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Impact of GLP-1 Receptor Agonists on Postoperative Complications and Long-Term Outcomes in Total Knee Arthroplasty: A Retrospective Cohort Study Stratified by BMI

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ABSTRACT

Purpose:

Obesity is a recognized risk factor for adverse outcomes after total knee arthroplasty (TKA), including increased postoperative complications and revision rates. Glucagon-like peptide-1 (GLP-1) receptor agonists reduce obesity-related health risks; however, their impact on postoperative outcomes in TKA patients, particularly across different body mass index (BMI) categories, remains unclear. This study evaluates the association between GLP-1 receptor agonist use and short- and long-term outcomes following TKA, stratified by BMI.

Methods:

A retrospective cohort study was performed using the PearlDiver database, identifying patients who underwent primary TKA between 2010 and 2021 using ICD-9/10 and CPT codes. GLP-1 receptor agonist users were matched 4:1 to non-users based on age, sex, and Charlson Comorbidity Index. Patients were stratified into six BMI categories (<19.9, 20.0–24.9, 25.0–29.9, 30.0–34.9, 35.0–39.9, and ≥40.0 kg/m²). Outcomes included 90-day medical complications and two-year surgical events.

Results:

Among 47,359 GLP-1 users and 12,032 matched controls, GLP-1 use was associated with significantly lower 90-day postoperative complication rates across BMI categories, particularly among patients with BMI ≥30 who had reduced incidences of renal failure, anemia, cardiac arrhythmias, pulmonary embolism, pneumonia, and stroke ($p<0.05$). At two years, GLP-1 users

demonstrated significantly lower rates of periprosthetic fractures, revision surgeries, mechanical loosening, and prosthetic joint infections, most notably in patients with BMI 25–29.9 and ≥30 ($p<0.05$).

Conclusion:

GLP-1 receptor agonist use is associated with reduced postoperative complications and improved long-term surgical outcomes, especially in patients with higher BMI, suggesting a potential role in perioperative optimization for obese TKA patients.

Level of Evidence: III

Keywords: Total Knee Arthroplasty; GLP-1 Receptor Agonists; Postoperative Complications; Body Mass Index; Outcomes

INTRODUCTION

Total knee arthroplasty (TKA) is a widely performed surgical procedure for managing advanced osteoarthritis. However, postoperative complications and the risk of long-term implant failure remain concerning, particularly among patients with obesity. Elevated body mass index (BMI) has consistently been associated with adverse outcomes, including higher rates of infection, thromboembolic events, and revision surgeries[1,2]. As the prevalence of obesity continues to rise, the need for effective perioperative strategies to mitigate these risks has become increasingly important.

While numerous studies have documented the relationship between obesity and poor postoperative outcomes in TKA, few have explored pharmacologic interventions aimed at reducing this risk[11,12]. Glucagon-like peptide-1 (GLP-1) receptor agonists, originally developed for type 2 diabetes management, have gained recognition for their ability to induce weight loss and improve metabolic parameters[3]. Recent research suggests potential benefits of GLP-1 agents in the preoperative setting; however, existing studies are limited in scale, often lack stratification by BMI, and fail to address whether these agents influence specific surgical outcomes such as complications or revisions after TKA.

Despite their promise, the impact of GLP-1 receptor agonists on postoperative and long-term outcomes in TKA patients remains poorly characterized, particularly when stratified by BMI. While some evidence supports their general health benefits, few studies have investigated whether GLP-1 use can translate into measurable improvements in surgical recovery. Understanding this relationship is especially relevant for patients with obesity, who often face significant perioperative risk and stand to benefit most from effective preoperative optimization.

In this retrospective cohort study, we evaluate the association between GLP-1 receptor agonist use and postoperative outcomes in patients undergoing primary TKA, using a large national administrative claims database. By stratifying patients across six BMI categories, we aim to determine whether GLP-1 therapy is linked to reduced 90-day complications and improved two-year surgical outcomes. Through this analysis, we seek to clarify the potential therapeutic role of GLP-1 agents in the perioperative management of TKA patients and contribute to the development of targeted strategies for reducing obesity-related surgical risks.

METHODS

Study Design

This retrospective cohort study was performed using the Mariner170 dataset within the PearlDiver national administrative claims database (PearlDiver Technologies, Colorado Springs, CO), which includes deidentified patient-level data spanning from 2010 to 2023. The database comprises over 170 million patients from diverse payer sources, including commercial insurance, Medicare, Medicaid, self-pay, and other government-sponsored programs. The M170Ortho subset was utilized to capture diagnoses, procedures, and outcomes relevant to orthopedic interventions. Patients were queried using ICD-9, ICD-10, and CPT codes. As all patient data were fully deidentified and Health Insurance Portability and Accountability Act compliant, the study was exempt from institutional review board approval.

Patient Population

Patients who underwent TKA were identified using relevant CPT and ICD codes (Supplemental Table 1). Inclusion was limited to those undergoing primary TKA between January 2010 and December 2021, with a requirement of at least two years of continuous

enrollment following the index surgery to ensure complete follow-up. Patients receiving GLP-1 receptor agonists prior to surgery were identified via pharmacy claims and formed the GLP-1 group. Preoperative GLP-1 receptor agonist use was defined as ≥1 pharmacy claim for a GLP-1 receptor agonist in the two years preceding the TKA index date. GLP-1 receptor agonists were evaluated as a therapeutic class; individual agents, dosage, medication adherence, and exact duration of therapy could not be reliably determined from the available claims data. Those without prescriptions for GLP-1 medications served as controls. Both groups were stratified by BMI based on CDC classifications: underweight (<19.9 kg/m2), normal weight (20.0-24.9 kg/m2), overweight (25.0-29.9 kg/m2), class I obesity (30.0-34.9 kg/m2), class II obesity (35.0-39.9 kg/m2), and class III obesity (≥40.0 kg/m2).

Demographic variables, including age, sex, and the Charlson Comorbidity Index (CCI), were recorded for each BMI cohort. Comorbidities such as hypertension, heart failure, pulmonary and renal conditions, diabetes, and others were identified using ICD codes and also stratified by BMI subgroups. To reduce selection bias, a 4:1 matching ratio was implemented using the PearlDiver MATCH function, aligning GLP-1 users with non-users within each BMI group based on age bracket, sex, and CCI. Post-matching balance was assessed using appropriate statistical methods. Matching and multivariate regression accounted for age, sex, BMI, Charlson Comorbidity Index, and diabetes; however, residual confounding may remain.

