care

Part of Diabetes ONTHENET

Diolch!

https://www.pcdsociety.org/diabetes-distilled