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Korean doctor says those who haven't contracted COVID-19 have no friends

Rebecca Moon · 14 hours ago

Image: KAIST Mommyson


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Disclosures 2022/23

Speaker fees: Amarin, Amgen, AstraZeneca, Boehringer Ingelheim, Daiichi Sankyo, Dexcom, GSK, Lilly, Menarini, Napp, Novartis, Novo Nordisk

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Conference attendance: AstraZeneca, Novo Nordisk

I have many doubts about modern medicine

Type 2 Diabetes Cardiovascular Renal Metabolic Review Checklist

Medscape UK X Guidelines
Primary Care Hacks

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Consider the following during T2D CVRM shared decision making:

Lifestyle Considerations

- ☐ Assess weight (e.g. BMI or WHR) and discuss individualised weight loss goals as appropriate. Remember to ethnically adjust these goals where indicated[1]
- ☐ Discuss the importance of 24-hour physical behaviours for T2D[2]
  - o sitting/breaking up prolonged sitting
  - o sweating
  - o strengthening
  - o sleep
  - o stepping
- ☐ Strive for remission of T2D if possible,[3] irrespective of weight.[4] Weight loss of 5–10% confers metabolic improvement; weight loss of 10–15% or more can have a disease-modifying effect and lead to remission of T2D[2]

Individualised HbA_{1c} Goals

- ☐ Review the person's current HbA_{1c} and trend, and consider other factors when individualising HbA_{1c} goals, e.g.:
  - o risks potentially associated with hypoglycaemia and other drug adverse effects
  - o life expectancy
  - o comorbidities
  - o established vascular complications
  - o patient preference, resources, and support systems[5]
- ☐ See the expert consensus statement on diabetes and frailty for individualising management in older adults and/or adults with frailty and T2D

Kidneys

- ☐ Individualise HbA_{1c} targets in people with diabetic kidney disease
  - o be aware that all SGLT2is have negligible glucose-lowering effect once eGFR falls below 45 ml/min, so consider adding in an additional glucose-lowering medication such as a GLP-1 RA
- ☐ If eGFR <60 ml/min/1.73 m^2 **or** clinically significant proteinuria (ACR ≥3 mg/mmol) **and** on maximally tolerated dose of ACEi/ARB: consider adding SGLT2i with renal protective benefits,[2] irrespective of HbA_{1c}
  - o see the Primary Care Hack, *Extra-Glycaemic Indications of SGLT2 Inhibitors*
- ☐ If CKD present, offer atorvastatin 20 mg for primary or secondary prevention of CVD[6]
- ☐ Offer aspirin or clopidogrel to adults with CKD for the secondary prevention of CVD,[7] but be aware of the risk of bleeding
- ☐ Consider referral as per NICE criteria, or if 5-year risk of requiring renal replacement therapy is >5% (measured using the Four-Variable Kidney Failure Risk Equation)

Blood Pressure

There is considerable debate around optimal BP targets for people living with diabetes, with several conflicting guidelines published

- ☐ **First instance:** aim for a HBPM average target of <135/85 mmHg (<140/90 mmHg clinic target) in all people[8]
- ☐ **Provided treatment is well tolerated:** then aim for HBPM average of 125/75 mmHg (130/80 mmHg clinic target) or lower in most people[8]
- ☐ **For adults aged >80 years:** consider a clinic BP target of <150/90 mmHg[9]
- ☐ **For people living with T2D:** start drug treatment with an ACEi/ARB,[9] irrespective of age or ethnic background
- ☐ Measure sitting and standing BP in people with hypertension and T2D.[9] In those with a significant postural drop in BP (i.e., ≥20 mmHg systolic and/or ≥10 mmHg diastolic that occurs on standing[10]), treat to a BP target based on the standing BP

Note: SGLT2is have a modest impact on BP, lowering it by around 4/2 mmHg[11]

Lipids

- ☐ LDL-C targets for people living with T2D:[12]
  - o moderate risk: <2.6 mmol/l
  - o high risk: ≥50% reduction from baseline **and** <1.8 mmol/l
  - o very high risk: ≥50% reduction from baseline **and** <1.4 mmol/l
- ☐ Patient's QRISK3 is ≥10%: offer atorvastatin 20 mg for primary prevention of CVD[6][13]
- ☐ If LDL-C targets are not achieved on maximally tolerated dose statin, consider combination lipid-lowering therapy e.g., add in ezetimibe, bempedoic acid, or PCSK9 inhibitor[12]
- ☐ For secondary prevention of CVD, offer atorvastatin 80 mg[12]

Continued overleaf...

NAFLD

- ☐ Noninvasive tests for liver fibrosis risk may be advisable due to the strong association of T2D with NAFLD[14][15][16]
- ☐ Consider FIB-4 test to assess for underlying fibrosis risk in people aged 35–65 years
- ☐ If identified as intermediate or high risk, consider referral to secondary care gastroenterology for transient elastography (FibroScan)
- ☐ Strongly encourage and facilitate weight loss where possible: weight loss 3–5% reduces hepatic steatosis, ≥5–7% can lead to resolution of NASH, and ≥10% improves hepatic fibrosis[17]
- ☐ There is emerging evidence for the benefits of metabolic surgery and GLP-1 RAs, and pioglitazone[2] for NAFLD

Comorbidities and Life Story

- ☐ Consider presence of:
  - o CVD or high risk of CVD:[2][18]
    - ASCVD (i.e. IHD/TIA/stroke/PVD): if present, offer early combination therapy with metformin and an SGLT2i, irrespective of HbA_{1c}[18]
    - all subtypes of HF: if present, offer early combination therapy with metformin and an SGLT2i, irrespective of HbA_{1c}[18]
    - QRISK3 ≥10% and age >40 years, or presence of hypertension, dyslipidaemia, smoking, obesity, or family history (in a first-degree relative) of premature cardiovascular disease: consider early combination therapy with metformin and an SGLT2i, irrespective of HbA_{1c}[18]
  - o CKD and proteinuria[2][18] (see Kidney section)
  - o obesity:[2][17] both SGLT2is and GLP-1 RAs can facilitate weight loss in people living with T2D
  - o retinopathy:[18] be aware of the possibility of worsening of pre-existing retinopathy if HbA_{1c} is rapidly lowered
  - o OSAHS; these conditions are commonly associated with T2D.[2][19] Consider using the Epworth sleepiness scale and the STOP–BANG questionnaire to exclude underlying OSAHS
- ☐ Educate women of childbearing age that many medications (e.g. ACEis, ARBs, statins, SGLT2is, and GLP-1 RAs) are contraindicated in pregnancy, and counsel them regarding contraception.[20][21] If planning pregnancy, refer to pre-pregnancy services
- ☐ Consider age, functional and frailty status, occupation, literacy level, and other social determinants of health during shared decision making[2][7][18]

Prescribing Considerations

- ☐ Discuss adherence and if necessary explore barriers/preferences[2][18][21]
- ☐ Review history of hypoglycaemia/hypoglycaemia awareness, DVLA adherence, and CBG monitoring where appropriate, and consider CGM in all people with T2D on insulin[2][18]
- ☐ Sick-day guidance[20][21]
  - o for people with T2D on insulin
  - o review the SADMANS mnemonic. Consider temporarily pausing these drugs during any significant intercurrent illness, but remind individuals to restart once they are eating and drinking normally and recovered from their illness
- ☐ SGLT2i or GLP-1 RA commenced:
  - o consider reduction in SU or insulin dose. If on insulin, consider cautiously reducing insulin dose, increase CBG monitoring, and contact DSN as required[17][22][23]
  - o consider adjustment of any dose of diuretic when introducing an SGLT2i[20][24][25]
- ☐ Ensure appropriate/optimal prescribing; consider de-intensifying in the context of functional dependence and frailty[26]

MDT Referrals

- ☐ DSMES (e.g. DESMOND or X-Pert)
- ☐ Consider any locally available physical activity referral pathway
- ☐ Regular retinopathy screening
- ☐ Regular foot screening
- ☐ Consider secondary care as required, e.g., diagnostic uncertainty or treatment option advice
- ☐ Consider dietician referral, and psychological counselling for diabetes distress

Coding

- ☐ Code identified conditions as 'priority 1'
- ☐ Do not code 'diabetes resolved'; instead, code 'diabetes in remission'

Follow Up

- ☐ Goal setting—Diabetes UK information prescriptions can help to facilitate goal setting, information sharing, and care planning
- ☐ Set a defined timescale for follow up and consider regular monitoring as clinically indicated
- ☐ Regular monitoring of weight, BP, HbA_{1c}, renal function (both eGFR and urinary ACR), and lipid profile as clinically indicated (at least annually).

Abbreviations: **ACEi**=angiotensin-converting enzyme inhibitor; **ACR**=albumin to creatinine ratio; **ARB**=angiotensin receptor blockers; **ASCVD**=atherosclerotic cardiovascular disease; **BP**=blood pressure; **CBG**=capillary blood glucose; **CGM**=continuous glucose monitoring; **CHF**=congestive heart failure; **CKD**=chronic kidney disease; **CVD**=cardiovascular disease; **CVRM**=cardiovascular, renal, and metabolism; **DESMOND**=diabetes education and self-management for ongoing and newly diagnosed; **DSMES**=diabetes self-management, education, and support; **DSN**=diabetes specialist nurse; **DVLA**=Driver and Vehicle Licensing Agency; **eGFR**=estimated glomerular filtration rate; **FIB-4**=Fibrosis-4; **GLP-1 RA**=glucagon-like peptide-1 receptor agonist; **HbA_{1c}**=haemoglobin A_{1c}; **HBPM**=home blood pressure monitoring; **HDL-C**=high-density lipoprotein cholesterol; **HF**=heart failure; **HFpEF**=heart failure with preserved ejection fraction; **HFrEF**=heart failure with reduced ejection fraction; **IHD**=ischaemic heart disease; **LDL-C**=low-density lipoprotein cholesterol; **MDT**=multidisciplinary team; **NAFLD**=nonalcoholic fatty liver disease; **OSAHS**=obstructive sleep apnoea hypopnoea syndrome; **PARS**=Physical Activity Referral Service; **PVD**=peripheral vascular disease; **QRISK3**=Cardiovascular Risk Score 3; **SGLT2i**=sodium–glucose cotransporter-2 inhibitor; **STOP–BANG**=snoring history, tired during the day, observed stop breathing while sleep, high blood pressure, BMI >35 kg/m^2, age >50 years, neck circumference >40 cm, and male gender; **SU**=sulfonylurea; **TIA**=transient ischaemic attack; **T2D**=type 2 diabetes; **WHR**=waist to hip ratio.

For references, view the webpage for this Primary Care Hack at bit.ly/407CT9G

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Extra-Glycaemic Indications of SGLT2 Inhibitors

Medscape UK X Guidelines
Primary Care Hacks

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● **Initiate or continue as described** ● **Continue as described** ● **Not recommended**

SGLT2	Indication	CKD stage (mL/min/1.73 m²)				
		Stages G1 and G2 eGFR ≥60	Stage G3a eGFR 45–59	Stage G3b eGFR 30–44	Stage G4 eGFR 15–30	Stage G5 eGFR <15
Canagliflozin	Treatment of diabetic kidney disease in adults with T2D as add-on to standard of care	Initiate or continue 100 mg			If urinary ACR ≥30 mg/mmol, continue 100 mg and continue dosing until dialysis or renal transplantation. Do not initiate if eGFR <30	
Dapagliflozin	Treatment of symptomatic chronic heart failure regardless of ejection fraction (HFrEF and HFpEF) in adults with or without T2D	Initiate or continue 10 mg				No dose adjustment is required based on renal function. It is not recommended to initiate if eGFR <15
	Treatment of CKD in adults with or without T2D	Initiate or continue 10 mg*				No dose adjustment is required based on renal function. It is not recommended to initiate if eGFR <15
Empagliflozin	Treatment of symptomatic chronic heart failure regardless of ejection fraction (HFrEF and HFpEF) in adults with or without T2D	Initiate or continue 10 mg				Not recommended if eGFR <20
	Cardiovascular risk reduction as add-on to standard of care in adults with T2D and established cardiovascular disease	Initiate or continue 10 mg			Not recommended if eGFR <30	

- The glucose-lowering efficacy of all SGLT2 inhibitors is dependent on renal function and is reduced when eGFR <45 and likely absent in people with severe renal impairment. Therefore, if eGFR falls <45, additional glucose-lowering treatment should be considered in people living with T2D.
- SGLT2 inhibitors are not recommended for people living with T1D.

* 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)

Table based on author's interpretation of relevant summaries of product characteristics. At time of publication, ertugliflozin has no extra-glycaemic indications.

