

RESEARCH ARTICLE

Do Glucagon Like Peptide-1 Receptor Agonists Modify Progression of Primary Glenohumeral Osteoarthritis? A Propensity Score–Matched Evaluation of Shoulder Arthroplasty Incidence

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Abstract

Objectives: Glenohumeral osteoarthritis (OA) is a common degenerative condition, and total shoulder arthroplasty (TSA) often represents the definitive treatment for end-stage disease. The use of glucagon-like peptide-1 receptor agonists (GLP-1RA) has increased substantially, and recent evidence suggests potential disease-modifying effects and reduced arthroplasty rates in lower-extremity joints. This study evaluated whether GLP-1RA use is associated with progression from primary shoulder OA to TSA.

Methods: A retrospective database query was performed to identify patients diagnosed with primary shoulder OA, excluding those with other shoulder pathologies. Patients were stratified according to prediagnosis GLP-1RA prescription status and were 1:1 propensity-score matched to balance relevant comorbidities. Outcomes included the incidence of TSA, TSA-free survival assessed using Kaplan–Meier survival analysis, major joint injections, and mean levels of inflammatory biomarkers, including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and cortisol. A significance threshold of $P < 0.05$ was applied.

Results: After matching, each cohort included 24,669 patients. The GLP-1RA cohort had a significantly shorter follow-up duration than the non-GLP-1RA cohort (731 ± 694 vs. $1,220 \pm 1,006$ days; $P < 0.001$). TSA incidence was higher among GLP-1RA users than among non-users (2.25% vs. 1.77%; $P < 0.001$), and TSA-free survival was lower in the GLP-1RA cohort (95.50% vs. 97.23%; log-rank $P < 0.001$). A greater proportion of patients in the GLP-1RA cohort received major joint injections (18.93% vs. 16.87%; $P < 0.001$), although the mean number of injections per patient was lower in this group (2.48 ± 2.86 vs. 2.74 ± 3.23 ; $P < 0.001$). GLP-1RA users also demonstrated significantly lower mean CRP and ESR levels (both $P < 0.001$), while mean cortisol levels were similar between cohorts.

Conclusion: In contrast to findings reported for hip and knee OA, GLP-1RA use was not associated with a protective effect against progression to TSA in patients with primary shoulder OA. Further studies are warranted to clarify the joint-specific mechanisms that may underlie these differences.

Level of evidence: III**Keywords:** GLP-1 receptor agonist, Primary osteoarthritis, Progression, Shoulder osteoarthritis, Shoulder Replacement**Introduction**

Shoulder osteoarthritis (OA) is a common and debilitating joint disease, affecting an estimated 16–21% of middle-aged and older adults, with prevalence increasing steadily with age.¹ It is characterized by progressive degeneration of the glenohumeral joint

cartilage resulting in chronic pain, stiffness, and functional decline.² Current management remains primarily symptomatic and includes analgesics, injections, and activity modification, whereas total shoulder arthroplasty (TSA) is generally reserved for patients with advanced

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disease who do not

respond adequately to nonoperative treatment.² TSA has become an increasingly common orthopedic procedure, and its incidence is projected to rise substantially in the coming decades.³ Despite this growing clinical burden, shoulder OA remains understudied compared with hip and knee OA, with relatively limited research on disease progression and modifiable risk factors.

Glucagon-like peptide-1 receptor agonists (GLP-1RAs) are increasingly prescribed for the treatment of type 2 diabetes and obesity.⁴ Accordingly, their use has expanded substantially over the past decade.⁵ Beyond their metabolic benefits, GLP-1RAs have demonstrated anti-inflammatory and chondroprotective properties.⁶ Preclinical studies have shown that GLP-1RAs may reduce chondrocyte apoptosis and suppress inflammatory and catabolic mediators, including NF- κ B, MMP-13, and iNOS.⁶ Moreover, a recent systematic review of 11 preclinical and clinical studies, limited to knee OA, reported consistent evidence supporting the potential structural protective, immunomodulatory, and analgesic effects of GLP-1RAs in OA.⁷ Collectively, these findings suggest a possible disease-modifying role for GLP-1RAs in joint OA, and recent studies have reported associations between GLP-1RA use and a lower incidence of lower-extremity arthroplasty.^{8,9}

