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The Importance of Continuity of Care Among Older Adults on Chronic Opioid Therapy

Max Mauney

THE IMPORTANCE OF CONTINUITY OF CARE AMONG OLDER ADULTS ON CHRONIC OPIOID THERAPY

By

Max Joseph Mauney

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Approved By

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Advisor: Professor Yi Yang

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Reader: Professor Sujith Ramachandran

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Reader: Professor John Bentley

DEDICATION

This thesis is dedicated to my parents, Joey and Jennifer Mauney. From a young age, they placed a heavy emphasis on education and without their guidance I would not be anywhere close to where I am today. I am forever grateful for their longstanding and continued support.

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ABSTRACT

MAX MAUNEY: The Importance of Continuity of Care Among Older Adults on Chronic Opioid Therapy

(Under the Direction of Dr. Yi Yang)

Objective: The purpose of this study was to define continuity of care and prescriber characteristics among older adults with chronic non-cancer pain who are on long-term opioid therapy. Also, it will evaluate the connection between continuity of care and prescriber characteristics on the risk of opioid-related adverse events among older adults on chronic opioid therapy. The main goal is to observe the relationship between continuity and the related adverse events that may arise.

Methods: This study utilized a nested case-control using a 5% random sample of the National Medicare data between 2012 and 2016. This data used a random sample of beneficiaries in the United States and included a plethora of information regarding their provider visits. The control group was defined as those who entered the study cohort but did not experience any related adverse events or death. There were two numerical ways to determine COC (COCI and HI). Statistical comparisons through a Chi-Square test and Conditional logistic regression models were used to visually compare COC and opioid-related adverse events.

Results: The mean COCI score was 0.65 in the 6-month period prior to cohort entry. Those with low COC were found to have higher odds of the outcome compared to those with higher COC. Those seeing a pain specialist had lower odds of the composite outcome. The adjusted results showed similar findings that were expected.

Conclusion: It was found that there was a positive correlation between continuity of care and having less opioid-related adverse events for patients with CNCP. Also, provider specialty was not as significant to COC.

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LIST OF ABBREVIATIONS

CNCP	Chronic Non-Cancer Pain
COC	Continuity of Care
COCI	Continuity of Care Index
OIRD	Opioid-Induced Respiratory Depression
OD	Opioid-Related Overdose
MBSF	Master Beneficiary Summary File
HI	Herfindahl Index
LIS	Low-Income Subsidy
CCI	Charlson Comorbidity Index
COPD	Chronic Obstructive Pulmonary Disorder
MME	Morphine Milligram Equivalents
CDC	Centers for Disease Control and Prevention
SD	Standard Deviation
LTOT	Long-Term Opioid Therapy
OR	Odds Ratio
P	Statistical Significance
NSAID	Non-Steroidal Anti-Inflammatory Drugs

Introduction

Approximately 20% of people worldwide are affected by chronic non-cancer pain and around one in five adults in the United States suffer from this pain (Mathieson, et al. & Bonezzi et al. 2020). As the prevalence of chronic pain increases with age, CNCP commonly affects older adults and is most frequently associated with musculoskeletal disorders, such as degenerative spine conditions and arthritis (American Geriatrics Society Panel 2009). In addition to a significant impact on functionality and autonomy, chronic pain is associated with substantial disability in the elderly population (Reid, Eccleston, Pillemer 2015). Opioid analgesics are often used to manage such persistent pain even though there is limited evidence to support the long-term use in older adults (Chou et al. 2015). As stated by the American Geriatrics Society Panel, "persistent pain commonly affects older people and is most frequently associated with musculoskeletal disorders, such as degenerative spine conditions and arthritis" (Els et al. 2017). Long-term opioid therapy in older adults can lead to increased risks and adverse events like cognitive impairment, fall injuries, nausea, constipation, etc. (Baldini, Von Korff, Lin 2012). As stated by Dunn et al., long-term opioid therapy is more common, especially in adults with chronic noncancer pain;" this can lead one to hypothesize a positive correlation with long-term opioid therapy and negative effects (Dunn, Saunders, Rutter 2010). Managing non-cancer chronic pain in older adults, particularly in those with several comorbidities and polypharmacy is difficult. Existing research identifies risk

