Original Work

Analysis of Opioid Prescription Practices After Mailed Intervention by a Pharmacy Benefit Manager to Prescribers of Commercial Health Plan Members

by Caitlin C. Albrecht, PharmD, Marleen K. Wickizer, PharmD, AE-C, CDCES, Agata Siwak, PharmD, Maria L. Hurst, CPhT, PMC, Robert V. Topp, PhD, RN

Abstract

Objective: High-dose opioid prescriptions are associated with increased risk of opioid misuse and overdose. With access to members' complete prescription claims histories, a pharmacy benefit manager (PBM) is in a unique position to intervene with members receiving high doses of opioids. This study investigates how a PBM-led intervention impacted members' future opioid therapy.

Methods: Members were included if they had opioid claims averaging ≥ 90 morphine milligram equivalents (MME) per day from July 1, 2019, through October 31, 2019. Sixty-five members qualified for the study; 33 in the intervention group and 32 in the control group. In November 2019, letters containing information about the members' opioid claims history were sent to prescribers of intervention group members. Outcomes were collected from July 1, 2020, through October 31, 2020. The primary outcome was mean decrease in daily MME; secondary outcomes included change in number of opioid prescribers.

Results: The average decrease in daily MME in the intervention group (33.3 ± 102.8) was not statistically different than the control group (13.4 ± 36.2, p = 0.30). The number of opioid prescribers was similar at baseline among the intervention (1.39 ± 0.14) and the control group members (1.63 ± 0.14) and statistically different following the intervention (1.18 ± 0.12 vs. 1.59 ± 0.12, p = 0.04).

Conclusions: Mailings to prescribers of members with high daily MME values were not found to be associated with a significant decrease in average daily MME but did result in a decrease in average number of opioid prescribers.

Though there have been improvements in opioid prescribing practices over the past several years, the opioid epidemic continues to be a major problem within the United States, with more than 68,000 deaths involving opioids occurring in 2020.[1] Additionally, non-fatal opioid overdoses substantially contribute to the number of hospitalizations and emergency department (ED) visits that occur annually; ED visits related to opioids increased by an average of 12% per year between 2014 and 2017.[2]

Higher average daily doses of opioids are associated with an increased risk of opioid-related mortality; doses of greater than 200 morphine milligram equivalents (MME) have been associated with a 2.9-fold increase in opioid-related death, and doses between 50 and 99 MME per day have been associated with a 1.9-fold increase in opioid-related death, compared to doses of less than 20 MME per day.[3] Higher daily doses of opioids are also associated with increased risk of overdose.[4] One study found that patients taking 50-99 MME per day had a 3.7-fold increase in overdose risk and patients taking more than 100 MME per day had an 8.9-fold increase in overdose risk, compared to patients receiving less than 20 MME per day.

The Centers for Disease Control and Prevention (CDC) published guidelines on opioid prescribing for patients with pain in 2016 and updated these guidelines in 2022.[5,6] The guidelines specifically discuss the use of high doses of opioids, defined in the 2016 guidelines as greater than 90 MME per day. Per the CDC, there has not been found to be a clear benefit associated with opioid doses of greater than 50 MME when compared to lower doses, despite substantial evidence of increased risk.[6] The CDC recommends prescribing the lowest effective dose possible when starting opioid therapy; they state that 20-30 MME per day for an opioid-naïve patient is often sufficient. Benefits and risks should be carefully evaluated when increasing dosing, and clinicians should closely monitor patients who are on high-dose opioid therapy and should provide strategies, including education, to reduce overdose risk when possible.

Rates of high-dose opioid prescribing were trending downward prior to the publication of the CDC's 2016 guidelines and continued to decrease following publication.[7,8] This and other studies support the idea that educational

programming targeted to providers on the risks associated with opioid use can impact prescribing practices and encourage lower levels of average daily MME.[9,10]

