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Initiation of Long-Acting Opioids Following Hospital Discharge Among Medicare Beneficiaries

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Scholarly Report submitted in partial fulfillment of the MD Degree at Harvard Medical School

Date: 2 April 2020

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Title: Initiation of Long-Acting Opioids following Hospital Discharge among Medicare Beneficiaries

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ABSTRACT

Background: Opioids with a longer duration of effect ("long-acting opioids") are associated with risk of overdose and morbidity compared to short-acting opioids even at equivalent dosing. Guidelines recommend against initiating long-acting opioids during hospitalization. We evaluated the prescription of long-acting opioids following hospitalization among opioid-naïve older adults.

Methods: We used a 20% random sample of fee-for-service Medicare beneficiaries with an acute care hospitalization in 2016 who were ≥65 years old, did not have cancer or hospice claims, and had not filled an opioid prescription in the 30 days prior to hospitalization. We used a multivariable generalized estimating equation model to identify characteristics associated with prescription of a long-acting opioid within 7 days of hospital discharge compared to those prescribed only short-acting opioids. Predictors included sociodemographics, chronic conditions and medication claims, markers of medical complexity and functional status, indication for hospitalization, and prior opioid use.

Results: Of 300,715 hospitalizations in our cohort, 60,305 (20%) had a claim for short-acting opioids only and 1,651 (0.6%) had at least one claim for a long-acting opioid within 7 days of discharge. 64.9% of hospitalizations resulting in long-acting opioid prescription were surgical in nature. Compared to patients with receipt of short-acting opioids after discharge, patients with receipt of long-acting opioids had higher incidence of known risk factors for opioid-related adverse events, including history of mood and anxiety disorders, opioid use disorder, prior long-term high-dose opioid use, and co-administration of multiple sedating medications. Characteristics with the strongest positive associations with long-acting, compared to short-acting opioid receipt included previous high-dose long-term opioid use (aOR 34.99, 25.99-47.11), history of opioid use disorder (aOR 2.43, 1.87-3.15), medical DRG (aOR 2.94, 2.35-3.67), principal diagnosis of diseases of the musculoskeletal system and connective tissue (aOR 2.14, 1.63-2.80), and operations on the musculoskeletal system (aOR 2.68, 2.04-3.51).

Conclusions: The majority of opioid-naïve individuals discharged with long-acting opioids after acute hospitalization are surgical patients, for whom pain is typically acute and self-limited. Moreover, patients started on long-acting opioids at discharge had higher incidence of known risk factors for opioid-related adverse events, highlighting the necessity to develop systems-based solutions to improve guideline-concordant prescribing of long-acting opioids.

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GLOSSARY OF ABBREVIATIONS

- aOR: Adjusted odds ratio
- CSS: (Agency for Healthcare Research and Quality) Clinical Classification System
- CDC: Centers for Disease Control and Prevention
- DRG: Diagnosis-related group
- ICU: Intensive Care Unit
- MCC: Medicare chronic condition

STUDENT ROLE

Our goal was to identify, among opioids-naïve Medicare beneficiaries who received a new prescription for opioids following acute hospitalization, patient-level characteristics that were associated with the prescription of long-acting opioids as compared to short-acting opioids.

The study design was developed in collaboration with my mentor, Dr. Herzig, who took me on as a mentee following my medicine subinternship in the Spring 2019. We developed the idea for the project jointly in the knowledge that Dr. Herzig had just been awarded a grant from the Agency for Healthcare Research and Quality to evaluate the role of opioids in the post-acute hospitalization period. We soon obtained a claims-based cohort of a random sample of Medicare beneficiaries from the Centers for Medicare and Medicaid Services. Over the summer and early fall 2019, the division biostatistician Dr. Jung created the variables necessary for our analysis, with input from members of the study team. I participated and provided input in several of the planning meetings.

We developed a working dataset that allowed me to program the analysis in SAS. There were several rounds of data reanalysis as we realized that additional variables were needed or variable modifications were required. By January 2020, we had sufficient data to submit an abstract to the Society for General Internal Medicine's annual meeting in May 2020. The abstract was accepted for presentation, but the conference was ultimately cancelled due to COVID-19. Dr. Herzig helped with primary statistical analysis and with revision of the abstract. I also received substantial assistance in critical evaluation of the abstract from Dr. McCarthy and Dr. Anderson, two collaborators for the broader project aims. We are actively editing the manuscript and presently aim to submit it to a peer-reviewed journal by May 2020.