factors of opioid-related adverse outcomes for patients on long-term opioid therapy. These factors include treatment characteristics such as dosage of opioids and type of opioids, patient characteristics such as disability status, comorbidities, and use of other medications. In addition, the number and types of providers managing long-term opioid therapy may be critical. Previous research has indicated that obtaining prescriptions from multiple prescribers or pharmacies, termed provider shopping, may be an indicator of opioid misuse. In fact, the pharmacy quality alliance has endorsed the number of prescribers as a measure indicative of quality of opioid use. The use of multiple prescribers also leads to a lack in continuity of care which may lead to poor management of opioid therapy and higher risk of adverse outcomes. Similarly, whether a pain specialist is involved in the care of the patient may influence the risk of adverse outcomes associated with long-term opioid therapy.

The American Academy of Family Physicians defined continuity of care as "the process by which the patient and the physician are cooperatively involved in ongoing health care management toward the goal of high quality, cost-effective medical care" (Gulliford et al. 2006). Continuity of care can be measured quantitatively. Bice and Boxerman proposed a formula to measure the continuity of care (COC) through the equation given in figure 1.

$$COCI = \frac{\sum^{S}(n_j)^2 - n}{n(n-1)}$$

Figure 1: Bice and Boxerman COC Equation (Sudhakar-Krishnan, Vidya, Rudolf 2007)

In this equation, n is the total number of visits, nj is the number of visits to a provider (j), s is the total number of providers (s above the sigma), and the maximum value for continuity is 1" (Bice, Boxerman). The index represents the extent to which an individual patient visits single or group of providers over a specified period (Pollack et al. 2016).

Continuity of care is found to be associated with a high degree of patient satisfaction, higher rates of medication compliance, decrease adverse events and better management of elderly patients with chronic conditions (Dreiher, et al. 2012).It is noted that patients using multiple prescribers and multiple pharmacies are more likely to experience adverse events due to more variability and room for error.

Prescribing continuity is fundamental to high-quality care and better care experiences. Fragmented care from multiple providers and increment in number of providers are associated with a greater risk of adverse events caused by drugs (Beadles, et al. 2014). A study by Hallvik et al. found out that lower prescribing continuity in long-term opioid use, as measure by COCI, was associated with the likelihood of receiving risky opioid prescriptions and opioid-related adverse events including overdose-related hospitalizations and other adverse events (Hallvik, et al.) Clear comprehension of the association between continuity of opioid prescribing and opioid-related adverse events is necessary to effectively management of CNCP through chronic opioid therapy. Therefore, the overall goal of this paper is to evaluate the importance of appropriate patient management while undergoing safe use of long-term opioid prescribed therapy. The specific aims are to describe the continuity of care and prescriber characteristics among older adults on long-term opioid therapy with CNCP and to also evaluate the

relationship between COC and prescriber characteristics on the risk of opioid-induced adverse outcomes among older adults on chronic opioid therapy with CNCP.

Methods

Study Design and Data Source

This study used a nested case-control design using a 5% random sample of the National Medicare data between 2012-2016. The data includes demographic characteristics from a 5% random sample of all Medicare beneficiaries in the United States, and their inpatient, outpatient, and pharmacy claims containing information on diagnosis codes, procedure codes, and medication fills, linked using an encrypted beneficiary identifier. An institutional review board approved the study and a data use agreement for use of Medicare data was obtained from the Centers for Medicare & Medicaid Services prior to the study.

Cohort Definition

Medicare beneficiaries identified to be on a new chronic opioid therapy episode between July 1, 2012 and December 31, 2016 were deemed eligible for cohort entry. Based on extant literature, a new chronic opioid therapy episode was defined as presence of at least three prescription claims fills for opioids and a cumulative 45 days of opioid possession in any 90-day period during the study, with no history of opioid prescription fills in the 6-month period prior to start of the chronic opioid therapy episode (Dunn, Kate M., et al. 2010 & Ramachandran, S., et al. 2021) The 91st day after initiation of the chronic opioid therapy episode was considered as the "cohort entry date" for beneficiaries that were at least 65 years of age or older as of the start date of the opioid use episode and

continuously enrolled in Medicare Parts A, B, and D in the 12-month period prior to cohort entry. Additionally, beneficiaries were required to have no history of cancer and at least two claims with diagnoses for a chronic non-cancer pain (CNCP) condition within a 30-day window in the 12-month period prior to the beginning of the chronic opioid use episode. Beneficiaries entering the study cohort remained a part of the cohort until the first occurrence of one of the following events – outcome of interest, death, cancer diagnosis, loss of Medicare eligibility, or end of the study period.

