GLP-1RA'S-NON-SCIENTIC STUFF

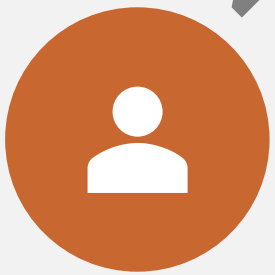
Naresh Kanumilli

PRESENTER DISCLOSURES

- **Current Roles:** PCDS- Trustee, DUKPCOC- committee member, GM-Diabetes Board chair, GM&EC SCN- clinical Lead. Honorary Clinical Advisor for primary care- GMCRN
- **Honoraria/Travel grants**: AstraZeneca, Boehringer Ingelheim, Lilly, MSD, Novartis, Novo Nordisk, Roche, Sanofi and Menarini.
- **Research Support**: AstraZeneca, Boehringer Ingelheim, Lilly, MSD, Novartis, Janssen, Novo Nordisk, Roche and Sanofi
- **Speaker's Bureau**: AstraZeneca, Menarini Group, Boehringer Ingelheim, Lilly, MSD, Napp, Novartis, Novo Nordisk, Roche, Amgen and Sanofi

REAL-LIFE PRACTICALITIES OF GLP-1 RAS AND THEIR IMPACT

WHY AND WHEN TO PRESCRIBE



WHO TO PRIORITISE

EFFECTS ON WORKLOAD

PRIVATE PRESCRIBING AND THE BLACK MARKET: CHALLENGES FOR HCPS

GLP-1RAS: MULTIFACTORIAL EFFECTS BEYOND GLYCAEMIC CONTROL

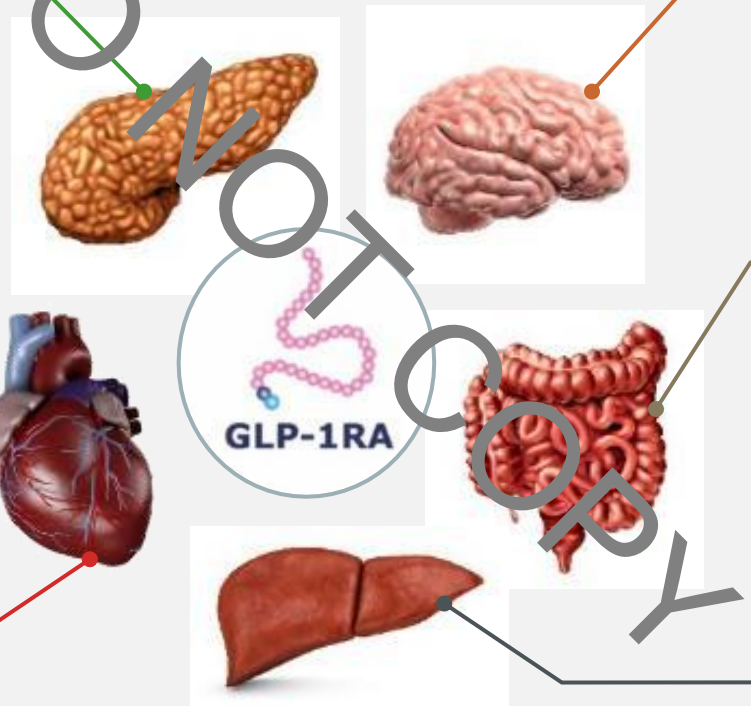
DATA ORIGINATING FROM HUMAN AND NON-HUMAN (i.e. ANIMAL AND IN-VITRO) STUDIES

Pancreas

- ↑ Beta-cell function[1*]
- ↓ Beta-cell death[1]
- ↑ Insulin production[1*]
- ↓ Glucagon secretion[1]

Brain

- ↓ Body weight[5*]
- ↓ Food intake[6]
- ↓ Appetite[7,8]



Incretin system

Replacement of deficient GLP-1 response[9]

- ↓ Glucose production[10]
- ↑ Insulin sensitivity[10]
- ↓ Conversion carbohydrate to fat[10]
- ↓ Accumulation of lipids[10]
- ↓ Retention of lipids[11]

Heart

- ↓ Cardiovascular risk[2]
- ↓ Fatty acid metabolism[3]
- ↑ Cardiac function[3]
- ↓ Systolic blood pressure[3]
- ↓ Inflammation[4]
- ↓ Plaque progression[4]

Liver

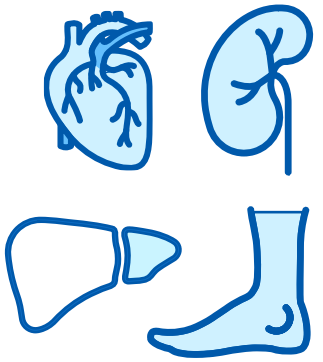
*Data from non-human studies. GLP-1, glucagon-like peptide-1; GLP-1RA, glucagon-like peptide-1 receptor agonist.

1. Campbell JE, DJ Drucker. *Cell Metab* 2013;17:819–837; 2. Marso SP et al. *N Engl J Med* 2016;375:311–322; 3. Ryan D, Acosta A. *Obesity* 2015;23:1119–1129; 4. Hogan AE et al. *Diabetologia* 2014;57:781–784; 5. Baggio LL, Drucker DJ. *J Clin Invest* 2014;124:4223–4226; 6. Bagger JI et al. *Clin Endocrinol Metab* 2015;100:4541–4552; 7. Flint A et al. *J Clin Invest* 1998;101:515–520; 8. Blundell J et al. Presented at the 76th Scientific Sessions of the American Diabetes Association. June 10–14, 2016. New Orleans, Louisiana, USA: Oral Presentation 23-OR; 9. Tong J, D'Alessio D. *Diabetes* 2014;63:407–409; 10. Armstrong MJ et al. *J Hepatol* 2016;64:399–408; 11. Armstrong MJ et al. *Lancet* 2016;387:679–90.

Chronic cardiovascular-renal-metabolic diseases are a consequence of complex and interlinked pathophysiological processes[1]

Each condition can increase the risk of another[2,3]

These are all important risk factors for end-organ damage[4-7]



Weight gain, adiposity and **inflammation** are conditions that can initiate a **decline in metabolic health**[1,2]

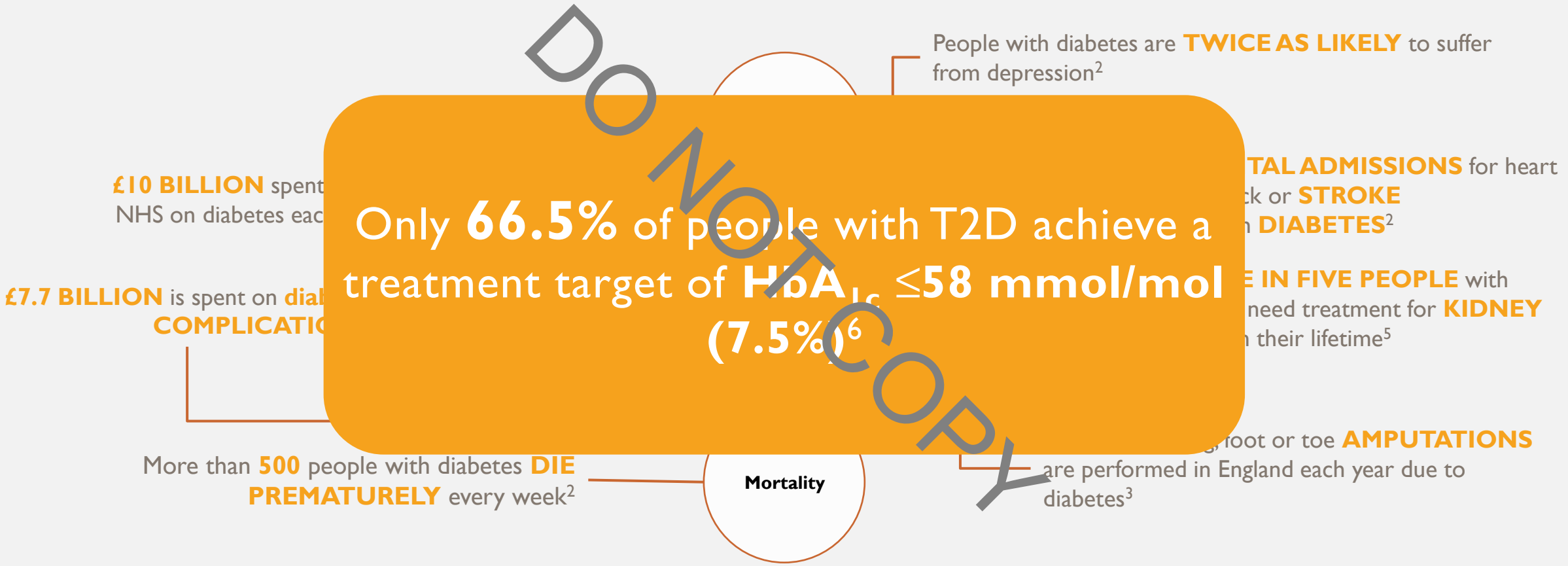
Adiposity and **insulin resistance** can promote **hypertension**, and are associated with **dyslipidaemia** and **T2D** as well as **inflammation**[4-7]

