TIRZEPATIDA Y EL NUEVO ESTÁNDAR DE EFICACIA EN OBESIDAD

Implicancias para la cirugía metabólica

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Clinica Las Condes - NOVAMED

SCCBM-ACHINUMET-IFSO-LAC

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La presentación tiene un carácter académico científico y no busca fomentar ni promover el uso de productos ni dispositivos médicos farmacéuticos.

Otras consideraciones

- No vivo ni he vivido con obesidad.
- El tratamiento de la obesidad **DEBE incluir otros parámetros además del la pérdida de peso como objetivo de tratamiento.**

Sobre tratamientos para la obesidad

Enfermedad crónica, multifactorial, progresiva y recidivante.

Limitaciones históricas del tratamiento farmacológico

La llegada de terapias con eficacia “quirúrgica”

Nuevo estándar de eficacia

Sobre tratamientos para la obesidad

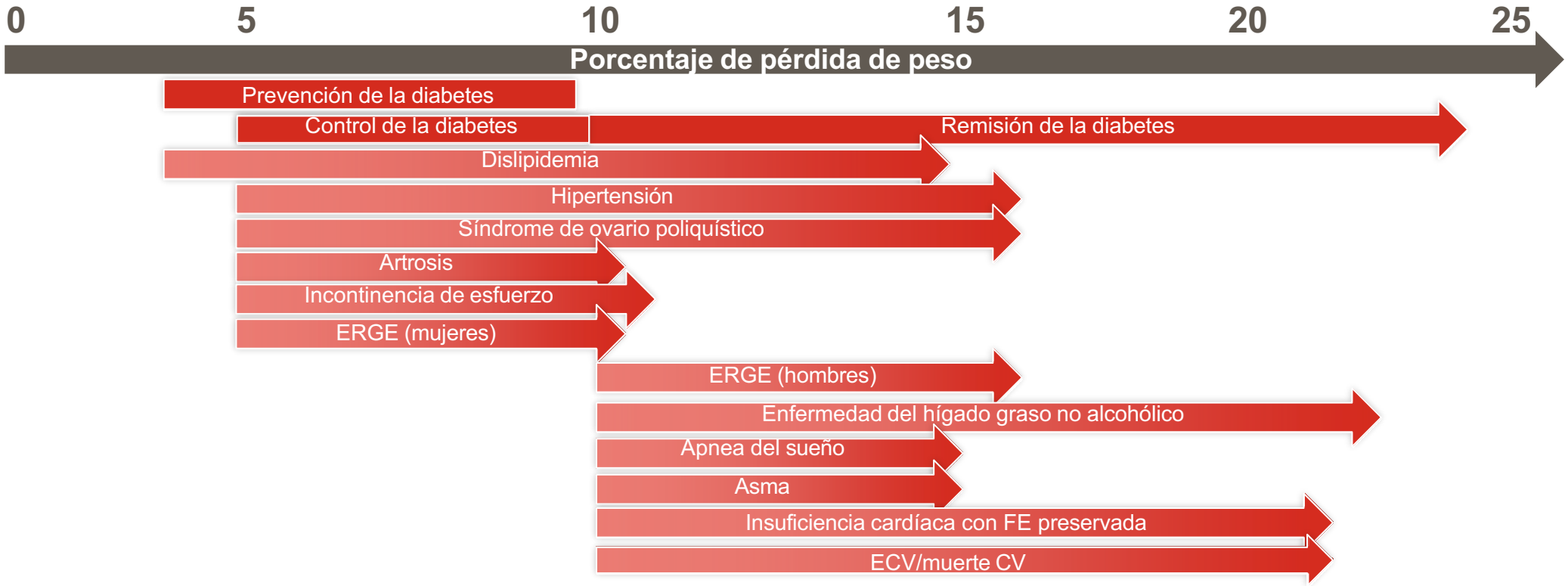
- La cirugía era claramente superior desde el punto de vista de pérdida de peso corporal

Intervención	%TWL aproximado
Dieta/CEV	5–8%
Liraglutida	6-8%
Semaglutida 2.4 mg	12–15%
Tirzepatide	18-21%
Gastrectomía vertical	20-30%
Bypass gástrico	30-35%

De Luca, M., Cohen, R. V., Belluzzi, A., et al. (2026). Efficacy and safety of pharmacological, endoscopic, and surgical treatments for obesity: A GRADE-based network meta-analysis. Obesity, 34(2)

Beneficio de la pérdida de peso

Mayor beneficio con una mayor pérdida de peso



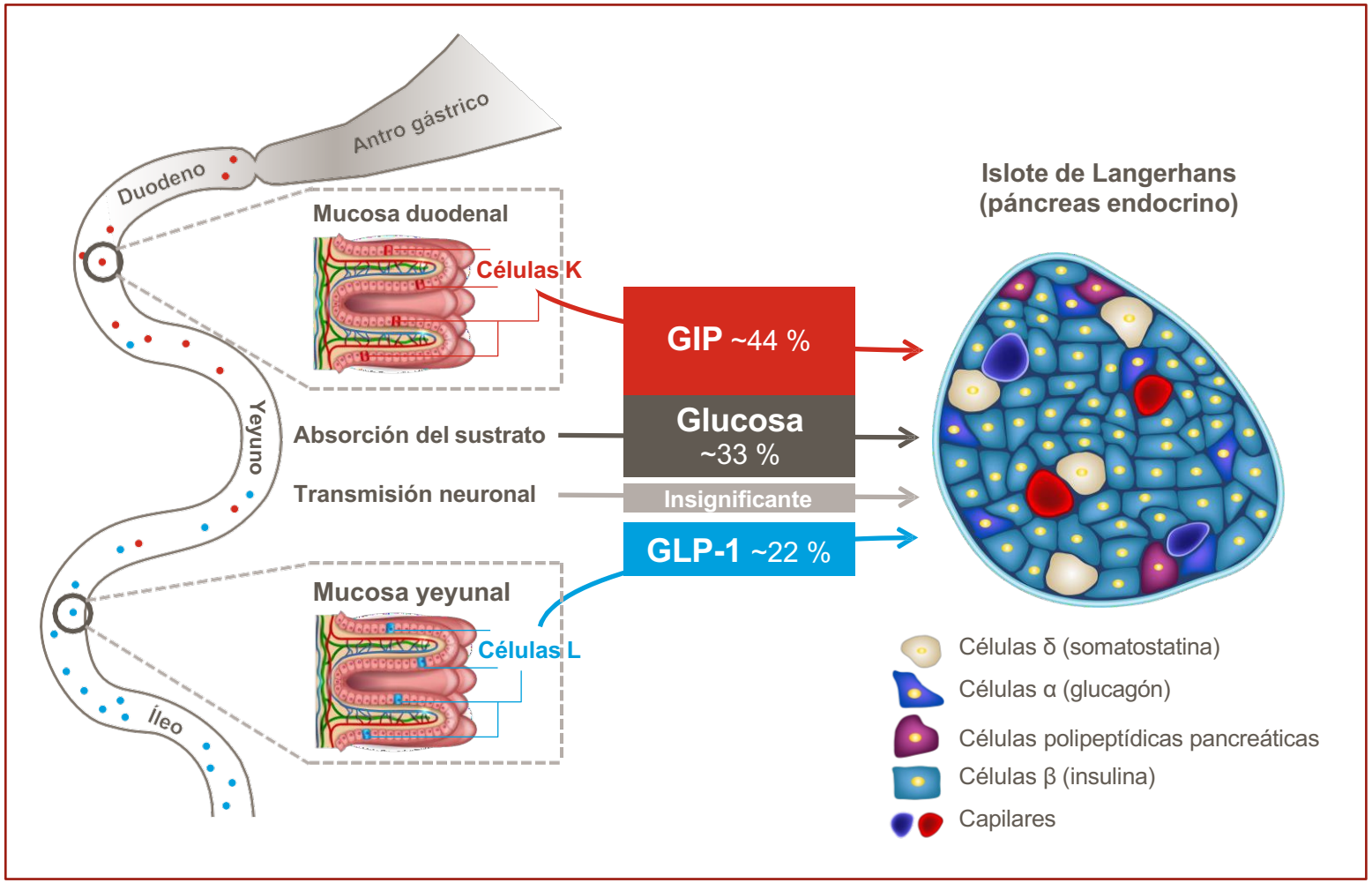
CV = cardiovascular; ECV = enfermedad cardiovascular; ERGE = Enfermedad por reflujo gastroesofágico; FE = fracción de eyección.

Lingvay I, *et al*. *Lancet* 2022; 399: 394-405

“Twincretinas”

Agonismo rGIP y rGLP1LP-1

El eje intestino-páncreas
GIP y GLP1 no son gemelos idénticos



- **Bloqueo GLP-1**
  Ligero aumento de glucosa postcarga. Disminución leve de secreción de insulina.
- **Bloqueo GIP**
  Aumento sustancial de glucosa pp.
  Reducción marcada de secreción de insulina.
  Impacto significativamente mayor que el bloqueo de GLP-1.
- **El efecto incretina total es ≈ 67% de la respuesta insulinotrópica tras glucosa oral.**

GIP = polipéptido insulinotrópico dependiente de la glucosa; GLP-1 = péptido similar al glucagón tipo 1; GPP = glucosa posprandial.
Nauck MA, Meier JJ. *Diabetes*. 2019;68(5):897-900.

