Morello CM, Mnatzaganian CL, Painter NA. Emerging and Off-Label Uses Of Glucagon-Like Peptide-1 Receptor Agonists (GLP1-RA) and Dual GIP/GLP1-RAs. *JABFM*. 2026;39(1). doi:10.3122/jabfm.2025.250158R1

EVIDENCE-BASED CLINICAL MEDICINE

Emerging and Off-Label Uses Of Glucagon-Like Peptide-1 Receptor Agonists (GLP1-RA) and Dual GIP/GLP1-RAs

Candis M Morello, PharmD[1], Christina L Mnatzaganian, PharmD[1], Nathan A Painter, PharmD[1]

[1] Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California San Diego

https://doi.org/10.3122/jabfm.2025.250158R1

Journal of the American Board of Family Medicine

Vol. 39, Issue 1, 2026

Background: Glucagon-like peptide-1 receptor agonists (GLP1-RAs) and the glucagon-dependent insulinotropic polypeptide (GIP)/GLP1-RA are approved for type 2 diabetes (T2D) and obesity given their profound impact on glycemic weight management. Additional indications include reducing cardiovascular disease risk and progression of chronic kidney disease (CKD) in T2D as well as obstructive sleep apnea in patients with obesity. These enhanced effects are likely due to their pleiotropic effects, leading to decreased inflammation and other benefits. This review explored emerging evidence for uses of GLP1-RAs and GIP/GLP1-RA that have been researched but not yet approved. Clinicians may use this information to guide treatment decisions.

Review Process: PubMed and Embase literature searches were conducted using Medical Subject Heading terms. Studies referencing GLP1-RAs and GIP/GLP1-RA were included if they were published in approximately the last decade, included adults, and were either a randomized controlled trial, meta-analysis, or observational study. Of 319 articles reviewed, 27 met inclusion criteria.

Emerging and Compelling Uses: Initial positive impacts have been noted for the following conditions: liver disease/liver transplant, CKD/kidney transplant, Alzheimer's disease, Parkinson's disease, substance use disorders, osteoarthritis, rheumatoid arthritis, psoriasis, COVID-19 virus, asthma, chronic obstructive pulmonary disorder, polycystic ovarian syndrome, and short bowel syndrome.

Considerations: Large randomized controlled trials may lead to approvals of these conditions and are encouraged. Safety and adverse effects of these medications must be assessed when initiating or modifying doses.

Conclusion: GLP1-RAs and GIP/GLP1-RA have demonstrated early benefits to several conditions beyond their current approved indications. Clinicians can use this information to determine treatment options for patients, particularly in those with T2D, cardiovascular disease, and/or obesity.

Keywords: Alzheimer Disease, Glucagon-Like Peptide-1 Receptor Agonists, Liver Diseases, Off-Label Use, Parkinson Disease, Polycystic Ovarian Syndrome, Respiratory Diseases, Substance Use Disorders, Chronic Disease, Clinical Medicine

Background

Glucagon-like peptide-1 receptor agonists (GLP1-RAs) have emerged since the early 2000s as a promising treatment for patients with type 2 diabetes (T2D). In the United States (US), these currently approved medications include exenatide, liraglutide, dulaglutide, and semaglutide. GLP1-RAs are incretin hormones that work by mimicking the glucagon-like peptide-1 hormone, which stimulates insulin production and reduces glucagon release, while slowing gastric emptying and reducing food intake. A dual hormone agent, also known as "twincretin", tirzepatide, has also been more recently developed, and incorporates GLP1-RA activity with a second incretin hormone, the glucose-dependent insulinotropic polypeptide (GIP). GIP increases the production of insulin as well as sensitivity to insulin.

Due to these multiple mechanisms of action and impact on weight loss, GLP1-RAs and GIP/GLP1-RA have also been approved by the US Food and Drug Administration (FDA) for use in obesity and obstructive sleep apnea (Table 1). There have been additional indications for some agents based on benefits noted for patients with T2D and a history of cardiovascular events as well as to prevent chronic kidney disease. GLP1-RAs have demonstrated pleiotropic effects, including anti-inflammatory properties and benefits beyond glycemic management. As such, multiple studies have begun to show the early positive impacts of these agents on non-approved uses of GLP1-RAs and GIP/GLP1-RA.

Table 1. **Summary of FDA approved GLP1-RA and Dual GIP/GLP1-RA Indications.**

Generic (Brand)	MOA	Dosing Frequency and Route	T2D	CVD/ MACE	CKD	Obesity	OSA
Exenatide (Byetta)	Short-acting GLP1-RA	Twice daily injection	Yes	No	No	No	No
Exentatide ER (Bydureon)	Long-acting GLP1-RA	Once weekly injection	Yes	No	No	No	No
Liraglutide (Victoza)	Short-acting GLP1-RA	Once daily injection	Yes	Yes	No	No	No
Liraglutide (Saxenda)	Short-acting GLP1-RA	Once daily injection	No	No	No	Yes	No
Dulaglutide (Trulicity)	Long-acting GLP1-RA	Once weekly injection	Yes	Yes	No	No	No
Semaglutide (Ozempic)	Long-acting GLP1-RA	Once weekly injection	Yes	Yes	Yes	No	No
Semaglutide (Wegovy)	Long-acting GLP1-RA	Once weekly injection	No	Yes	No	Yes	No
Semaglutide (Rybelsus)	Short-acting GLP1-RA	Once daily oral	Yes	Yes	No	No	No
Tirzepatide (Monjouro)	Long-acting Dual GIP/GLP1-RA	Once weekly injection	Yes	No	No	No	No
Tirzepatide (Zepbound)	Long-acting Dual GIP/GLP1-RA	Once weekly injection	No	No	No	Yes	Yes

Abbreviations: FDA, Food and Drug Administration; GLP1-RA, Glucagon-like peptide-1 receptor agonist; GIP, glucose-dependent insulinotropic peptide; MOA, mechanism of action, T2D, type 2 diabetes; CVD, cardiovascular disease, MACE; major adverse cardiac events, CKD, chronic kidney disease; OSA, obstructive sleep apnea

The aim of this review is to explore emerging and early evidence for use in disease states or comorbidities beyond T2D, cardiovascular disease, and obesity. Family medicine and internal medicine clinicians, in particular, may find this summary helpful as they consider treatment options for their patients. Highlighted areas in health care that are being explored include liver disease and liver transplant, kidney disease and kidney transplant, Alzheimer's disease, Parkinson's disease, substance use disorders, osteoarthritis, rheumatoid arthritis, psoriasis, COVID-19 virus, asthma, chronic obstructive pulmonary disorder (COPD), polycystic ovarian syndrome (PCOS), and short bowel syndrome.

Review Process

A literature search was conducted using PubMed and Embase databases to identify studies on GLP1-RAs and dual GIPGLP1-RA. The search encompassed articles published in approximately the last decade with the final search performed on March 18, 2025. The search strategy combined Medical Subject Headings (MeSH) terms and free-text keywords, including "GLP-1 receptor agonist" OR "glucagon-like peptide-1 receptor agonist" OR "incretin mimetics," specific drug names such as exenatide, liraglutide, semaglutide, dulaglutide, exenatide, albiglutide, lixisenatide, tirzepatide, and the disease states listed in the inclusion criteria below. Boolean operators (AND, OR) were utilized to refine the search results. Additionally, the reference lists of key articles were manually screened to identify studies not captured in the initial database search.

Studies were included based on the following criteria: adults (≥18 years) and use of any GLP1-RA or GIP/GLP1-RA medication. Eligible study designs included randomized controlled trials (RCTs), meta-analyses, and observational studies. Only articles published in English were considered. Additional inclusion criteria encompassed studies related to GIP/GLP1-RA (tirzepatide) and GLP1-RAs (all injectables and oral semaglutide), off-label use, liver-related outcomes, kidney-related outcomes, PCOS, neuropsychiatric conditions, Alzheimer's disease, Parkinson's disease, eating disorders, substance use disorder, gastrointestinal conditions (e.g., Crohn's disease, short bowel syndrome), and autoimmune conditions (e.g., osteoarthritis, rheumatoid arthritis, systemic lupus erythematosus, psoriasis).

