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

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Guidelines recommend against initiating long-acting opioids during acute hospitalization, owing to higher risk of overdose and morbidity compared to shortacting opioid initiation. We investigated the incidence of long-acting opioid initiation following hospitalization in a retrospective cohort of Medicare beneficiaries with an acute care hospitalization in 2016 who were \geq 65 years old, did not have cancer or hospice care, and had not filled an opioid prescription within the preceding 90 days. Among 258,193 hospitalizations, 47,945 (18.6%) were associated with a claim for a new opioid prescription in the week after hospital discharge: 817 (0.3%) with both short- and longacting opioids, 125 (0.1%) with long-acting opioids only,

ransition out of the hospital is a vulnerable time for older adults. Medications, particularly opioids, are a common cause of adverse events during this transitionary period.^{1,2} For hospitalized patients with acute noncancer pain that necessitates opioid treatment, guidelines recommend using short-acting, rather than long-acting, opioids.^{3,4} 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 when total daily dosing is identical.^{5,6} This risk is highest in the first 2 weeks following initial prescription.^{7,8}

Despite the recent decrease in overall prescription of opioids,⁹ a small but significant proportion continue to be prescribed as long-acting formulations.¹⁰⁻¹² We sought to understand the incidence of, and patient characteristics associated with, long-acting opioid initiation following hospital discharge among opioid-naïve older adults.

METHODS

We examined the 20% random sample of US Medicare beneficiaries ${\geq}65$ years old who were hospitalized in 2016 and

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and 47,003 (18.2%) with short-acting opioids only. Most long-acting opioid claims occurred in surgical patients (770 out of 942; 81.7%). Compared with beneficiaries prescribed short-acting opioids only, beneficiaries prescribed long-acting opioids were younger, had a higher prevalence of diseases of the musculoskeletal system and connective tissue, and had more known risk factors for opioid-related adverse events, including anxiety disorders, opioid use disorder, prior long-term high-dose opioid use, and benzodiazepine co-prescription. These findings may help target quality-improvement initiatives. *Journal of Hospital Medicine* 2021;16:724-726. © 2021 Society of Hospital Medicine

continuously enrolled in Parts A, B, and D for 1 year prior and 1 month following discharge, excluding beneficiaries with cancer or hospice care, those transferred from or discharged to a care facility, and those who had filled a prescription for an opioid within 90 days prior to hospitalization. We identified beneficiaries with a Part D claim for an opioid, excluding methadone and buprenorphine, within 7 days of discharge. We compared beneficiaries with at least one claim for a long-acting opioid (including extended-release formulations) within 7 days of hospital discharge to those with short-acting opioid claims only.

We used a multivariable, generalized estimating equation to determine patient-level factors independently associated with prescription of any long-acting opioids. We selected characteristics that we hypothesized to be associated with new opioid prescription, based on clinical experience and previous literature, including sociodemographics, patient clinical characteristics such as a modified Elixhauser index (a composite index of nearly 30 comorbidities, excluding cancer),¹³ substance use-related factors, co-prescribed medications, and hospitalization-related factors. The latter included being hospitalized for a medical vs surgical reason, defined based on diagnosis-related group (DRG), primary diagnosis, and primary procedure, grouped using the Agency for Healthcare Research and Quality Clinical Classification System¹⁴ (Table 1).

We conducted a sensitivity analysis, excluding beneficiaries with high-dose long-term opioid use in the year before hospitalization.

RESULTS

Of 258,193 hospitalizations meeting eligibility criteria, 47,945 (18.6%) had an opioid claim within 7 days of discharge and

TABLE 1. Characteristics of Hospitalizations With at Least One Claim for a New Opioid Prescription Within 7 Days of Hospital Discharge, Stratified by Opioid Duration of Action