Abbreviations: ACR: albumin/creatinine ratio; **CKD:** chronic kidney disease; **eGFR:** estimated glomerular filtration rate; **HFpEF:** heart failure with preserved ejection fraction; **HFrEF:** heart failure with reduced ejection fraction; **NICE TA:** NICE technology appraisal; **SGLT2:** sodium–glucose cotransporter 2; **SMC:** Scottish Medicines Consortium; **T1D:** type 1 diabetes; **T2D:** type 2 diabetes.

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What Next After Metformin?

Medscape UK X Guidelines

Primary Care Hacks

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This Medscape UK Primary Care Hack is intended to help guide our choice of medication for the management of people living with type 2 diabetes. As always, we should take an individualised and holistic approach to the care of people living with type 2 diabetes.

	Biguanides (Metformin)	SGLT2 Inhibitors (Canagliflozin, Dapagliflozin, Empagliflozin, Ertugliflozin)	GLP-1 Receptor Agonists (Dulaglutide, Exenatide, Liraglutide, Lixisenatide, Semaglutide)	DPP-4 Inhibitors or 'Gliptins' (Alogliptin, Linagliptin, Saxagliptin, Sitagliptin, Vildagliptin)	Thiazolidinediones (Pioglitazone)	Sulfonylureas (Gliclazide, Glimepiride, Glipizide)
	Reinforce the importance of 24-hour physical behaviours for T2D. See: *Management of Hyperglycemia in Type 2 Diabetes, 2022. A Consensus Report by the American Diabetes Association and the European Association for the Study of Diabetes*					
Mode of Action	Decreases hepatic glucose production and reduces IR	Insulin-independent; inhibits renal glucose reabsorption by blocking SGLT2 transporter	Stimulates glucose dependent insulin release from the pancreas	Increases GLP-1 levels by blocking DPP-4 enzyme that inactivates GLP-1	Insulin-dependent; reduces hepatic and peripheral IR at a molecular level	Stimulates insulin secretion from pancreatic beta-cells
Glycaemic Efficacy	Moderate/high	Moderate/high	High	Low/moderate	Moderate	High
Impact on	Weight loss +	Weight loss ++	Weight loss +++	Weight neutral	Weight gain +++	Weight gain ++

The Diagnosis and Classification of Diabetes in Primary Care

Medscape UK X Guidelines

Primary Care Hacks

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	T1D	LADA	T2D	Monogenic Diabetes	GDM	T3cD (Pancreatogenic)
Pathophysiology	Autoimmune destruction of pancreatic beta cells Clinical diagnosis ± PG and ketone levels. Urgent specialist discussion required It is increasingly challenging to differentiate T1D from T2D, partly due to the obesity	LADA is essentially 'slow-onset' T1D Gradual autoimmune destruction of pancreatic beta cells. Diagnosis and management similar to T1D See Diabetes UK's *Latent autoimmune diabetes in adults*	IR with relative insulin deficiency T2D is usually diagnosed when HbA_{1c} ≥48 mmol/mol. If use of HbA_{1c} is inappropriate (e.g. pregnant women, genetic variants [HbS or HbC trait], acute or chronic blood loss, end-stage kidney disease) than T2D	Genetic mutation leading to diabetes. Most common is MODY See diabetesgenes.org for diagnosis guidance	Impaired glucose tolerance in pregnancy due to pancreatic beta-cell dysfunction on background of IR NICE NG3[1] diagnostic criteria: FPG ≥5.6 mmol/l or 2-hour PG post 75 g OGTT ≥7.8 mmol/l, i.e. much lower than the diagnostic criteria for	Diabetes associated with disease, trauma or surgery of the exocrine pancreas Causes include acute and chronic pancreatitis, pancreatic surgery, cystic fibrosis, haemochromatosis and pancreatic cancer See Pancreatic

The Pharmacological Management of Hyperglycaemia in People Living with Type 2 Diabetes and Chronic Kidney Disease

Medscape UK X Guidelines
Primary Care Hacks

Author: Dr Kevin Fernando, GP Partner, North Berwick Health Centre; Content Advisor, Medscape Global and UK. Email: kfernando@webmd.net

● No dose adjustment needed ● Dose adjustment or further action recommended ● Not recommended

	CKD stage (ml/min/m²)				
	Stages G1 and G2 eGFR ≥60	Stage G3a eGFR 45–59	Stage G3b eGFR 30–44	Stage G4 eGFR 15–30	Stage G5 eGFR <15
Metformin	3 g total maximum daily dose (in 2–3 daily doses)	2 g total maximum daily dose (in 2–3 daily doses)	1 g total maximum daily dose (in 2–3 daily doses)		
Sulfonylureas		Increased risk of hypoglycaemia if eGFR <60. Consider reducing dose. Gliclazide and glipizide preferred as metabolised in the liver			
Repaglinide					
Acarbose					Avoid if CrCl <25 ml/min/1.73 m²
Pioglitazone					Avoid in those on dialysis
Alogliptin			Reduce to 12.5 mg od if CrCl ≤50 ml/min	Reduce to 6.25 mg od if CrCl <30 ml/min or dialysis required	
Linagliptin					
Saxagliptin		Reduce to 2.5 mg od			Avoid in those on dialysis
Sitagliptin			Reduce to 50 mg od	Reduce to 25 mg od	
Vildagliptin			Reduce to 50 mg od if CrCl <50 ml/min		
Canagliflozin	Initiate 100 mg and titrate to 300 mg if additional glycaemic improvement required	Initiate or continue 100 mg only	All SGLT2 inhibitors have negligible glucose-lowering effects once eGFR falls below 45. Consider adding an additional glucose-lowering agent if further glycaemic improvement is required		
Dapagliflozin	Recommended dose is 10 mg		Certain SGLT2 inhibitors have beneficial cardio–renal effects at all stages of renal impairment and should be continued *See The Medscape UK Primary Care Hack, Extra-Glycaemic Indications of SGLT2 Inhibitors,* for use of SGLT2 inhibitors in this context		

Diabetologia
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CONSENSUS REPORT

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)

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Abstract
The American Diabetes Association and the European Association for the Study of Diabetes convened a panel to update the previous consensus statements on the management of hyperglycaemia in type 2 diabetes in adults, published since 2006 and last updated in 2019. The target audience is the full spectrum of the professional healthcare team providing diabetes care in the USA and Europe. A systematic examination of publications since 2018 informed new recommendations. These include additional focus on social determinants of health, the healthcare system and physical activity behaviours including sleep. There is a greater emphasis on weight management as part of the holistic approach to diabetes management. The results of cardiovascular and kidney outcomes trials involving sodium–glucose cotransporter-2 inhibitors and glucagon-like peptide-1 receptor agonists, including assessment of subgroups, inform broader recommendations for cardiorenal protection in people with diabetes at high risk of cardiorenal disease. After a summary listing of consensus recommendations, practical tips for implementation are provided.

Keywords Cardiovascular disease · Chronic kidney disease · Glucose-lowering therapy · Guidelines · Heart failure · Holistic care · Person-centred care · Social determinants of health · Type 2 diabetes mellitus · Weight management

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A consensus report of a particular topic contains a comprehensive examination and is authored by an expert panel and represents the panel's collective analysis, evaluation and opinion. MJD and JBB were co-chairs for the Consensus Report Writing Group. VRA, BSC, RAG, JG, NMM and SER were the writing group members for ADA. SDP, CM, GM, PR, TT and AT were the writing group members for EASD. The article was reviewed for EASD by its Committee on Clinical Affairs and approved by its Executive Board. The article was reviewed for ADA by its Professional Practice Committee.

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Extended author information available on the last page of the article

Abbreviations

BGM	Blood glucose monitoring
CGM	Continuous glucose monitoring
CSII	Continuous subcutaneous insulin infusion
CVOT	Cardiovascular outcomes trial
DKA	Diabetic ketoacidosis
DPP-4i	Dipeptidyl peptidase-4 inhibitors
DSMES	Diabetes self-management education and support
ETD	Estimated treatment difference
GIP	Glucose-dependent insulinotropic polypeptide
GLP-1 RA	Glucagon-like peptide-1 receptor agonist(s)
HF	Heart failure
HHF	Hospitalisation for heart failure
MACE	Major adverse cardiovascular events
MNT	Medical nutrition therapy
NAFLD	Non-alcoholic fatty liver disease
NASH	Non-alcoholic steatohepatitis
SGLT1i	Sodium–glucose cotransporter-1 inhibitor

IMPORTANCE OF 24-HOUR PHYSICAL BEHAVIOURS FOR TYPE 2 DIABETES

SITTING/BREAKING UP PROLONGED SITTING

Limit sitting. Breaking up prolonged sitting (every 30 min) with short regular bouts of slow walking/simple resistance exercises can improve glucose metabolism.

STEPPING

- An increase of only 500 steps/day is associated with 2-9% decreased risk of cardiovascular morbidity and all-cause mortality.
- A 5 to 6 min brisk intensity walk per day equates to ~4 years' greater life expectancy.

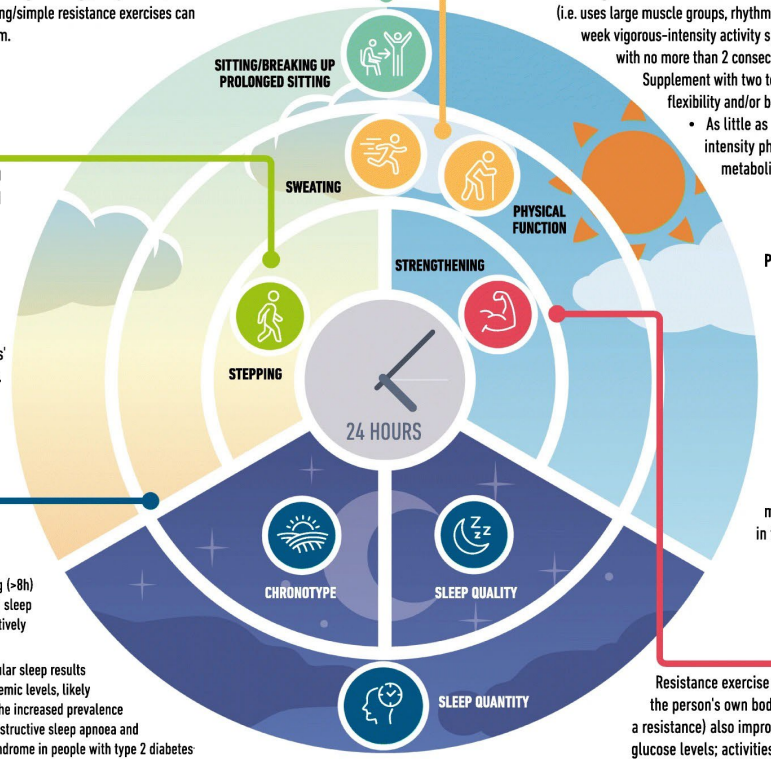
SLEEP

Aim for consistent, uninterrupted sleep, even on weekends.

Quantity – Long (>8h) and short (<6h) sleep durations negatively impact HbA_{1c}.

Quality – Irregular sleep results in poorer glycaemic levels, likely influenced by the increased prevalence of insomnia, obstructive sleep apnoea and restless leg syndrome in people with type 2 diabetes

Chronotype – Evening chronotypes (i.e. night owl: go to bed late and get up late) may be more susceptible to inactivity and poorer glycaemic levels vs morning chronotypes (i.e. early bird: go to bed early and get up early).



SWEATING (MODERATE-TO-VIGOROUS ACTIVITY)

- Encourage ≥150 min/week of moderate-intensity physical activity (i.e. uses large muscle groups, rhythmic in nature) OR ≥75 min/week vigorous-intensity activity spread over ≥3 days/week, with no more than 2 consecutive days of inactivity. Supplement with two to three resistance, flexibility and/or balance sessions.
- As little as 30 min/week of moderate-intensity physical activity improves metabolic profiles.

Physical function/frailty/ sarcopenia

- The frailty phenotype in type 2 diabetes is unique, often encompassing obesity alongside physical frailty, at an earlier age. The ability of people with type 2 diabetes to undertake simple functional exercises in middle-age is similar to that in those over a decade older.

STRENGTHENING

Resistance exercise (i.e. any activity that uses the person's own body weight or works against a resistance) also improves insulin sensitivity and glucose levels; activities like tai chi and yoga also encompass elements of flexibility and balance.

	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 BEHAVIOURS ON CARDIOMETABOLIC HEALTH IN PEOPLE WITH TYPE 2 DIABETES

↑ **Higher levels/improvement** (physical function, quality of life); ↓ **Lower levels/improvement** (glucose/insulin, blood pressure, HbA_{1c}, lipids, depression); ? no data available;
↑ **Green arrows = strong evidence;** ↑ **Yellow arrows = medium strength evidence;** ↑ **Red arrows = limited evidence.**

Sleep behaviours and associated habits and the progression of pre-diabetes to type 2 diabetes mellitus in adults: A systematic review and meta-analysis

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SAGE

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Abstract

Introduction: Certain sleep behaviours increase risk of type 2 diabetes mellitus (T2DM) in the general population, but whether they contribute to the progression from pre-diabetes to T2DM is uncertain. We conducted a systematic review to assess this.