Studies were excluded if they focused solely on animal models or in vitro experiments, evaluated combination therapies without separate analysis of GLP1-RA effects, or were case reports, editorials, or non-peer-reviewed articles. Further exclusions included studies focusing on type 1 diabetes, pediatrics and adolescents, pregnancy, non-FDA-approved drugs, prescribing trends, animal studies, and shortages and insurance coverage. Reviewers screened the titles and abstracts for relevance, and full-text articles meeting the inclusion criteria were retrieved for detailed assessment. Extracted data included study design, sample size, intervention specifics, outcomes measured, and key findings.

Reviewers independently screened titles and abstracts for relevance. A full-text review was performed for studies meeting inclusion criteria. Discrepancies were resolved through discussion and consensus. Data were extracted into a standardized spreadsheet format that included study

characteristics, intervention details, primary and secondary outcomes measured, and other key findings. The initial literature search yielded 319 articles (167 from Embase and 152 from PubMed), 110 of which were included that met the above criteria. An additional 83 were excluded using the established criteria. The final review included 27 articles that met inclusion criteria.

Emerging and Compelling Uses of GLP1-RAs and Dual GIP/GLP1-RA

Table 2 details the findings of the review on emerging and compelling uses of GLP1-RAs and dual GIP/GLP-RA.

Liver Disease and Liver Transplant

Recently, the American Association for the Study of Liver Diseases introduced new nomenclature for describing liver disease. Previously known as non-alcoholic fatty liver disease (NAFLD) and non-alcohol steatohepatitis (NASH), it is now known as metabolic dysfunction–associated liver disease (MASLD) and metabolic dysfunction–associated steatohepatitis (MASH). While GLP-1RAs have not yet received FDA indication for MASLD or MASH, they have shown promise in treating MASLD/MASH and improving liver histology, decreasing hepatic steatosis, and reducing fibrosis progression in patients with metabolic liver disease.[27] The American Diabetes Association has even added considerations for liver health as part of their guidelines and pharmacologic management.[28] The proposed mechanisms occur via weight loss by reducing hepatic fat accumulation by promoting appetite suppression and caloric intake reduction, insulin sensitization by enhancing glucose metabolism, reducing hepatic de novo lipogenesis, hepatic fat reduction by decreasing triglyceride synthesis and promotes lipid oxidation, and anti-inflammatory and anti-fibrotic effects by reducing pro-inflammatory cytokines (e.g., TNF-α, IL-6) and oxidative stress, slowing fibrosis progression.[29]

In a nested case control study (n = 5730), there was a non-significant trend to favor GLP1-RAs in preventing new cases of MASLD/MASH in patients with T2D (adjusted odds ratio [aOR] 0.84 [95% CI: 0.46-1.52]).[1] The study also showed a dose-dependent reduction in liver enzyme biomarkers, such as alanine transferase (ALT) and aspartate aminotransferase (AST). GLP1-RAs may be useful in patients with T2D, especially those with obesity, at the maximum tolerated dose (e.g., for gastrointestinal side effects) as a preventive strategy against MASLD/MASH.

In a retrospective cohort study of patients with T2D and MASLD (n=53,249), GLP1-RAs were associated with similar reductions in cardiovascular events, including heart failure (hazard ratio [HR] 0.92; 95% CI: 0.88, 0.96), major atherosclerotic cardiovascular events (MACE) (HR 0.95; 95% CI: 0.90, 1.08), cerebrovascular events (HR 0.91; 95% CI: 0.87, 0.95), and all-cause mortality (HR 0.62; 95% CI: 0.58, 0.56) as SGLT-2 inhibitors.[2] While not demonstrating an impact in MASLD progression, this study provided important data for the long-term complications of both T2D and MASLD.

Regarding the safety of GLP1-RAs in patients with a history of liver transplant, a retrospective review looked at efficacy and safety of GLP1-RAs for weight loss in patients without diabetes. Compared to placebo, the patients receiving GLP1-RAs saw significantly more weight loss (7.87% vs 4.24%) while maintaining a similar side effect profile.[3] Another retrospective analysis looking at patients (n=338) with a history of liver transplant and T2D demonstrated that over an eight-year study period, the risk of MACE/peripheral vascular disease and all-cause mortality were significantly lower in GLP1-RAs users (HR 0.92; 95% CI: 0.88, 0.96).[4]

Notably, GLP1-RAs are not well studied in decompensated cirrhosis, but studies have shown the benefit of GLP1-RAs in liver transplant recipients without major safety concerns. While showing promise, additional studies are needed to confirm histologic improvement and fibrosis regression.

Kidney Disease and Transplantation

There is growing use and study of GLP1-RAs in acute and chronic kidney disease as well as kidney transplant. Most recently, injectable semaglutide received FDA approval to reduce the risk of worsening kidney disease in adults with T2D and chronic kidney disease (CKD). T2D that is not well managed can accelerate the decline in kidney function and GLP1-RAs have demonstrated protection in patients with T2D and CKD.[30] A large longitudinal study (GLP1-RA users; n = 7,511) evaluated the impact of both short- and long-acting GLP1-RAs on MACE and major adverse kidney events (MAKE) in patients with acute kidney disease.[8] GLP1-RA users had reduced risk of both MACE and MAKE with aHR of 0.88 and 0.73, respectively. While a lower risk of MAKE was found, it was less pronounced in patients with proteinuria and with short-acting GLP1-RA (daily exenatide and lixisenatide) use. A three-year large retrospective cohort study in 29,146 propensity score matched veterans with CKD compared kidney endpoints in patients with T2D and use of GLP1-RA or sodium-glucose cotransporter-2 inhibitors (SLGT2i).[5] GLP1-RAs used were liraglutide, semaglutide, dulaglutide, and exenatide, although impact of individual drugs was not studied. The GLP1-RA group noted a decreased composite endpoint of all-cause mortality, end-stage renal disease event and ⩾40% decline event in estimated glomerular filtration rate (eGFR). In a retrospective cross-sectional propensity score matching study (n= 250), dulaglutide was evaluated in patients with T2D and moderate to severe CKD.[6] The primary outcome was the measurement of the eGFR slope. Over the three-year period, dulaglutide demonstrated renoprotection by slowing the eGFR decline. Mean (95% CI) in eGFR slope was 0.11 (−0.34, 0.56) mL/min/1.73 m^2 per year in the dulaglutide group (n = 120) and − 1.29 (−1.64, −0.94) mL/min/1.73 m^2 per year in the non-dulaglutide group (n = 130). The impact was more profound in patients with concomitant macro-albuminuria and/or SGLT2i use. In a review of RTCs and observational studies evaluating the use of GLP1-RAs in patients with end-stage kidney disease (ESKD) (on dialysis) and kidney transplantation, GLP1-RAs were found to be

