

# **Type 2 Diabetes Mellitus**

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# Learning objectives

- Diagnose Diabetes Mellitus
- Obesity and diabetes syndemic
- Define the potential complications of diabetes
- Designing a treatment plan for type 2 diabetes

## A person with hyperglycemia and hypertension

Mr. Smith, a 52-year-old man, presents to you after a community screen reveals FBG 185mg/dl and HbA1c 7.9%. He has been overweight ever since but has gained more weight after the age of 40. He has hypertension for 7 years and is on a beta blocker. No history of coronary heart disease, but complains about left knee pain for which he is taking non-steroidal anti-inflammatory drugs. His feet have been burning for about a year. He is married and has 4 children. Drinks alcohol occasionally and has never used tobacco. His father has type 2 diabetes and mother has had CABG. He does office work and moves only during lunch and coffee breaks. On weekends he is engaged in playing computer games with his son and watching movies at home with the family.

## How do you interpret Mr. Smith's FBG and A1c values?

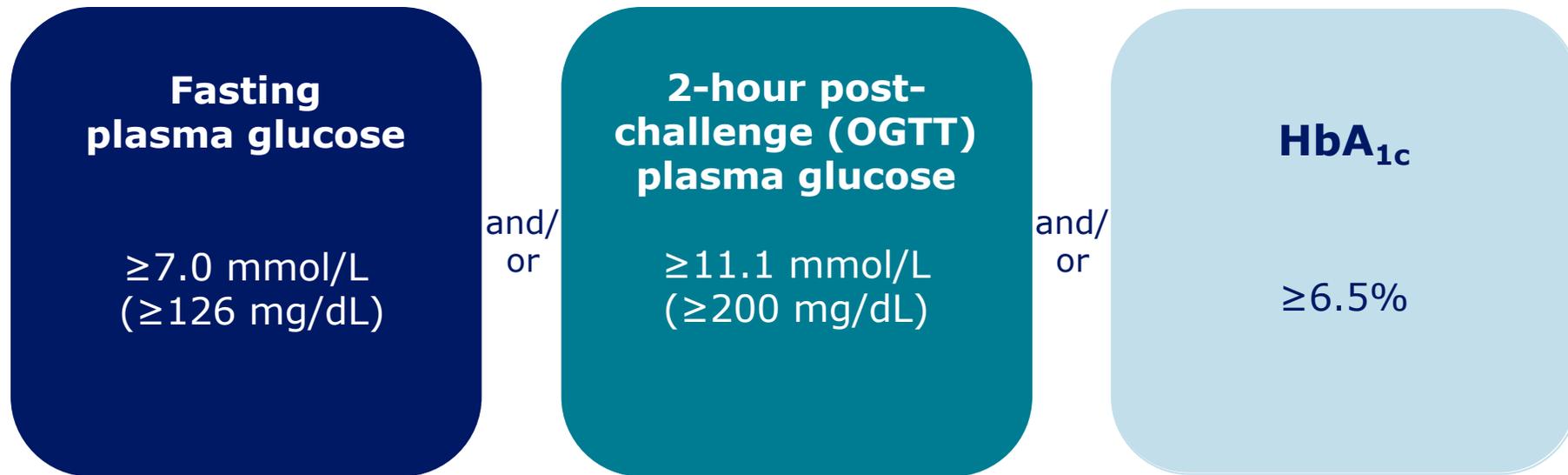
FBG: 185 HbA1c: 7.9%

- a. Quite normal
- b. Impaired glucose tolerance
- c. Impaired fasting glucose
- d. Type 2 diabetes
- e. Need to do OGTT

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# Diagnosis of type 2 diabetes



All assessments were to be confirmed by repeated measurements

# Physical exam

Vital signs are unremarkable except for a BP of 150/100mmHg. Weight 130kg, height 178cm, Body Mass Index (BMI) is 41.0. His waist circumference is 110 cm. No stigmata for Cushing's Syndrome. No facial or pretibial edema. There is loss of vibration bilaterally on lower extremities assessed with a 128Hz tuning fork. The rest of the examination is unremarkable.

