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Prolonged Use of Newly Prescribed Gabapentin After Surgery

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Abstract

Background—Surgeons have made substantial efforts to decrease postoperative opioid prescribing, largely because it can lead to prolonged use. These efforts include adoption of non-opioid pain medication including gabapentin. Like opioids, gabapentin use may be prolonged, increasing the risk of altered mental status and even overdose and death when taken concurrently with opioids. However, little is known about postoperative prolonged use of gabapentin in older adults.

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Conflict of Interest:

The authors have no conflicts of interest. Dr Finlayson is co-founder of Ooney Inc.

Methods—We merged a 20% sample of Medicare Carrier, MedPAR and Outpatient Files with Part D for 2013-2018. We included patients >65 years old without prior gabapentinoid use who underwent common non-cataract surgical procedures. We defined new postoperative gabapentin as fills for 7 days before surgery until 7 days after discharge. We excluded patients whose discharge disposition was hospice or death. The primary outcome was prolonged use of gabapentin, defined as a fill>90 days after discharge. To identify risk factors for prolonged use we constructed logistic regression models, adjusted for procedure and patient characteristics, length of stay, disposition location and care complexity.

Results—Overall, 17,970 patients (3% of all eligible patients) had a *new* prescription for gabapentin after surgery. Of these, the mean age was 73 years-old and 62% were female. The most common procedures were total knee (45%) and total hip (21%) replacements. Prolonged use occurred in 22%. Those with prolonged use were more likely to be women (64% vs 61%), be non-white (14% vs 12%), have concurrent prolonged opioid use (44% vs 18%), and have undergone emergency surgery (8% vs 4%). On multivariable analysis, being female, having a higher Charlson comorbidity score, having an opioid prescription at discharge and at >90 days and having a higher care complexity were associated with prolonged use of gabapentin.

Conclusions—More than one-fifth of older adults prescribed gabapentin postoperatively filled a prescription >90 days after discharge, especially among patients with more comorbidities and concurrent prolonged opioid use, increasing the risk of adverse drug events and polypharmacy.

Keywords

pain control; postoperative care; deprescribing; older adults **(3-5)**

Introduction

In a recent nationwide shift, surgeons have sought to decrease postoperative opioid prescribing by adopting the use of non-opioid ‘multimodal’ pain regimens.[1–4] Gabapentinoids (gabapentin and pregabalin) are now commonly administered during the postoperative period for many surgical patients, especially with the rise in adoption of ‘enhanced recovery after surgery’ pathways.[4] Multimodal pain medication use, including that of gabapentin, has tripled in the U.S. over the past decade.[5] Studies indicate that a single preoperative dose of a gabapentinoid is associated with a decrease in postoperative pain and opioid consumption at 24 hours.[6] However, gabapentinoids also increase postoperative sedation and dizziness in both the short and long-term.[7,8]

In older adults (age ≥ 65), who account for almost half of all surgical patients each year in the US,[9] gabapentinoids are often poorly tolerated because of pharmacokinetic and pharmacodynamic changes associated with aging, comorbidities, and interactions with other medications.[10] In fact, gabapentinoids are included in the AGS Beers Criteria list, explicitly detailing potentially inappropriate medications (PIMs) for older adults. There are strong recommendations to avoid using with opioids, due to risk of overdose, respiratory depression and death, except when transitioning from one to the other,[11,12] and to dose reduce in older adults with poor kidney function.[11] The use of PIMs has been associated with adverse drug reactions and increased mortality across a wide variety of surgical procedures.[13,14]

Nevertheless, older age is one of several risk factors for receiving more opioids and multimodal pain medication in the postoperative period.[5,15] While short-term use has all of these inherent risks, much like opioids, gabapentin can be continued long-term with the risk of altered mental status, dizziness, and drowsiness.[11,16] Prolonged use also has its own unique hazards by contributing to polypharmacy, shown to increase adverse events and hospitalizations.[17,18]

The shift towards multimodal pain regimens, including gabapentin, has taken place without attention to ensuring that they, like opioids, are appropriately discontinued soon after surgery. The prevalence of prolonged use of post-operative gabapentin among older adults is unknown, as are the factors associated with prolonged use. Finally, the incidence of prolonged use in conjunction with opioids, a combination found to lead to serious adverse events including overdose and death,[11,12] has not been studied. Therefore, we sought to describe prolonged use of postoperatively prescribed gabapentin and characterize the associated patient and medication-related factors.