Table 2. **Summary of GLP1-RA or Dual GIP/GLP1-RA Studies in Off Label Uses.**

Disease/Use	Study	Study Type	Country	GLP1-RA(s) or Dual GIP/ GLP1-RA	N (study group/ control group)	Follow-up Period	Primary Aim Outcome(s)
Liver Disease and Transplant							
NAFLD / NASH	Chang 2024[1]	Nested case-control study	Taiwan	Not specified	50,693	1.8 years	• Use of GLP-1RAs was associated with an insignificantly lower risk of NAFLD/NASH events (adjusted OR: 0.84 [95% CI: 0.46–1.52]). • A longer duration (> 183 days) and a higher cumulative dose (> 180 defined daily dose) of GLP-1RA therapy were associated with an insignificantly reduced risk of NAFLD/NASH events (i.e., 0.56 [0.19–1.64] and 0.62 [0.23–1.62].
Liver disease	Krishnan 2024[2]	Population-based propensity-matched retrospective cohort study	USA	dulaglutide, exenatide, liraglutide, lixisenatide or semaglutide	2,835,398	4.8 years	• In patients with liver disease, new onset of heart failure (HR 0.92; 95% CI 0.88, 0.96) and composite cerebrovascular diseases (HR 0.91; 95% CI 0.87, 0.95) was significantly lower in the GLP-1RAs group. • GLP-1RAs group had a lower rate of adverse cardiovascular events, including new-onset heart failure (HR 0.88; 95% CI 0.85, 0.92), composite incidence MACE (HR 0.89; 95% CI 0.85, 0.94) and composite cerebrovascular events (HR 0.93; 95% CI 0.89, 0.96) • Mortality rate was also significantly lower in the GLP-1RAs group (HR 0.70; 95% CI 0.66, 0.75).
Liver transplant	Richardson 2024[3]	Retrospective review	USA	Not specified	44	3, 6, 9, and 12 months	• The GLP-1RA group lost 7.87% of TBW at the 1-year time point compared with baseline ($p < 0.01$). • No t-cell mediated organ rejection was observed during the study
Solid organ transplant	Dotan 2024[4]	retrospective analysis	Israel	liraglutide, dulaglutide, semaglutide	338	10 years	• The incidence of MACE was 101 events/1000 patient-years in GLP1-RAs users compared with 134 events/1000 patient-years in the control group (HR 0.46; 95% CI, 0.27-0.78; P = 0.004).
Kidney Disease and Transplant							
CKD	Morello 2024[5]	Retrospective cohort, propensity scored matched, real-world study	USA	liraglutide, semaglutide, dulaglutide and exenatide	29,146; 14,573 each group	36 months	• GLP-1RA group decreased composite endpoint, all-cause mortality, ESKD event and ≥40% decline event in eGFR, although notably SGLT2i performed better.

Disease/Use	Study	Study Type	Country	GLP1-RA(s) or Dual GIP/ GLP1-RA	N (study group/ control group)	Follow-up Period	Primary Aim Outcome(s)
Moderate to Severe CKD	Tsuchida 2022[6]	Retrospective, cross-sectional database analysis, propensity score matching	Japan	dulaglutide	dulaglutide: 120, non-dulaglutide 130	36 months	• Mean (95% CI) in eGFR slope was 0.11 (−0.34, 0.56) mL/min/1.73 m^2 per year in dulaglutide group and − 1.29 (−1.64, −0.94) mL/min/1.73 m^2 per year in non-dulaglutide group. • Difference between groups was 1.40 (0.83, 1.97) mL/min/1.73 m^2 per year, and a statistically significant reduction was observed in the non-dulaglutide group (P < 0.0001). • The categorical analysis of eGFR, the percentage of stage 4 (<30 mL/min/1.73 m^2 per year) tended to be higher in group non-dulaglutide group.
ESKD and Transplant	Clemens 2023[7]	Small RCTs, retrospective cohort studies	Canada	Liraglutide, oral and injectable semaglutide	multiple	3 to 12 months	• Small RCTs and retrospective cohort studies observed glycemic and weight benefits with use of liraglutide in dialysis populations. • 24 patients with ESKD receiving hemo- or peritoneal dialysis, liraglutide (max dose of 1.8 mg) reduced time in hyperglycemia from 81.3% ± 2.4 to 78.1% ± 5.8 compared to placebo. • Kidney Transplant: Small retrospective cohort studies of GLP-1RA have been conducted in kidney transplant recipients with T2D. In a cohort study of liraglutide 1.8 mg daily, fasting blood glucose was lowered from 12.8 mmol/L±2.17 to 9.22 mmol/L ± 1.48 with the addition of the GLP-1RA. • In a retrospective cohort study of solid organ transplant recipients of whom 80% were kidney transplant recipients, HbA1c was reduced by up to 1.08% at 3 months following the addition of a GLP-1RA. Dulaglutide also appears to help reduce insulin requirements in transplant recipients. A variable amount of weight loss (0–4.86 kg) has been described across retrospective cohort studies of GLP-1RA in the transplant population.
AKD	Pan 2024[8]	Longitudinal investigation	Taiwan	short-acting: exenatide and lixisenatide, long acting: exenatide once-weekly, liraglutide, albiglutide, dulaglutide, and semaglutide	7,511 GLP-1 RAs users to non-users among 165,860 AKD patients.	median follow up 2.3 years	• GLP-1RAs users exhibited reduced risks of mortality (aHR): 0.57), MACE (aHR: 0.88), and MAKE (aHR: 0.73). • Primary outcome: morbidity GLP1-RA 6.8% vs 12.9% control group [0.57 (0.51-6.4)] MACE: The findings consistently indicated an association between the GLP1-RAs use and a lower risk of mortality. • An association between a lower risk of MACEs and GLP1-RAs use persisted regardless of HTN, advanced CKD, or insulin/ metformin use. This association was notable among younger

Disease/Use	Study	Study Type	Country	GLP1-RA(s) or Dual GIP/ GLP1-RA	N (study group/ control group)	Follow-up Period	Primary Aim Outcome(s)
							GLP-1RA users without proteinuria and those not receiving SU, DPP-4i, or RAAS blockers. • Similar association observed between GLP-1RAs use and lower risk of MAKEs, although less pronounced in patients with proteinuria and those receiving short-acting GLP-1RAs.
Neurodegenerative Diseases							
Parkinson's Disease and Alzheimer's Disease	Siddeeque 2024[9]	Retrospective cohort study utilized data from a global collaborative	17 countries and 127 health care organizations	semaglutide, liragutide, dulaglutide	>102K (n= 102,935), obesity	GLP1-RA group was observed for an average of 17.5 months (SD 18.4 months), with a median follow-up of 11.8 months	• Obese patients treated with GLP-1RAs showed significantly lower risks of developing Alzheimer's disease (RR = 0.627, 95 %CI = 0.481-0.817). • Risk reduction for PD was not statistically significant overall (RR = 0.784, 95 %CI = 0.580-1.058) but was significant for semaglutide users (RR = 0.574, 95% CI = 0.369-0.893). • Semaglutide consistently showed the most pronounced protective effects in PD, AD Lewy body and vascular diseases. • Significant reduction in all-cause mortality was observed (HR = 0.525, 95% CI = 0.493-0.558) for all four neurodegenerative disorders.
Parkinson's Disease	Aviles-Olmos 2014[10]	Open label, RCT	United Kingdom	exenatide 10 mg twice daily	20 exenatide and 24 control group	12 months post- exenatide discontinuation	• Blinded video rating of MDS-UPDRS part 3 "off medication" evaluated. Exenatide group had a mean improvement at 24 months (12 months post exenatide discontinuation) compared with baseline of 1.1 points (SD, 5.9) on the MDS-UPDRS part 3 motor score, while controls had a mean decline of 4.5 points (SD, 5.3) (a difference of 5.6 points (95% CI, 2.2–9.0; p=0.002). • Open label rating of rigidity scores to the blinded data equated to a decline of 0.5 points (SD, 7.3) in the exenatide group, compared with a decline of 8.5 points (SD, 6.3) in control group (difference, 8.0points; 95% CI,3.8–12.2; p<0.001). • Repeat analysis of the MDS-UPDRS part 3 motor score off medication/ off stimulation including data from the 3 patients who had undergone DBS showed a persistent advantage for the exenatide group (difference of 5.2 points; 95% CI, 1.0–9.1; p<0.01).
Alzheimer's Disease	Bi 2023[11]	Systematic review and meta analysis	Not provided	exenatide and liraglutide	5 small studies: 21-57 participants	in 5 studies: 12-26 weeks	• Cognitive function: MD = 2.16 (95% CI: 1.45–2.88) • GLP-1RAs may help slow the progression of AD • BMI change: MD = −1.16 (95% CI: −1.71−−0.61)