However, whether these effects extend to the shoulder joint, and the role of GLP-1RAs in shoulder OA, remain unclear. Unlike weight-bearing joints such as the hip and knee, the shoulder is exposed to lower mechanical loading, which may alter the relationship between GLP-1RA use and OA progression in this joint. To address this gap, we leveraged the TriNetX database, a large multi-institutional real-world dataset, to investigate whether GLP-1RA exposure before OA diagnosis is associated with the subsequent risk of undergoing TSA. We hypothesized that patients prescribed GLP-1RAs would have a lower incidence of TSA compared to matched controls.

Materials and Methods

Data source

We queried the TriNetX Research Network, which aggregates deidentified patient data from more than 100 healthcare organizations, including diagnoses, procedures, medications, laboratory values, and genomic data from more than 100 million patients. Because the database contains only deidentified data, this study was deemed exempt from Institutional Review Board approval. Current Procedural Terminology (CPT), Systematized Nomenclature of Medicine (SNOMED), and International Classification of Diseases, 10th Revision (ICD-10) codes were used to query the database.

Inclusion/exclusion criteria and cohort formation

The data query was performed on December 5, 2025. We identified patients aged 18 years or older who were diagnosed with primary shoulder OA between December 2005 and December 2025. Patients with any diagnosis of proximal humerus fracture, aseptic necrosis of the humerus, secondary shoulder OA, or other shoulder pathologies, such as adhesive capsulitis or rotator cuff tear, at any time during the study period were excluded. The included patients were then stratified into two cohorts: GLP-1RA users, defined as patients with a GLP-1RA prescription within 5 years and up

to 2 weeks before shoulder OA diagnosis, and non-user controls. Both cohorts were followed for up to 10 years after the diagnosis of shoulder OA. The query codes used in this study are provided in [Supplementary Table 1].

1:1 Propensity Score Matching (PSM)

A 1:1 propensity-score matching procedure was performed to control for several covariates, including demographic characteristics, specifically age at diagnosis and sex, and relevant comorbidities, including type 2 diabetes mellitus, insulin use, body mass index (BMI; 20–25, 25–30, 30–40, and ≥ 40 kg/m²), dyslipidemia, hypertensive diseases, nicotine use, chronic kidney disease stages 1 through 5, heart failure, ischemic heart disease, liver disease, and HbA1c levels ($\leq 5.6\%$, 5.6%–6.5%, 6.5%–7.5%, 7.5%–8.5%, 8.5%–9%, and $\geq 9\%$). The TriNetX platform uses a greedy nearest-neighbor matching algorithm with a caliper of 0.01 with adequate covariate balance defined as a standardized mean difference of ≤ 0.1 .

Outcomes of interest

The primary outcomes assessed in this study were the incidence of TSA and TSA-free survival. Secondary outcomes included inflammatory marker levels, including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and cortisol, as well as the incidence and number of major joint injections.

Statistics

Statistical analyses were performed using the built-in analytics tools of the TriNetX platform. Risk percentages, odds ratios (ORs), 95% confidence intervals (CIs), and P values were calculated for all outcomes. TSA-free survival analyses were performed using Kaplan–Meier survival curves with log-rank testing, and hazard ratios (HRs) were estimated. Categorical variables were compared using chi-square tests, whereas continuous variables were compared using Student's t tests. Statistical significance was defined as $P < 0.05$.

Results

A total of 667,363 patients were initially included, comprising 24,825 GLP-1RA users and 642,538 non-user controls. Before matching, the two groups differed significantly across multiple included baseline characteristics. After 1:1 propensity-score matching, each cohort consisted of 24,669 patients, and baseline characteristics were well balanced, with no statistically significant differences between the groups, as shown in [Table 1].

