

Anti-obesity drugs



Risk factors for coronary heart disease (CHD)

Età

Uomini > 45 anni o donne > 55 anni

Fumo di sigaretta

Ipertensione

Pressione arteriosa $\geq 140/90$ o uso di farmaci antipertensivi indipendentemente dai valori pressori

Bassi livelli di colesterolo HDL

< 40 mg/dl (< 50 mg/dl nelle donne)

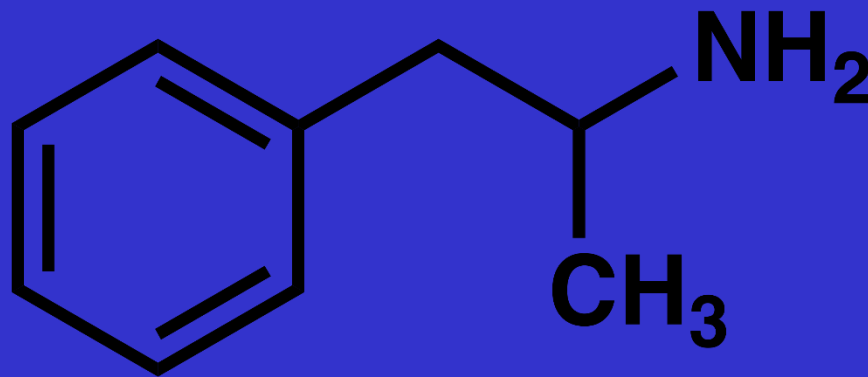
Obesità

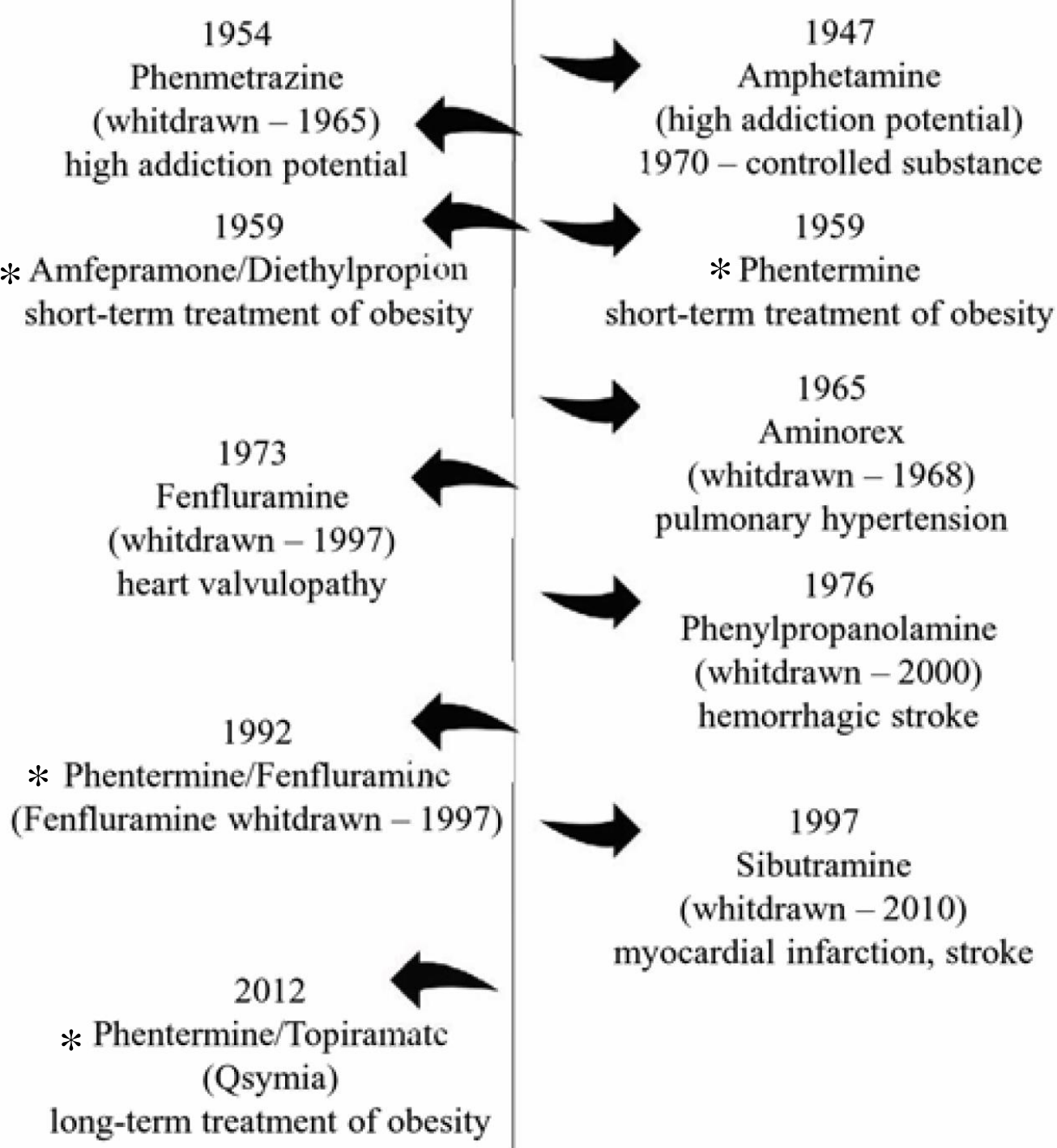
indice di massa corporea > 25 Kg/m² e circonferenza vita superiore a 102 (uomini) o 88 (donne)