CITATION

Deshpande BR, McCarthy EP, Jung Y, Anderson TS, Herzig SJ. Initiation of Long-Acting Opioids following Hospital Discharge among Medicare Beneficiaries. [submission pending].

APPENDIX: Manuscript

Initiation of Long-Acting Opioids following Hospital Discharge among Medicare Beneficiaries

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Dr. Herzig had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Author Contributions:
Conception and design: Deshpande, Herzig
Analysis and interpretation of the data: all authors
Drafting of the article: Deshpande

Critical revision of the article for important intellectual content: all authors
Final approval of the article: all authors
Provision of study materials or patients: Herzig
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Competing Interests Statement:
Deshpande: none
McCarthy: TBD
Jung: TBD
Anderson: TBD
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INTRODUCTION

The transition out of the hospital is a vulnerable time for older individuals. Medications, particularly opioids, are a common cause of adverse events in this transitionary period.[1,2] For opioid-naïve patients who require opioids for acute non-cancer pain, guidelines recommend against initiating treatment with long-acting opioids.[3–5] Long-acting opioids have a longer duration of action but also have a significantly elevated risk of unintentional overdose and morbidity compared to short-acting opioids, even at identical total daily dosing.[6,7] This risk is highest in the first two weeks following initial prescription.[8,9] Worryingly, despite the recent decrease in overall prescription of opioids,[10] the proportion prescribed as long-acting formulations appears to be disproportionately increasing in frequency.[11] We sought to understand the incidence of long-acting opioid prescription following hospital discharge among opioid-naïve older adults and patient characteristics associated with this practice.

METHODS

Study Population

We used a 20% random sample of U.S. Medicare beneficiaries who were hospitalized in 2016 using the Center for Medicare and Medicaid Services' Medicare Provider Analysis and Review file. All beneficiaries were at least 65 years old and had been continuously enrolled in Medicare Parts A, B, and D for at least one year prior and one month following discharge (except those who died). We excluded persons with hospice claims or cancer diagnosis codes, as guidelines that recommend against initiation of long-acting opioids do not address care for those populations. We excluded individuals who had filled a prescription for an opioid within 30 days prior to hospitalization to ensure that our study population was relatively opioid-naïve. We further excluded patients who were transferred in from, or discharged to any type of care facility, as medication claims would have been unavailable during these periods.[12] Upon applying these inclusion and exclusion criteria, we identified patients with a Part D claim for an opioid within 7 days of discharge from an acute care hospital (Figure 1).

Defining Population Characteristics and Prescriptions

We selected characteristics that we hypothesized might be associated with new opioid prescription, based on clinical experience as well as prior literature. These characteristics included:

- Sociodemographic: age, sex, race; initial reason for Medicare entitlement, Medicaid eligibility
- Medical complexity over the preceding year: Elixhauser Comorbidity Index excluding drug abuse (measured separately) and cancer (these individuals excluded);[13] Medicare chronic condition (MCC) indicators for osteoporosis, hip/pelvic fracture, migraine & chronic headache, bipolar disorder, anxiety disorders; number of previous hospitalizations
- Functional status over the preceding year through 2 days after discharge: MCC indicator for mobility impairment; home healthcare claims; skilled nursing facility claims
- Substance use-related variables over the preceding year: previous high-dose long-term opioid use (a 90-day period of at least 120 morphine milligram equivalents between 30-365 days prior to hospitalization); MCC indicators for opioid use disorder, other drug use disorders
- Hospitalization: length of stay; critical care; diagnosis-related group (DRG)-based reason for hospitalization (medical, procedural); primary discharge diagnosis and procedures using the Clinical Classification System (CCS),[14] excluding groupings with prevalence <2%
- Medications: number of medications in 90 days prior to and 7 days after hospitalization; presence of any claim for benzodiazepines, muscle relaxants, stimulants, zolpidem, antidepressants, or antipsychotics within 7 days of discharge[15]

Outcomes and Statistical Analyses

The primary outcome was the frequency of prescription of a long-acting opioid among opioid-naïve patients who were filled an opioid prescription within 7 days of hospital discharge. We report cohort characteristics stratified by opioid duration of action. We used a multivariable generalized estimating equation model with a logit link and exchangeable correlation structure to determine patient-level factors independently associated with prescription of long-acting opioids (compared with short-acting opioids), accounting for correlation across multiple hospitalizations for patients who were hospitalized more than once. We report adjusted odds ratios with 95% confidence intervals. Analyses were completed in SAS version 9.4.

