Lorcaserin

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渡邊直美推特

Outline

- 肥胖的藥物治療
- Lorcaserin 安全性& 療效
- Lorcaserin 注意事項

Pharmacological Management of Obesity

Use weight loss medications only as adjunct to lifestyle modification.

- > 6 months of chronic management of obesity
- Medication + lifestyle > lifestyle therapy alone
- weight-related complications→ consider lifestyle +medication at the same time
- Short term medication not recommended

1. American Association of Clinical Endocrinologists/American College of Endocrinology (AACE/ACE) 2016 recommendations
2. Endocrine Society

Drug therapy for obesity

GLP-1 receptor agonists

- Liraglutide

Drugs that alter fat digestion

- Orlistat

Combination drugs

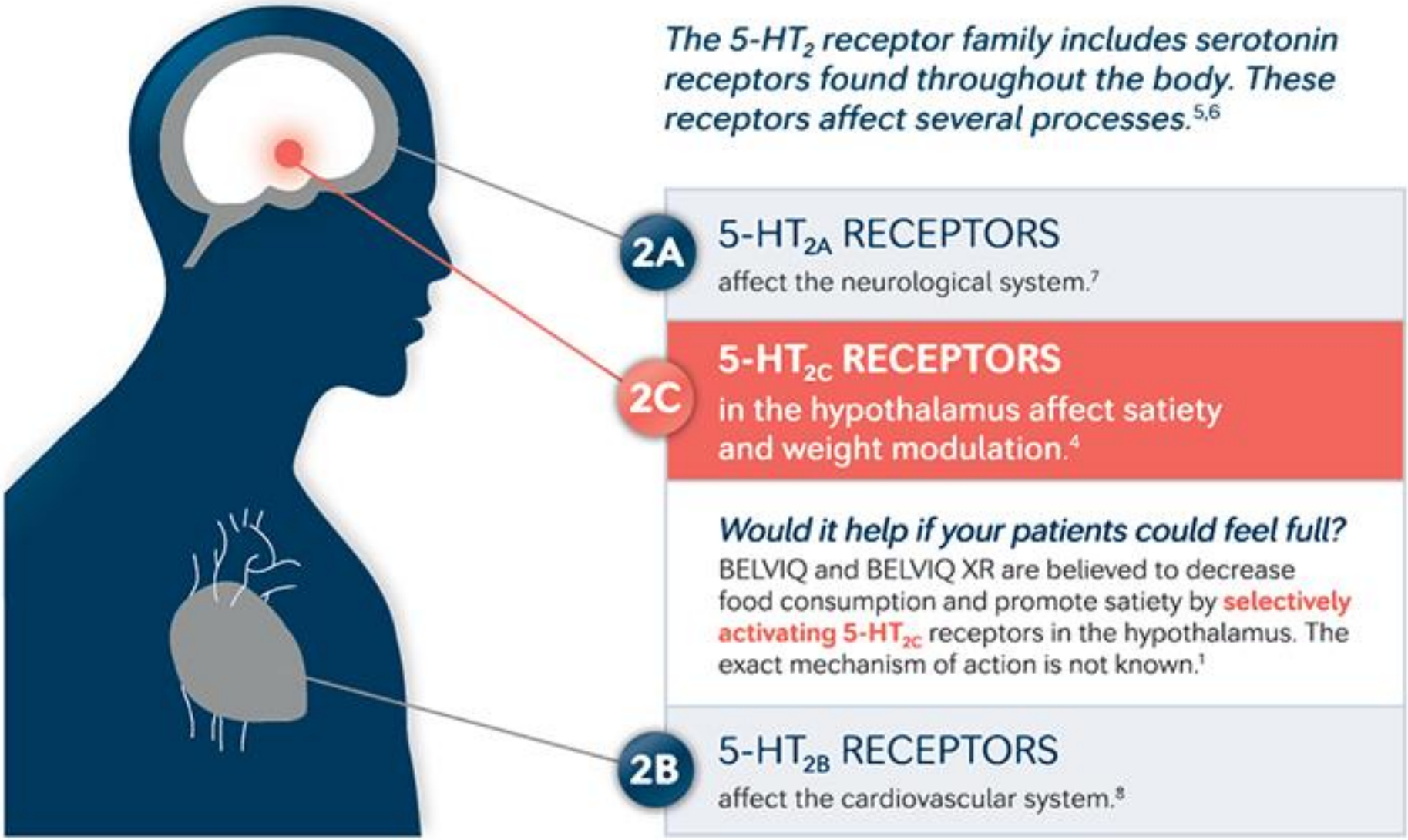
- Phentermine-topiramate
- Bupropion-naltrexone

Serotonin agonist

- Lorcaserin

Drug therapy for obesity

- GLP-1 receptor agonists
  - Liraglutide
- Drugs that alter fat digestion
  - Orlistat
- Combination drugs
  - Phentermine-topiramate
  - Bupropion-naltrexone
- Serotonin agonist
  - Lorcaserin



