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ORIGINAL RESEARCH

Patient Knowledge of Safe Use of ER/LA Opioid Analgesics Following Implementation of the Class-Wide REMS: A Survey Study

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Background/Rationale: The US Food and Drug Administration (FDA) approved a Risk Evaluation and Mitigation Strategy (REMS) for extended release/long-acting (ER/LA) opioids in 2012. The purpose of this study was to assess patient knowledge of the safe use of these products following implementation of the REMS and to determine possible effects of the REMS, including impact on medication access.

Objective: To assess patient knowledge of safe use of ER/LA opioids and use of REMS patient education tools such as the Medication Guide (MG) and Patient Counseling Document (PCD).

Methods: This was a cross-sectional survey of commercially insured (Commercial) and Medicare Advantage-insured (Medicare) adults with ≥1 pharmacy claim for an ER/LA opioid (10/01/2015 – 02/28/2017) in the HealthCore Integrated Research Database and Medicaid-insured (Medicaid) adult members of a research panel, about their knowledge of safe use of ER/LA opioids and receipt/comprehension of the MG and PCD.

Results: Survey respondents consisted of 382 Commercial, 43 Medicare and 40 Medicaid adults. While ≥95% of respondents received and read the MG, fewer were aware of the PCD (Commercial: 47%, Medicare: 65%, Medicaid: 53%). Almost 75% of the knowledge questions were answered correctly by ≥80% of all respondents; fewer respondents recognized that use of opioids as directed can lead to death (Commercial: 73%, Medicare: 56%, Medicaid: 63%), the MG should be read at each dispensing (Commercial: 78%, Medicare: 53%, Medicaid: 75%), opioids should not be stored in the medicine cabinet (Commercial: 77%, Medicare: 79%, Medicaid: 58%), missed doses should not be taken as soon as possible (Commercial: 56%, Medicare: 51%, Medicaid: 50%), and pills should not be crushed (Commercial: 85%, Medicare: 67%, Medicaid: 52%).

Conclusion: Although most respondents reported reading and understanding the MG and exhibited knowledge of safe use of ER/LA opioids, providers' use of the PCD and increased understanding of safe use core messages need reinforcement.

Keywords: Risk Evaluation and Mitigation Strategy, opioids, patient knowledge

Introduction

Extended release (ER) and long-acting (LA) opioid analgesics are used in the United States (US) for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.[1] These medications include buprenorphine, fentanyl, hydromorphone, hydrocodone, methadone, morphine, oxycodone, oxymorphone, and tapentadol. A Risk Evaluation and Mitigation Strategy (REMS) for ER/LA opioid

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medications was approved by the US Food and Drug Administration (FDA) on 09 July 2012[2,3] as one element of a national response to increasing rates of opioid overdose and death.[4–6] In 2018, this opioid REMS was further expanded to include immediate release opioid analgesics, a program now known as the Opioid Analgesic REMS; however, this study was conducted under the ER/LA Opioid Analgesics REMS. The REMS comprises class-wide safety labeling changes as well as educational efforts that include (1) Medication Guides (MG), FDA-approved printed materials that are provided by pharmacies at the point of medication dispensing with the intent that patients read them prior to taking the dispensed medication that address issues specific to particular drugs and drug classes, and contain information for helping patients avoid serious adverse events; (2) Patient Counseling Documents (PCDs) to be used by ER/LA opioid prescribers and other healthcare providers for facilitating education of and discussions with patients; and (3) voluntary additional prescriber training on all ER/LA opioid analgesics. The educational documents are available online (www.er-la-opioidrems.com).

The purpose of this study was to assess (1) whether patients had received the MG and PCD documents intended to educate them about the safe use of ER/LA opioids; and (2) patients' knowledge of the safe use of these products following the start of REMS implementation. This study was one of the several studies[7] assessing the impact of ER/LA opioid analgesic REMS following its implementation in July 2012.

Methods

Study Design and Patient Population

A cross-sectional survey of adults who had used ER/LA opioid analgesics between October 1, 2015 and February 28, 2017 was conducted. The Commercial and Medicare Advantage patient populations were identified from medical and pharmacy claims in the HealthCore Integrated Research Database (HIRD), a large administrative claims database with longitudinal claims data from members of 14 geographically dispersed US health plans.

