GLP-1 Receptor Agonists: Efficacy, and Cost-effectiveness in Obesity Management – A Systematic Review

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Introduction

- Glucagon-like peptide-1 (GLP-1) receptor agonist are effective for weight loss and prevention/delay of type 2 diabetes in adult patients with obesity.
- Obesity is a major global health problem that is associated with multiple comorbidities such as type 2 diabetes, heart disease, stroke, etc.
- According to CDC, in 2021, 41.9% of U.S. adults had obesity, and 7.7% had severe obesity. GLP-1 agonists are a class of incretin-based pharmaceutical agents that reported efficacy in the management of obesity.
- GLP 1 agonist has also been shown to be effective for prevention/delay of type 2 diabetes in multiple clinical trials.

Objectives

- The aim of this systematic review is to determine the long-term efficacy, safety, and cost-effectiveness of GLP-1 for weight loss and prevention/delay of type 2 diabetes.

Methods

- Searches using specific search terms were conducted using OVID SP platform for Medline, Embase, Cochrane DSR, DARE, CCA, CCTR, CMR, HTA, NHSEED and Econlit.
- All abstracts and full papers were reviewed according to the eligibility criteria by two reviewers.
- Data were extracted independently into a customized extraction sheet in Microsoft Excel.
- A risk-of-bias assessment was conducted using Cochrane Guide for Systematic Reviews and revised Cochrane risk-of-bias tool for randomized trials.

Table 1: Study eligibility criteria

PICOS	Inclusion criteria
Populations	Overweight (BMI 25-29.9) and obese (BMI ≥ 30)
Interventions/ Comparators	**Parenteral GLP 1 agonists** • Dulaglutide • Exenatide extended release • Exenatide • Semaglutide (Injectable and Oral) • Liraglutide • Lixisenatide • Efpeglenatide **Dual GLP-1/GIP receptor agonists** • Tirzepatide
Study designs	Randomized controlled trials, Cost effective analysis studies
Outcomes	• The long-term efficacy of GLP-1 agonist in weight loss and prevention/delay of type 2 diabetes. • Cost-effectiveness of GLP-1 treatment.
Other Limits	2013 to 2023 Nov, articles published in English.

Results

- The search identified 1940 abstracts, of which 1550 were included after deduplication. Following screening, 94 full texts were selected, and from those, 25 studies were included.
- Additional hand searching revealed 13 more relevant articles, bringing the total count to 38 articles, consisting of six cost-effectiveness analyses (CEAs) and 32 randomized controlled trials (RCTs).
- The drugs studied were semaglutide (8 studies), liraglutide (18 studies), semaglutide & liraglutide (1 study), efpeglenatide (1 study), tirzepatide (1 study), and exenatide (3 studies).
- Most studies reported that GLP-1 receptor agonists led to weight reduction.
- For liraglutide, weight reduction ranged from 0.7 kg in 52 weeks to 8.4 kg in 68 weeks.
- For semaglutide, weight reduction ranged from 3.5 kg to 15.3 kg in 68 weeks.
- Additionally, for liraglutide, the reduction in BMI ranged from 1.0 to 4.2 kg/m^2 in 52 weeks, and for semaglutide, the reduction in BMI ranged from 2.9 to 6.6 kg/m^2 in 68 weeks.
- Other GLP-1 agonists (efpeglenatide, tirzepatide, and exenatide) also reported consistent weight reductions ranging from 1.7 to 7.3 kg and a reduction in BMI ranging from 2.3 to 2.6 kg/m^2.
- Overall analysis results demonstrated that GLP-1 receptor agonists improved control of blood glucose, blood pressure, and plasma levels of LDL, HDL, and triglycerides.
- GLP-1 receptor agonists are safe to use in comorbid conditions such as congestive heart failure and kidney disease.
- However, GLP-1 receptor agonists were reported to be less cost-effective in treating obesity compared to other anti-obesity medications (phentermine and topiramate) due to the high pricing of these drugs.