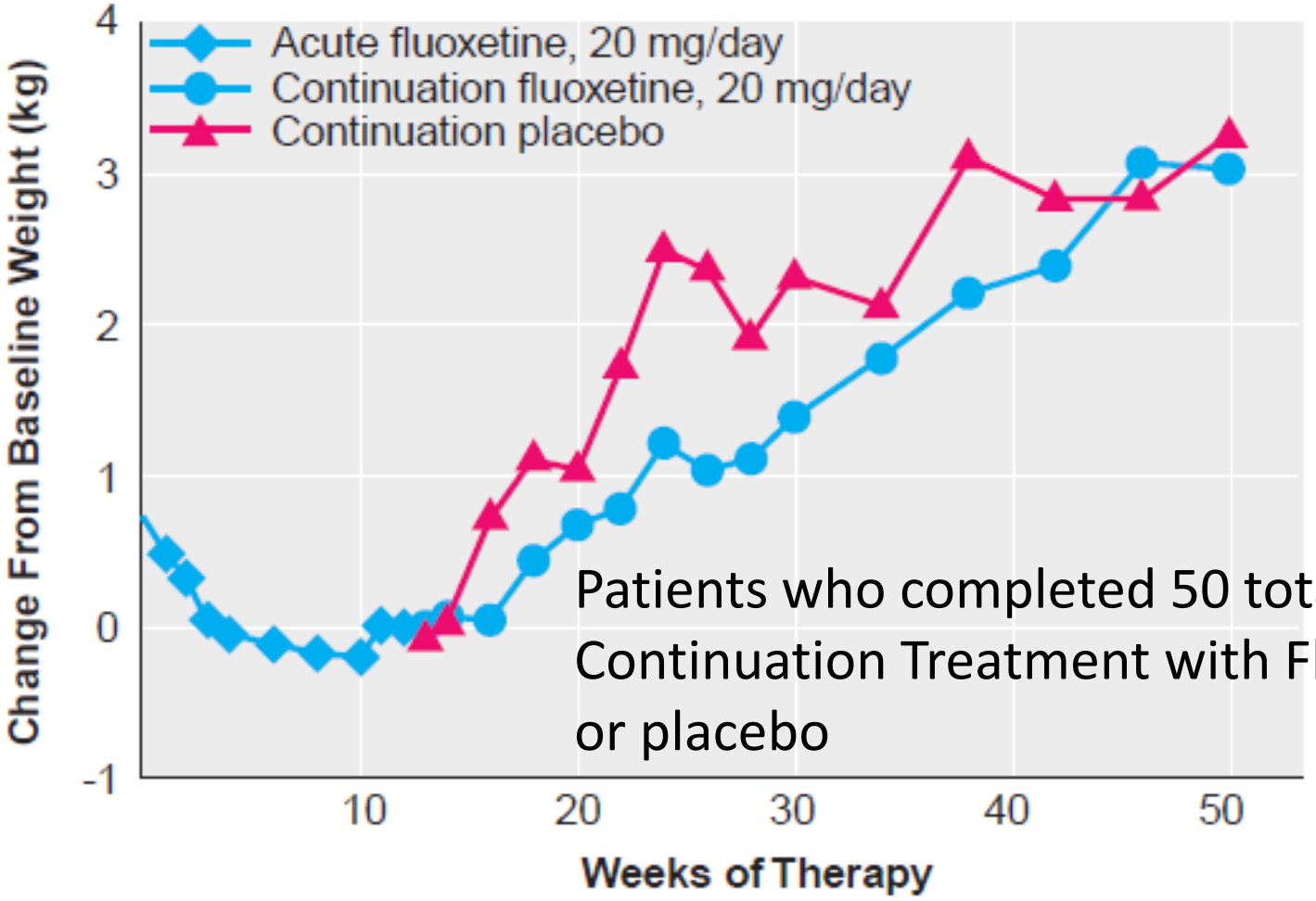
www.belviq.com

沛麗婷作用相關機制？
認識 血清素三種受器的作用

MedPartner美的好朋友

https://www.medpartner.club/

Fluoxetine (百憂解): Change in Weight Over Time



Patients who completed 50 total weeks of Continuation Treatment with Fluoxetine or placebo

Am J Psychiatry. 1999 Aug;156(8):1170-6.

