

What can we expect from new drugs?

Volkan Demirhan Yumuk, MD

Learning objectives

- Learn when to use anti-obesity medications
- Explain the benefits and potential risks of pharmacotherapy for obesity
- Identify patients who may benefit from anti-obesity medications
- Recognize barriers to the effective use of medications

A person with obesity considering medication for weight loss

Ms. Smith is a 40-year-old woman who is going to see her doctor to discuss how she can lose weight and whether there are medications she can take for this matter. She had tried dieting on her own and had also tried several commercial weight loss programs with little long term success. She is relatively healthy except for depression. She does not have a history of coronary artery disease or diabetes. No history for eating disorders or personality disorder. She has regular menses. She does not take any medications or non-prescription supplements. She does not smoke but drinks alcohol as 4 or 5 drinks a week. Her parents have type 2 diabetes. She says she always feels she is hungry. She reads the nutritional labels on food packaging. She orders take-out meals most of the time. She has her own business working from her home office. She is a member of a fitness club but she visits the place infrequently.

Physical exam

Vital signs are unremarkable. Weight 100 kg, height 167 cm, Body Mass Index (BMI) is 35.9. Her waist circumference is 94cm. No stigmata for Cushing's Syndrome. There is acanthosis nigricans on the neck and arm pits. No facial or pretibial edema. The rest of the examination is unremarkable.

Laboratory

FBG: 110mg/dl, HbA1c: 5.9%, HOMA-IR: 3.5

Total kolesterol: 200mg/dl, Triglycerides:100mg/dl

HDL-K: 70mg/dl, LDL-K:110mg/dl,VLDL-K:20mg/dl

Creatinine: 0.8mg/dl, Na 140mEq/l K: 4.1mEq/l, Uric acid: 5.0mg/dl

ALT: 76 IU/l, AST: 32IU/l, CPK: 130 IU/l

Ca: 9.2mg/dl, P: 3.9mg/dl, Albumin: 4.0g/dl, 25-OH Vitamin D:10ng/ml, iPTH: 97ng/l

