ENVISION PHARMA GROUP
Driven by evidence, enabled by technology

Overview of Recent Systematic Literature Reviews on Anti-obesity Medications in Adults

Karen Smoyer,[1] Lauren Moubarak,[2] Sheena Singh,[2] Suki Kandola[2]
[1]Envision Pharma Group, Philadelphia, PA, USA; [2]Envision Pharma Group, London, UK

CO101

Background

- The global prevalence of obesity has soared in the past 40 years and presents a large morbidity and mortality burden[1]
- Lifestyle-based interventions have had limited success
- To address this need, several anti-obesity medications (AOMs) have been approved or are in development, resulting in a large volume of published research on AOM effectiveness and safety

Objective

- This research aims to identify key trends in recently published systematic literature reviews (SLRs) on AOMs in adults

Methods

- Literature searches in Embase, Medline, and Cochrane were conducted using a NICE-published search strategy for obesity[2] and using intervention and SLR terms to identify English-language SLRs published between January 1, 2018, and January 3, 2023
- SLRs of adults with obesity treated with AOMs were included. SLRs covering exclusively surgical, lifestyle, or herbal/supplemental treatments were excluded
- A single reviewer screened titles and abstracts then screened full text of SLRs against predefined inclusion/exclusion criteria. A second reviewer conducted a 10% check

Results

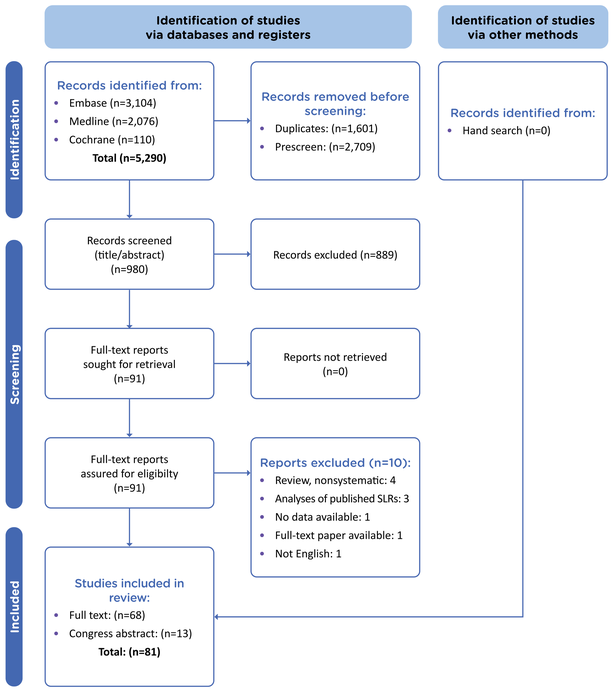
- After the removal of duplicates and obvious irrelevant publications, 980 titles and abstracts were screened according to eligibility criteria, and 889 were excluded
- Of 91 full-text reports assessed for eligibility, 81 SLRs (full text: 68; congress abstract: 13) met the eligibility criteria for inclusion (**Box, Figure 1**)

