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C04

Overview of Recent Systematic Literature Reviews on Glucagon-Like Peptide-1 Receptor Agonists for Weight Loss in Adults With Obesity

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Background

- The global prevalence of obesity has drastically increased over the past three decades, increasing the risk of obesity-related morbidity and premature mortality[1]
- Lifestyle and behavioural interventions for weight loss have had limited success
- Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are emerging as highly effective anti-obesity medications (AOMs)

Objective

- To identify key trends in systematic literature reviews (SLRs) on GLP-1 RAs in adults with obesity

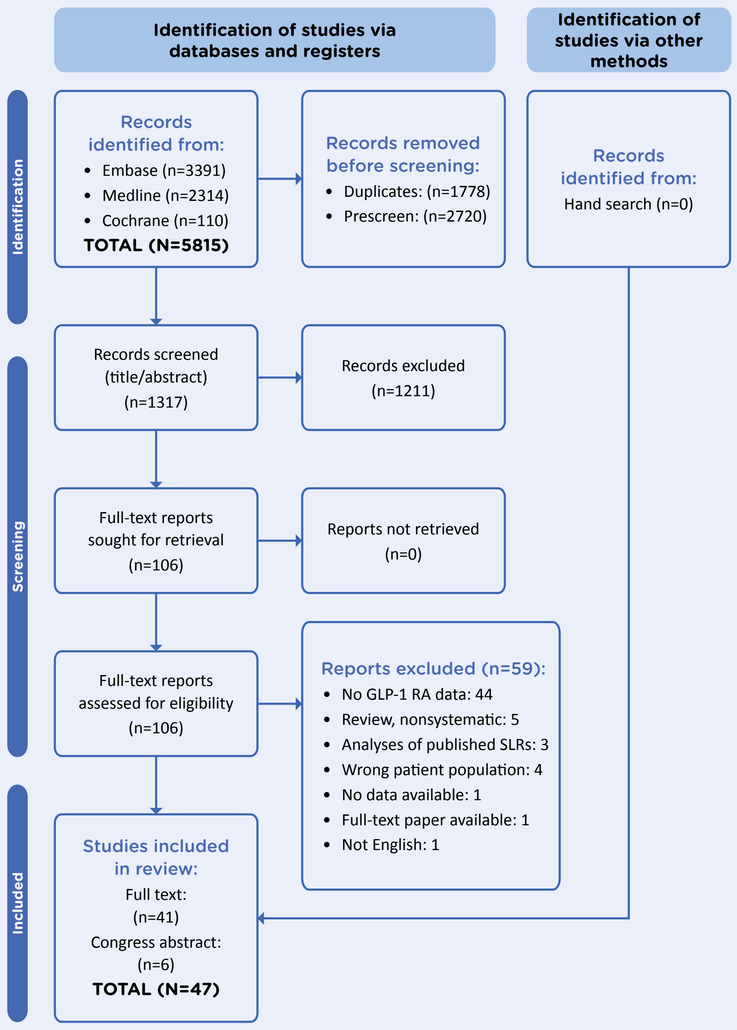
Methods

- Literature searches in Embase, Medline, and Cochrane databases were conducted using a National Institute for Health and Care Excellence (NICE)–published search strategy for obesity,[2] along with intervention and SLR terms to identify English-language SLRs published between 01 January 2018 and 16 May 2023
- SLRs of adults with obesity treated with GLP-1 RAs were included; SLRs focusing exclusively on other AOMs, herbal treatments, or nonpharmacological interventions were excluded
- A single reviewer screened titles and abstracts then screened full text of SLRs against prespecified inclusion/exclusion criteria, with a 10% check by a second reviewer