FT4: 1.2ng/dl, TSH: 7.8mIU/l

Hb: 13.2g/dl, Ferritin: 55ng/ml, WBC: 8.700, Platelet: 310,000

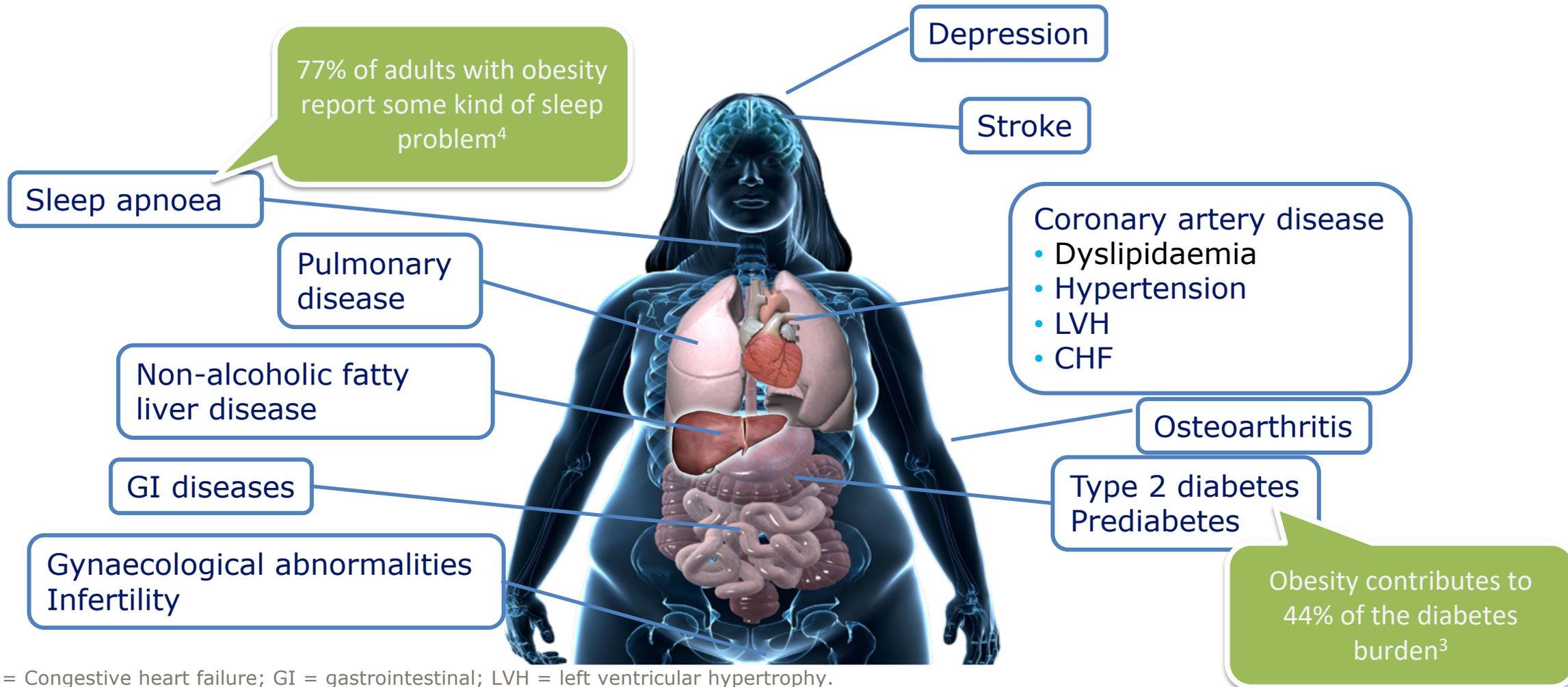
Urinalysis: normoalbuminuria, no casts,

Ultrasound upper abdomen: Grade 2 hepatosteatosis

Diagnoses

1. Obesity
2. Prediabetes
3. Insulin resistance
4. Fatty liver
5. Vitamin D deficiency
6. Secondary hyperPTH
7. Subclinical hypothyroidism
8. Depression

Obesity is associated with multiple chronic complications



1. NIH. *Obes Res* 1998;6 (Suppl 2):51S-209S; 2. Schelbert. *Prim Care* 2009;36:271-85; 3. WHO. Global health risks report 2009. Available at: http://www.who.int/healthinfo/global_burden_disease/global_health_risks/en/ 4. National Sleep Foundation. 2013 Sleep in America Poll. Available at: <http://sleepfoundation.org/sleep-topics/obesity-and-sleep/page/0%2C3/>

Question 1

Is Ms. Smith a candidate for an antiobesity drug?