FDA 核准適應症

Chronic weight management as adjunct to reduced-calorie diet and exercise:

- initial BMI of ≥30 kg/m2

or

- initial BMI of ≥27 kg/m2

with Hypertension/ dyslipidemia/ type 2 diabetes

In Taiwan

2006
Phenylpropanolamine (PPA)下市

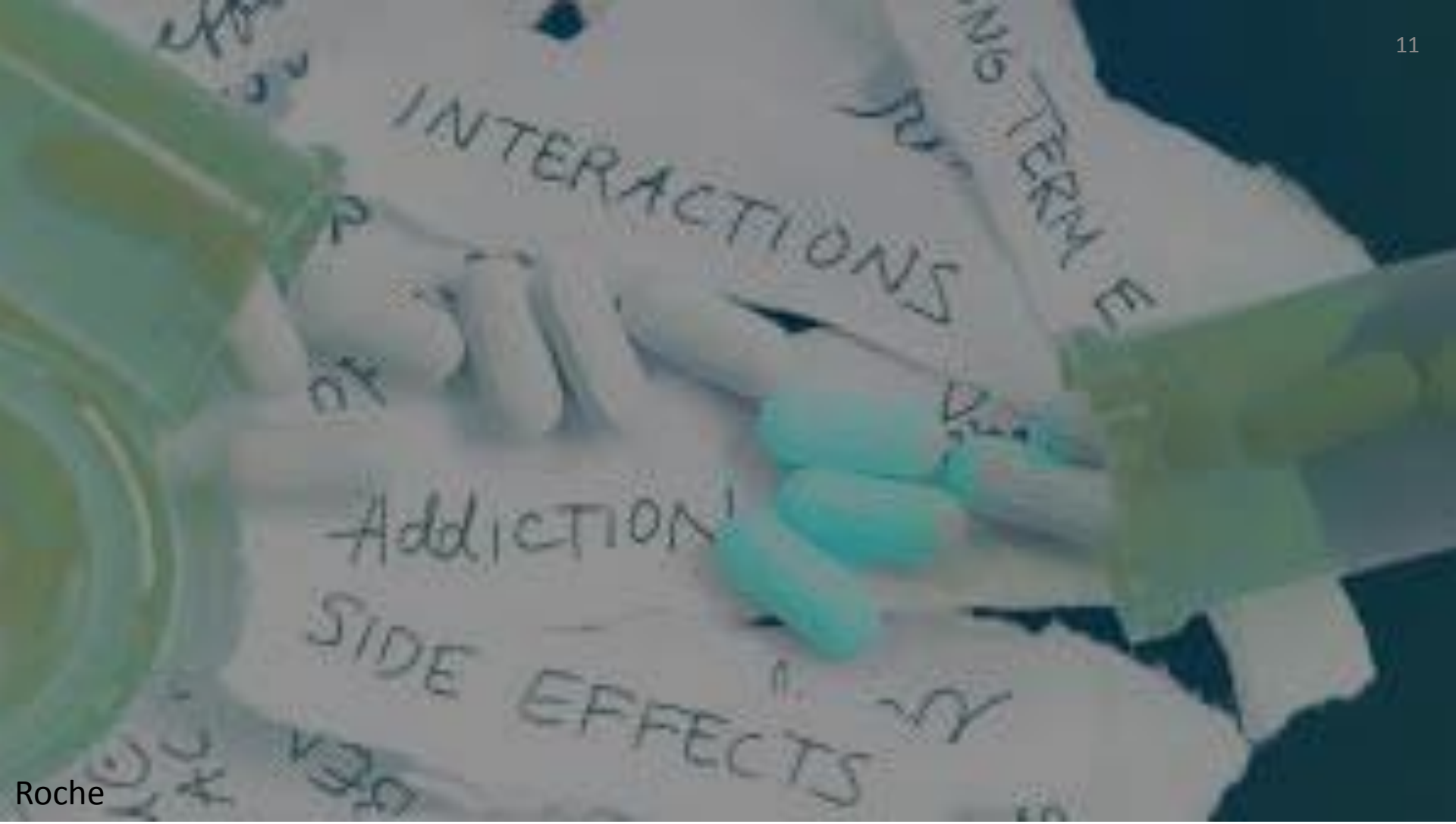
羅氏鮮諾美婷

2010
諾美婷下市

2017
臺灣FDA核准
沛麗婷

Need-to-knows

- 10 mg BID
- Should be discontinued if failure to lose 5% body weight after 12 weeks
- Avoid in pregnancy: category X
- Drug interactions: CYP2D6, 5-HT receptors
- Toxicity: 5-HT2A, 5-HT2B
- Special precautions: DM, psychiatrics, hepatic/ renal function impairment



Roche

Safety issues

AACE/ACE 2016 recommendations

American Association of Clinical Endocrinologists/ American College of Endocrinology	
Adjunct to lifestyle for chronic (> 6 months) management of obesity	(grade A, level 1)
Avoid lorcaserin in patients with alcohol or other substance addictions	(grade A, level 1)
Use caution with/ avoid lorcaserin in patients who are taking medication for depression	(grade A, level 1)
Use caution with/ avoid severe renal impairment (eGFR< 30 ml/minute)	(grade B, level 2)