Case Definition

Multiple opioid-related adverse events – opioid-induced respiratory depression (OIRD), opioid-related overdose (OD), all-cause mortality, and a composite outcome of the first occurrence of any of the three stated events, were assessed in this study. Separate cases and matching controls were determined for each of the events. Cases were defined as beneficiaries from the cohort who had an episode of either OIRD or OD, or died before the end of the study period. The date of the first occurrence of an event of interest was considered as the "index date".

Based on prior literature, an OIRD episode was identified based on presence of a diagnosis code for prescription opioid-related poisoning and a procedure code for life-threatening respiratory or central nervous system depression, or mechanical ventilation or critical care within one day of the prescription opioid-related poisoning (Zedler, B., et al. 2014 and 2018). Consistent with previous literature, OD was determined based on presence of a diagnosis code for opioid-related poisoning, or a diagnosis code for opioid-related adverse event with a diagnosis code for opioid overdose on the same day (Dunn,

Kate, et al. 2010). For beneficiaries who died during the study period, date of death was obtained from the Master Beneficiary Summary File (MBSF).

Control Definition

Controls were defined as beneficiaries who entered the study cohort but did not experience any opioid-related adverse event or death as of the index date of their matched case. Incidence density sampling was employed to select one control for each case, to allow for random sampling from the pool of eligible controls, such that the time at risk of an opioid-related adverse event or death for each control beneficiary was equal to or more than that of their matched case. This technique allows for beneficiaries that were selected as controls at the given time at risk to also serve as a case at a future time point. Moreover, it is possible for a particular beneficiary to serve as a control for more than one case. Cases and controls were matched on age and time of cohort entry.

Continuity of Care

Opioid prescribing continuity was determined using the Continuity of Care Index (COCI) proposed by Bice and Boxerman, and captures "the extent to which a given individual's total number of visits for an episode of illness or a specific time period are with a single or group of referred providers" (Bice, Boxerman 1977). In the context of the present study, COCI was calculated based on opioid prescriptions filled and its value ranged from 0 (complete fragmentation of care) to 1 (perfect continuity of care). COCI scores were classified into quartiles and beneficiaries were assigned to three categories – bottom quartile (0-25th percentile), middle quartile (25th–75th percentile), and top quartile (more than 75th percentile).

The Continuity of Care Index was calculated at different time points for the two different aims of the study. For aim 1, COCI was calculated in the 6-month period prior to the cohort entry date. For aim 2, COCI was assessed in the 6-month hazard period prior to the index date for the case and its matched control.

Sensitivity analysis was conducted using a different measure of continuity of care – the Herfindahl Index (HI). Even though the HI is conceptually similar to that of the COCI, in the sense that both measure "the degree of coordination required between different providers during an episode" (Pollack, et al. 2016), it is calculated slightly differently.

Control Variables

Covariates included in the study included beneficiary sociodemographic characteristics, clinical characteristics, and opioid medication use characteristics. Sociodemographic characteristics included race, sex, Medicare low-income subsidy (LIS) status, and region of residence. Clinical characteristics controlled for in the study include comorbidity score – assessed using the Deyo adaptation of the Charlson Comorbidity Index (CCI) in addition to separate indicators for presence of – multiple CNCP conditions, mental illnesses, renal insufficiency, hypnosis, substance abuse disorder, hepatic insufficiency, Parkinson's disease, chronic obstructive pulmonary disorder (COPD), sleep apnea or other sleep disorders. Additionally, history of overdose and OIRD were assessed (Deyo et al. 1992). Opioid medication uses characteristics included average daily dose of opioids prescribed – in morphine milligram equivalent (MME) units, and type of opioid prescribed. Based on CDC guidance and prior research, average daily dose of opioids was divided into the following categories: less than 20 MME, 20-50

MME, and 50 MME or above (CDC 2021). Type opioid prescribed were categorized into – short-acting, long-acting, and combination products. All covariates were assessed prior to the index date.