The Medicaid population was identified from members of an online survey research panel who indicated they had Medicaid insurance at some time during the past year. Panel members consisted of a pre-screened group of individuals who expressed willingness to participate in surveys, were identified through a recruitment process that complied with standards published by the European Society for Opinion and Marketing Research and Market Research Society and were characterized by a number of attributes, including type of health insurance.[8]

The claims-based Commercial and Medicare Advantage populations consisted of currently active, survey eligible adults, age 18 years and older, with Commercial or Medicare Advantage health insurance who filled at least one prescription for an ER/LA opioid analgesic, including transdermal patch, transmucosal film, methadone, and oral formulations, within the most recent 12 months of claims data available at the time the sample was identified. Patients with claims for drug or substance abuse were excluded to comply with Title 42 of the Code of Federal Regulations Part 2 (42 CFR Part 2) Rule which protects the privacy of individuals undergoing substance and alcohol abuse treatment.

The Medicaid panel population consisted of adults, age 18 or older, who indicated they were covered by Medicaid insurance at some time during the most recent 12-month period and had used at least one ER/LA opioid analgesic, including transdermal patch, transmucosal film, methadone, and oral formulations, in the most recent 12-months.

Since the Commercial patient population may not be representative of the total patient population using ER/LA opioid analgesics, the Medicaid and Medicare Advantage patient populations were added to supplement the Commercial population. The targeted number of completed surveys from each of these populations was at least 40 in addition to the targeted number of 400 completed Commercial surveys.

Survey Process

Recruitment letters and emails were sent to Commercial (age 18 years and older) and Medicare Advantage (age 65 and older) patients meeting the criteria described above to inform them of the study and solicit their participation. Patients who did not respond to the recruitment letter and/or email and had valid landline telephone numbers were called by interviewers and recruited over the telephone. Survey administration was either via the internet or over the telephone with an interviewer.

Medicaid (age 18 years and older) panel members were recruited by email and completed the survey via the internet. The recruitment email was similar to the letter and email used to recruit Commercial and Medicare Advantage respondents and their survey process was similar to that of the Commercial and Medicare Advantage respondents.

All respondents had to provide electronic or verbal consent and meet study inclusion criteria before starting the 20-minute survey that assessed their level of knowledge about the serious risks associated with the use of their ER/LA opioid analgesic medications and their experiences with the MG and PCD. Screening questions excluded respondents who reported they did not fill a prescription for an ER/LA opioid analgesic within the past 12 months, were employed as a licensed physician, could not speak or understand English, or indicated current or past employment for themselves or their immediate family that posed a conflict of interest (e.g., pharmaceutical company). Once the targeted number of completed surveys was reached (at least 400 Commercial respondents; 40 Medicare respondents and 40 Medicaid respondents), the survey was closed.

The protocol and all survey-related materials were approved by the New England Institutional Review Board (NEIRB) prior to the conduct of the study and all patient data were handled in compliance with the regulations of the US Insurance Portability and Accountability Act of 1996.

Knowledge Assessment Statements

Respondents' level of knowledge about the serious risks associated with the use of ER/LA opioid analgesics was assessed with 23 questions in which they were asked to identify whether the question was true, false, or do not know. Questions were related to the following key risk messages: (1) The patient understands the serious risks associated with the use of their ER/LA opioid analgesics (7 questions); (2) The patient knows what to do if they take too much drug (2 questions); (3) The patient understands the need to store the drug in a safe place (3 questions); (4) The patient knows they should not share the drug with anyone (2 questions); and (5) The patient understands how to use the drug safely (9 questions).

In addition, there were 5 additional questions that were tailored to the type of ER/LA opioid analgesic used. For example, only patients using a transdermal delivery system were presented with the statement "it is okay to cut your patch in half if you want to use less medicine."

Table 1 presents the knowledge assessment questions and their correct responses by risk message.