Figure 1: Prisma Flow Chart

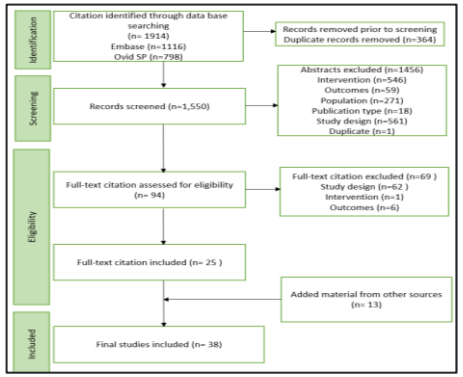


Table 2: Overview of results from all included clinical studies

Drug name	Dosage	Primary author	Year	Country	Time point	Reduction in weight (kg)	Reduction in BMI (kg/m²)	Reduction in weight (%)	% Reporting weight loss
Efpeglenatide	4-8 mg	Pratley	2019	Multiple countries	20 w	-6.6 to -7.1	-2.4 to -2.6	-6.7% to -7.4	71.06
Exenatide	10 µg	Basolo	2018	USA	24 w	-1.72	NR	NR	NR
	2 mg	Lundkvist	2017	Sweden	52 w	-5.7	NR	NR	NR
	NA	Rodgers	2021	USA	12 w	-1.9 to -6.2	-0.7 to -2.3	NR	100
Liraglutide	3 mg	Chao	2019	USA	24-52 w	NR	NR	-5.4% to -12.2	NR
	3 mg	Wadden	2020	USA	56 w	NR	NR	-7.50	NR
	3 mg	Kolotkin	2018	Multiple countries	160 w	NR	NR	NR	82.90
	3 mg	Lundgren	2021	Denmark	52 w	-0.7	NR	NR	83.67
	3 mg	Farr	2019	Israel	5 w	-2.5	-1.72	-4.84	100
	3 mg	Blackman	2016	USA & Canada	32 w	NR	NR	-5.70	NR
	3 mg	Chao	2019	USA	1 y	NR	NR	-11.50	NR
	3 mg	Lean	2014	Multiple countries	20 w	-7.8	NR	NR	NR
	3 mg	Wadden	2013	USA & Canada	56 w	-6	-2.1	-6.20	50.50
	3 mg	Utzschneider	2022	USA	12 m	NR	-2.6	NR	NR
	3 mg	Wadden	2019	USA	52 w	-12.2	-4.3	-11.50	100
	1.8-3 mg	Davies	2015	Multiple countries	56 w	-5.0 to 6.4	-1.7 to -2.2	-4.7 to -6.0	100
	3 mg	Garvey	2020	Multiple countries	56 w	NR	NR	-5.8	96.46
	3 mg	Gudbergsen	2021	Denmark	52 w	-2.8	-1	NR	100
	1.8 mg	Kim	2013	USA	14 w	-6.8	NR	NR	68.57
	3 mg	le Roux	2017	Multiple countries	160 w	-6.5	-2.4	-6.10	52.56
	1.78 mg	Marso	2017	Multiple countries	48 m	-2.89	NR	NR	NR
	3 mg	Pi-Sunyer	2015	Multiple countries	56 w	-8.4	-3	-8.00	100
	3 mg	Rubino	2022	USA	68 w	-15.3	NR	-15.80	92.13
Semaglutide	2.4 mg	Wilding	2021	Multiple countries	68 w	-15.3	-5.54	-14.90	100
	2.4 mg	Wadden	2021	USA	68 w	NR	-6.6	-0.16	0.86
	2.4 mg	Borlaug	2023	Multiple countries	52 w	NR	-15.10	-13.30	NR
	1.0-2.4 mg	Davies	2021	Multiple countries	68 w	-6.9 to -9.7	-2.5 to -3.5	6.99 to -9.64	NR
	1.7-2.4 mg	Kadowaki	2022	Japan and South Korea	68 w	NR	NR	-9.6 to -13.2	97
	2.4 mg	Lincoff	2023	Multiple countries	104 w	NR	NR	-9.39	100
	2.4 mg	Weghuber	2022	Multiple countries	68 w	-15.3	NR	-14.70	73
	2.4 mg	Rubino	2023	Multiple countries	68 w	-8	-2.9	-8.8	100
	2.4 mg	Rubino	2022	USA	68 w	-6.8	NR	-6.40	92.86
Tirzepatide	5-15 mg	Jastreboff	2022	Multiple countries	72 w	NR	NR	-15.0 to -20.9	100

Abbreviations: BMI: Body Mass Index; NR: Not Reported; m: months; w: weeks; y:years; time point means time at which outcomes were measured

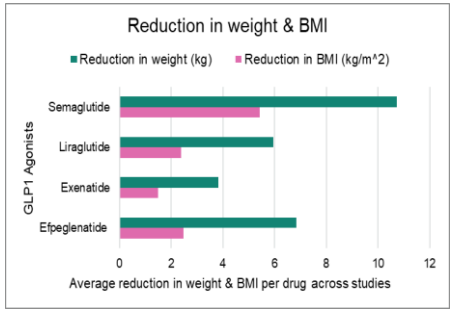
Table 3: Overview of results from all included cost effectiveness analysis studies

Drug name	Primary author	Year	Country	Time horizon	Currency, Year	Cost of medication	Incremental QALYs	Incremental costs	ICER (Cost/QALY)
Liraglutide	Lumbreras	2023	USA	40 years	USD, 2021	$236	0.003	$133,246	$39,665,285
	Lee	2020	USA	5 years	USD, 2019	$17,090	NA	NA	Dominated
	Nuijten	2021	Switzerland	Lifetime	CHF, 2021	CHF 548,881	0.734	-$15,382	Dominated
	Nuijten	2018	USA	3 years	USD, 2016	$11,695	NR	$9,285	Dominated
	Lim	2023	USA	5 years	USD, 2022	$1,294	0.032	$53,089	Dominated
Semaglutide	Lumbreras	2023	USA	40 years	USD, 2021	$236	0.008	$189,867	$24,274,467
	Lee	2020	USA	5 years	USD, 2019	$8,273	NA	NA	$17,880.00
	Lim	2023	USA	5 years	USD, 2022	$1,295	0.113	$62,350	$1,094,349
	Saumoy	2023	USA	30 years	USD, 2021	$1,826	-0.795	$2,20,727	Dominated
Tirzepatide	Lumbreras	2023	USA	40 years	USD, 2021	$171	0.324	$115,184	$355,616.00

Abbreviations: CHF: Swiss Franc; NA: Not available; QALY: Quality adjusted life year USD: United States Dollar

Results

Figure 2: Overview of results from all included clinical studies



Conclusions

- GLP-1 receptor agonists, particularly liraglutide and semaglutide, demonstrated significant efficacy in causing reduction in weight and BMI.
- GLP-1 receptor agonists also helped improve metabolic parameters in Type 2 diabetes mellitus, hypertension and hyperlipidemia.
- The overall analysis supported their safety in comorbid conditions, but their cost-effectiveness in treating obesity was reported to be lower compared to alternative medications.
- Despite the economic considerations, the findings emphasize the potential clinical benefits of GLP-1 receptor agonists in managing obesity and associated metabolic conditions

References

https://ispor.confex.com/data/extendedabstract/ispor/intl2024/Paper_137181_extendedabstract_668_0.pdf

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