American Association of Clinical Endocrinologists/American College of Endocrinology

American Association of Clinical Endocrinologists/ American College of Endocrinology (AACE/ACE) Levels of evidence	
Level 1	Randomized trials or meta-analysis of randomized trials
Level 2	Non-randomized controlled trial, prospective cohort study, retrospective case-control study, or meta-analysis of these types of studies
Level 3	Cross-sectional study, surveillance study, consecutive case series, or single case reports
Level 4	No evidence (theory, opinion, consensus, review, or preclinical study)

American Association of Clinical Endocrinologists/ American College of Endocrinology (AACE/ACE) Grades of Recommendation	
Grade A	Best evidence level 1, or best evidence level 2 but adjusted upward for positive subjective factors
Grade B	Best evidence level 2, or best evidence level 1 adjusted downward for negative subjective factors, or best evidence level 3 adjusted upward for positive subjective factors
Grade C	Best evidence level 3, or best evidence level 2 adjusted downward for negative subjective factors, or best evidence level 4 adjusted upward for positive subjective factors
Grade D	Best evidence level 4, or best evidence level 3 adjusted downward for negative subjective factors, or < two-thirds consensus (regardless of evidence level)

AACE/ACE 2016 recommendations

Consider lorcaserin in addition to lifestyle therapy for patients with overweight and obesity and of following conditions.

High risk for type 2 diabetes (prediabetes or metabolic syndrome)	(grade A, level 1)
Risk for seizure disorders	(grade B, level 1)
Chronic opioid or opiate medication	(grade B, level 1)
Risk for nephrolithiasis	(grade D)
Hypertension	(grade B, level 1)
Atherosclerotic cardiovascular disease	(grade A, level 1)
Increased risk for cardiac arrhythmia	(grade B, level 1)
Risk for glaucoma	(grade B, level 2)

Avoid Drug Therapy

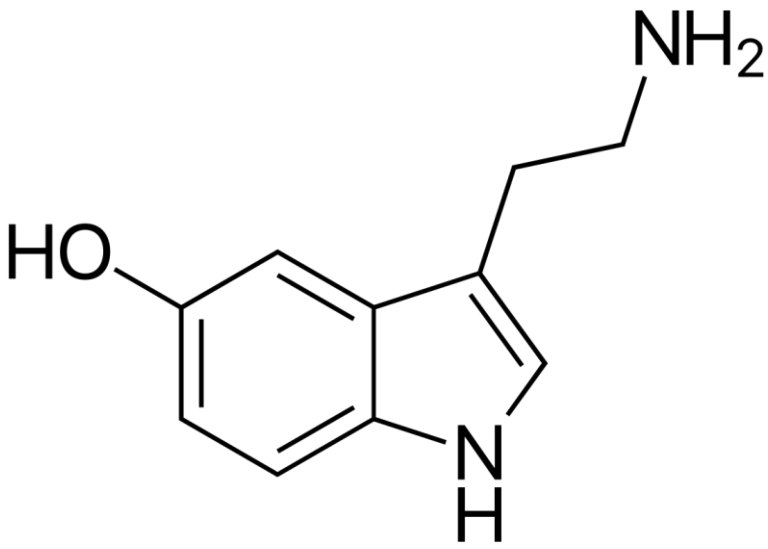
American Association of Clinical Endocrinologists/ American College of Endocrinology	
Pregnancy	(grade A, level 1)
Breast feeding	(grade A, level 1)
Severe hepatic impairment (Child-Pugh score >9)	(grade A, level 1)

Common Side Effects

In patient without diabetes:	In patient with diabetes:
✓ headache	✓ hypoglycemia
✓ dizziness	✓ headache
✓ fatigue	✓ back pain
✓ nausea	✓ cough
✓ dry mouth	✓ fatigue
✓ constipation	

Serious but Uncommon side effects

- Serotonin syndrome
- Disturbances in attention or memory



Original Investigation

FREE

June 14, 2016

Association of Pharmacological Treatments for Obesity With Weight Loss and Adverse Events

A Systematic Review and Meta-analysis

Rohan Khera, MD[1]; Mohammad Hassan Murad, MD, MPH[2,3]; Apoorva K. Chandar, MBBS, MPH[4]; et al

» Author Affiliations | Article Information

JAMA. 2016;315(22):2424-2434. doi:10.1001/jama.2016.7602

Aim	**To compare weight loss and adverse events among drug treatments for obesity**
Population	Overweight & obese adults Follow up >= 1 year RCTs
Intervention	Orlistat, Lorcaserin, naltrexone-bupropion, phentermine- topiramate, liraglutide
Comparison	Another active agent/ placebo
Outcome	5%, 10% Weight loss Discontinuation of therapy due to adverse events at 1 year