The **association** of **T2D** and **obesity** with cardiovascular-renal-metabolic diseases such as **CKD, CVD, PAD** and **MASH** has been well-documented[1,8]

CKD, chronic kidney disease; CVD, cardiovascular disease; MASH, metabolic dysfunction-associated steatohepatitis; T2D, type 2 diabetes; PAD, peripheral artery disease.

1. Lingvay I, *et al. Lancet*. 2022;**399**;394-405; 2. Li M, *et al. Sig Transduct Target Ther*. 2022;**7**:216; 3. Schönknecht YB, *et al. Eur J Nutr*. 2022;**61**:3077-3083; 4. Tasic I, *et al. Front. Biosci.* 2018;10(1):166–174; 5. Musunuru K. *Lipids*. 2010;**45**(10):907–14; 6. Mendrick DL, *et al. Toxicol Sci*. 2018;162(1):36–42. 7. Sorriento D, *et al. Int J Mol Sci*. 2019;**20**(16):3879; 8. Ndumele CE, *et al. Circulation*.2023;**148**:1606-1635.

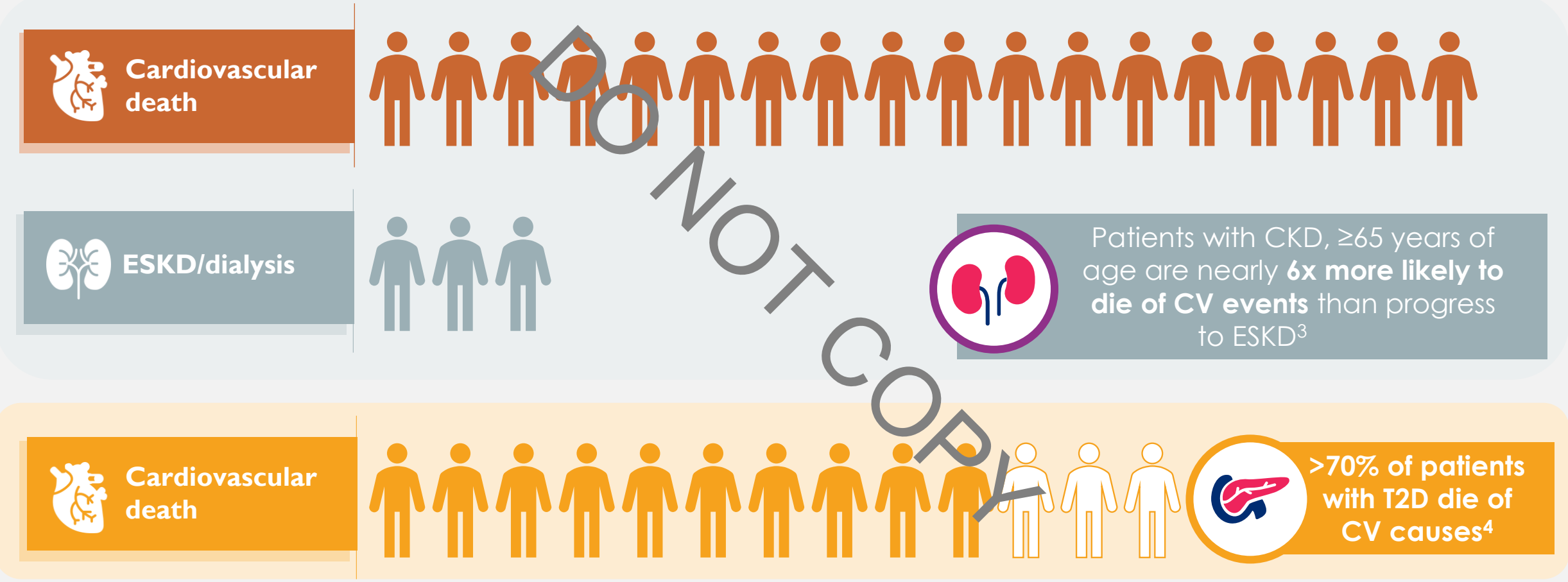
DIABETES IS ONE OF THE MOST SIGNIFICANT PUBLIC HEALTH CHALLENGES OF OUR TIME[1]



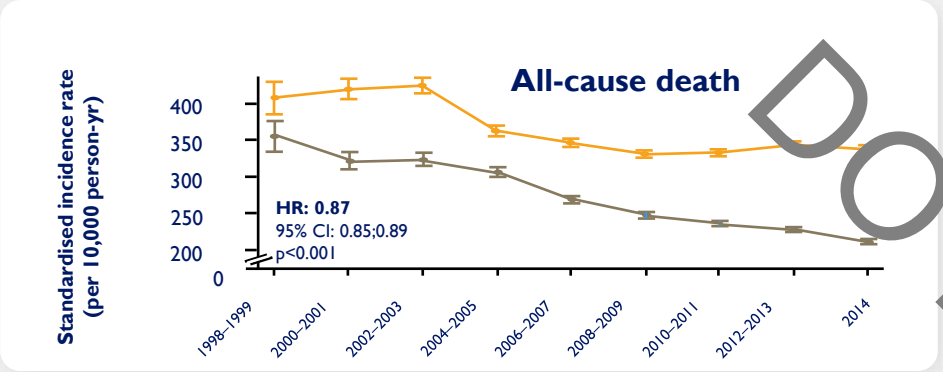
HbA$_{1c}$, glycated haemoglobin; T2D, type 2 diabetes.

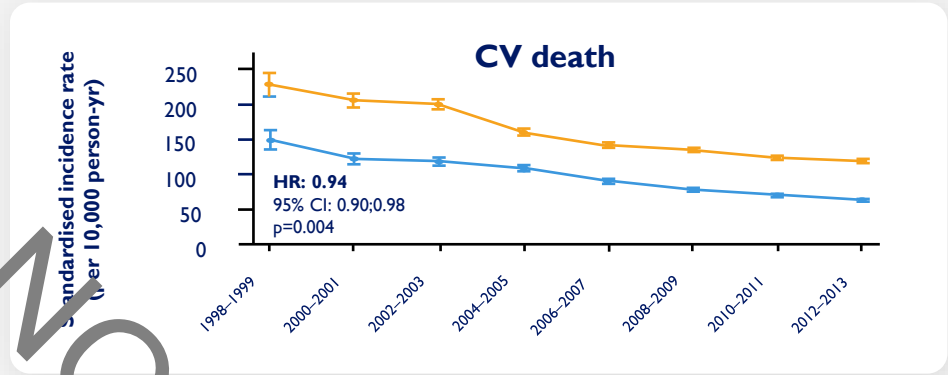
1. National Institute for Health Research, NIHR Dissemination Centre—THEMED REVIEW. On the level: Evidence for action on type 2 diabetes. September 2016; 2. Diabetes UK. Us, diabetes and a lot of facts and stats. https://www.diabetes.org.uk/resources-s3/2019-02/1362B_Facts%20and%20stats%20Update%20Jan%202019_LOW%20RES_EXTERNAL.pdf. Accessed May 2020; 3. National Diabetes Foot Care Audit Third Annual Report. Available at: https://www.hqip.org.uk/wp-content/uploads/2018/03/National-Diabetes-Foot-Care-Audit-2014-2017.pdf. Accessed May 2020; 4. Hex N *et al. Diabet Med* 2012;29:855–62; 5. Diabetes UK. Kidney disease (nephropathy). Available at: https://www.diabetes.org.uk/kidneys. Accessed May 2020; 6. Diabetes UK. State of the Nation 2016: Time to take control of diabetes. Available at: https://www.diabetes.org.uk/professionals/position-statements-reports/statistics/state-of-the-nation-2016-time-to-take-control-of-diabetes. Accessed May 2020.