Ethical Approval

This study was approved by the Beth Israel Deaconess Medical Center institutional review board.

RESULTS

Incidence of Long-Acting Opioid Prescription

Of the 300,715 hospitalizations meeting inclusion and exclusion criteria (Figure 1), 60,305 (20%) resulted in a claim for short-acting opioids only and 1,651 (0.6%) resulted in a claim for a long-acting opioid within 7 days of discharge (362 for only long-acting opioids and 1,289 for both short- and long-acting opioids). Among the 61,956 patients with any opioid claim within 7 days of hospital discharge, 16,546 (26.7%) had a medical DRG and the remaining 45,410 (73.3%) had a procedural DRG (Table 1). The most common primary discharge diagnoses were musculoskeletal (41.1%), cardiovascular (17.7%), and gastrointestinal (12.8%).

Cohort Characteristics by Opioid Duration of Action

Compared to beneficiaries with only short-acting opioid claims in the week after discharge, beneficiaries with long-acting opioid claims were younger, more likely to be female, more likely to be white, and more likely to have qualified for Medicare for reasons other than age (Table 1). Beneficiaries prescribed long-acting opioids were more likely to have several mental health conditions, including opioid and other substance use disorders, a greater number of hospitalizations in the preceding year, and greater use of home healthcare and skilled nursing facility care. They were less likely to have had an ICU stay and more likely to have been hospitalized for a medical rather than procedural reason. Beneficiaries prescribed a long-acting opioid were prescribed more medications on average in both the 90 days prior to and 7 days after hospitalization and were more likely to have been co-prescribed each of the other sedating medications examined.

Adjusted Associations Between Candidate Risk Factors and Long-Acting Opioid Prescription

On multivariable analysis, there were several independent factors associated with long-acting, compared to short-acting opioid prescription (Table 2). The 5 characteristics with the strongest positive associations included previous high-dose long-term opioid use (aOR 34.99, 25.99-47.11), history of opioid use disorder (aOR 2.43, 1.87-3.15), medical DRG (aOR 2.94, 2.35-3.67), principal diagnosis of diseases of the musculoskeletal system and connective tissue (aOR 2.14, 1.63-2.80), and operations on the musculoskeletal system (aOR 2.68, 2.04-3.51).

In two sensitivity analyses, one excluding beneficiaries with any opioid claim within 90 days prior to hospitalization and another excluding beneficiaries with previous high-dose long-term opioid use in the year before hospitalization, the associations between the remaining factors and long-acting opioid prescription remained qualitatively similar (eTable 1).

DISCUSSION

Among 300,715 hospitalizations of opioid-naïve, non-cancer, non-hospice Medicare beneficiaries in 2016, one-fifth filled a new opioid prescription within 7 days of hospital discharge. Consistent with guideline recommendations, prescription of long-acting opioids was uncommon in the week after hospitalization, occurring in fewer than 1% of patients. However, about three-quarters of patients who filled a prescription for a long-acting opioid had been hospitalized for a procedure, which is concerning since post-operative pain is typically acute and self-limited. Additionally, patients started on long-acting opioids at discharge had higher incidence of known risk factors for opioid-related adverse events, including history of mood and anxiety disorders, opioid use disorder, prior long-term high-dose opioid use, and co-prescription of sedating medications. Taken together, these findings suggest that although long-acting opioids are infrequently initiated after hospital discharge, they tend to be prescribed to patients with high risk for harm. With nearly half of patients with a long-acting opioid claim having been hospitalized for musculoskeletal disorders or related procedures, this population represents a key target for quality improvement interventions.

To our knowledge, this is the first study to examine the incidence of long-acting opioid receipt shortly after hospital discharge. Although our study is large and nationally representative, there are several limitations. Although we excluded patients with a diagnosis of cancer or hospice care, reliance on claims-based data precluded characterization of the appropriateness of long-acting opioid therapy. Furthermore, we could not capture claims made to other health or prescription drug insurance plans.

In conclusion, although receipt of long-acting opioids following hospitalization was uncommon in this large national sample of Medicare beneficiaries, the majority of use was in patients with acute post-operative pain and risk factors for opioid-related adverse outcomes. These findings highlight the necessity to develop systems-based solutions to improve guideline-concordant prescribing of long-acting opioids.