From: **Association of Pharmacological Treatments for Obesity With Weight Loss and Adverse Events: A Systematic Review and Meta-analysis**

JAMA. 2016;315(22):2424-2434. doi:10.1001/jama.2016.7602

Table 3. Summary of Direct Meta-analysis for All Weight Loss and Adverse Event Outcomes

Pharmacological Intervention	No. of Studies	Active Intervention		Control (Placebo Unless Otherwise Noted)		OR or Weighted Mean Difference, kg (95% CI)
		No. With Event	Total No.	No. With Event	Total No.	
≥5% Weight Loss						
Orlistat	16	3140	5315	1694	4694	2.69 (2.36 to 3.07)
Lorcaserin	3	1562	3350	729	3288	3.09 (2.49 to 3.83)
Naltrexone-bupropion	4	1081	2044	274	1319	3.90 (2.91 to 5.22)
Phentermine-topiramate	2	1019	1479	290	1477	9.10 (7.68 to 10.78)
Liraglutide	3	vs Placebo: 1798 vs Orlistat: 53	2921 72	Placebo: 380 Orlistat: 29	1503 67	5.09 (4.07 to 6.37) 3.66 (1.79 to 7.46)
≥10% Weight Loss						
Orlistat	14	1520	4859	684	4249	2.41 (2.08 to 2.78)
Lorcaserin	3	742	3350	276	3288	3.17 (2.53 to 3.97)
Naltrexone-bupropion	4	599	2044	112	1319	4.11 (2.80 to 6.05)
Phentermine-topiramate	2	702	1479	109	1477	11.34 (9.10 to 14.13)
Liraglutide	3	vs Placebo: 930 vs Orlistat: 27	2921 72	Placebo: 146 Orlistat: 9	1503 67	4.36 (3.61 to 5.26) 3.87 (1.65 to 9.04)

Summary of Direct Meta-analysis for All Weight Loss and Adverse Event Outcomes

From: **Association of Pharmacological Treatments for Obesity With Weight Loss and Adverse Events: A Systematic Review and Meta-analysis**

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		No. With Event	Total No.	No. With Event	Total No.	
Mean Weight Loss in Excess of Placebo[a]						
Orlistat	14		3391		2777	−2.63 (−2.94 to −2.32)[b]
Lorcaserin	3		3350		3288	−3.25 (−3.55 to −2.95)[b]
Naltrexone-bupropion	2		1297		967	−4.95 (−5.54 to −4.36)[b]
Phentermine-topiramate	1		981		979	−8.80 (−9.62 to −7.98)[b]
Liraglutide	3		2921 72		1503 67	−5.24 (−5.60to−4.87)[b] −3.90 (−5.18 to −2.62)[b]
Discontinuation of Therapy Due to Adverse Events						
Orlistat	16	439	5323	224	4704	1.84 (1.55 to 2.18)
Lorcaserin	3	250	3350	190	3288	1.40 (0.96 to 2.03)
Naltrexone-bupropion	4	501	2044	175	1319	2.60 (2.15 to 3.14)
Phentermine-topiramate	2	274	1479	132	1477	2.32 (1.86 to 2.89)
Liraglutide	3	vs Placebo: 292 vs Orlistat: 7	2921 72	Placebo: 57 Orlistat: 2	1503 67	2.82 (2.10 to 3.77) 3.50 (0.70 to 17.49)

Summary of Direct Meta-analysis for All Weight Loss and Adverse Event Outcomes

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From: **Association of Pharmacological Treatments for Obesity With Weight Loss and Adverse Events: A Systematic Review and Meta-analysis**

