Retrospective Claims Analysis of Opioid Prescribing Patterns: Single and Combination Agents for Acute Pain and Subsequent Conversion to Chronic Opioid Usage Among Commercial Members

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BACKGROUND

- Pain is a complex phenomenon that must be managed through a unique and individualized approach for each patient.[1]
- For opioid naïve patients, physical dependence can occur in as little as 4-8 weeks.[2]
- According to the 2022 Centers for Disease Control and Prevention (CDC) Opioid Prescribing Guidelines, non-opioid therapies are found to be at least as effective as opioids in many types of acute pain and should be maximized.[1]
- Opioid therapy should only be initiated for acute pain if necessary. If an opioid is initiated, an immediate release form should be prescribed at the lowest effective dosage for no greater quantity than needed for the expected duration of pain (<7 days is usually sufficient).[1]
- A traditional prescribing approach is to combine a non-opioid with an opioid to produce additive analgesia by activating multiple pain-inhibitory pathways to provide relief for a broader spectrum of pain and reduced adverse effects.[3]
- The variations in physician prescribing for combination and single opioid agents in acute pain and the subsequent implications for long-term opioid use are still mostly unknown.[4]

OBJECTIVES

To assess the impact of initiation with a combination agent (CA) vs. a single agent (SA) in opioid naïve members with acute pain and subsequent conversion to opioid dependence

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METHODS

- Observational retrospective analysis of paid pharmacy claims in a commercial health plan from 10/01/2021–12/31/2022
- Study Population:
  - Continuously enrolled members aged 18 to 64
  - Opioid naïve (no opioid claims from look-back period of 10/01/2021–12/31/2021)
  - Prescribed a combination agent (oxycodone/acetaminophen, oxycodone/ibuprofen, tramadol/acetaminophen, hydrocodone/aspirin, oxycodone/aspirin, tramadol/celecoxib) OR single agent (oxycodone, hydrocodone, tramadol) during baseline period of 01/01/2022–06/30/2022 for acute pain (≤7 days' supply)
- Baseline characteristics of age, gender, chronic disease score (measures the level of comorbid burden at a patient level), days' supply of first claim for SA or CA, and morphine milligram equivalents (MME) of first claim for SA or CA were assessed between cohorts.
- Primary outcome: Compare the proportion of opioid naïve members that started on an SA or CA and subsequently converted to a chronic user (≥3 months of continuous opioid use) from 07/01/2022–12/31/2022.
- Secondary outcomes: Assessed during evaluation period 07/01/2022–12/31/2022.
  - Average daily morphine milliequivalents (MME) for those who converted to chronic users
  - Proportion of members engaging in pharmacy or prescriber shopping (defined as ≥3 prescribers or pharmacies)
  - Proportion of members prescribed a concurrent benzodiazepine with overlap use (≥30 days)
  - Proportion of members prescribed a concurrent skeletal muscle relaxant (SMR) with overlap use (≥30 days)
- Continuous outcomes (average daily MME) were analyzed using linear regression (t-statistic reported) and dichotomous outcomes (% converting to chronic users, pharmacy/prescriber shopping, concurrent benzodiazepine or SMR use) were assessed using logistic regression (Wald chi-square reported).
- A significance level of a = 0.05 was used to assess outcomes.

FIGURE 1

Study Design

Sample Identification Window:
- Commercial health plan, continuously enrolled members during entire measurement period

Exclusion Window:
- Under age 18 or over 65, based on start of baseline period, one or more opioid claim(s) from 10/01/21–12/31/2021 (non-opioid naïve members)

Inclusion Window:
- One claim for acute pain (<7-day supply) for combination agent (oxycodone/acetaminophen, oxycodone/ibuprofen, tramadol/acetaminophen, hydrocodone/aspirin, oxycodone/aspirin, tramadol/celecoxib) OR single agent (oxycodone, hydrocodone, tramadol) from 01/01/2022–06/30/2022

Baseline Characteristics Assessed:
- Age, Gender, Chronic Disease Score, Day Supply – First Claim, MME – First Claim

Primary Outcome:
- Proportion of members who converted to a chronic user (≥3 months of continuous opioid use) during the evaluation period (07/01/2022–12/31/2022)

Secondary Outcomes:
- Average daily morphine milliequivalents (MME), Proportion of members engaging in pharmacy or prescriber shopping (defined as ≥3 prescribers or pharmacies), Proportion of members prescribed a concurrent benzodiazepine, Proportion of members prescribed a concurrent skeletal muscle relaxant

Measurement Period: 10/01/21–12/31/22

Baseline Period – 9 Months → | ← Evaluation Period – 6 Months

3 Months – Confirm no opioid prescribed	6 Months – PT on combo or single opioid	6 Months – Assess if PT converts to chronic user (≥3 Months of continuous opioid use)
Oct 1, 2021 – Dec 31, 2021	Jan 1, 2022 – Jun 30, 2022	Jul 1, 2022 – Dec 31, 2022