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TABLES AND FIGURES

Table 1. Characteristics of Hospitalizations with At Least One Claim for a New Opioid Prescription within 7 Days of Hospital Discharge

Variable[1]	Short-Acting Opioid Only		Long-Acting Opioid		Total	
Sample size	60305	97.3%	1651	2.7%	61956	100%
Sociodemographics						
Age						
65–69	16157	26.8%	554	33.6%	16711	27.0%
70–74	18783	31.2%	554	33.6%	19337	31.2%
75–79	12966	21.5%	287	17.4%	13253	21.4%
80–84	7174	11.9%	145	8.8%	7319	11.8%
85–89	3575	5.9%	76	4.6%	3651	5.9%
90+	1650	2.7%	35	2.1%	1685	2.7%
Sex						
Female	34539	57.3%	996	60.3%	35535	57.4%
Male	25766	42.7%	655	39.7%	26421	42.6%
Race/Ethnicity						
White	53000	87.9%	1490	90.3%	54490	88.0%
Black	3950	6.6%	90	5.5%	4040	6.5%
Other	3355	5.6%	71	4.3%	3426	5.5%
Initial Reason for Medicare Entitlement						
Age > 65yo	51749	85.8%	1319	79.9%	53068	85.7%
Other	8556	14.2%	332	20.1%	8888	14.4%
Medicaid Dual Eligibility						
No subsidy	50915	84.4%	1395	84.5%	52310	84.4%
Medicaid	9390	15.6%	256	15.5%	9646	15.6%
Medical Complexity						
Elixhauser Comorbidity Index	4.5	SD 3.2	4.8	SD 3.6	4.5	SD 3.2
Medicare Chronic Conditions						
Osteoporosis	4845	8.0%	184	11.1%	5029	8.1%
Hip/pelvic fracture	1493	2.5%	40	2.4%	1533	2.5%
Migraine and chronic headache	1398	2.3%	55	3.3%	1453	2.4%
Bipolar disorder	855	1.4%	41	2.5%	896	1.5%
Anxiety disorders	9694	16.1%	386	23.4%	10080	16.3%
Previous hospitalizations within the past 12 months						
0	42478	70.4%	1039	62.9%	43517	70.2%
1	10823	18.0%	322	20.0%	11145	18.0%
2 or more	7004	11.6%	290	17.6%	7294	11.8%

Functional Status Indicators						
Mobility limitations	1429	2.4%	47	2.9%	1476	2.4%
Home Healthcare claims[2]	9658	16.0%	376	22.8%	10034	16.2%
Skilled Nursing Facility claims[2]	2843	4.7%	123	7.5%	2966	4.8%
Substance Use-Related Variables						
Previous high-dose long-term opioid use[3]	183	0.3%	188	11.4%	371	0.6%
Opioid use disorder	1237	2.1%	155	9.4%	1392	2.3%
Non-opioid drug use disorders	1398	1.3%	55	2.4%	1453	1.3%
Hospitalization Characteristics						
Index hospitalization length of stay more than 7 days	5190	8.6%	142	8.6%	5332	8.6%
ICU stay during index hospitalization	11987	19.9%	209	12.7%	12916	19.7%
Primary DRG						
Surgical	44339	73.5%	1071	64.9%	45410	73.3%
Medical	15966	26.5%	580	35.1%	16546	26.7%
Primary discharge diagnosis[4]						
Infectious and parasitic diseases	1451	2.4%	53	3.2%	1504	2.4%
Diseases of the circulatory system	10855	18.0%	127	7.7%	10982	17.7%
Diseases of the respiratory system	2338	3.9%	88	5.3%	2426	3.9%
Diseases of the digestive system	7802	12.9%	101	6.1%	7903	12.8%
Diseases of the genitourinary system	2590	4.3%	37	2.2%	2627	4.2%
Diseases of the musculoskeletal system and connective tissue	24520	40.7%	921	55.8%	25441	41.1%
Injury and poisoning	6616	11.0%	187	11.3%	6803	11.0%
Principal discharge procedure[4]						
Operations on the nervous system	1697	2.8%	22	1.3%	1719	2.8%
Operations on the cardiovascular system	9334	15.5%	79	4.8%	9413	15.2%
Operations on the digestive system	7235	12.0%	80	4.9%	7315	11.8%
Operations on the musculoskeletal system	26222	43.5%	979	59.3%	27201	43.9%
Miscellaneous diagnostic and therapeutic procedures	2048	3.4%	73	4.4%	2121	3.4%
Medication Variables						
Number of medication fills within 90 days pre-hospitalization	9.9	SD 8.1	11.6	SD 10.1	10.0	SD 8.1
Medication in 7 Days Post-Discharge						
Number of Medications	3.1	SD 2.2	4.0	SD 2.5	3.1	SD 2.2
Benzodiazepines	3176	5.3%	140	8.5%	3316	5.4%
Muscle relaxants	1871	3.1%	68	4.1%	1939	3.1%
Stimulants	39	0.1%	4	0.2%	43	0.1%