Daily MME values of 90 or higher may be the result of more than one opioid prescription taken concurrently, and doses of this magnitude are sometimes prescribed by multiple clinicians and filled at multiple pharmacies. Consequently, a clinician prescribing an opioid or a pharmacist filling an opioid prescription may not be aware of the patient's complete opioid history, as information stored within the electronic health record at one clinic may not be accessible to clinicians at other locations. A pharmacy benefit manager (PBM) may therefore be well positioned to identify members receiving high doses of opioids and to notify prescribers of the patient's complete opioid fill history. Navitus Health Solutions, a PBM, has a retrospective drug utilization review safety program, called the MME Safety Program, that identifies members who have received at least 90 MME per day in a given 4-month time period. This program includes standardized letters mailed to prescribers of identified members, which include information about the patient, their opioid and potentiator medication profiles, their opioid and naloxone fill histories, and the risks associated with high doses of opioids. The purpose of this study was to determine the effect of targeted mailings sent to the prescribers of members with high doses of opioid prescriptions on the member's future opioid prescriptions. A prior study evaluated the impact of mailed prescriber letters on opioid and benzodiazepine prescription rates in individuals receiving both classes of medications; this study differs from that one, as it evaluated members taking only high doses of opioids, not opioids and benzodiazepines.[11]

Methods

Study Design

This study was a retrospective analysis of prescription claims data from commercial health plan members. IRB exemption was obtained prior to accessing data. The study compared members of commercial health plans that participate in the MME Safety Program (the intervention group) to members of similar commercial health plans that did not participate in the program (the control group). Members within these commercial health plans were identified using the PBM's claims database. Eligible members had prescription claims totaling greater than or equal to 90 MME per day during the 4-month pre-intervention period, from July 1, 2019, through October 31, 2019. Members were excluded if they were under the age of 18 or were not enrolled in their respective commercial health plan throughout the entire study period, from July 1, 2019, through October 31, 2020. Members were also excluded if they had claims for oncology medications, had claims from a long-term care pharmacy in the past 4 months, or were currently receiving hospice care.

On November 1, 2019, the MME Safety intervention letters were mailed to providers. Prescribers of the intervention group's members were contacted via letter if the member had filled a prescription for an opioid written by the prescriber in the pre-intervention period. The letter included a list of the opioid medications the member had filled during the previous 4 months, as well as the fill date, drug name, quantity and days' supply, the name and address of the prescriber, and the name and address of the pharmacy where the medication was filled. Total number of opioid prescribers used, total number of pharmacies used, and any potentiator medications filled during the time period were also included. The letter contained several recommendations to the prescriber, including recommendations that the prescriber provide education to the member on opioid overdose, that they discuss and offer naloxone to the member, that they consider creating a plan to gradually taper down the member's opioid doses, and that they review the prescription drug monitoring (PDMP) database and coordinate therapy with different prescribers on the included profile as appropriate. The prescribers of control group members were not mailed a letter and no additional action was taken on these members as a part of the MME Safety program. The health plans included in the intervention and control groups were not within the same state nor in nearby states, so it is unlikely prescribers would have had members in both groups.

In November of 2021, data from the post-intervention period, from July 1, 2020, to October 31, 2020, were analyzed and compared to data from the pre-intervention period. Data collected from the pre- and post-intervention periods included member age, member gender, average daily MME, number of opioid prescribers, number of pharmacies used and specific opioids filled, including quantity per script and number of fills.

Statistical Analysis

The primary hypothesis was that members whose opioid prescribers received a letter with information about the member's opioid fill history would decrease their average daily MME nine months after the mailing (in the post-intervention period) compared to members whose opioid prescribers did not receive a letter. Additional outcome variables compared between the two groups in the pre- and post-intervention period included the average number of opioid prescriptions,

TABLE 1. Baseline Demographics

Characteristic	*Intervention Group (n = 33)*	*Control Group (n = 32)*
Age (years)	52.0 ± 10.9	53.2 ± 12.2
Female	24 (73%)	17 (53%)
Average Daily MME	188	145
Average Number of Opioid Prescriptions	2.36	1.84
Average Number of Opioid Prescribers	1.39	1.63
Has At Least 1 Long-Acting Opioid	27 (82%)	23 (72%)

MME = morphine milligram equivalents

the average number of opioid prescribers and the percentage of members with at least one prescription for a long-acting opioid. Univariate repeated measures ANOVA statistics were calculated to determine if either of the groups changed on measures of average MME, number of opioid prescriptions, or the number of prescribers over the duration of the study. Significant ($p < 0.05$) time, group, or group by time interaction effects indicated post hoc comparisons of the appropriate means using Tukey's least significant differences. Chi-square statistics were calculated to compare the percentage of members with a prescription for at least one fill for a long-acting opioid.