# Laboratory results

FBG: 167mg/dl, 2hr. Post-prandial BG: 235mg/dl, HbA1c: 8.0%

Total kolesterol: 236mg/dl, Triglycerides: 250mg/dl

HDL-K: 30mg/dl, LDL-K:156mg/dl,VLDL-K: 50mg/dl

Creatinine: 0.7mg/dl, Na 140mEq/l K: 4.0mEq/l, Uric acid: 9.0mg/dl

ALT: 66 IU/l, AST: 30 IU/l, CPK: 130 IU/l

Ca: 9.2mg/dl, P: 3.9mg/dl, Albumin: 4.0g/dl, 25-OH Vitamin D:40ng/ml

FT4: 1.0ng/dl, TSH: 2.4mIU/l

Hb: 15.2g/dl, Ferritin: 102ng/ml, WBC: 7.700, Platelet: 300,000

Urinalysis: normoalbuminuria, no casts,

Ultrasound upper abdomen: Grade 2 hepatosteatosi

# Diagnoses

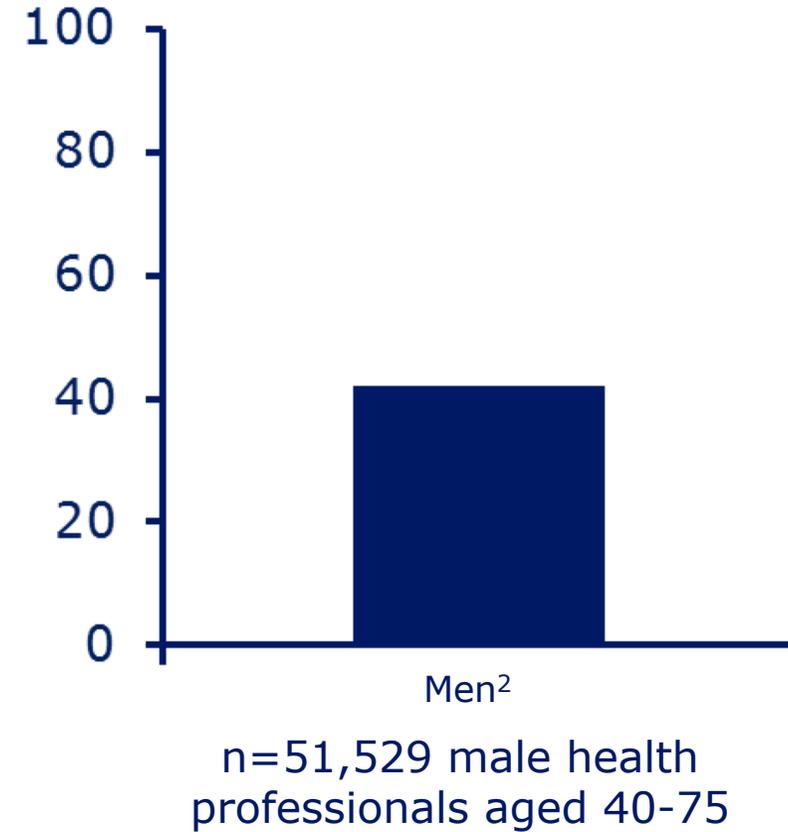
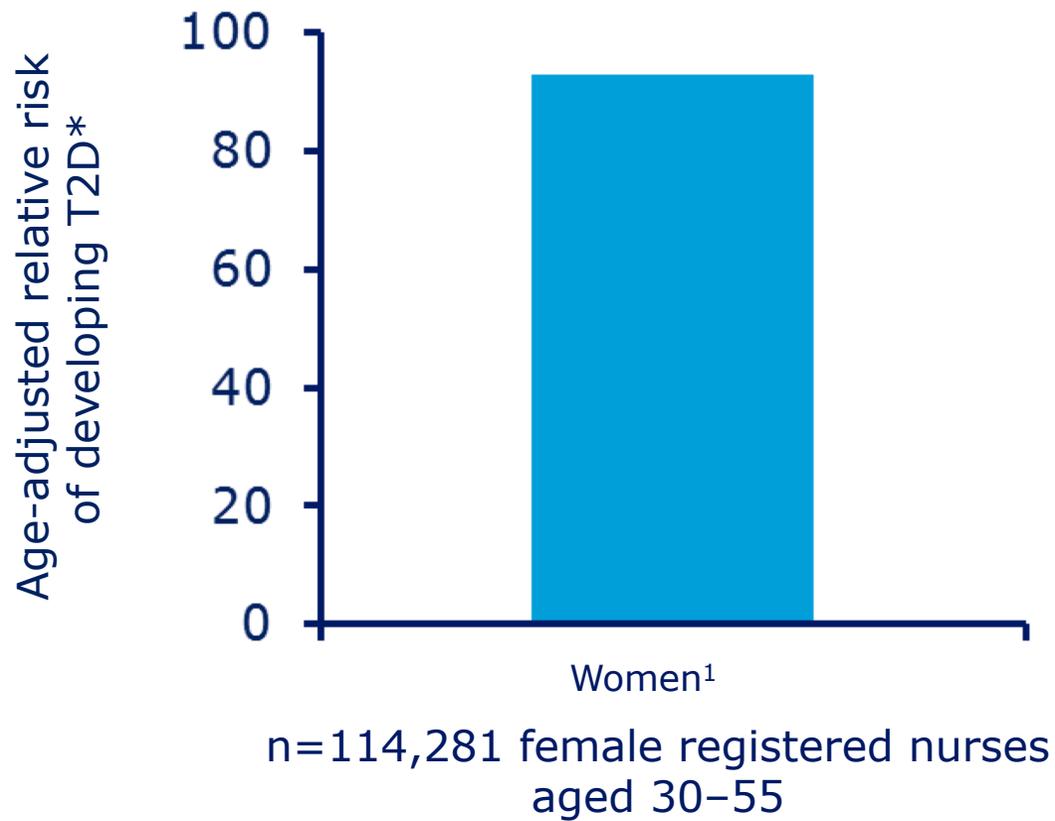
1. Obesity
2. Type 2 diabetes
3. Hypertension
4. Hyperlipidemia
5. Hyperuricemia
6. NAFLD
7. Peripheral diabetic neuropathy
8. Osteoarthritis