JAMA. 2016;315(22):2424-2434. doi:10.1001/jama.2016.7602

Network Meta-analysis

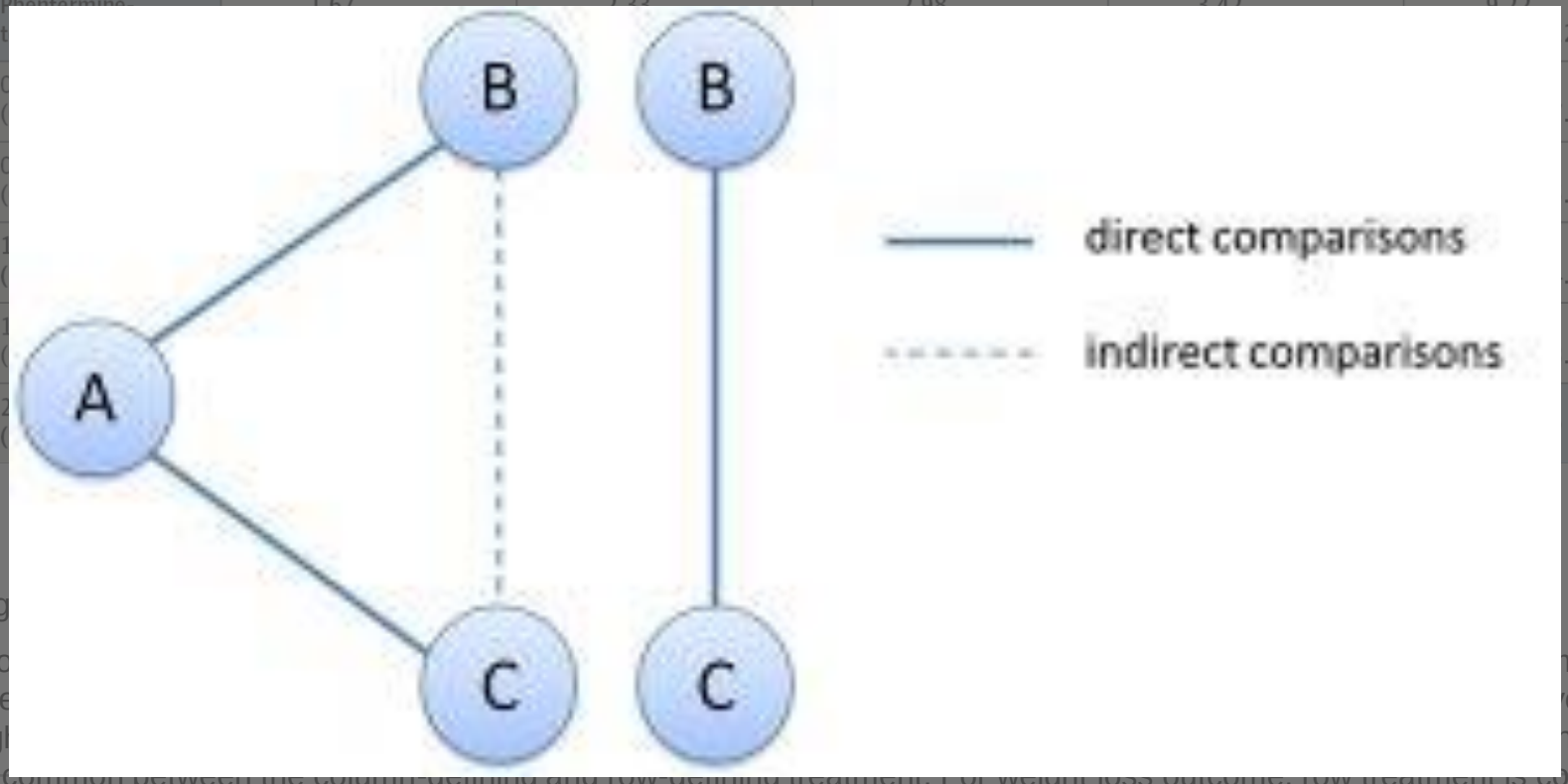

Figure Leg

Comparisc nmary estimate re verse events (ligh ns are in the cell in common between the column-defining and row-defining treatment. For weight loss outcome, row treatment is compared with column treatment (ie, column treatment is reference). For adverse event outcome, column treatment is compared with row treatment (ie, row treatment is reference). Numbers in parentheses indicate 95% credible intervals (95% CrIs). Numbers in bold represent statistically significant results.

From: **Association of Pharmacological Treatments for Obesity With Weight Loss and Adverse Events: A Systematic Review and Meta-analysis**

JAMA. 2016;315(22):2424-2434. doi:10.1001/jama.2016.7602

Odds ratio (95% CrI) for discontinuation due to adverse events	Odds ratio (95% CrI) for achieving at least 5% weight loss					
	Phentermine-topiramate	1.67 (1.03-2.56)	2.33 (1.54-3.59)	2.98 (1.95-4.54)	3.42 (2.40-4.91)	9.22 (6.63-12.85)
0.78 (0.48-1.20)	Liraglutide	1.4 (0.96-2.18)	1.78 (1.22-2.78)	2.06 (1.51-2.96)	5.54 (4.16-7.78)	
0.87 (0.59-1.25)	1.11 (0.74-1.72)	Naltrexone-bupropion	1.28 (0.87-1.84)	1.47 (1.09-1.96)	3.96 (3.03-5.11)	
1.71 (1.14-2.49)	2.2 (1.43-3.39)	1.97 (1.38-2.76)	Lorcaserin	1.15 (0.86-1.55)	3.1 (2.38-4.05)	
1.25 (0.88-1.76)	1.6 (1.10-2.40)	1.44 (1.07-1.95)	0.73 (0.54-1.02)	Orlistat	2.7 (2.34-3.09)	
2.29 (1.71-3.06)	2.95 (2.11-4.23)	2.64 (2.1-3.35)	1.34 (1.05-1.76)	1.84 (1.53-2.21)	Placebo	

Figure Legend:

Comparison of Weight Loss and Adverse Events With Pharmacological Weight Loss Agents in Network Meta-analysisSummary estimate represents odds ratio of achieving at least 5% weight loss (light gray background) and discontinuation due to adverse events (light blue background). Agents are ordered by rankings for the 5% weight loss outcome. Odds ratio for comparisons are in the cell in common between the column-defining and row-defining treatment. For weight loss outcome, row treatment is compared with column treatment (ie, column treatment is reference). For adverse event outcome, column treatment is compared with row treatment (ie, row treatment is reference). Numbers in parentheses indicate 95% credible intervals (95% CrIs). Numbers in bold represent statistically significant results.