Similitudes entre GIP y GLP-1

Efectos similares sugeridos en estudios clínicos y preclínicos

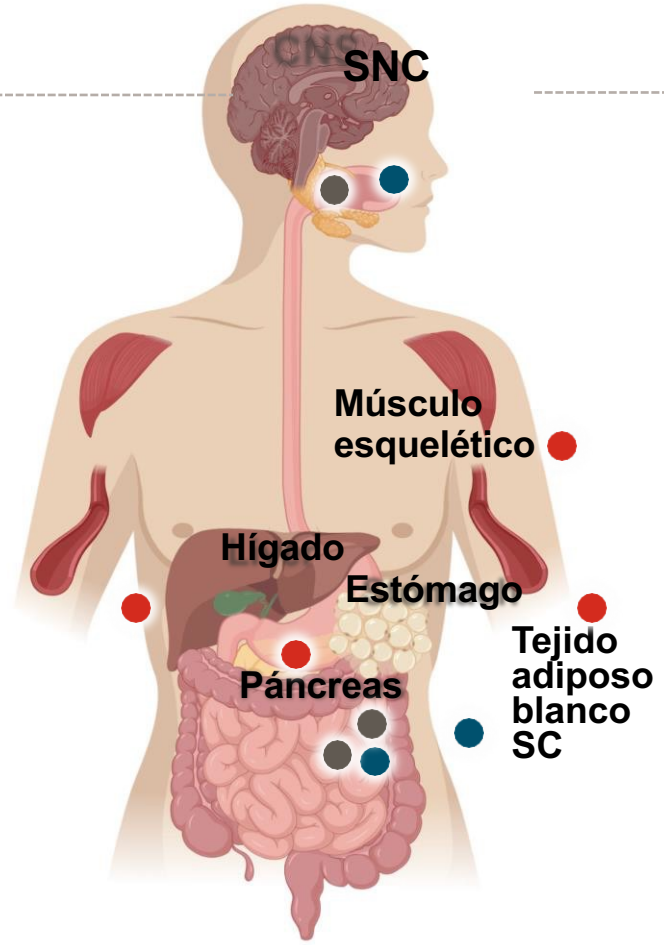
GLP-1

SNC
- ↓ Ingesta de alimentos
- ↓ Peso corporal

Páncreas
- ↑ Insulina

Sistémico
- ↓ Hiperglicemia

Hígado
- ↑ Sensibilidad a la insulina
- ↓ Acumulación ectópica de lípidos



GIP

SNC
- ↓ Ingesta de alimentos
- ↓ Peso corporal

Páncreas
- ↑ Insulina

Sistémico
- ↓ Hiperglicemia

Músculo esquelético
- ↑ Sensibilidad a la insulina
- ↓ Acumulación ectópica de lípidos

Data presented in this figure come from human and animal studies.
Adapted from: Samms RJ, Coghlan MP, Sloop KW. *Trends Endocrinol Metab*. 2020;31(6):410-421.

Diferencias GIP y GLP-1

Efectos diferentes de GIP y GLP-1 sugeridos por datos preclínicos y clínicos

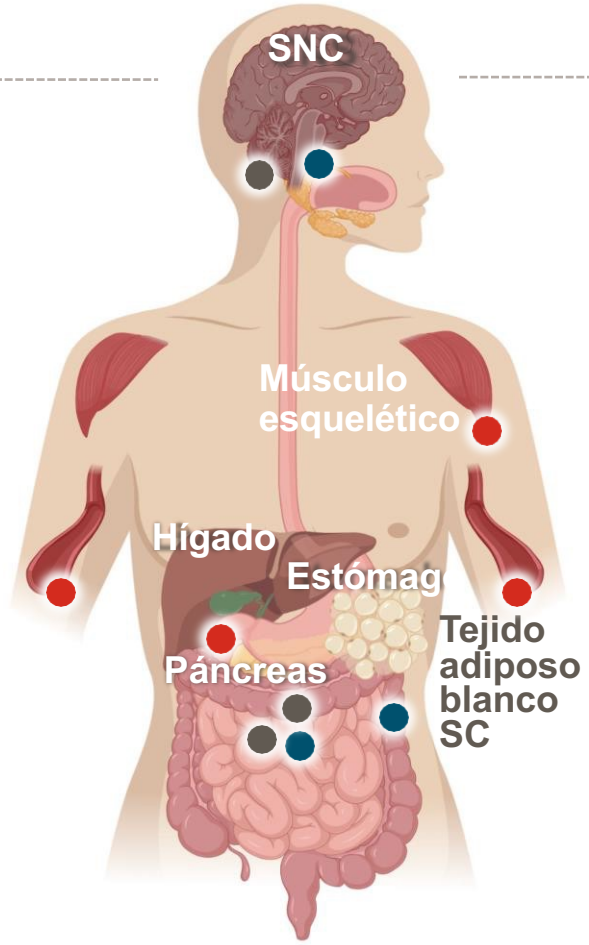
GLP-1

SNC
- ↑ Saciedad
- ↑ Náusea

Páncreas
- ↓ Glucagón

Estómago
- ↓ Vaciamiento gástrico

Hígado *
- ↓ Producción hepática de glucosa



GIP

SNC
- ↓ Nausea

Páncreas
- ↑ Glucagón

Tejido adiposo blanco SC
- ↑ Sensibilidad a la insulina
- ↑ Capacidad tampón lipídica
- ↑ Flujo sanguíneo
- ↑ Capacidad de almacenamiento
- ↓ Infiltración de células inmunitarias proinflamatorias

Sistémico *
- ↓ Triglicéridos dietéticos

Músculo esquelético *
- ↑ Flexibilidad metabólica

Los datos presentados en esta figura provienen de estudios en humanos y animales. SC = subcutáneo.
Adaptado de: Samms RJ, Coghlan MP, Sloop KW. Tendencias Endocrinol Metab. 2020; 31(6):410-421.

Programa de Ensayos Clínicos SURMOUNT

Resultados de Eficacia

Programa SURMOUNT

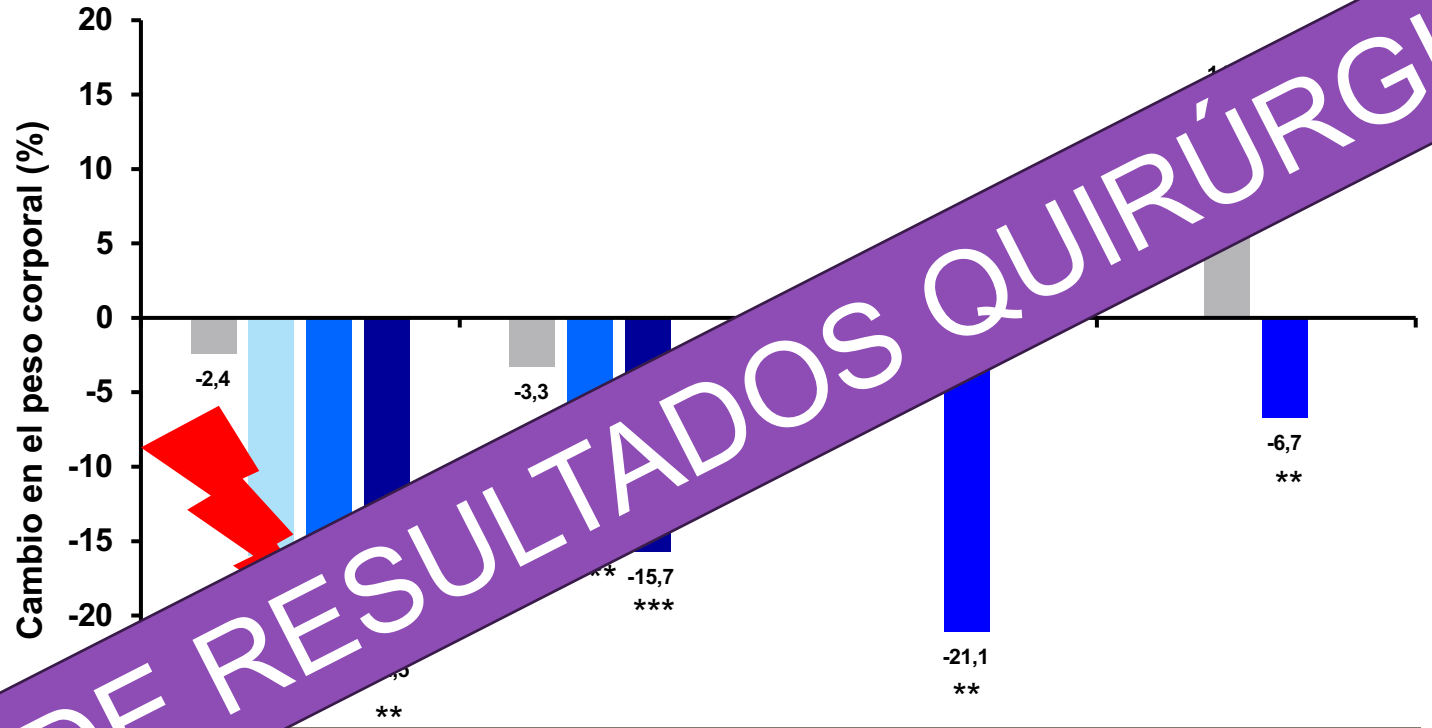
Desarrollo clínico Fase 3 en Obesidad

	SURMOUNT-1: Control de Peso[1]	SURMOUNT-2: Control de Peso en DM2[2]	SURMOUNT-3: Control de Peso Después de una Intervención Intensiva en el Estilo de Vida[3]	SURMOUNT-4: Mantenimiento de la Pérdida de Peso[4]	SURMOUNT-5: Control de Peso en Participantes con Comorbilidades Relacionadas con el Peso[5]
Fecha de finalización de la primaria:	April 2022	April 2023	May 2023	May 2023	November 2024
Número de Participantes del estudio:	2539	938	806	783	751
Duración del tratamiento:	72 sem ↓ Prediabetes Extension to 176 Weeks	72 sem	72 sem	88 sem (36 weeks open-label treatment followed by 52 weeks double-blind treatment)	72 sem
Intervención/tratamiento	TZP 5, 10, 15 mg QW PBO QW	TZP 10, 15 mg QW PBO QW	TZP MTD (10 or 15 mg) QW PBO QW	TZP MTD (10 or 15 mg) QW PBO QW	TZP QW SEMA QW