# Obesity and Diabetes: A global syndemic

## What is a syndemic?

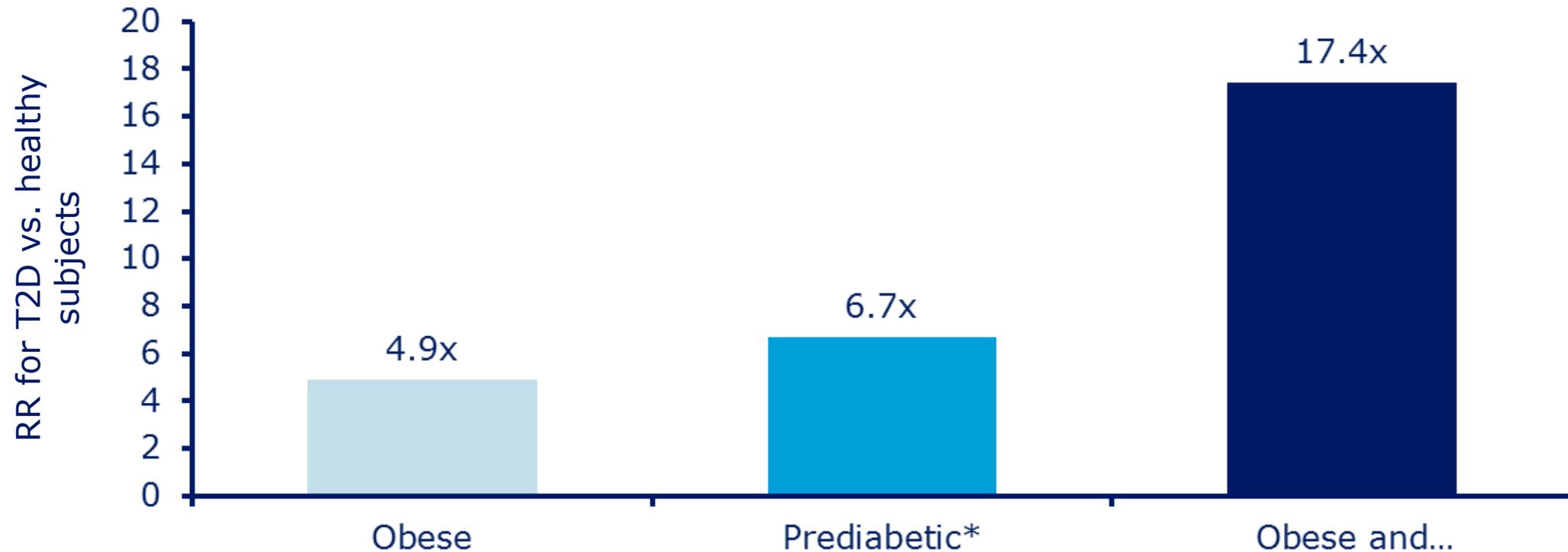
- Two or more epidemics interacting synergistically and contributing as a result of their interaction to excess disease burden in a population