Outcome Variables

Primary outcomes included 90-day medical complications and 2-year surgical outcomes, comparing GLP-1 users to matched controls within each BMI subgroup. Ninety-day complications assessed included readmission, renal failure, anemia, arrhythmias (with and without atrial fibrillation), blood transfusion, deep vein thrombosis (DVT), congestive heart

failure, pulmonary embolism (PE), pneumonia, sepsis, stroke, urinary tract infection (UTI), and hypoglycemia. Two-year surgical endpoints included incidence of periprosthetic fractures, revision procedures, mechanical loosening, and prosthetic joint infection (PJI). A two-year follow-up was chosen to capture long-term surgical outcomes, including revision procedures, mechanical loosening, and periprosthetic fractures. These events were identified using validated ICD and CPT codes (Supplemental Table 2). To maintain data privacy per PearlDiver policy, any category with fewer than 11 patients is represented as "<11".

Statistical Analysis

Descriptive statistics were used to summarize demographic and clinical data, presented as means with standard deviations (SD) for continuous variables, and frequencies with percentages for categorical variables. Differences in continuous variables were evaluated using Welch's t-test, while chi-square (χ^2) tests with Yates' continuity correction were used to compare categorical variables and complication rates between cohorts. A p-value <0.05 was used to denote statistical significance. All analyses were conducted using R software (R Foundation for Statistical Computing, Vienna, Austria) embedding within the PearlDiver database. Postoperative complications were identified using validated ICD-9, ICD-10, and CPT codes recorded within predefined postoperative follow-up intervals; 90-day medical complications were captured from claims occurring within 90 days following the index procedure, whereas revision procedures and surgical complications were identified during the two-year postoperative follow-up period using standardized coding definitions. Because administrative claims capture any diagnosis coded during the follow-up window, reported rates reflect all coded events in that interval and should be interpreted as relative comparisons between matched cohorts rather than absolute institutional benchmarks.

RESULTS

From a total of 1,203,421 patients who underwent primary TKA between 2010 and 2021 in the PearlDiver database, 47,359 patients had preoperative GLP-1 receptor agonist prescriptions. After 4:1 matching, a total of 47,359 GLP-1 users and 12,032 control patients undergoing TKA were identified across six BMI strata (<19.9, 20–24.9, 25–29.9, 30–34.9, 35–39.9, ≥40). Demographic characteristics including age, sex, and CCI were well-balanced between GLP-1 and control cohorts, with no significant differences across all BMI groups (Table 1).

Comorbidity Differences

GLP-1 users consistently demonstrated lower rates of multiple comorbidities compared to matched controls, particularly in patients with BMI ≥30.0. Specifically, GLP-1 users had significantly lower rates of congestive heart failure, cardiac arrhythmia, heart valve disorders, pulmonary disease, peripheral vascular disease, hypertension, coagulopathy, metastatic and non-metastatic cancer, peptic ulcer disease, lymphoma, rheumatoid arthritis, and electrolyte abnormalities across most BMI ≥30.0 categories ($p<0.001$). Notably, GLP-1 cohorts showed significantly reduced substance-related disorders, tobacco use, and alcohol disorders in the majority of BMI subgroups ≥25.0 ($p<0.05$). Depression rates were similar between GLP-1 and control cohorts across all BMI categories. Interestingly, liver disease was more prevalent in the GLP-1 group at BMI 30.0–39.9 ($p<0.05$), while acute blood loss anemia was less common among GLP-1 patients at higher BMI ranges. A full overview of these comorbidities stratified by BMI category is depicted in Table 2.

Ninety-Day Complications

At 90 days postoperatively, GLP-1 users experienced significantly lower rates of several medical complications compared to controls, with variation in effect by BMI category (Table

3; Figure 1). Among patients with BMI ≥20.0, GLP-1 users demonstrated consistently reduced rates of renal failure, anemia, cardiac arrhythmias with atrial fibrillation, and UTI ($p<0.001$). In the BMI ≥25.0 cohort, significant reductions were observed in cardiac arrhythmias without atrial fibrillation, transfusion requirements, DVT, heart failure, and hypoglycemia ($p<0.01$). Additionally, among patients with BMI >40.0, GLP-1 users experienced significantly lower rates of PE ($p<0.001$) and pneumonia ($p=0.001$), as well as reduced incidence of sepsis ($p<0.001$) and stroke ($p=0.002$). Readmission rates were also significantly reduced in the GLP-1 group for BMI ≥30.0 ($p<0.05$).

Two-Year Surgical Outcomes

GLP-1 users exhibited improved surgical outcomes two years after TKA, demonstrating significantly lower rates of periprosthetic fractures, revision surgery, mechanical loosening, and PJI compared to matched controls (Table 3; Figure 2). Specifically, periprosthetic fracture rates were lower in GLP-1 users with BMI ≥30.0 ($p<0.05$). Revision TKA occurred less frequently in GLP-1 patients with BMI ≥25.0 ($p<0.001$), as did mechanical loosening ($p<0.001$) and PJI ($p<0.001$) across the same BMI range. These associations were most consistent in patients with BMI ≥30.0; however, given the observational design, they should be interpreted as a possible protective association rather than a demonstrated causal effect, and residual confounding cannot be excluded.

DISCUSSION

We found that preoperative GLP-1 use in primary TKA patients was associated with consistently lower rates of 90-day postoperative complications, including renal failure, anemia, cardiac arrhythmias, and infectious complications, especially in patients with BMI ≥25. In addition, two-year surgical outcomes such as revision TKA, mechanical loosening,

periprosthetic fractures, and prosthetic joint infection were significantly improved in GLP-1 users. Unlike prior studies, this study provides BMI-stratified analysis across six categories and evaluates both short-term (90-day) and long-term (2-year) outcomes in a large national cohort, offering new insight into the potential impact of GLP-1 receptor agonists in perioperative management. These findings suggest that GLP-1 therapy may serve as a valuable tool in the perioperative optimization of patients undergoing TKA, particularly in overweight and obese patients, and should be considered as part of multidisciplinary care strategies to reduce surgical risk.