Methods: Structured searches were performed on bibliographic databases (MEDLINE, EMBASE and CINAHL) from inception to 26/04/2021 for longitudinal studies/trials consisting of adults≥18 years with pre-diabetes and sleep behaviours (short or long sleep duration (SD), late chronotype, insomnia, obstructive sleep apnoea, daytime napping and/or night shift employment) that reported on incident T2DM or glycaemic changes. The Newcastle-Ottawa Scale was used for quality assessment.

Results: Six studies were included. Meta-analysis of three studies ($n = 20,139$) demonstrated that short SD was associated with greater risk of progression to T2DM, hazard ratio (HR) 1.59 (95% CI 1.29–1.97), I^2 heterogeneity score 0%, $p < 0.0001$, but not for long SD, HR 1.50 (0.86–2.62), I^2 heterogeneity 77%, $p = 0.15$. The systematic review showed insomnia and night shift duty were associated with higher progression to T2DM. Studies were rated as moderate-to-high quality.

Conclusions: Progression from pre-diabetes to T2DM increases with short SD, but only limited data exists for insomnia and night shift duty. Whether manipulating sleep could reduce progression from pre-diabetes to T2DM needs to be examined.

Keywords
Pre-diabetes, type 2 diabetes mellitus, sleep disorders, systematic review

Introduction

Pre-diabetes (also known as non-diabetic hyperglycaemia) represents a state where glucose levels are above the normal defined range, but lower than the diagnostic thresholds for type 2 diabetes mellitus (T2DM).[1–5] People with pre-diabetes are at higher risk of progressing to T2DM than people with normoglycaemia. Thus, pre-diabetes is considered an important target for T2DM prevention strategies.[5,6] As the prevalence of T2DM is increasing

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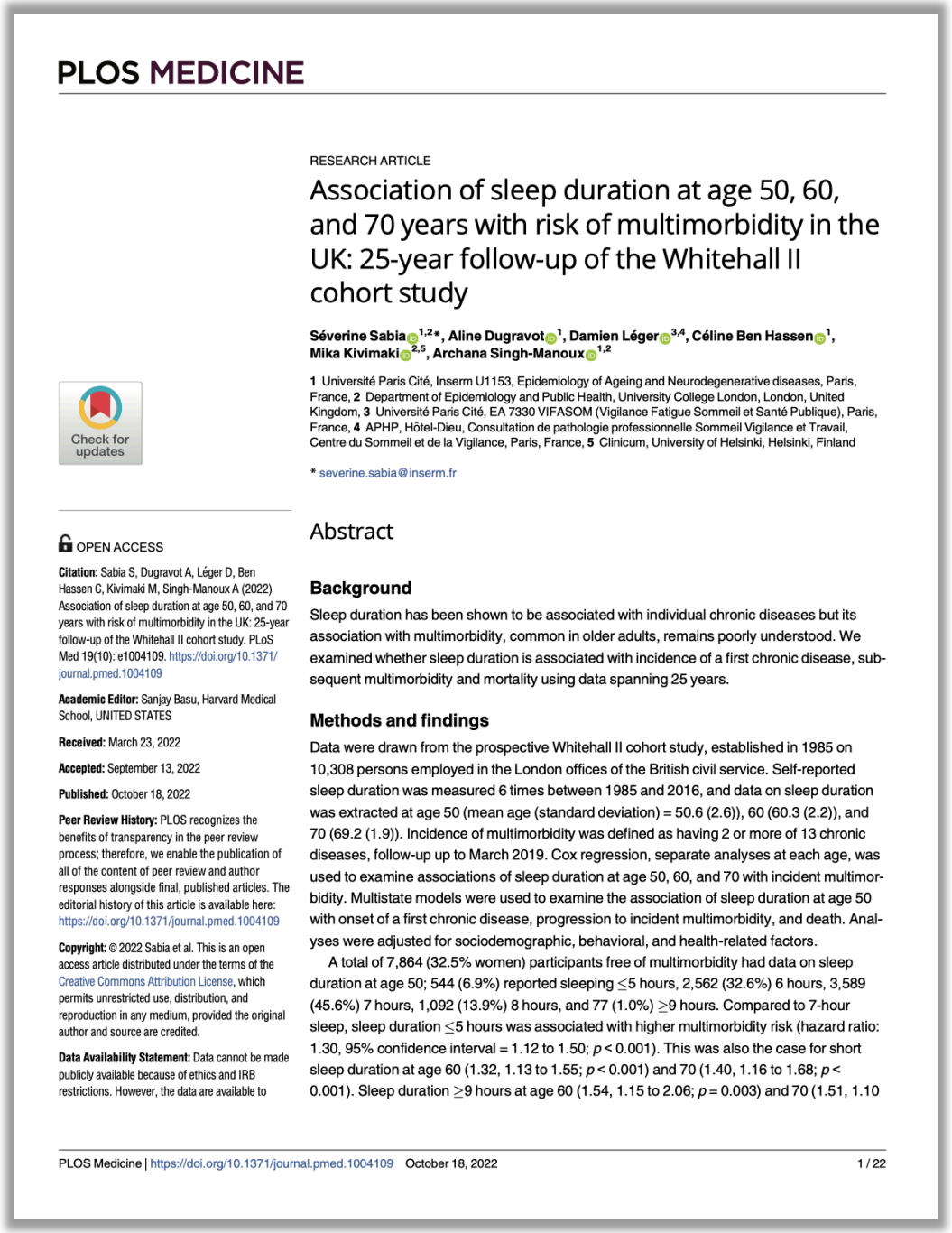
- Short sleep duration (<5-6 hours/night) 59% ↑ risk of progression from pre-diabetes to T2D
- Shift work also impacts risk – do we know which of our patients work shifts?



PLOS MEDICINE

RESEARCH ARTICLE

Association of sleep duration at age 50, 60, and 70 years with risk of multimorbidity in the UK: 25-year follow-up of the Whitehall II cohort study

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Data Availability Statement: Data cannot be made publicly available because of ethics and IRB restrictions. However, the data are available to

Abstract

Background

Sleep duration has been shown to be associated with individual chronic diseases but its association with multimorbidity, common in older adults, remains poorly understood. We examined whether sleep duration is associated with incidence of a first chronic disease, subsequent multimorbidity and mortality using data spanning 25 years.

Methods and findings

Data were drawn from the prospective Whitehall II cohort study, established in 1985 on 10,308 persons employed in the London offices of the British civil service. Self-reported sleep duration was measured 6 times between 1985 and 2016, and data on sleep duration was extracted at age 50 (mean age (standard deviation) = 50.6 (2.6)), 60 (60.3 (2.2)), and 70 (69.2 (1.9)). Incidence of multimorbidity was defined as having 2 or more of 13 chronic diseases, follow-up up to March 2019. Cox regression, separate analyses at each age, was used to examine associations of sleep duration at age 50, 60, and 70 with incident multimorbidity. Multistate models were used to examine the association of sleep duration at age 50 with onset of a first chronic disease, progression to incident multimorbidity, and death. Analyses were adjusted for sociodemographic, behavioral, and health-related factors.

A total of 7,864 (32.5% women) participants free of multimorbidity had data on sleep duration at age 50; 544 (6.9%) reported sleeping ≤5 hours, 2,562 (32.6%) 6 hours, 3,589 (45.6%) 7 hours, 1,092 (13.9%) 8 hours, and 77 (1.0%) ≥9 hours. Compared to 7-hour sleep, sleep duration ≤5 hours was associated with higher multimorbidity risk (hazard ratio: 1.30, 95% confidence interval = 1.12 to 1.50; $p < 0.001$). This was also the case for short sleep duration at age 60 (1.32, 1.13 to 1.55; $p < 0.001$) and 70 (1.40, 1.16 to 1.68; $p < 0.001$). Sleep duration ≥9 hours at age 60 (1.54, 1.15 to 2.06; $p = 0.003$) and 70 (1.51, 1.10

- Short sleep duration (≤5 hours) is associated with risk of chronic disease & multimorbidity at all ages
- Long sleep duration (≥9 hours) was associated with multimorbidity only ≥60 years

WHY SLEEPING NAKED COULD CUT YOUR RISK OF DIABETES

Centre and author of Sound Asleep: The Expert Guide To Sleeping Well.

'If anything prevents that decline in temperature, the brain will wake itself up to see what's going on, meaning you'll struggle to get to sleep or you'll have disturbed sleep.

'The advantage of sleeping naked is it's easier for the body to cool and maintain the lower temperature the brain wants to achieve,' Russell Foster, professor of circadian neuroscience at the University of Oxford, says ditching nightwear may improve your slumber.

'If you're wearing lots of bedclothes it's going to be more difficult to regulate your temperature, so wear the least you can get away with.'

Disrupted sleep from being too hot doesn't just mean you'll get less sleep overall, but it might mean less deep sleep, the most restorative type.

Deep sleep is key for memory consolidation and the production of growth hormone — important for cell repair and growth.

Why does the body cool down during sleep? One theory is that it evolved to do this because our ancestors in Africa would grab some rest in the afternoon, and needed to keep cool in the savanna heat.

SWAP BED SOCKS FOR A HOT WATER BOTTLE

THOUGH it's important not to get too hot at night, make sure you have warm hands and feet.

That's because for your temperature to lower to the level that triggers sound sleep, your body needs to lose excess heat.

It does this by sending blood to the vessels near skin — in particular, those on the hands and feet — where heat is lost through the skin surface.

. . . not to mention ward off infections, trim your waistline

Picture: CORBIS

If you just can't go without PJs

■ CHOOSE pyjamas made from brushed cotton, says George Havenith, professor of environmental physiology and ergonomics at Loughborough University.

'The roughened surface provides a warmer feel as it holds air that insulates you.'

Natural fibres such as wool, cotton or silk 'have a good humidity buffering capacity (they absorb moisture), which will feel better in bed'.

■ COVER the torso, arms and legs. Instead of heavy quilts, choose blankets, which you can remove in layers if you get too hot. Mike Tipton, professor of human and applied physiology at the University of Portsmouth, says: 'You want clothing and bedding that provide insulation, but also

USE OF GLUCOSE-LOWERING MEDICATIONS IN THE MANAGEMENT OF TYPE 2 DIABETES

HEALTHY LIFESTYLE BEHAVIOURS; DIABETES SELF-MANAGEMENT EDUCATION AND SUPPORT (DSMES); SOCIAL DETERMINANTS OF HEALTH (SDOH)

TO AVOID THERAPEUTIC INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3–6 MONTHS)

Goal: Cardiorenal Risk Reduction in High-Risk Patients with Type 2 Diabetes (In addition to comprehensive CV risk management)*

+ASCVD†

Defined differently across CVOTs but all included individuals with established CVD (e.g. MI, stroke, any revascularisation procedure). Variably included: conditions such as transient ischaemic attack, unstable angina, amputation, symptomatic or asymptomatic coronary artery disease.

+Indicators of high risk

While definitions vary, most comprise ≥ 55 years of age with two or more additional risk factors (including obesity, hypertension, smoking dyslipidaemia or albuminuria)

+ASCVD/Indicators of High Risk

GLP-1 RA# with proven CVD benefit **EITHER/OR** SGLT2i§ with proven CVD benefit

If HbA_{1c} above target

- For patients on a GLP-1 RA consider adding SGLT2i with proven CVD benefit or vice versa
- TZD^

+HF

Current or prior symptoms of HF with documented HFrEF or HFpEF

+HF

SGLT2i§ with proven HF benefit in this population

+CKD

eGFR < 60 ml/min per 1.73 m^2 OR albuminuria (ACR ≥ 3.0 mg/mmol (30mg/g)). These measurements may vary over time; thus, a repeat measure is required to document CKD.