Variable	Short-acting opioids only	Any long-acting opioids	Variable	Short-acting opioids only	Any long-acting opioids
Sample size	47,003 (98.0)	942 (2.0)	Sample size	47,003 (98.0)	942 (2.0)
Age, y			Index hospitalization characteristics		
65-69	12,434 (26.5)	337 (35.8)	Length of stay, mean (SD), d	3.5 (3.3)	3.2 (3.9)
70-74	14,813 (31.5)	330 (35.0)	Length of stay more than 7 d	4051 (8.6)	63 (6.7)
75-79	10,157 (21.6)	159 (16.9)	Intensive care unit stay	9466 (20.1)	79 (8.4)
80-84	5606 (11.9)	63 (6.7)			
85+	3993 (8.5)	53 (5.6)	Primary DRG	10 742 (22 0)	172 (10.2)
			Medical	10,742 (22.9)	172 (18.3)
Sex	20 752 (44 2)	200 (42 4)	Surgical	36,261 (77.2)	770 (81.7)
Male	20,753 (44.2)	399 (42.4) 543 (57.6)	Principal discharge diagnosis ^c		
Female	26,250 (55.9)	543 (57.6)	Infectious disease	989 (2.1)	14 (1.5)
Race			Circulatory system	8591 (18.3)	38 (4.0)
White	41,570 (88.4)	862 (91.5)	Respiratory system	1443 (3.1)	20 (2.1)
Black	2720 (5.8)	39 (4.1)	Digestive system	6217 (13.2)	28 (3.0)
Other	2713 (5.8)	41 (4.4)	Genitourinary system ^a	_	_
		()	Musculoskeletal system and connective tissue	19,633 (41.8)	685 (72.7)
Medicare-Medicaid dual eligible	6386 (13.6)	82 (8.7)	Injury and poisoning	5331 (11.3)	119 (12.6)
Elixhauser Comorbidity Index, mean (SD)	4.2 (3.0)	3.5 (2.9)	Principal discharge procedure ^c		
Selected Medicare chronic conditions			Nervous system ^a	_	—
Osteoporosis	3518 (7.5)	86 (9.1)	Cardiovascular system	7670 (16.3)	26 (2.8)
Hip/pelvic fracture	1200 (2.6)	19 (2.0)	Digestive system	5872 (12.5)	29 (3.1)
Mobility impairment	1016 (2.2)	12 (1.3)	Musculoskeletal system ^e	21,096 (44.9)	732 (77.7)
Migraine and chronic headache	979 (2.1)	21 (2.2)	Miscellaneous diagnostic and therapeutic	1418 (3.0)	24 (2.6)
Bipolar disorder ^a			procedures		
Anxiety disorders	6540 (13.9)	164 (17.4)	Other medication claims within 7 days of — discharge	2024 (4.5)	
Substance use history			Benzodiazepines	2091 (4.5)	60 (6.4)
Previous high-dose long-term opioid use ^{a,b}	_	_	Muscle relaxants	1315 (2.8)	29 (3.1)
Opioid use disorder	720 (1.5)	37 (3.9)	Antidepressants	1976 (4.2)	31 (3.3)
Nonopioid drug use disorders ^a		57 (5.5)	Antiocpicoodito		

Results are expressed as No. (%), except where stated to be mean (SD).

^aCells with sample size ≤10 have been omitted, per Centers for Medicare & Medicaid Services policy.

^bA 90-day period with a prescribed morphine milligram equivalents of at least 120 within the preceding year, but >90 days prior to hospitalization.

^cBased on the Agency for Healthcare Research and Quality Clinical Classification System.¹⁴

^dIncludes septic arthritis and osteomyelitis, nontraumatic joint disorders, spondylosis, intervertebral disc disorders, other back problems, osteoporosis, pathological fracture, acquired deformities, connective tissue diseases, other bone disease and musculoskeletal deformities.

*Includes bone excision; treatment of fracture or dislocation; arthroscopy, arthroplasty, arthrocentesis; division of joint capsule, ligament, or cartilage; injections and aspirations of muscles, tendons, bursa, joints, and soft tissue; amputation; spinal fusion; other diagnostic or therapeutic procedures on musculoskeletal system.

Abbreviation: DRG, diagnosis-related group.

comprised our analytic cohort (see the Appendix Figure for the study consort diagram), including 47,003 (18.2%) with short-acting opioids only and 942 (0.4%) with at least one claim for long-acting opioids, of whom 817 received both short- and long-acting opioids (Table 1).