# The relative risk of developing diabetes is high in men and women with BMI >35



Data are based on subjects with a BMI >35 kg/m<sup>2</sup> compared with subjects with a BMI of <22 (women)<sup>1</sup> and <23 (men)<sup>2</sup>

# Obese people with prediabetes are at 17 times greater risk of type 2 diabetes



\*Prediabetes defined as fasting plasma glucose of 110 mg/dL (6.1 mmol/L) and 2-h plasma glucose less than 140 mg/dL (7.8 mmol/L); impaired glucose regulation: fasting plasma glucose concentration 110–126 mg/dL (6.1–6.99 mmol/L) and/or 2-h plasma glucose concentration 140–200 mg/dL (7.8–11.09 mmol/L).  
RR, relative risk; T2D, type 2 diabetes

# What other tests would you like to run on Mr. Smith in the first place?

- a. Eye exam
- b. Albumin creatinine ratio
- c. Stress EKG
- d. EMG
- e. Chest X-ray

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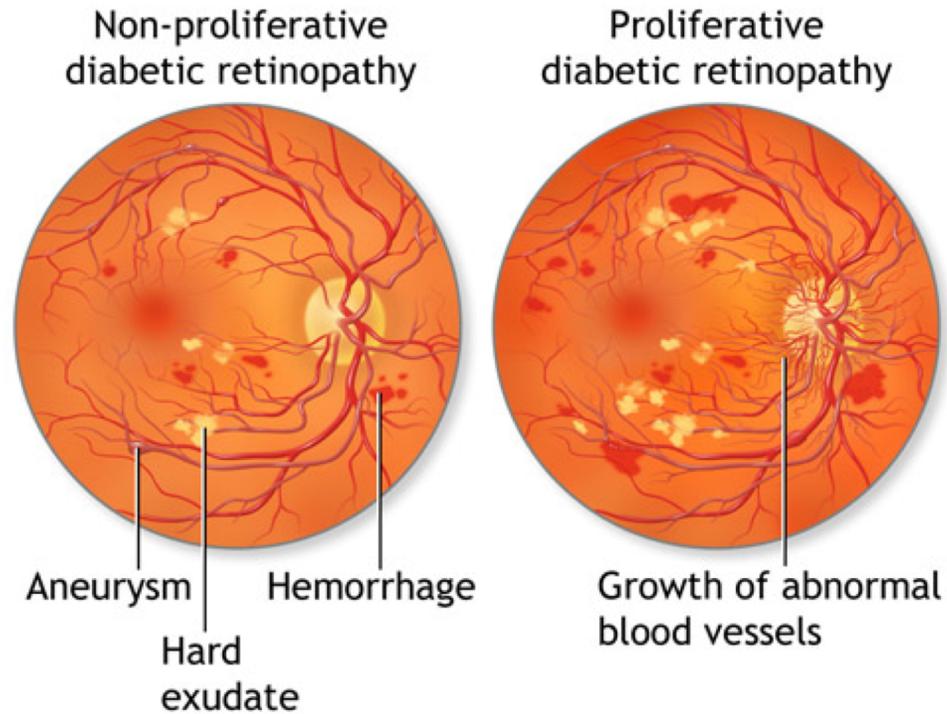
# Classification of Diabetic Retinopathy

## ○ Pre-proliferative

- Microaneurysms
- Venous beading
- Intraretinal hemorrhages
- Flame-shaped hemorrhages
- Cotton wool spots
- Retinal edema