Zolpidem	573	1.0%	28	1.7%	601	1.0%
Antipsychotics	616	1.0%	32	1.9%	648	1.1%
Antidepressants	3054	5.0%	107	6.5%	3161	5.1%

[1] Expressed as either “mean (standard deviation)” or “number (percentage)” as appropriate
[2] Measured in 365 days prior to hospital discharge, through 2 days after hospital discharge
[3] A 90-day period with a prescribed morphine milligram equivalents of at least 120 within the preceding year, but >30 days prior to hospitalization
[4] Based on the Agency for Healthcare Research and Quality Clinical Classification System

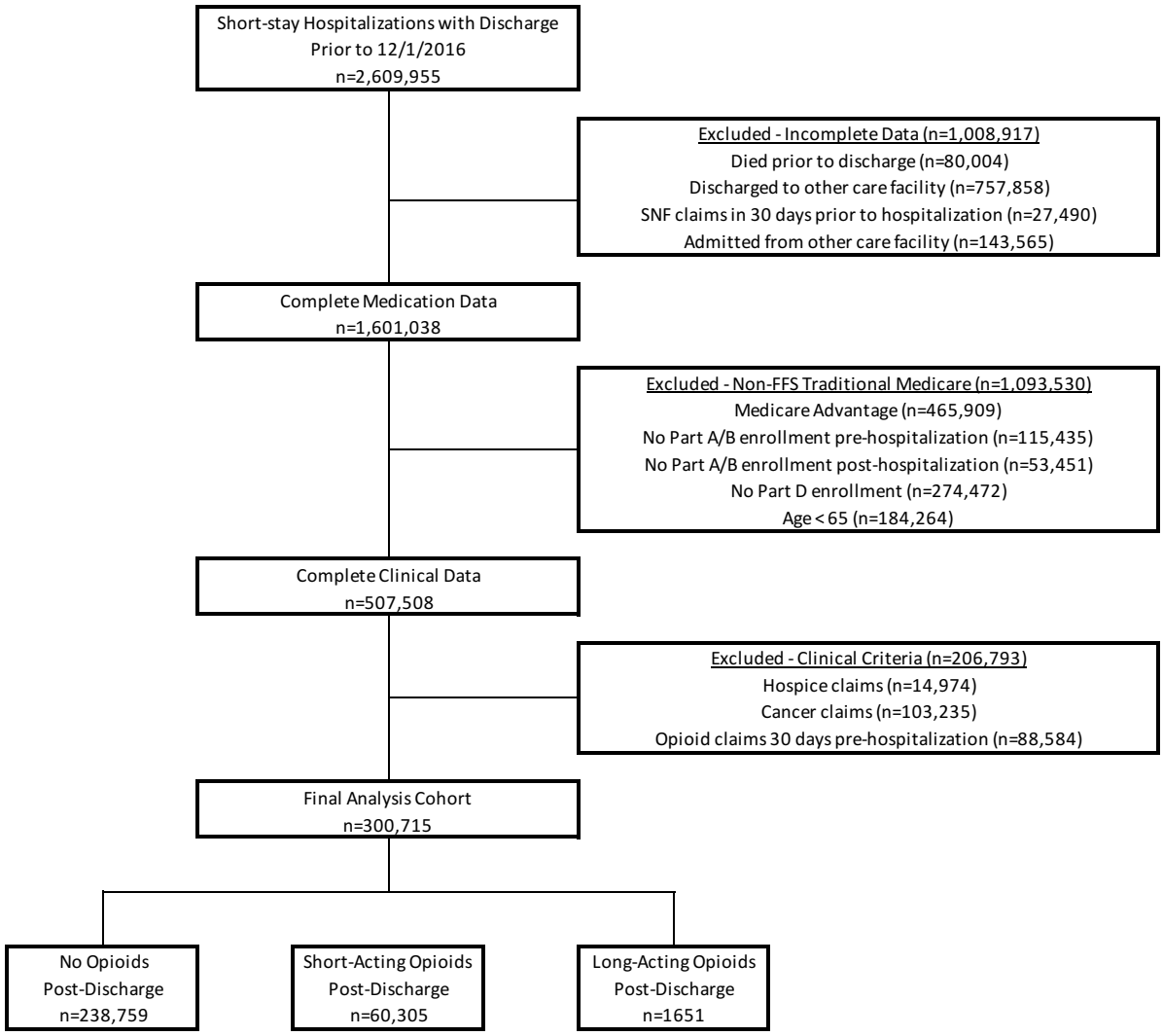
Table 2. Factors Associated with Long-Acting Opioid Prescription (Compared to Short-Acting) Within 7 Days of Hospital Discharge (n=61,956)