+CKD (on maximally tolerated dose of ACEi/ARB)

PREFERABLY

SGLT2i§ with primary evidence of reducing CKD progression

Use SGLT2i in people with an eGFR ≥ 20 ml/min per 1.73 m^2; once initiated should be continued until initiation of dialysis or transplantation

OR

GLP-1 RA with proven CVD benefit if SGLT2i not tolerated or contraindicated

If HbA_{1c} above target, for patients on SGLT2i, consider incorporating a GLP-1 RA or vice versa

If additional cardiorenal risk reduction or glycaemic lowering needed

Goal: Achievement and Maintenance of Glycaemic and Weight Management Goals

Glycaemic Management: Choose approaches that provide the efficacy to achieve goals:

Metformin OR Agent(s) including COMBINATION therapy that provide adequate EFFICACY to achieve and maintain treatment goals

Consider avoidance of hypoglycaemia a priority in high-risk individuals

In general, higher efficacy approaches have greater likelihood of achieving glycaemic goals

Efficacy for glucose lowering

Very High:
Dulaglutide (high dose), Semaglutide, Tirzepatide

Insulin

Combination Oral, Combination Injectable (GLP-1 RA/Insulin)

High:
GLP-1 RA (not listed above), Metformin, SGLT2i, Sulfonylurea, TZD

Intermediate:
DPP-4i

Achievement and Maintenance of Weight Management Goals:

Set individualised weight management goal

General lifestyle advice: medical nutrition therapy/eating patterns/ physical activity

Intensive evidence based structured weight manageme programme

Consider medication for weight loss

Consider metabol surgery

When choosing glucose-lowering therapi

Consider regimen with high-to-very-high du glucose and weight efficacy

Efficacy for weight loss

Very High:
Semaglutide, Tirzepatide

High:
Dulaglutide, Liraglutide

Intermediate:
GLP-1RA (not listed above), SGLT2i

Neutral:
DPP-4i, Metformin

If HbA_{1c} above target

Identify barriers to goals:

- Consider DSMES referral to support self-efficacy in achievement of goals
- Consider technology (e.g. diagnostic CGM) to identify therapeutic gaps and tailor the
- Identify and address SDOH that impact on achievement of goals

ACEi, Angiotensin-Converting Enzyme Inhibitor; ACR, Albumin/Creatinine Ratio; ARB, Angiotensin Receptor Blocker; ASCVD, Atherosclerotic Cardiovascular Disease; CGM, Continuous Glucose Monitoring; CKD, Chronic Kidney Disease; CV, Cardiovascular; CVD, Cardiovascular Disease; CVOT, Cardiovascular Outcomes Trial; DPP-4i, Dipeptidyl Peptidase-4 Inhibitor; eGFR, Estimated Glomerular Filtration Rate; GLP-1 RA, Glucagon-Like Peptide-1 Receptor Agonist; HF, Heart Failure; HFpEF, Heart Failure with preserved Ejection Fraction; HFrEF, Heart Failure with reduced Ejection Fraction; HHF, Hospitalisation for Heart Failure; MACE, Major Adverse Cardiovascular Events; MI, Myocardial Infarction; SDOH, Social Determinants of Health; SGLT2i, Sodium-Glucose Cotransporter-2 Inhibitor; T2D, Type 2 Diabetes; TZD, Thiazolidinedione.

* In people with HF, CKD, established CVD or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be independent of background use of metformin;† A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high CV risk. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. See text for details; ^ Low-dose TZD may be better tolerated and similarly effective; § For SGLT2i, CV/renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, all-cause mortality, MI, HHF and renal outcomes in individuals with T2D with established/high risk of CVD; # For GLP-1 RA, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke and renal endpoints in individuals with T2D with established/high risk of CVD.

PROACTIVE CARE: AVOIDING INERTIA

Consider initial combination therapy with glucose-lowering agents, especially in those with high HbA_{1c} (i.e., >70mmol/mol [8.5%]) at diagnosis, in younger people with type 2 diabetes (regardless of HbA_{1c}), and in those in whom a stepwise approach would delay access to agents that provide cardiorenal protection beyond their glucose-lowering effects.

Avoid therapeutic inertia and reevaluate health behaviors, individuals' medication-taking behaviors, and side effects of agents at every clinic visit.

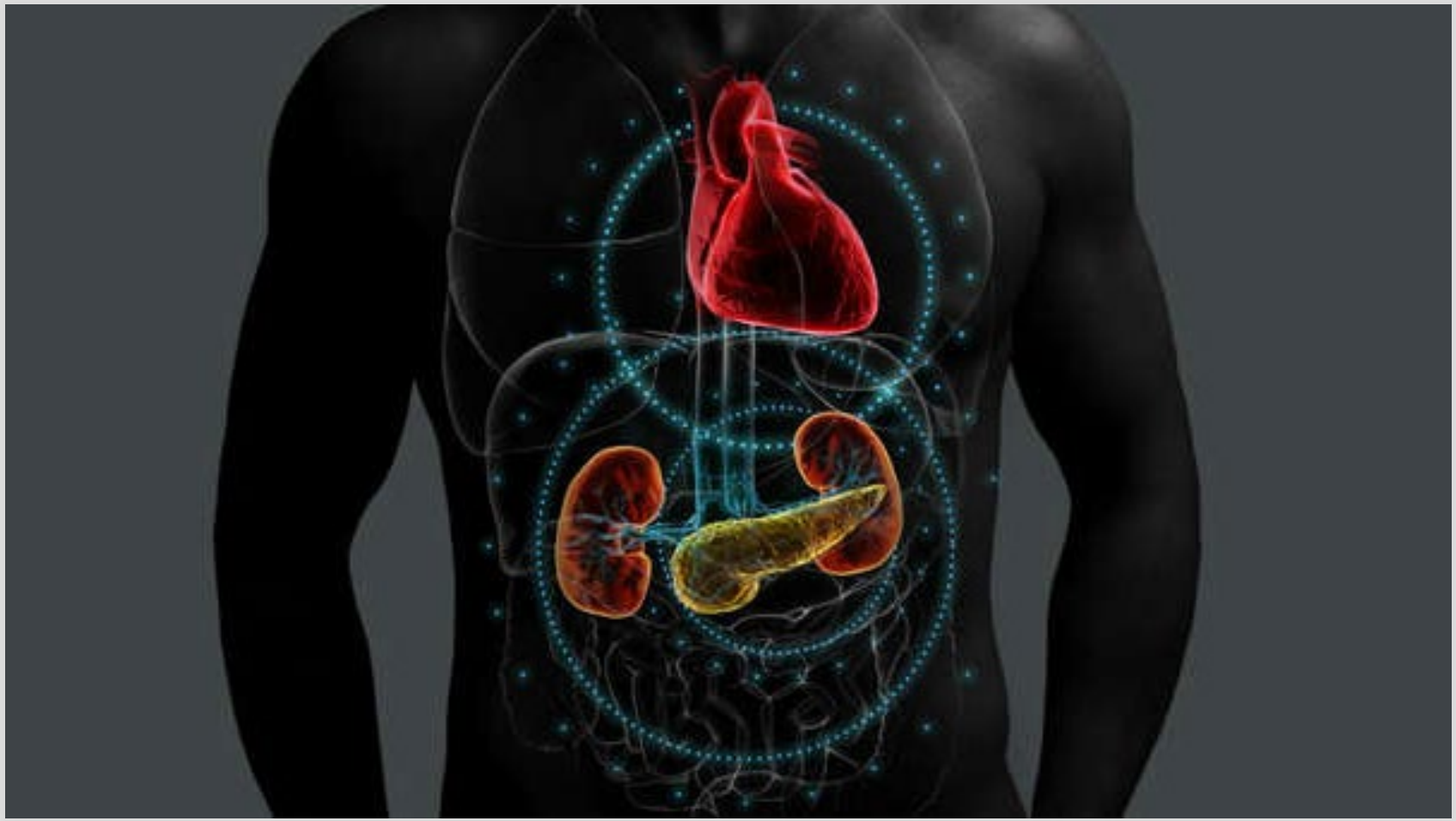
When additional glycemic lowering is needed, incorporate, rather than substitute, glucose-lowering therapies with complementary mechanisms of action.

Consider fixed-dose combinations to reduce prescription burden.

Consider de-intensification of therapy, e.g., in frail older adults, in the setting of hypoglycemia-causing medications, and in those with glycemic metrics substantially better than target.

Type 2 diabetes in adults: management

NICE guideline [NG28] Published: 02 December 2015 Last updated: 29 June 2022



Assess HbA1c, cardiovascular risk and kidney function

CONSIDER

- DPP-4 inhibitor ('gliptin') — or
- Pioglitazone — or
- Sulfonylurea

An SGLT2 inhibitor ('flozin') for some people:

- TA 390 Canagliflozin
- TA 390 Dapagliflozin
- TA 390 Empagliflozin
- TA 572 Ertugliflozin

Not at high CVD risk

OFFER

- Metformin

or if GI disturbance

- Metformin MR

If metformin contraindicated

OFFER

- SGLT2 inhibitor alone

Chronic heart failure or established atherosclerotic CVD

OFFER

- Metformin

or if GI disturbance

- Metformin MR

and as soon as metfomin tolerability is confirmed, offer

- SGLT2 inhibitor ('flozin')

with proven cardiovascular benefit

If metformin contraindicated

CONSIDER

- SGLT2 inhibitor alone

High risk of CVD QRISK2 of 10% or higher

OFFER

- Metformin

or if GI disturbance

- Metformin MR

and as soon as metfomin tolerability is confirmed, offer

- SGLT2 inhibitor ('flozin')

with proven cardiovascular benefit

If metformin contraindicated

ADA/EASD and NICE Recommendations on the Pharmacological Management of Type 2 Diabetes in Adults

Medscape UK X Guidelines
Primary Care Hacks

Authors: *Guidelines* editorial team, email: guidelines@webmd.net; Dr Kevin Fernando, GP Partner, North Berwick Health Centre; Content Advisor, Medscape Global and UK, email: kfernando@webmd.net

This Medscape UK Primary Care Hack highlights key recommendations from the American Diabetes Association/European Association for the Study of Diabetes and NICE on the management of hyperglycaemia in adults with T2D. As always, we should take an individualised and holistic approach to the care of people living with T2D.

ADA/EASD (2022)	NICE (2022)		
INITIAL THERAPY	**FIRST-LINE TREATMENT** Assess HbA_{1c}, CV risk, and kidney function[F] Reinforce advice about diet, lifestyle, and adherence to drug treatment if HbA_{1c} levels are not adequately controlled by a single drug and rise to ≥58 mmol/mol (7.5%)		
Implement comprehensive lifestyle measures for all people with T2D, including physical activity, weight reduction (including weight reduction medications), treatment adherence, nutrition, adequate sleep, and smoking cessation DSMES should be offered on an ongoing basis, and be provided by trained diabetes care and education specialists For treatment of hyperglycaemia, metformin remains the agent of choice in most people with diabetes Other classes of agents are useful in combination with metformin or when metformin is contraindicated or not tolerated, with agent selection determined by the balance between the glucose-lowering efficacy and the side-effect profile of the individual agents[A] Consider initial combination therapy with glucose-lowering agents, especially in those with high HbA_{1c} at diagnosis (i.e., >70 mmol/mol [>8.5%]), in younger people with T2D (regardless of HbA_{1c}), and in those in whom a stepwise	**Not at High CVD Risk**	**CHF or Established ASCVD[H]**	**High Risk of CVD (QRISK2 ≥10%)**
	Offer standard-release metformin or if GI disturbance, metformin MR If metformin contraindicated consider: • DPP-4 inhibitor **or** • pioglitazone **or** • sulfonylurea • an SGLT2i for some people (canagliflozin, dapagliflozin, empagliflozin, ertugliflozin)[G]	Offer standard-release metformin or if GI disturbance, metformin MR And, as soon as metformin tolerability is confirmed,[I] **offer** SGLT2i with proven CV benefit	Offer standard-release metformin or if GI disturbance, metformin MR And, as soon as metformin tolerability is confirmed,[I] **consider** SGLT2i with proven CV benefit

SGLT2 inhibitors as the bedrock of therapy for heart failure

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See Online/Articles
https://doi.org/10.1016/S0140-6736(22)01429-5

The evolution of SGLT2 inhibitors from glucose-lowering agents to heart failure therapies is a rare story of serendipity. It began with a requirement by the US Food and Drug Administration in 2008 to show cardiovascular safety of new glucose-lowering agents after their regulatory approval for treatment of hyperglycaemia.[1] Although the initial focus was on cardiovascular safety, it became quickly apparent that SGLT2 inhibitors were not only safe, but they were also effective for reducing cardiovascular risk in type 2 diabetes. Important gains included substantially improving clinical outcomes for heart failure and chronic kidney disease.[2,3]

Research moved quickly to dedicated outcome trials for heart failure and chronic kidney disease in patients with and without type 2 diabetes. Across the board, SGLT2 inhibitors delivered with relative risk reductions for composite outcomes of heart failure hospitalisations and cardiovascular death by approximately 25%, or of substantial loss of kidney function or kidney failure by approximately 40%.[2,3] As a result, these agents were codified as a pillar of heart failure therapies, irrespective of diabetes status, supported by high-level and strong guideline recommendations.[4,5] However, heart failure trials were first done in patients with reduced ejection fraction, leaving supported therapies for heart failure with preserved or mildly reduced ejection fraction as a major gap.[6] The next step was extension of trials to this group of patients in EMPEROR-Preserved and DELIVER.[7,8] A prespecified meta-analysis by Muthiah Vaduganathan and colleagues,[9] reported in *The Lancet*, builds the evidence base for the benefit of SGLT2 inhibitors on hospitalisation for heart failure and cardiovascular death in patients with preserved or mildly reduced ejection fraction. Additionally, trials in patients with reduced ejection fraction (DAPA-HF and EMPEROR-Reduced) and those admitted to the hospital with worsening heart failure with any ejection fraction (SOLOIST-WHF) were added post hoc, for a combined meta-analysis providing power to assess various clinical outcomes. All trials compared an SGLT2 inhibitor with placebo. The mean age of participants was 66–72 years, with 55–77% men and 23–45% women. The lower limit of estimated glomerular filtration rate for inclusion was 20–30 mL/min per 1·73m^2 and diabetes was present in 45–50% of participants. Increased natriuretic peptide concentrations were required for inclusion, although the threshold varied widely (300–5000 pg/mL). Despite the differences in patient populations and study designs, the evidence is strikingly consistent and resoundingly clear—SGLT2 inhibitors are the bedrock of therapy for heart failure regardless of ejection fraction or care setting.