Obesity

Amphetamine-like drugs

Sympathomimetic (appetite suppression)





Time-line of amphetamine-like drugs used in the therapy of obesity from beginning until today

Aminorex and fenfluramine (5HT)

- **Amfepramone:** indirect sympathomimetic stimulant drug NA > DA. Structurally related with bupropion (antidepressant)
- **Benzphetamine:** indirect sympathomimetic stimulant drug NA > DA from storage sites in the lateral hypothalamic feeding center, producing a decrease in appetite
- **Phentermine:** one of the most frequently prescribed anti-obesity drugs. Combination with other drugs. Up to 12 weeks treatment

Anorectic drugs:

Phentermine \uparrow DA > NA > 5HT

Sibutramine \uparrow 5HT > NA (reuptake)

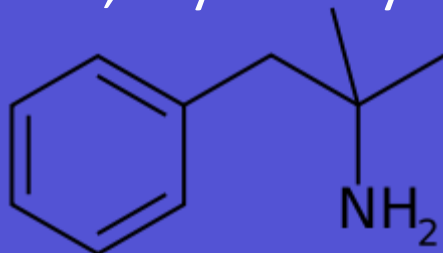
(active metabolites)

Low dependence

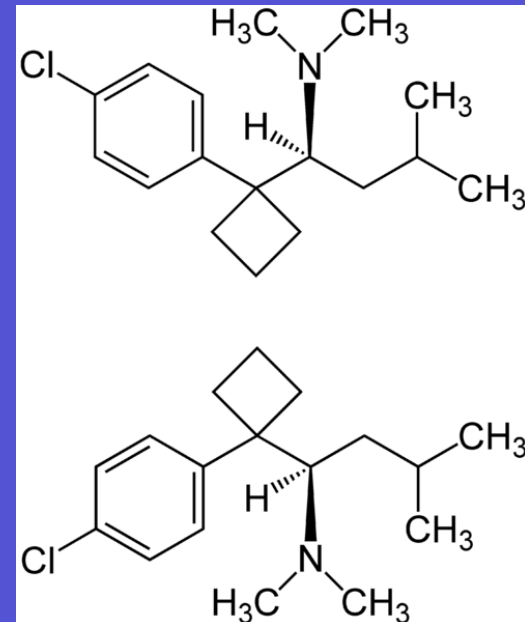
S.E.: heart rate, pressure, headache, insomnia, constipation

Interactions with: fluoxetine, inhibit. MAO, sumatriptan, lithium, pentazocine, dextromethorphan

Interactions with inhibitors CYP3A4 (ketoconazole, cimetidine, erythromycin)