1) Jastreboff AM, Aronne LJ, Ahmad NN, Wharton S, Connery L, Alves B, Kiyosue A, Zhang S, Liu B, Bunck MC, Stefanski A; SURMOUNT-1 Investigators. Tirzepatide Once Weekly for the Treatment of Obesity. N Engl J Med. 2022 Jul 21;387(3):205-216. doi: 10.1056/NEJMoa2206038. Epub 2022 Jun 4. PMID: 35658024. 2)Garvey WT, Frias JP, Jastreboff AM, le Roux CW, Sattar N, Aizenberg D, Mao H, Zhang S, Ahmad NN, Bunck MC, Benabbad I, Zhang XM; SURMOUNT-2 investigators. Tirzepatide once weekly for the treatment of obesity in people with type 2 diabetes (SURMOUNT-2): a double-blind, randomised, multicentre, placebo-controlled, phase 3 trial. Lancet. 2023 Aug 19;402(10402):613-626. doi: 10.1016/S0140-6736(23)01200-X. Epub 2023 Jun 26. PMID: 37385275. 3)Wadden TA, Chao AM, Machineni S, Kushner R, Ard J, Srivastava G, Halpern B, Zhang S, Chen J, Bunck MC, Ahmad NN, Forrester T. Author Correction: Tirzepatide after intensive lifestyle intervention in adults with overweight or obesity: the SURMOUNT-3 phase 3 trial. Nat Med. 2024 Jun;30(6):1784. doi: 10.1038/s41591-024-02883-1. Erratum for: Nat Med. 2023 Nov;29(11):2909-2918. doi: 10.1038/s41591-023-02597-w. PMID: 38409593; PMCID: PMC11186756. 4) Aronne LJ, Sattar N, Horn DB, Bays HE, Wharton S, Lin WY, Ahmad NN, Zhang S, Liao R, Bunck MC, Jouravskaya I, Murphy MA; SURMOUNT-4 Investigators. Continued Treatment With Tirzepatide for Maintenance of Weight Reduction in Adults With Obesity: The SURMOUNT-4 Randomized Clinical Trial. JAMA. 2024 Jan 2;331(1):38-48. doi: 10.1001/jama.2023.24945. PMID: 38078870; PMCID: PMC10714284. 5)Aronne LJ, Horn DB, le Roux CW, Ho W, Falcon BL, Gomez Valderas E, Das S, Lee CJ, Glass LC, Senyucel C, Dunn JP; SURMOUNT-5 Trial Investigators. Tirzepatide as Compared with Semaglutide for the Treatment of Obesity. N Engl J Med. 2025 Jul 3;393(1):26-36. doi: 10.1056/NEJMoa2416394. Epub 2025 May 11. PMID: 40353578.

Cambio porcentual en el peso corporal

Programa de Ensayos Clínicos SURMOUNT



Estudio	SURMOUNT-1[1,a]	SURMOUNT-2[2,a]	SURMOUNT-3[3,a]	SURMOUNT-4[4,b]
Sup…	Placebo	Placebo	Placebo	Placebo
	72	72	72	88
…l medio(kg)	104.8 kg	100.8 kg	101.9 kg	85.2 kg

*/**P<.0001 vs. placebo. [a]Los datos provienen de la línea de base; [b]Los datos provienen de la aleatorización en la semana 36 después de un período abierto. Los valores son estimaciones de eficacia; Los datos son LSM (SE). LSM=Mínimos cuadrados de la m… Dosis Máxima Tolerada; SE=Error stándar; TZP=Tirzepatida. 1. Jastreboff AM, et al. *N Engl J Med*. 2022;387(3):205-216. 2. Garvey TM, et al. *Lancet*. 2023;402(10402):613-626. 3. Wadden TA, et al. *Nat Med*. 2023;29:2909-2918. 4. Aronne LJ, et al. *JAMA*. 2024;…(1)38-48.

Mantención de la pérdida de peso

CLINICAL PERSPECTIVE

Treatment of obesity: will incretin agonists make bariatric surgery a thing of the past?

Siehoon Lah [1] and Samantha L. Hocking [1,2,3]

[1]Metabolism and Obesity Service, Royal Prince Alfred Hospital, and [2]Central Clinical School, Faculty of Medicine and Health, and [3]Charles Perkins Centre, University of Sydney, Sydney, New South Wales, Australia

Key words
bariatric surgery, GLP-1 agonist, incretin agonist, semaglutide, tirzepatide, obesity.

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Abstract

The prevalence of obesity continues to increase worldwide. Obesity is associated with an increased risk of cardiometabolic and other diseases, reduced quality of life and shortened life expectancy. Highly effective therapies are required to achieve meaningful and sustained weight reduction to prevent, slow or reverse disease associated with obesity. Bariatric surgery is a highly effective intervention to induce weight loss, with observational data demonstrating durability of weight loss over 10 or more years. In addition, bariatric surgery improves cardiometabolic risk factors, including hyperglycaemia and type 2 diabetes, hypertension and dyslipidaemia. Observational data have shown a reduction in all-cause mortality, cardiovascular events and mortality and a reduction in cancer risk and mortality in patients who have undergone bariatric surgery compared to matched patients who did not have surgery. The emergence of newer incretin agonists, particularly semaglutide and tirzepatide, have demonstrated remarkable efficacy in inducing and maintaining weight loss with ongoing use. As for bariatric surgery, incretin agonist therapies also improve type 2 diabetes outcomes, cardiovascular mortality and other obesity-related complications, with new evidence emerging and long-term outcome data awaited. This perspective compares bariatric surgery and incretin agonist therapy, assessing their relative efficacies in weight reduction, impact on obesity-related complications, their respective risk profiles and considerations of cost-effectiveness and equity of access. These comparisons seek to evaluate whether these increasingly popular medications could make bariatric surgery a thing of the past.

Introduction

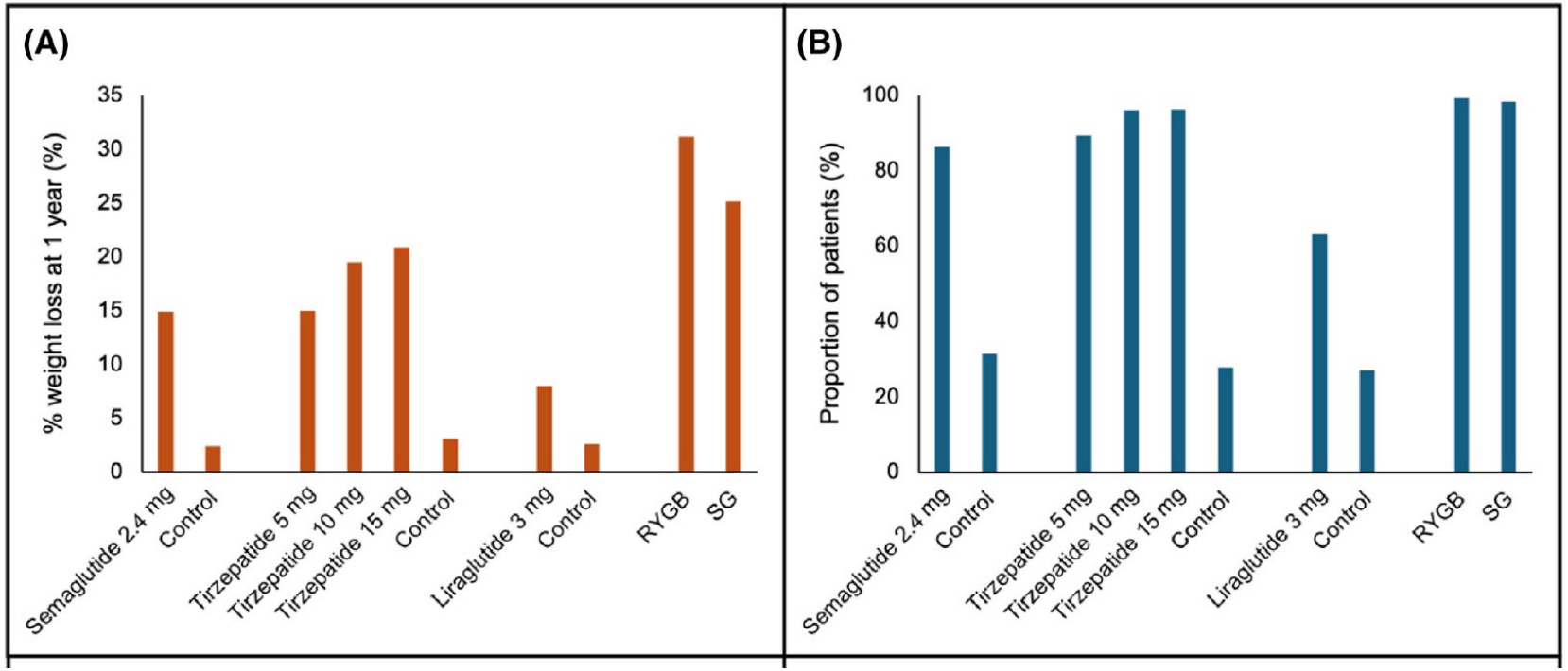
Obesity is a chronic complex disease which continues to increase in prevalence worldwide. Obesity is driven by changes in our environment, principally ubiquitous and continuous access to highly palatable energy-dense and affordable foods and is underpinned by genetic and epigenetic predisposition.[1,2] However, this may oversimplify the pathophysiological drivers of obesity, which disproportionately affect individuals from socially disadvantaged communities, highlighting the important contributions from food insecurity, obesogenic environments, economic disadvantage and poor access to healthcare, with the risk of obesity developing and worsening fuelled by the stigma and discrimination people with obesity face, creating a vicious cycle.[1] In addition to the diverse drivers of obesity, the phenotype, complications and, in particular, response to obesity treatment can differ widely among individuals.[3]