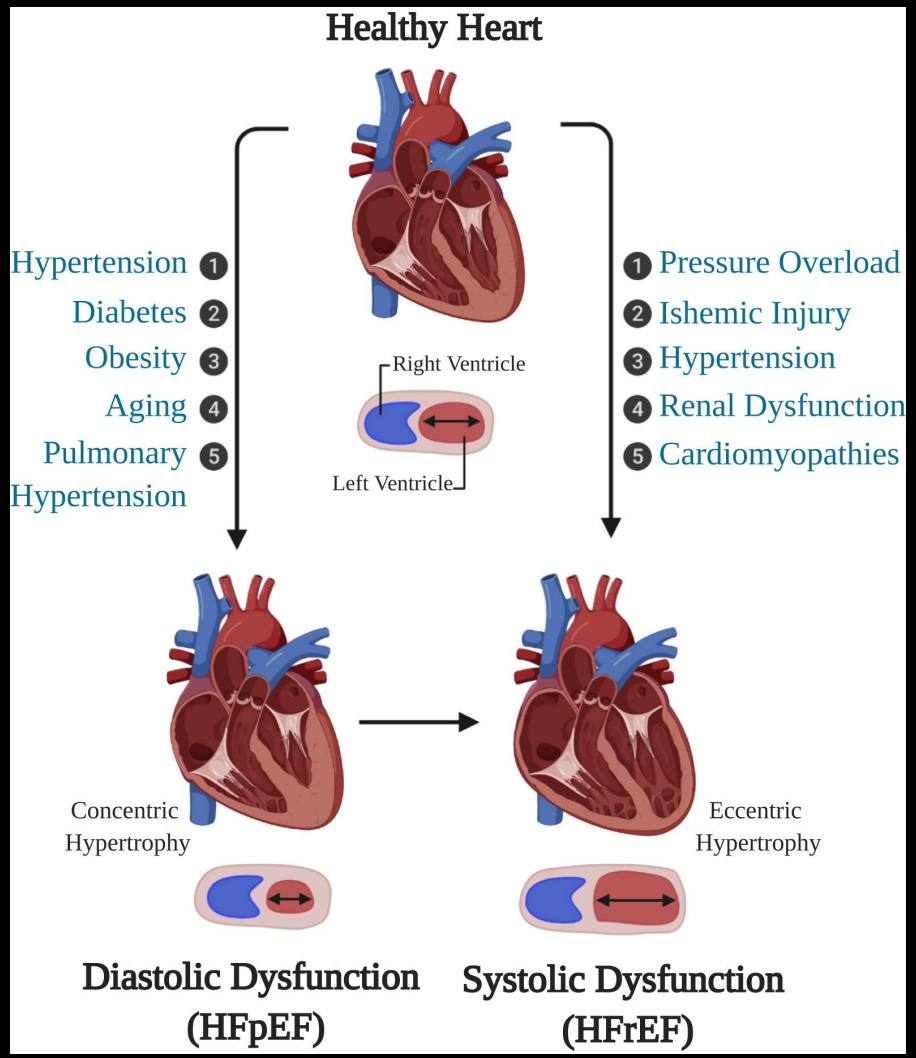
The strengths of the prespecified (n=12 251) and combined (21 947) meta-analyses include large sample sizes and use of different agents, making the case for generalisability across the SGLT2 inhibitor class.[9] In addition, to benefit on the primary outcome of hospitalisation for heart failure or cardiovascular death (hazard ratio 0·77 [95% CI 0·72–0·82]), significant risk reductions were found for the individual components of the primary outcome as well as all-cause death (0·92 [0·86–0·99]) in the broader analysis across five trials. Risk reductions were similar in subgroups defined by different heart-failure phenotypes (eg, ejection fraction, New York Heart Association functional class, other heart failure therapies, and atrial fibrillation) and concurrent conditions (eg, diabetes, low kidney function, and obesity). Additionally, self-reported health status was more likely to improve with SGLT2 inhibitor treatment compared with placebo.

Nevertheless, demographic representation remains problematic in these studies, a challenge shared by the clinical trial enterprise overall.[10] In DELIVER and EMPEROR-Preserved, representation of women at 44–45% reflects progress considering the high burden of heart failure with preserved ejection fraction in women. Yet, non-White or non-Asian groups were woefully small. There were 417 (3.4%) Black participants of the 12 251 included across both trials. Although Black people have high risk for heart failure, scant attention has been paid to their trial enrolment. The authors indicate that the study population was representative for the sites, but we contend that concerted efforts should be made to find study sites that enrol Black and other groups at high risk. New ways of thinking and cultural shifts are needed to include under-represented groups in clinical trials as a path to health equity.[10] Another concern is the minor emphasis on kidney disease, especially given its common co-occurrence with heart failure, and these diseases' combined impact

The Four Pillars of Heart Failure

Consider additional therapies

Figure 2



The American Journal of Pathology 2020 1901596-1608DOI: (10.1016/j.ajpath.2020.04.006)

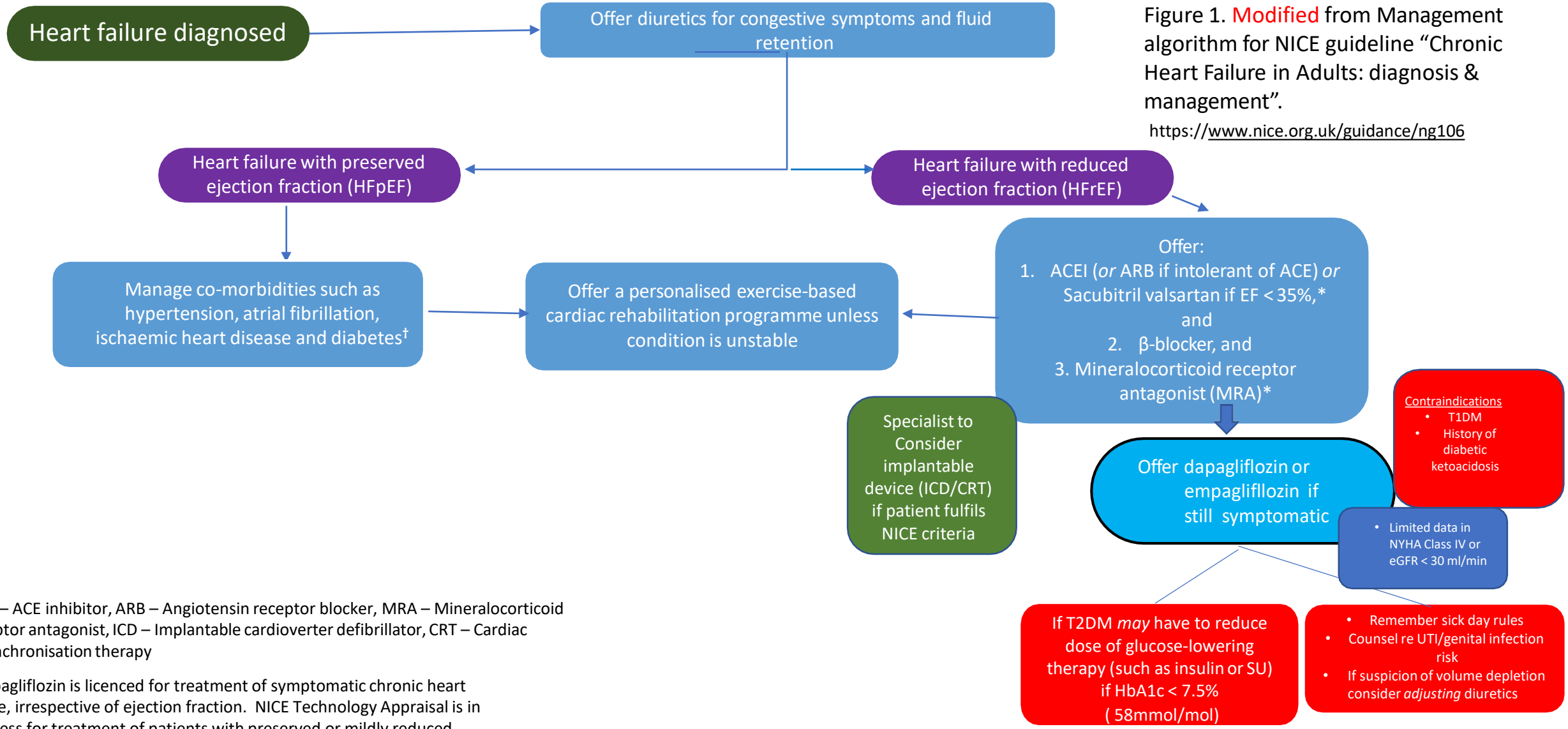


Figure 1. Modified from Management algorithm for NICE guideline "Chronic Heart Failure in Adults: diagnosis & management".

https://www.nice.org.uk/guidance/ng106

ACEi – ACE inhibitor, ARB – Angiotensin receptor blocker, MRA – Mineralocorticoid receptor antagonist, ICD – Implantable cardioverter defibrillator, CRT – Cardiac resynchronisation therapy

†Empagliflozin is licenced for treatment of symptomatic chronic heart failure, irrespective of ejection fraction. NICE Technology Appraisal is in progress for treatment of patients with preserved or mildly reduced ejection fraction.

*Measure serum sodium, potassium and assess renal function before and after starting and after each dose increment. If eGFR is 30 to 45 ml/min/1.73 m^2, consider lower doses or slower titration of ACEI/ARBs/sacubitril valsartan or MRAs

Date of publication: March 2021. Updated October 2022

Chronic

NICE guideline

d guidance (PDF)

Next >

associated with CKD.

Adult with Diabetes

ACR less than 3 mg/mmol

Monitor ACR, creatinine and blood pressure annually

ACR 3 mg/mmol or more

Offer an ACE inhibitor or ARB (titrated to the highest licensed dose they can tolerate)

Offer an SGLT2 inhibitor if type 2 diabetes & ACR 30 mg/mmol or more, and criteria in licence met.

Consider an SGLT2 inhibtor if type 2 diabetes & ACR between 3 mg/mmol and 30 mg/mmol, and critera in licence met.

UK Kidney Association

UK Kidney Association Clinical Practice Guideline: Sodium-Glucose Co-transporter-2 (SGLT-2) Inhibition in Adults with Kidney Disease

Final version: 18 October 2021
Review date: 18 October 2026

Summary of recommendations

RECOMMENDATIONS FOR USE IN PEOPLE WITH AN eGFR ≥25mL/min/1.73m^2		
Section 2	**PEOPLE WITH TYPE 2 DM**	**Grade**
1.	We recommend initiating SGLT-2inhibition* in those with: (a) uACR of ≥25 mg/mmol attributed to diabetic nephropathy (b) Established coronary disease or stable symptomatic heart failure (irrespective of ejection fraction).	**1A**
2.	We recommend initiating SGLT-2 inhibition in those with a uACR of ≥25 mg/mmol attributable to a non-diabetic cause‡	**1B**
3.	We suggest initiating SGLT-2 inhibition to modify cardiovascular risk in those with an eGFR 25-60 mL/min/1.73m^2 and uACR <25 mg/mmol, recognising effects on glycaemic control will be limited.	**2B**
Section 3	**PEOPLE WITHOUT DM**	
1.	We recommend initiating SGLT-2 inhibition* in those with stable symptomatic heart failure (irrespective of ejection fraction).	**1A**
2.	We recommend initiating SGLT-2 inhibition* in those with a uACR of ≥25 mg/mmol, excluding people with polycystic kidney disease or on immunological therapy for renal disease.‡	**1B**
** See section 4 for summary of indications/licensed uses* *‡ DAPA-CKD provides the key clinical evidence and excluded people with a kidney transplant, polycystic kidney disease, lupus nephritis, ANCA-associated vasculitis, and those receiving immunological therapy for renal disease in the last 6 months.*		

SGLT2 Inhibitors and Renal Outcomes : A comparison of RCTs

Infographic by-: Priti Meena, M.D @Priti899

CREDENCE

Double-blind, Placebo-controlled,
Multicentric RCT
(N=4401)