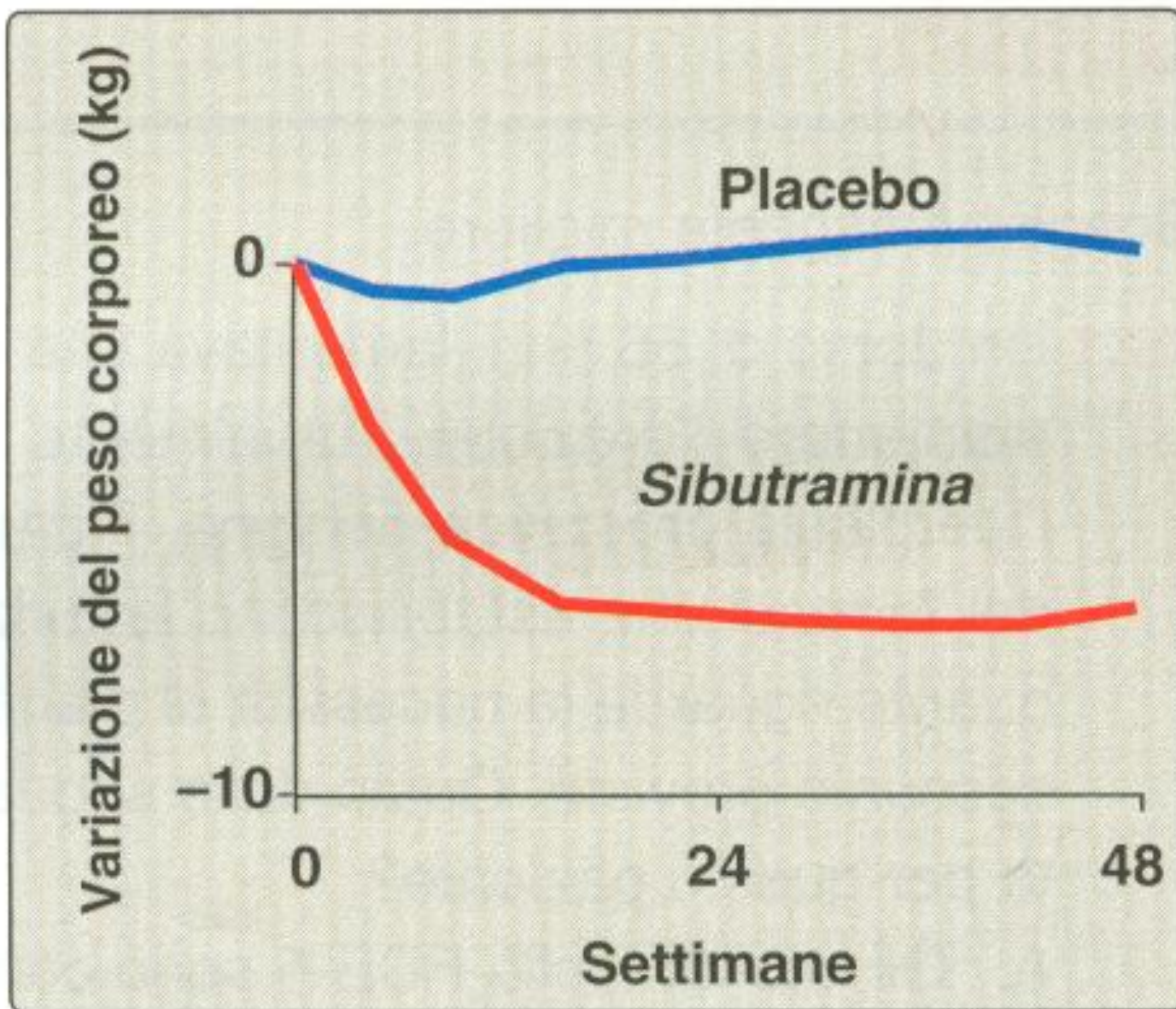


Phentermine



Sibutramine

Effect of treatment with *sibutramine*

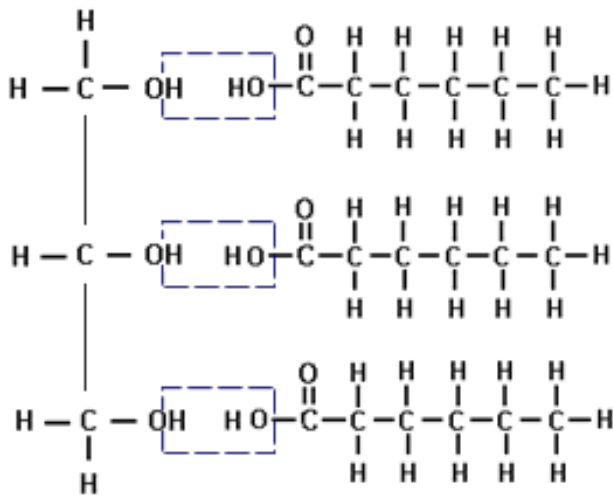


Past drug therapy

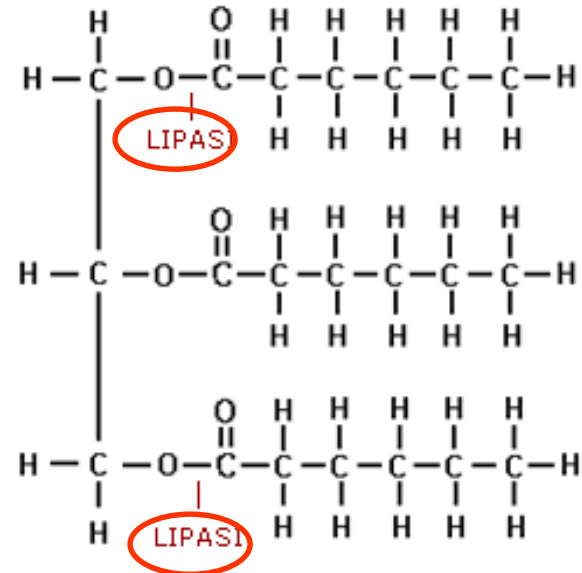
Drug	Mechanism of action	Withdrawal reason
Amphetamine, Metamphetamine	Sympathomimetic - appetite suppression	High abuse and dependence potential, cardiovascular effects
Aminorex	Sympathomimetic - appetite suppression	Pulmonary hypertension
Fenfluramine, Dexfenfluramine	Sympathomimetic - appetite suppression	Valvular heart disease, pulmonary hypertension