Statistical analysis

Descriptive statistics were used to report beneficiary characteristics, and continuity of care. For categorical variables, frequency and percentage distributions were reported. Statistical comparisons were conducted between the groups using Chi-Square tests. For continuous variables, mean and standard deviation (SD), or median and interquartile range were reported, as appropriate. Statistical comparisons for continuous variables were conducted using paired t-tests. Conditional logistic regression models were used to examine the relationship between continuity of care and opioid-related adverse events accounting for the matched case-control data. All analyses were conducted using SAS version 9.4 (Cary, NC).

Results

Study Cohort

Characteristics of the 35,189 Medicare beneficiaries who were new LTOT users are shown in Table 1. The mean was 77 years in this group; 24,342 were female (69%), 29,321 were white (83%), and 15,054 had a low-income status (43%). This sample had an average COCI score of 0.65 in the 6-month period prior to cohort entry. 2,165 (9%) of beneficiaries received at least one prescription from a pain specialist.

Table 1. Description of Patient Demographic and Clinical Characteristics

Patient Characteristics	**Full Cohort**	**Composite outcome**		
	N=35,189	Control N=1,122	Cases N=1,122	
	N (%)	N (%)	N (%)	*P*
COCI				<0.001*
Low	13,721 (38.99)	271 (46.01)	318 (53.99)	
Medium	5,365 (15.25)	263 (44.50)	328 (55.50)	
High	16,103 (45.76)	588 (55.26)	476 (44.74)	
HI				<0.001*
Low	8,623 (24.50)	245 (43.91)	313 (56.09)	
Medium	10,463 (29.73)	289 (46.46)	333 (53.54)	
High	16,103 (45.76)	588 (55.26)	476 (44.74)	

Pain Specialist^	2,884 (9.18)	90 (56.25)	70 (43.75)	0.087
Opioid Formulation Combination LA SA		 97 (25.94) 40 (39.60) 985 (55.68)	 277 (74.06) 61 (60.40) 784 (44.32)	<0.001*
Avg MME 20 – 50 ≥ 50 < 20		 507 (47.47) 125 (35.01) 490 (59.83)	 561 (52.53) 232 (64.99) 329 (40.17)	<0.001*
Age (SD)	77.19 (8.60)	82.44 (9.30)	82.50 (9.40)	0.07
Sex (Female)	24,342 (69.18)	868 (50.49)	851 (49.51)	0.40
Race Black White Other	 3,686 (10.47) 29,321 (83.32) 2,182 (6.20)	 78 (41.49) 968 (49.69) 76 (70.37)	 110 (58.51) 980 (50.31) 32 (29.63)	<0.001*
LIS	15,054 (42.78)	571 (43.13)	753 (56.87)	<0.0001*
Region North-East South West Mid-West		 161 (52.44) 519 (50.98) 183 (53.04) 259 (45.12)	 146 (47.56) 499 (49.02) 162 (46.96) 315 (54.88)	0.05*
Mental Illness		525 (43.32)	687 (56.68)	<0.001*
Renal Insufficiency		341 (37.97)	557 (62.03)	<0.001*
Hypnotic Medications		3 (25.00)	9 (75.00)	0.08
Substance Abuse		33 (54.10)	28 (45.90)	0.513
Sleep Apnea		115 (40.78)	167 (59.22)	<0.001*

Other Sleep Disorder		447 (38.27)	721 (61.73)	<0.001*
Hepatic Insufficiency		74 (38.34)	119 (61.66)	<0.001*
Parkinson		56 (43.08)	74 (56.92)	0.104
Respiratory Infection		0 (0.00)	10 (100.0)	0.001*
COPD		443 (41.29)	630 (58.71)	<0.001*
Anticonvulsants		462 (45.65)	550 (54.35)	<0.001*
Antidepressants		494 (43.26)	648 (56.74)	<0.001*
NSAIDs		237 (63.20)	138 (36.80)	<0.001*
Sedative Hypnotics		113 (54.07)	96 (45.93)	0.217
Benzodiazepines		145 (46.47)	167 (53.53)	0.18
Muscle Relaxants		92 (49.46)	94 (50.54)	0.88
Multiple CNCP		1,005 (49.34)	1,032 (50.66)	0.05*
History of OIRD		6 (23.08)	20 (76.92)	0.006*
History of Overdose		6 (26.09)	17 (73.91)	0.02*