- a. Yes
- b. No
- c. Maybe
- d. Never
- e. I am against antiobesity drugs

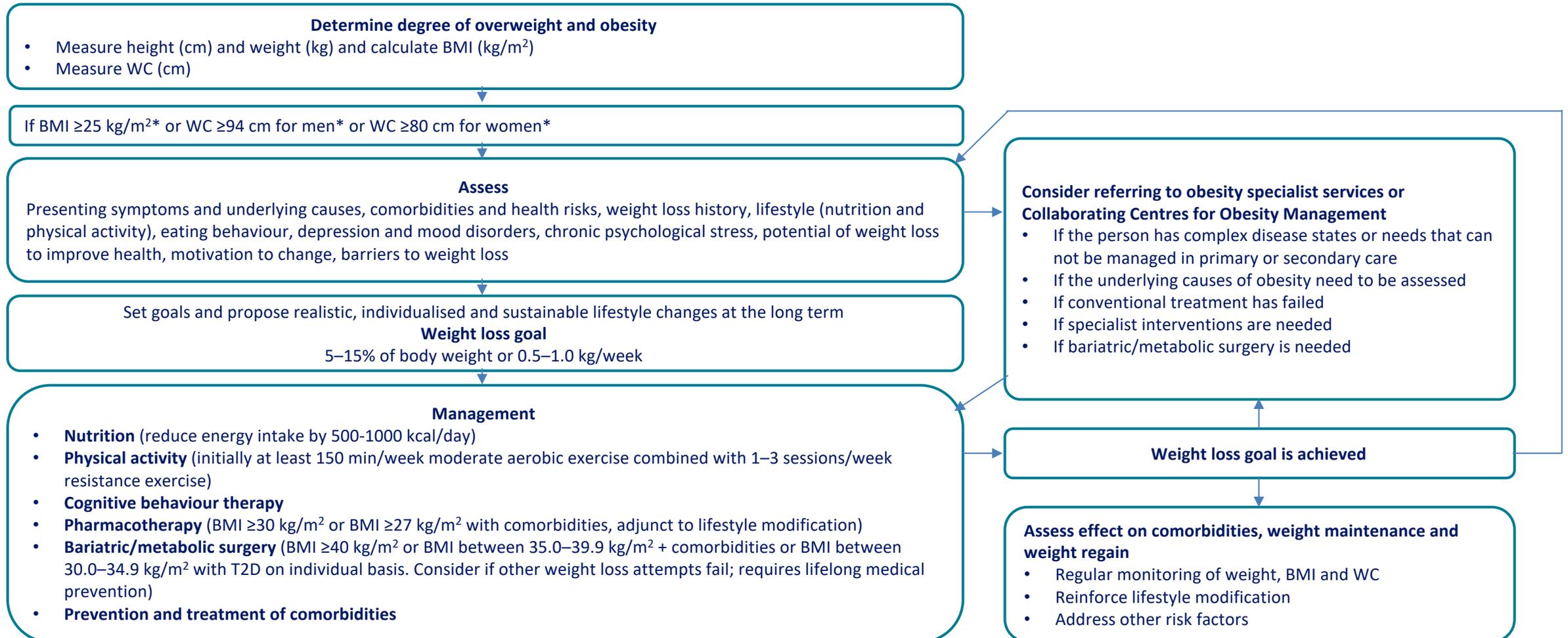
Question 1

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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

Question 2

What are the novel anti-obesity drug(s) in Europe, approved by European Medicines Agency (EMA)?

- a. Phentermine
- b. Liraglutide
- c. Lorcaserin
- d. Naltrexone/bupropion
- e. Phentermine/Topiramate

Question 2

What are the novel anti-obesity drug(s) in Europe, approved by European Medicines Agency (EMA)?

- a. Phentermine
- b. Liraglutide (Saxenda)**
- c. Lorcaserin
- d. Naltrexone/bupropion (Mysimba)**
- e. Phentermine/Topiramate

Anti-obesity drugs

Drugs	Status	Mechanism	Dosing	Response evaluation	Warnings	Contraindications	Side-effects
Orlistat	FDA & EMA approved	pancreatic, gastric lipase inhibitor	120 mg tid 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 _{2c} R agonist	10 bid	3.6% 1 year stop if <%5 weight loss at 12 weeks	serotonin syndrome, cognitive impairment, depression, valvulopathy hypoglycaemia, priapism	pregnancy, breast feeding, use with caution: MAOIs, SSRIs, SNRIs	headache, nausea dry mouth, dizziness fatigue, constipation
Phentermine/ topiramate	FDA approved	NE release (P) GABA modulation (T)	starting dose: 3.75/23 qd recommended dose: 7.5/46 qd *high dose: 15/92 qd	6.6% (recommended dose) 1 year 8.6% (high dose) 1 year 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 constipation, paresthesia, dizziness, dysgeusia
Bupropione/ naltrexone	FDA & EMA approved	DA/NE reuptake inhibitor(B) opioid antagonist (N)	8/90 mg tb 2 tb bid	4.8% 1 year 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 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_{2c}-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