The GLP-1RA cohort had a significantly shorter follow-up duration than the control cohort (730.73 ± 693.84 vs. $1,220.31 \pm 1,005.87$ days; $P < 0.001$). In the GLP-1RA cohort, 556 patients underwent TSA (2.25%), compared to 436 patients in the control cohort (1.77%; $P < 0.001$), corresponding to an odds ratio of 1.28 (95% CI, 1.13–1.46). Kaplan–Meier survival analysis [Figure 1] demonstrated a lower TSA-free survival rate at the end of the observation window in the GLP-1RA cohort than in the control cohort (95.50% vs. 97.23%; log-rank $P < 0.001$; HR, 1.52; 95% CI, 1.34–1.73).

Table 1. Patient characteristics before and after propensity score matching

Variable	GLP-1RAs (n=24,825) (%)	Control (n=642,538) (%)	Std diff	GLP-1Ras (n=24,669) (%)	Control (n=24,669) (%)	Std diff
Age at Index (Mean +/- SD)	63.5 +/- 10.8	65.7 +/- 14.0	0.171	63.6 +/- 10.8	63.8 +/- 11.7	0.022
Female	59.50%	51.10%	0.169	59.30%	60.60%	0.026
Male	40.50%	48.90%	0.169	40.70%	39.30%	0.027
Type 2 diabetes mellitus	79.50%	19.00%	1.52	79.40%	80.10%	0.016
Hypertensive diseases	84.10%	48.70%	0.809	84.00%	85.20%	0.032
Disorders of lipoprotein metabolism and other lipidemias	81.30%	42.90%	0.861	81.20%	82.00%	0.022
Diseases of liver	20.80%	7.90%	0.376	20.60%	19.50%	0.028
Chronic kidney disease, stage 1	1.10%	0.30%	0.095	1.10%	1.10%	<0.001
Chronic kidney disease, stage 2 (mild)	5.50%	1.70%	0.205	5.50%	5.00%	0.019
Chronic kidney disease, stage 3 (moderate)	18.40%	7.30%	0.337	18.40%	18.20%	0.006
Chronic kidney disease, stage 4 (severe)	4.50%	1.70%	0.163	4.50%	4.50%	0.001
Chronic kidney disease, stage 5	1.10%	0.50%	0.062	1.10%	1.10%	0.003
Ischemic heart diseases	32.30%	17.60%	0.344	32.30%	32.40%	0.003
Heart failure	19.10%	9.40%	0.282	19.20%	19.30%	0.002
Nicotine dependence	16.50%	11.50%	0.144	16.50%	16.50%	<0.001
Insulin use	53.00%	11.50%	0.991	52.70%	53.10%	0.008
BMI						
20 - 25 kg/m ²	9.10%	19.90%	0.309	9.20%	8.20%	0.036
25 - 30 kg/m ²	28.00%	32.10%	0.089	28.10%	27.50%	0.013
30 - 40 kg/m ²	58.20%	30.40%	0.583	58.10%	60.50%	0.048
> 40 kg/m ²	34.60%	8.60%	0.665	34.20%	35.80%	0.032
Hemoglobin A1c/Hemoglobin.total in Blood						
< 5.60%	22.10%	16.30%	0.149	22.10%	25.30%	0.075
5.60 - 6.50%	46.10%	20.20%	0.572	45.90%	48.10%	0.044
6.50 - 7.50%	50.00%	8.60%	1.02	49.80%	48.10%	0.033
7.50 - 8.50%	42.80%	4.70%	1	42.50%	39.70%	0.055
8.50 - 9%	19.30%	1.60%	0.607	19.00%	16.50%	0.066
> 9%	33.50%	3.10%	0.854	33.10%	30.20%	0.063

