



Cómo tratar obesidad en atención primaria?

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Conflictos de interés

- Conferencista: Astra Zeneca, Abbott Nutrición, Novartis Oncology, Novo Nordisk, Merck Sharp & Dohme, Roche, Glaxo SmithKline, Sanofi Aventis, Bayer, Pfizer, Novartis
- Advisory Board: Novartis Oncology, Sanofi Aventis, Astra Zeneca, Novo Nordisk, Stendhal, Pfizer
- Investigación clínica: Astra Zeneca, Novartis Pharma Logistics Inc., Merck Sharp & Dohme, Glaxo SmithKline, Organon, Boehringer Ingelheim, Roche, Novo Nordisk

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Agenda

- Consecuencias médicas de obesidad
- Abordaje psicológico
- Abordaje práctico en estilos de vida
- Fármacos
- Cirugía bariátrica

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Definición

- Basado en IMC, que tiene sus limitantes
- IMC= kg/m²
- Interpretación
 - Normal 18.5-24.9 kg/m²
 - Sobrepeso 25-29.9 kg/m²
 - Obesidad grado I: 30-34.9 kg/m²
 - Obesidad grado II: 35-39.9 kg/m²
 - Obesidad grado III: >40 kg/m²
- Limitantes del IMC

Weight Regulation in Humans

- The human body is hardwired to know how many fat cells are on board and to keep the body weight stable
- At about 5% to 10% of weight loss the human body will respond by:
 - Lowering metabolic rate (more than 5%-10%)
 - Lower the hormones that signal satiety or fullness after eating
 - Increase thoughts and hormones to make humans seek out and eat more food
 - All part of defense of body weight
 - This does not get better with time (always trying to get back to that highest weight)

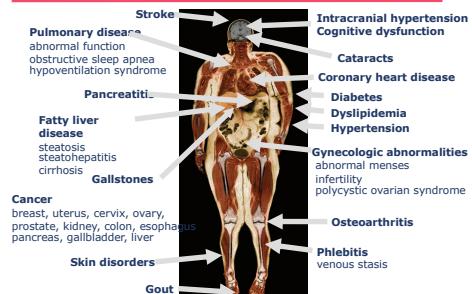
Sumithran P et al. *N Engl J Med.* 2011;365:1597-1604

The Good News on 5% to 10% Weight Loss

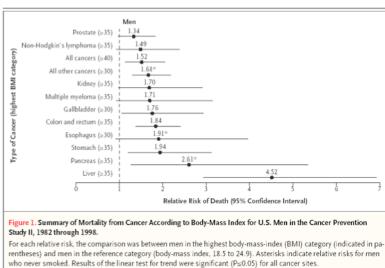
- Sustained weight loss of 3%-5% is likely to result in clinically meaningful reductions in triglycerides, blood glucose, HbA1C, and the risk of developing type 2 diabetes
- Greater amounts of weight loss will reduce blood pressure, improve LDL-C and HDL-C, and reduce the need for medications to control blood pressure, blood glucose and lipids as well as further reduce triglycerides and blood glucose

Jensen MD, et al.
2013 AHA/ACC/TOS Obesity Guideline

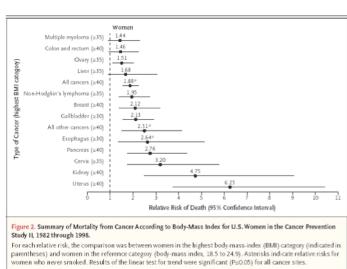
Medical Complications of Obesity



Obesidad y mortalidad por cancer



Obesidad y mortalidad por cáncer



Complications of Obesity

Metabolic

Structural

Inflammatory

Degenerative

Neoplastic

Psychological

Several of these complications exacerbate the underlying obesity, creating a vicious cycle:

Diabetes Many diabetes drugs cause weight gain

PCOS Insulin resistance promotes lipogenesis

Sleep apnea Disrupted sleep can cause weight gain

Limit exercise capacity

Arthritis Steroids often cause weight gain

Back pain Inflammatory disorders

Depression Eating disorders and many psychotropic agents cause weight gain

Psychological

Cuál es el objetivo de la pérdida de peso?