Disease/Use	Study	Study Type	Country	GLP1-RA(s) or Dual GIP/ GLP1-RA	N (study group/ control group)	Follow-up Period	Primary Aim Outcome(s)
							• Blood glucose change: standard MD = −0.64 (95% CI: −1.21–−0.88)
Substance Use Disorder and Alcohol Use Disorder							
OUD and AUD	Qeadan 2025[12]	Retrospective cohort study	USA	albiglutide, dulaglutide, exenatide, liraglutide, lixisenatide, semaglutide, and tirzepatide	503,747 patients with history of OUD and 817,309 patients with history of AUD	24 months	• Among individuals with OUD, those with a GIP/GLP-1 RA prescription had a 40% lower rate of incident opioid overdose compared to those without a GIP/GLP-1 RA prescription (aIRR [95% CI] = 0.60 [0.43, 0.83]).
OUD	Wang 2024[13]	Cohort	USA	semaglutide, liraglutide, dulaglutide	33,006	12 months	• Semaglutide was associated with a significantly lower risk of opioid overdose during a 1-year follow-up compared with other diabetes medications, including other GLP-1RAs, with HRs ranging from 0.32 (95% CI, 0.12-0.89) to 0.58 (95% CI, 0.38-0.87).
AUD	Klausen 2022[14]	RCT	USA	exenatide long-acting	127	26 weeks	• Exenatide did not significantly reduce the number of heavy drinking days compared with placebo, it significantly attenuated fMRI alcohol cue reactivity in the ventral striatum and septal area, which are crucial brain areas for drug reward and addiction. • Dopamine transporter availability was lower in the exenatide group compared with the placebo group. • Exploratory analyses revealed that exenatide significantly reduced heavy drinking days and total alcohol intake in a subgroup of obese patients (BMI > 30 kg/m^2).
AUD	Hendershot 2025[15]	RCT	USA	semaglutide	48	10 weeks	• Semaglutide reduced posttreatment laboratory consumption with a medium to large effect size for grams of alcohol consumed (95% CI, −0.85 to −0.11; P = .01) and peak breath alcohol concentration (95% CI, −0.87 to −0.06; P = .03)
Gastrointestinal							
Short Bowel Syndrome	Merlo 2023[16]	Pilot observational study	Italy	liraglutide	39 (19/20)	1 month and 6 months	• Median ostomy/fecal output was significantly reduced by 550 mL/day after 6 months of treatment (vs. -200 mL/day in untreated, p = 0.04).

Disease/Use	Study	Study Type	Country	GLP1-RA(s) or Dual GIP/ GLP1-RA	N (study group/ control group)	Follow-up Period	Primary Aim Outcome(s)
							• 52.6% (10/19) achieved ≥20% output reduction (p = 0.013) at 1 month and 63.2% (12/19) achieved ≥20% output reduction (p = 0.038) at 6 months.
Osteoarthritis, Rheumatoid Arthritis, and Psoriasis							
Osteoarthritis	Bliddal 2024[17]	Double blinded RCT	9 countries	semaglutide	407 (271/ 136)	68 weeks plus 7 week follow up	• Mean change of -13.7% baseline body weight at week 68 in the semaglutide group and -3.2% in the placebo group (estimated difference, -10.5 percentage points; 95% CI, −12.3 to −8.6; p<0.001). • Mean change of -41.7 points from baseline in the WOMAC pain score at week 68 in the semaglutide group and -27.5 points in the placebo group (estimated difference, -14.1 points; 95% CI, -20.0 to -8.3; p<0.001).
Osteoarthritis	Baser 2024[18]	Retrospective cohort study	USA	semaglutide, liraglutide, tirzepatide	111,799 (39,394/ 72,405)	6 months	• Adjusted osteoarthritis risk was 27% % lower in anti-obesity medication users than in non-users (HR= 0.73, 95% CI (0.67–0.79), p<0.01).
Rheumatoid arthritis and psoriasis	Karacabeyli 2024[19]	Review	Canada	liraglutide, exenatide	19 studies	n/a	• Liraglutide improved DAS-28 in the majority (9/15) of patients in an uncontrolled prospective cohort study of patients with RA (11/15) or PsA (4/15), as well as in a case report of a patient with diabetes and RA. • One study found a mean improvement from 4.2 to 2.7 in the 9 DAS-28 responders, whereas another described a decrease from 5.5 to 3. Weight in the 9 DAS-28 responders decreased significantly from 94 to 90.6 kg with liraglutide 1.2 mg subcutaneously daily, but not in the 6 DAS-28 non-responders. • In longitudinal cohorts and RCTs, statistically significant improvements in PASI were seen in 4 of 5 studies and 3 of 4 studies demonstrated significant improvements in DLQI. Statistically significant weight loss or change in BMI was noted in 4 of 5 studies.
COVID-19 Virus							
COVID-19	Foresta 2023[20]	Retrospective cohort study	Italy	Not reported	32,853 (1,925 GLP1-RA users/4,711 DPP-4i	n/a	• Reduction of the risk for COVID-19 outcomes for users of DPP-4i, GLP1-RA, and SGLT-2i compared with nonusers, although statistical significance was reached only in DPP-4i users for total mortality (OR, 0.89; 95% CI, 0.82–0.97).

Disease/Use	Study	Study Type	Country	GLP1-RA(s) or Dual GIP/ GLP1-RA	N (study group/ control group)	Follow-up Period	Primary Aim Outcome(s)
					users/2,143 SGLT-2i users/ 22,925 control)		• Sensitivity analysis confirmed the main results reaching significant reductions in hospital admissions in GLP-1 RA users.
COVID-19	Chen 2022[21]	Systematic review - meta-analysis	China	Unclear without reviewing individual studies	35 studies	n/a	• SGLT2i or GLP1-RA significantly associated with a reduction in mortality compared to non-users; pooled OR, 0.82; 95% CI: 0.76-0.88; p=0.00, GLP1RA: pooled OR, 0.91; 95% CI: 0.84-0.98; p=0.02).
Respiratory Diseases							
COPD	Yen 2024[22]	Retrospective cohort of insurance database	Taiwan	Not provided in manuscript nor supplementary materials	16,120 (8,060/ 8,060)	2.51 and 2.46 years for GLP-1 RA users and non-users, respectively.	• 150 (1.86%) GLP1-RA users and 399 (4.95%) non-users died during follow-up (7.31 vs 19.79 per 1000 patient-years). • The aHR for death between GLP1-RA users and non-users was 0.46 (95% CI 0.38 to 0.56, p<0.001). • GLP1-RA users had a significantly lower risk of MACE (aHR 0.73, 95% CI 0.65 to 0.82), NIPPV (aHR 0.66, 95% CI 0.47 to 0.93), IMV (aHR 0.64, 95% CI 0.51 to 0.8) and bacterial pneumonia (aHR 0.76, 95% CI 0.65 to 0.88) than GLP-1 RA non-users. • The cumulative incidence of IMV, bacterial pneumonia, MACE and death was significantly lower in GLP1-RA users than in non-users (p<0.001).
Asthma	Zhang 2024[23]	Meta-analysis	70 of the 192 World Health Organization member states	lixisenatide, tirzepatide, exenatide, semaglutide, dulaglutide, albiglutide, others not approved in US	n=39 RCTs; (47,499/ 38,256)		• Trend of reduced risk of asthma observed in patients with GLP1-RA (RR = 0.91, 95% CI: 0.68 to 1.24), which was consistent with the result after excluding the dual GIP/GLP1-RA (RR = 0.88, 95% CI: 0.64 to 1.20), although a statistical significance was not reached.
COPD	Foer 2023[24]	Observational, retrospective analysis of EHR data from an integrated healthcare system	USA	albiglutide, dulaglutide, exenatide, liraglutide, lixisenatide, and semaglutide	1,642 (328 GLP1-RA users/260 DPP-4i users/353 SGLT2i users/701	10 years	• Lower unadjusted COPD exacerbation counts in GLP1-RA users. • Adjusted exacerbation rates were significantly higher in DPP-4i (incidence rate ratio, 1.48 [95% confidence interval, 1.08-2.04]; *p*=0.02) and sulfonylurea (incidence rate ratio, 2.09

Disease/Use	Study	Study Type	Country	GLP1-RA(s) or Dual GIP/ GLP1-RA	N (study group/ control group)	Follow-up Period	Primary Aim Outcome(s)
					sulfonylurea users)		[95% confidence interval, 1.62-2.69]; $p<0.0001$) users versus GLP1-RA users. • GLP1-RAs were associated with significantly reduced risk of severe exacerbations versus DPP-4is and sulfonylureas, and of moderate exacerbations versus sulfonylureas.
Polycystic Ovarian Syndrome (PCOS)							
PCOS	Tong 2024[25]	Review	USA, Slovenia, and China	exenatide, liraglutide	8 RCTs of 519 obese patients with PCOS	8-16 weeks	• GLP1-RAs were more effective at improving insulin sensitivity, reducing BMI, and resulting in a smaller waist circumference versus control.
PCOS	Bader 2024[26]	Review	USA, Slovenia, and China	liraglutide, exenatide	8 studies of 486 patients with PCOS	12-32 weeks	• Results were comparable for reduction in body mass index, waist circumference, fat mass, and visceral fat mass; however, it was more in combination therapy versus comparator. • Combined treatment with GLP1-RA and metformin had significant effects on weight loss and favorable results on endocrine and metabolic parameters.