SD: Standard deviation; BMI: Body mass index; Std diff: standardized difference

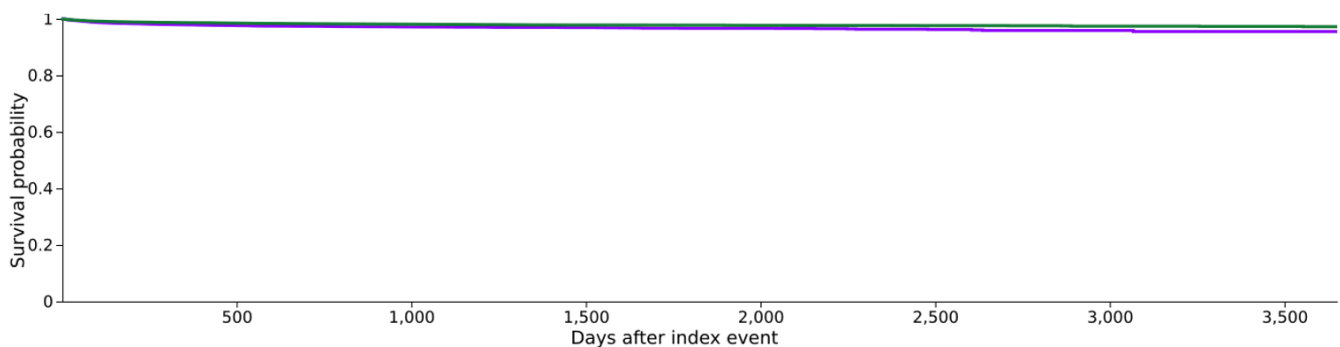
Purple: GLP-1RAs cohort; Green: Control cohort; log-rank $p < 0.001$ 

Figure 1. Kaplan-Meier Survival Curve

Major joint injections were significantly more common in the GLP-1RA cohort than in the control cohort (18.93% vs. 16.87%; OR, 1.15; 95% CI, 1.10–1.21; $P < 0.001$). However, the mean number of injections per patient was higher in the control cohort than in the GLP-1RA cohort (2.74 ± 3.23 vs. 2.48 ± 2.86 ; $P < 0.001$).

The availability of inflammatory biomarker data differed significantly between cohorts. CRP and ESR values were available for a lower proportion of patients in the GLP-1RA cohort than in the control cohort (CRP: 16.27% vs. 22.87%; ESR: 17.07% vs. 22.93%; both $P < 0.001$), whereas cortisol values were also less frequently available in the GLP-1RA cohort (2.68% vs. 4.02%; $P <$

0.001). Among patients with available laboratory values, mean CRP levels were significantly higher in the control cohort than in the GLP-1RA cohort (39.03 ± 63.41 vs. 30.66 ± 55.49 mg/L; $P < 0.001$). Mean ESR levels were also higher in the control cohort (37.45 ± 29.97 vs. 33.78 ± 28.03 mm/h; $P < 0.001$). Mean cortisol levels were numerically higher in the control cohort than in the GLP-1RA cohort (13.41 ± 8.90 vs. 12.80 ± 8.58 µg/dL), but this difference was not statistically significant ($P = 0.164$).

A summary of these findings is presented in [Tables 2 and 3].

Table 2. Summary of outcome comparison between the two groups

Outcome	GLP1-RAs	Control	Odds Ratio (95%CI)	p-value
Follow-up (days)	730.73 +/- 693.84	1220.31 +/- 1005.87	-	<0.001
Incidence of TSA	2.25%	1.77%	1.28 (1.13, 1.46)	<0.001
Major joint injection	18.93%	16.87%	1.15 (1.10, 1.21)	<0.001
Number of injections (mean +/- SD)	2.48 +/- 2.86	2.74 +/- 3.23	-	<0.001

TSA: Total shoulder arthroplasty; SD: Standard deviation, CI: Confidence interval

Table 3. Summary of lab values between the two groups

Lab values	GLP1-RAs (Mean +/- SD)	Control (Mean +/- SD)	p-value
CRP	30.66 +/- 55.49	39.03 +/- 63.41	<0.001
ESR	33.78 +/- 28.03	37.45 +/- 29.97	<0.001
Cortisol	12.80 +/- 8.58	13.41 +/- 8.90	0.164

ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, SD: Standard deviation

Discussion

In this large database cohort study, GLP-1RA users had a significantly higher incidence of TSA despite a shorter follow-up duration. In addition, Kaplan-Meier analysis demonstrated lower TSA-free survival in the exposed group, corresponding to a hazard ratio of 1.52. GLP-1RA users also had significantly higher odds of receiving a major joint injection; however, among patients who received injections, GLP-1RA users had a significantly lower mean number of injections. GLP-1RA use was also associated with significantly lower systemic inflammatory marker levels. Although prior studies have suggested that GLP-1RAs may have protective effects in knee OA, including pain improvement and reduced surgical intervention,⁷ their role in shoulder OA remains poorly defined. This study provides novel insights into the association between prior GLP-1RA exposure and progression of shoulder OA, highlighting a previously underexplored aspect of how these widely prescribed medications may relate to outcomes in this common shoulder condition.

Preclinical studies have provided mechanistic evidence supporting a potential structural protective role for GLP-1RAs in OA. In vitro experiments using human, murine, and rat chondrocytes have demonstrated attenuation of catabolic

pathways through suppression of extracellular matrix-degrading enzymes, including MMP-3, MMP-13, ADAMTS-4, and ADAMTS-5, as well as endoplasmic reticulum stress proteins, alongside dose-dependent upregulation of anabolic markers such as type II collagen and aggrecan.¹⁰⁻¹⁵ In vivo models have further supported these findings, with liraglutide shown to mitigate cartilage destruction and proteoglycan loss in rat models¹⁰ and to decrease synovitis in a mouse model of knee OA.¹³ Consistent with these mechanistic findings, Zhu et al., in a clinical study of 1,807 patients with diabetes, reported that GLP-1RA exposure was associated with greater weight loss, a lower incidence of knee surgery, improvements in pain and function, and slower cartilage-loss velocity.¹⁶ In addition, semaglutide demonstrated significant improvements in pain, body weight, and physical function over 68 weeks in patients with obesity compared with placebo.¹⁷ Similarly, in a secondary analysis of a randomized controlled trial, GLP-1RA recipients achieved higher Knee injury and Osteoarthritis Outcome Score (KOOS) function scores than placebo-treated patients, although no between-group differences in physical activity were observed over one year.¹⁸ Collectively, these findings support potential structural and symptomatic benefits of GLP-1RA therapy in knee OA and underscore the importance

of investigating its potential relevance to shoulder OA.

Few studies have examined progression from OA to arthroplasty among patients receiving GLP-1RAs compared with controls using the TriNetX database. Among patients with pre-existing OA, Lavu et al. reported no difference in 5-year arthroplasty incidence in either the hip or knee between GLP-1RA users and controls.⁸ In contrast, Porto et al. reported reduced odds of both hip and knee arthroplasty among patients receiving GLP-1Ras.⁹ Davis et al. similarly found that GLP-1RA use was not associated with lower rates of shoulder OA or subsequent arthroplasty. Instead, GLP-1RA users had a higher 5-year incidence of OA across all subgroups; non-obese patients with diabetes showed higher rates of shoulder arthroplasty than non-users, whereas no differences were observed among patients with obesity.¹⁹ However, these studies did not specify the subtype of OA, such as primary versus post-traumatic OA, and did not exclude other potential indications for arthroplasty. This lack of diagnostic specificity limits the interpretability of the findings and may confound their applicability to patients with primary OA. In the present study, we attempted to better isolate the association between GLP-1RA exposure and shoulder OA progression by excluding other possible indications for TSA, including rotator cuff disease. In addition, we adjusted for comorbidities that could influence surgical eligibility, including cardiovascular disease, thereby strengthening the clinical relevance of our findings.