- 5%?
- 10%?
- 20%?
- Volver al peso ideal?
- En cuánto tiempo?
- Por qué?

Benefits of Modest Intentional Weight Loss

- Improvement in comorbid diseases
 - Type 2 diabetes
 - Hypertension
 - Dyslipidemia
 - Fatty liver disease
 - Obstructive sleep apnea
 - Asthma
 - Osteoarthritis
 - Cancer risk
- Improved quality of life
 - Decreased health care costs
 - Decreased surgical complication rates
 - Orthopedic surgery
 - Heart surgery
 - General and thoracic surgery

• The effect on cardiovascular risk is less clear

Cómo abordarlo en atención primaria?

Factores a tomar en cuenta

- Historia familiar
- Historia previa de intentos de pérdida de peso
- Identificar causas secundarias
- Cuáles son las limitantes que han llevado a que la persona no haya tenido éxito en los intentos previos?
 - Psicológicos?
 - Físicos?
 - Económicos?
 - Laborales?

Causas secundarias

- Fármacos:
 - Antipsicóticos
 - Glucocorticoides orales
 - Beta bloqueadores?
 - Antiretrovirales
 - Anticonceptivos orales? (usar menor dosis posible)
- Endocrinopatías
 - Cushing
 - Hipotiroidismo
- Síndromes genéticos: síndrome de Prader Willi

Tratamiento psicológico

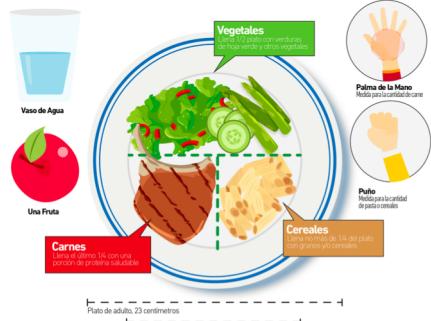
La obesidad como adicción a la comida

- El modelo psicológico es el mismo de una adicción
- Un estímulo que lleva a una acción que resulta gratificante pero que lleva a producir daño (a sí mismo o a otros)
- Hay pacientes que le dicen a uno que son adictos al azúcar
- El azúcar tiene las mismas consecuencias metabólicas igual que el alcohol, sin el efecto psicológico del alcohol
 - Aumento de peso
 - Aumento de grasa visceral
 - Aumento de triglicéridos
 - Hígado graso y cirrosis!



Modificación de estilos de vida

- Cómo ser práctico?
- Fuentes importantes de “calorías ocultas”
 - Jugos y refrescos de frutas
 - Alcohol
 - Golosinas

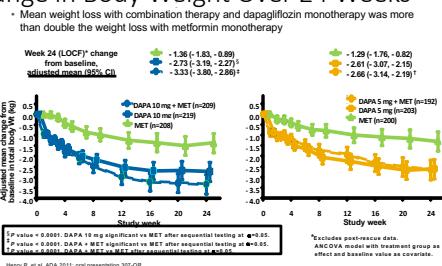


Recomendaciones de actividad física

- Cuánto tiempo?
- Cómo adaptarlo a cada individuo?
- Limitaciones físicas
- Limitaciones económicas
- Limitaciones sociales
- Una clave es que tiene que ser placentero y fácilmente accesible!