Beneficiaries with long-acting opioid claims were more likely to be younger (ages 65-69 and 70-74 years) and White than those with claims for short-acting opioids only. They had a lower mean number of Elixhauser comorbidities but a higher prevalence of mental health conditions, including anxiety disorders and opioid use disorder, as well as a higher prevalence of previous highdose long-term opioid use (occurring more than 90 days prior to hospitalization). They were more likely to have been hospitalized for a procedural rather than a medical reason, with 770 of the 942 (81.7%) beneficiaries receiving long-acting opioids having been hospitalized for a procedural reason (based on DRG). They were also more likely to have benzodiazepine co-prescription.

Factors independently associated with receipt of long-acting opioids compared to short-acting opioids only included younger age, having been admitted for a musculoskeletal problem, and presence of known risk factors for opioid-related adverse events, including anxiety disorders, opioid use disorder, prior long-term high-dose opioid use, and benzodiazepine coprescription (Table 2). After excluding 33 beneficiaries with previous high-dose long-term opioid use in the year before hospitalization, associations were unchanged (Appendix Table).

TABLE 2. Factors Significantly Associated with Long-Acting Opioid Prescription (Compared to Short-Acting Only) Within 7 Days of Hospital Discharge in the Overall Cohort (47,945 hospitalizations; 942 longacting opioid prescriptions)

Characteristic	Adjusted odds ratio (95% CI) ^a	
Sociodemographics		
Age, y		
65-69	Reference	
70-74	0.80 (0.69-0.94)	
75-79	0.60 (0.49-0.73)	
80-84	0.46 (0.35-0.60)	
85-89	0.64 (0.48-0.86)	
Selected Medicare chronic conditions		
Osteoporosis	1.28 (1.01-1.63)	
Anxiety disorders	1.32 (1.10-1.58)	
Substance use history		
Previous high-dose long-term opioid use ^b	11.5 (4.29-30.85)	
Opioid use disorder	2.20 (1.50-3.22)	
Index hospitalization characteristics		
Length of stay >7 days (vs <7)	1.82 (1.36-2.43)	
Principal discharge diagnosis ^c		
Genitourinary system	0.23 (0.09-0.60)	
Musculoskeletal system and connective tissue	2.70 (1.77-4.11)	
Injury and poisoning	1.99 (1.33-2.99)	
Principal discharge procedure ^c		
Nervous system	0.25 (0.12-0.52)	
Cardiovascular system	0.31 (0.17-0.55)	
Other medication claims within 7 days of discharge		
Benzodiazepines	1.47 (1.12-1.93)	

*Based on a multivariable, generalized estimating equation model with logit link and ex-changeable correlation structure, including all variables listed in Table 1 simultaneously. ^bA 90-day period with a prescribed morphine milligram equivalents of at least 120 within the preceding year, but >90 days prior to hospitalization

^cBased on the Agency for Healthcare Research and Quality Clinical Classification System.¹⁴

DISCUSSION

Among a nationally representative sample of opioid-naïve Medicare beneficiaries without cancer, almost 20% filled a new opioid prescription within 7 days of hospital discharge. While prescription of long-acting opioids was uncommon, 81.7% who were prescribed a long-acting opioid had a procedural reason for hospitalization, raising concern since postoperative pain is typically acute and limited. Beneficiaries started on long-acting opioids more frequently had risk factors for opioid-related adverse events, including history of opioid use disorder and benzodiazepine co-prescription. With nearly three-quarters of patients with a long-acting opioid claim having been hospitalized for musculoskeletal disorders or orthopedic procedures, this population represents a key target for quality improvement interventions.

This is the first analysis describing the incidence and factors associated with long-acting opioid receipt shortly after hospital discharge among Medicare beneficiaries. Given that our data predate the publication of the Society of Hospital Medicine's consensus statement on safe opioid prescribing in hospitalized patients,³ it is possible that there have been changes to prescribing patterns since 2016 that we are unable to characterize with our data. We are also limited by an inability to determine the appropriateness of any individual long-acting opioid prescription, though previous research has shown that long-acting opioids are frequently inappropriately initiated in older adults.¹⁵ Finally, our findings may not be generalizable to non-Medicare populations.

While long-acting opioid initiation following hospitalization is uncommon, these medications are most often prescribed to individuals with pain that is typically of limited duration and those at high risk for harm. Our findings highlight potential targets for systems-based solutions to improve guidelineconcordant prescribing of long-acting opioids.