Abbreviations: GLP-1RA; Glucagon-like peptide-1 receptor agonist, GIP; glucose-dependent insulinotropic polypeptide, NAFLD; non-alcoholic fatty liver disease, NASH; non-alcoholic steatohepatitis, OR; Odds ratio, CI; confidence interval, USA; United States of America, SGLT2i; sodium-glucose cotransporter-2 inhibitors, HR; hazard ratio, MACE; major adverse cardiovascular events, TBW; total body weight, CKD; chronic kidney disease, eGFR; estimated glomerular filtration rate, ESKD; end stage kidney disease, RCT; randomized controlled trial, AKD; Acute kidney disease, aHR; adjusted hazard ratio, HTN; hypertension, MAKE; major adverse kidney events, SD; standard deviation, RR; risk ratio, PD; Parkinson's disease; AD; Alzheimer's disease, MDS-UPDRS; movement disorders society modified unified Parkinson's disease rating scale, MD; mean difference, BMI; body mass index, OUD; opioid use disorder, AUD; alcohol use disorder, aIRR; adjusted incidence rate ratio, FMRI; functional magnetic resonance imaging, WOMAC; Western Ontario and McMaster Universities Arthritis Index, DAS-28; Disease Activity Score 28, RA; rheumatoid arthritis, PsA; psoriatic arthritis, PASI; Psoriasis Area Severity Index, DLQI; Dermatology Life Quality Index, COVID-19; coronavirus disease 2019, DPP-4i; dipeptidyl-peptidase-4 inhibitors, COPD; chronic obstructive pulmonary disease, NIPPV; non-invasive positive pressure ventilation, IMV; invasive mechanical ventilation, EHR; electronic health record, PCOS; polycystic ovarian syndrome.

effective and safe.[7] The most reported adverse events were gastrointestinal in nature in both groups; however, hypoglycemia was prevalent in ESKD users especially with concomitant insulin use but were not present in kidney transplant studies.

Neurodegenerative Disorders: Parkinson's Disease

Following FDA approval of GLP1-RAs in the early 2000's, observations were made that patients with neurodegenerative disorders, such as Parkinson's Disease (PD) and Alzheimer's Disease (AD), who concomitantly were treated with a GLP1-RA for T2D or obesity demonstrated improvement in neurodegenerative symptoms. Since GLP1-RAs cross the blood brain barrier and the brain contains GLP1-RA receptors, studies have been conducted to determine if neuroprotective properties exist. Several complementary mechanisms have been identified at the cellular level improving neural-inflammation; increased efficiency of ATP production, reduced oxidative stress, improved synaptic activity and neuronal survival, as well as an association between metabolism and insulin sensitivity.[9,31,32]

PD is a progressive multifactorial neurodegenerative condition with clinical characteristics including tremors at rest, gait dysfunction, speech difficulty, cognitive impairment, and dementia. While dopamine replacement has served as the hallmark treatment, more focus has been on slowing the disease progression rather than restoring dopamine levels. In a small open label study examining exenatide 10 mcg twice daily use for 12 months in patients with PD, both motor and non-motor improvements were found.[33] Motor severity was measured using the Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS). In a follow-up study evaluating subjects (20 in the study group versus 24 in the control group) 12 months post-discontinuation of exenatide, MDS-UPDRS improvements continued and were sustained despite no exposure to exenatide for one year.[10] A large-scale retrospective propensity-matched cohort study involving 17 countries and 127 healthcare organizations evaluated real-world use of semaglutide, dulaglutide, and liraglutide in over 102,000 obese patients with neurodegenerative disorders, including PD, AD, Lewy body dementia, and vascular dementia.[9] The primary aim was to investigate the association between the use of GLP1-RAs and the risk of developing neurodegenerative disorders in obese patients. In the PD cohort, semaglutide was the only GLP1-RA associated with a significant neurodegenerative risk reduction compared to the control group (relative risk [RR]=0.574, 95% CI=0.369-0.893 versus (RR=0.784, 95% CI=0.580-1.058); while dulaglutide and liraglutide did not demonstrate any risk reduction. In the full cohort, including all four neurodegenerative disorders, semaglutide and dulaglutide demonstrated significant reduction in fatality rates compared to non-GLP1-RA users.

Neurodegenerative Disorders: AD

AD, the most common type of dementia, is a slow progressive brain disorder with clinical characteristics of memory loss, confusion, difficulty finding words, completing tasks and exerting fine motor skills. Like PD, there has been an increased interest in repurposing GLP1-RAs to assess the impact on clinical improvement in AD, with many preclinical studies and trials now published.[34] In the previously discussed large-scale retrospective propensity-matched study, semaglutide was also the only GLP1-RA that significantly improved neurodegenerative risk of AD.[9] While dulaglutide showed a similar trend, it did not reach significance and liraglutide showed no significant difference. In a systematic review and meta-analysis, comparisons were made of five small randomized clinical trials from 2012-2019 in patients (n=177) with diagnosed AD or cognitive impairment without an AD diagnosis.[11] The primary aim of evaluating change in cognitive function was assessed using at least one of the Mini-Mental State Examination (MMSE), Activities of Daily Living (ADL), or Wechsler Memory Scale-Fourth Edition (WMS-IV) tools in patients exposed to exenatide or liraglutide versus placebo. Use of GLP1-RAs was associated with improved cognitive function in patients with AD (Mean Difference = 2.16; 95% CI: 1.45-2.88). These findings may help inform clinical use of GLP1-RAs in AD; however, additional larger scale clinical studies would be useful to identify optimal drugs, dosing, and treatment duration.

Substance Use Disorders

GLP1-RAs have gained some attention for their use in substance use disorders. GLP-1 receptors in the brain's mesolimbic system are responsible for regulating motivated behaviors and reward processing through a dopamine response, which plays a key role in food satiety and appetite control. This region of the brain overlaps with pathways involved in addiction and substance use disorders. Due to similarities in the reward mechanism, it is thought that GLP1-RAs may influence substance satiety and alter the reward related responses and change substance use behaviors.[14]

One cohort study of patients (n=33,006) with T2D and opioid use disorder treated with a GLP1-RA compared to other diabetes medications showed that semaglutide was associated with a significantly lower risk of opioid overdose (range from HR 0.32; 95% CI: 0.12-0.89 to HR 0.58; 95% CI: 0.38-0.87) during a 1-year follow-up compared with other diabetes medications, including other GLP1-RAs.[13]

In another cohort study, patients (n=503,747) with a history of opioid or alcohol use disorder (AUD) treated with GLP1-RAs had a 40% lower rate of incident opioid overdose and a 50% lower rate of incident alcohol intoxication compared to those without a GLP1-RA prescription (adjusted incidence rate ration; 95% CI=0.60 [0.43-0.83]).[12] Another review article in patients with alcohol use disorder found a significant reduction in the number of heavy drinking days and total alcohol intake.[35]