Methods

Data Source

We used the 20% Medicare sample for years 2013-2018. Medicare is a federal health insurance program which covers approximately 97% of all US citizens ≥65[19] and the dataset is a 20% representative sample. We merged Medicare Carrier, MedPAR and Outpatient Files with Part D files and used the Master Beneficiary Summary File (MBSF) base file, the chronic conditions segment, the other chronic or potentially disabling conditions segment, and the National Death Index segment to determine cohort composition regarding age, gender, race and comorbidity score, identify hospitalizations and fee-for service claims at free-standing ambulatory surgical centers for specifically identified procedures, discharge location and identify prescription fills. The study was approved by the University of California San Francisco Institutional Review Board.

Study Population

We included patients ≥ 66 years at time of the procedure undergoing one of the 14 most common non-cataract surgeries performed in older adults,[20,21] (Supplementary Appendix1) who had at least one prescription filled in the system 3 months prior to surgery. To ensure we had patients who were using their Part D benefit, we only included patients with continuous Part D coverage for 3 months before and 6 months after the procedure date. For patients who had multiple procedures over the time period, we considered only their first procedure date. We excluded patients whose discharge disposition was death or hospice,[22] who died within 30 days after discharge and patients who had ≥ 3 procedures on the same day. We excluded new pregabalin prescriptions from the analysis as these were only 0.34% of our original cohort and may represent important differences in prescribing habits.

We included patients ≥ 66 years to allow for one year prior to the procedure to compile comorbidities to calculate a Charlson comorbidity score[23] using an updated 17 disease version more appropriate for use in administrative databases.[24] The 14 surgical procedures

included represent a wide range of surgical risk, anatomic regions and surgical specialties. We defined outpatient procedures using HCPCS/CPT codes, and inpatient procedures using ICD9-CM or ICD10-PCS codes (Supplementary Appendix2). We included specific groups of patients who had two different procedures on the same day if those procedures both fell into our inclusion criteria (specifically Total Shoulder Arthroplasty/Total Knee Arthroplasty and Total Shoulder Arthroplasty/Total Hip Arthroplasty) and we combined the spinal procedures (laminectomy and laminotomy) into one category for analysis given their extensive overlap.

From this cohort (Supplementary Appendix3), we analyzed patients who had a *new* discharge prescription for gabapentin at the time of surgery. We considered a discharge prescription as any fill between 7 days before and 7 days after the surgery (or discharge for inpatients), as some surgical practices prescribe medications preoperatively. We defined a *new* fill of a gabapentin if the medication had not been prescribed in the 3 months prior to surgery.[20] We pulled the NDC codes from Part D claims and then linked them with Medispan crosswalk files to identify generic drug names and prescription information including dosage information.

Outcomes and Data Analyses

The primary outcome is prolonged use of gabapentin in the postoperative period, defined as a prescription refilled at 90-180 days after discharge from surgery, a time period based on definitions of prolonged use of opioids after surgical procedures.[20,25,26] We calculated the days' supply and average daily dose. We defined which procedures most commonly had gabapentin prescribed postoperatively, and the unadjusted risk of prolonged use for each medication category and for type of surgery. Additionally, we assessed concomitant prolonged use of opioids since that can increase the risk of adverse drug events (Supplementary Appendix4).

To identify risk factors for prolonged use we constructed logistic regression models, adjusted for procedure characteristics (surgery type), patient characteristics (age, sex, race/ethnicity, Charlson comorbidity score), length of stay, disposition location and care complexity[17,27,28] (number of physicians seen in prior 6 months). We handled competing risks through a descriptive model as the number of deaths within 30 days were too small for a Fine-Grey calculation.

Results

Patient Demographics

Of 604,356 older adults meeting inclusion criteria (Supplementary Appendix 2), 17,481 (3%) of patients had a *new* prescription for gabapentin after the index procedure and were included in our final cohort (Table 1). Of these, the mean age was 73 years old, 62% were women and 85% were white. The median Charlson comorbidity score was 1 (q1, q3; 0, 2) and the marker of care complexity, the average number of physicians seen in the prior 6 months was a median of 13 (q1, q3; 2, 17). The average length of stay was 2.9 days (sd 4.6 days). Most patients were discharged home (94%) with 41% being discharged with

home health. Surgery was planned in 94% of the cohort. Seventy-three percent of patients were also discharged with an opioid prescription, and at 90 days, 24% were still receiving an opioid. The most common two procedures with gabapentin prescribed at discharge were total knee (43%) and total hip (20%) replacements (Table 2).