Tratamiento farmacológico

Dapagliflozin in Combination with Metformin: Change in Body Weight Over 24 Weeks

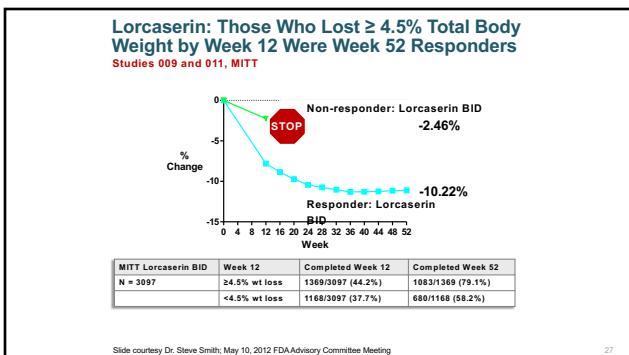
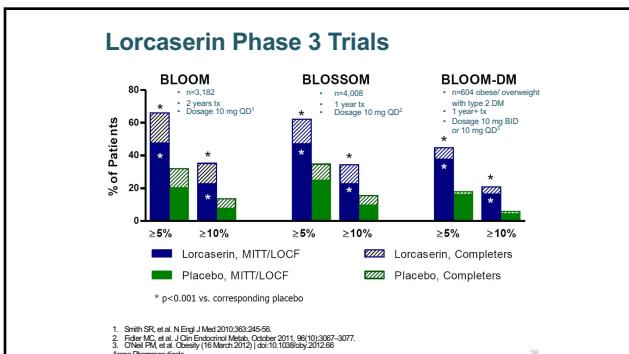
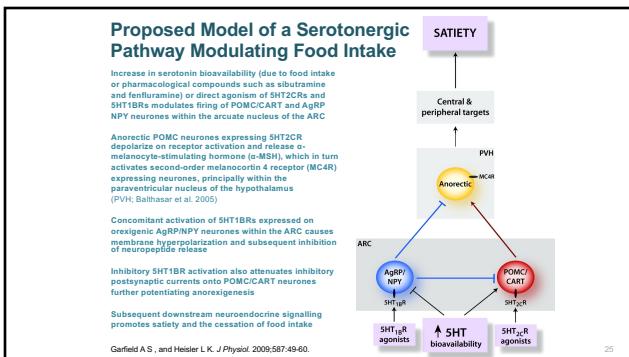


Lorcaserin

Mechanism of Action	Indications and Dose	Contraindications and Warnings
<ul style="list-style-type: none"> Selective 5-HT2C receptor agonist Stimulates α-MSH production from POMC neurons resulting in activation of MC4R Increases satiety 	<ul style="list-style-type: none"> Approved by FDA June 2012 Indication: Weight loss in patients with BMI ≥ 30 kg/m2 or BMI ≥ 27 kg/m2 with weight-related co-morbid condition(s) 10 mg po bid Schedule IV Discontinue if 5% weight loss is not achieved in 12 wks 	Contraindications <ul style="list-style-type: none"> Pregnancy Warnings Co-administration with other serotonergic or anti-dopaminergic agents Valvular heart disease Cognitive impairment Psychiatric disorders (euphoria, suicidal thoughts, depression) Pruritis Risk of hypoglycemia with diabetes meds

Lorcaserin hydrochloride [package insert]. Woodcliff Lake, NJ: Eisai Inc.; 2012.

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**Lorcaserin – BLOOM Study:
Key Secondary Endpoints**

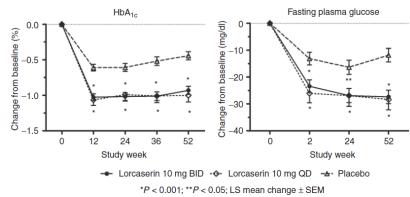
Endpoint		Lorcaserin	Placebo	P value
Waist circumference (cm)	↓	-6.8	-3.9	<0.001
SBP/DBP (mm Hg)	↓	-1.4 / -1.1	-0.8 / -0.6	0.04/0.01
Cholesterol (% Δ)				
Total	↓	-0.90	0.57	0.001
LDL	↓	2.87	4.03	0.049
HDL		0.05	-0.21	0.72
Triglycerides (%)	↓	-6.15	-0.14	<0.001
Safety				
HR (beats/min)	↓	-2.0	-1.6	0.049
Beck depression II		-1.1	-0.9	0.26

Intention-to-Treat Analysis with LOCF Imputation

Smith SR, et al. NEJM. 2010;363:245-256.