FIGURE 2

Frequency of Prescriber Specialties for Index Opioid Claim at Baseline

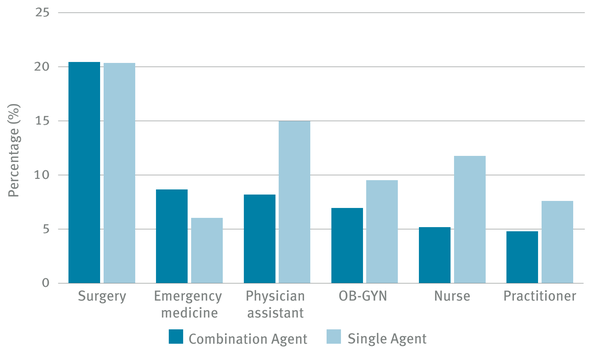

TABLE 1

Baseline Characteristics

	Combination Opioid Agent n=13,561		Single Opioid Agent n=5,099		Total N=18,660	
	Mean/%	SD/Count	Mean/%	SD/Count	Mean/%	SD/Count
Age (baseline)	43.17	13.34	45.29	12.69	43.75	13.20
% Female	54.88	7,442	60.01	3,060	56.28	10,502
Chronic disease score	2.17	1.79	3.00	1.79	2.40	1.83
Days' supply – Index claim	3.55	1.67	3.99	1.82	3.67	1.72
MME – Index claim	31.51	14.52	30.74	17.38	31.30	15.36

TABLE 2

Outcomes Regression Analysis Results Comparing Combination Agent Utilizers to Single Agent Utilizers*

Outcomes	Count	Test Statistic	P-Value	Odds Ratio	95% CI for Odds Ratio
% Converted to chronic user	22 members	0.26	0.61	0.82	0.38-1.77
Average daily MME	23.36 MME	1.57	0.12		
Benzodiazepine & opioid overlap use	8 members	0.92	0.34	1.60	0.612-4.18
Skeletal muscle relaxant & opioid overlap use	22 members	1.10	0.30	0.65	0.29-1.46
Pharmacy/Prescriber shopping	63 members	2.10	0.147	1.35	0.90-2.03

*Combination agent users: experimental group
*Odds ratios represent the odds for the combination agent utilizers relative to single agent utilizers

RESULTS

- 18,660 members met the study inclusion criteria, with 13,561 and 5,099 in the CA and SA groups, respectively.
- At baseline, the CA group was slightly younger and had fewer females, a lower level of comorbidity, a lower days' supply, and a higher MME for the first claim. (Table 1)
- Of the total sample, **only 33 (0.18%) members converted to continuous opioid users.** (Table 2)
- Of the 33 total members who converted to continuous opioid users, 22 (0.16%) members were in the CA group and 11 (0.22%) members were in the SA group; however, there was no significant difference between groups.
- No statistically significant difference was observed in the secondary outcomes.

LIMITATIONS

- It is unknown to what extent members identified as single agent opioid users may have been supplementing their pain management regimen with over-the-counter pain relievers.
- Opioid utilization patterns could be impacted by members paying cash for their prescription fills. Only paid opioid fills adjudicated through the member's pharmacy benefit are captured in this analysis.
- Findings are generalizable only to commercially insured members and may not be representative of members within different lines of business.

DISCUSSION

- Following the passage of the 2016 CDC opioid guidelines and large increase in opioid-related overdose deaths, the number of states with laws that impose enforceable limitations on opioid prescriptions for pain treatment have increased rapidly from 10 in 2016 to 39 by the end of 2019.[5,6]
- Across all 50 states in the U.S., there were varied laws on acute pain, MME dosage limits, and first-time prescription fills with 46% of states requiring days' supply limits of 7 days.[5,6]
- The updated 2022 CDC opioid guidelines acknowledged the misapplication of the 2016 recommendations in the form of government legislations or absolute limits for policies by managed care organizations or health care systems that may have resulted in increased patient burden and worse patient outcomes.
- After assessing different factors that may contribute to a member converting to chronic usage, the extremely small number of members who actually converted suggests that no factors can be used as definitive guideposts to predict chronic usage.
- Maximizing non-opioid therapies like ibuprofen or acetaminophen, as recommended in the CDC guidelines, may have some role in the low number of subsequent chronic users due to their additional analgesic benefits.
- However, the study's results suggest that lower 3-4 day durations and dosages around 30 MME/day may be more beneficial guideposts as it may be sufficient for many opioid naive patients with common types of acute pain found in primary care or emergency department settings.

CONCLUSIONS

- The study's results did not find that a combination with a non-opioid played a significant role in predicting chronic opioid usage.
- Less than 1% of members from both cohorts converted to chronic use indicating a days' supply of <7 and average 30 MME/day may be more important than maximizing non-opioid therapies to prevent conversion to continuous use.
- However, there may be additive analgesic benefits with CAs due to their multiple mechanisms of action.

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