Characteristic	Adjusted Odds Ratio[1]	[95% Confidence Interval]
Sociodemographics		
Age		
65–69	Reference	
70–74	0.90	[0.79 – 1.02]
75–79	0.68	[0.59 – 0.80]
80–84	0.65	[0.53 – 0.79]
85–89	0.72	[0.56 – 0.93]
90+	0.63	[0.43 – 0.91]
Sex		
Female		
Male	0.96	[0.86 – 1.07]
Race/Ethnicity		
White		
Black	0.85	[0.67 – 1.08]
Other	0.84	[0.65 – 1.10]
Initial Reason for Medicare Entitlement		
Age $\geq$ 65yo		
Other	1.17	[1.00 – 1.37]
Medicaid Dual Eligibility		
No subsidy		
Medicaid	0.75	[0.63 – 0.90]
Medical Complexity		
Elixhauser Comorbidity Index (per unit)	1.00	[0.97 – 1.02]
Medicare Chronic Conditions		
Osteoporosis	1.25	[1.05 – 1.50]
Hip/pelvic fracture	0.75	[0.52 – 1.07]
Migraine and chronic headache	0.96	[0.69 – 1.32]
Bipolar disorder	0.97	[0.67 – 1.40]
Anxiety disorders	1.19	[1.03 – 1.37]
Previous hospitalizations within past 12 months		
0		
1	1.13	[0.97 – 1.31]
2 or more	1.29	[1.04 – 1.60]
Functional Status Indicators		
Mobility limitations	1.10	[0.78 – 1.55]
Home Healthcare claims[2]	1.14	[0.96 – 1.35]
Skilled Nursing Facility claims[2]	1.00	[0.77 – 1.29]

Substance Use-Related Variables		
Previous high-dose long-term opioid use[3]	34.99	[25.99 – 47.11]
Opioid use disorder	2.43	[1.87 – 3.15]
Non-opioid drug use disorders	0.78	[0.50 – 1.21]
Hospitalization Characteristics		
Index hospitalization length of stay more than 7 days	1.15	[0.92 – 1.43]
ICU stay during index hospitalization	0.89	[0.75 – 1.06]
Primary DRG		
Surgical		
Medical	2.94	[2.35 – 3.67]
Primary discharge diagnosis[4]		
Infectious and parasitic diseases	1.01	[0.70 – 1.47]
Diseases of the circulatory system	0.80	[0.60 – 1.07]
Diseases of the respiratory system	0.86	[0.62 – 1.19]
Diseases of the digestive system	0.84	[0.59 – 1.19]
Diseases of the genitourinary system	0.58	[0.38 – 0.87]
Diseases of the musculoskeletal system and connective tissue	2.14	[1.63 – 2.80]
Injury and poisoning	1.40	[1.08 – 1.83]
Principal discharge procedure[4]		
Operations on the nervous system	0.85	[0.52 – 1.38]
Operations on the cardiovascular system	0.60	[0.43 – 0.84]
Operations on the digestive system	0.83	[0.57 – 1.20]
Operations on the musculoskeletal system	2.68	[2.04 – 3.51]
Miscellaneous diagnostic and therapeutic procedures	0.92	[0.69 – 1.24]
Medication Variables		
Number of medication fills within 90 days pre-hospitalization	1.00	[0.99 – 1.01]
Medication in 7 Days Post-Discharge		
Number of Medications	1.23	[1.20 – 1.26]
Benzodiazepines	0.93	[0.75 – 1.16]
Muscle relaxants	0.71	[0.53 – 0.94]
Stimulants	1.09	[0.16 – 7.60]
Zolpidem	0.95	[0.59 – 1.55]
Antipsychotics	0.66	[0.40 – 1.10]
Antidepressants	0.44	[0.33 – 0.59]