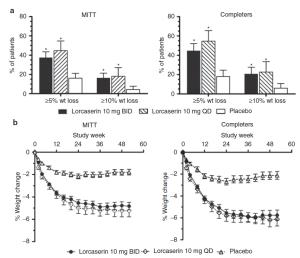
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**Randomized Placebo-Controlled Clinical Trial of Lorcaserin for Weight Loss in Type 2 DM
BLOOM-DM Study - HbA_{1c}**



O'Neill PM, et al. Obesity (Silver Spring). 2012 Jul;20(7):1426-36.

**Randomized Placebo-Controlled Clinical Trial of Lorcaserin for Weight Loss in Type 2 DM
BLOOM-DM Study
Weight Loss**



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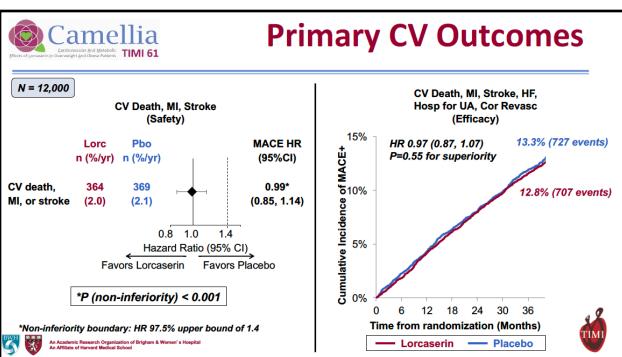
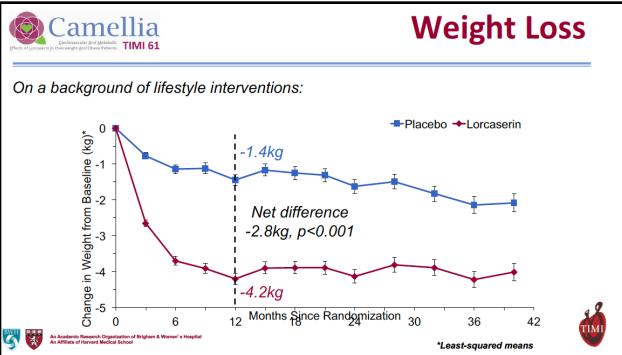
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Lorcaserin: Adverse Events Reported by $\geq 5\%$ in Any Group

N (%)	Lorcaserin (N = 3195)	Placebo (N = 3185)
Headache	537 (16.8)	321 (10.1)
Dizziness	270 (8.5)	122 (3.8)
Nausea	264 (8.3)	170 (5.3)
Constipation	186 (5.8)	125 (3.9)
Fatigue	229 (7.2)	114 (3.6)
Dry mouth	169 (5.3)	74 (2.3)

Intention-to-Treat Analysis with LOCF Imputation
Smith SR, et al. NEJM. 2010;363:245-256.

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Phentermine/Topiramate ER

Mechanism of Action

- Phentermine
 - Sympathomimetic amine, NE release
 - Blunts appetite

- Topiramate
 - Increases GABA activity, antagonize AMPA/kainate glutamate receptor, carbonic anhydrase inhibitor
 - Prolongs satiety

Indications and Dose

- Approved by FDA, July 2012, schedule IV

Indication

Weight loss in pts with BMI $\geq 30 \text{ kg/m}^2$ or $\geq 27 \text{ kg/m}^2$ with weight-related co-morbid condition(s)