Phenylpropanolamine	Sympathomimetic - appetite suppression	Increased risk of haemorrhagic stroke
Sibutramine	Sympathomimetic - appetite suppression	Cardiovascular effects – increased risk of heart attack and stroke
Rimonabat	Inverse agonist of CB1 cannabinoid receptor	Psychiatric disorders

Other Anti-obesity drugs

Lipase



Glycerol + 3 fatty acids - 3 H₂O



= triglyceride

Anti-obesity drugs

Orlistat

* *Fentermina*

Sibutramina

*Rimonabant**

*Antidepressives
(bulimia)*

Lipase inhibitors

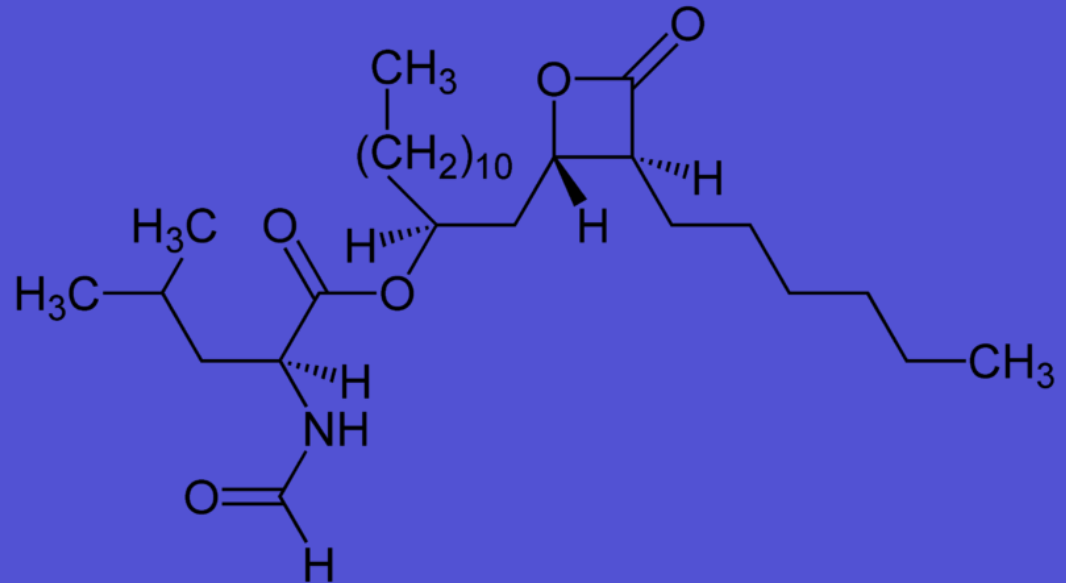
Anorexic

Lipase inhibitor drugs:

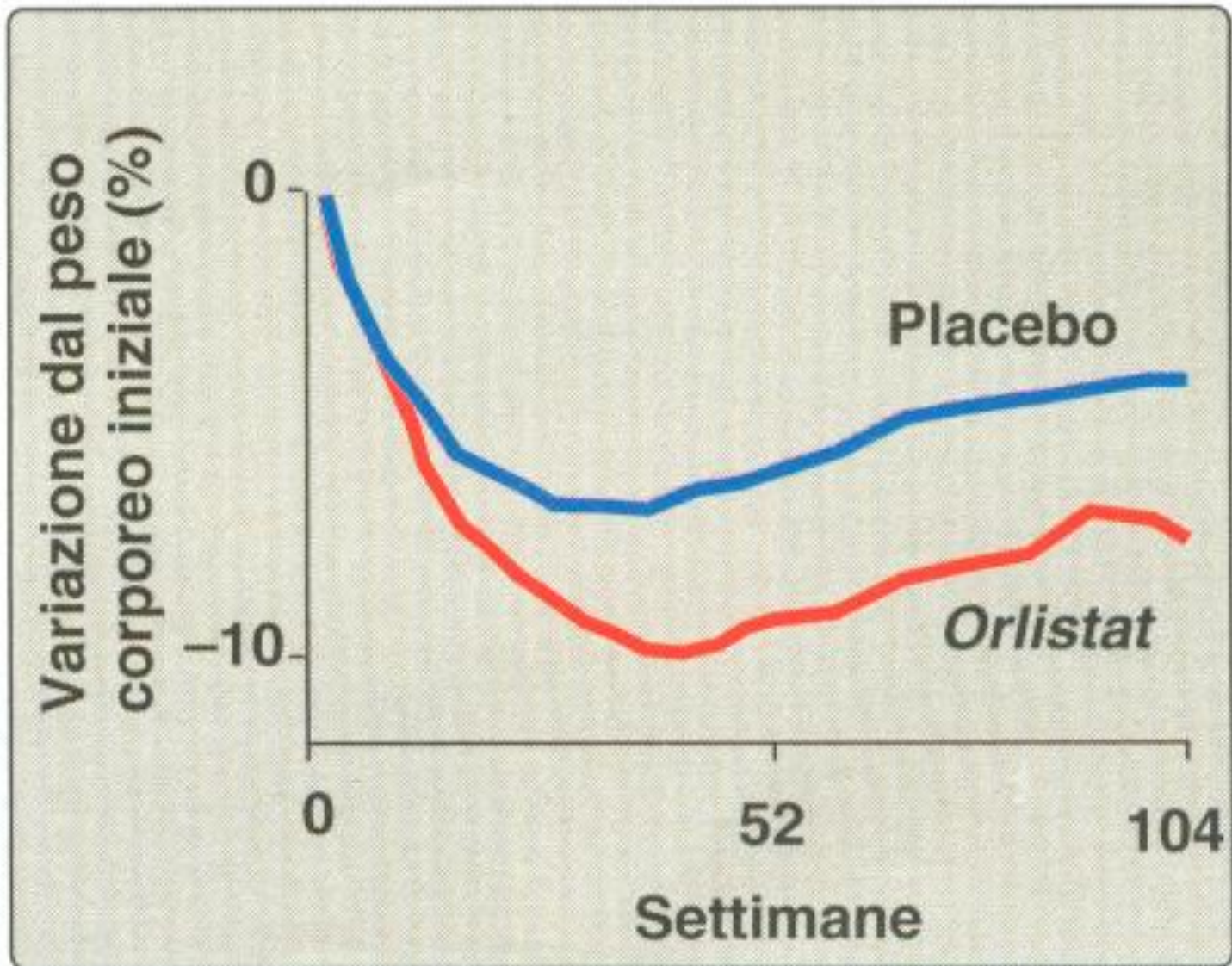
Orlistat: gastric and pancreatic lipases;