The findings of this study highlight the potential benefits of GLP-1 usage in reducing the burden of various comorbidities, namely in patients with a BMI ≥30.0 who undergo primary TKA. Notably, the significantly lower rates of conditions such as congestive heart failure, cardiac arrhythmia, pulmonary disease, and several types of cancer in the GLP-1 cohort may reflect broader systemic benefits of GLP-1 therapy beyond weight loss alone. However, it is important to consider the potential for selection bias, as individuals who are prescribed GLP-1 receptor agonists might be more health-conscious and more likely to engage with healthcare, which could independently contribute to the reduced prevalence of these comorbidities. Thus, while the observed reductions in these conditions are promising, further research is needed to control for these potential biases and clarify the direct impact of GLP-1 on these outcomes. It is important to acknowledge the increased prevalence of liver disease in the GLP-1 cohort at BMI 30.0–39.9, which warrants further investigation into the long-term effects of GLP-1 therapy on liver function. One retrospective cohort study by Kanwal et al. noted GLP-1 use may be protective for progression to cirrhosis in patients with liver disease, however, the protective association was not observed in patient with prior cirrhosis, possibly suggesting a complicated relationship between liver disease and GLP-1 usage[15]. Additionally, the reduced

incidence of acute blood loss anemia in GLP-1 users at higher BMI ranges provides intriguing insights into potential protective mechanisms, though the underlying causes remain unclear due to a lack of literature regarding this particular complication. These results stress the need for further research into GLP-1 usage and comorbid conditions, specifically the long-term implications of GLP-1 therapy across diverse patient populations.

Mechanistically, the outcomes observed here may reflect the broad systemic and metabolic effects of GLP-1 receptor agonists beyond weight loss—including improvements in glycemic control, cardiovascular and renal risk factors, and inflammatory pathways—although these mechanisms remain incompletely understood[13,14]. GLP-1 receptor agonists may also influence skeletal health, with several studies suggesting that they promote bone formation and reduce bone resorption, which could plausibly contribute to the lower rates of periprosthetic fracture, mechanical loosening, and revision observed in our cohort[6,7,8]. These mechanistic links remain hypothesis-generating and require confirmation in dedicated prospective studies.

In our analysis of 90-day postoperative complications following TKA, we found that GLP-1 receptor agonist users had significantly lower rates of major medical complications, including renal failure, anemia, urinary tract infections, cardiopulmonary events, and readmission rates. These differences were most pronounced in patients with a BMI ≥40 and may reflect a protective association in higher-risk surgical candidates, although residual confounding cannot be excluded. Our data shares similarities with other recently published literature. One retrospective cohort study by Kim et al. focused on morbidly obese patients (BMI ≥40 kg/m^2) undergoing primary TKA using a large claims database. The research found that GLP-1 receptor agonist use for at least 3 months before and after surgery was associated with significant reductions in 90-day periprosthetic joint infection, medical complications,

pulmonary embolism, and readmissions compared to non-users[4]. A similar study utilizing the TriNetX research network evaluated patients undergoing primary TKA and total hip arthroplasty (THA) and found that preoperative GLP-1 receptor agonist use was associated with a decreased 90-day risk of periprosthetic joint infection and readmission compared to non-users. However, they found that there were no significant differences in other postoperative complications between the groups[5]. Collectively, these results suggest that GLP-1 receptor agonists may offer a dual benefit in optimizing metabolic profiles and improving early postoperative outcomes in patients undergoing TKA, particularly among those at highest risk.

When evaluating long-term surgical outcomes two years after TKA, GLP-1 users again demonstrated significantly better results, with lower rates of revision procedures, periprosthetic fractures, PJI, and mechanical loosening. Interestingly, our findings contrast with those of the previously mentioned study by Kim et al., which found no difference in 2-year surgical outcomes in GLP-1 users versus controls[4]. This discrepancy may reflect differences in population size, stratification by BMI, or length of exposure to therapy before and after surgical intervention. These differences in outcomes highlight the need for further research to better understand the potential role of GLP-1 agonists in long-term TKA outcomes.

While results regarding GLP-1 receptor agonists have been encouraging, there are conflicting findings concerning their impact on surgical complications. Chokshi et al. conducted a retrospective cohort study using the TriNetX Research Network to investigate the optimal timing for cessation of GLP-1 agonists before total knee and hip arthroplasty. They found that discontinuing Ozempic more than seven days prior to surgery significantly reduced the risk of anesthesia-related adverse events, including intubation, delayed emergence from anesthesia, and aspiration pneumonitis. The highest risk for these complications was observed in patients

who continued GLP-1 therapy throughout the perioperative period[9]. Conversely, a separate retrospective cohort study utilizing a national database found differing results. This study analyzed patients with type 2 diabetes undergoing TKA, comparing those on GLP-1 therapy to those not receiving GLP-1 agents. They reported no significant differences in surgical or medical complication rates between groups at 90 days. The control group exhibited higher odds of extended hospital stays, though no significant differences were found in rates of all-cause or aseptic revision at one-year postoperatively[10]. These mixed findings highlight the need for further research to clarify the perioperative management of GLP-1 agonists and their true impact on short- and long-term outcomes after total joint arthroplasty.

Despite matching and multivariable adjustment, residual confounding remains an inherent limitation of observational claims-based studies. Patients prescribed GLP-1 receptor agonists may represent a more health-conscious population with greater healthcare engagement, improved medication adherence, and more comprehensive metabolic optimization, all of which could contribute to improved postoperative outcomes independent of GLP-1 therapy itself. Consequently, the observed associations should not be interpreted as evidence of a direct causal effect but rather as hypothesis-generating findings that warrant confirmation in prospective randomized studies.

This study has limitations, with a significant one being the retrospective design and reliance on administrative claims data, which confers a risk of coding errors which can lead to inaccurate clinical details, such as specific complications, glycemic control, or surgical techniques. Another limitation is the inability to distinguish between GLP-1 agents or dosages, which may differ in efficacy. Moreover, medication adherence and duration of therapy could not be directly measured. Despite statistical adjustments, residual confounding cannot be fully

excluded, particularly regarding unmeasured factors such as medication adherence, A1c control, and hospital-level variables. The preoperative interval of GLP-1 therapy may influence outcomes; patients with shorter exposure durations may have less benefit, which is a limitation of the retrospective design. PearlDiver cannot confirm actual medication adherence, dosage, or duration; we used prescription fill data as a proxy, which may overestimate true exposure. Coding inaccuracies may under- or overestimate complication rates. BMI, while widely used, does not fully capture body composition or central adiposity, which may influence surgical outcomes. However, the use of a large, nationally representative database and BMI stratification strengthens our findings and improves generalizability. Despite the limitations, this study benefits from a large sample size and long follow-up duration. Because this is an observational study, residual confounding by unmeasured factors (e.g., diabetes severity, lifestyle) cannot be excluded. Because complications were identified using administrative claims rather than prospectively adjudicated clinical records, reported event rates may differ from those observed in institutional registries or clinical trials; consequently, these findings should be interpreted as claims-based outcome estimates within a large, nationally representative population.