## ○ Proliferative

- Neovascularization
- Vitreous hemorrhage
- Fibrous proliferation



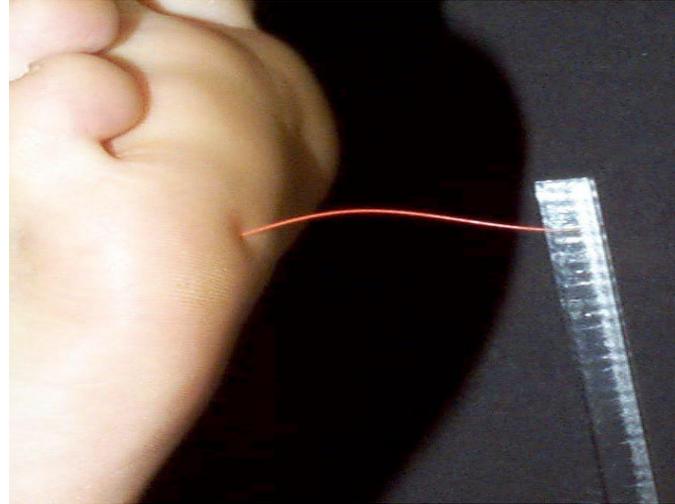
# Albuminuria

|             | Urine on spot                | 24 hr urine     |
|-------------|------------------------------|-----------------|
| Albuminuria | Albumin/creatinine<br>(mg/g) | UAE<br>(mg/day) |
| Normal      | <30                          | <30             |
| Low grade   | 30-299                       | 30-299          |
| High grade  | >300                         | >300            |

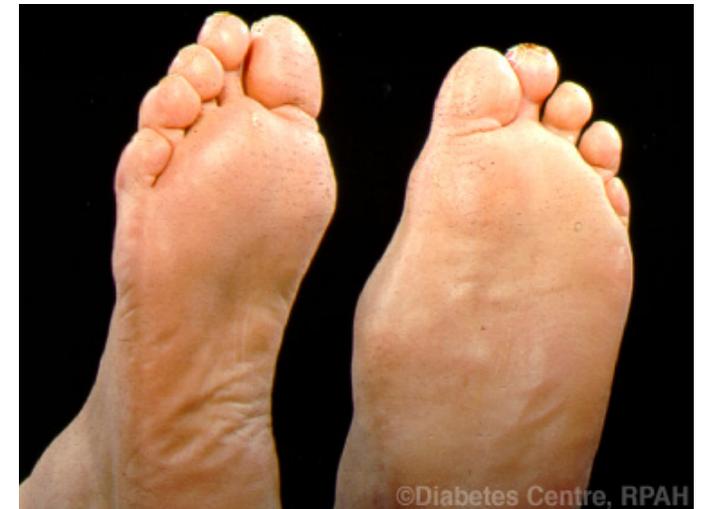
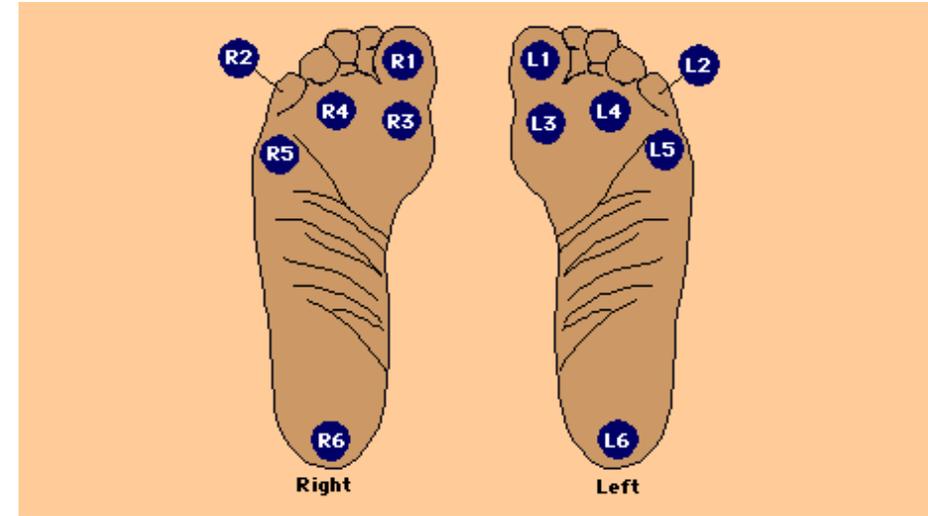
# Peripheral neuropathy