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References

- 1. Tsilimingras D, Schnipper J, Duke A, et al. Post-discharge adverse events among urban and rural patients of an urban community hospital: a pro-spective cohort study. J Gen Intern Med. 2015;30(8):1164-1171. https:// doi.org/10.1007/s11606-015-3260-3
- 2. Forster AJ, Murff HJ, Peterson JF, Gandhi TK, Bates DW. The incidence and severity of adverse events affecting patients after discharge from the hospi-tal. Ann Intern Med. 2003;138(3):161-167. https://doi.org/10.7326/0003-4819-138-3-200302040-00007
- 3. Herzig SJ, Mosher HJ, Calcaterra SL, Jena AB, Nuckols TK. Improving the safety of opioid use for acute noncancer pain in hospitalized adults: a consensus statement from the Society of Hospital Medicine. J Hosp Med. 2018;13(4):263-271. https://doi.org/10.12788/jhm.2980
 Herzig SJ, Calcaterra SL, Mosher HJ, et al. Safe opioid prescribing for acute
- noncancer pain in hospitalized adults: a systematic review of existing guide-lines. J Hosp Med. 2018;13(4):256-262. https://doi.org/10.12788/jhm.2979
- Barnett ML, Olenski AR, Thygeson NM, et al. A health plan's formulary led to reduced use of extended-release opioids but did not lower overall opioid use. Health Aff (Millwood). 2018;37(9):1509-1516. https://doi.org/10.1377/ hlthaff.2018.0391
- Carey CM, Jena AB, Barnett ML. Patterns of potential opioid misuse and subsequent adverse outcomes in Medicare, 2008 to 2012. Ann Intern Med. 2018;168(12):837-845. https://doi.org/10.7326/M17-3065 Miller M, Barber CW, Leatherman S, et al. Prescription opioid duration of
- action and the risk of unintentional overdose among patients receiving opioid therapy. JAMA Intern Med. 2015;175(4):608-615. https://doi.org/10.1001/ amainternmed.2014.8071
- pamainternmed.2014.80/1
 Ray WA, Chung CP, Murray KT, Hall K, Stein CM. Prescription of long-act-ing opioids and mortality in patients with chronic noncancer pain. JAMA. 2016;315(22):2415-2423. https://doi.org/10.1001/jama.2016.7789
 Zhu W, Chernew ME, Sherry TB, Maestas N. Initial opioid prescriptions among U.S. commercially insured patients, 2012-2017. N Engl J Med. 2019;380(11):1043-1052. https://doi.org/10.1056/NEJMsa1807069
 Starret L Gleason P. Short-acting long-acting and abuse_deterret opioid
- Starner I, Gleason P. Short-acting, long-acting, and abuse-deterrent opioid utilization patterns among 15 million commercially insured members. Pre-sented at: Academy of Managed Care Pharmacy (AMCP) Nexus; October 3-6, 2016; National Harbor, MD
- 11. Young JC, Lund JL, Dasgupta N, Jonsson Funk M. Opioid tolerance and clinically recognized opioid poisoning among patients prescribed extended-re-lease long-acting opioids. *Pharmacoepidemiol Drug Saf.* 2019;28(1):39-47. https://doi.org/10.1002/pds.4572
- 12. Hwang CS, Kang EM, Ding Y, et al. Patterns of immediate-release and extended-release opioid analgesic use in the management of chronic pain, 2003-2014. JAMA Netw Open. 2018;1(2):e180216. https://doi.org/10.1001/ amanetworkopen.2018.0216
- Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. Med Care. 1998;36(1):8-27. https://doi. org/10.1097/00005650-199801000-00004
- 14. Agency for Healthcare Research and Quality. Clinical Classifications Software (CCS) for ICD-10-CM/PCS. Healthcare Cost and Utilization Project (HCUP).
 October 2018. www.hcup-us.ahrq.gov/toolssoftware/ccs10/ccs10.jsp
 Willy ME, Graham DJ, Racoosin JA, et al. Candidate metrics for evaluating
- the impact of prescriber education on the safe use of extended-release/ long-acting (ER/LA) opioid analgesics. *Pain Med.* 2014;15(9):1558-1568. https://doi.org/10.1111/pme.12459