In a recent phase 2 clinical trial that evaluated the effects of semaglutide in non–treatment-seeking adults with AUD, semaglutide was associated with a decrease in overall alcohol intake per drink and a decrease in cravings. However, there was no difference in overall drinking days versus abstinence days.[15] One factor slowing research in AUD is that patients with AUD are already at a higher risk for developing pancreatitis or pancreatic cancer, both of which are known precautions for the use of GLP-1 RAs.[36]

Inflammation: Osteoarthritis, Rheumatoid Arthritis, and Psoriasis

Given the propensity for weight loss, GLP1-RAs may be suitable treatment options for diseases that are caused by or worsened by obesity and its pro-inflammatory impact. As such, literature demonstrates the expanding role of GLP1-RAs in obesity and inflammatory conditions, particularly osteoarthritis (OA), rheumatoid arthritis (RA), and psoriasis. In a double-blinded RCT that included 407 participants with obesity and knee OA, 271 received once weekly semaglutide escalated to maximum of 2.4 mg target and 136 received placebo.[17] Semaglutide users noted significantly decreased pain and improved weight loss (Western Ontario and McMaster Universities Arthritis Index pain score decreased by 41.7 points with semaglutide versus 27.5 points with placebo, p<0.001). Another study found a reduced risk of OA in a retrospective cohort study (n=39,394 patients with obesity) assessing diagnosis and prescription claims for tirzepatide, semaglutide, or liraglutide.[18] Specifically, adjusted OA risk was significantly decreased (27%) in patients using a GLP1-RA than in non-users (HR=0.73, p=0.0019), with tirzepatide demonstrating lowest risk of the three GLP1-RAs studied (HR=0.57 versus semaglutide, p<0.0001; liraglutide HR 1.63 versus tirzepatide, p=0.0007). Finally, a scoping review of GLP1-RAs across eight studies in patients with RA and psoriasis demonstrated similar positive impacts.[19] The review found that patients with RA or psoriatic arthritis who used liraglutide had reduced disease activity noted via assessment of Disease Activity Score (DAS-28). Additionally, four of five clinical studies of patients with psoriasis who used liraglutide or exenatide had significant improvements in Psoriasis Area Severity Index and weight/body mass index.

Inflammation: COVID-19 Virus

The anti-inflammatory properties seen in GLP1-RAs could theoretically decrease the exaggerated response caused by the COVID-19 virus.[37] One systematic review of 32,853 patients with at least two prescriptions of dipeptidyl peptidase-4 (DPP-4) inhibitors, GLP1-RAs, SGLT2-is, or any other antihyperglycemic drug analyzed these medications' effects on COVID-19 prognosis.[20] Authors demonstrated a reduction in risk of COVID-19 outcomes for patients who had used DPP-4 inhibitors, GLP-1RAs, and SGLT2-is versus nonusers, although findings were only significant for DPP-4 inhibitor users for total mortality (OR 0.89; 95% CI 0.82-0.97) as well as for reduction in hospital admissions in GLP1-RA users (OR 0.79, 95% CI 0.67-0.94) and in-hospital mortality in SGLT2-i users (OR 0.73, 95% CI 0.56-0.96).[20] It was proposed that this positive impact could be due to GLP1-RA reduction of cytokine-induced lung injury through interference with the NF-KB pathway or via anti-inflammatory effects.[20,38,39] Further, a meta-analysis of 18 studies assessed the mortality risk of COVID-19 in patients with diabetes treated with anti-diabetes medications.[21] GLP1-RA treatment was associated with reduced mortality risk (OR 0.91, p=0.02) compared to non-use and had the most significant protective effect against death, followed by SGLT2-is and metformin.

Inflammation: Asthma and Chronic Obstructive Pulmonary Disease (COPD)

Literature has further outlined that the anti-inflammatory effects previously described have also been noted in respiratory diseases including asthma and COPD. A recent meta-analysis that included 39 RCTs of 85,755 patients with T2D or patients with obesity assessed the effects of GLP1-RAs (lixisenatide, exenatide, semaglutide, dulaglutide, and albiglutide) and dual GLP-1RA/GIP (tirzepatide) on asthma.[23] Investigators noted a trend of reduced asthma risk in patients who used a GLP1-RA, though statistical significance was not achieved (relative risk [RR]=0.91, 95% CI 0.68-1.24). Further studies are warranted to further elucidate the impact on asthma.

Respiratory outcomes in COPD patients have been favorable among those who used GLP1-RAs. The impact of GLP1-RAs on airway inflammation includes decreased airway hyperreactivity, mucous metaplasia, and lung IL-33 expression, all of which are associated with COPD.[24,40-44] A retrospective, observational study of electronic health records (n=1,642 patients) found that unadjusted COPD exacerbation counts were significantly higher in patients with T2D who used DPP-4 inhibitors (incidence rate ratio 1.48, 95% CI 1.08-2.04, p=0.02) and sulfonylureas (incidence rate ratio 2.09, 95% CI 1.62-2.69, p<0.0001) compared to those who used GLP1-RAs, including albiglutide, dulaglutide, exenatide, liraglutide, semaglutide, and lixisenatide.[24] Further, a nationwide cohort study of 8,060 patients with COPD and T2D found that GLP1-RA users had a significantly lower risk of all-cause mortality (adjusted HR [aHR] 0.46, 95% CI 0.38-0.56), MACE (including composite of hospitalization for stroke, coronary artery disease, and heart failure) (aHR 0.73, 95% CI 0.65-0.82), non-invasive positive pressure ventilation (aHR 0.66, 95% CI 0.47-0.93), invasive mechanical ventilation (aHR 0.64, 95% CI 0.51-0.8), and bacterial pneumonia (aHR 0.76, 95% CI 0.65-0.88) than non-GLP1-RA users.[22] These findings may help inform treatment decisions for patients with comorbid inflammatory respiratory disorders and T2D.

Polycystic Ovary Syndrome (PCOS)

Insulin resistance, obesity and abdominal obesity, metabolic disorders, and cardiovascular risk factors are associated with PCOS.[25,45] Given the propensity to improve insulin resistance and weight loss, GLP1-RAs are a promising treatment to consider for overweight or obese patients with

PCOS. A systematic review of eight randomized controlled trials found that GLP1-RAs (liraglutide or exenatide) were more effective at improving insulin sensitive and reducing body mass index and waist circumference than metformin or dapagliflozin in adults with PCOS.[25] Another review also assessed eight studies of adult patients with PCOS and found that GPL1-RAs (liraglutide or exenatide) effectively reduced body weight and improved some endocrine parameters (reduced total testosterone and improved sex hormone binding globulin levels) and insulin resistance.[26] The most compelling treatment for this population included a combination of GLP1-RA and metformin, which improved menstrual cyclicity, insulin sensitivity, glucose metabolism, and anthropometric measures.

Gastrointestinal

One pilot observational study found that adult patients (n=19) with newly diagnosed short bowel syndrome after surgical resection benefited from a GLP1-RA.[16] Deficiencies in GLP-1, as well as GLP-2, are noted in short bowel syndrome.[46] In the pilot study, liraglutide was titrated from doses varying 0.6 mg/day to 1.8 mg/day.[16] After six months of treatment, the median ostomy/fecal output decreased significantly by 550 mL/day in patients treated with a GLP1-RA (versus reduction of 200 mL/day in untreated patients, p=0.04). Given this paucity of literature, further studies will add to the growing evidence for use in short bowel syndrome.