Tuning fork 128Hz



Esthesiometer 10g



# What is/are your treatment plan(s) for diabetes in Mr. Smith?

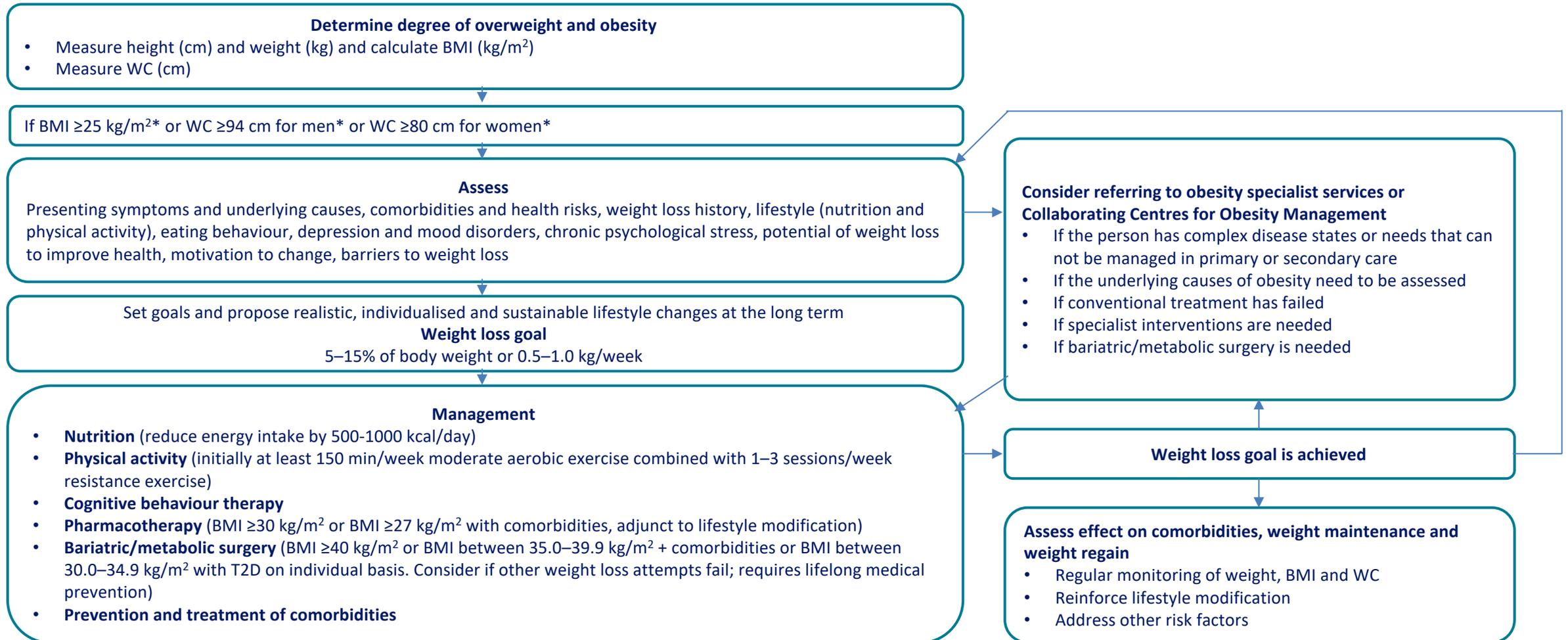
- a. Lifestyle modification
- b. Pharmacotherapy
- c. Bariatric/metabolic surgery

# I treat obesity first with:

- a. **Lifestyle modification**
- b. **Pharmacotherapy**
- c. Bariatric/metabolic surgery

# EASO European guidelines

## Clinical care pathway for overweight and adults with obesity



\*BMI and WC cut-off points are different for some ethnic groups. T2D, type 2 diabetes; WC, waist circumference