Results

A total of 65 members were included in the study, 33 in the intervention arm and 32 in the control arm. The majority of members in both groups were female and the average age was 52 in the intervention group and 53 in the control group. Additional baseline demographics are provided in Table 1. The primary outcome, decrease in daily MME, was not statistically significantly different between the intervention group (33.3 ± 102.8) and the control group (13.4 ± 36.2, $p = 0.30$). Table 2 presents the R-ANOVA analysis comparing average daily MME, number of opioid prescriptions and number of opioid prescribers between study groups over time. As this table indicates, there was a significant time effect ($p = 0.02$) for average daily MME with post hoc analysis indicating that the intervention group exhibited a significant decline in average daily MME from 188.2 ± 15.3 to 154.9 ± 15.7. The control group did not significantly change their average daily MME over the duration of the study (145.1 ± 15.6 vs. 131.7 ± 16.0). This table also indicates a significant group effect ($p = 0.04$) for the number of opioid prescriptions: the intervention group (2.36 ± 0.15) had a greater number of opioid prescriptions compared to the control group (1.84 ± 0.15) prior to the intervention, and both groups had a similar number of opioid prescriptions post-intervention (intervention group: 2.18 ± 0.16 vs. control group: 1.88 ± 0.16). Neither the intervention nor the control group significantly changed their number of opioid prescriptions over the duration of the study. There was a significant group effect ($p = 0.04$) for number of opioid prescribers: pre-intervention, the study groups had similar numbers of opioid prescribers (intervention group: 1.39 ± 0.14 vs. control group: 1.63 ± 0.14), and post-intervention, the intervention group had significantly fewer opioid prescribers than the control group (intervention group: 1.18 ± 0.12 vs. control group: 1.59 ± 0.12).

Table 3 presents a chi-square analysis comparing the percentage of long-acting opioids between the two groups pre- and post-intervention. This table indicates that the percentage of the intervention group (82%) and the control group (72%) prescribed at least one long-acting opioid was similar at both the pre-intervention ($p = 0.34$) and post- intervention (intervention group: 73% vs. control group: 66%, $p = 0.54$) data collection points.

Discussion

This study examined how mailed communications sent to prescribers of commercial health plan members receiving high daily doses of opioids impact the members' future opioid medication claims. One endpoint studied, change in number of opioid prescribers, was found to be significantly improved in the intervention group. The primary endpoint, change in daily MME, as well as the other secondary endpoints, did not show a statistically significant difference between the two groups, though numerically, the intervention group outperformed the control group. A prior study to identify factors associated with risk of prescription opioid abuse found that opioid prescriptions from two or more pharmacies or two or more prescribers within a 3-month period were associated with increased risk of abuse.[12] There may therefore be benefit in interventions that encourage the use of fewer opioid prescribers. The outcomes of this study differ somewhat from a prior study that evaluated the effect of prescriber mailings on opioid and benzodiazepine prescribing rates in members taking both classes of medication; that study found that there was a significant decrease in the average daily MME between the intervention and control groups.[11] This difference may be related to the fact that the earlier study specifically evaluated members

TABLE 2. R-ANOVA Comparing Daily MME, Number of Opioid Prescriptions and Number of Opioid Prescribers Between Study Groups Over Time

Outcome	*Intervention Group*		*Control Group*		*Statistical Interpretation*	
	Pre-intervention Mean ± SE	*Post-Intervention Mean ± SE*	*Pre-intervention Mean ± SE*	*Post-Intervention Mean ± SE*	*F*	*P*
Daily MME	188.2 ± 15.3	154.9 ± 15.7*	145.1 ± 15.6	131.7 ± 16.0	G: 2.77 T: 5.59 GxT: 1.08	0.10 0.02 0.30
Number of Opioid Prescriptions	2.36 ± 0.15#	2.18 ± 0.16	1.84 ± 0.15	1.88 ± 0.16	G: 4.52 T: 0.51 GxT: 1.01	0.04 0.48 0.32
Number of Opioid Prescribers	1.39 ± 0.14	1.18 ± 0.12#	1.63 ± 0.14	1.59 ± 0.12	G: 4.43 T: 1.36 GxT: 0.75	0.04 0.25 0.39

*# Groups were different at a specific time; *A specific group changed over time; MME = morphine milligram equivalents; G = Main effect of group; T = Main effect of Time; GxT = Group by Time interaction effect*

receiving both opioids and benzodiazepines, and concurrent use of opioid and benzodiazepines have been shown to put an individual at increased risk of adverse outcomes, including fatal overdose, compared to opioid use alone.[13,14]

Limitations

This study has a number of limitations to consider. For one, the sample size was fairly small, at 33 and 32 members in the intervention and control groups respectively. With smaller sample sizes, the risk of type II error increases; it is therefore possible that the lack of a significant difference in the primary outcome was related to the small sample size. Sample size was limited by the control group arm, specifically, as the majority of Navitus' commercial clients participate in the MME Safety Program. Health plans generally choose not to participate in the MME Safety Program if they have their own, internal opioid monitoring programs. These programs would have been in place prior to the start of the study and may have impacted baseline prescribing habits and outcomes.