This perspective examines the current evidence regarding bariatric surgery and emerging incretin agonists to determine if the latter could render bariatric surgery obsolete. Specifically, it explores their respective impacts on weight loss, type 2 diabetes (T2D) outcomes, cardiovascular outcomes, cancer and all-cause mortality. The risks of each intervention, along with cost-effectiveness and equity of access, will also be discussed. Within the scope of bariatric surgery, the focus is primarily on the most common procedures: sleeve gastrectomy (SG) and gastric bypass, which includes Roux en Y gastric bypass (RYGB) and single or one anastomosis gastric bypass. For the

Funding: None.
Conflict of interest: None.

Porcentaje de pérdida de peso a 1 año de tratamiento.

Proporción de pacientes que mantienen ≥5% de pérdida de peso al año.



*RCT para datos de fármacos
*Estudio observacional para datos de Qx.
Data presented are not direct head-to-head comparisons between medications and surgery

Treatment of obesity: will incretin agonists make bariatric surgery a thing of the past? doi:10.1111/imj.16625

Mantención de la pérdida de peso

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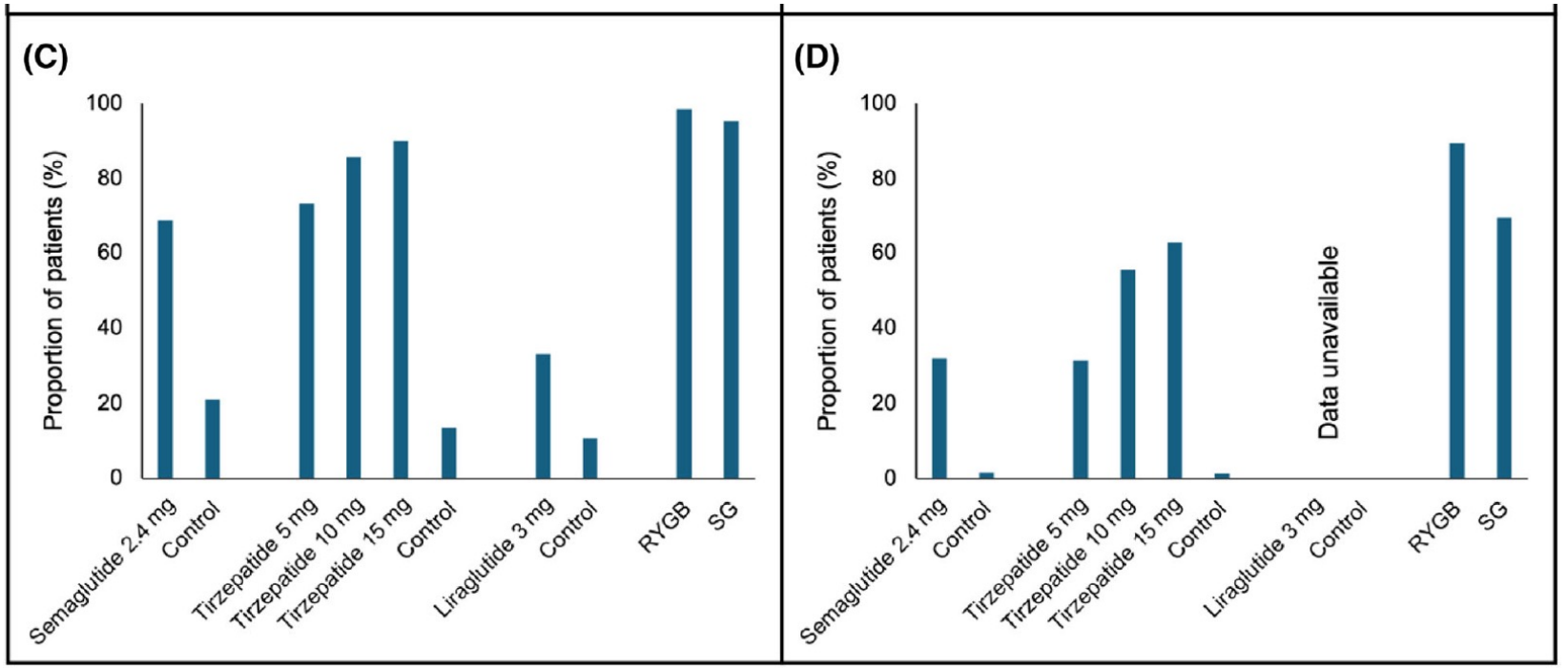
Funding: None.
Conflict of interest: None.

Proporción de pacientes que mantienen ≥10 de pérdida de peso al año

Proporción de pacientes que mantienen ≥20 de pérdida de peso al año



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Pero… no es sólo peso

DM2

Impacto CV

Ganancia de peso recurrente

Resultados más allá del peso

	Cirugía bariátrica y metabólica	Tratamiento farmacológico (incretinas)
DM2	**Stampede-trial** HbA1c ≤6% at 1 year: • 37% GV • 42% BPG • 12% tto médico	**Originalmente diseñados para la DM2.** Semaglutide: ~67% logra HbA1c ≤6.5% **Tirzepatide:** **~79–80% lograHbA1c ≤6.5**
Impacto CV	**Estudios observacionales** • Menor riesgo de IAM • Menor riesgo de ACV • Menor riesgo de ICC • Disminución mortalidad por todas las causas	Tratamientos basados en incretinas **han demostrado beneficios cardiovasculares** más allá de la baja de peso corporal y el control glicémico. Estudios aún on going para moléculas innovadoras

Tirzepatida Mounjaro, está aprobado en Chile por ISP en Adultos para manejo crónico del peso y Diabetes tipo 2.

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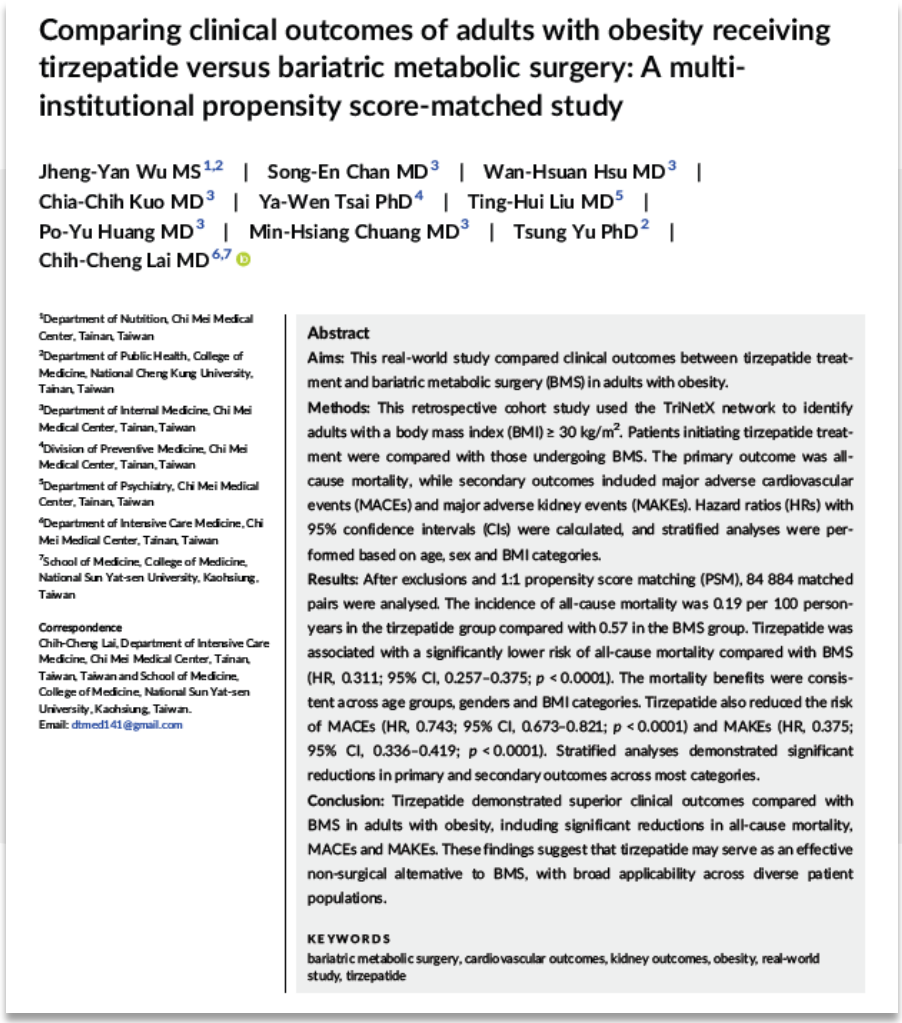
Resultados más allá del peso