# Anti-obesity drugs

| Drugs                      | Status             | Mechanism  | Dosing  | Response evaluation  | Warnings  | Contraindications  | Side-effects   |
|----------------------------|--------------------|--|---|--|---|--|--|
| Orlistat                   | FDA & EMA approved | pancreatic, gastric lipase inhibitor                 | 120 mg tid<br>60 mg tid (OTC)   | 2.9–3.4% 1 year  | hepatitis, liver failure (rare), concomitant multivitamin advised                             | pregnancy, breast feeding, chronic malabsorption syndrome, cholestasis   | decreased absorption of fat soluble vitamins, steatorrhoea, faecal urgency |
| Lorcaserin                 | FDA approved       | 5HT <sub>2c</sub> R agonist                          | 10 bid  | 3.6% 1 year<br>stop if <%5 weight loss at 12 weeks   | serotonin syndrome, cognitive impairment, depression, valvulopathy<br>hypoglycaemia, priapism | pregnancy, breast feeding, use with caution: MAOIs, SSRIs, SNRIs   | headache, nausea dry mouth, dizziness<br>fatigue, constipation             |
| Phentermine/<br>topiramate | FDA approved       | NE release (P)<br>GABA modulation (T)                | starting dose:<br>3.75/23 qd<br>recommended dose:<br>7.5/46 qd<br>*high dose:<br>15/92 qd | 6.6% (recommended dose) 1 year<br>8.6% (high dose) 1 year<br>stop if <%5 weight loss at 12 weeks | fetal toxicity, acute myopia, cognitive dysfunction, metabolic acidosis, hypoglycaemia        | pregnancy, breast feeding, glaucoma, hyperthyroidism, use with caution: MAOIs  | insomnia, dry mouth<br>constipation, paresthesia, dizziness, dysgeusia     |
| Bupropione/<br>naltrexone  | FDA & EMA approved | DA/NE reuptake inhibitor(B)<br>opioid antagonist (N) | 8/90 mg tb<br>2 tb bid  | 4.8% 1 year<br>stop if <%5 weight loss at 12 weeks   | fetal toxicity, increased seizure risk, glaucoma, hepatotoxicity                              | uncontrolled hypertension, seizure, anorexia nervosa / bulimia, drug or alcohol withdrawal, use with caution: MAO inhibitors | nausea, constipation, headache, vomiting, dizziness                        |
| Liraglutide                | FDA & EMA approved | GLP-1 agonist  | 3 mg sc   | 5.8 kg 1 year<br>stop if <%4 weight loss at 14 wks   | acute pancreatitis, acute gall bladder disease  | medullary thyroid cancer history, MEN type 2 history   | nausea, vomiting, pancreatitis   |

FDA = Food & Drug Administration; EMA= European Medicinal Agency; OTC = over the counter; 5HT<sub>2c</sub>-R = 5 hydroxytryptamine 2c receptor; MAOI = monoamine oxidase inhibitor; SSRI = selective serotonin reuptake inhibitor; SNRI = serotonin norepinephrine reuptake inhibitor; NE = norepinephrine; GABA = gamma amino butyric acid; DA = dopamine; GLP-1 = glucagon-like peptide-1; MEN = multiple endocrine neoplasia.

\*Careful observation.

## European Guidelines for Obesity Management in Adults

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Karin Schindler<sup>d</sup> Luca Busetto<sup>e</sup> Dragan Mijic<sup>f</sup>  
Hermann Toplak<sup>g</sup> for the Obesity Management Task Force of  
the European Association for the Study of Obesity

# What is/are your drug choice(s) to treat diabetes?

- a. Metformin
- b. Sulphonylureas
- c. DPP-4 inhibitors
- d. Alpha-1 glycosidase inhibitors
- e. Glinides
- f. Thiozolidindiones
- g. GLP-1 analogues
- h. SGLTP-2 inhibitors
- i. Insulin

# What may be your drug choice(s) to treat diabetes?

- a. **Metformin**
- b. Sulphonylureas
- c. **DPP-4 inhibitors**
- d. **Alpha-1 glycosidase inhibitors**
- e. Glinides
- f. **Thiazolidindiones**
- g. **GLP-1 analogues**
- h. **SGLTP-2 inhibitors**
- i. Insulin

# Current anti-diabetic medications & their influence on body weight

| Medication                       | Weight change seen     |
|----------------------------------|------------------------|
| Metformin                        | loss                   |
| Sulphonylureas                   | gain                   |
| Thiazolidinediones               | gain, subcutaneous fat |
| Meglitinides                     | gain,                  |
| Insulin                          | gain                   |
| $\alpha$ -Glucosidase inhibitors | neutral                |
| DPP- 4 inhibitors                | neutral                |
| GLP-1 agonists                   | loss                   |
| SGLT2 inhibitors                 | loss                   |