Conclusion

Our findings demonstrate an association between preoperative GLP-1 receptor agonist use and improved postoperative outcomes following primary TKA, particularly among patients with elevated BMI. Because this is an observational study, these results should be regarded as hypothesis-generating; prospective studies are warranted to determine whether they reflect direct therapeutic effects of GLP-1 therapy or residual differences in patient characteristics and perioperative optimization. If validated, GLP-1 receptor agonists may have a role in the preoperative optimization of higher-risk patients undergoing TKA.

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FIGURE LEGENDS

Figure 1. Incidence of 90-day postoperative complications stratified by BMI subgroups (A-F). In cases where no bars are shown, data was <11 (NA). ns = not significant; * = p<0.05; ** = p<0.01; *** = p<0.001

Figure 2. Incidence of 2-year revision outcomes stratified by BMI subgroups. ns = not significant; * = p<0.05; ** = p<0.01; *** = p<0.001

Table 1. Demographic data of matched TKA GLP-1 cohorts stratified by BMI

Demographics	BMI										
	< 19.9			20.0 – 24.9			25.0 – 29.9			30.0 – 34.9	
	GLP-1 (n=183)	Control (n=57)	*P* Value	GLP-1 (n=815)	Control (n=225)	*P* Value	GLP-1 (n=4,093)	Control (n=1,049)	*P* Value	GLP-1 (n=11,045)	Control (n=2,802
Age, mean (SD)	63.6 (7.5)	64.0 (7.7)	0.735	65.3 (8.3)	65.4 (8.8)	0.859	65.1 (8.3)	65.2 (8.4)	0.725	63.8 (7.9)	63.9 (8.1
Sex, n (%)			0.843			0.864			0.930		
Male	50 (27.3)	17 (29.8)		250 (30.7)	71 (31.6)		1,408 (34.4)	363 (34.6)		3,935 (35.6)	1,004 (35.
Female	133 (72.7)	40 (70.2)		565 (69.3)	154 (68.4)		2,685 (65.6)	686 (65.4)		7,110 (64.4)	1,798 (64.
CCI, mean (SD)	2.8 (1.9)	2.9 (2.0)	0.700	3.0 (2.1)	3.2 (2.3)	0.214	3.0 (2.3)	3.1 (2.4)	0.435	3.0 (2.3)	3.0 (2.4)
CCI Cohorts, n (%)											
0	11 (6.0)	<11 (NA)	1.000	78 (9.6)	20 (8.9)	0.856	357 (8.7)	93 (8.9)	0.932	1,013 (9.2)	258 (9.2
1	44 (24.0)	12 (21.1)	0.774	159 (19.5)	41 (18.2)	0.735	845 (20.6)	214 (20.4)	0.895	2,233 (20.2)	561 (20.0
2	39 (21.3)	12 (21.1)	1.000	150 (18.4)	39 (17.3)	0.786	753 (18.4)	190 (18.1)	0.867	2,202 (19.9)	554 (19.8
> 3	89 (48.7)	29 (50.9)	0.885	428 (52.5)	125 (55.6)	0.463	2,138 (52.3)	552 (52.6)	0.850	5,597 (50.7)	1,429 (51.

Samples with n < 11 are not shown to protect patient privacy.

Table 2. Comorbidity differences between matched TKA GLP-1 cohorts stratified by BMI