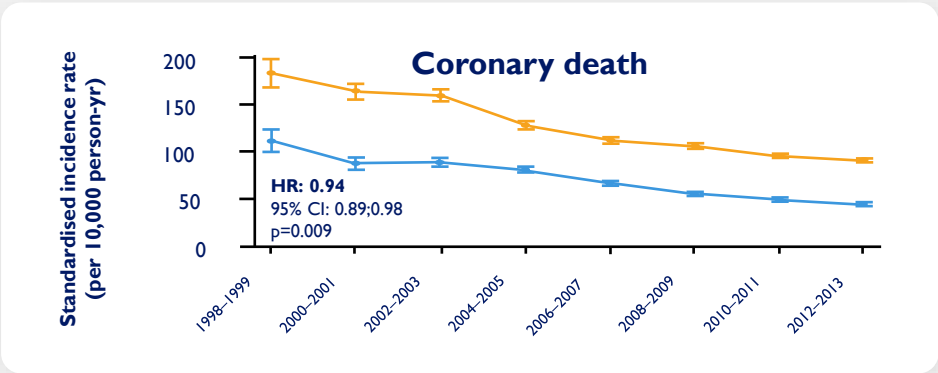
CV COMPLICATIONS ARE THE LEADING CAUSE OF MORBIDITY AND MORTALITY IN PATIENTS WITH CKD* AND T2D[1,2]

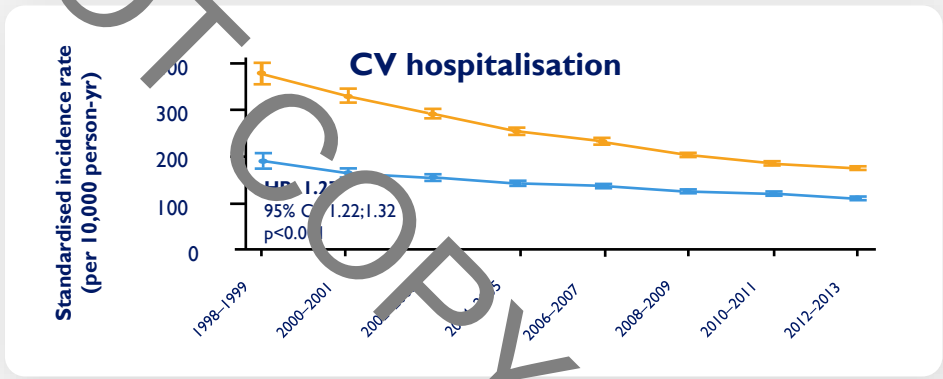


Individuals with Type 2 Diabetes are at increased risk of CVD vs. those without[1]









Individuals with T2D

Matched controls

Values are ratios of hazard ratios for patients with type 2 diabetes vs. controls, during a 10-year time period. A value above 1 means a greater event rate reduction, and a value below 1 a lesser event-rate reduction, in the patients with diabetes than in the matched controls[1]

The P value is for the interaction between time period and group — that is, patients with type 2 diabetes and matched controls[1]

Data are mean ± 95% CI; HR (95% CI), patients in Sweden with T2D vs. matched controls.

Adapted from Rawshani A *et al. N Engl J Med* 2017;**376**:1407–18.

Although CV death rate is declining in general, the difference in CV death between individuals with and without T2D is still evident

CI, confidence interval; CV, cardiovascular; CVD, cardiovascular disease; HR, hazard ratio; yr, years.

1. Rawshani A, *et al. N Engl J Med.* 2017;**376**:1407–18.

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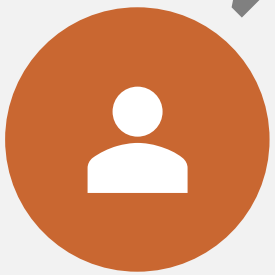
WHY AND WHEN TO PRESCRIBE



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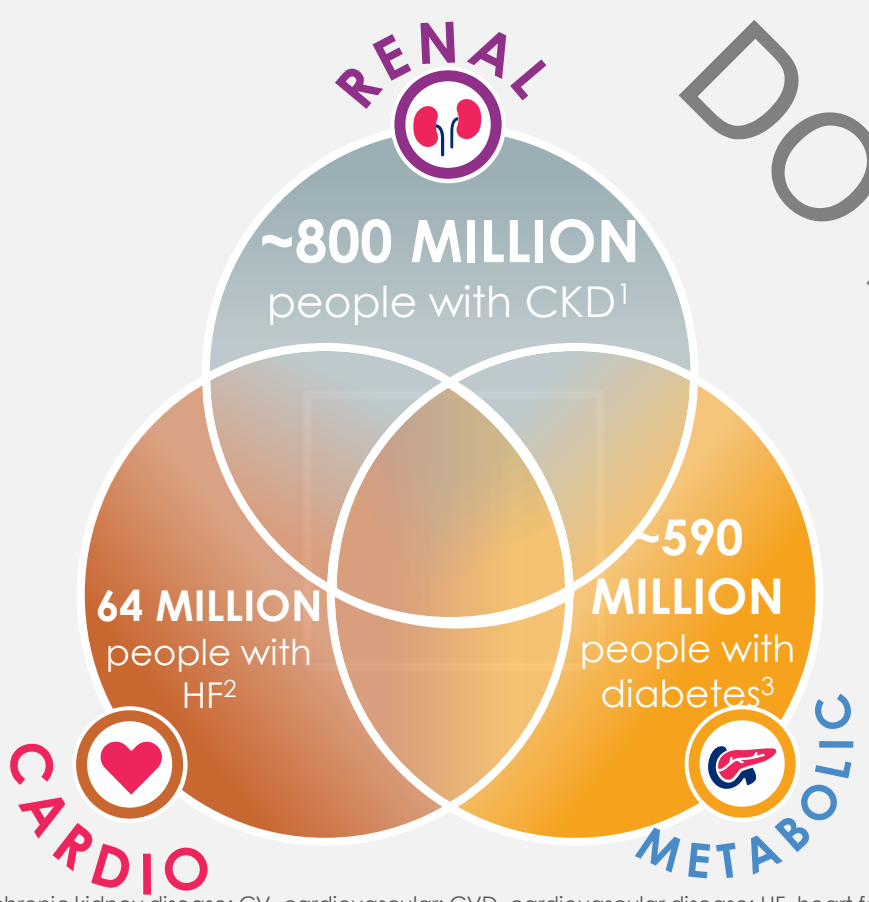
PRIMARY CARE IS A KEY OPPORTUNITY FOR EARLY AND EFFECTIVE CV RISK IDENTIFICATION



Vascular damage may already be present before a patient is diagnosed with T2D and/or CKD[4,5]

Risks of CV death, CV events and hospitalisation exponentially increase with progressively worsening kidney function[6]