Inclusion:
Type 2 DM
eGFR: ≥30-90
and UACR: >300-≤5000 mg/g

Canagliflozin VS placebo

2019

Median follow-up: 2.62 yrs

Renal-specific composite of ESKD, 2* S. Cr or death from renal causes:
HR 0.66; (0.53 to 0.81)

CV death, MI, or stroke:
HR 0.80 (0.67 -0.95)
Hospitalization for heart failure:
HR 0.61; (0.47 to 0.80)

DAPA-CKD

Double-blind, Placebo-controlled,
Multicentric RCT
(N=4304)

Inclusion:
eGFR: ≥25-75 and
UACR: ≥200-≤5000 mg/g

With or without DM

Dapagliflozin VS placebo

2020

Median follow up : 2.4 yrs

Composite of sustained decline in eGFR of at least 50%, ESKD, or death from renal causes:
HR 0.56; (0.45 to 0.68)

Composite of death from CV causes or hospitalization for heart failure:
HR 0.71; (0.55 to 0.92)

EMPA-KIDNEY

Double-blind, Placebo-controlled,
Multicentric parallel group RCT
(N=6609)

Inclusion:
eGFR: ≥20-45 or
eGFR ≥45 to <90 with UACR ≥200 mg/g

With or without DM

Empagliflozin VS placebo

2022

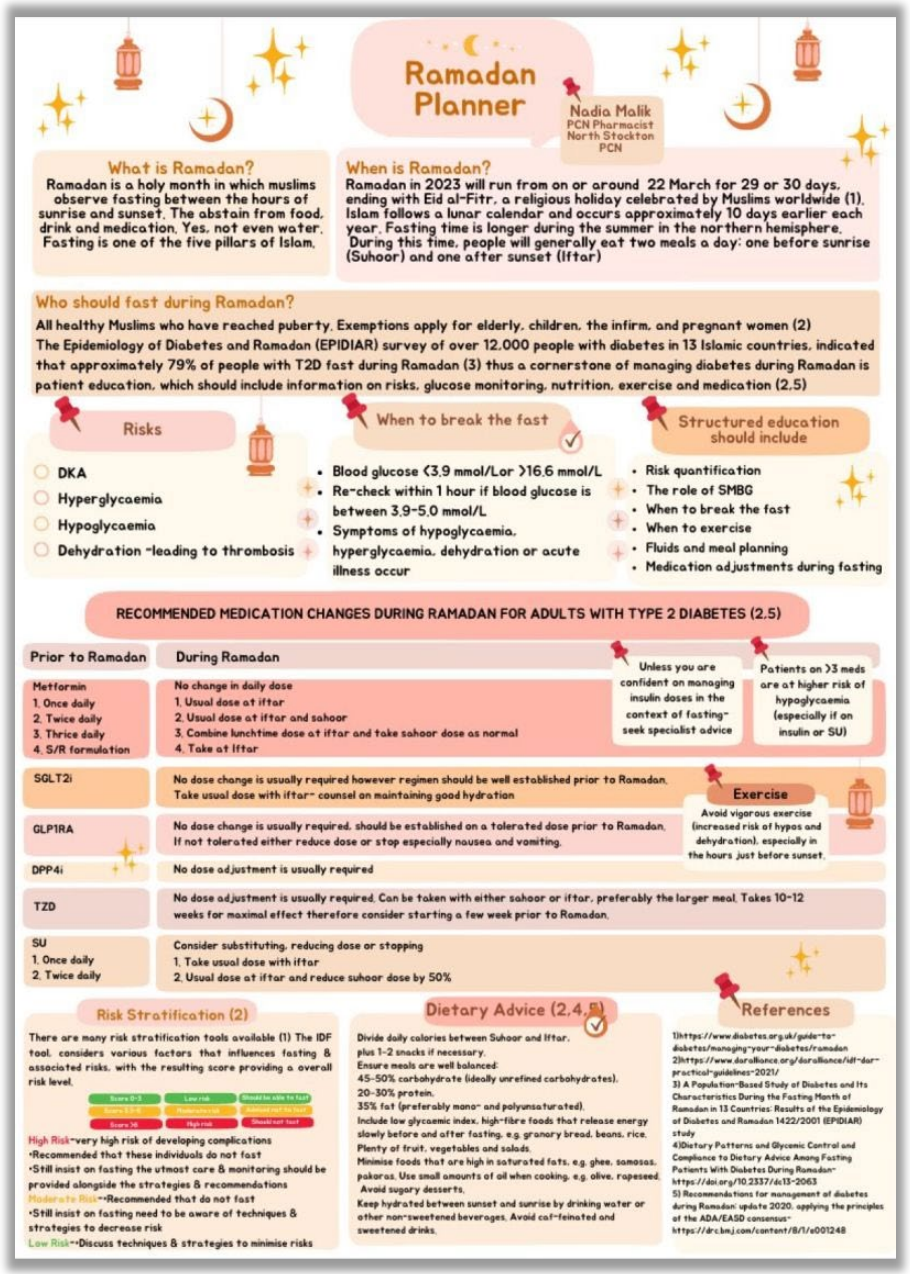
Median follow-up: 2 yrs

Progression of kidney disease or death from CV causes:
HR 0.72; (0.64 to 0.82)

Rate of hospitalization from any cause:
HR 0.86; (0.78 to 0.95)

CV: cardiovascular, ESKD: End-stage kidney diseases, eGFR: estimated glomerular filtration rate in ml per minute per 1.73 m^2, HR: Hazard ratio, MI: Myocardial infarction, RCT: Randomized Controlled Trials, S.Cr: Serum creatinine, SGLT2: Sodium-glucose Cotransporter-2 (SGLT2) Inhibitors, UACR: urinary albumin-to-creatinine ratio

General Practice Bingo



- Nadia Malik, PCN Pharmacist, North Stockton PCN
- @nadia_malik6

diabetesdistilled
the latest developments filtered for you

I would walk 10 000 steps but should I walk 10 000 more?

In this prospective cohort study published in *JAMA Internal Medicine*, del Pozo Cruz and colleagues describe the associations of step count and intensity with mortality, cancer and cardiovascular disease (CVD) in 78 500 individuals recruited from the UK Biobank database. Over a median of 7 years' follow-up, increasing daily step count was associated with reductions in mortality (all-cause, cardiovascular and cancer-related) and incidence of CVD and cancer. These benefits were observed with a clear dose–response relationship up to around 10 000 steps per day. Furthermore, increased stepping intensity was associated with further risk reduction, particularly for incidence of CVD and cancer. Notably, there was no minimum daily step count associated with these morbidity and mortality benefits. These findings will hopefully help us motivate and facilitate change in our less active patients in primary care; daily step count goals should be individualised to ensure they remain realistic and achievable, yet still provide improvements in morbidity and mortality.

Kevin Fernando
GP in North Berwick

Walking 10 000 steps daily is exercise lore and is recommended by many as a core activity to maintain our physical and mental wellbeing. Wearable fitness trackers are well entrenched in modern society and often routinely set 10 000 steps as a daily activity target. However, this concept of 10 000 daily steps is not evidence-based and was created as part of a very successful marketing campaign for a pedometer sold shortly after the Tokyo Olympics in 1964. The device was called *manpo-kei*, which translates into English as "10 000-step meter". The Japanese character for 10 000 looks like a person walking, which is thought to be how the number was chosen.

Several guidelines and consensus statements do recommend increasing daily step count to improve cardiometabolic health; for example, the ADA/EASD 2022 consensus report on the management of hyperglycaemia in type 2 diabetes reminds us that an increase of just 500 steps per day is associated with a 2–9% reduction in the risk of cardiovascular morbidity and all-cause mortality (Davies et al, 2022). Moreover, a 5–6-minute brisk-intensity walk per day equates to around 4 years' greater life expectancy. However, high-quality evidence for improved cardiometabolic and cancer outcomes by undertaking 10 000 steps daily remains, hitherto, sparse.

This recently published, well-conducted, population-based, prospective cohort study aimed to describe the associations of step count and intensity with all-cause mortality, cancer and cardiovascular disease (CVD). It interrogated data from the well-established UK Biobank biomedical database, so the results are generalisable to healthcare professionals working within the UK.

A total of 78 500 individuals were recruited; mean age was 61 years, 55% were female and 97% identified as White ethnicity. This lack of ethnic diversity is disappointing, as it is well known that adequate physical activity levels and resultant cardiometabolic outcomes vary between different ethnic groups.

Participants were invited by email to participate in an accelerometer study, in which a wrist-worn accelerometer measured daily step count and intensity (steps/minute). It should be noted that step count data were only collected at baseline for 7 days, and the authors do acknowledge this may not be representative of usual walking habits. However, repeat accelerometer measurements were undertaken 4 years later in a small sample of the recruited

Citation: Fernando K (2023) Diabetes Distilled: I would walk 10 000 steps but should I walk 10 000 more? *Diabetes & Primary Care* **25**: [early view publication]

- 10,000 steps daily is exercise lore but evidence for improved outcomes is sparse
- UK prospective cohort study
- ↑ daily step count & intensity associated with ↓ in mortality (all-cause, cancer & CVD) and incidence of CVD & cancer up to around 10,000 steps
- No minimum step count for benefits

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Prediabetes is more than just dysglycaemia

Prediabetes, which is increasing in prevalence, is associated with an increased risk of all-cause mortality and cardiovascular disease. This large study set out to investigate the associations between changes in prediabetes status and risk of death, and to clarify the roles of modifiable risk factors in these associations in a Taiwanese cohort. Participants with prediabetes were recruited and followed for a median of 8 years. Within 3 years, 3.9% of the cohort developed type 2 diabetes and 37.2% reverted to normoglycaemia. Reversion to normoglycaemia was not associated with a lower overall risk of death compared to those with persistent prediabetes. However, reversion to normoglycaemia in combination with physical activity was associated with a lower risk of death compared to persistent prediabetes and inactivity. In those with obesity, risk of death varied between those who reverted to normoglycaemia and those who had persistent prediabetes. The findings support the importance of lifestyle modifications in individuals with prediabetes.

Kevin Fernando
GP in North Berwick

Prediabetes is very common; a cross-sectional study suggested that more than a third of adults in England had prediabetes and that the prevalence had tripled over the preceding 8 years (Mainous et al, 2014). However, because of the nature of the study, it was not possible to identify how many of these individuals progressed to type 2 diabetes.

A previous high-quality meta-analysis (Cai et al, 2020) demonstrated that prediabetes is associated with an increased risk of all-cause mortality and cardiovascular disease (CVD) in the general population, and in those with atherosclerotic CVD. This has significant implications for the screening and management of prediabetes in the primary and secondary prevention of CVD (see my earlier *Diabetes Distilled* piece).

However, high-quality evidence exploring the impact of reversion from prediabetes to normoglycaemia on cardiovascular and mortality outcomes remained, hitherto, sparse.

This recently published, well-conducted, population-based prospective cohort study aimed to investigate the associations between changes in prediabetes status and the risk of death, as well as to clarify any modifiable risk factors in these associations (Cao et al, 2023). It interrogated data from a well-established Taiwanese cohort, so the results are not immediately generalisable to healthcare professionals working within the UK.

Nearly 46 000 individuals with prediabetes were recruited. The mean age was 44.6 years, 37.1% were females and all identified as being from an Asian ethnic background. Recruited individuals were also generally from higher socioeconomic backgrounds. Median follow-up was 8 years.

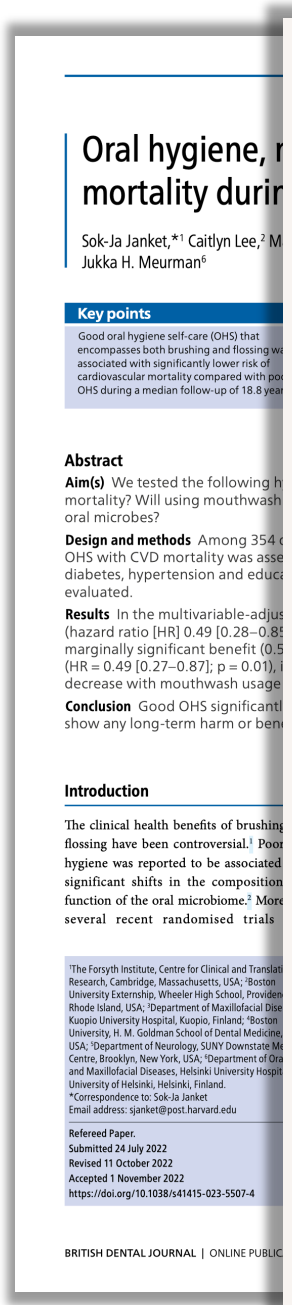
Within 3 years of recruitment, 1786 individuals (3.9%) developed type 2 diabetes and 17 021 (37.2%) reverted to normoglycaemia. Unsurprisingly, the authors found that progression from prediabetes to type 2 diabetes within 3 years was associated with higher risks of all-cause death and CVD-related death, compared with a persistent diagnosis of prediabetes.