Comorbidity	BMI																
	< 19.9			20.0 – 24.9			25.0 – 29.9			30.0 – 34.9			35.0 – 39.9			> 40.0		
	GLP-1 (n=183)	Control (n=57)	*P* Value	GLP-1 (n=815)	Control (n=225)	*P* Value	GLP-1 (n=4,093)	Control (n=1,049)	*P* Value	GLP-1 (n=11,045)	Control (n=2,802)	*P* Value	GLP-1 (n=11,544)	Control (n=2,935)	*P* Value	GLP-1 (n=19,679)	Control (n=4,964)	*P* Value
Congestive Heart Failure	56 (30.6)	26 (45.6)	0.054	218 (26.7)	66 (29.3)	0.493	1,021 (24.9)	298 (28.4)	**0.024**	2,739 (24.8)	822 (29.3)	**<0.001**	3,018 (26.1)	936 (31.9)	**<0.001**	5,991 (30.4)	1,727 (34.8)	**<0.001**
Cardiac Arrhythmia	105 (57.4)	36 (63.2)	0.535	438 (53.7)	137 (60.9)	0.067	2,189 (53.5)	612 (58.3)	**0.005**	5,776 (52.3)	1,644 (58.7)	**<0.001**	5,968 (51.7)	1,685 (57.4)	**<0.001**	10,266 (52.2)	2,811 (56.6)	**<0.001**
Heart Valve Disorders	80 (43.7)	24 (42.1)	0.951	344 (42.2)	102 (45.3)	0.446	1,644 (40.2)	476 (45.4)	**0.002**	4,174 (37.8)	1,237 (44.1)	**<0.001**	4,275 (37.0)	1,230 (41.9)	**<0.001**	6,983 (35.5)	1,994 (40.2)	**<0.001**
Pulmonary Disease	36 (19.7)	15 (26.3)	0.376	118 (14.5)	46 (20.4)	**0.038**	606 (14.8)	164 (15.6)	0.534	1,633 (14.8)	514 (18.3)	**<0.001**	1,798 (15.6)	605 (20.6)	**<0.001**	3,795 (19.3)	1,159 (23.4)	**<0.001**
Peripheral Vascular Disease	80 (43.7)	34 (59.6)	0.051	370 (45.4)	107 (47.6)	0.618	1,681 (41.1)	490 (46.7)	**0.001**	4,180 (37.8)	1,212 (43.3)	**<0.001**	4,160 (36.0)	1,256 (42.8)	**<0.001**	6,677 (33.9)	1,876 (37.8)	**<0.001**
Hypertension	177 (96.7)	54 (94.7)	0.772	765 (93.9)	194 (86.2)	**<0.001**	3,897 (95.2)	933 (88.9)	**<0.001**	10,542 (95.4)	2,593 (92.5)	**<0.001**	11,071 (95.9)	2,763 (94.1)	**<0.001**	19,020 (96.7)	4,727 (95.2)	**<0.001**
Paralysis	19 (10.4)	<11 (NA)	1.000	52 (6.4)	16 (7.1)	0.810	198 (4.8)	57 (5.4)	0.475	481 (4.4)	145 (5.2)	0.070	431 (3.7)	145 (4.9)	**0.003**	757 (3.8)	251 (5.1)	**<0.001**
Nervous System Disorders	167 (91.3)	57 (100.0)	**0.045**	758 (93.0)	207 (92.0)	0.711	3761 (91.9)	980 (93.4)	0.112	10,159 (92.0)	2,588 (92.3)	0.527	10,640 (92.2)	2,733 (93.1)	0.091	17,995 (91.4)	4,540 (91.4)	0.994
Lung Disease	<11 (NA)	<11 (NA)	0.515	11 (1.3)	<11 (NA)	0.872	40 (1.0)	16 (1.5)	0.174	118 (1.1)	37 (1.3)	0.302	128 (1.1)	42 (1.4)	0.177	227 (1.2)	52 (1.0)	0.579
Thyroid Disorders	91 (49.7)	26 (45.6)	0.696	420 (51.5)	114 (50.7)	0.877	2,052 (50.1)	490 (46.7)	0.052	5,275 (47.8)	1,286 (45.9)	0.081	5,470 (47.4)	1,300 (44.3)	**0.003**	9,199 (46.8)	2,260 (45.5)	0.128
Chronic Kidney Disease	64 (35.0)	22 (38.6)	0.734	13 (1.6)	<11 (NA)	0.897	14 (0.3)	<11 (NA)	1.000	22 (0.2)	<11 (NA)	0.661	24 (0.2)	<11 (NA)	0.162	20 (0.1)	<11 (NA)	0.544
Liver Disease	67 (36.6)	19 (33.3)	0.770	268 (32.9)	66 (29.3)	0.353	1,311 (32.0)	308 (29.4)	0.105	3,621 (32.8)	839 (29.9)	**0.004**	3,974 (34.4)	933 (31.8)	**0.007**	6,440 (32.7)	1,548 (31.2)	**0.039**
Peptic Ulcer Disease	<11 (NA)	<11 (NA)	0.163	33 (4.0)	15 (6.7)	0.140	165 (4.0)	53 (5.1)	0.168	391 (3.5)	122 (4.4)	**0.047**	376 (3.3)	133 (4.5)	**<0.001**	578 (2.9)	183 (3.7)	**0.007**
Lymphoma	<11 (NA)	<11 (NA)	1.000	15 (1.8)	<11 (NA)	0.924	71 (1.7)	30 (2.9)	**0.026**	178 (1.6)	67 (2.4)	**0.007**	184 (1.6)	60 (2.0)	0.107	295 (1.5)	112 (2.3)	**<0.001**
Metastatic Cancer	<11 (NA)	<11 (NA)	1.000	33 (4.0)	<11 (NA)	1.000	177 (4.3)	59 (5.6)	0.087	387 (3.5)	150 (5.4)	**<0.001**	351 (3.0)	128 (4.4)	**<0.001**	551 (2.8)	257 (5.2)	**<0.001**

Non-Metastatic Cancer	37 (20.2)	17 (29.8)	0.182	175 (21.5)	68 (30.2)	**0.008**	892 (21.8)	288 (27.5)	**<0.001**	2,208 (20.0)	704 (25.1)	**<0.001**	2,143 (18.6)	710 (24.2)	**<0.001**	3,372 (17.1)	1,128 (22.7)	**<0.001**
Rheumatoid Arthritis	26 (14.2)	19 (33.3)	**0.002**	135 (16.6)	48 (21.3)	0.118	563 (13.8)	195 (18.6)	**<0.001**	1,509 (13.7)	453 (16.2)	**<0.001**	1,502 (13.0)	510 (17.4)	**<0.001**	2,505 (12.7)	821 (16.5)	**<0.001**
Coagulopathy	42 (23.0)	21 (36.8)	0.056	197 (24.2)	62 (27.6)	0.341	816 (19.9)	249 (23.7)	**0.007**	1,943 (17.6)	639 (22.8)	**<0.001**	1,950 (16.9)	659 (22.5)	**<0.001**	3,264 (16.6)	1,043 (21.0)	**<0.001**
Electrolyte Abnormalities	113 (61.7)	43 (75.4)	0.083	485 (59.5)	126 (56.0)	0.384	2,131 (52.1)	563 (53.7)	0.371	5,361 (48.5)	1,433 (51.1)	**0.015**	5,493 (47.6)	1,523 (51.9)	**<0.001**	9,624 (48.9)	2,635 (53.1)	**<0.001**
Acute Blood Loss Anemia	18 (9.8)	<11 (NA)	0.780	81 (9.9)	25 (11.1)	0.696	379 (9.3)	109 (10.4)	0.291	936 (8.5)	260 (9.3)	0.188	923 (8.0)	283 (9.6)	**0.004**	1,664 (8.5)	461 (9.3)	0.066
Anemia	119 (65.0)	42 (73.7)	0.292	549 (67.3)	151 (67.1)	1.000	2,505 (61.2)	654 (62.3)	0.520	6,268 (56.7)	1,708 (61.0)	**<0.001**	6,331 (54.9)	1,765 (60.2)	**<0.001**	11,036 (56.1)	3,007 (60.6)	**<0.001**
Alcohol Disorders	20 (10.9)	11 (19.3)	0.156	80 (9.8)	31 (13.8)	0.114	262 (6.4)	91 (8.7)	**0.011**	670 (6.1)	222 (7.9)	**<0.001**	656 (5.7)	253 (8.6)	**<0.001**	989 (5.0)	380 (7.7)	**<0.001**
Substance Related Disorders	74 (40.4)	35 (61.4)	**0.008**	280 (34.4)	102 (45.3)	**0.003**	1,225 (29.9)	398 (37.9)	**<0.001**	3,256 (29.5)	961 (34.3)	**<0.001**	3,378 (29.3)	994 (33.9)	**<0.001**	5,591 (28.4)	1,670 (33.6)	**<0.001**
Psychosis	15 (8.2)	<11 (NA)	0.077	40 (4.9)	16 (7.1)	0.259	187 (4.6)	65 (6.2)	**0.036**	502 (4.5)	145 (5.2)	0.174	507 (4.4)	167 (5.7)	**0.003**	865 (4.4)	321 (6.5)	**<0.001**
Depression	115 (62.8)	42 (73.7)	0.179	474 (58.2)	129 (57.3)	0.884	2,263 (55.3)	573 (54.6)	0.725	5,975 (54.1)	1,557 (55.6)	0.169	6,430 (55.7)	1,627 (55.4)	0.812	11,247 (57.1)	2,904 (58.5)	0.089
Tobacco Use	96 (52.5)	38 (66.7)	0.083	420 (51.5)	129 (57.3)	0.142	1,953 (47.7)	581 (55.4)	**<0.001**	5,313 (48.1)	1,497 (53.4)	**<0.001**	5,531 (47.9)	1,523 (51.9)	**<0.001**	8,884 (45.2)	2,473 (49.8)	**<0.001**