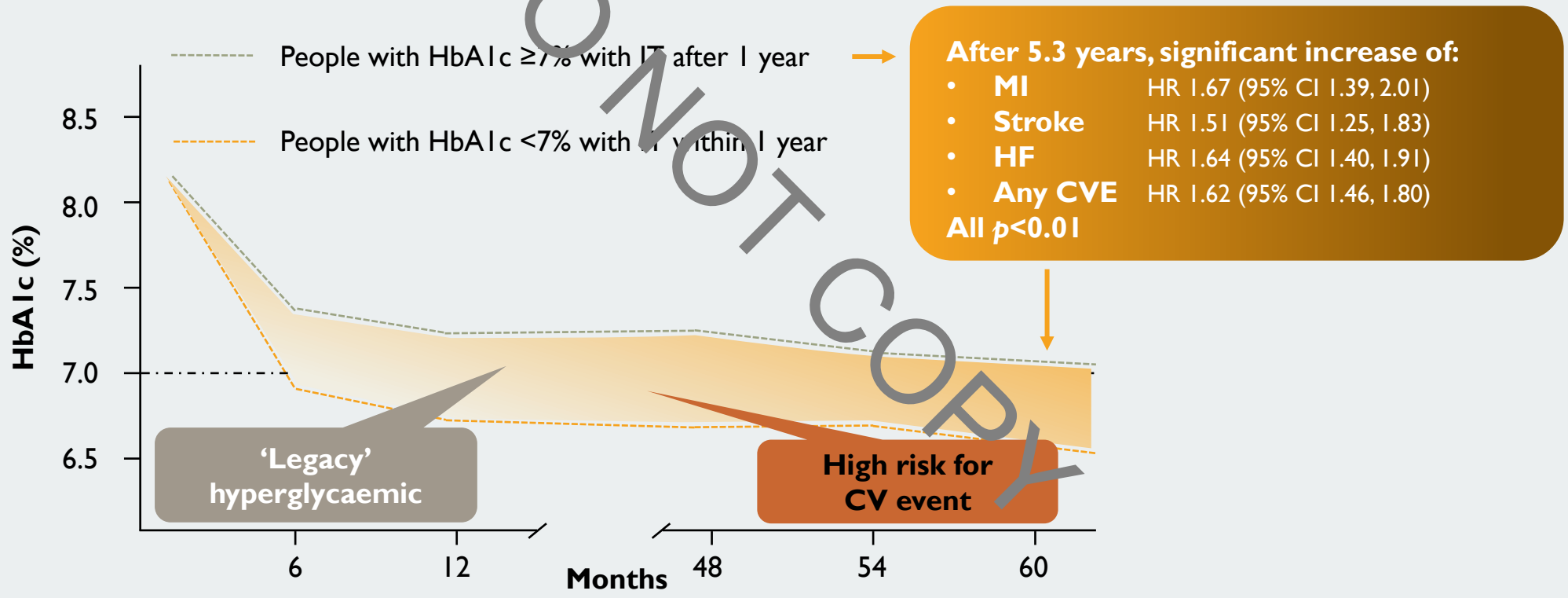
People with T2D without pre-existing cardio-renal disease have an 80% lifetime risk of developing CVD or renal events and a 41% risk of CV death[7]

CKD, chronic kidney disease; CV, cardiovascular; CVD, cardiovascular disease; HF, heart failure; T2D, type 2 diabetes

1. American Society of Nephrology. The hidden epidemic: worldwide, over 850 million people suffer from kidney diseases. 2018. https://www.asn-online.org/news/2018/0626-Joint_Hidden_Epidem.pdf (accessed Sep 2025); 2. Vijay K *et al. Cardiorenal Med* 2022;12:1; 3. *International Diabetes Federation. IDF Diabetes Atlas* 11th edition. 2025. https://diabetesatlas.org/resources/idf-diabetes-atlas-2025/(accessed Sep 2025); 4. Claudel SE & Verma A. *Circulation* 2025;151:716; 5. Kotwal SS & Perkovic V. *Circulation* 2024;150:975; 6. Go AS *et al. N Engl J Med* 2004;351:1296; 7. International Diabetes Federation. Global clinical practice recommendations. https://idf.org/download-global-clinical-practice-recommendations/ (accessed Sep 2025)

DELAY IN T2D-OPTIMISING TREATMENT AND POOR GLYCAEMIC CONTROL SIGNIFICANTLY INCREASES THE RISK OF HF, MI AND STROKE[1,2]

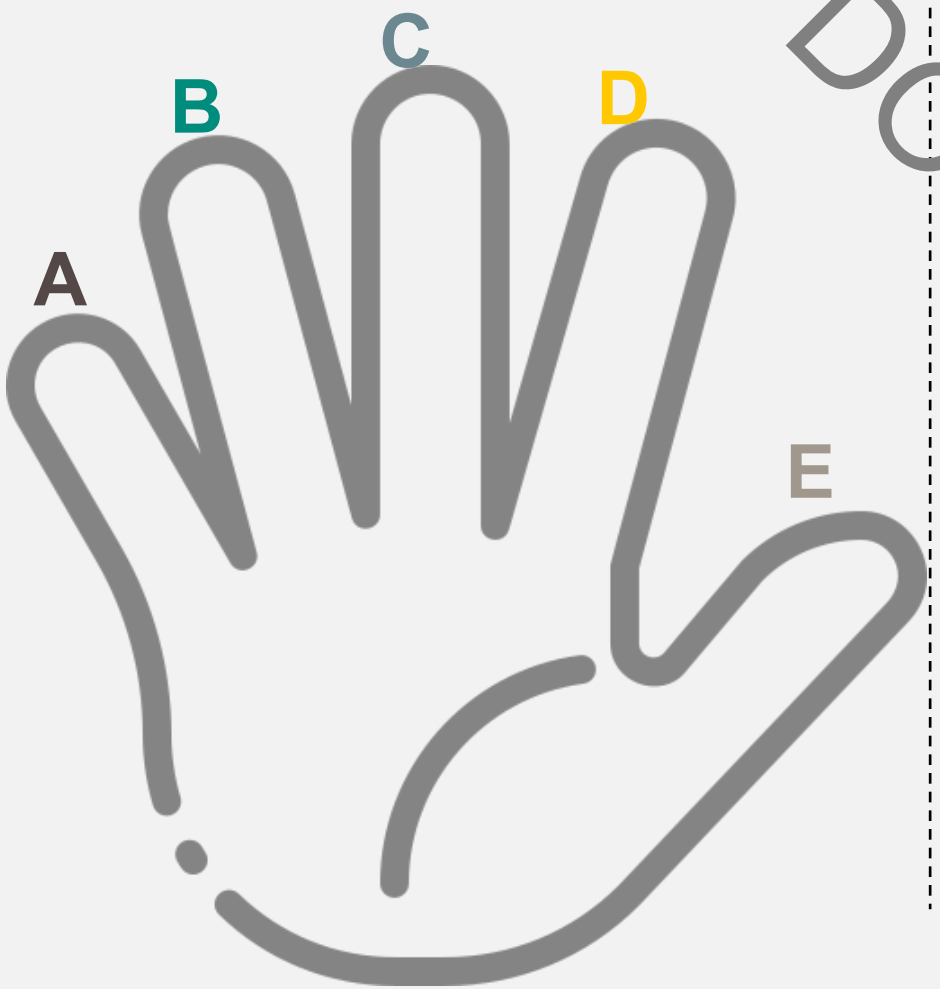
Retrospective cohort study of 105,477 people with T2D in the UK between 1990 and 2012



The reference group was those with a time to treatment intensification <12 months and HbA1c <7 or 7.5% (<53 or 58 mmol/mol)
CV, cardiovascular; CVE, macrovascular event; HbA1c, glycated haemoglobin; HF, heart failure; HR, hazard ratio; IT, treatment intensification; MI, myocardial infarction; T2D, type 2 diabetes
1. Paul SK *et al. Cardiovasc Diabetol* 2015;14:100; 2. Khunti K & Millar-Jones D. *Prim Care Diabetes* 2017;11:3

CONNECT THE DOTS

THE ABCDE OF CKD AND CV RISK



A Albuminuria

B Blood pressure

C Cholesterol

D Diabetes

E eGFR status

Aim: to encourage early intervention

ABCDE is applicable to:

- Men aged >40 years
- Women after menopause or aged >50 years

ABCDE is used to:

- Identify risk of CV disease
- Diagnose CKD

The **ABCDE** profile can be extended with ‘F’ for ‘fat’ and ‘N’ for ‘nicotine’.