Treatment Dose Daily

phentermine 7.5 mg

topiramate ER 46 mg

Max Dose Daily

phentermine 15 mg

topiramate ER 92 mg

Contraindications and Warnings

- Contraindications**
 - Pregnancy, glaucoma, hyperthyroidism, MAOIs

Warnings

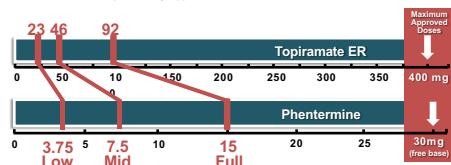
- Fetal toxicity**
 - Increased heart rate
 - Suicide and mood and sleep disorders
 - Acute myopia and glaucoma
 - Cognitive impairment
 - Metabolic acidosis
 - Creatinine elevations
 - Hypoglycemia with diabetes meds

Phentermine and topiramate extended-release [package insert]. Mountain View, CA: Vius; 2012.

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Phentermine/Topiramate ER

- Once-a-day, oral, extended release topiramate
- Low doses of previously approved medications to minimize side effects



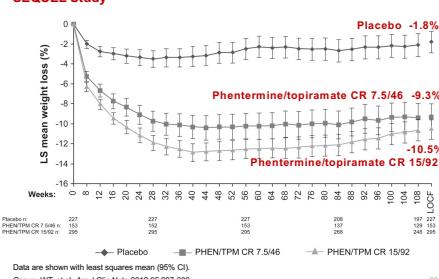
DOSING

- Begin with low dose for 2 wks phentermine 3.75/ topiramate ER 46
- Advance to treatment dose phentermine 7.5/ topiramate ER 46
- If <3% weight loss after 12 wks, either discontinue or advance to full dose phentermine 15/ topiramate ER 92 (transition dose phentermine 11.25/ topiramate ER 69 for 2 wks)
- If <5% weight loss after 12 wks on full dose, discontinue (take every other day for one wk)

Phentermine and topiramate extended-release [package insert]. Mountain View, CA: Vius; 2012.

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Effect of Phentermine/Topiramate ER on Weight Loss in Obese Adults Over 2 Years SEQUEL Study



Data are shown with least squares mean (95% CI).
Garvey WT, et al. Am J Clin Nutr. 2012;95:297-308.

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Phentermine/Topiramate ER: EQUIP and CONQUER Most Commonly Reported Treatment Emergent Adverse Events

Adverse Event (%) (N=749)	Placebo	PHEN/TPM ER 3.7/23	PHEN/TPM ER 7.5/6	PHEN/TPM ER 15/92
Paresthesia	1.9	4.2	13.7	19.9
Dry mouth	2.8	6.7	13.5	19.1
Constipation	6.1	7.9	15.1	16.1
Upper respiratory tract infection	12.8	15.8	12.2	13.5
Headache	9.3	10.4	7.0	10.6
Dysgeusia	1.1	1.3	7.4	9.4
Nasopharyngitis	8.0	12.5	10.6	9.4
Insomnia	4.7	5.0	5.8	9.4
Dizziness	3.4	2.9	7.2	8.6
Sinusitis	6.3	7.5	6.8	7.8
Nausea	4.4	5.8	3.6	7.2
Back pain	5.1	5.4	5.6	6.6
Fatigue	4.2	5.0	4.4	5.0
Blurred vision	3.5	6.3	4.0	5.4
Diarrhea	4.9	5.0	6.4	5.6

Phentermine and topiramate extended-release [package insert]. Mountain View, CA: Vivus; 2012.