*Significant at α=0.05 level, COCI=Continuity of Care Index, HI= Herfindahl Index, ^Beneficiaries who received at least one opioid prescription from a pain specialist, SA=Short Acting, LA=Long Acting, MME=Morphine Milligram Equivalents, LIS=Low Income Status, COPD=Chronic Obstructive Pulmonary Disease, OIRD=Opioid Induced Respiratory Depression, Avg=Average, CNCP=Chronic Non-Cancer Pain, NSAIDs= Nonsteroidal Anti-Inflammatory Drugs.

Outcomes

1,122 patients experienced the composite outcome. After selection of matched cases and controls, the median duration of time between cohort entry and the index date for study subjects who experienced the composite outcome was 254.5 days (IQR: 77-519). The mean COCI for cases was 0.70 (SD of 0.26) and for controls was 0.75 (SD of 0.30). Similarly, the mean HI for cases was 0.74 (SD of 0.26) and for controls was 0.79 (SD of 0.25).

Unadjusted Analysis

Unadjusted results of the conditional logistic regression models are reported in Table 2. It was found that beneficiaries with low COC (OR= 1.61 [95% CI 1.28 - 2.02]) had higher odds of the outcome relative to those with a higher COC. Beneficiaries with medium COC had 65% (OR= 1.65 [95% CI 1.33 - 2.04]) higher likelihood of experiencing the composite outcome relative to high continuity of care. Beneficiaries with medium continuity of care had 65% (OR = 1.65 [95% CI 1.33–2.04]) higher likelihood of experiencing the composite outcome relative to high continuity of care. Additionally, beneficiaries who received at least one opioid prescription from a pain specialist had 34% (OR = 0.66 [95% CI 0.48 - 0.93]) lower odds of the composite

outcome compared to those who did not receive any opioid prescription from a pain specialist.

Table 2. Conditional Logistic Regression Model Results

using Continuity of Care Index (COCI) (Unadjusted)

Patient characteristics	**Composite outcome**	
	OR (95% CI)	*P*
COCI		
High	Reference	
Low	1.61 (1.28-2.02)	<0.001*
Medium	1.65 (1.33-2.04)	<0.001*
Pain Specialist[%]		
No	Reference	
Yes	0.66 (0.48-0.93)	0.016*

*Significant at α=0.05 level, COCI=Continuity of Care Index, Ref=Reference category,

[%] Beneficiaries who received at least one opioid prescription from a pain specialist.

Adjusted Analysis

Table 3 presents adjusted results of the conditional logistic regression model for the composite outcome. After adjusting for all control variables, low continuity of care (OR = 1.46 [95% CI 1.09 – 1.96]) and medium continuity of care (OR = 1.38 [95% CI 1.05 – 1.81]) were found to be significantly associated with the composite outcome, respectively compared to high continuity of care. Receiving at least one opioid prescription from a pain specialist had 28% (OR = 0.72 [95% CI 0.47 – 1.10]) lower odds of composite outcome relative to those who did not receive any opioid prescription from a pain specialist. However, this finding was not significant. We also tested an interaction between the COCI term and presence of a prescription from a pain specialist, but this

term was not found to be significant and was subsequently dropped from the model for reasons of parsimony.

Sensitivity analysis using the Herfindahl Index (HI) showed results similar to COCI (Tables 4 & 5) demonstrating the robustness of our analyses.

Table 3. Conditional Logistic Regression Model Results using Continuity of Care Index (COCI) (Adjusted)