In our analysis, GLP-1RA users had a higher incidence of TSA, although the GLP-1RA cohort had a significantly shorter follow-up duration than controls, warranting cautious interpretation. Notably, Kaplan-Meier analysis demonstrated lower TSA-free survival in the GLP-1RA cohort despite the shorter follow-up period. One possible explanation is that patients receiving GLP-1RAs may have had more advanced OA at baseline, predisposing them to surgical intervention regardless of subsequent treatment. Additionally, improvements in weight, glycemic control, and overall health associated with GLP-1RA use may have made these individuals more suitable candidates for elective surgery. As such, the increased incidence of TSA in this group may reflect enhanced surgical eligibility rather than accelerated disease progression. Another possible explanation for the increased incidence of shoulder arthroplasty among GLP-1RA users, despite lower systemic inflammatory marker levels, is the non-weight-bearing nature of the shoulder. Unlike the hip and knee, where load-bearing and mechanical forces may interact with metabolic modulation to influence OA progression, the shoulder is exposed to relatively lower mechanical loading, which may limit the potential protective effect of GLP-1RAs. These findings highlight the complexity of real-world associations and underscore the need for further research to clarify the role of GLP-1RAs in the clinical trajectory of OA.

Furthermore, we found that GLP-1RA users had lower inflammatory marker levels. This finding is consistent with previous reports describing the anti-inflammatory properties of these agents.⁶ However, the relationship between inflammatory marker levels and the risk of joint

arthroplasty remains uncertain. Elevated inflammatory marker levels have been associated with greater pain^{20,21} and more inflamed tissue in the knee.^{22,23} Greater pain may, in turn, increase the likelihood of proceeding to arthroplasty; however, this relationship has primarily been investigated in the knee joint. Notably, a prior study evaluating metformin use in the setting of shoulder OA reported a higher incidence of TSA in the metformin cohort despite lower inflammatory marker levels,²⁴ similar to our findings. These observations suggest that factors driving OA progression may differ across joints and highlight the complex relationship between systemic inflammation and OA progression.

GLP-1RA users had a higher incidence of major joint injections, despite having fewer injections on average than non-users. This pattern may suggest that patients receiving GLP-1RAs may have had more symptomatic disease at presentation, resulting in a greater likelihood of initial intervention, but subsequently underwent fewer repeat injections over time. One possible explanation is the proposed anti-inflammatory effect of GLP-1RAs, as supported by the lower ESR and CRP levels observed in this study and by findings from previous studies.⁶ To our knowledge, the combination of a higher incidence of major joint injections but a lower mean number of injections among GLP-1RA users has not been previously reported. Porto et al. and Lavu et al. both reported an increased risk of joint injections among GLP-1RA users compared with controls in hip and knee OA^{8,9}; however, the mean number of injections was not reported. It is important to note that the injection code used in the present study was not specific to the shoulder; therefore, injections administered to other major joints may have been included in the analysis.

This study has several limitations. First, because of limitations inherent to the database, we were unable to control for the severity of shoulder OA at baseline or confirm patient adherence to prescribed medications. In addition, the retrospective design introduces inherent limitations regarding causal inference and may be subject to unmeasured confounding and other potential biases. Furthermore, as noted above, the procedural code used to identify joint injections was not specific to the shoulder joint and may have captured injections administered to other major joints. Finally, inflammatory marker data were not available for all patients, and measured levels may have varied depending on the timing of assessment, potentially introducing measurement bias and residual confounding.

Conclusion

In patients with primary shoulder OA, GLP-1RA use was not associated with a reduced risk of TSA and was associated with a higher likelihood of major joint injections, despite lower inflammatory marker levels among users. These findings highlight the need for further investigation to clarify the clinical significance of these associations and to support evidence-based patient counseling. A deeper understanding of this relationship may help clinicians guide treatment decisions and manage expectations for patients receiving GLP-1RA therapy.