Comparing clinical outcomes of adults with obesity receiving tirzepatide versus bariatric metabolic surgery: A multi-institutional propensity score-matched study

Jheng-Yan Wu MS[1,2] | Song-En Chan MD[3] | Wan-Hsuan Hsu MD[3] | Chia-Chih Kuo MD[3] | Ya-Wen Tsai PhD[4] | Ting-Hui Liu MD[5] | Po-Yu Huang MD[3] | Min-Hsiang Chuang MD[3] | Tsung Yu PhD[2] | Chih-Cheng Lai MD[6,7]

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[6]Department of Intensive Care Medicine, Chi Mei Medical Center, Tainan, Taiwan
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Email: dtmed141@gmail.com

Abstract

Aims: This real-world study compared clinical outcomes between tirzepatide treatment and bariatric metabolic surgery (BMS) in adults with obesity.

Methods: This retrospective cohort study used the TriNetX network to identify adults with a body mass index (BMI) ≥ 30 kg/m^2. Patients initiating tirzepatide treatment were compared with those undergoing BMS. The primary outcome was all-cause mortality, while secondary outcomes included major adverse cardiovascular events (MACEs) and major adverse kidney events (MAKEs). Hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated, and stratified analyses were performed based on age, sex and BMI categories.

Results: After exclusions and 1:1 propensity score matching (PSM), 84 884 matched pairs were analysed. The incidence of all-cause mortality was 0.19 per 100 person-years in the tirzepatide group compared with 0.57 in the BMS group. Tirzepatide was associated with a significantly lower risk of all-cause mortality compared with BMS (HR, 0.311; 95% CI, 0.257–0.375; $p < 0.0001$). The mortality benefits were consistent across age groups, genders and BMI categories. Tirzepatide also reduced the risk of MACEs (HR, 0.743; 95% CI, 0.673–0.821; $p < 0.0001$) and MAKEs (HR, 0.375; 95% CI, 0.336–0.419; $p < 0.0001$). Stratified analyses demonstrated significant reductions in primary and secondary outcomes across most categories.

Conclusion: Tirzepatide demonstrated superior clinical outcomes compared with BMS in adults with obesity, including significant reductions in all-cause mortality, MACEs and MAKEs. These findings suggest that tirzepatide may serve as an effective non-surgical alternative to BMS, with broad applicability across diverse patient populations.

KEYWORDS
bariatric metabolic surgery, cardiovascular outcomes, kidney outcomes, obesity, real-world study, tirzepatide

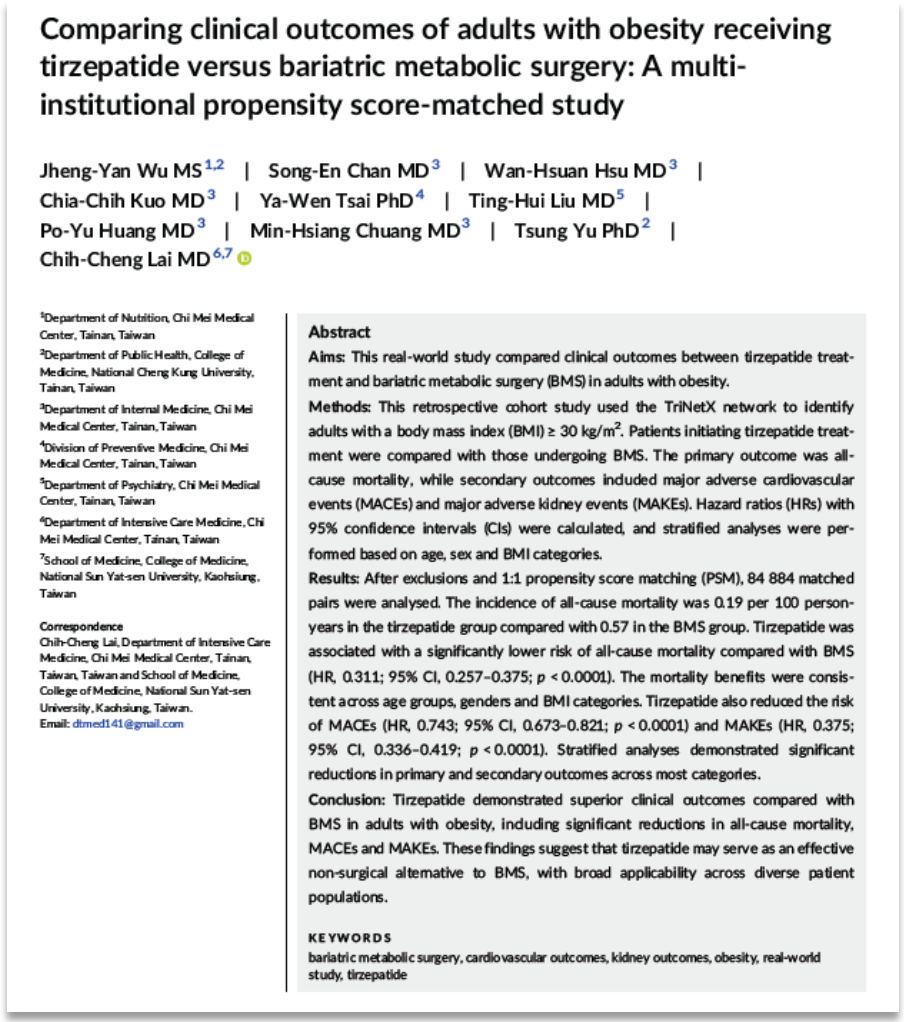
Diseño del estudio

- Estudio retrospectivo
- Adultos con IMC ≥ 30 kg/m²
- Se compararon:
  - Pacientes tratados con tirzepatida.
  - Pacientes sometidos a cirugía bariátrica (bypass gástrico o gastrectomía vertical).
- Seguimiento de hasta 2 años

Tirzepatida Mounjaro, está aprobado en Chile por ISP en Adultos para manejo crónico del peso y Diabetes tipo 2.

Wu JY, Chan SE, Hsu WH, et al. Comparing clinical outcomes of adults with obesity receiving tirzepatide versus bariatric metabolic surgery: A multi-institutional propensity score-matched study. Diabetes Obes Metab. 2025;27(6):3357-3366. doi:10.1111/dom.16353

Resultados más allá del peso



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Results: After exclusions and 1:1 propensity score matching (PSM), 84 884 matched pairs were analysed. The incidence of all-cause mortality was 0.19 per 100 person-years in the tirzepatide group compared with 0.57 in the BMS group. Tirzepatide was associated with a significantly lower risk of all-cause mortality compared with BMS (HR, 0.311; 95% CI, 0.257–0.375; $p < 0.0001$). The mortality benefits were consistent across age groups, genders and BMI categories. Tirzepatide also reduced the risk of MACEs (HR, 0.743; 95% CI, 0.673–0.821; $p < 0.0001$) and MAKEs (HR, 0.375; 95% CI, 0.336–0.419; $p < 0.0001$). Stratified analyses demonstrated significant reductions in primary and secondary outcomes across most categories.

Conclusion: Tirzepatide demonstrated superior clinical outcomes compared with BMS in adults with obesity, including significant reductions in all-cause mortality, MACEs and MAKEs. These findings suggest that tirzepatide may serve as an effective non-surgical alternative to BMS, with broad applicability across diverse patient populations.

KEYWORDS
bariatric metabolic surgery, cardiovascular outcomes, kidney outcomes, obesity, real-world study, tirzepatide

Mortalidad por cualquier causa (resultado primario)

- Tirzepatida **redujo el riesgo de muerte en 68%** comparado con cirugía.
- Resultado consistente en todas las edades, sexos y categorías de IMC

Eventos cardiovasculares mayores (MACE)

- **Reducción del riesgo en 25%** con tirzepatida.

Efectos adversos

- Tirzepatida presentó **menor riesgo de complicaciones gastrointestinales** comparado con la cirugía,

Tirzepatida Mounjaro, está aprobado en Chile por ISP en Adultos para manejo crónico del peso y Diabetes tipo 2.