Patient characteristics	**Composite outcome**	
	OR (95% CI)	P
COCI		
High	Ref	
Low	1.46 (1.09-1.96)	0.011*
Middle	1.40 (1.05-1.81)	0.020*
Pain Specialty (Ref=No)		
Yes	0.72 (0.47-1.10)	0.125
Average MME		
<20	Ref	
20 - 50	1.80 (1.40-2.30)	<0.001*
≥ 50	2.44 (1.63-3.64)	<0.001*
Opioid Formulation		
SA	Ref	
Combination	2.58 (1.81-3.66)	<0.001*
LA	0.87 (0.50-1.57)	0.635
Sex (Ref=Male)		
Female	0.88 (0.66-1.18)	0.400
Race		
White	Ref	
Black	1.35 (0.88-2.07)	0.166
Other	0.27 (0.15-0.47)	<0.001*
Region		
Northeast	Ref	
Midwest	1.45 (1.00-2.11)	0.263
South	1.04 (0.73-1.46)	0.784
West	1.28 (0.85-1.93)	0.347
LIS (Ref=No)		
Yes	2.12 (1.66-2.70)	<0.001*

CCI 0 1-2 ≥3	 Ref 2.01 (1.44-2.81) 2.86 (1.94-4.22)	 <0.001* <0.001*
Mental Illness (Ref=No) Yes	 1.26 (0.98-1.63)	 0.074
Renal Insufficiency (Ref=No) Yes	1.35 (1.06-1.72)	0.015*
Hypnotic Medications (Ref=No) Yes	1.06 (0.20-5.50)	0.946
Substance Abuse (Ref=No) Yes	 0.72 (0.37-1.38)	 0.315
Sleep Apnea (Ref=No) Yes	 0.89 (0.62-1.40)	 0.502
Other Sleep Disorders (Ref=No) Yes	2.04 (1.60-2.60)	<0.001*
Hepatic Insufficiency (Ref=No) Yes	0.92 (0.61-1.40)	0.697
Parkinson (Ref=No) Yes	 1.16 (0.74-1.81)	 0.518
COPD (Ref=No) Yes	 1.14 (0.89-1.47)	 0.304
Anticonvulsants (Ref=No) Yes	 1.09 (0.86-1.38)	 0.462
Antidepressants (Ref=No) Yes	 1.32 (1.03-1.70)	 0.030*

NSAIDs (Ref=No) Yes	 0.67 (0.50-0.90)	 0.009*
Sedative Hypnotics (Ref=No) Yes	 0.73 (0.50-1.10)	 0.130
Benzodiazepines (Ref=No) Yes	 1.15 (0.83-1.60)	 0.387
Muscle Relaxants (Ref=No) Yes	 1.04 (0.69-1.57)	 0.841
Multiple CNCP (Ref=No) Yes	 0.73 (0.48-1.09)	 0.127*
History of OIRD (Ref=No) Yes	 0.65 (0.20-2.18)	 0.50

History of Overdose (Ref=No) Yes	 1.12 (0.32-3.90)	 0.856

*Significant at α=0.05 level, COCI=Continuity of Care Index, Ref=Reference category, SA=Short Acting, LA=Long Acting, MME=Morphine Milligram Equivalents, LIS=Low Income Status, CCI=Charlson Comorbidity Index, COPD=Chronic Obstructive Pulmonary Disease, OIRD= Opioid Induced Respiratory Depression, CNCP=Chronic Non-Cancer Pain, NSAIDs= Nonsteroidal Anti-Inflammatory Drugs.

Table 4. Conditional Logistic Regression Model Results using Herfindahl Index (HI) (Unadjusted)

Patient characteristics	**Composite outcome**	
	OR (95% CI)	*P*
HI High Low Medium	 Reference 1.79 (1.42-2.26) 1.52 (1.23-1.88)	 <0.001* <0.001*
Pain Specialist[%] No Yes	 Reference 0.65 (0.47-0.91)	 0.012*

*Significant at α=0.05 level, HI=Herfindahl Index, Ref=Reference category,

[%] Beneficiaries who received at least one opioid prescription from a pain specialist.

Table 5. Conditional Logistic Regression Model Results for Composite Outcome using Herfindahl Index (HI) (Adjusted)

Patient characteristics	**Composite outcome**	
	OR (95% CI)	*P*
HI High Low Middle	 Ref 1.51 (1.12-2.03) 1.35 (1.04-1.77)	 0.007* 0.026*
Pain Specialty (Ref=No) Yes	 0.71 (0.46-1.09)	 0.119