Samples with n < 11 are not shown to protect patient privacy.

Table 3. Analysis of 90-day postoperative complications and 2-year surgical outcomes between matched TKA GLP-1 cohorts stratified by BMI

Outcome	BMI																
	< 19.9			20.0 – 24.9			25.0 – 29.9			30.0 – 34.9			35.0 – 39.9			> 40.0		
	GLP-1 (n=183)	Control (n=57)	*P* Value	GLP-1 (n=815)	Control (n=225)	*P* Value	GLP-1 (n=4,093)	Control (n=1,049)	*P* Value	GLP-1 (n=11,045)	Control (n=2,802)	*P* Value	GLP-1 (n=11,544)	Control (n=2,935)	*P* Value	GLP-1 (n=19,679)	Control (n=4,964)	*P* Value
90-Day																		
Readmission	<11 (NA)	<11 (NA)	1.000	<11 (NA)	<11 (NA)	1.000	<11 (NA)	<11 (NA)	0.655	17 (0.2)	<11 (NA)	**0.004**	18 (0.2)	<11 (NA)	**0.007**	28 (0.1)	14 (0.3)	**0.031**
Renal Failure	15 (8.2)	14 (24.6)	0.853	104 (12.8)	49 (21.8)	**<0.001**	509 (12.4)	232 (22.1)	**<0.001**	1,351 (12.2)	639 (22.8)	**<0.001**	1,361 (11.8)	703 (24.0)	**<0.001**	2,050 (10.4)	1,232 (24.8)	**<0.001**
Anemia	38 (20.8)	26 (45.6)	0.134	183 (22.5)	84 (37.3)	**<0.001**	781 (19.1)	368 (35.1)	**<0.001**	1,975 (17.9)	949 (33.9)	**<0.001**	1,955 (16.9)	953 (32.5)	**<0.001**	3,474 (17.6)	1,792 (36.1)	**<0.001**
Arrhythmia with Atrial Fibrillation	20 (10.9)	13 (22.8)	0.223	69 (8.5)	35 (15.6)	**<0.001**	315 (7.7)	184 (17.5)	**<0.001**	836 (7.6)	435 (15.5)	**<0.001**	895 (7.8)	484 (16.5)	**<0.001**	1,457 (7.4)	895 (18.0)	**<0.001**
Arrhythmia without Atrial Fibrillation	<11 (NA)	<11 (NA)	0.763	41 (5.0)	34 (15.1)	0.419	218 (5.3)	131 (12.5)	**<0.001**	546 (4.9)	362 (12.9)	**<0.001**	541 (4.7)	346 (11.8)	**<0.001**	917 (4.7)	674 (13.6)	**<0.001**
Transfusion	<11 (NA)	<11 (NA)	0.782	15 (1.8)	16 (7.1)	0.858	70 (1.7)	40 (3.8)	**0.004**	150 (1.4)	111 (4.0)	**0.016**	159 (1.4)	112 (3.8)	**0.004**	455 (2.3)	272 (5.5)	**<0.001**
Deep Vein Thrombosis	<11 (NA)	<11 (NA)	0.257	15 (1.8)	<11 (NA)	0.317	79 (1.9)	45 (4.3)	**0.002**	204 (1.8)	119 (4.2)	**<0.001**	217 (1.9)	124 (4.2)	**<0.001**	491 (2.5)	279 (5.6)	**<0.001**
Heart Failure	<11 (NA)	15 (26.3)	0.144	43 (5.3)	34 (15.1)	0.305	193 (4.7)	134 (12.8)	**0.001**	624 (5.6)	424 (15.1)	**<0.001**	693 (6.0)	503 (17.1)	**<0.001**	1,332 (6.8)	1,047 (21.1)	**<0.001**
Pulmonary Embolism	<11 (NA)	<11 (NA)	1.000	<11 (NA)	<11 (NA)	1.000	11 (0.3)	<11 (NA)	0.827	45 (0.4)	28 (1.0)	**0.047**	45 (0.4)	31 (1.1)	0.108	181 (0.9)	123 (2.5)	**<0.001**
Pneumonia	<11 (NA)	<11 (NA)	1.000	25 (3.1)	25 (11.1)	1.000	92 (2.2)	77 (7.3)	0.249	249 (2.3)	219 (7.8)	0.166	267 (2.3)	250 (8.5)	0.455	469 (2.4)	575 (11.6)	**0.001**
Sepsis	<11 (NA)	<11 (NA)	1.000	11 (1.3)	12 (5.3)	0.835	47 (1.1)	45 (4.3)	0.835	141 (1.3)	143 (5.1)	0.906	139 (1.2)	161 (5.5)	0.204	248 (1.3)	348 (7.0)	**<0.001**
Stroke	<11 (NA)	<11 (NA)	1.000	14 (1.7)	14 (6.2)	1.000	77 (1.9)	65 (6.2)	0.314	159 (1.4)	123 (4.4)	**0.032**	149 (1.3)	125 (4.3)	0.147	202 (1.0)	268 (5.4)	**0.002**
Urinary Tract Infection	19 (10.4)	16 (28.1)	0.612	77 (9.5)	52 (23.1)	**0.028**	378 (9.2)	241 (23.0)	**<0.001**	878 (7.9)	599 (21.4)	**<0.001**	886 (7.7)	565 (19.2)	**<0.001**	1,636 (8.3)	1,109 (22.3)	**<0.001**
Hypoglycemia	<11 (NA)	<11 (NA)	1.000	<11 (NA)	<11 (NA)	0.058	19 (0.5)	<11 (NA)	**0.009**	47 (0.4)	<11 (NA)	**<0.001**	40 (0.3)	11 (0.4)	**<0.001**	105 (0.5)	59 (1.2)	**<0.001**
2-Year																		