Among patients with new prescriptions, 23% (n=4,031) continued to receive gabapentin prescriptions at 90+ days after surgery. Those with prolonged use were more likely to be women (24% vs 21%), be non-white (24% vs 23%) and have undergone emergency surgery (38% vs 22%). (Table 1). While only 20% of those with prolonged use had an opioid prescription at discharge (compared to 81% without prolonged use), this number rose to 41% for prolonged concomitant opioid use. The procedures with the highest proportion of prolonged use were carotid endarterectomy (64%) and laparoscopic cholecystectomy (53%). Another 5 categories of procedures had prolonged use rates in the 40-50% range including: lumbar laminotomy/laminectomy, open ventral hernia repair, open inguinal hernia repair, laparoscopic prostatectomy and laparoscopic hysterectomy (Table 2).

Associations with Prolonged Use

The univariate analysis identified multiple variables associated with prolonged use of gabapentin including older age, female sex, non-white race, higher Charlson comorbidity score, concomitant opioid use at 90 days, a procedure performed in-hospital, non-home discharge, higher care complexity and emergency surgery as risk factors for prolonged use of gabapentin (Supplementary Appendix5). The days supply at discharge was not associated with prolonged use, however variation was high between surgical populations and in some procedures those with prolonged use were discharged with more days' supply compared to those without prolonged use (Figure 1). The procedures most associated with prolonged use of gabapentin were carotid endarterectomy, laparoscopic cholecystectomy and open inguinal hernia repair.

On multivariable logistic regression, we found that female sex, higher Charlson comorbidity score, concomitant opioid use at 90 days, and emergency surgery were associated with prolonged use (Table 3). Discharge to SNF was also associated with prolonged use on multivariable analysis, however this population represented only 5% of the overall cohort. The same procedures remained with the highest odds of prolonged gabapentin use in multivariable regression.

Competing Risks

We handled competing risks descriptively. Among 604,356 patients who were hospitalized and survived thru discharge, 17,481 filled a prescription for gabapentin at discharge. Among those, 0 had died by 90 days and 17, 970 were alive at 90 days and still Part D.

Discussion

In this study, we investigated the incidence of and associations with prolonged use of gabapentin in the postoperative period. We found that prolonged use of gabapentin is high in older adults in the postoperative period with over one fifth of older adults in our cohort having prolonged use. Although prescribing was relatively infrequent, once the medication

was started it was likely to be continued. This is especially concerning given it was most likely to be continued in populations at highest risk for adverse events, such as those with a higher Charlson comorbidity score and those who underwent emergency surgery. While the procedures at highest odds for prolonged use represent a small portion of the overall population of procedures for which gabapentin is prescribed they represent procedures that may be more likely done in the emergent setting (carotid endarterectomy, laparoscopic cholecystectomy, as examples). These patients may greatly benefit from interventions that clearly prescribe pain medication for short-term use and increase communication between surgeon and PCP. While sex and race had statistically significant associations with prolonged use, the percentage differences were small between these groups and may not be clinically significant. However, we show that prolonged use of gabapentin is associated with prolonged use of opioids, especially dangerous since concomitant use of gabapentin and opioids has been found to increase the risk of opioid related overdose and death.[11,12,29]

Concerningly, our study has similar findings to many studying prolonged use of opioids. Like opioids, we found that once started, the continuation of gabapentin is relatively common. While gabapentin has some misuse potential, there are other reasons that gabapentin may be continued in the postoperative period. Transitions of care, such as discharge after a surgical procedure, are associated with medication errors or discrepancies,[30] and 19-23% of patients suffer an adverse event, most commonly an adverse drug event.[30] Prolonged use can also occur due to patients' poor understanding of medications[31] or guidance on how long to continue medications,[32] as well as lack of clinician awareness, including poor insight into why medications were originally prescribed, lack of guidelines, fear of making a change, work practice of prescribing without review, and a culture of prescribing more as opposed to reviewing lists and stopping unnecessary medications.[31] This may be especially acute in surgical procedures that aren't usually known to have neurologic pain, so physicians don't associate the prescription as short-term use connected to the surgery. Currently, little is known about why patients have prolonged use, however, this and concomitant opioid use is dangerous, especially in older adults due to the sedating effects and risk of respiratory depression.[11,12,29] Finally, the use of gabapentin has been touted as a vehicle to decrease opioid use. However, in our study, the two were often used together.