Wu JY, Chan SE, Hsu WH, et al. Comparing clinical outcomes of adults with obesity receiving tirzepatide versus bariatric metabolic surgery: A multi-institutional propensity score-matched study. Diabetes Obes Metab. 2025;27(6):3357-3366. doi:10.1111/dom.16353

Resultados más allá del peso

Comparing clinical outcomes of adults with obesity receiving tirzepatide versus bariatric metabolic surgery: A multi-institutional propensity score-matched study

Jheng-Yan Wu MS[1,2] | Song-En Chan MD[3] | Wan-Hsuan Hsu MD[3] | Chia-Chih Kuo MD[3] | Ya-Wen Tsai PhD[4] | Ting-Hui Liu MD[5] | Po-Yu Huang MD[3] | Min-Hsiang Chuang MD[3] | Tsung Yu PhD[2] | Chih-Cheng Lai MD[6,7]

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Abstract

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Results: After exclusions and 1:1 propensity score matching (PSM), 84 884 matched pairs were analysed. The incidence of all-cause mortality was 0.19 per 100 person-years in the tirzepatide group compared with 0.57 in the BMS group. Tirzepatide was associated with a significantly lower risk of all-cause mortality compared with BMS (HR, 0.311; 95% CI, 0.257–0.375; $p < 0.0001$). The mortality benefits were consistent across age groups, genders and BMI categories. Tirzepatide also reduced the risk of MACEs (HR, 0.743; 95% CI, 0.673–0.821; $p < 0.0001$) and MAKEs (HR, 0.375; 95% CI, 0.336–0.419; $p < 0.0001$). Stratified analyses demonstrated significant reductions in primary and secondary outcomes across most categories.

Conclusion: Tirzepatide demonstrated superior clinical outcomes compared with BMS in adults with obesity, including significant reductions in all-cause mortality, MACEs and MAKEs. These findings suggest that tirzepatide may serve as an effective non-surgical alternative to BMS, with broad applicability across diverse patient populations.

KEYWORDS
bariatric metabolic surgery, cardiovascular outcomes, kidney outcomes, obesity, real-world study, tirzepatide

Limitaciones

- Estudio observacional (no ensayo clínico aleatorizado).
- Posible confusión residual.
- Seguimiento limitado a 2 años.
- No se evaluó costo-efectividad a largo plazo.
- No se analizó adherencia al tratamiento.

Conclusiones

- Aunque la cirugía bariátrica es un tratamiento muy eficaz para la obesidad, este estudio sugiere que **tirzepatida podría ser superior en términos de supervivencia y protección cardiovascular y renal**, además de ser una alternativa menos invasiva.

Tirzepatida Mounjaro, está aprobado en Chile por ISP en Adultos para manejo crónico del peso y Diabetes tipo 2.

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Reganancia de peso

	Cirugía bariátrica y metabólica	Tratamiento farmacológico (incretinas)
Respuesta clínica subóptima y/ó ganancia de peso recurrente	Def: Menos del 20% del TWL Def: Más del 30% de ganancia del peso inicial perdido*. Prev: 15-40% dependiendo de múltiples factores.	Precoz al suspender el tratamiento Muy frecuente

**IFSO Consensus on Definitions and Clinical Practice Guidelines for Obesity Management—an International Delphi Study. /doi.org/10.1007/s11695-023-06913-8*

Reganancia de peso

Review

Weight Regain After Liraglutide, Semaglutide or Tirzepatide Interruption: A Narrative Review of Randomized Studies

Massimo Quarenghi [1,2,*], Silvia Capelli [2], Giulia Galligani [2], Arianna Giana [1], Giorgia Preatoni [1,2] and Rosamaria Turri Quarenghi [3]

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Abstract: Objectives: The primary objective of this review is to analyze the effects on body weight of discontinuing therapy with glucagon-like peptide-1 receptor agonists (GLP-1 RAs) or tirzepatide in patients treated for obesity. In recent months, there has been a considerable increase in the utilization of GLP-1 RAs and GIP/GLP-1 RAs. However, the paucity of available data regarding their medium- to long-term safety remains a salient concern. Of particular significance is the observation of the weight curve following their suspension, a subject that has received scant attention to date. **Methods:** For this, a bibliographic search was carried out in three electronic databases: PubMed, Cochrane Library and Google Scholar. The following filters were applied: **in the last 10 years, Randomized Controlled Trial, Adult: 19+ years. The review was restricted to randomized controlled trials to reduce bias and ensure the high quality of the studies examined.** A total of 427 references were identified, 178 articles were read in full, and 13 articles were included in the analysis. **Results and Conclusions:** The analysis showed a rapid regain of weight after cessation of therapy, regardless of the duration of the treatment with GLP-1 RA or GIP/GLP-1 RA. This rebound is likely to substantially mitigate the metabolic benefits attained through weight loss. Given the efficacy of these drugs, it is essential for future research to focus on elucidating the optimal duration of these treatments or identifying techniques or schemes that involve a reduction in dosages to prevent weight regain.

Keywords: glucacon like peptide (GLP1 RA); GIP/GLP-1 RA; tirzepatide; liraglutide; semaglutide; weight regain; bariatric surgery

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1. Introduction

The prevalence of overweight and obesity has been increasing on a global scale, substantially influencing both the health status of the population and the financial costs associated with healthcare [1–3]. It is estimated that an individual with obesity has a life expectancy that is several years shorter than that of a person with a healthy weight [4]. The treatment of overweight and obese individuals not only exerts an economic impact but also enhances quality of life and reduces morbidity and mortality [5,6].

Although the modification of lifestyle, specifically the improvement in the diet and the introduction of physical activity, still constitutes the cornerstone of obesity management, its ineffectiveness when implemented in isolation has been well documented [7,8]. In contrast, the efficacy of bariatric surgical therapy over a period of up to two decades post-surgery

Diseño del estudio

- 13 RCT
- Liralgutida, semaglutida, tirzepatida

Resultados

- Liraglutida: **En las 12 semanas de seguimiento, post estudio**, quienes cambiaron a placebo, **GRP de 3%**
- Semaglutida: **GRP 11.6%** en el grupo que descontinuó el fármaco en la semana 68 a 120 (52 semanas). **Pérdida de peso neta 5.6% (120 semanas)**
- Tirzepatida: Grupo que cambió a placebo en la semana 36, presentaron **GRP de 14%** (52 semanas), vs quienes continuaron con el fármaco que siguieron perdiendo un 5.5% extra. **Pérdida de peso neta 9,9% (88 semanas)**

Quarenghi M, Capelli S, Galligani G, et al. Weight Regain After Liraglutide, Semaglutide or Tirzepatide Interruption: A Narrative Review of Randomized Studies. J Clin Med. 2025;14(11):3791. doi:10.3390/jcm14113791

Reganancia de peso

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[3] Private Medical Office, 6600 Locarno, Switzerland; rosyturri@hotmail.com
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Abstract: Objectives: The primary objective of this review is to analyze the effects on body weight of discontinuing therapy with glucagon-like peptide-1 receptor agonists (GLP-1 RAs) or tirzepatide in patients treated for obesity. In recent months, there has been a considerable increase in the utilization of GLP-1 RAs and GIP/GLP-1 RAs. However, the paucity of available data regarding their medium- to long-term safety remains a salient concern. Of particular significance is the observation of the weight curve following their suspension, a subject that has received scant attention to date. **Methods:** For this, a bibliographic search was carried out in three electronic databases: PubMed, Cochrane Library and Google Scholar. The following filters were applied: **in the last 10 years, Randomized Controlled Trial, Adult: 19+ years. The review was restricted to randomized controlled trials to reduce bias and ensure the high quality of the studies examined.** A total of 427 references were identified, 178 articles were read in full, and 13 articles were included in the analysis. **Results and Conclusions:** The analysis showed a rapid regain of weight after cessation of therapy, regardless of the duration of the treatment with GLP-1 RA or GIP/GLP-1 RA. This rebound is likely to substantially mitigate the metabolic benefits attained through weight loss. Given the efficacy of these drugs, it is essential for future research to focus on elucidating the optimal duration of these treatments or identifying techniques or schemes that involve a reduction in dosages to prevent weight regain.

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Conclusiones

- Esta revisión de estudios RCT muestra una GRP significativa luego de la descontinuación de tratamientos GIP-rA o GIP/GLP1 rA.
- Es probable que también disminuyan los efectos metabólicos inducidos por la pérdida de peso y el efecto del medicamento

Quarenghi M, Capelli S, Galligani G, et al. Weight Regain After Liraglutide, Semaglutide or Tirzepatide Interruption: A Narrative Review of Randomized Studies. J Clin Med. 2025;14(11):3791. doi:10.3390/jcm14113791

Reganancia de peso

Obesity Surgery (2025) 35:808–822
https://doi.org/10.1007/s11695-025-07733-8

IFSO

RESEARCH

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Glucagon-Like Peptide-1 Receptor Agonists for the Treatment of Suboptimal Initial Clinical Response and Weight Gain Recurrence After Bariatric Surgery: a Systematic Review and Meta-analysis

Yuntao Nie[1] · Yiran Zhang[2] · Baoyin Liu[1] · Hua Meng[1]

Received: 27 August 2024 / Revised: 28 January 2025 / Accepted: 4 February 2025 / Published online: 13 February 2025

Abstract

Background Suboptimal initial clinical response (SICR) and weight gain recurrence (WGR) are challenging issues following bariatric surgery. Recently, the promising weight loss effects of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have been applied to bariatric patients. We aimed to conduct a systematic review and meta-analysis to evaluate the efficacy and safety of GLP-1 RAs in the treatment of SICR and WGR after bariatric surgery.