CKD, chronic kidney disease; CV, cardiovascular; eGFR, estimated glomerular filtration rate

European Renal Association. Do you know your ABCDE profile? 2025. https://www.era-online.org/publications/do-you-know-your-abcde-profile/ (accessed Sep 2025)

COMMUNICATION BETWEEN CLINICIANS IS CRITICAL TO ENSURE CRM CONDITIONS ARE TREATED HOLISTICALLY

Multidisciplinary team: communication between all members is needed (phone call, email, text message, letter)

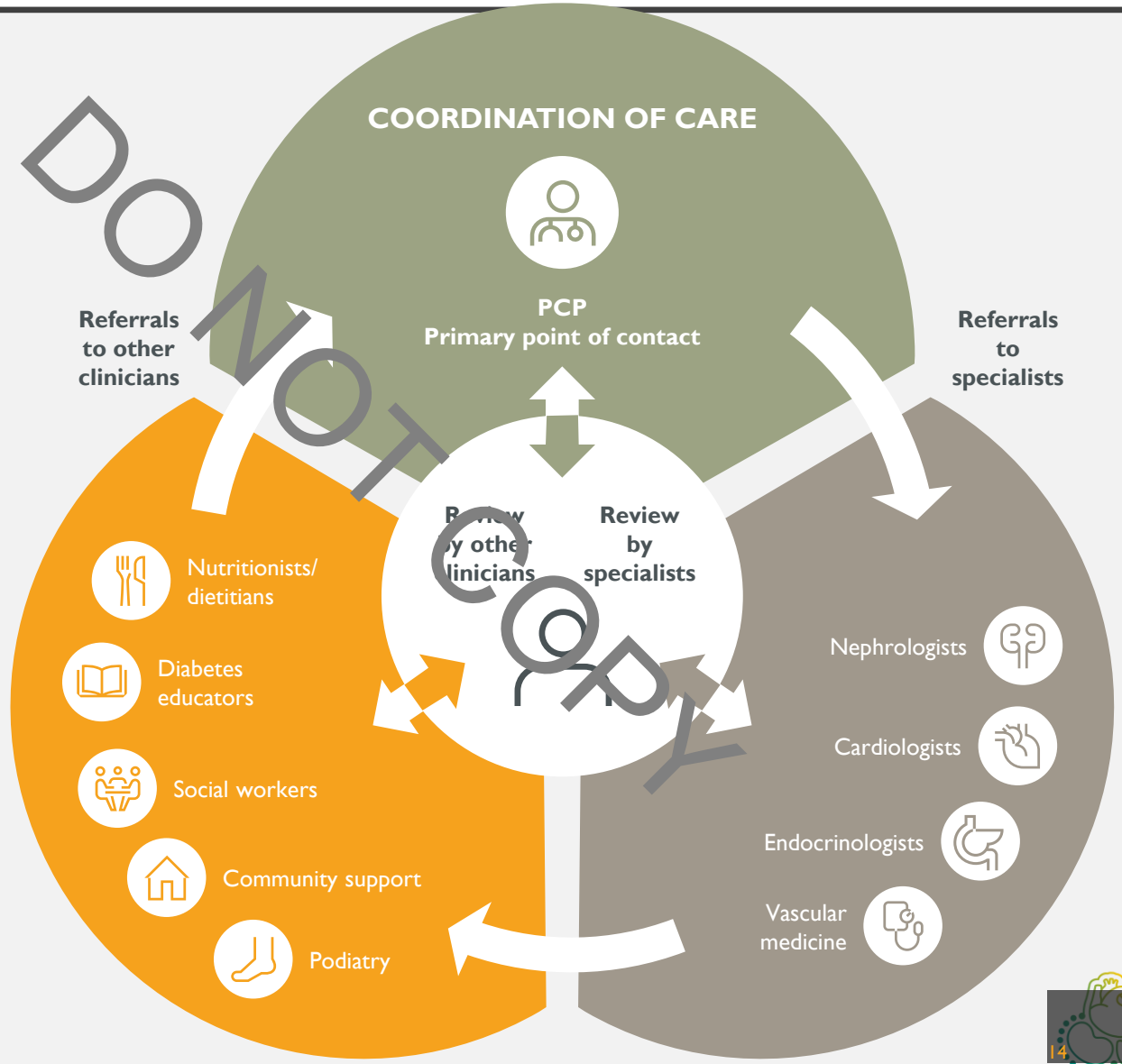


Figure adapted from Kushner PR *et al. Clin Diabetes* 2022;40:401
CRM, cardio, renal and metabolic; PCP, primary care physician
Kushner PR *et al. Clin Diabetes* 2022;40:401

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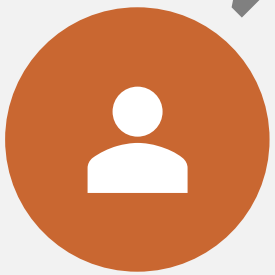

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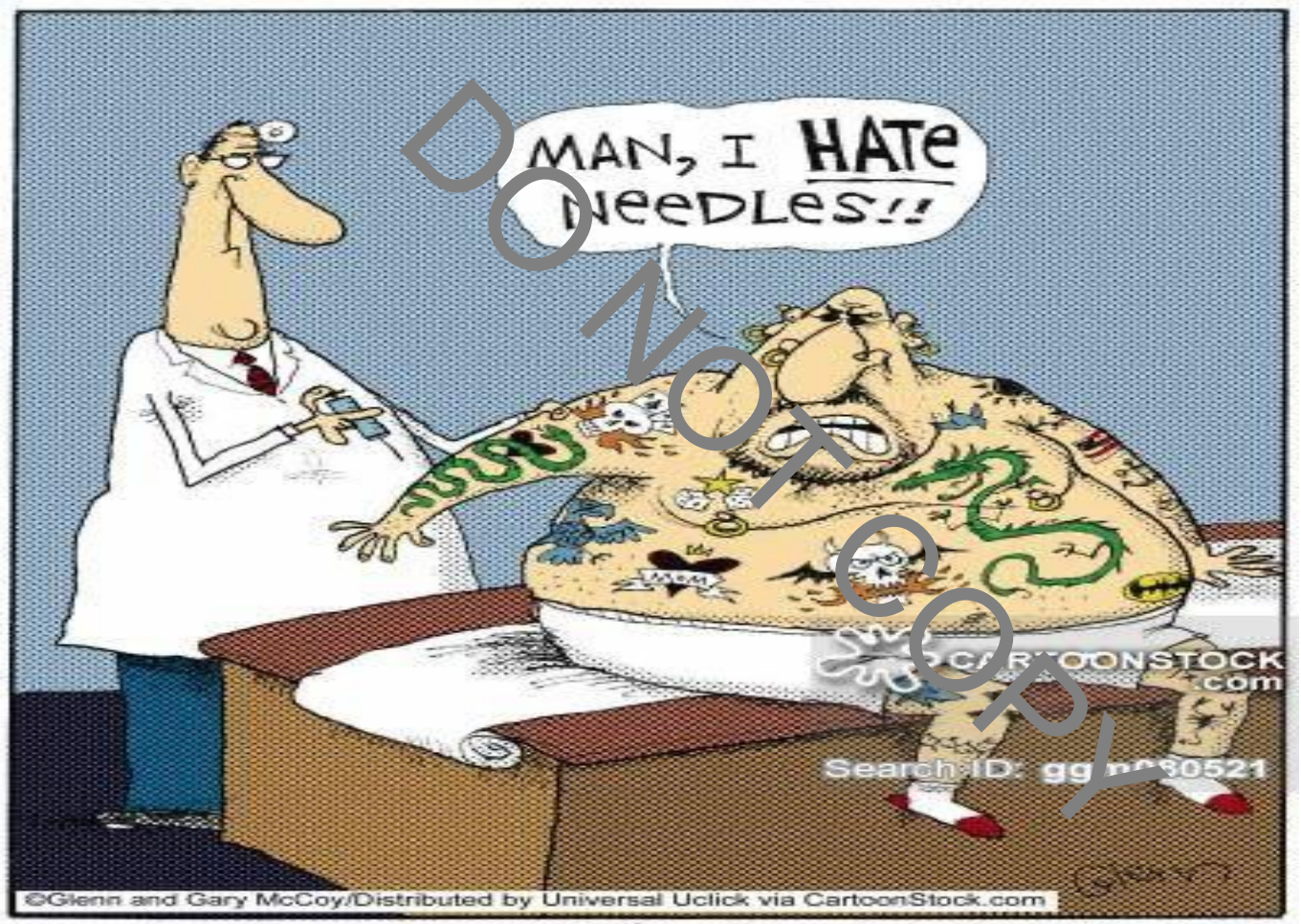

MAN, I HATe NeedLes!!
©Glenn and Gary McCoy/Distributed by Universal Uclick via CartoonStock.com

INITIATION CHECKLIST

- Continue to promote T2DM lifestyle/ remission and education
- Review medical history
- Assess for any contraindications or cautions (e.g. severe GI disease, pancreatitis)
- Consider severe hepatic impairment
- Explain the rationale for recommending therapy

- Explain the mode of action including GI effects
- Advise on weekly dosing regimen
- Discuss self-monitoring of blood glucose if on insulin and/or sulphonylureas and look to empower self-titration of therapies
- Provide sick day guidance
- Arrange appropriate monitoring of response and a review date

- Consider effect on absorption of warfarin and other drugs with a narrow therapeutic index (e.g. digoxin) due to slow gastric emptying and monitor when initiating or increasing tirzepatide.