There were also some baseline differences between the groups. Specifically, in the pre-intervention period, the intervention group had a higher average daily MME, higher average number of opioid prescriptions and a greater percentage of members with one or more claims for a long-acting opioid. There was also variability within the intervention and control groups. For example, the average daily MME in the intervention group, pre-intervention, ranged from 91.9 MME per day to 472.0 MME per day, and the average daily MME within the control group ranged from 92.2 MME per day to 339.2 MME per day.

As this study was conducted as a retrospective review of claims data, if any participants paid out-of-pocket for opioid prescriptions in the pre- or post-intervention periods, those medications would not have been included in the analysis. Data are limited to commercial populations within specific geographical locations, and therefore, findings may not be generalizable to Medicare or Medicaid populations or other geographical regions. The intervention relied on mailed letters to the prescriber's clinic or office, and it is therefore possible that letters were unread by the prescriber. In the future, potentially there would be value in surveying prescribers to gather opinions and feedback on what information within the letter is most pertinent or how the letter or means of delivery could be improved. Additionally, future directions could include telephonic and other omni-channel interventions.

Successful tapering of opioids requires time and careful collaboration with the member, as is discussed in detail in the CDC's guidelines for opioid prescribing.[6] Since it is necessary to taper slowly, potentially a greater decrease in average daily MME would have occurred if there had been more time between the pre- and post-intervention periods studied. It is also possible that opioid doses of greater than 90 MME per day were clinically appropriate for some of these members; in these situations, the letters may have provided a reminder to the prescriber to reaffirm that the member was benefiting from their current regimen and to potentially provide additional education on overdose or to prescribe naloxone.

TABLE 3. Chi-Square Analysis Comparing the Percentage of Long-Acting Opioids Between Groups at Pre-Intervention and Post-Intervention

	Pre-Intervention		*Post-Intervention*	
	No Long-acting Opioids	*At Least 1 Long-acting Opioid*	*No Long-acting Opioids*	*At Least 1 Long-acting Opioid*
Control	9 (28%)	23 (72%)	11 (34%)	21 (66%)
Intervention	6 (18%)	27 (82%)	9 (27%)	24 (73%)
Statistical Interpretation	$X^2 = 0.9$, $p = 0.34$		$X^2 = 0.39$, $p = 0.54$	

Conclusion

Mailed letters to opioid prescribers of members with high average daily MME values were not found to be associated with a significant decrease in average daily MME but did result in a decline in average number of opioid prescribers. Further studies may be necessary to determine the full impact of mailed interventions, and adjustments to the intervention, such as including more or different information within the letter, may result in a greater decrease in opioid prescribing. As a new program, the main goal of the mailings was to educate and increase awareness among prescribers of quantities of opioids being used by their patients. As prescribers become more familiar with the program, potentially more impact on measured outcomes will be seen.

Caitlin Albrecht is a Clinical Pharmacy Resident at Navitus Health Solutions, LLC in Madison, WI. Marleen Wickizer is the Director of Clinical Services at Navitus Health Solutions, LLC in Madison, WI. Agata Siwak is a Population Health Pharmacist & Residency Program Coordinator at Navitus Health Solutions, LLC in Madison, WI. Maria Hurst is a Senior Product Manager, Population Health at Navitus Health Solutions, LLC in Madison, WI. Robert Topp is a Professor at the University of Toledo, College of Nursing in Toledo, OH.

Acknowledgments: This research was previously presented as a podium presentation at the Wisconsin Pharmacy Residency Conference on April 6, 2022, and as a resident research poster at the America College of Clinical Pharmacy Virtual Poster Symposium on May 25, 2022. This research has not been published elsewhere.

Disclosure: The authors declare no real or potential conflicts or financial interest in any product or service mentioned in the manuscript, including grants, equipment, medications, employment, gifts, and honoraria. The corresponding author had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

PR *This article has been peer-reviewed. The contribution in reviewing is greatly appreciated!*

Corresponding Author:
Caitlin Albrecht - Caitlin.albrecht@navitus.com

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