Summary and Considerations

GLP1-RAs and GIP/GLP1-RAs show early and compelling evidence in the previously described studies for several conditions beyond those currently approved for use by the FDA. Future studies, ideally RCTs, conducted on larger cohorts may lead to approvals of these conditions and should be encouraged. Additionally, the emerging data on these agents can help inform primary care clinicians, including physicians, physician associates, nurse practitioners, and clinical pharmacists, in selecting treatment and providing education for patients with T2D who present with comorbidities highlighted in this review. The American Diabetes Association advocates for interdisciplinary care in treating patients with diabetes as displayed in Table 1.[28]

In studies and clinical practice, the most common adverse event associated with GLP1-RA and dual GIP/GLP1-RA is gastrointestinal discomfort, which can present as mild to severe. Proper patient education can improve tolerability. For example, to prevent nausea, vomiting, and heartburn, eating smaller meals (i.e., the size of a fistful) more often, avoiding irritating foods and drinks (i.e., spicy, fatty, or greasy foods or carbonated beverages), and avoid lying down or going to bed 2-3 hours after eating. For patients using these drugs for obesity, monitoring blood pressure is essential. Weight loss often results in improved blood pressure and dyslipidemia resulting in the need for reassessment of hypertension and dyslipidemia medications. Another important consideration with GLP1-RA and GIP/GLP1-RA use is holding the medication prior to surgery or other medical procedures (i.e., colonoscopy, endoscopy). These drugs delay gastric emptying and may predispose patients to lung aspiration. Generally, short-acting GLP-1 RAs should be held the day of surgery/procedure and once-weekly GLP-1 RAs should be held one week prior.

Specific limitations are inherent in any literature review. Reported outcomes could be skewed since studies with positive outcomes may be more likely published than those without, creating an inadvertent publication and/or selection bias. Both positive and negative outcomes were provided in this review. A time lag bias may also occur to due to additional studies published during this manuscripts review process, which we attempted to mitigate by including the most up to date data at the time of submission. Since all authors are clinical pharmacist practitioners working in collaborative practices with patients with diabetes, there could also be a discipline bias.

Conclusion

This review provided evidence that GLP1-RAs and GIP/GLP1-RAs have demonstrated early benefits to several conditions beyond their current FDA approved indications. Primary care clinicians can use this information to determine treatment options for patients, particularly in those with T2D, cardiovascular disease, and/or obesity.

Funding

The authors have no funding to report.

Conflicts of Interest

The authors have no conflict of interests.

Corresponding Author

Candis M. Morello, PharmD, University of California San Diego Skaggs School of Pharmacy and Pharmaceutical Sciences, La Jolla, CA, cmmorello@health.ucsd.edu

Peer Review

This manuscript was externally peer reviewed.

Submitted: April 24, 2025 EDT. Accepted: September 08, 2025 EDT.

References

1. Chang KC, Kuo FC, Yang CY, et al. Non-alcoholic fatty liver disease risk with GLP-1 receptor agonists and SGLT-2 inhibitors in type 2 diabetes: a nationwide nested case–control study. *Cardiovasc Diabetol*. 2024;23:367. doi:10.1186/s12933-024-02461-2

2. Krishnan A, Schneider CV, Hadi Y, Mukherjee D, AlShehri B, Alqahtani SA. Cardiovascular and mortality outcomes with GLP-1 receptor agonists vs other glucose-lowering drugs in individuals with NAFLD and type 2 diabetes: a large population-based matched cohort study. *Diabetologia*. 2024;67(3):483-493. doi:10.1007/s00125-023-06057-5

3. Richardson SH, Wong G, Garner E, Izzy M, Srivastava G. Utility of glucagon-like peptide 1 receptor agonists as anti-obesity medications in liver transplant recipients. *Liver Transplantation*. 2024;30(2):226-228. doi:10.1097/LVT.0000000000000233

4. Dotan I, Rudman Y, Turjeman A, et al. Glucagon-like Peptide 1 Receptor Agonists and Cardiovascular Outcomes in Solid Organ Transplant Recipients With Diabetes Mellitus. *Transplantation*. 2024;108(7):e121-e128. doi:10.1097/TP.0000000000004945

5. Morello CM, Awdishu L, Lam S, Heman A, Bounthavong M. Sodium-Glucose Cotransporter-2 Inhibitors versus Glucagon-Like Peptide 1 Receptor Agonists Effects on Kidney and Clinical Outcomes in Veterans with Type 2 Diabetes. *Kidney360*. 2024;5(11):1633-1643. doi:10.34067/KID.0000000597

6. Tsuchida KI, Taneda S, Yokota I, et al. Japan Diabetes Clinical Data Management Study Group (JDDM study group). The renoprotective effect of once-weekly GLP-1 receptor agonist dulaglutide on progression of nephropathy in Japanese patients with type 2 diabetes and moderate to severe chronic kidney disease (JDDM67). *J Diabetes Investig*. 2022;13(11):1834-1841. doi:10.1111/jdi.13877

7. Clemens KK, Ernst J, Khan T, et al. Glucagon-like peptide 1 receptor agonists in end-staged kidney disease and kidney transplantation: A narrative review. *Nutr Metab Cardiovasc Dis*. 2023;33(6):1111-1120. doi:10.1016/j.numecd.2023.03.023

8. Pan HC, Chen JY, Chen HY, et al. GLP-1 receptor agonists' impact on cardio-renal outcomes and mortality in T2D with acute kidney disease. *Nat Commun*. 2024;15:5912. doi:10.1038/s41467-024-50199-y

9. Siddeeque N, Hussein MH, Abdelmaksoud A, et al. Neuroprotective effects of GLP-1 receptor agonists in neurodegenerative Disorders: A Large-Scale Propensity-Matched cohort study. *Int Immunopharmacol*. 2024;143(Pt 3):113537. doi:10.1016/j.intimp.2024.113537

10. Aviles-Olmos I, Dickson J, Kefalopoulou Z, et al. Motor and cognitive advantages persist 12 months after exenatide exposure in Parkinson's disease. *J Parkinsons Dis*. 2014;4(3):337-344. doi:10.3233/JPD-140364

11. Bi Z, Wang L, Wang W. Evaluating the effects of glucagon-like peptide-1 receptor agonists on cognitive function in Alzheimer's disease: A systematic review and meta-analysis. *Adv Clin Exp Med*. 2023;32(11):1223-1231. doi:10.17219/acem/161734

12. Qeadan F, McCunn A, Tingey B. The association between glucose-dependent insulinotropic polypeptide and/or glucagon-like peptide-1 receptor agonist prescriptions and substance-related outcomes in patients with opioid and alcohol use disorders: A real-world data analysis. *Addiction*. 2025;120(2):236-250. doi:10.1111/add.16679. PMID:39415416

13. Wang W, Volkow ND, Wang Q, et al. Semaglutide and Opioid Overdose Risk in Patients With Type 2 Diabetes and Opioid Use Disorder. *JAMA Netw Open*. 2024;7(9):e2435247. doi:10.1001/jamanetworkopen.2024.35247. PMID:39320894

14. Klausen MK, Thomsen M, Wortwein G, Fink-Jensen A. The role of glucagon-like peptide 1 (GLP-1) in addictive disorders. *Br J Pharmacol*. 2022;179(4):625-641. doi:10.1111/bph.15677

15. Hendershot CS, Bremmer MP, Paladino MB, et al. Once-Weekly Semaglutide in Adults With Alcohol Use Disorder: A Randomized Clinical Trial. *JAMA Psychiatry*. Published online February 12, 2025. doi:10.1001/jamapsychiatry.2024.4789

16. Merlo FD, Aimasso U, Ossola M, et al. Effects of Treatment with Liraglutide Early after Surgical Intervention on Clinical Outcomes in Patients with Short Bowel Syndrome: A Pilot Observational "Real-Life" Study. *Nutrients*. 2023;15(12):2740. doi:10.3390/nu15122740

17. Bliddal H, Bays H, Czernichow S, et al. Once-weekly semaglutide in persons with obesity and knee osteoarthritis. *N Engl J Med*. 2024;391(17):1573-1583. doi:10.1056/NEJMoa2403664

18. Baser O, Rodchenko K, Vivier E, Baser I, Lu Y, Mohamed M. The impact of approved anti-obesity medications on osteoarthritis. *Expert Opinion on Pharmacotherapy*. 2024;25(11):1565-1573. doi:10.1080/14656566.2024.2391524