- Ensure robust contraception for women, transmen and non-binary people of childbearing potential.

- Switch to a non-oral contraceptive method or add a barrier method to oral contraceptive (for four weeks) when initiating or increasing tirzepatide. See FSRH Guidance

- Review oral HRT, consider switching to transdermal. See BMS guidance

- Review and adjust other glucose-lowering therapies

CONTRAINDICATIONS

Pregnancy and breastfeeding

Some form of contraception is recommended in women of childbearing age[1]

Severe GI diseases

Avoid GLP-1 RAs in disorders such gastroparesis and inflammatory bowel disease because of their effect of slowed gastric emptying and potential exacerbation of GI symptoms[1]

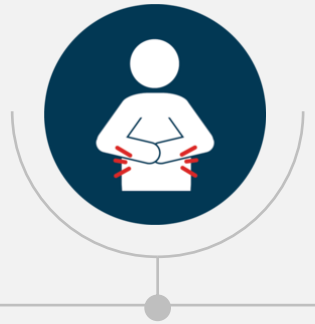
History of pancreatitis[1]

Personal or family history of medullary thyroid cancer [2]

Personal or family history of multiple endocrine neoplasia type 2 (MEN2) [2]

- 1. Marx N, et al. Circulation. 2022;146:1882-1894; 2. Das SR, et al. J Am Coll Cardiol. 2020;76:1117-1145.

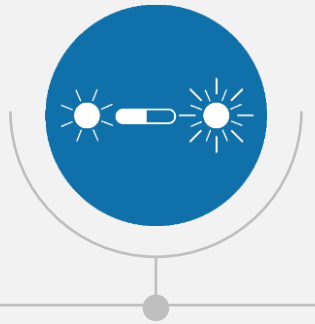
GI SIDE EFFECTS ARE COMMON



GI side effects can manifest as:

- Nausea
- Vomiting
- Diarrhea
- Constipation

These GI side effects are often dose dependent



GI side effects are often mild to moderate in intensity

These effects are often transient and tend to occur during initiation or uptitration of treatment

- Nauck MA, et al. Mol Metab. 2021;46:101102; Nauck MA, et al. Eur J Endocrinol. 2019;181:R211-R234; Bettge K, et al. Diabetes Obes Metab. 2017;19:336-347; Wilding JPH, et al. N Engl J Med. 2021;384:989; Davies M, et al. Lancet. 2021;397:971-984; Wadden TA, et al. JAMA. 2021;325:1403-1413; Pi-Sunyer X, et al. N Engl J Med. 2015;373:11-22.

Reducing GI AEs With GLP-1 RAs

Guidelines for Patients

Eating Habits

- Eat slowly
- Only if really hungry
- Smaller portions
- No lying down after meal
- Stop when satiated
- No straw
- No distractions, enjoy savoring
- Not too active after meal
- No meals near bedtime

Food Composition

- Low-fat diet
- Boiling, oven, griddle
- Water-rich foods
- Avoid sweets, dressings, spicy, or canned foods
- Clear drinks (small sips, not too much)

Lifestyle

- Fresh air, light exercise
- Food diary to identify what works better

Gorgojo-Martínez JJ, et al. J Clin Med. 2023;12:145.

Managing GI AEs With GLP-1 RAs

Guidance for Practitioners

Before

Take time to talk with the patient

- Manage expectations
- Discuss anticipated adverse effects
- Emphasize importance of following the diet recommendations

Dose Escalation

- Wait 2-4 more weeks before increasing dose
- Stop treatment temporarily
- If GI AEs start just after escalation, consider reducing dose again temporarily
- Some patients may need a reduced dose long term

Dose Escalation or Maintenance Phase

- Rule out alternative cause
- Check if the patient is following diet and lifestyle guidance
- Short-term pharmacological support

Nausea

- Anti-emetics
- Prokinetics

Vomiting

- Anti-emetics
- Prokinetics
- Standard procedures for severe cases

Diarrhea

- Probiotics
- Antidiarrheals
- Consider metformin dose reduction where pertinent

Constipation

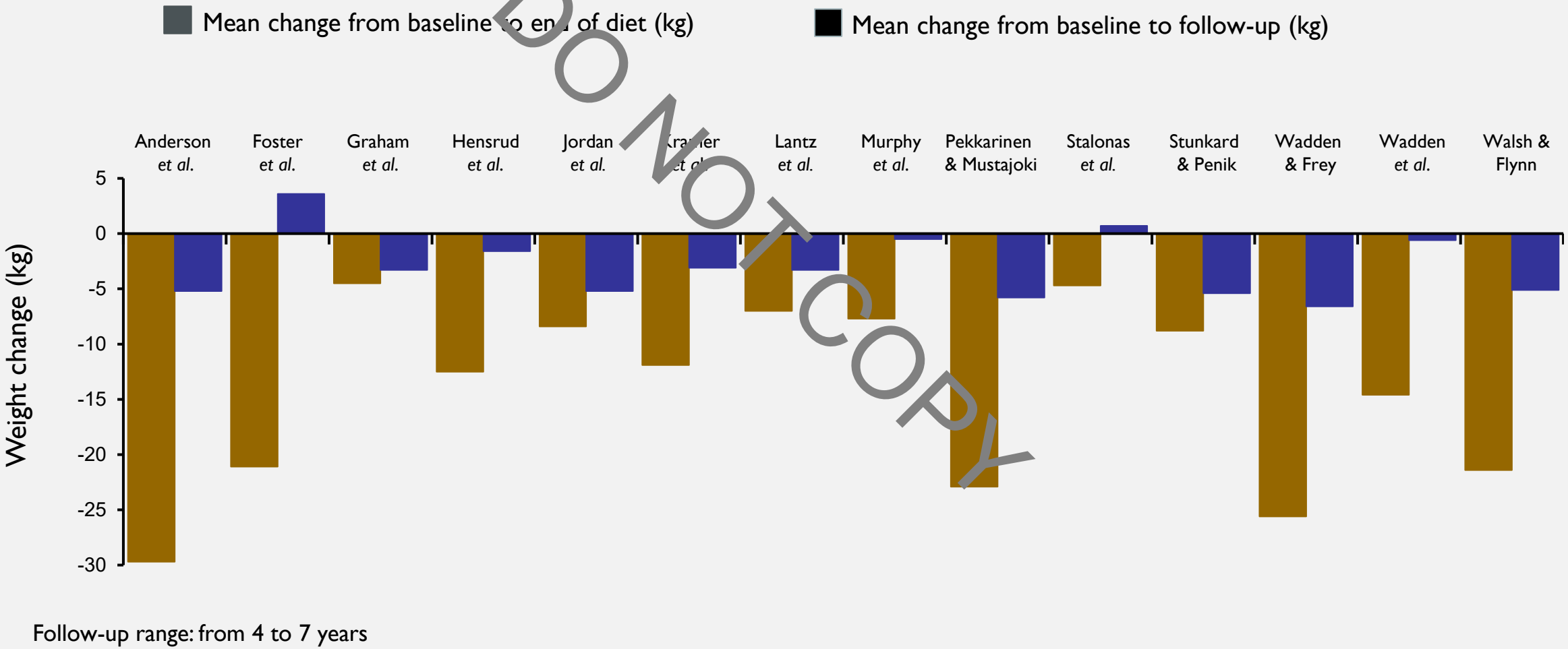
- Stool softeners
- Consider reducing GLP-1 RA dose

If GI AEs persist beyond normal in time/severity, implement additional measures

AE, adverse event.