Methods A literature search was performed across online databases. The primary outcomes were percentage of total weight loss (%TWL) and absolute weight loss. Secondary outcomes included changes in biochemical markers and adverse effects (AEs).

Results Nineteen studies including 1290 patients were included. After at least 3 months of treatment, the pooled %TWL was 9.24% for liraglutide, 11.38% for semaglutide, and 15.50% for tirzepatide, with corresponding weight reductions of 8.56 kg, 11.62 kg, and 12.60 kg, respectively. Additionally, %TWL and weight loss with liraglutide use were 7.65% and 7.47 kg for ≤ 6 months, 10.22% and 9.30 kg for 6–12 months, and 10.80% and 9.72 kg for ≥ 12 months. For semaglutide, the %TWL and weight reduction were 10.18% and 9.43 kg at 6 months, and 13.15% and 14.68 kg at 12 months. Biochemical markers including triglycerides, total cholesterol, low-density lipoprotein cholesterol, glycated hemoglobin, and alanine aminotransferase levels showed significant reductions after GLP-1 RA treatment. Common AEs were nausea (23%), vomiting

Key Points
- GLP-1 RAs are effective for SICR or WGR after bariatric surgery, while tirzepatide and semaglutide showed superior outcomes.
- Lipid profiles, glycemic profiles, and liver function all improved following GLP-1 RA treatment.
- AEs were mainly gastrointestinal, with incidence remaining within an acceptable range.

Metodología

- 19 estudios - 1290 pacientes
- Se evaluaron:
  - Porcentaje de pérdida total de peso (%TWL)
  - Pérdida de peso en kg
  - Cambios metabólicos
  - Efectos adversos

Fármaco	% pérdida total de peso	Pérdida promedio	Resultados según duración
Liraglutide	9.24%	8.56 kg	≤6 meses: ~7.65% pérdida 6–12 meses: ~10.22% ≥12 meses: ~10.80%
Semaglutide	11.38%	11.62 kg	6 meses: ~10.18% 12 meses: ~13.15%
Tirzepatide	15.50%	12.60 kg	*6 meses: 15.5% estudios corto plazo en contexto post quirúrgico

Nie Y, Zhang Y, Liu B, Meng H. Glucagon-like peptide-1 receptor agonists for the treatment of suboptimal initial clinical response and weight gain recurrence after bariatric surgery: a systematic review and meta-analysis. Obes Surg. 2025;35(3):808-822. doi:10.1007/s11695-025-07733-8

Reganancia de peso

Obesity Surgery (2025) 35:808–822
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RESEARCH

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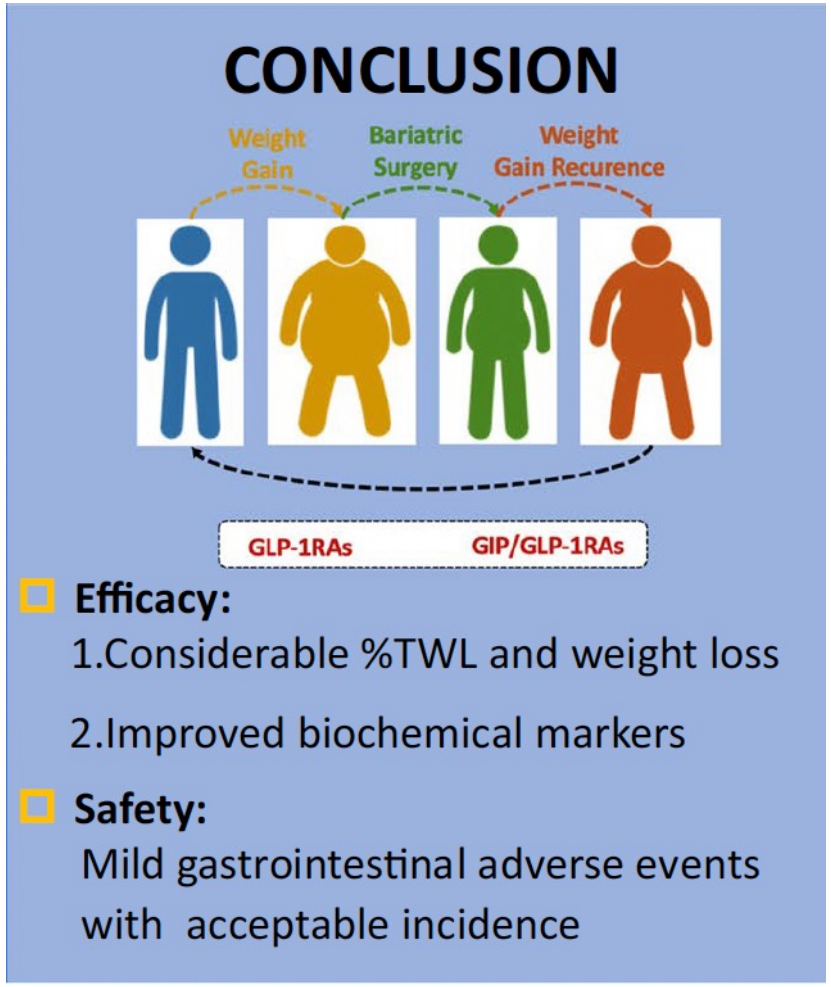

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Reganancia de peso

Obesity Surgery (2025) 35:5596–5605
https://doi.org/10.1007/s11695-025-08414-2

IFSO

REVIEW

Effects of Semaglutide and Tirzepatide on Recurrent Weight Gain After Bariatric Surgery: A Systematic Review and Meta-analysis

Angel Alois Osorio Manyari[1] · Azucena Lirio Armas Alvarez[2] · Joel Davis Osorio Manyari[3] · Francisco Onieva Gonzalez[1] · Sjaak Pouwels[4,5]

Received: 1 September 2025 / Revised: 24 October 2025 / Accepted: 24 November 2025 / Published online: 28 November 2025

Abstract
Fifteen to forty% of patients experience recurrent weight gain (RWG) after metabolic bariatric surgery (MBS). Glucagon-like peptide receptor agonists (GLP-1 RAs) are effective treatments for obesity in nonsurgical patients. To assess the effects of semaglutide and tirzepatide after MBS, we conducted a meta-analysis of data from inception to August 2025. Eight retrospective studies and 964 patients were included. The percentage total weight loss (%TWL) was −10.97% [95% CI, −13.41 to −8.53; $p<0.05$] for semaglutide and −13.63% [95% CI, −22.59 to −4.67; $p<0.05$] for tirzepatide. The evidence suggests that semaglutide and tirzepatide result in weight reduction in patients with RWG after MBS.

Key Points
Newer GLP-1 RAs can be effective in patients with RWG after MBS.
Tirzepatide could be more effective than semaglutide against RWG after MBS.

Introduction

Overweight and obesity pose major global health challenges. In 2021, they were responsible for 3.71 million deaths and 129 million disability-adjusted life-years worldwide [1].

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Metabolic bariatric surgery (MBS) is the most effective treatment for patients with obesity, obesity-related comorbidities, and all-cause mortality [2, 3]. Roux-en-Y gastric bypass (RYGBP) and sleeve gastrectomy (SG) are the most common types of MBS and are associated with approximately 28.4% and 23% total weight loss (%TWL) [4]. After achieving an adequate postoperative nadir weight, some patients experience a suboptimal initial clinical response (SICR) or, more commonly, recurrent weight gain (RWG), previously known as weight regain (WR). The prevalence of RWG can vary because of its multiple definitions [5, 6]. One study of 300 patients who underwent RYGBP revealed that 37% of them had RWG at 7 years [7]. A systematic review revealed that the prevalence of RWG ranged from 5.7% at 2 years to 75.6% at 6 years post-SG [8]. RWG results in the recurrence of associated medical problems, and because its causes are multifactorial, its management requires an individualized, tailored approach. In cases of anatomical causes, revisional surgery has been used to manage RWG, with a %TWL of 17.1–26.1% but a higher risk of complications than primary surgery [9, 10]. More recently, endoscopic procedures have emerged as alternatives to revisional surgery for RWG; however, these procedures are not free of potential complications [11]. Glucagon-like peptide receptor agonists (GLP-1 RAs) have been demonstrated to be effective

Diseño del estudio

- Revisión sistemática y metaanálisis.
- Se incluyeron **8 estudios retrospectivos**.
- Variable principal: porcentaje de pérdida total de peso (%TWL).
- Total de 964 pacientes con RWG

Resultados

Semaglutida:

- %TWL: −10.97%
- IC 95%: −13.41 a −8.53
- P<0.05

Tirzepatida:

- %TWL: −13.63%
- IC 95%: −22.59 a −4.67
- P<0.05

Osorio Manyari AA, Armas Alvarez AL, Osorio Manyari JD, et al. Effects of Semaglutide and Tirzepatide on Recurrent Weight Gain After Bariatric Surgery: A Systematic Review and Meta-analysis. Obes Surg. 2025;35:5596–5605. doi:10.1007/s11695-025-08414-2.

Reganancia de peso

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IFSO

REVIEW

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Introduction

Overweight and obesity pose major global health challenges. In 2021, they were responsible for 3.71 million deaths and 129 million disability-adjusted life-years worldwide [1].