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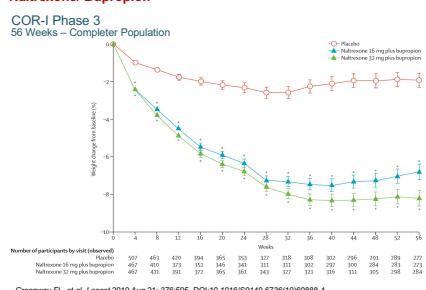
Naltrexone/Bupropion

- Mechanism of Action
 - Naltrexone – Opioid receptor antagonist
 - Bupropion – Dopamine/noradrenaline reuptake inhibitor
- Approved by FDA committee but FDA did not approve until a CVD outcome study is performed due to concerns about blood pressure and pulse in some patients
- The Light Study (CVD outcomes) is under way; estimated completion: July 2017

Apovian C, et al. Obesity. 2013.
Clinicaltrials.gov. Cardiovascular Outcomes Study of Naltrexone SR/Bupropion SR in Overweight and Obese Subjects With Cardiovascular Risk Factors (The Light Study). 2012. <http://clinicaltrials.gov/show/NC10160179>

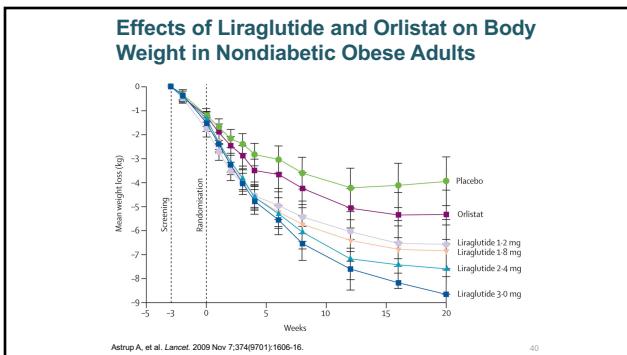
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Mean Weight Loss Naltrexone/ Bupropion

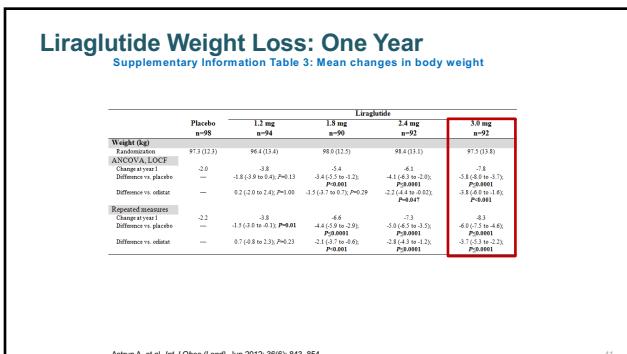


Greenway FL, et al. Lancet 2010 Aug 21; 376:595. DOI:10.1016/S0140-6736(10)60888-4.

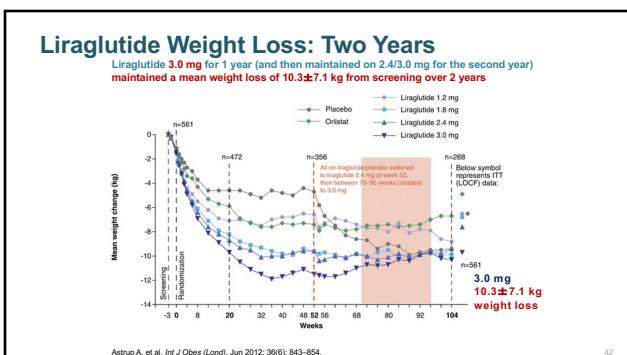
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Cirugía bariátrica

Indicaciones

- IMC mayor a 40 kg/m²
- IMC mayor a 35 kg/m² asociado a comorbilidades
- Descartar depresión!!!
- No es la solución fácil que todos piensan!
- Reganancia de peso
- Mantenimiento a largo plazo
- Consecuencias metabólicas
 - Osteoporosis
 - Deficiencias de micronutrientes

Conclusiones

- Obesidad es una patología compleja
- El modelo psicológico es igual a la adicción
- Se debe abordar desde el punto de vista psicológico, motivacional, social, farmacológico
- El único agente disponible en el mercado nacional que es seguro es lorcaserina
- Candidatos a cirugía bariátrica

Preguntas...

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Puede descargar la
presentación en:



www.EndoDrChen.com