Average MME		
<20	Ref	
20 - 50	1.79 (1.40-2.29)	<0.001*
≥ 50	2.43 (1.63-3.63)	<0.001*
Opioid Formulation		
SA	Ref	
Combination	2.56 (1.80-3.64)	<0.001*
LA	0.87 (0.48-1.59)	0.653
Sex (Ref=Male)		
Female	0.88 (0.66-1.17)	0.382
Race		
White	Ref	
Black	1.35 (0.88-2.07)	0.170
Other	0.27 (0.15-0.47)	<0.001*
Region		
Northeast	Ref	
Midwest	1.45 (1.00-2.10)	0.049*
South	1.04 (0.73-1.47)	0.841
West	1.28 (0.85-1.93)	0.234
LIS (Ref=No)		
Yes	2.11 (1.65-2.70)	<0.001*
CCI		
0	Ref	
1-2	2.01 (1.44-2.82)	<0.001*
≥3	2.86 (1.94-4.22)	<0.001*
Mental Illness (Ref=No)		
Yes	1.26 (0.98-1.63)	0.073
Renal Insufficiency (Ref=No) Yes	1.35 (1.06-1.72)	0.015*
Hypnotic Medications (Ref=No) Yes	1.05 (0.20-5.47)	0.950
Substance Abuse (Ref=No)		
Yes	0.72 (0.37-1.38)	0.317
Sleep Apnea (Ref=No)		
Yes	0.88 (0.62-1.26)	0.486
Other Sleep Disorders (Ref=No) Yes	2.05 (1.60-2.61)	<0.001*
Hepatic Insufficiency (Ref=No) Yes	0.92 (0.62-1.40)	0.702
Parkinson (Ref=No)		
Yes	1.16 (0.74-1.81)	0.522
COPD (Ref=No)		

Yes	1.14 (0.89-1.47)	0.303
Anticonvulsants (Ref=No) Yes	1.09 (0.86-1.38)	0.464
Antidepressants (Ref=No) Yes	1.32 (1.03-1.70)	0.034*
NSAIDs (Ref=No) Yes	0.67 (0.49-0.91)	0.009*
Sedative Hypnotics (Ref=No) Yes	0.74 (0.49-1.10)	0.137
Benzodiazepines (Ref=No) Yes	1.15 (0.83-1.60)	0.388
Muscle Relaxants (Ref=No) Yes	1.04 (0.69-1.57)	0.852
Multiple CNCP (Ref=No) Yes	0.73 (0.48-1.09)	0.124
History of OIRD (Ref=No) Yes	0.65 (0.19-2.16)	0.476
History of Overdose (Ref=No) Yes	1.11 (0.32-3.87)	0.866

*Significant at α=0.05 level, HI= Herfindahl Index, Ref=Reference category, SA=Short Acting, LA=Long Acting, MME=Morphine Milligram Equivalents, CCI= Charlson Comorbidity Index, LIS=Low Income Status, COPD=Chronic Obstructive Pulmonary Disease, OIRD= Opioid Induced Respiratory Depression, CNCP=Chronic Non-Cancer Pain, NSAIDs= Nonsteroidal Anti-Inflammatory Drugs.

Discussion

Throughout recent years, the word “epidemic” seemed to only apply to viral diseases such as COVID-19. The thought of something this severe is seen as something obvious, even though the United States has been dealing with a silenced self-created epidemic of its own. Addiction is not uncommon nor is it new, but the way it has become so centered around medicine has become alarming. In today’s world, there are many substances placed on a list considering them “illegal,” and for good reason. However, some “legal” substances that are still being prescribed and given out are statistically just as dangerous. Opioids are increasingly attracting more victims, and it seems to have no end in sight. It is not just about the drug itself, but how it ended up in so many hands of American citizens.

This study observed the safety of opioid use in the long-term. This was obtained using a nationally representative cohort of Medicare-eligible older adults with CNCP. The evaluation of prescribing characteristics along with the incidence of opioid-related adverse events was important to the data. It was found that less than 1 out of 10 adults starting a new LTOT episode received at least one prescription from a pain specialist. The COC of opioid prescribing was obtained two different ways – through COCI and HI. It was also found that participants had a moderate degree of continuity during their initial long-term opioid use episode. It was also found that those with greater COC had lower odds of experiencing any opioid-related adverse event, but the presence of a prescription

from a pain specialist did not significantly impact risk of any adverse events. These findings present significant evidence to help improve safety of LTOT among older adults suffering from CNCP.