# Other medications *Mr. Smith* may need for treatment of complications of obesity and diabetes?

- a. Metformin
- b. ACEIs or ARBs
- c. Statins
- d. Xanthine oxidase inhibitor

# What is your treatment plan for obesity and diabetes if you see previous interventions are not working?

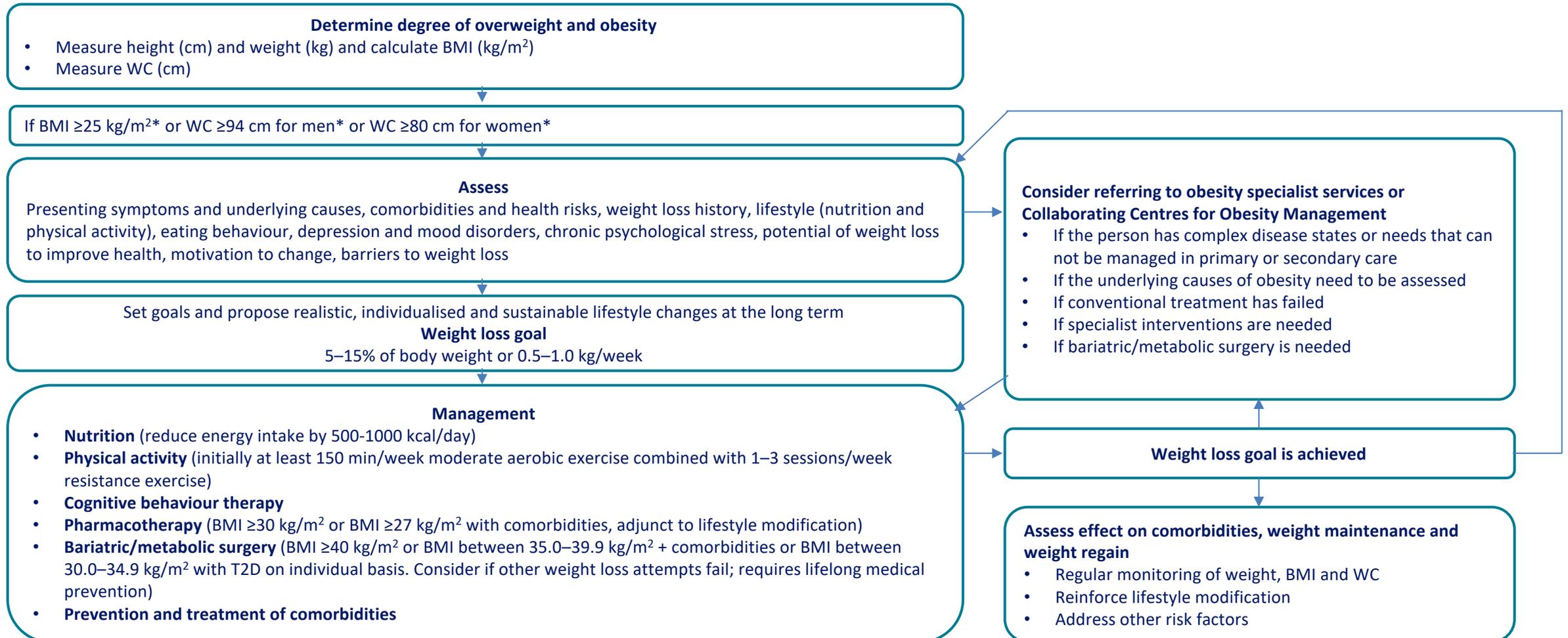
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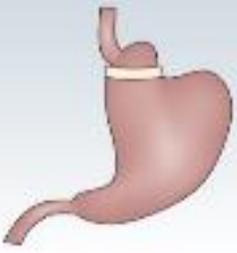
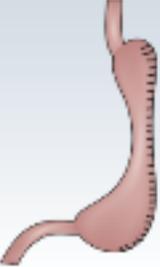
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# Common bariatric surgery procedures

| Procedure <sup>1</sup>     |  | Description <sup>2,3</sup>  | Type <sup>2,3</sup>         |
|----------------------------|--|---|-----------------------------|
| Adjustable gastric banding |   | Silicone band is placed around proximal stomach outlet to restrict food intake                      | Restrictive                 |
| Sleeve gastrectomy         |   | Stomach is constructed into a thin tube and most of the greater curvature of the stomach is removed | Restrictive                 |
| Roux-en-Y gastric bypass   |  | Small pouch is created from the stomach and connected to the small intestine                        | Restrictive + malabsorptive |

1. Field BC et al. *Nat Rev Endocrinol* 2010;6:444–53; 2. Lodhia NA et al. *Int J Obes* 2012;2:S47–50; 3. Mechanick JI et al. *Obes (Silver Spring)* 2013;21(Suppl 1):S1–27

# Take home messages

- Obesity and type 2 diabetes are a global syndemic
- Obesity management is crucial in prevention and treatment of type 2 diabetes
- Lifestyle modification and pharmacotherapy are first line treatment modalities
- Bariatric/metabolic surgery may be administered when indicated