Periprosthetic Fracture	<11 (NA)	<11 (NA)	0.564	<11 (NA)	<11 (NA)	0.655	14 (0.3)	12 (1.1)	0.695	41 (0.4)	23 (0.8)	**0.024**	48 (0.4)	28 (1.0)	**0.022**	87 (0.4)	41 (0.8)	**<0.001**
Revision	<11 (NA)	<11 (NA)	0.564	34 (4.2)	<11 (NA)	**<0.001**	124 (3.0)	37 (3.5)	**<0.001**	359 (3.2)	118 (4.2)	**<0.001**	387 (3.4)	137 (4.7)	**<0.001**	792 (4.0)	256 (5.2)	**<0.001**
Mechanical Loosening	<11 (NA)	<11 (NA)	0.257	25 (3.1)	<11 (NA)	**0.001**	105 (2.6)	51 (4.9)	**<0.001**	245 (2.2)	117 (4.2)	**<0.001**	250 (2.2)	120 (4.1)	**<0.001**	692 (3.5)	253 (5.1)	**<0.001**
Prosthetic Joint Infection	<11 (NA)	<11 (NA)	0.706	14 (1.7)	<11 (NA)	**0.008**	66 (1.6)	28 (2.7)	**<0.001**	169 (1.5)	76 (2.7)	**<0.001**	171 (1.5)	89 (3.0)	**<0.001**	426 (2.2)	191 (3.8)	**<0.001**

Samples with n < 11 are not shown to protect patient privacy.

Supplemental Table 1. ICD and CPT codes used to define cohorts.

Diagnosis/Procedure	ICD/CPT Code
BMI < 19.9	ICD-10-D-Z681,ICD-9-D-V850
BMI 20 – 24.9	ICD-10-D-Z6820, ICD-10-D-Z6821, ICD-10-D-Z6822, ICD-10-D-Z6823, ICD-10-D-Z6824,ICD-9-D-V851
BMI 25 – 29.9	ICD-10-D-Z6825, ICD-10-D-Z6826, ICD-10-D-Z6827, ICD-10-D-Z6828,ICD-10-D-Z6829,ICD-9-V8521,ICD-9-V8522,ICD-9-V8523,ICD-9-V8524,ICD-9-V8525
BMI 30 – 34.9	ICD-10-D-Z6830, ICD-10-D-Z6831, ICD-10-D-Z6832, ICD-10-D-Z6833,ICD-10-D-Z6834,ICD-9-V8530,ICD-9-D-Z6831,ICD-9-D-Z6832,ICD-9-D-Z6833,ICD-9-D-Z6834
BMI 35 – 39.9	ICD-10-D-Z6835, ICD-10-D-Z6836, ICD-10-D-Z6837, ICD-10-D-Z6838, ICD-10-D-Z6839 ICD-9-V8535, ICD-9-D-Z6836, ICD-9-D-Z6837,ICD-9-D-Z6838,ICD-9-D-Z6839
BMI > 40	ICD-10-D-Z6841,ICD-10-D-Z6842,ICD-10-D-Z6843, ICD-10-D-Z6844, ICD-10-D-Z6845, ICD-9-D-V8541, ICD-9-D-V8542,ICD-9-D-V8543, ICD-9-D-V8544, ICD-9-D-V8545
GLP-1	GENERIC_DRUG-EXENATIDE, GENERIC_DRUG-EXENATIDE_MICROSPHERES, GENERIC_DRUG-LIXISENATIDE, GENERIC_DRUG-ALBIGLUTIDE, GENERIC_DRUG-DULAGLUTIDE, GENERIC_DRUG-LIRAGLUTIDE, GENERIC_DRUG-SEMAGLUTIDE, GENERIC_DRUG-TEDUGLUTIDE
Total Knee Arthroplasty	CPT-27447

CPT, *Current Procedural Terminology*; ICD-9, *International Classification of Diseases*, *Ninth Revision*; ICD-10, *International Classification of Diseases*, *Tenth Revision*.

Supplemental Table 2. ICD and CPT codes used to define 2-year outcomes.

Comorbidity	ICD/CPT Code
Periprosthetic Fracture	ICD-9-D-99644,ICD-10-D-M9711XA, ICD-10-D-M9712XA, ICD-10-D-M978XXA, ICD-10-D-M979XXA
Revision	CPT-27486, CPT-27487, CPT-27488, ICD-10-P-0SWC07Z, ICD-10-P-0SWC0JC, ICD-10-P-0SWC0JZ, ICD-10-P-0SWC0KZ, ICD-10-P-0SWC37Z, ICD-10-P-0SWC3JC, ICD-10-P-0SWC3JZ, ICD-10-P-0SWC3KZ, ICD-10-P-0SWC47Z, ICD-10-P-0SWC4JC, ICD-10-P-0SWC4JZ, ICD-10-P-0SWC4KZ, ICD-10-P-0SWCX7Z, ICD-10-P-0SWCXJC, ICD-10-P-0SWCXJZ, ICD-10-P-0SWCXKZ, ICD-10-P-0SWD07Z, ICD-10-P- 0SWD0JC, ICD-10-P-0SWD0JZ, ICD-10-P-0SWD0KZ, ICD-10-P-0SWD37Z, ICD-10-P-0SWD3JC, ICD-10-P-0SWD3JZ, ICD-10-P-0SWD3KZ, ICD-10-P-0SWD47Z, ICD-10-P-0SWD4JC, ICD-10-P-0SWD4JZ, ICD-10-P-0SWD4KZ, ICD-10-P-0SWDX7Z, ICD-10-P-0SWDXJC, ICD-10-P- 0SWDXJZ, ICD-10-P-0SWDXKZ, ICD-9-P-0080, ICD-9-P-0081, ICD-9-P-0082, ICD-9-P-0083, ICD-9-P-0084, ICD-9-P-0085, ICD-9-P-8155
Mechanical Loosening	ICD-9-D-99647, ICD-10-D-T84098A, ICD-9-D-99641, ICD-9-D-99677, ICD-10-D-T84038A, ICD-9-D-99649, ICD-10-D-T84498A, ICD-10-D-T8489XA
Prosthetic Joint Infection	ICD-10-D-T8450XA, ICD-10-D-T8450XD, ICD-10-D-T8450XS, ICD-10-D-T8459XA, ICD-10-D-T8459XD, ICD-9-D-99666

CPT, *Current Procedural Terminology*; ICD-9, *International Classification of Diseases*, *Ninth Revision*; ICD-10, *International Classification of Diseases*, *Tenth Revision*.