Notably, reversion to normoglycaemia was not associated with a lower risk of all-cause death, cancer-related death or CVD-related death. However, in individuals who were physically active, reversion to normoglycaemia was associated with a lower risk of all-cause death, compared to those who had a persistent diagnosis of prediabetes but remained physically inactive. High levels of physical activity translated to around 2 years longer life expectancy in this study.

Furthermore, normoglycaemia did not offset the risks of smoking. Current smokers had a

Citation: Fernando K (2023) Diabetes Distilled: Prediabetes is more than just dysglycaemia. *Diabetes & Primary Care* **25**: [early view publication]

- What happens to risk of death when revert to normoglycaemia from prediabetes?
- Reversion to normoglycaemia was associated with a lower risk of death only in those who remained physically active
- Normoglycaemia did not offset the risks of smoking
- Risk of death was higher in those living with obesity and reversion to normoglycaemia



Oral hygiene, r
mortality durir

Sok-Ja Janket,*[1] Caitlyn Lee,[2] M
Jukka H. Meurman[6]

Key points

Good oral hygiene self-care (OHS) that encompasses both brushing and flossing w
associated with significantly lower risk of
cardiovascular mortality compared with po
OHS during a median follow-up of 18.8 yea

Abstract

Aim(s) We tested the following h
mortality? Will using mouthwash
oral microbes?

Design and methods Among 354
OHS with CVD mortality was asse
diabetes, hypertension and educa
evaluated.

Results In the multivariable-adjus
(hazard ratio [HR] 0.49 [0.28–0.8
marginally significant benefit (0.5
(HR = 0.49 [0.27–0.87]; p = 0.01),
decrease with mouthwash usage

Conclusion Good OHS significantl
show any long-term harm or ben

Introduction

The clinical health benefits of brushing
flossing have been controversial.[1] Poo
hygiene was reported to be associated
significant shifts in the composition
function of the oral microbiome.[5] More
several recent randomised trials

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1.8 Managing complications

Periodontitis

1.8.1 Advise adults with type 2 diabetes at their annual review that:

- they are at higher risk of periodontitis
- if they get periodontitis, managing it can improve their blood glucose control and can reduce their risk of hyperglycaemia. **[2022]**

1.8.2 Advise adults with type 2 diabetes to have regular oral health reviews (their oral healthcare or dental team will tell them how often, in line with the NICE guideline on dental checks: intervals between oral health reviews). **[2022]**

1.8.3 For guidance for oral healthcare and dental teams on how to provide oral health advice, see the NICE guideline on oral health promotion. **[2022]**

1.8.4 For adults with type 2 diabetes who have been diagnosed with periodontitis by an oral healthcare or dental team, offer dental appointments to manage and treat their periodontitis (at a frequency based on their oral health needs). **[2022]**

Periodontitis

For a short explanation of why the committee made these recommendations, see the rationale and impact section on periodontitis.

Full details of the evidence and the committee's discussion are in evidence review D: periodontitis.

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I can see CLEAR-ly now the LDL is down

Atherosclerotic cardiovascular disease (ASCVD), a consequence of elevated LDL-cholesterol levels, is associated with considerable morbidity and mortality. The cornerstone of its prevention and treatment is the lowering of LDL-cholesterol levels through the high-intensity use of statins. However, a sizeable percentage of those who would benefit from statins report side-effects from their use. The CLEAR Outcomes trial aimed to establish the effects of bempedoic acid, an alternative LDL-cholesterol-lowering agent, on cardiovascular outcomes in a cohort at high risk of ASCVD, but unable or unwilling to take optimal doses of statins for primary or secondary prevention. A 21.1% greater reduction in LDL-cholesterol was recorded in those receiving bempedoic acid compared with placebo. The primary composite endpoint of four-point major adverse cardiovascular events was significantly reduced by 13% with bempedoic acid over a median follow-up of 40.6 months. It also reduced the risk of secondary endpoint events. While bempedoic acid is not a substitute for a statin, and despite higher incidences of some adverse effects, these results suggest that it is a viable alternative for statin-intolerant individuals.

Kevin Fernando
GP in North Berwick

Elevated LDL-cholesterol levels are a proven direct cause of atherosclerotic cardiovascular disease (ASCVD) and mortality. Contemporary lipid guidelines, such as the 2019 ESC/EAS recommendations (Mach et al, 2020), have driven down LDL-cholesterol targets for people at highest CV risk; for secondary prevention in very high-risk people, an LDL-cholesterol reduction of ≥50% from baseline **and** an LDL-cholesterol target of <1.4 mmol/L are now recommended.

Moreover, for every 1 mmol/L reduction in LDL-cholesterol, there is a 22% reduction in the annual rate of major vascular events (Cholesterol Treatment Trialists' Collaboration et al, 2010). Furthermore, there was no evidence of any threshold within the cholesterol target range studied, suggesting that reducing LDL-cholesterol by 2–3 mmol/L would reduce annual CV risk by up to 50%.

Statins are the cornerstone of CV risk reduction strategies, and we can expect around a 50% reduction in LDL-cholesterol with a high-intensity statin approach, such as atorvastatin 40 mg. However, the "rule of 6" tells us the response to dose increase of a statin is not proportional and, in general, doubling a statin dose above the minimally effective dose reduces LDL-cholesterol by only an additional 6% (Knopp, 1999). Therefore, for many of our patients at the highest CV risk, statins alone will be inadequate to achieve these tighter LDL-cholesterol targets.

Whilst it is increasingly accepted that most side-effects attributed to statins are due to a "nocebo" effect (an expectation of adverse side effects, rather than actual adverse events *per se*), it is estimated that around 9% of patients are truly statin-intolerant (Bytyçi et al, 2022). These individuals remain at significant risk of a future major adverse CV event (MACE) and would benefit from alternative LDL-cholesterol-lowering therapy.

Bempedoic acid is a newer addition to our armamentarium to lower LDL-cholesterol. It is a pro-drug that inhibits liver cholesterol synthesis upstream of statins. However, bempedoic acid is activated in the liver, and not peripheral muscle, and therefore is not associated with significant muscle-related adverse effects. The phase 3 clinical trial programme investigating bempedoic acid has demonstrated 17–28% reductions in LDL-cholesterol with bempedoic acid alone, and a 38% reduction when used in combination with ezetimibe (Ballantyne, 2020). In the clinical trial programme, bempedoic acid was generally well

Citation: Fernando K (2023) Diabetes Distilled: I can see CLEAR-ly now the LDL is down. *Diabetes & Primary Care* **25**: [early view publication]

- CVOT for bempedoic acid (Nilemdo) in high CV risk statin-intolerant individuals
- 21% ↓ in LDL-cholesterol
- 13% ↓ (RRR) in MACE
- 1.6% ↓ (ARR) NNT 63 over 40 months

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Health

Weight loss drug semaglutide approved for NHS use

7 days ago

By Annabel Rackham
BBC News

A weight loss jab that has gained popularity in the US has been approved for use by the NHS in England.

The National Institute for Health and Care Excellence (NICE) concluded semaglutide, marketed as Wegovy, is safe, effective and affordable.

Delivered via an injection into the skin, the drug makes people feel fuller and more satisfied, so they eat less.

Famous personalities such as **Elon Musk claim to have used it** - with a "craze" allegedly developing in Hollywood.

Lifestyle changes

Semaglutide for managing overweight and obesity

Technology appraisal guidance [TA875] Published: 08 March 2023

Guidance

Download guidance (PDF)

Next

1 Recommendations

1.1 Semaglutide is recommended as an option for weight management, including weight loss and weight maintenance, alongside a reduced-calorie diet and increased physical activity in adults, only if:

- it is used for a maximum of 2 years, and within a specialist weight management service providing multidisciplinary management of overweight or obesity (including but not limited to tiers 3 and 4), and
- they have at least 1 weight-related comorbidity and:
  - a body mass index (BMI) of at least 35.0 kg/m^2, or
  - a BMI of 30.0 kg/m^2 to 34.9 kg/m^2 and meet the criteria for referral to specialist weight management services in NICE's guideline on obesity: identification, assessment and management.

  Use lower BMI thresholds (usually reduced by 2.5 kg/m^2) for people from South Asian, Chinese, other Asian, Middle Eastern, Black African or African-Caribbean family backgrounds.

1.2 Consider stopping semaglutide if less than 5% of the initial weight has been lost after 6 months of treatment.

Research

JAMA Cardiology | Brief Report

Association of Dapagliflozin Use With Clinical Outcomes and the Introduction of Uric Acid–Lowering Therapy and Colchicine in Patients With Heart Failure With and Without Gout

A Patient-Level Pooled Meta-analysis of DAPA-HF and DELIVER

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IMPORTANCE Gout is common in patients with heart failure (HF), and sodium-glucose cotransporter 2 inhibitors, a foundational treatment for HF, reduce uric acid levels.

OBJECTIVE To examine the reported prevalence of gout at baseline, the association between gout and clinical outcomes, and the effect of dapagliflozin in patients with and without gout and the introduction of new uric acid–lowering therapy and colchicine.

DESIGN, SETTING, AND PARTICIPANTS This post hoc analysis used data from 2 phase 3 randomized clinical trials conducted in 26 countries, DAPA-HF (left ventricular ejection fraction [LVEF] ≤40%) and DELIVER (LVEF >40%). Patients with New York Heart Association functional class II through IV and elevated levels of N-terminal pro–B-type natriuretic peptide were eligible. Data were analyzed between September 2022 and December 2022.

INTERVENTION Addition of once-daily 10 mg of dapagliflozin or placebo to guideline-recommended therapy.

MAIN OUTCOMES AND MEASURES The primary outcome was the composite of worsening HF or cardiovascular death.

RESULTS Among 11 005 patients for whom gout history was available, 1117 patients (10.1%) had a history of gout. The prevalence of gout was 10.3% (488 of 4747 patients) and 10.1% (629 of 6258 patients) in those with an LVEF up to 40% and greater than 40%, respectively. Patients with gout were more often men (897 of 1117 [80.3%]) than those without (6252 of 9888 [63.2%]). The mean (SD) age was similar between groups, 69.6 (9.8) years for patients with gout and 69.3 (10.6) years for those without. Patients with a history of gout had a higher body mass index, more comorbidity, and lower estimated glomerular filtration rate and were more often treated with a loop diuretic. The primary outcome occurred at a rate of 14.7 per 100 person-years (95% CI, 13.0-16.5) in participants with gout compared with 10.5 per 100 person-years (95% CI, 10.1-11.0) in those without (adjusted hazard ratio [HR], 1.15; 95% CI, 1.01-1.31). A history of gout was also associated with a higher risk of the other outcomes examined. Compared with placebo, dapagliflozin reduced the risk of the primary end point to the same extent in patients with (HR, 0.84; 95% CI, 0.66-1.06) and without a history of gout (HR, 0.79; 95% CI, 0.71-0.87; *P* = .66 for interaction). The effect of dapagliflozin use with other outcomes was consistent in participants with and without gout. Initiation of uric acid–lowering therapy (HR, 0.43; 95% CI, 0.34-0.53) and colchicine (HR, 0.54; 95% CI, 0.37-0.80) was reduced by dapagliflozin compared with placebo.

CONCLUSIONS AND RELEVANCE This post hoc analysis of 2 trials found that gout was common in HF and associated with worse outcomes. The benefit of dapagliflozin was consistent in patients with and without gout. Dapagliflozin reduced the initiation of new treatments for hyperuricemia and gout.

TRIAL REGISTRATION ClinicalTrials.gov Identifiers: NCT03036124 and NCT03619213

Supplemental content

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JAMA Cardiol. doi:10.1001/jamacardio.2022.5608
Published online February 22, 2023.

- Post hoc analysis of DAPA-HF & DELIVER (dapagliflozin HF studies)
- Prevalence of gout was around 10%
- Worsening HF or CV death was significantly higher in those with gout
- Dapagliflozin reduced the initiation of medication to reduce urate levels or treat gout flares

SURPASS CLINICAL PROGRAM

DESIGNED TO DELIVER ROBUST DATASET WITH MULTIPLE HEAD-TO-HEAD TRIALS

Comparison of Proposed Actions of GIP And GLP-1[5]

Brain

GIP Activity
- ⬇ Reduced food intake

GLP-1 Activity
- ⬇ Reduced food intake
- ⬆ Increased satiety

Whole-Body

GIP Activity
- ⬆ Increased insulin sensitivity

Pancreas

GIP Activity
- ⬆ Increased insulin
- ⬆ Increased glucagon

GLP-1 Activity
- ⬆ Increased insulin
- ⬇ Reduced glucagon

Stomach

GLP-1 Activity
- ⬇ Reduced gastric emptying

Derived from preclinical studies: Samms RJ, Coghlan MP, Sloop KW. How may GIP enhance the therapeutic efficacy of GLP-1? *Trends Endocrinol Metab*. 2020;31(6):416.4

SURPASS CV Outcomes Trial (event driven, CV indication) (2025)

2019 2020 2021 2022

Finerenone for treating chronic kidney disease in type 2 diabetes

Technology appraisal guidance [TA877] Published: 23 March 2023

Guidance

Download guidance (PDF)

Next

1 Recommendations

1.1 Finerenone is recommended as an option for treating stage 3 and 4 chronic kidney disease (with albuminuria) associated with type 2 diabetes in adults. It is recommended only if:

- it is an add-on to optimised standard care; this should include, unless they are unsuitable, the highest tolerated licensed doses of:
  - angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs) and
  - sodium–glucose cotransporter-2 (SGLT2) inhibitors and
- the person has an estimated glomerular filtration rate (eGFR) of 25 ml/min/1.73 m^2 or more.