Receipt and Usage of MG and PCD and Healthcare Provider Behaviors

Respondents answered questions about their most recent use of ER/LA opioids and their understanding of the MG and PCD. They were also asked about how often their prescribing health care providers provided counseling on a variety of topics (i.e., risks, discontinuation, side effects, safe disposal, and medication handling storage) in the past 12 months.

Analysis

Descriptive analyses were conducted that determined the proportion of respondents who reported receiving, reading and understanding the MG, and whether providers referred to and/or the extent that patients understood the PCD at visits where opioids were prescribed. We calculated a Knowledge Assessment Score (KAS) from the knowledge assessment questions that was defined as the proportion of the 23 questions that respondents answered correctly using unweighted addition and converted the proportion to a percentage after dichotomizing responses as correct or incorrect. Respondents received a score of 1 for each correct response; an incorrect response was defined as any response other than the correct response and received a score of 0. A threshold of at least 80% correct was considered "acceptable knowledge."[9] We assessed the distribution of KAS scores and determined the proportion of respondents correctly answering each individual question. The results were stratified by insurance type (Commercial, Medicare Advantage, Medicaid).

All analyses were conducted using SAS® Enterprise Guide version 7.12 (SAS Institute Inc., Cary, NC, USA).

Results

Participation

The survey sample list consisted of the contact information of 21,293 Commercial and Medicare Advantage patients who met the study inclusion/exclusion criteria. Recruitment letters or emails were sent to 14,242 of these patients, and 2615 (18%) responded to the letter or email request. Of the patients who responded, 1939 (74%) refused to participate, 676 (26%) provided verbal or electronic consent to participate of which 197 (29%) did not meet survey screening criteria. Of the 479 patients who qualified, 54 (11%) started the survey but did not complete it and 425 (89%) completed the survey (Figure 1). Patients who completed the survey were compensated for their time.

An additional 40 patients with Medicaid insurance were separately recruited through an online survey research panel and completed the survey online.

Table 1 Knowledge Assessment Questions by REMS Risk Message

Risk Message (RM)/Knowledge Question	Correct Answer
RM-1. The patient understands the serious risks associated with the use of their ER/LA opioid analgesic	
a. Taking or using too much ER/LA opioid, also called overdose, may cause life-threatening breathing problems, respiratory depression, or abnormally slow breathing that can lead to death.	True
b. ER/LA opioid analgesics can make you dizzy, lightheaded or sleepy.	True
c. Constipation is a possible side effect when using [OPIOID]	True
d. [OPIOID] can cause serious side effects that can lead to death, even when used as recommended	True
e. Addiction is a risk associated with use of [OPIOID]	True
f. Death is a risk associated with use of [OPIOID]	True
g. Unintentional overdose is a risk associated with use of [OPIOID]	True
RM-2. The patient knows what to do if they take too much drug	
h. You should get emergency medical help if you take or use too much or overdose on [OPIOID], even if you feel fine.	True
i. You should get emergency medical help if you experience side effects such as trouble breathing, shortness of breath, fast heartbeat, chest pain or swelling of your face, tongue or throat, after taking or using [OPIOID].	True
RM-3. The patient understands the need to store the drug in a safe place	
j. You should store [OPIOID] in a medicine cabinet with other medications in the household.	False
k. After you stop taking or using [OPIOID], it is okay to throw any unused medicine in the trash.	False
l. If a child takes or uses your [OPIOID], they could die.	True
RM-4. The patient knows they should not share the drug with anyone	
m. It is okay for you to give [OPIOID] to other people who have the same condition as you have.	False
n. Selling or giving away your [OPIOID] is against the law.	True
RM-5. The patient understands how to use the drug safely	
o. It's okay to stop taking or using [OPIOID] without talking to your healthcare provider.	False
p. If the dose you are taking or using does not control the pain, it is okay to take or use more medicine without talking to your healthcare provider.	False
q. It's okay to drink alcohol while taking or using [OPIOID].	False
r. It's not necessary to read the attached Medication Guide every time you fill your [OPIOID] prescription.	True
s. You do not have to tell your healthcare provider about all the other medications you use.	False
t. You do not have to tell your healthcare provider if you have a history of abuse of street or prescription drugs, alcohol addiction, or mental health problems.	False
u.You do not have to tell your healthcare provider about over-the-counter medicines, vitamins, and dietary supplements.	False
v. It's okay to drink caffeine while using [OPIOID].	True
w. If you miss a dose of the ER/LA opioid analgesic, you should take the missed dose as soon as possible.	True
x. (ORAL Only) If you have trouble swallowing your medication, you should split or crush the pill.	False
y. (ORAL Only) If you miss a dose of [OPIOID], you can take more when it is time for your next dose.	False
z. (PATCH Only) You need to tell your healthcare provider if you have a fever.	True
aa. (PATCH Only) If you still have pain, you should try using a hot tub or sauna while using [OPIOID].	False
bb. (PATCH Only) It is okay to cut your patch in half if you want to use less medicine.	False