Results

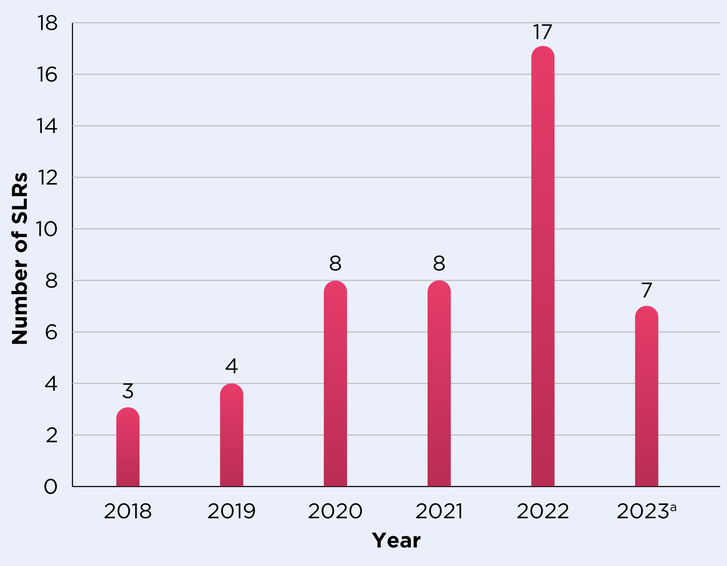
- After the removal of duplicates and obvious irrelevant publications, 1317 publications were identified and screened, with 106 retained for assessment of full text
- Of 106 publications, 47 SLRs (41 full texts; 6 congress abstracts) met the eligibility criteria for inclusion (**Figure 1**, **Box**)

Figure 1. PRISMA diagram



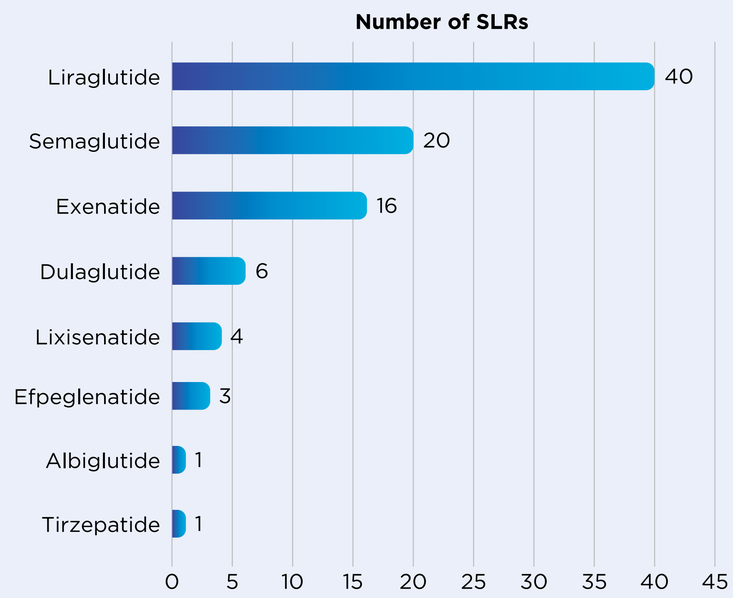
GLP-1 RA, glucagon-like peptide-1 receptor agonist; SLRs, systematic literature reviews

Figure 2. Number of SLRs published between 1 January 2018 and 16 May 2023



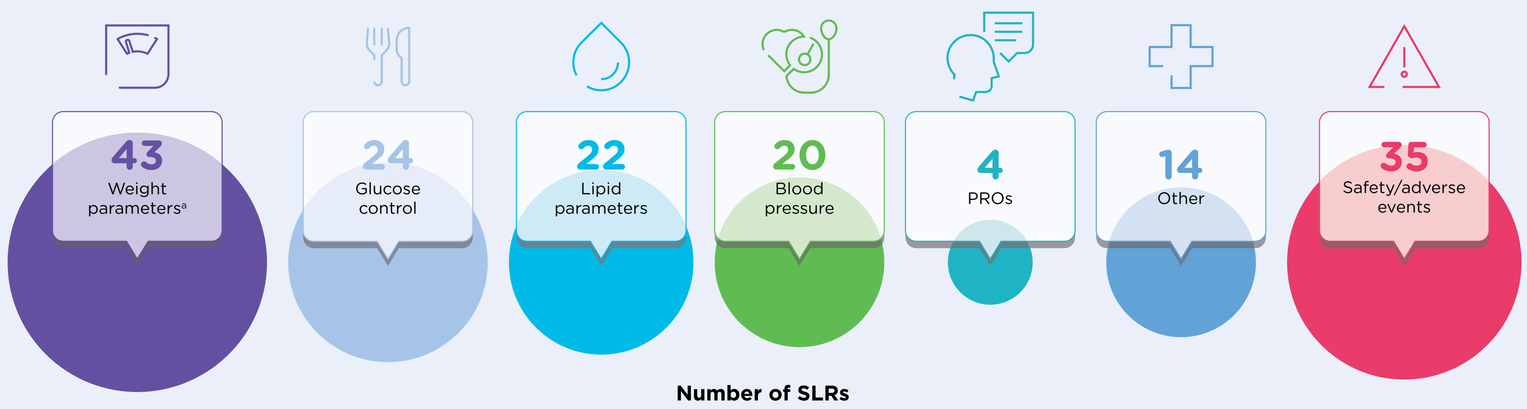
[a]Published as of 16 May 2023
SLRs, systematic literature reviews