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References

- Ibounig T, Simons T, Launonen A, Paavola M. Glenohumeral osteoarthritis: an overview of etiology and diagnostics. *Scand J Surg.* 2021;110(3):441-451. doi:10.1177/1457496920935018.
- Chillemi C, Franceschini V. Shoulder osteoarthritis. *Arthritis.* 2013;2013:370231. doi:10.1155/2013/370231.
- Wagner ER, Farley KX, Higgins I, Wilson JM, Daly CA, Gottschalk MB. The incidence of shoulder arthroplasty: rise and future projections compared with hip and knee arthroplasty. *J Shoulder Elbow Surg.* 2020;29(12):2601-2609. doi:10.1016/j.jse.2020.03.049.
- Collins L, Costello RA. Glucagon-Like Peptide-1 Receptor Agonists. *StatPearls.* 2025.
- Watanabe JH, Kwon J, Nan B, Reikes A. Trends in glucagon-like peptide 1 receptor agonist use, 2014 to 2022. *J Am Pharm Assoc.* 2024;64(1):133-138. doi:10.1016/j.japh.2023.10.002.
- Mehdi SF, Pusapati S, Anwar MS, et al. Glucagon-like peptide-1: a multi-faceted anti-inflammatory agent. *Front Immunol.* 2023;14:1148209. doi:10.3389/fimmu.2023.1148209.
- Cheng J, Solomon T, Estee M, Cicuttini FM, Lim YZ. Effect of glucagon-like peptide-1 receptor agonists in osteoarthritis: A systematic review of pre-clinical and human studies. *Osteoarthritis Cartilage Open.* 2025;7(1):100567. doi:10.1016/j.ocarto.2025.100567.
- Lavu MS, Porto JR, Hecht II CJ, et al. The Five-Year Incidence of Progression to Osteoarthritis and Total Joint Arthroplasty in Patients Prescribed Glucagon-Like Peptide 1 Receptor Agonists. *J Arthroplasty.* 2024;39(10):2433-2439.e1. doi:10.1016/j.arth.2024.06.008.
- Porto JR, Lavu MS, Hecht CJ, et al. The Impact of Contemporary Glucagon-like Peptide-1 Receptor Agonists on the Onset, Severity, and Conversion to Arthroplasty in Hip and Knee Osteoarthritis. *Orthop J Sports Med.* 2025;13(1):23259671241297157. doi:10.1177/23259671241297157.
- Chen J, Xie JJ, Shi KS, et al. Glucagon-like peptide-1 receptor regulates endoplasmic reticulum stress-induced apoptosis and the associated inflammatory response in chondrocytes and the progression of osteoarthritis in rat. *Cell Death Dis.* 2018;9(2):212. doi:10.1038/s41419-017-0217-y.
- Li H, Chen J, Li B, Fang X. The protective effects of dulaglutide against advanced glycation end products (AGEs)-induced degradation of type II collagen and aggrecan in human SW1353 chondrocytes. *Chem Biol Interact.* 2020;322:108968. doi:10.1016/j.cbi.2020.108968.
- Mei J, Sun J, Wu J, Zheng X. Liraglutide suppresses TNF-alpha-induced degradation of extracellular matrix in human chondrocytes: a therapeutic implication in osteoarthritis. *Am J Transl Res.* 2019;11(8):4800-4808.
- Meurot C, Martin C, Sudre L, et al. Liraglutide, a glucagon-like peptide 1 receptor agonist, exerts analgesic, anti-inflammatory and anti-degradative actions in osteoarthritis. *Sci Rep.* 2022;12(1):1567. doi:10.1038/s41598-022-05323-7.
- Tong C, Liang H, Liu X, et al. The protective effects of exenatide against AGEs-induced articular matrix degradation in human primary chondrocytes. *Am J Transl Res.* 2019;11(4):2081-2089.
- Zhang X, Jiang J, Xu J, Chen J, Gu Y, Wu G. Liraglutide, a glucagon-like peptide-1 receptor agonist, ameliorates inflammation and apoptosis via inhibition of receptor for advanced glycation end products signaling in AGEs induced chondrocytes. *BMC Musculoskelet Disord.* 2024;25(1):601. doi:10.1186/s12891-024-07640-6.
- Zhu H, Zhou L, Wang Q, et al. Glucagon-like peptide-1 receptor