Effects of Weight-Loss Medications on Cardiometabolic Risk Profiles: A Systematic Review and Network Meta-analysis

Rohan Khera,[1,*] **Ambarish Pandey**,[1,*] Apoorva K. Chandar,[2] Mohammad H. Murad,[3,4] Larry J. Prokop,[3] Ian J. Neeland,[1] Jarett D. Berry,[1] Michael Camilleri,[5] and Siddharth Singh[6,7]

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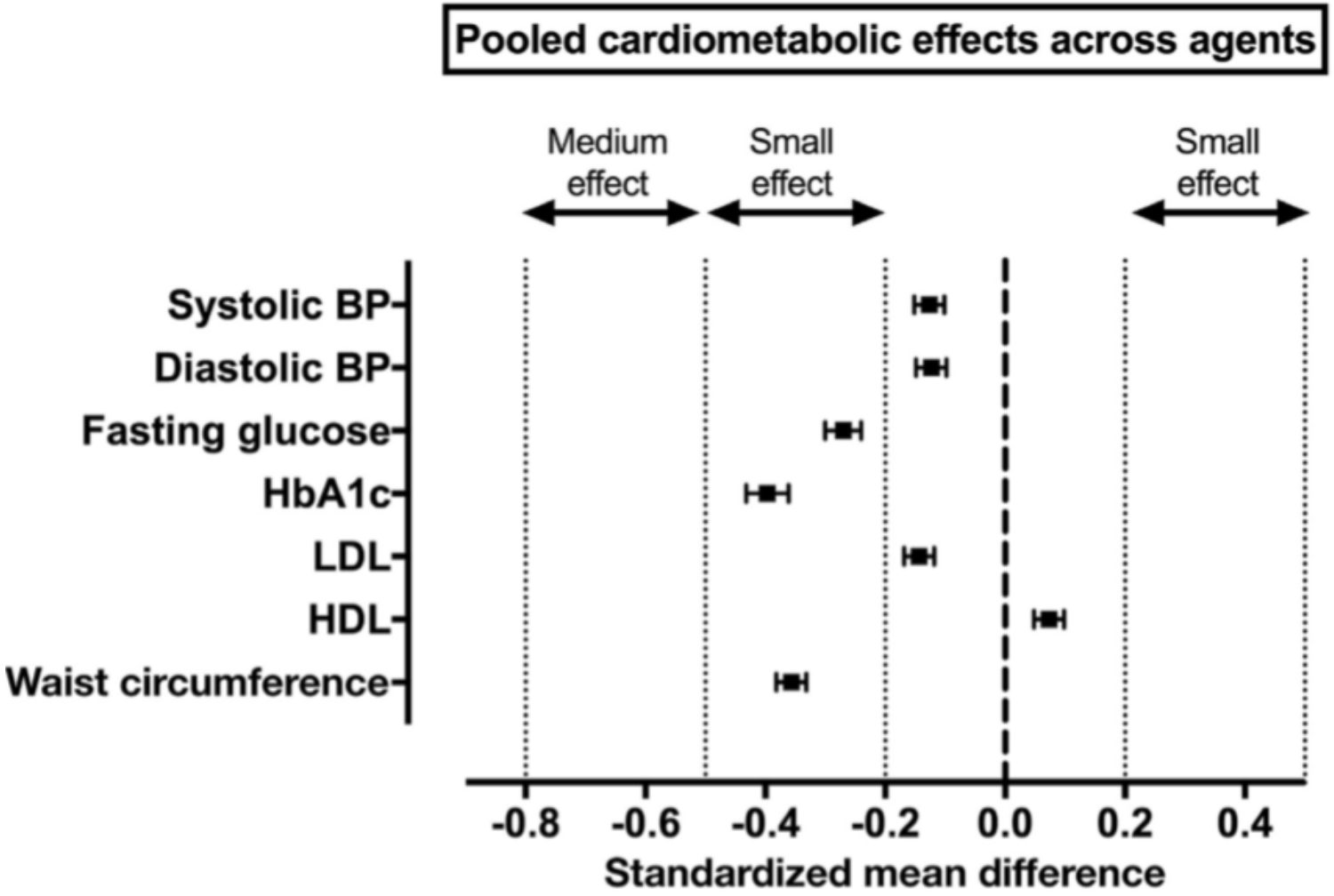
Aim	**To evaluate overall and comparative effects of weight loss medications for long term use on cardiometabolic risk profiles of obese patients**
Population	Overweight & obese adults Follow up >= 1 year RCTs
Intervention	Orlistat, Lorcaserin, naltrexone-bupropion, phentermine- topiramate, liraglutide
Comparison	Another active agent/ placebo
Outcome	Changes in blood glucose (FBG, HbA1c), cholesterol profile (LDL, HDL), BP, Waist circumference