Volkan Yumuk^a Constantine Tsigos^b Martin Fried^c

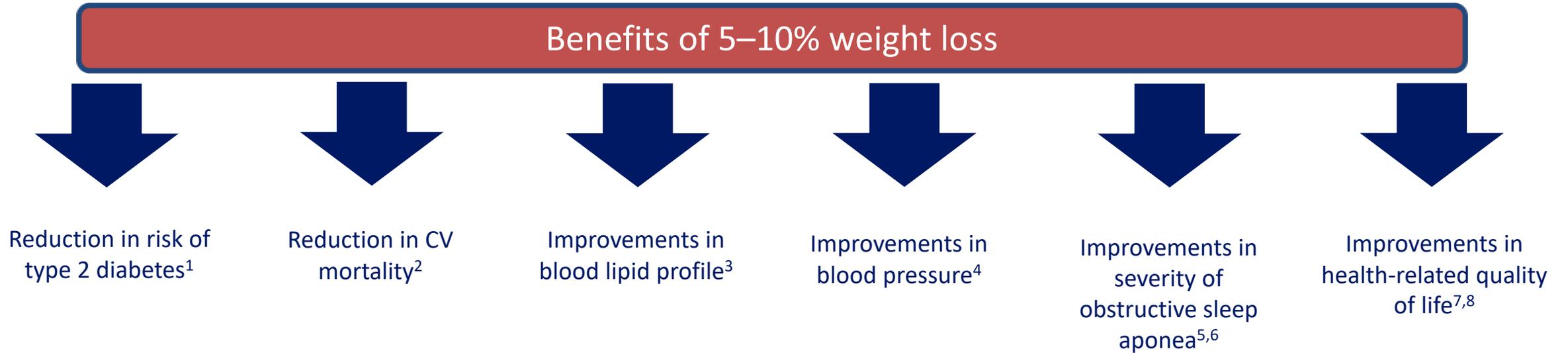
Karin Schindler^d Luca Busetto^e Dragan Mijic^f

Hermann Toplak^g for the Obesity Management Task Force of the European Association for the Study of Obesity

Who is suitable for which: Any clues?

- **Phentermine/Topiramate**: Reduces hunger, reduces cravings; may lead the patient to portion size reduction and to avoid nibbling
- **Liraglutide**: Increases satiety, regulates blood glucose
- **Naltrexone/Bupropion**: Increases satiety; may reduce stress eating, cravings

Management & outcome



1. Knowler *et al.* *N Engl J Med* 2002;346:393–403; 2. Li *et al.* *Lancet Diabetes Endocrinol* 2014;2:474–80; 3. Datillo *et al.* *Am J Clin Nutr* 1992;56:320–8; 4. Wing *et al.* *Diabetes Care* 2011;34:1481–6; 5. Foster *et al.* *Arch Intern Med* 2009;169:1619–26; 6. Kuna *et al.* *Sleep* 2013;36:641–9; 7. Warkentin *et al.* *Obes Rev* 2014;15:169–82; 8. Wright *et al.* *J Health Psychol* 2013;18:574–86

Barriers to optimal medical care in obesity

- Patient factors
 - Fear of failure, treatment risks
 - Lack of family or community support
 - Lack of time devoted to self care
 - Lack of motivation
- Physician factors
 - Lack of time to provide counseling
 - Lack of knowledge about treatment options
 - Scepticism about efficacy of treatment
 - Fear of offending the patient
- Medical system factors
 - Lack of facilities, specialised HCPs
 - Lack of coverage for counseling and obesity medications and bariatric surgery

Take home messages

- Obesity is a chronic disease with complications
- Patient centered approach to treatments is essential
- Life long treatment plans and follow-up must be instituted
- Lifestyle modification is a must
- Pharmacotherapy is an adjunct to lifestyle modification may help weight loss and weight maintenance and may have beneficial effects on complications of obesity, including pre-diabetes, type 2 diabetes and CV risk factors