Our study has several limitations. Specific procedures, even some which were associated with prolonged use, were too small of a subgroup to meaningful interpret the results. Additionally, some patients may have received a short supply of medications from the hospital pharmacy which will not be captured in Part D data. We excluded patients with Medicare Advantage as they may not necessarily use Part D to fill medication prescriptions, which may limit our generalizability to fee-for-service beneficiaries. However, our sample size remains large despite this exclusion to allow to make robust assessments of the non-Medicare Advantage population. Finally, our ability to detect differences between racial/ethnic groups is limited by the manner in which Medicare traditionally categorized patients and has low validity in some groups.[33]

In summary, we have shown for the first time that older adults discharged with a prescription for gabapentin are likely to have prolonged use of the medication, especially if they have

more comorbid conditions, and that these patients also continue opioids. These findings suggest that broad-based shifts in pain management to avoid opioid prescribing has potential long-term effects and that close attention needs to be paid to medications meant to be used short-term in the post-surgical discharge period. While gabapentin may have some benefit in the short-term and some older adults may have persistent pain that warrants prolonged use of gabapentin, particularly after spinal surgery, we speculate that a large proportion of this prolonged use is not intentional, and that the system needs to be improved to prevent both polypharmacy and unintentional continuation. This is especially evident in the fact that the non-orthopedic procedures are at higher odds of having prolonged use, suggesting that this prolonged use may be unintentional and therefore an area important to intervene upon. As non-opioid medications are increasingly used after surgery, careful attention needs to be paid to ensuring that these medications are in fact substituting for opioids and are appropriately discontinued.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Disclosures:

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Sponsor's Role

The sponsor had no role in the design, methods, subject recruitment, data collections, analysis or preparation of the paper.

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Key Points:

Prolonged use of medications for older adults can lead to adverse events and polypharmacy yet is relatively common among older surgical patients who receive a gabapentin prescription at discharge.

Gabapentin is most commonly prescribed in patients going orthopedic or spine surgeries.

Patients undergoing surgery are more likely to have prolonged use of gabapentin if they are women, have increased comorbidities, increased care complexity or who are prescribed opioids at discharge.

Why does this matter?

Prolonged use contributes to polypharmacy in an already at-risk population. As non-opioid medications are increasingly used in the surgical patient population, careful attention needs to be paid to ensuring that these medications are in fact substituting for opioids as opposed to be given together and that the medications are then appropriately discontinued. These findings suggest that broad-based shifts in pain management to avoid opioid prescribing has potential long-term effects and that close attention needs to be paid to medications meant to be used short-term in the post-surgical discharge period, especially those that are potentially inappropriate medications.

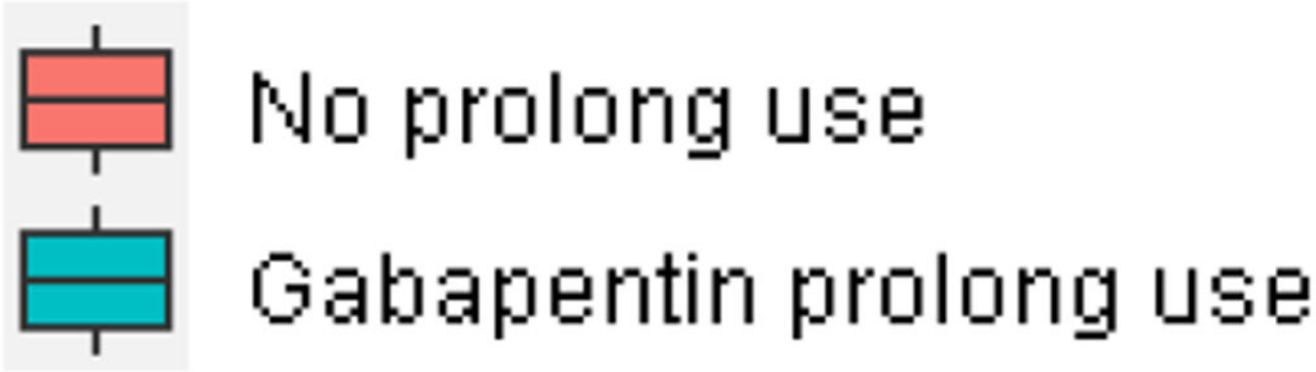

Figure 1:
Total Days Supply of Discharge Gabapentin Prescription for No prolonged Use versus Prolonged Use groups for each surgical procedure. (Median and IQR)