Note: When answering the survey, respondents saw the name of the product that they used in the place of "[OPIOID]."

Patient Characteristics

The mean ages of the Commercial, Medicare Advantage and Medicaid respondents were 53.1, 72.5 and 47.5 years, respectively (Table 2). A large proportion of respondents were female (Commercial: 64%, Medicare Advantage: 70% and Medicaid: 58%) and white (Commercial: 87%, Medicare Advantage: 86% and Medicaid: 93%). In terms of marital status, 62% among Commercial versus 35% among Medicare Advantage and 43% among Medicaid respondents were married/living with a partner. Only 25% of the Commercial versus 51% and 43% of Medicare Advantage and Medicaid respondents, respectively, had an annual income under $25,000. Thirty five percent of Commercial, 19% of Medicare Advantage, and 48% of Medicaid respondents had an education level of college graduate or higher. Oral ER/LA opioid use was more common among Commercial (68%) and Medicaid (63%) respondents whereas only

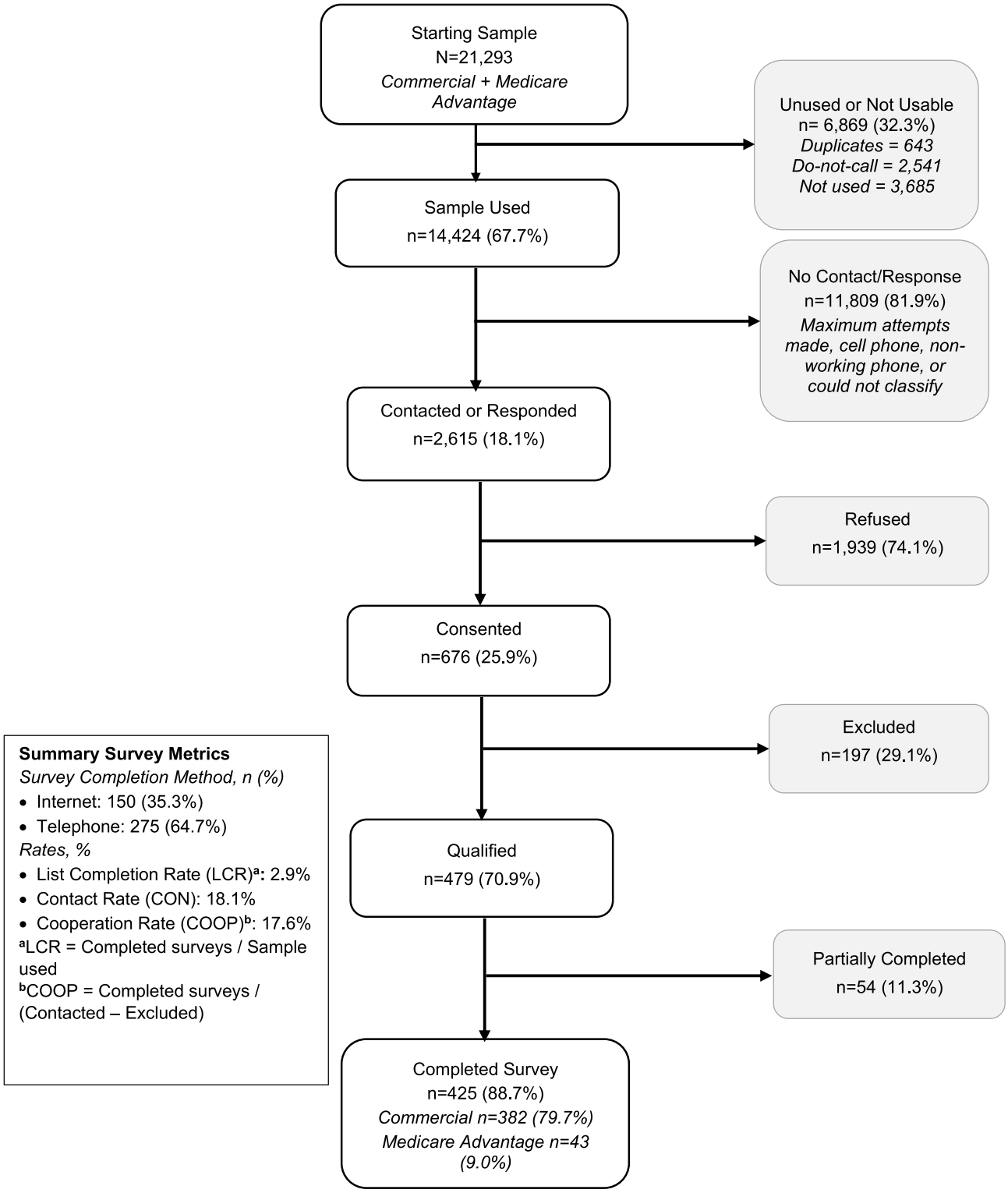

Figure 1 Survey sample disposition.

49% of Medicare Advantage respondents were oral ER/LA opioid users. Slightly over half of all respondents had their most recent prescription dispensed within one month prior to the survey (Table 2).

Receipt and Usage of MG and PCD

Nearly all respondents reported receiving and/or reading the MG (98% Commercial, 100% Medicare Advantage, 95% Medicaid). A majority in all groups

Table 2 Demographic and Clinical Characteristics of Survey Respondents

	Commercial		Medicare Advantage		Medicaid	
	N	**(%)**	**N**	**(%)**	**N**	**(%)**