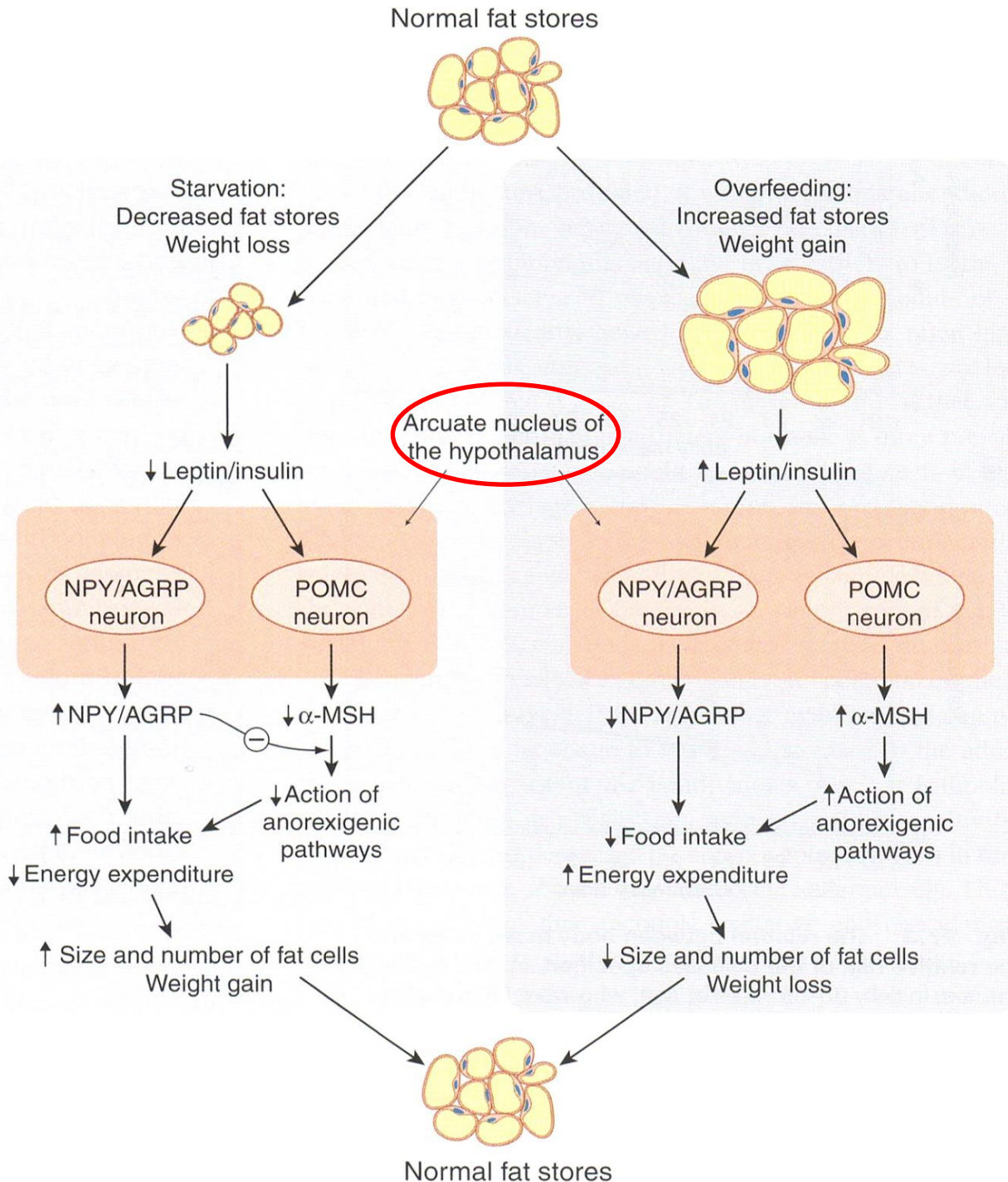
In diabetes protects against weight loss changes (leptin levels, blood pressure etc..)

S.E.: interference with absorption of fat-soluble vitamins, gastrointestinal effects



Effect of treatment with *orlistat*





Leptin:

Role in regulation of energy balance

-lipogenesis

+lipolysis

-gluconeogenesis

+oxidation AG

NPY= neuropeptide Y

AGRP= agouti-related protein

POMC= proopiomelanocortin

α-MSH= α-melanocyte-stimulating hormone