Table 1:

Overall Cohort for New Gabapentin prescription, prolonged vs no prolonged use

	New gabapentin prescription (N=17,481, col%)	Prolonged use (N=4,031, row%)	No prolonged use (N=13,450, row%)	p-value
Age, mean (sd)	73.0 (5.4)	73.4 (5.7)	72.9 (5.4)	<0.001[a]
Gender				<0.001[b]
Female	10750 (61.5%)	2602 (24.2%)	8148 (75.8%)	
Male	6731 (38.6%)	1429 (21.2%)	5302 (78.8%)	
Race				0.01[b]
White	14931 (85.4%)	3421 (22.9%)	11510 (77.1%)	
Black	965 (5.5%)	241 (25%)	724 (75%)	
Hispanic	859 (4.9%)	226 (26.3%)	633 (73.7%)	
Other	726 (4.2%)	143 (19.7%)	583 (80.3%)	
Race (White/Non-white)				0.26[b]
White	14931 (85.4%)	3421 (22.9%)	11510 (77.1%)	
Non-white	2550 (14.6%)	610 (23.9%)	1940 (76.1%)	
Charlson Comorbidity Score median (q1, q3)	1 (0, 2)	1 (0, 4)	1 (0, 2)	<0.001[b]
0	8119 (46.4%)	1580 (19.5%)	6539 (80.5%)	
1-2	5112 (29.2%)	1075 (21%)	4037 (79%)	
3-4	2350 (13.4%)	652 (27.7%)	1698 (72.3%)	
5+	1900(10.9%)	724 (38.1%)	1176 (61.9%)	
Gabapentin days supply	mean (sd), median (q1, q3)			
+/− 7 days around discharge	31.0 (24.6) 30 (14, 30)	50.5 (32.3) 30 (30, 90)	25.1 (18.0) 30 (14, 30)	<0.001[a]
8-89 days after discharge	56.7 (33.5) 60 (30, 90)	68.5 (31.1) 60 (30, 90)	45.4 (30.7) 30 (30, 60)	<0.001[a]
90-180 days after discharge	76.4 (37.5) 90 (45, 90)	76.4 (37.5) 90 (45, 90)	N/A	
Concurrent medication use (opioid use)				
Prescription +/− 7 days around discharge	12804 (73.3%)	2500 (19.5%)	10304 (80.5%)	<0.001[b]
90-180 days after discharge	4246 (24.3%)	1750 (41.2%)	2496 (58.8%)	<0.001[b]
Facility type				<0.001[b]
Inpatient	14224 (81.4%)	2922 (20.5%)	11302 (79.5%)	
Outpatient	3257 (18.6%)	1109 (34%)	2148 (66%)	
LOS (Inpatient only) mean (sd) median (q1, q3)	2.9 (4.6) 2 (1, 3)	4.4 (7.5) 3 (2, 4)	2.6 (3.4) 2 (1, 3)	<0.001[a]
Surgery planned				<0.001[b]
Yes	16407 (93.9%)	3619 (22.1%)	12788 (77.9%)	

	New gabapentin prescription (N=17,481, col%)	Prolonged use (N=4,031, row%)	No prolonged use (N=13,450, row%)	p-value
No	1074 (6.1%)	412 (38.4%)	662 (61.6%)	
Care complexity, median (q1, q3)				<0.001[b]
q1 (1-2)	4837 (27.7%)	1077 (22.3%)	3760 (77.7%)	
q2 (3-12)	3472 (19.9%)	658 (19%)	2814 (81%)	
q3 (13-18)	5274 (30.2%)	1119 (21.2%)	4155 (78.8%)	
q4 (19 or more)	3898 (22.3%)	1177 (30.2%)	2721 (69.8%)	

[*] Care complexity: (number of physicians seen in prior 6 months).

sd = standard deviation. q = quartile. LOS = length of stay.