Gorgojo-Martínez JJ, et al. J Clin Med. 2023;12:145.

MAINTENANCE OF WEIGHT LOSS IS CHALLENGING



Follow-up range: from 4 to 7 years

Mann T, *et al. Am Psychol* 2007;62:220–33

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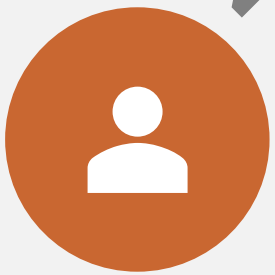

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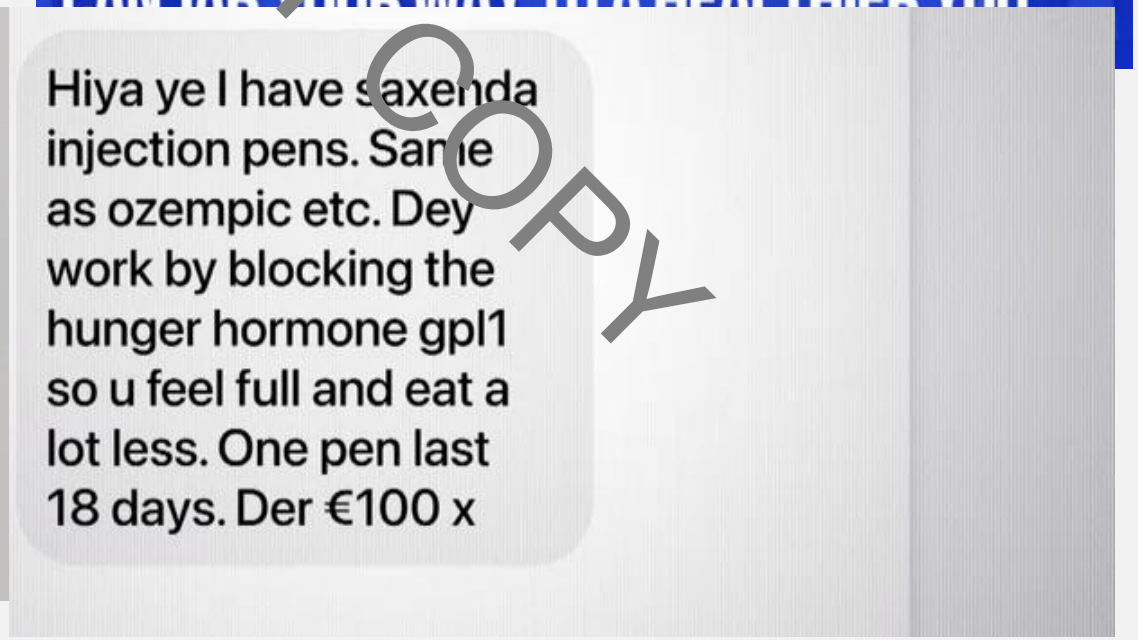
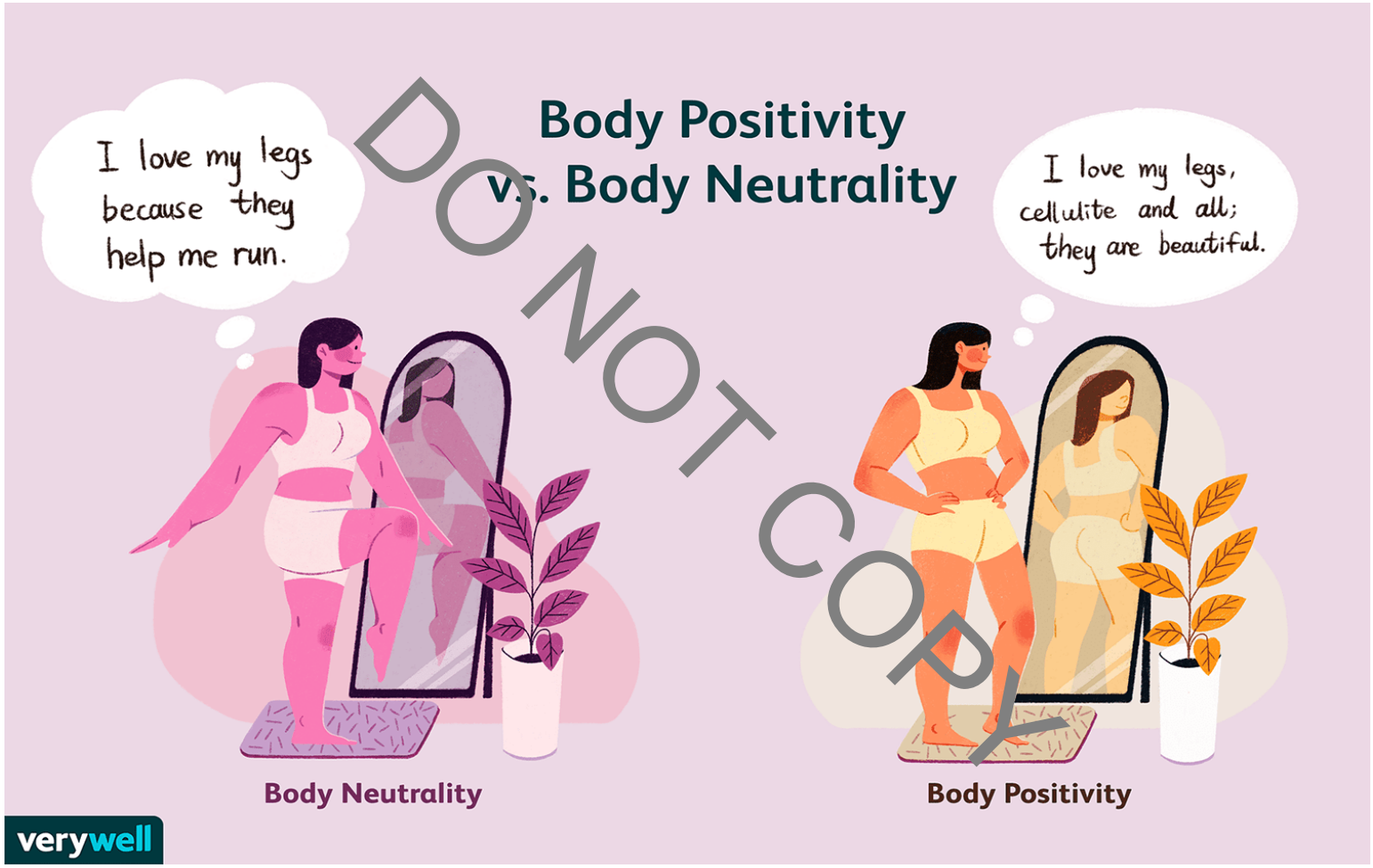
OZEMPIC
0.5 mg
solution for injection in pre-filled pen
semaglutide
subcutaneous use
once weekly
1 pen and 4 disposable needles
novo nordisk
FAKE