Gastroenterology. 2018 Apr;154(5):1309-1319.e7

Cardiometabolic risk



Gastroenterology. 2018 Apr;154(5):1309-1319.e7

Ongoing study on CV effect

Am Heart J. 2018 Mar 29;202:39-48. doi: 10.1016/j.ahj.2018.03.012. [Epub ahead of print]

Design and rationale for the Cardiovascular and Metabolic Effects of Lorcaserin in Overweight and Obese Patients-Thrombolysis in Myocardial Infarction 61 (CAMELLIA-TIMI 61) trial.

Bohula EA[1], Scirica BM[2], Fanola C[2], Inzucchi SE[3], Keech A[4], McGuire DK[5], Smith SR[6], Abrahamsen T[2], Francis BH[7], Miao W[7], Perdomo CA[7], Satlin A[7], Wiviott SD[2], Sabatine MS[2].

Author information

Abstract

OBJECTIVES: Lorcaserin, a selective serotonin 2C receptor agonist, is an effective pharmacologic weight-loss therapy that improves several cardiovascular risk factors. The long-term clinical cardiovascular and metabolic safety and efficacy in patients with elevated cardiovascular risk are unknown.

RESEARCH DESIGN AND METHODS: CAMELLIA-TIMI 61 (NCT02019264) is a randomized, double-blind, placebo-controlled, multinational clinical trial designed to evaluate the safety and efficacy of lorcaserin with regard to major adverse cardiovascular events and progression to diabetes in overweight or obese patients at high cardiovascular risk. Overweight or obese patients either with established cardiovascular disease or with diabetes and at least 1 other cardiovascular risk factor were randomized in a 1:1 ratio to lorcaserin 10 mg twice daily or matching placebo. The primary safety objective is to assess for noninferiority of lorcaserin for the composite end point of cardiovascular death, myocardial infarction, or stroke (major adverse cardiovascular event [MACE]) (with noninferiority defined as the upper bound of a 1-sided 97.5% CI excluding a hazard ratio of 1.4) compared with placebo assessed at an interim analysis with 460 adjudicated events. The efficacy objectives, assessed at study completion, will evaluate the superiority of lorcaserin for the primary composite end point of cardiovascular death, myocardial infarction, stroke, hospitalization for unstable angina, heart failure, or any coronary revascularization (MACE+) and the key secondary end point of conversion to diabetes. Recruitment began in January 2014 and was completed in November 2015 resulting in a total population of 12,000 patients. The trial is planned to continue until at least 1,401 adjudicated MACE+ events are accrued and the median treatment duration exceeds 2.5 years.

CONCLUSION: CAMELLIA-TIMI 61 is investigating the safety and efficacy of lorcaserin for MACEs and conversion to diabetes in overweight or obese patients with established cardiovascular disease or multiple cardiovascular risk factors.

PMID: 29803985 DOI: 10.1016/j.ahj.2018.03.012

Am Heart J. 2018 Mar 29;202:39-48.

減肥藥品比較

Drug	Orlistat	Lorcaserin	Phentermine / Topiramate	Liraglutide
Label	Xenical	Belviq	Qsymian	Saxenda
Mechanism	Gastric/ pancreatic lipase inhibitor	5-HT2c agonist	CNS stimulant	GLP-1 agonist
	↓TG hydrolyzation	↓Appetite	↓Appetite	↓Appetite
Who are they for	initial BMI of ≥30 kg/m2 **or** initial BMI of ≥27 kg/m2 **+** Hypertension/ dyslipidemia/ type 2 diabetes			
Common side effects	Oil spotting, GI discomfort, Fecal incontinence	Hypoglycemia, Headache, N/V	HR↑, Paresthesia, Insomnia	HR↑, Headache, Hypoglycemia

總結一下...

使用Lorcaserin 必須注意的事

安全性

特別族群可不可以用?

交互作用

BMI< 27可否使用?

減重藥品可否併用?

References

- **DynaMed：Weight loss medications for obesity in adults. Fatima Cody Stanford, MD, MPH, MPA, FAAP, FACP, FTOS; updated 2018 Mar 21**
- **MedPartner**

  https://www.medpartner.club/
- **葉峻樁醫師**

  https://chunting.me/

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THANKS FOR YOUR ATTENTION