Figure 3. GLP-1 RAs assessed in included SLRs (n=47)



GLP-1 RAs, glucagon-like peptide-1 receptor agonists; SLRs, systematic literature reviews

Figure 4. Outcomes reported in included SLRs (n=47)



[a]Four SLRs did not report weight parameters. The focus of these SLRs were other outcomes (blood pressure [n=2], arrhythmias [n=1], and appetite regulation [n=1])
PROs, patient-reported outcomes; SLRs, systematic literature reviews

Publication details

- The SLRs were published in a range of journals, of which 7 (14.9%) were obesity specific, and 15 (31.9%) were endocrinology/metabolic journals
- Obesity-specific journals included *Obesity*, *Obesity Reviews*, and *Obesity Medicine*
- One SLR was published in *JAMA* (LeBlanc et al, 2018) and 1 SLR was published in *The Lancet* (Shi et al, 2022)

SLR characteristics

- The number of SLRs more than quadrupled from 2018 to 2022, and as of 16 May 2023, 7 additional SLRs had been published (**Figure 2**)
- The majority included meta-analysis (n=38, 80.9%)
- The number of GLP-1 RA studies included in the SLRs ranged from 1 (Haywood et al, 2019) to 64 (Vosoughi et al, 2021)
- Eight SLRs did not report the number of studies assessing GLP-1 RAs
- For the majority of the SLRs, literature databases were searched from inception; the date the search was conducted ranged from February 2017 (Khera et al, 2018) to January 2023 (Long et al, 2023)

Subgroups

- The most common subpopulations were those without diabetes (21.3%), diabetes (10.6%), polycystic ovary syndrome (8.5%), and schizophrenia or psychosis (6.4%)
- Subgroups such as older populations, persons with genetic variants, and those with hypothalamic obesity were studied in 1 SLR each

Interventions

- The most commonly assessed GLP-1 RA was liraglutide (85.1%), followed by semaglutide (42.6%), exenatide (34.0%), and dulaglutide (12.8%) (**Figure 3**)
- Lixisenatide (8.5%) and efpeglenatide (6.4%) were also identified
- One SLR included albiglutide, which was discontinued in 2018 for commercial reasons[3]
- One SLR assessed the use of tirzepatide, a newer AOM targeting both glucose-dependent insulinotropic peptide and GLP-1 receptors (Lin et al, 2023)
- Currently, for adults, liraglutide and semaglutide are approved by the European Medicines Agency and the US Food and Drug Administration for weight loss in individuals with body mass index (BMI) ≥30 kg/m² or BMI ≥27 to <30 kg/m² and one or more weight-related comorbidity

Outcomes

- The majority of studies (91.5%) assessed weight parameters, including change in weight, BMI, or waist circumference (**Figure 4**), and found GLP-1 RAs to be effective for these outcomes
- Four studies did not report change in weight. These studies focused on other outcomes, including blood pressure (Kennedy et al, 2023; Usman et al, 2022), cardiac arrhythmias (Wu et al, 2022), and appetite regulation (Aldawsari et al, 2023)
- Also assessed were glucose control (51.1%), lipid parameters (46.8%), and blood pressure (42.6%)
- Approximately three-fourths of included SLRs (74.5%) reported information on adverse events (AEs), noting that GLP-1 RAs were generally well tolerated, with gastrointestinal-related events being the most common AEs
- Four SLRs included patient-reported outcomes or health-related quality of life (HRQOL) after treatment with GLP-1 RAs (Jobanputra 2022; Martenstyn 2020; Shi 2022; Zhong 2022). The most commonly used tools were the Short-Form 36 (SF-36) and Impact of Weight on Quality of Life (IWQOL)-Lite
- Where assessed, GLP-1 RAs were associated with an improvement in selected domains of HRQOL and physical function; however, few SLRs reported these outcomes