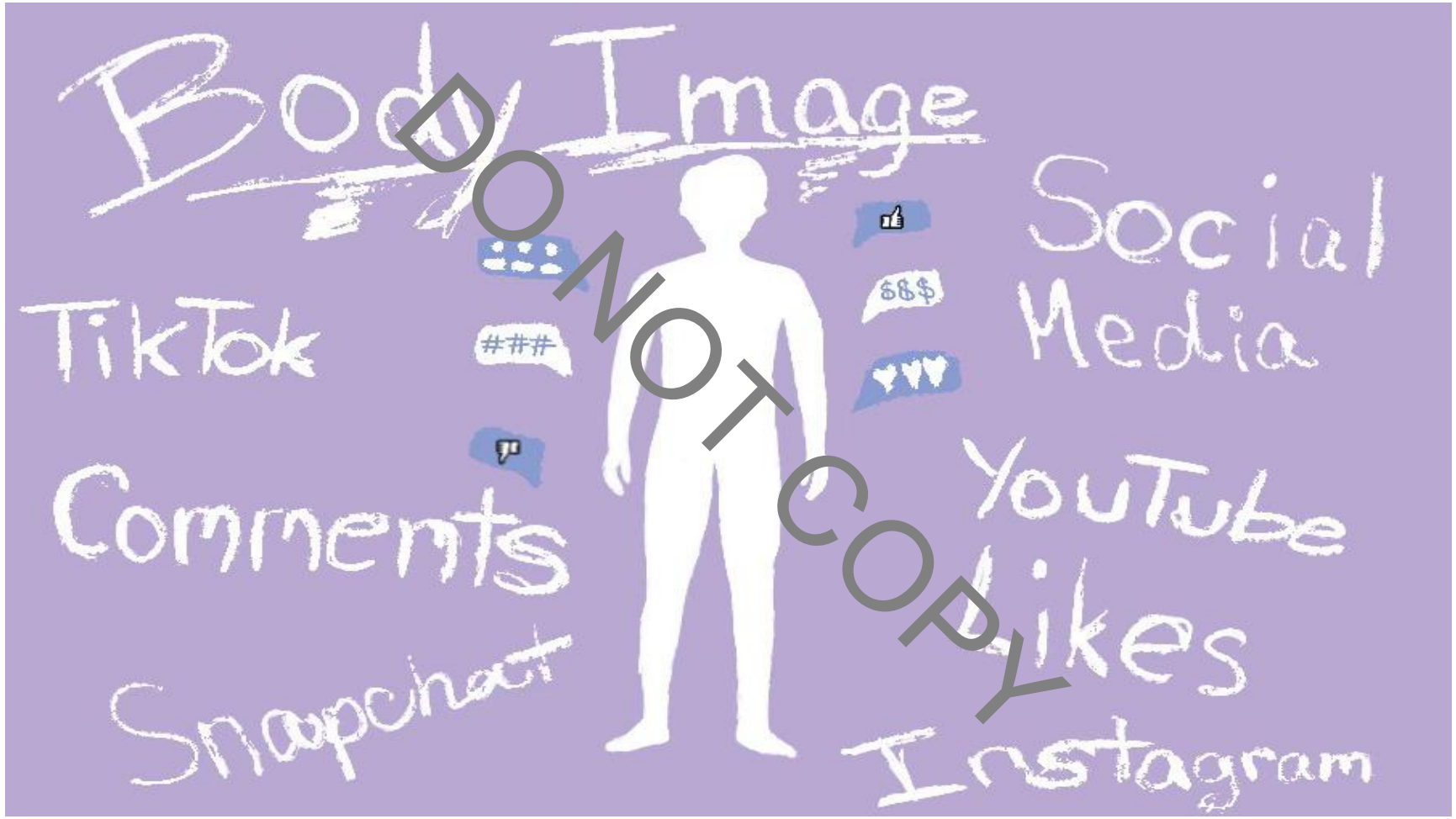

TOM WARBRICK
'FORGET BROCCOLI, FORGET EXERCISE - YOU
CAN JAB YOUR WAY TO A HEALTHIER YOU'


Retatrutide
injection 2.5 mg
2.5


Hiya ye I have saxenda injection pens. Same as ozempic etc. Dey work by blocking the hunger hormone gpl1 so u feel full and eat a lot less. One pen last 18 days. Der €100 x

"I don't think injecting your weight loss drug into a cake, is quite the idea."


Body Positivity
vs. Body Neutrality
I love my legs because they help me run.
I love my legs, cellulite and all; they are beautiful.
Body Neutrality
Body Positivity
verywell


Body Image
Social Media
TikTok
Comments
Snapchat
YouTube
Likes
Instagram
$$$
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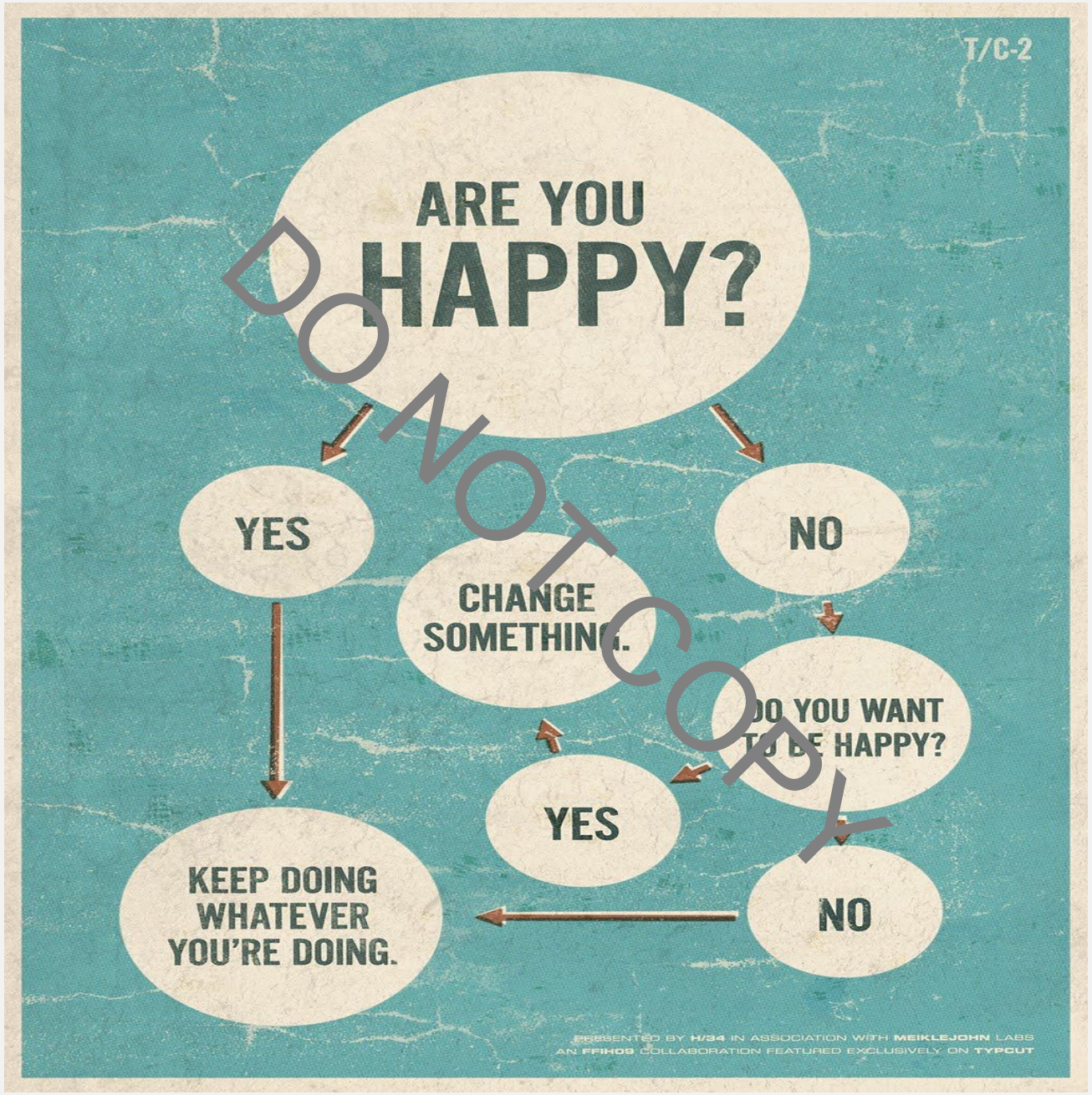
T/C-2
ARE YOU HAPPY?
YES
NO
CHANGE SOMETHING.
DO YOU WANT TO BE HAPPY?
YES
NO
KEEP DOING WHATEVER YOU'RE DOING.
PRESENTED BY H/34 IN ASSOCIATION WITH MEIKLEJOHN LABS
AN FFIH09 COLLABORATION FEATURED EXCLUSIVELY ON TYPCUT

THE END