[a] t-test;

[b] chi-square test

Table 2:

Cohort by Procedure Type for New Gabapentin prescription, prolonged vs no prolonged use

	New gabapentin prescription (N=17,481, col%)	With gabapentin prolonged use (N=4,031, row%)	No gabapentin prolonged use (N=13,450, row%)	p-value
Type of procedure				<0.001[a]
Total Knee Arthroplasty	7432 (42.5%)	1305 (17.6%)	6127 (82.4%)	
Total Hip Arthroplasty	3509 (20.1%)	556 (15.8%)	2953 (84.2%)	
Total Shoulder Arthroplasty/Total Knee Arthroplasty	2191 (12.5%)	896 (40.9%)	1295 (59.1%)	
Lumbar Laminotomy/Lumbar Laminectomy	1591 (9.1%)	340 (21.4%)	1251 (78.6%)	
Cholecystectomy, Laparoscopic	808 (4.6%)	131 (16.2%)	677 (83.8%)	
Initial Inguinal Hernia Repair, Open	557 (3.2%)	164 (29.4%)	393 (70.6%)	
Total Shoulder Arthroplasty /Total Hip Arthroplasty	341 (2.0%)	179 (52.5%)	162 (47.5%)	
Carotid Endarterectomy	298 (1.7%)	125 (41.9%)	173 (58.1%)	
Ventral Hernia Repair, Open	207 (1.2%)	133 (64.3%)	74 (35.7%)	
Total Shoulder Arthroplasty	165 (0.9%)	76 (46.1%)	89 (53.9%)	
Initial Inguinal Hernia Repair, Laparoscopic	146 (0.8%)	31 (21.2%)	115 (78.8%)	
Hysterectomy	99 (0.6%)	40 (40.4%)	59 (59.6%)	
Prostatectomy, Laparoscopic	76 (0.4%)	29 (38.2%)	47 (61.8%)	
Low Anterior Resection, Laparoscopic	61 (0.4%)	26 (42.6%)	35 (57.4%)	

NR = not reported as values are too small,

[a] = chi-square test

Table 3:

Multivariable analysis for prolonged use of gabapentin

	Adjusted OR (95% CI)	p-value
Age	1.00 (1.00, 1.01)	0.59
Gender		<0.001
Male	ref.	
Female	1.26 (1.16, 1.36)	
Race		0.10
White	ref.	
Non-white	0.91 (0.82, 1.02)	
Charlson Comorbidity Score		<0.001
0	ref.	
1-2	1.09 (0.98, 1.22)	
3-4	1.39 (1.22, 1.60)	
5+	1.76 (1.52, 2.03)	
Concurrent medication use (opioid use)		
+/− 7 days around discharge		<0.001
No	ref.	
Yes	0.61 (0.56, 0.66)	
90-180 days after discharge		<0.001
No	ref.	
Yes	3.10 (2.86, 3.36)	
Facility type		0.05
Inpatient	ref.	
Outpatient	1.15 (1.00, 1.31)	
Disposition location		<0.001
Home	ref.	
Home under care of organized home health service organization	0.93 (0.85, 1.03)	
Transfer to acute care	1.74 (0.82, 3.70)	
Skilled nursing Facility	1.80 (1.56, 2.08)	
Other	0.28 (0.06, 1.30)	
Surgery planned		<0.001
Yes	ref.	
No	1.38 (1.19, 1.60)	
Care complexity (number of physicians seen in prior 6 months)		<0.001
q1 (1-2)	ref.	
q2 (3-12)	0.69 (0.61, 0.79)	
q3 (13-18)	0.72 (0.63, 0.82)	
q4 (19 or more)	0.79 (0.69, 0.91)	
Type of procedure		<0.001

	Adjusted OR (95% CI)	p-value
Total Knee Arthroplasty	ref.	
Total Hip Arthroplasty	0.85 (0.76, 0.96)	
Total Shoulder Arthroplasty/Total Knee Arthroplasty	2.49 (2.19, 2.84)	
Lumbar Laminotomy/Lumbar Laminectomy	1.14 (0.99, 1.32)	
Cholecystectomy, Laparoscopic	0.80 (0.65, 0.98)	
Initial Inguinal Hernia Repair, Open	1.51 (1.22, 1.88)	
Total Shoulder Arthroplasty/Total Hip Arthroplasty	3.37 (2.62, 4.33)	
Carotid Endarterectomy	2.20 (1.70, 2.85)	
Ventral Hernia Repair, Open	5.59 (4.11, 7.61)	
Total Shoulder Arthroplasty	3.67 (2.61, 5.18)	
Initial Inguinal Hernia Repair, Laparoscopic	1.00 (0.66, 1.53)	
Hysterectomy	2.15 (1.40, 3.32)	
Prostatectomy, Laparoscopic	2.67 (1.62, 4.39)	
Low Anterior Resection, Laparoscopic	2.79 (1.63, 4.78)	

OR: Odds Ratio, CI: Confidence Interval, ref: Reference group, q: Quartile