Total number of respondents	**382**	**(100)**	**43**	**(100)**	**40**	**(100)**
Age in years, mean (SD)	53.1	(10.17)	72.5	(7.09)	47.5	(12.83)
Gender, n (%)						
Female	243	(64)	30	(70)	23	(58)
Male	138	(36)	13	(30)	17	(43)
Refused	1	(0)	0	(0)	0	(0)
U.S. Census region of residence, n (%)						
Northeast	68	(18)	4	(9)	0	(0)
South	115	(30)	11	(26)	0	(0)
Midwest	121	(32)	28	(65)	0	(0)
West	78	(20)	0	(0)	0	(0)
Unknown	0	(0)	0	(0)	40	(100)
Race/Ethnicity, n (%)						
White, Caucasian	332	(87)	37	(86)	37	(93)
Other	50	(13)	6	(14)	3	(7)
Marital status, n (%)						
Married/Living with partner	235	(62)	15	(35)	17	(43)
Single, separated, divorced, widowed	147	(38)	28	(65)	23	(58)
Income level, U.S. dollars						
Less than $25,000	94	(25)	22	(51)	17	(43)
$25,000 or more	258	(68)	16	(37)	23	(58)
Don't know	30	(8)	5	(12)	0	(0)
Education level						
High school or less	101	(26)	19	(44)	8	(20)
Some college	145	(38)	16	(37)	13	(33)
College graduate/Graduate school	132	(35)	8	(19)	19	(48)
Other	4	(1)	0	(0)	0	(0)
Specific ER/LA opioid analgesic(s) used, n (%)						
Oral drugs that are not methadone only	259	(68)	21	(49)	25	(63)
Patch and no methadone	77	(20)	15	(35)	4	(10)
Methadone	44	(12)	7	(16)	11	(28)
Patch and methadone	2	(1)	0	(0)	0	(0)
New user, n (%)						
First use	77	(20)	8	(19)	11	(28)
Used before	301	(79)	35	(81)	29	(73)
Not sure	4	(1)	0	(0)	0	(0)
Time since last prescription, n (%)						
Less than one month ago	210	(55)	23	(53)	21	(53)
One month to less than six months ago	96	(25)	15	(35)	12	(30)
Six months to less than 12 months ago	60	(16)	2	(5)	6	(15)
12 months or more ago	13	(3)	2	(5)	1	(3)
Not sure	3	(1)	1	(2)	0	(0)

(*Continued*)

Table 2 (Continued).