Box. List of included SLRs

Abdelfattah W. *Diabet Med.* 2021;38(suppl 1):15-16. **Abdel-Maboud M et al.** *PLoS ONE.* 2021;16(7):e0254412. **Abiri B et al.** *Curr Med Res Opin.* 2022;38(11):1853-1863. **Aceves Martins M et al.** *Obesity Facts.* 2019;12(suppl 1):69-70. **Agarwal SM et al.** *Biol Psychiatry.* 2018;83(9 suppl 1):S443. **Ahmad NN et al.** *Obes Rev.* 2021;22(11):e13326. **Arastu N et al.** *Int J Clin Pharm.* 2022;44(4):852-859. **Barboza JJ et al.** *J Clin Med.* 2022;11(11):2998. **Cao B et al.** *J Affect Disord.* 2022;314:222-232. **Capristo E et al.** *Nutr Metab Cardiovasc Dis.* 2021;31(9):2587-2595. **Chen MB et al.** *Medicine.* 2021;100(6):e24593. **Cheong AJY et al.** *Obesity.* 2022;30(1):117-128. **Chin YH et al.** *eClinicalMedicine.* 2022;54:101685. **Cho YK et al.** *J Obes Metab Syndr.* 2021;30(4):336-344. **Conley MM et al.** *Cochrane Database Syst Rev.* 2021;3:CD013119. **Deng Y et al.** *Ther Adv Chronic Dis.* 2022;13. **Ding L et al.** *Int J Endocrinol.* 2020:1626484. **Farah D et al.** *Value Health.* 2019;22(suppl 2):S164. **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. **Guan Y et al.** *Int J Endocrinol.* 2020:5150684. **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. **Janani L et al.** *Drug Res.* 2021;71(9):477-488. **Jeong G et al.** *medRxiv.* 2022;28. **Kane JA et al.** *Int J Clin Res Trials.* 2019;4(1). **Keszytus D et al.** *Dtsch Arztebl Int.* 2018;115(29-30):487-493. **Khera R et al.** *Gastroenterology.* 2018;154(5):1309-1319.e1307. **Kulak-Bejda A et al.** *Arch Med Sci.* 2021;17(4):940-953. **Kuo HH et al.** *J Clin Pharm Ther.* 2020;45(1):35-44. **LeBlanc ES et al.** *JAMA.* 2018;320(11):1172-1191. **Lee K et al.** *Gen Hosp Psychiatry.* 2022;78:58-67. **Lei XG et al.** *Obesity.* 2021;29(6):985-994. **Lin Q et al.** *Expert Rev Clin Pharmacol.* 2022;15(12):1461-1469. **Lyu X et al.** *Int J Endocrinol.* 2021;2021:6616693. **Martenstyn J et al.** *J Behav Med.* 2020;43(6):873-891. **McDowell K et al.** *Obes Rev.* 2018;19(9):1189-1204. **Ni W et al.** *World Neurosurg.* 2018;118:e59-e71. **Ning HH et al.** *Endocrine.* 2018;62(3):528-534. **Noori S et al.** *Int J Clin Pract.* 2021;75(11):e14674. **Onakpoya U et al.** *Obesity.* 2018;26(3):513-521. **Onakpoya U et al.** *Br J Clin Pharmacol.* 2020;86(4):646-667. **Panda SR et al.** *J Obstet Gynaecol India.* 2018;68(5):336-343. **Perreault L et al.** *medRxiv.* 2022;03. **Pormento MK et al.** *Endocr Pract.* 2021;27(12 suppl):S6-S7. **Pu R et al.** *Ther Adv Endocrinol Metab.* 2020;11:2042018820926000. **Ramirez AVG et al.** *Curr Diabetes Rev.* 2020;16(7):750-758. **Robertson C et al.** *Obesity Facts.* 2019;12(suppl 1):178. **Romantsova T et al.** *Obes Rev Conference: ECOICO.* 2020;21(suppl 1):EP-227. **Sahebkar A et al.** *J Am Soc Hypertens.* 2018;12(2):80-96. **Salari N et al.** *Diabetol Metab Syndr.* 2021;13(1):110. **Serralde-Zuniga AE et al.** *Cochrane Database Syst Rev.* 2019;2019(10):CD011688. **Shaikh H et al.** *Cochrane Database Syst Rev.* 2020;2020(12):CD012110. **Shi Q et al.** *Lancet.* 2022;399(10321):259-269. **Singh AK et al.** *Expert Rev Clin Pharmacol.* 2020;13(2):183-190. **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(9 suppl):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. **Wang A et al.** *Endocrine.* 2019;64(2):220-232. **Wong J et al.** *Obes Rev.* 2021;22(12):e13336. **Wu S et al.** *Diabetol Metab Syndr.* 2022;14(1):195. **Xie Z et al.** *Clin Epidemiol.* 2022;14:1463-1476. **Yoshida N et al.** *Ann Transl Med.* 2020;8(17):1059. **Yu AQ et al.** *Adv Ther.* 2021;38(2):1275-1289. **Zhang F et al.** *Front Endocrinol.* 2020;11:00288. **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.

Results (continued)

Figure 1. PRISMA Diagram



Publication details

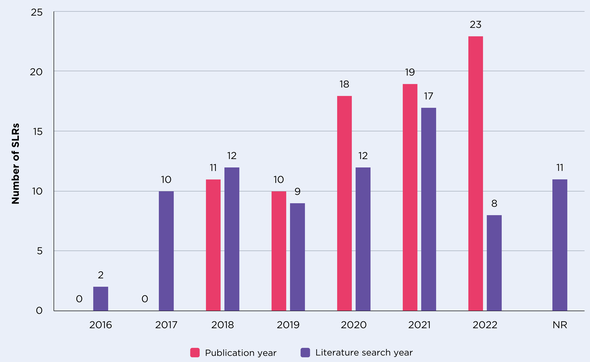
- The SLRs were published in a wide range of journals
- The most common journal types were endocrinology journals (n=21; 25.9%), followed by general medicine/multispecialty (n=19; 23.5%) and obesity-specific journals (n=15; 18.5%)
- Obesity-specific journals included *Obesity Reviews*, *Obesity, Obesity Facts,* and *Journal of Obesity and Metabolic Syndrome*
- One SLR was published in *JAMA* (LeBlanc et al, 2018), and one was published in *The Lancet* (Shi et al, 2022)
- Of the 68 full-text publications, 16 did not report sponsorship and 21 received no funding; only 3 (4.4%) were industry sponsored (Ahmad et al, 2021, Eli Lilly and Company; Smith et al, 2022, Novo Nordisk; Zhang et al, 2020, Bayer China Ltd)

SLR characteristics

- Overall, 65 SLRs were of RCTs only, and 2 SLRs included observational studies only
- Eleven SLRs included both RCTs and observational studies, whereas 3 lacked details on the study design
- The majority of SLRs included meta-analysis (80.3%)
- The number of studies in the SLRs ranged from 2 (Yoshida et al, 2020; Uy Lim et al, 2020) to 143 (Shi et al, 2022)

- The number of SLRs published during the past 5 years increased by 109%, with 11 (13.6%) published in 2018 and 23 (28.4%) published in 2022 (**Figure 2**)
- Among the included SLRs, the literature search period was most often from database inception, with the year of search ranging between 2016 and 2022 (**Figure 2**)

Figure 2. Year of SLR publication and literature search



NR, not reported; SLR, systematic literature review.