[1] Based on a multivariable generalized estimating equation model with logit link and exchangeable correlation structure, including all variables simultaneously
[2] Measured in 365 days prior to hospital discharge through 2 days after hospital discharge
[3] A 90-day period with a prescribed morphine milligram equivalents of at least 120 within the preceding year, but >30 days prior to hospitalization
[4] Based on the Agency for Healthcare Research and Quality Clinical Classification System

Figure 1. Study Flow Diagram



eTable 1. Factors Associated with Long-Acting Opioid Prescription (Compared to Short-Acting) Within 7 Days of Hospital Discharge in (1) the overall cohort, (2) after excluding beneficiaries with any opioid claim within 90 days prior to hospitalization, and (3) after excluding beneficiaries with previous high-dose long-term opioid use in the year before hospitalization.

	Model 1	Model 2	Model 3
	n=61,956	n=47,945	n=61,585
Characteristic	Adjusted Odds Ratio[1] [95% CI]	Adjusted Odds Ratio[1] [95% CI]	Adjusted Odds Ratio[1] [95% CI]
Sociodemographics			
Age			
65–69	Reference	Reference	Reference
70–74	0.90 [0.79 – 1.02]	0.81 [0.69 – 0.94]	0.89 [0.78 – 1.02]
75–79	0.68 [0.59 – 0.80]	0.60 [0.49 – 0.73]	0.65 [0.55 – 0.76]
80–84	0.65 [0.53 – 0.79]	0.45 [0.34 – 0.60]	0.62 [0.50 – 0.76]
85–89	0.72 [0.56 – 0.93]	0.61 [0.43 – 0.87]	0.73 [0.56 – 0.94]
90+	0.63 [0.43 – 0.91]	0.59 [0.34 – 1.04]	0.58 [0.38 – 0.87]
Sex			
Female	Reference	Reference	Reference
Male	0.96 [0.86 – 1.07]	0.93 [0.81 – 1.07]	0.95 [0.85 – 1.06]
Race/Ethnicity			
White	Reference	Reference	Reference
Black	0.85 [0.67 – 1.08]	0.82 [0.58 – 1.18]	0.82 [0.64 – 1.05]
Other	0.84 [0.65 – 1.10]	0.82 [0.58 – 1.15]	0.82 [0.62 – 1.08]
Initial Reason for Medicare Entitlement			
Age $\geq$ 65yo	Reference	Reference	Reference
Other	1.17 [1.00 – 1.37]	1.09 [0.86 – 1.37]	1.22 [1.04 – 1.43]
Medicaid Dual Eligibility			
No subsidy	Reference	Reference	Reference
Medicaid	0.75 [0.63 - 0.90]	0.70 [0.52 – 0.93]	0.76 [0.62 – 0.92]
Medical Complexity			
Elixhauser Comorbidity Index (per unit)	1.00 [0.97 – 1.02]	0.98 [0.95 – 1.02]	1.00 [0.97 – 1.02]
Medicare Chronic Conditions			
Osteoporosis	1.25 [1.05 – 1.50]	1.29 [1.01 – 1.64]	1.23 [1.02 – 1.48]
Hip/pelvic fracture	0.75 [0.52 – 1.07]	0.61 [0.37 – 1.00]	0.73 [0.50 – 1.06]
Migraine and chronic headache	0.96 [0.69 – 1.32]	0.83 [0.52 – 1.33]	0.95 [0.68 – 1.33]
Bipolar disorder	0.97 [0.67 – 1.40]	0.78 [0.39 – 1.55]	0.85 [0.55 – 1.29]
Anxiety disorders	1.19 [1.03 – 1.37]	1.39 [1.16 – 1.68]	1.25 [1.08 – 1.44]

