Anti-obesity drugs
## Risk factors for coronary heart disease (CHD)

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Uomini &gt; 45 anni o donne &gt; 55 anni</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>Pressione arteriosa $\geq$ 140/90 o uso di farmaci antipertensivi indipendentemente dai valori pressori</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>Bassi livelli di colesterolo HDL $&lt; 40$ mg/dl ($&lt; 50$ mg/dl nelle donne)</td>
</tr>
<tr>
<td>Obesity</td>
<td>indice di massa corporea $&gt; 25$ Kg/m$^2$ e circonferenza vita superiore a 102 (uomini) o 88 (donne)</td>
</tr>
</tbody>
</table>
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)

1954
Phenmetrazine
(whitdrawn – 1965)
high addiction potential

1959
* Amfetramone/Diethylpropiion
short-term treatment of obesity

1973
Fenfluramine
(whitdrawn – 1997)
heart valvulopathy

1992
* Phentermine/Fenfluramine
(Fenfluramine withdrawn – 1997)

2012
* Phentermine/Topiramate
(Qsymia)
long-term treatment of obesity

1947
Amphetamine
(high addiction potential)
1970 – controlled substance

1959
* Phentermine
short-term treatment of obesity

1965
Aminorex
(whitdrawn – 1968)
pulmonary hypertension

1976
Phenylpropanolamine
(whitdrawn – 2000)
hemorrhagic stroke

1997
Sibutramine
(whitdrawn – 2010)
myocardial infarction, stroke
• **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: DA> NA> 5HT
Sibutramine: 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)
Effect of treatment with *sibutramine*
# Past drug therapy

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism of action</th>
<th>Withdrawal reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamine, Metamphetamine</td>
<td>Sympathomimetic - appetite suppression</td>
<td>High abuse and dependence potential, cardiovascular effects</td>
</tr>
<tr>
<td>Aminorex</td>
<td>Sympathomimetic - appetite suppression</td>
<td>Pulmonary hypertension</td>
</tr>
<tr>
<td>Fenfluramine, Dexfenfluramine</td>
<td>Sympathomimetic - appetite suppression</td>
<td>Valvular heart disease, pulmonary hypertension</td>
</tr>
<tr>
<td>Phenylpropanolamine</td>
<td>Sympathomimetic - appetite suppression</td>
<td>Increased risk of haemorrhagic stroke</td>
</tr>
<tr>
<td>Sibutramine</td>
<td>Sympathomimetic - appetite suppression</td>
<td>Cardiovascular effects – increased risk of heart attack and stroke</td>
</tr>
<tr>
<td>Rimonabat</td>
<td>Inverse agonist of CB1 cannabinoid receptor</td>
<td>Psychiatric disorders</td>
</tr>
</tbody>
</table>
Other Anti-obesity drugs
Lipase

Glycerol + 3 fatty acids -3 H2O = triglyceride
Anti-obesity drugs

- Orlistat
- *Fentermina*
- Sibutramina

Lipase inhibitors

Anorexic

Rimonabant*

Antidepressives (bulimia)
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 = proopio-melanocortin
α-MSH = α-melanocyte-stimulating hormone