This study was able to find that after accounting for dose and type of opioid therapy, some individuals had nearly 50% greater odds of experiencing an adverse event as compared to those who had perfect COC. These same individuals were in the lowest quartile of continuity of opioid prescribing as well. Hallvik and colleagues' findings did represent unadjusted results from one state, this study confirms the important of COC regarding opioid prescribing using two different measurements (Hallvik et al., 2018). Previous studies have examined the impact of COC and have found that patients with high COC have lower rates of mortality (Gray et al., 2018), preventable hospitalizations (Cheng et al., 2010; Nyweide et al., 2013), receive fewer unnecessary medical services (Romano et al., 2015), have more emergency room visits (Kern et al., 2019), higher healthcare costs and adverse outcomes (Amjad et al., 2016). Most previous research examining continuity regarding opioid prescribing gives an approach that quantifies the number of prescribers or pharmacies used per individual. Those individuals that use multiple prescribers are engaging in a behavior that may be indicative of harmful drug use (Cepeda et al., 2012). However, this may not be reflective of non-medical use of prescription opioids among older adults as prevalence would be assumed to be lower for this age group. Ensuring continuity of opioid prescribing for older adults is a way to ensure safety. Measures that can evaluate quantitatively, such as COCI or HI, can be more applicable rather than using the number of unique prescribers. This can be

supported in that continuity of care has been found to be more appropriate for control of CNCP (Satterwhite et al., 2019).

This study found that individuals having at least one opioid prescription from a pain specialist were not less likely to experience and opioid-related adverse event. This may come as a surprise, but no previous studies have been able to correlate this relationship between prescriptions from pain specialists and adverse events. However, a significant amount of evidence supports the role that pain specialists play in being consulted for treatment of chronic pain (Patwardhan et al., 2018; Hanna et al., 2018). Findings from other research show that pain specialists prescribe opioid medications more often than primary care providers, but their prescriptions are likely to be for lower dosages (Alamanda et al., 2016; Pan, Blankey, & Hughes, 2019). Pain specialists have more training, knowledge, and less negative perceptions of LTOT (Hsu et al., 2021; McCarberg et al., 2013; Varrassi & Muller-Schwefe, 2012). It is possible that the findings in this study are indicative that having at least one prescription from a pain specialist does not confer more confidence in specialists being involved in treatment. The odds ratio for the pain specialist variable changed from significant to non-significant after adjustment of other covariates; this may suggest that a more complex relationship may be at play involving the pain specialist. It could be that after accounting for continuity of opioid prescribing, provider specialty does not significantly improve safety in LTOT. This could be a huge finding; previous studies have shown that pain specialists are not easily accessible (Wiznia et al., 2017) and have called for greater numbers of allied providers such as pain-specialist pharmacists (Atkinson, Gulum, & Forkum, 2016). Regardless, a centered focus on continuous patient management with higher COC,

regardless of provider specialty, may hold a potential for improving the safety for patients on LTOT.

However, this study's findings have to be interpreted with context of some limitations. First, this study operationalized continuity of opioid prescribing using COCI and HI. Both of these measures have limitations within them. Both of these assume that repeated visits to the same provider allow for greater continuity, but neither measure is able to capture the content for each visit with said provider. Management of chronic conditions requires a team of providers that work together in various aspects of care for said patient, and this itself cannot be captured by a number generated through COCI or HI. Next, this study design estimated COCI and HI during a 6-month duration prior to the index date during which individuals were required to have at least 3 prescriptions filled for opioid medications. If the number of prescriptions is low, the COCI and HI may yield unreliable results. The findings in this study are in line with the hypothesis, but studies done over longer durations would need to be able to validate these same results. Also, this study does not account for prescriptions paid for using cash per the administrative claims data limitation. This study also only utilized information for those enrolled in Medicare Advantage plans and also excluded those younger than 65 years of age. Both of these variables could have an effect on the overall reliability of the outcomes.

Conclusion

This study showed that Medicare-enrolled adults over the age of 65 who initiate LTOT have moderate levels of COC and only a small portion of them receive prescriptions from pain specialists. It was also found that continuity of care, but not provider specialty, was significantly associated with fewer opioid-related adverse event among older adults with Chronic Non-Cancer Pain.

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