Previous hospitalizations within past 12 months			
0	Reference	Reference	Reference
1	1.13 [0.97 – 1.31]	1.08 [0.88 – 1.33]	1.10 [0.95 – 1.29]
2 or more	1.29 [1.04 – 1.60]	1.24 [0.88 – 1.75]	1.33 [1.07 – 1.66]
Functional Status Indicators			
Mobility limitations	1.10 [0.78 – 1.55]	0.74 [0.39 – 1.40]	1.13 [0.79 – 1.60]
Home Healthcare claims[2]	1.14 [0.96 – 1.35]	1.30 [1.02 – 1.66]	1.24 [1.04 – 1.47]
Skilled Nursing Facility claims[2]	1.00 [0.77 – 1.29]	0.84 [0.53 – 1.32]	0.96 [0.73 – 1.25]
Substance Use-Related Variables			
Previous high-dose long-term opioid use[3]	34.99 [25.99 – 47.11]	8.19 [2.64 – 25.43]	---
Opioid use disorder	2.43 [1.87 – 3.15]	2.18 [1.47 – 3.24]	3.10 [2.42 – 3.95]
Non-opioid drug use disorders	0.78 [0.5 – 1.21]	0.83 [0.38 – 1.81]	0.68 [0.41 – 1.13]
Hospitalization Characteristics			
Index hospitalization length of stay more than 7 days	1.15 [0.92 – 1.43]	1.28 [0.93 – 1.75]	1.14 [0.91 – 1.43]
ICU stay during index hospitalization	0.89 [0.75 – 1.06]	0.84 [0.64 – 1.11]	0.85 [0.70 – 1.03]
Primary DRG			
Surgical	Reference	Reference	Reference
Medical	2.94 [2.35 – 3.67]	2.85 [2.01 – 4.03]	3.11 [2.46 – 3.92]
Primary discharge diagnosis[4]			
Infectious and parasitic diseases	1.01 [0.70 – 1.47]	1.08 [0.54 – 2.14]	0.98 [0.65 – 1.49]
Diseases of the circulatory system	0.80 [0.60 – 1.07]	0.74 [0.42 – 1.28]	0.79 [0.58 – 1.09]
Diseases of the respiratory system	0.86 [0.62 – 1.19]	0.98 [0.53 – 1.78]	0.87 [0.61 – 1.23]
Diseases of the digestive system	0.84 [0.59 – 1.19]	0.73 [0.37 – 1.43]	0.86 [0.58 – 1.28]
Diseases of the genitourinary system	0.58 [0.38 – 0.87]	0.33 [0.13 – 0.86]	0.52 [0.32 – 0.85]
Diseases of the musculoskeletal system and connective tissue	2.14 [1.63 – 2.80]	3.65 [2.36 – 5.63]	2.15 [1.62 – 2.85]

Injury and poisoning	1.40 [1.08 – 1.83]	2.53 [1.65 – 3.87]	1.46 [1.10 – 1.92]
Principal discharge procedure[4]			
Operations on the nervous system	0.85 [0.52 – 1.38]	0.62 [0.28 – 1.38]	0.91 [0.55 – 1.51]
Operations on the cardiovascular system	0.60 [0.43 – 0.84]	0.57 [0.31 – 1.04]	0.57 [0.39 – 0.83]
Operations on the digestive system	0.83 [0.57 – 1.20]	1.10 [0.59 – 2.03]	0.87 [0.58 – 1.30]
Operations on the musculoskeletal system	2.68 [2.04 – 3.51]	3.00 [2.00 – 4.48]	3.04 [2.30 – 4.03]
Miscellaneous diagnostic and therapeutic procedures	0.92 [0.69 – 1.24]	1.05 [0.65 – 1.69]	1.00 [0.74 – 1.35]
Medication Variables			
Number of medication fills within 90 days pre-hospitalization	1.00 [0.99-1.01]	0.98 [0.97 – 0.99]	0.99 [0.99 – 1.00]
Medication in 7 Days Post-Discharge			
Number of Medications	1.23 [1.20 – 1.26]	1.34 [1.30 – 1.38]	1.24 [1.21 – 1.27]
Benzodiazepines	0.93 [0.75 – 1.16]	0.98 [0.74 – 1.31]	0.98 [0.79 – 1.22]
Muscle relaxants	0.71 [0.53 – 0.94]	0.57 [0.39 – 0.84]	0.73 [0.56 – 0.97]
Stimulants	1.09 [0.16 – 7.60]	1.97 [0.25 – 15.66]	2.43 [0.68 – 8.70]
Zolpidem	0.95 [0.59 – 1.55]	0.94 [0.49 – 1.83]	0.99 [0.62 – 1.59]
Antipsychotics	0.66 [0.40 – 1.10]	0.45 [0.18 – 1.12]	0.77 [0.47 – 1.24]
Antidepressants	0.44 [0.33 – 0.59]	0.32 [0.20 – 0.52]	0.49 [0.36 – 0.65]

[1] Based on a multivariable generalized estimating equation model with logit link and exchangeable correlation structure, including all variables simultaneously

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