19. Karacabeyli D, Lacaille D. Glucagon-like peptide 1 receptor agonists in patients with inflammatory arthritis or psoriasis: A scoping review. *J Clin Rheumatol*. 2024;30(1):26-31. doi:10.1097/RHU.0000000000001949

20. Foresta A, Ojeda-Fernandez L, Macaluso G, et al. Dipeptidyl Peptidase-4 Inhibitors, Glucagon-like Peptide-1 Receptor Agonists, and Sodium-Glucose Cotransporter-2 Inhibitors and COVID-19 Outcomes. *Clin Ther*. 2023;45(4):e115-e126. doi:10.1016/j.clinthera.2023.02.007

21. Chen Y, Lv X, Lin S, Arshad M, Dai M. The Association Between Antidiabetic Agents and Clinical Outcomes of COVID-19 Patients With Diabetes: A Bayesian Network Meta-Analysis. *Front Endocrinol (Lausanne)*. 2022;13:895458. doi:10.3389/fendo.2022.895458

22. Yen FS, Hsu CC, Wei JC, et al. Glucagon-like peptide-1 receptor agonists may benefit cardiopulmonary outcomes in patients with COPD. *Thorax*. 2024;79(11):1017-1023. doi:10.1136/thorax-2023-221040

23. Zhang MQ, Lin C, Cai XL, et al. The association between GLP-1 receptor-based agonists and the incidence of asthma in patients with type 2 diabetes and/or obesity: a meta-analysis. *Biomed Environ Sci*. 2024;37(6):607-616. doi:10.3967/bes2024.067

24. Foer D, Strasser ZH, Cui J, et al. Association of GLP-1 receptor agonists with chronic obstructive pulmonary disease exacerbations among patients with type 2 diabetes. *Am J Respir Crit Care Med*. 2023;208(10):1088-1100. doi:10.1164/rccm.202303-0491OC

25. Tong X, Song X, Zhang Y, Zhao Q. Efficacy and safety of glucagon-like peptide-1 receptor agonists in the treatment of polycystic ovary syndrome-a systematic review and meta-analysis. *Arch Physiol Biochem*. 2024;130(6):1005-1011. doi:10.1080/13813455.2024.2380422

26. Bader S, Bhatti R, Mussa B, Abusanana S. A systematic review of GLP-1 on anthropometrics, metablic, and endocrine parameters in patients with PCOS. *Womens Health (Lond)*. 2024;20:17455057241234530. doi:10.1177/17455057241234530

27. Abushamat LA, Shah PA, Eckel RH, Harrison SA, Barb D. The Emerging Role of Glucagon-Like Peptide-1 Receptor Agonists for the Treatment of Metabolic Dysfunction-Associated Steatohepatitis. *Clin Gastroenterol Hepatol*. 2024;22(8):1565-1574. doi:10.1016/j.cgh.2024.01.032

28. American Diabetes Association (ADA) Standards of Care in Diabetes—2025 is Diabetes Care 2025. 2025;48(Supplement_1). doi:10.2337/dc25-SDIS

29. Nevola R, Epifani R, Imbriani S, et al. GLP-1 Receptor Agonists in Non-Alcoholic Fatty Liver Disease: Current Evidence and Future Perspectives. *Int J Mol Sci*. 2023;24(2):1703. doi:10.3390/ijms24021703

30. Shaman AM et al. Effect of the glucagon-like peptide-1 receptor agonists semaglutide and liraglutide on kidney outcomes in patients with type 2 diabetes: pooled analysis of SUSTAIN 6 and LEADER. *Circulation*. 2022;145:575-585. doi:10.1161/CIRCULATIONAHA.121.055459

31. Procaccini C, Santopaolo M, Faicchia D, et al. Role of metabolism in neurodegenerative disorders. *Metabolism*. 2016;65(9):1376-1390. doi:10.1016/j.metabol.2016.05.018

32. Ashok A, Andrabi SS, Mansoor S, Kuang Y, Kwon BK, Labhasetwar V. Antioxidant Therapy in Oxidative Stress-Induced Neurodegenerative Diseases: Role of Nanoparticle-Based Drug Delivery Systems in Clinical Translation. *Antioxidants*. 2022;11(2):408. doi:10.3390/antiox11020408

33. Aviles-Olmos I, Dickson J, Kefalopoulou Z, et al. Exenatide and the treatment of patients with Parkinson's disease. *J Clin Invest*. 2013;123(6):2730-2736. doi:10.1172/JCI68295

34. Katsenos AP, Davri AS, Simos YV, et al. New treatment approaches for Alzheimer's disease: preclinical studies and clinical trials centered on antidiabetic drugs. *Expert Opinion on Investigational Drugs*. 2022;31(1):105-123. doi:10.1080/13543784.2022.2022122

35. Klausen MK, Jensen ME, Møller M, et al. Exenatide once weekly for alcohol use disorder investigated in a randomized, placebo-controlled clinical trial. *JCI Insight*. 2022;7(19):e159863. doi:10.1172/jci.insight.159863. PMID:36066977

36. National Institute for Health and Care Excellence. *Alcohol-Use Disorders: Diagnosis, Assessment and Management of Harmful Drinking (High-Risk Drinking) and Alcohol Dependence. Clinical Guideline, Revised 2019*. Vol 4. Clinical guideline; 2011.

37. Banerjee Y, Pantea Stoian A, Silva-Nunes J, et al. The role of GLP-1 receptor agonists during COVID-19 pandemia: a hypothetical molecular mechanism. *Expert Opin Drug Saf*. 2021;20(11):1309-1315. doi:10.1080/14740338.2021.1970744

38. Lee YS, Jun HS. Anti-inflammatory effects of GLP-1-based therapies beyond glucose control. *Mediators Inflamm*. 2016;2016:3094642. doi:10.1155/2016/3094642

39. Drucker DJ. Coronavirus infections and type 2 diabetes—shared pathways with therapeutic implications. *Endocr Rev*. 2020;41(3):bnaa01. doi:10.1210/endrev/bnaa011

40. Toki S, Goleniewska K, Reiss S, Zhang J, Bloodworth MH, Stier MT, et al. Glucagon-like peptide 1 signaling inhibits allergen-induced lung IL-33 release and reduces group 2 innate lymphoid cell cytokine production in vivo. *J Allergy Clin Immunol*. 2018;142:1515-1528.e8. doi:10.1016/j.jaci.2017.11.043

41. Toki S, Newcomb DC, Printz RL, Cahill KN, Boyd KL, Niswender KD, et al. Glucagon-like peptide-1 receptor agonist inhibits aeroallergen-induced activation of ILC2 and neutrophilic airway inflammation in obese mice. *Allergy*. 2021;76:3433-3445. doi:10.1111/all.14879

42. Alshabanat A, Zafari Z, Albanyan O, Dairi M, FitzGerald JM. Asthma and COPD overlap syndrome (ACOS): a systematic review and meta analysis. *PLoS One*. 2015;10:e0136065. doi:10.1371/journal.pone.0136065

43. Tkacova R, Dai DLY, Vonk JM, et al. Airway hyperresponsiveness in chronic obstructive pulmonary disease: a marker of asthma-chronic obstructive pulmonary disease overlap syndrome? *J Allergy Clin Immunol*. 2016;138:1571-1579.e10. doi:10.1016/j.jaci.2016.04.022

44. Huang X, Guan W, Xiang B, Wang W, Xie Y, Zheng J. MUC5B regulates goblet cell differentiation and reduces inflammation in a murine COPD model. *Respir Res*. 2022;23:11. doi:10.1186/s12931-021-01920-8

45. Cena H, Chiovato L, Nappi RE. Obesity, polycystic ovary syndrome, and infertility: a new avenue for GLP-1 receptor agonists. *J Clin Endocrinol Metab*. 2020;105(8):e2695-2709. doi:10.1210/clinem/dgaa285

46. Jeppesen PB, Hartmann B, Thulesen J, et al. Elevated plasma glucagon-like peptide 1 and 2 concentrations in ileum resected short bowel patients with a preserved colon. *Gut*. 2000;47(3):370-376. doi:10.1136/gut.47.3.370