Metabolic bariatric surgery (MBS) is the most effective treatment for patients with obesity, obesity-related comorbidities, and all-cause mortality [2, 3]. Roux-en-Y gastric bypass (RYGBP) and sleeve gastrectomy (SG) are the most common types of MBS and are associated with approximately 28.4% and 23% total weight loss (%TWL) [4]. After achieving an adequate postoperative nadir weight, some patients experience a suboptimal initial clinical response (SICR) or, more commonly, recurrent weight gain (RWG), previously known as weight regain (WR). The prevalence of RWG can vary because of its multiple definitions [5, 6]. One study of 300 patients who underwent RYGBP revealed that 37% of them had RWG at 7 years [7]. A systematic review revealed that the prevalence of RWG ranged from 5.7% at 2 years to 75.6% at 6 years post-SG [8]. RWG results in the recurrence of associated medical problems, and because its causes are multifactorial, its management requires an individualized, tailored approach. In cases of anatomical causes, revisional surgery has been used to manage RWG, with a %TWL of 17.1–26.1% but a higher risk of complications than primary surgery [9, 10]. More recently, endoscopic procedures have emerged as alternatives to revisional surgery for RWG; however, these procedures are not free of potential complications [11]. Glucagon-like peptide receptor agonists (GLP-1 RAs) have been demonstrated to be effective

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Limitaciones

- Exclusivamente estudios retrospectivos.
- Heterogeneidad en definiciones de RWG.
- Tamaño muestral relativamente limitado.
- Ausencia de ensayos clínicos aleatorizados.
- No se reportan resultados metabólicos detallados ni de seguridad a largo plazo.

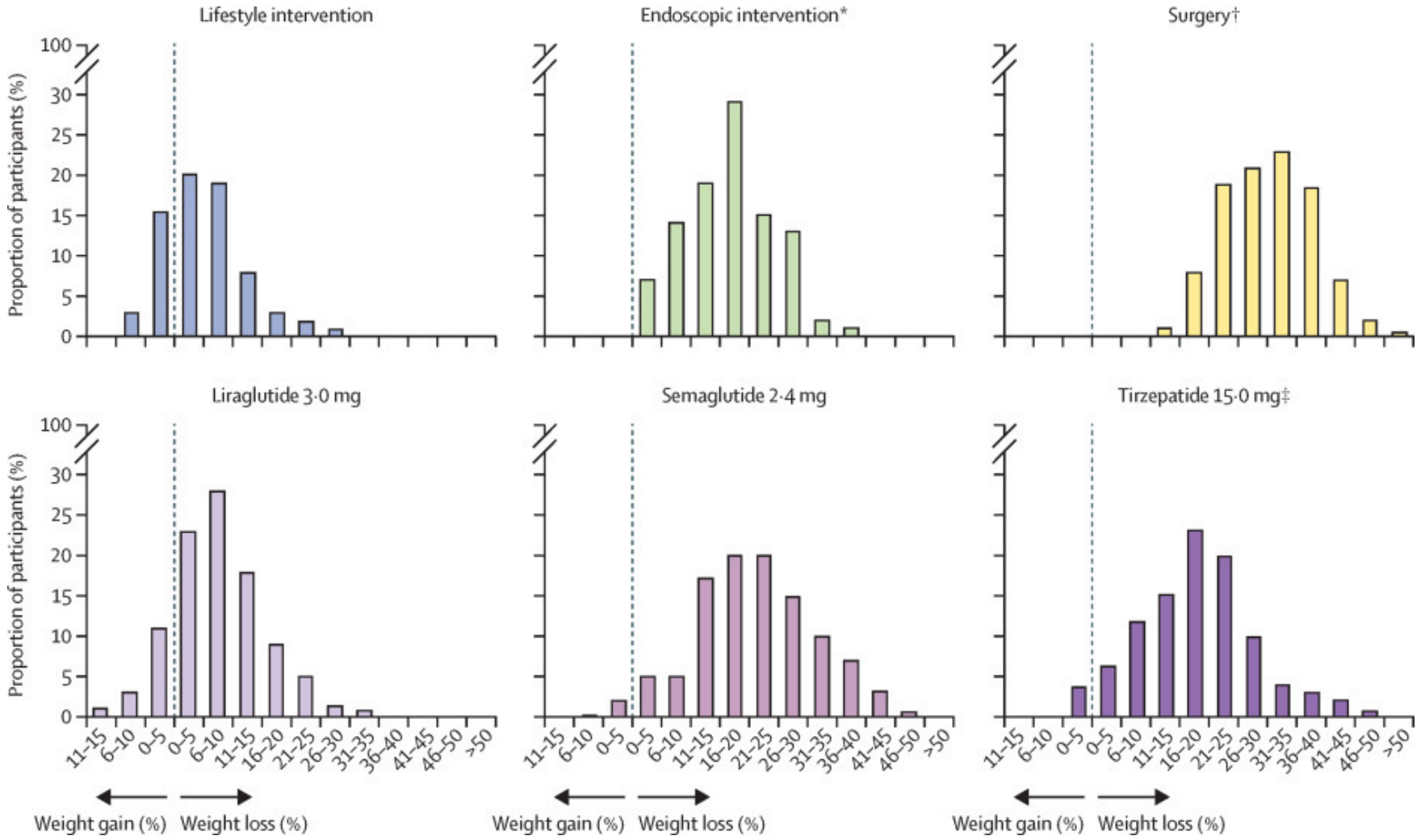
Conclusión

- La evidencia disponible sugiere que semaglutida y tirzepatida son **opciones terapéuticas efectivas para la recuperación de peso tras cirugía bariátrica, con posible superioridad de tirzepatida.**
- Se requieren estudios prospectivos y ensayos controlados aleatorizados para confirmar estos hallazgos y definir su papel en algoritmos terapéuticos post-bariátricos.

Osorio Manyari AA, Armas Alvarez AL, Osorio Manyari JD, et al. Effects of Semaglutide and Tirzepatide on Recurrent Weight Gain After Bariatric Surgery: A Systematic Review and Meta-analysis. Obes Surg. 2025;35:5596–5605. doi:10.1007/s11695-025-08414-2.

Opciones de tratamientos

La pérdida de peso media varía según el tipo de tratamiento para la obesidad



Tratamiento personalizado, incluído uso de combinaciones

Perdoma, Cohen R et al et al. Lancet 2023; 401:1116-1130.

Comparación terapéutica: Cirugía Bariátrica vs Agonistas GLP-1r / twincretinas

Parámetro	Cirugía Bariátrica	GLP-1 / Tirzepatida
Pérdida de peso promedio	25–40% TWL (según procedimiento)	15–28% en ensayos clínicos
Durabilidad del efecto	Alta (evidencia >10–20 años)	Dependiente de uso continuo
Impacto metabólico	Alta remisión de DM2 y comorbilidades	Mejoría metabólica significativa
Invasividad	Procedimiento quirúrgico	Tratamiento farmacológico
Costo a largo plazo	Costo único alto inicial. Considerar costos de suplementación.	Coste acumulativo crónico
Perfil de pacientes	Obesidad severa (BMI ≥40 o ≥35 + comorbilidades…(?))	BMI 25–40 o pacientes con exceso de adiposidad que genere enfermedad.

Perdoma, Cohen R et al et al. Lancet 2023; 401:1116-1130.

¿Competencia o integración?

No es cirugía vs fármacos

Es cirugía + farmacoterapia

Modelo futuro:

- Enfoque escalonado
- Terapia combinada
- Tratamiento crónico

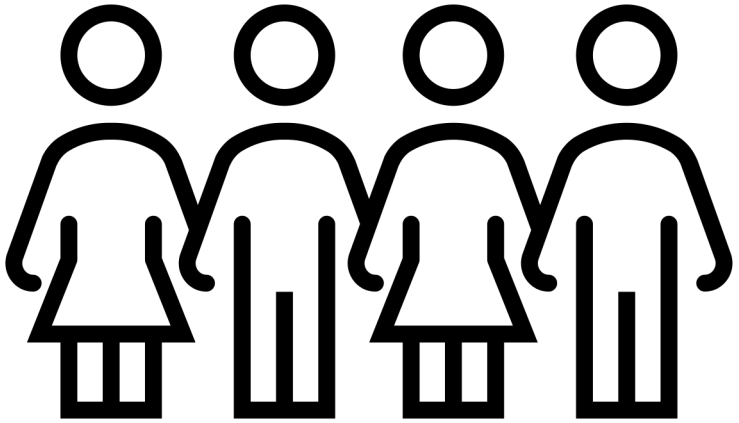
Conclusiones

- Tirzepatida alcanza ~20–22% TWL
- Reduce la brecha con cirugía
- Cambia la selección y el algoritmo terapéutico
- La cirugía metabólica sigue siendo el tratamiento más potente y definitivo
- El futuro es terapia combinada

- *Es esencial que la investigación se centre en dilucidad la duración óptima de estos medicamentos, identificar esquemas de retiro programado o disminución de dosis, o dosis de mantención para evitar GRP.*
- *Faltan de datos a 10–15 años*

Escenarios clínicos prácticos

- Mujer 38 años IMC 38 DM2 → ¿fármaco o cirugía?
- Hombre 45 años post-sleeve con RWG → Tirzepatida vs revisión
- Paciente IMC 55 → ¿combinación?



¿Estamos ante un nuevo estándar?

Tirzepatida redefine el estándar farmacológico,
pero no reemplaza el estándar quirúrgico.