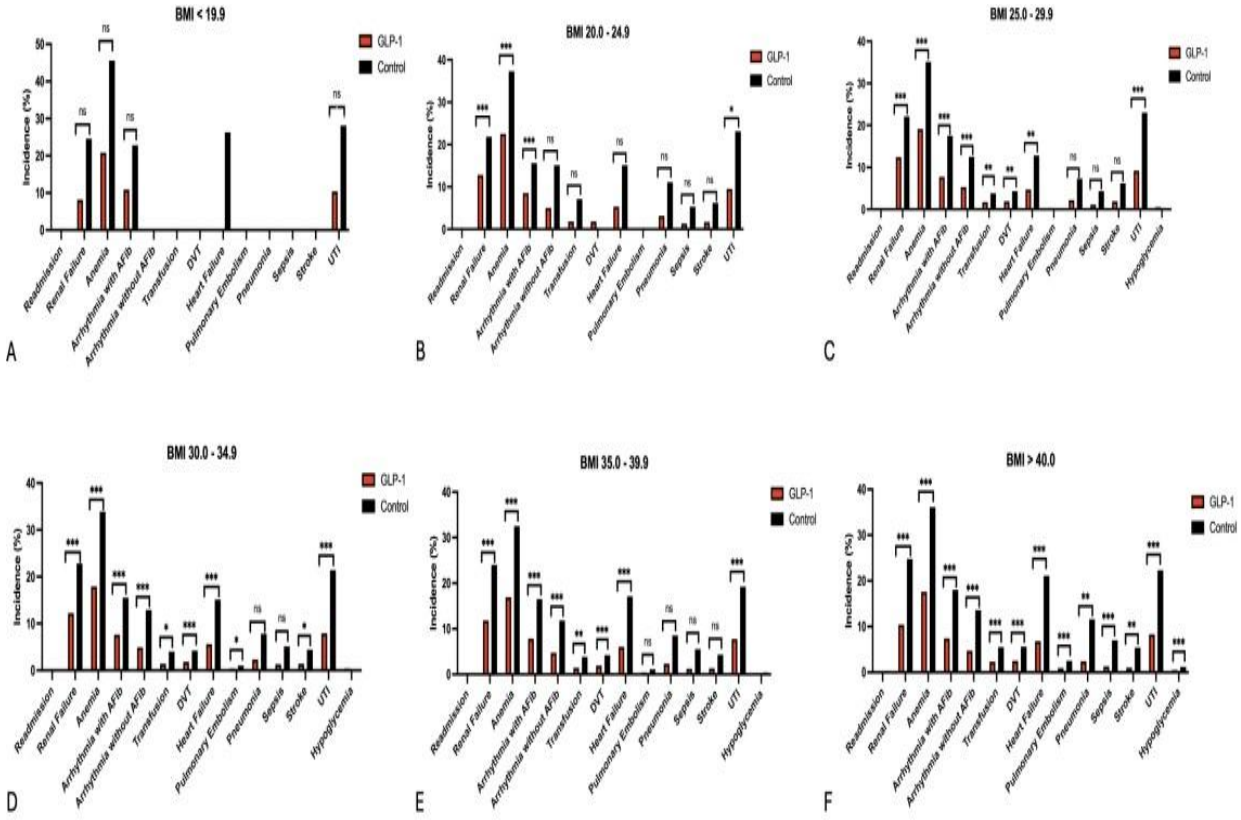

Figure 1. Incidence of 90-day postoperative complications stratified by BMI subgroups (A-F). In cases where no bars are shown, data was <11 (NA). ns = not significant; * = p<0.05; ** = p<0.01; *** = p<0.001

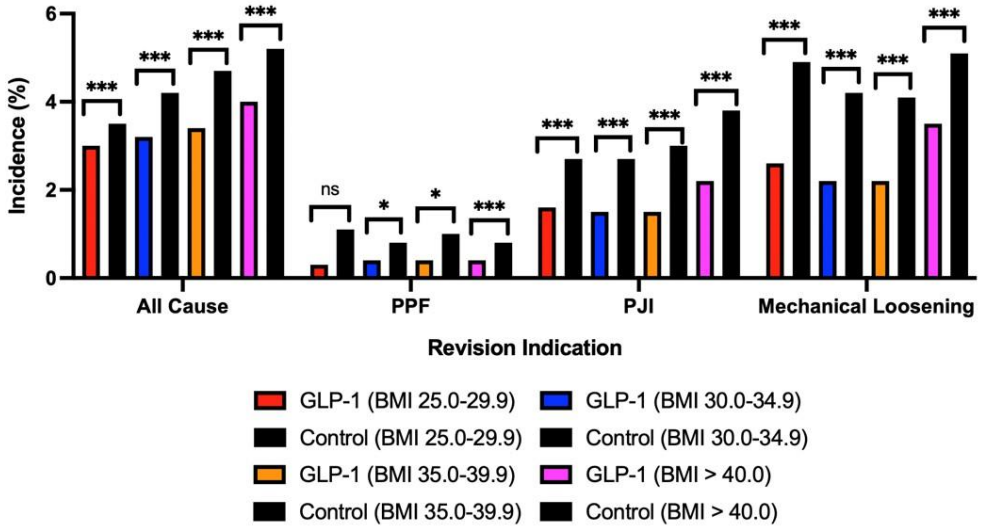

Figure 2. Incidence of 2-year revision outcomes stratified by BMI subgroups. ns = not significant; * = $p<0.05$; ** = $p<0.01$; *** = $p<0.001$