	Commercial		Medicare Advantage		Medicaid	
	N	(%)	N	(%)	N	(%)
Time since most recent visit to the healthcare provider who prescribed ER/LA opioid analgesic, n (%)						
Less than one month ago	190	(50)	18	(42)	14	(35)
One month to less than six months ago	144	(38)	18	(42)	23	(58)
Six months to less than 12 months ago	33	(9)	2	(5)	3	(8)
12 months or more ago	13	(3)	5	(12)	0	(0)
Not sure	2	(1)	0	(0)	0	(0)
Time since healthcare provider first prescribed ER/LA opioid analgesic, n (%)						
Less than one month ago	18	(5)	3	(7)	4	(10)
One months to less than six months ago	45	(12)	6	(14)	15	(38)
Six months to less than 12 months ago	85	(22)	4	(9)	4	(10)
12 months or more ago	222	(58)	28	(65)	17	(43)
Not sure	12	(3)	2	(5)	0	(0)
Type of healthcare provider that first prescribed the survey index ER/LA opioid analgesic drug, n (%)						
Pain specialist	187	(49)	17	(40)	13	(33)
Primary care physician, general practitioner, internal medicine specialist, or family practice physician	86	(23)	18	(42)	19	(48)
Other type of healthcare provider	107	(28)	6	(14)	8	(20)
Not sure	2	(1)	2	(5)	0	(0)

Note: Percentages may not sum to 100% due to rounding.
Abbreviations: ER/LA, extended-release/long-acting; GED, General Education Degree; N, number; SD, standard deviation; US, United States.

reported that they understood most of the information (Table 3).

Far fewer respondents indicated an awareness of the PCD. It was reported as received from and/or referenced by their healthcare provider by 47% of Commercial, 65% of Medicare Advantage, and 53% of Medicaid respondents. Fifty-seven percent of Commercial, 50% of Medicare Advantage and 76% of Medicaid respondents reported that their healthcare provider referred to or discussed the PCD within the last 12 months when prescribing their current ER/LA opioid analgesic (Table 3).

Healthcare Provider Behaviors

A large majority of the respondents stated that their healthcare providers always or regularly talked about how much medication to take or use when ER/LA opioid analgesics were prescribed (Commercial: 86%, Medicare Advantage: 81%, Medicaid: 88%), while fewer stated that their healthcare providers always or regularly cautioned them about important risks associated with the use of ER/LA opioid analgesics, including overdose or taking too much (Commercial: 68%, Medicare Advantage: 77%, Medicaid: 65%) and always or regularly instructed them about keeping ER/LA opioid analgesics safe and away from children (Commercial: 65%, Medicare Advantage: 74%, Medicaid: 63%; Table 3). While 79% percent of Commercial and 88% of Medicaid respondents reported that their physicians always or regularly asked about their medical history, only 65% of Medicare Advantage respondents reported the same. Deficits were also observed in several other healthcare provider behaviors across the groups. However, some behaviors were more often reported by Medicaid than Commercial and Medicare Advantage respondents, such as: healthcare provider always/regularly discussed how to safely discontinue ER/LA opioid analgesics if they are no longer needed (Medicaid: 68% vs. Commercial: 50% and Medicare Advantage: 49%); always or regularly instructed about the importance of how to safely dispose any unused ER/LA opioid analgesics (Medicaid: 60% vs. Commercial: 46% and Medicare Advantage: 56%); always or regularly talked about what to do with extra medication when ER/LA opioid analgesics were prescribed (Medicaid: 58% vs Commercial: 47% and Medicare Advantage: 51%). Healthcare provider behaviors such as always or regularly counseling on the most common

Table 3 Patient Recall of Medication Guide, Patient Counseling Document, and Specific Counseling Topics