- agonists as a disease-modifying therapy for knee osteoarthritis mediated by weight loss: findings from the
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. Bartholdy C, Overgaard A, Gudbergesen H, Bliddal H, Kristensen LE, Henriksen M. Changes in physical activity during a one-year weight loss trial with liraglutide vs placebo in participants with knee osteoarthritis: Secondary analyses of a randomised controlled trial. *Osteoarthritis Cartilage Open.* 2022;4(2):100255. doi:10.1016/j.ocarto.2022.100255.
 19. Davis WR, Bank NC, Lauck BJ, Creighton RA, Mistovich RJ. How do GLP-1 receptor agonists influence the progression of shoulder pathology? A matched cohort analysis. *JSES Rev Rep Tech.* 2025;6(1):100613. doi: 10.1016/j.xrrt.2025.100613.
 20. Dainese P, Mahieu H, De Mits S, Wittoek R, Stautemas J, Calders P. Associations between markers of inflammation and altered pain perception mechanisms in people with knee osteoarthritis: a systematic review. *RMD Open.* Shanghai Osteoarthritis Cohort. *Ann Rheum Dis.* 2023;82(9):1218-1226. doi: 10.1136/ard-2023-223845. 2023;9(2):e002945. doi:10.1136/rmdopen-2022-002945.
 21. Jin X, Beguerie JR, Zhang W, et al. Circulating C reactive protein in osteoarthritis: a systematic review and meta-analysis. *Ann Rheum Dis.* 2015;74(4):703-10. doi:10.1136/annrheumdis-2013-204494.
 22. Pearle AD, Scanzello CR, George SS, et al. Elevated C-reactive protein levels in osteoarthritis are associated with local joint inflammation. *Arthritis Res Ther.* 2004;6(Suppl 3):56. doi:10.1186/ar1391.
 23. Smith JW, Martins TB, Gopez E, Johnson T, Hill HR, Rosenberg TD. Significance of C-reactive protein in osteoarthritis and total knee arthroplasty outcomes. *Ther Adv Musculoskelet Dis.* 2012;4(5):315-25. doi:10.1177/1759720X12455959.
 24. Haj Shehadeh T, Chaudhry J, Abdeen A, Updegrave G, Armstrong A, Lanham N. Metformin does not decrease the incidence of shoulder arthroplasty in patients with glenohumeral joint osteoarthritis. *JSES Rev Rep Tech.* 2025;5(4):621-624. doi: 10.1016/j.xrrt.2025.07.006.

Supplementary Table

Supplementary Table 1. The diagnostic codes used to query the database.

Diagnoses	Code
Primary osteoarthritis, shoulder	ICD-10 - M19.01
Post-traumatic osteoarthritis, shoulder	ICD-10 - M19.11
Secondary osteoarthritis, shoulder	ICD-10 - M19.21
Fracture of upper end of humerus	ICD-10 - S42.2
Shoulder lesions	ICD-10 - M75
Idiopathic aseptic necrosis of shoulder	ICD-10 - M87.01
Idiopathic aseptic necrosis of humerus	ICD-10 - M87.02
Medications	Code
Glucagon-like peptide-1 (GLP-1) analogues	ATC: A10BJ
Outcomes	Code
Shoulder arthroplasty	CPT - 23472; ICD10 - ORRJ00Z, ORRJ07Z, ORRJ0JZ, ORRJ0KZ, ORRK00Z, ORRK07Z, ORRK0JZ, ORRK0KZ
Major joint injection	SNOMED: 119629003, 290035003, 308028008 CPT: 20610, 20611
C-reactive Protein	TNX - 9063
Erythrocyte sedimentation rate	TNX - 9066
Cortisol	TNX - 9035

ICD-10: International Classification of Diseases; CPT: Current Procedural Terminology; TNX: TriNetX Proprietary Code System