1.2 This recommendation is not intended to affect treatment with finerenone that was started in the NHS before this guidance was published. People having treatment outside this recommendation

PLACE OF TECHNOLOGY

Technology can be useful in people with type 2 diabetes but needs to be part of an holistic plan of care and supported by DSMES.

Consider CGM in people with type 2 diabetes on insulin.

Adapt the clinic/system to optimize effective use of technology among people with type 2 diabetes, particularly to support behavior change through self-monitoring.

Continuous glucose monitoring

1.6.17 Offer intermittently scanned continuous glucose monitoring (isCGM, commonly referred to as 'flash') to adults with type 2 diabetes on multiple daily insulin injections if any of the following apply:

- they have recurrent hypoglycaemia or severe hypoglycaemia
- they have impaired hypoglycaemia awareness
- they have a condition or disability (including a learning disability or cognitive impairment) that means they cannot self-monitor their blood glucose by capillary blood glucose monitoring but could use an isCGM device (or have it scanned for them)
- they would otherwise be advised to self-measure at least 8 times a day.

For guidance on continuous glucose monitoring (CGM) for pregnant women, see the NICE guideline on diabetes in pregnancy. **[2022]**

Offer isCGM to adults with insulin-treated type 2 diabetes who would otherwise need help from a care worker or healthcare professional to monitor their blood glucose. **[2022]**

Consider real-time continuous glucose monitoring (rtCGM) as an alternative to isCGM for adults with insulin-treated type 2 diabetes if it is available for the same or lower cost. **[2022]**

CGM should be provided by a team with expertise in its use, as part of supporting people to self-manage their diabetes. **[2022]**

Intermittent and real-time continuous glucose monitoring systems comparison chart

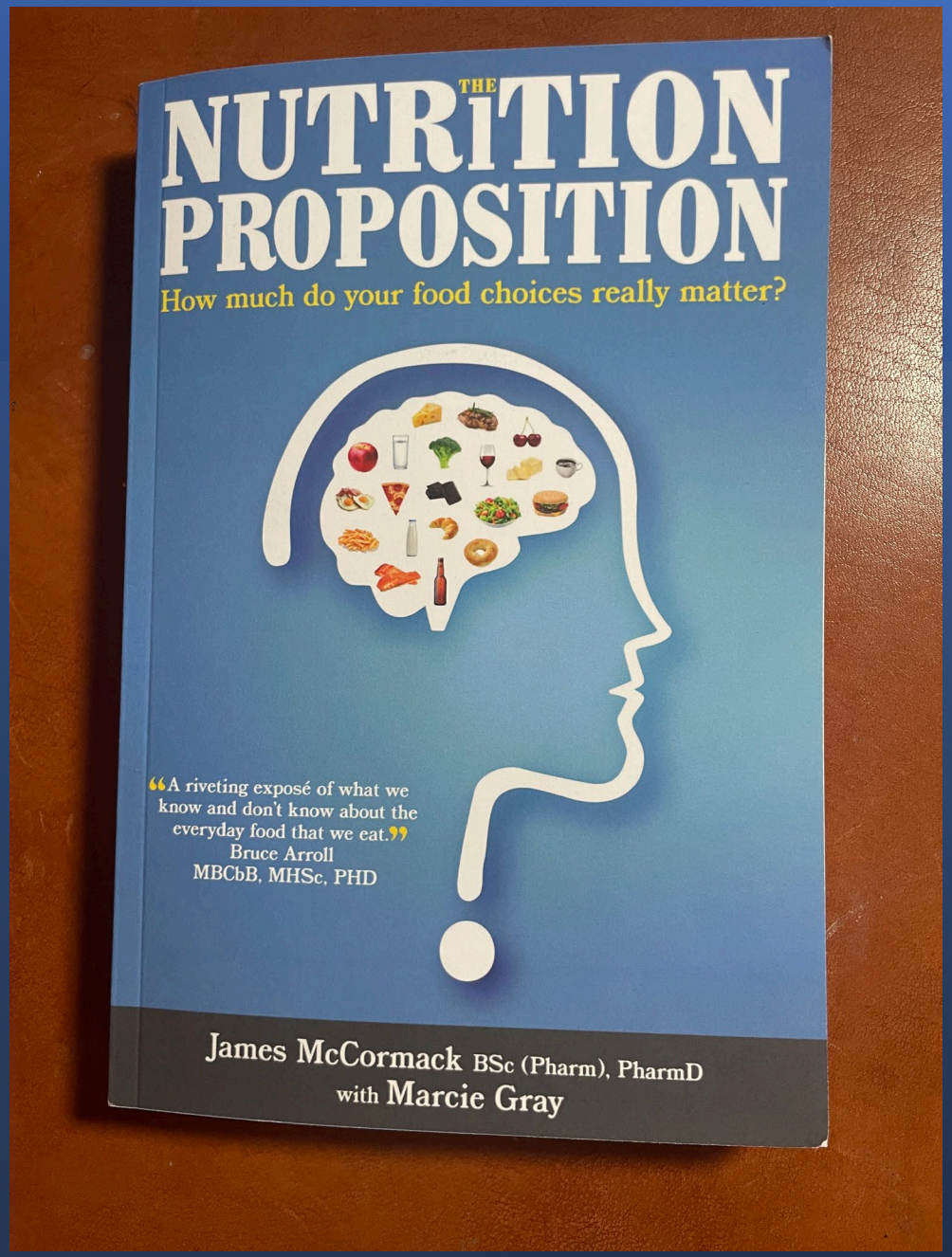
Diabetes Specialist Nurse Forum UK

	Freestyle Libre 2	Freestyle Libre 3	Dexcom One	Dexcom G6	Dexcom G7	Medtronic G4	GlucoRx AiDEX	GlucoMen Day *	Medtrum Touch Care Nano
Real-time CGM	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
MARD	9.2	7.8	9.0	9.0	8.2	10.6	9.1	9.7	9.1
Published accuracy data	Yes (T1 n=133)	Yes (T1 n=83)	Yes (T1 n=260)	Yes (T1 n=260)	Yes (T1 n=257)	Yes	Yes (T1 n=14)	Yes (T1 n=8)	Yes (T1 n=10)
Sensor life	14 days	14 days	10 days	10 days	10 days + 12 hr grace period	7 days	14 days	14 Days	7-14 days
Sensor warm up time	60 mins	60 mins	120 mins	120 mins	30 mins	120 mins	60 mins	55 mins	120 mins
Transmitter Life	N/A	N/A	3 months	3 months	N/A	12 months	4 years	5 years	12 months
Reader available	Yes	No	Yes	Yes	Yes	No	No	No	Yes
App needed	LibreLink	Libre 3	Dexcom One	Dexcom G6	Dexcom G7	MiniMed	GlucoRx AiDEX	GlucoMen Day CGM	EasySense
Capillary glucose calibration	No	No	No	No	No	No	No	Every 48 hours *	Every 12-24 hrs
High & low alarms	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Predictive alarms	No	No	No	Yes	Yes	Yes	No	Yes	Yes
Stand-alone use	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Pump compatibility	No	No	No	Tandem T:slim DANA-i YpsoPump	No	Medtronic 780G	No	No	Touch Care Nano pump
Closed loop compatibility	No	No	No	Yes	No	Yes	No	No	Auto-suspend
Data share HCP	Libreview	Libreview	Clarity	Clarity	Clarity	CareLink	CGM Viewer	GlucoLog web	EasyView
Data share friends/family	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
RCT data	Yes	Yes (FSL/FSL2)	Yes (G4/5/6)	Yes	No	No	No	No	No
UK approved wearable site	Upper arm	Upper arm	Buttocks [+] abdomen upper arm	Buttocks [+] abdomen upper arm	Buttocks [+] abdomen upper arm	Abdomen upper arm	Abdomen upper arm	Lower back abdomen upper arm	Abdomen upper arm

= available on prescription (FP10)

* From September 2022 [+] 2-17 years old , please check individual manufacturers' guidelines for age specific licences

Version 2.0 August 2022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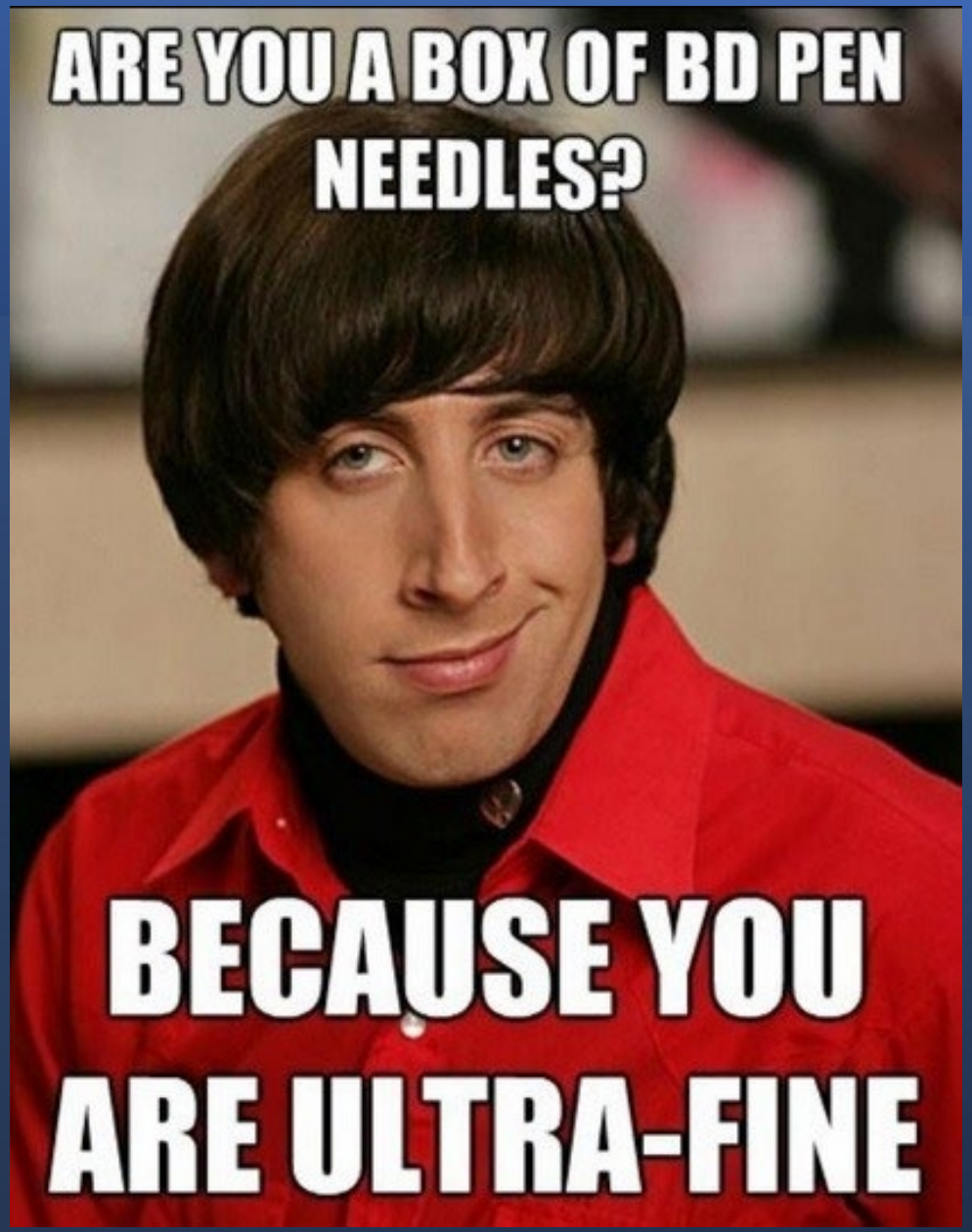
MBCbB, MHSc, PHD
James McCormack BSc (Pharm), PharmD
with Marcie Gray

“

The past is a foreign country: they do things differently there

L.P. Hartley “The Go-Between” Published 1957


ARE YOU A BOX OF BD PEN NEEDLES?
BECAUSE YOU ARE ULTRA-FINE

Thank you for listening & please get in touch if you have any questions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