Box. List of included SLRs

Abdel-Maboud M et al. *PLoS One*. 2021;16(7):e0254412. **Ahmad NN** et al. *Obes Rev.* 2021;22(11):e13326. **Aldawsari M** et al. *Diabetes Metab Syndr Obes*. 2023; 16:575-595. **Arastu N** et al. *Int J Clin Pharm*. 2022;44(4):852-859.**Barboza JJ** et al. *J Clin Med*. 2022;11(11):2998. **Bousaba J** et al. *Pharmacogenomics*. 2023;24(5):283-295. **Capristo E** et al. *Nutr Metab Cardiovasc Dis*. 2021;31(9):2587-2595. **Deng Y** et al. *Ther Adv Chronic Dis*. 2022;13 :20406223221108064. **Ding L** et al. *Int J Endocrinol*. 2020:1626484. **Gao X** et al. *Front Pharmacol*. 2022;13:935823. **Garcia-Oropesa EM** et al. *Front Med*. 2021;8:665023. **Ge JJ** et al. *J Endocrinol Invest*. 2022;45(2):261-273. **Guo M** et al. Endocrine. 2020;67(2):294-304. **Guo X** et al. *Horm Metab Res*. 2022;54(7):458-471. **Hasan B** et al. J *Clin Endocrinol Metab*. 2020;105(12):dgaa673. **Haywood C** et al. *Obes Rev*. 2019;20(4):588-598. **Heshmati H** et al. *Obesity*. 2020;28(suppl 2):102. **Iqbal J** et al. *Obes Rev*. 2022;23(6):e13435. **Jobanputra R** et al. *Obes Rev*. 2023:24(4):e13553. **Kennedy C** et al. *J Clin Med*. 2023:12(3):772. **Khera R** et al. *Gastroenterology*. 2018;154(5):1309-1319.e1307. **LeBlanc ES** et al. *JAMA*. 2018;320(11):1172-1191. **Lee K** et al. *Gen Hosp Psychiatry*. 2022;78:58-67. **Lin F** et al. *PLoS One* 2023:18(5):e0285197. **Lin Q** et al. *Expert Rev Clin Pharmacol*. 2022;15(12):1461-1469. **Long Y, Zhang Y.** *Irish J Med Sci*. 10 April 2023. **Lyu X** et al. *Int J Endocrinol*. 2021;2021:6616693. **Martenstyn J** et al. *J Behav Med*. 2020;43(6):873-891. **Patoulias D** et al. *Biomedicines*. 2023;11(3):22. **Salari N** et al. *Diabetol Metab Syndr*. 2021;13(1):110. **Shi Q** et al. *Lancet*. 2022;399(10321):259-269. **Singh AK** et al. *Expert Rev Clin Pharmacol*. 2020;13(1):53-64. **Smith I** et al. *Diabetes Metab Syndr Obes*. 2022;15:3961-3987. **Stogios N** et al. *Biol Psychiatry*. 2020;87(suppl 9):S357. **Tan HCQ** et al. *J ASEAN Fed Endocr Soc*. 2022;37(2):65-72. **Toor K** et al. *Value Health*. 2019;22(suppl 2):S140. **Upala S** et al. *Endocr Rev*. 2018;39(2 suppl 1):MON-265. **Usman MSS** et al. *Circulation*. 2022;146(suppl 1):15922. **Uy Lim AS** et al. *Obes Rev Conference*: ECOICO. 2020;21(suppl 1):EP-043. **Van Lersel L** et al. *Endocr Rev.* 2019;40(1):193-235. **Vosoughi K** et al. *eClinicalMedicine*. 2021;42:101213. **Vosoughi K** et al. *Obes Med*. 2022;35:100456. **Wu S** et al. *Diabetol Metab Syndr.* 2022;14(1):195. **Xie Z** et al. *Clin Epidemiol*. 2022;14:1463-1476. **Zhang L** et al. *Eur J Clin Pharmacol*. 2021;77(11):1611-1621. **Zhang P** et al. *Afr Health Sci*. 2019;19(3):2591-2599. **Zhong P** et al. *Endocrine*. 2022;75(3):718-724.

SLRs, systematic literature reviews

Conclusions

- Recent SLRs reflect the growing number of GLP-1 RAs, which uniquely target both peripheral and brain mechanisms involved in weight regulation
- GLP-1 RAs show promise as efficacious and safe pharmacological treatment for obesity; however, the long-term benefits are not yet known
- Subsequent SLRs are needed to synthesize evidence on newer AOMs, including dual-receptor agonists such as tirzepatide, once data are published

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