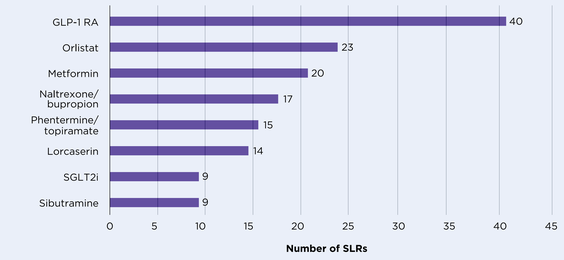
Subgroup

- Forty SLRs (49.4%) were conducted in a specific disease area subgroup, of which nondiabetic obesity was the most common (n=13, 16%), followed by polycystic ovary syndrome (n=7, 8.6%), type 2 diabetes (n=7, 8.6%), and schizophrenia or psychosis (n=3, 3.7%)
- Two SLRs reported on subpopulations with craniopharyngioma-related hypothalamic obesity (2.5%), while populations such as those with cancer, heart failure, depression, chronic kidney disease, and aged >60 years were included in 1 SLR each

Interventions assessed

- Of the included SLRs, 30 looked at a range of pharmacological agents, whereas 51 (63.0%) reported data for a specific drug intervention or drug class
- The most commonly assessed agents were glucagon-like peptide-1 receptor agonists (GLP-1 RAs; 49%), followed by orlistat (28.4%), metformin (22.7%), naltrexone/bupropion (21.0%), and phentermine/topiramate (18.5%). Several SLRs discussed the use of lorcaserin (17.3%), sibutramine (11.1%), and sodium-glucose cotransporter-2 inhibitors (11.1%) (**Figure 3**)
- Of the 40 SLRs that included GLP-1 RAs, liraglutide was the most common (80.0%), followed by semaglutide (40.0%)
- In the SLRs of multiple GLP-1 RAs, 27.5% included exenatide and 10% dulaglutide. Three SLRs each included lixisenatide and efpeglenatide, whereas albiglutide and taspoglutide were evaluated in 1 SLR each
- Examples of other interventions identified include appetite suppressants, antidepressants, and antidiabetics, such as dipeptidyl peptidase-4 inhibitors and acarbose
- In addition to weight loss, favorable and significant benefits on at least 1 cardiometabolic parameter, such as HbA1c, triglycerides, lipid parameters, and blood pressure, were observed across a range of AOMs, including orlistat, lorcaserin, GLP-1 RAs, phentermine/topiramate, and naltrexone/bupropion

Figure 3. Anti-obesity medications assessed in >10% of SLRs



GLP-1, glucagon-like peptide-1; RA, receptor agonist; SGLT2i, sodium-glucose cotransporter-2 inhibitor; SLRs, systematic literature reviews.

Drugs in development

- A targeted search of ClinicalTrials.gov conducted March 24, 2023 for phase 3 AOM trials in adults only that were recruiting, active, or complete as of 2021 or later identified 5 additional agents that were not reported in any of the included SLRs (**Table**)

Table. Phase 3 trials of AOMs not included in any identified SLRs

Drug	Mechanism of action	Sponsor
Tirzepatide	Glucose-dependent insulinotropic peptide/GLP-1 dual RA	Eli Lilly and Company
Benaglutide (now known as beinaglutide)	GLP-1 RA	Xiangya Hospital of Central South University, Changsha, China
Cagrilintide[a]	Long-acting amylin analog	Novo Nordisk A/S
IBI362/mazdutide[a]	GLP-1 and glucagon dual RA	Innovent Biologics (Suzhou) Co. Ltd.
Roflumilast	Phosphodiesterase type-4 inhibitor	Tanta University, Tanta, Egypt

[a]New molecular entity.
AOM, anti-obesity medication; GLP-1, glucagon-like peptide-1; RA, receptor agonist; SLRs, systematic literature reviews.

Conclusions

- Recent SLRs reflect a range of AOMs and highlight the promise of drug treatment, particularly GLP-1 RAs, for long-term weight loss to address the substantial burden of obesity
- Subsequent SLRs are needed to synthesize evidence on new AOMs that are currently in phase 3 trials, once data are published

References

1. World Health Organization. *Fact sheet – Obesity and overweight*. World Health Organization; 2018. Updated June 2021. Accessed March 30, 2023. https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight
2. National Institute for Health and Care Excellence (NICE). *Obesity: identification, assessment and management of overweight and obesity in children, young people and adults.* (NICE; 2014. Updated September 2022. NICE guideline CG189). Accessed March 30, 2023. https://www.nice.org.uk/guidance/cg189/evidence

Acknowledgments and disclosures
All of the authors are employees and shareholders of Envision Pharma Group.