Total Number of Respondents	Commercial		Medicare Advantage		Medicaid	
	N	(%)	N	(%)	N	(%)
	382	(100)	43	(100)	40	(100)
Received and/or read MG (Yes); N (%)	375	(98)	43	(100)	38	(95)
Received MG from pharmacist with last ER/LA opioid analgesic prescription fill (Yes); N (%)	356	(93)	39	(91)	32	(80)
Received MG from pharmacist in the last 12 months (Yes); N (%)	360	(94)	40	(93)	32	(80)
Received MG from any source besides pharmacist in the last 12 months (Yes); N (%)	38	(10)	4	(9)	11	(28)
Read MG; N (%)						
Read all, with each pharmacy fill	86	(23)	11	(26)	5	(13)
Read all, at least once	214	(56)	20	(47)	19	(48)
Read some, at least once	73	(19)	11	(26)	16	(40)
Never read MG	9	(2)	1	(2)	0	(0)
Usefulness of the information in the MG; N (%)						
Very useful	246	(64)	32	(74)	14	(35)
Somewhat useful	115	(30)	6	(14)	19	(48)
Not very useful/Not useful at all	13	(3)	5	(12)	7	(18)
Refused	3	(1)	0	(0)	0	(0)
Understood all/most information in the MG; N (%)	358	(94)	36	(83)	31	(78)
Received and/or healthcare provider referenced PCD (Yes); N (%)	180	(47)	28	(65)	21	(53)
Received PCD from healthcare provider when first prescribed current ER/LA opioid analgesic (Yes); N (%)	143	(79)	20	(71)	17	(81)
Healthcare provider referred to or discussed PCD when prescribing the current ER/LA opioid analgesic in the last 12 months (Yes); N (%)	103	(57)	14	(50)	16	(76)
Healthcare provider completed a Patient Prescriber Agreement (PPA) or patient contract when the current ER/LA opioid analgesic was prescribed in the last 12 months (Yes); N (%)	116	(64)	18	(64)	18	(86)
Frequency healthcare provider did following activities in the past 12 months when visited (Always or Regularly); N (%)						
a. Used the PCD on ER/LA opioids for discussions.	140	(37)	21	(49)	18	(45)
b. Cautioned about important risks associated with ER/LA opioid analgesics, including overdose or taking or using too much.	259	(68)	33	(77)	26	(65)
c. Discussed how to safely discontinue ER/LA opioid analgesics if they are no longer needed.	192	(50)	21	(49)	27	(68)
d. Counseled on the most common side effects from using ER/LA opioid analgesics.	260	(68)	28	(65)	27	(68)
e. Instructed about the importance and how to safely dispose of any unused ER/LA opioid analgesics.	175	(46)	24	(56)	24	(60)
f. Instructed about keeping ER/LA opioid analgesics safe and away from children.	250	(65)	32	(74)	25	(63)
g. Instructed not to share ER/LA opioid analgesics with anyone else.	242	(63)	29	(67)	26	(65)
h. Asked about medical history when prescribing ER/LA opioid analgesics.	300	(79)	28	(65)	35	(88)
i. Talked about how much medication to take or use when ER/LA opioid analgesics were prescribed.	327	(86)	35	(81)	35	(88)
j. Talked about what to do with extra medication when ER/LA opioid analgesics were prescribed.	180	(47)	22	(51)	23	(58)

Note: Percentages may not sum to 100% due to rounding.
Abbreviations: MG, medication guide; ER/LA, extended-release/long-acting; KAS, knowledge assessment score; PCD, patient counseling document; SD, standard deviation; N, number.

side effects of ER/LA opioids and always or regularly not sharing ER/LA opioid analgesic with anyone else were consistent across insurance groups (65–68% and 63–67%, respectively; Table 3).

Knowledge of Serious Risks of ER/LA Opioid Analgesics

Eighty-five percent of Commercial, 60% of Medicare Advantage and 53% of Medicaid respondents achieved

a KAS score (i.e., proportion of knowledge questions that a respondent answered correctly) of at least 80%, the threshold considered "acceptable knowledge." The mean KAS was 87 (standard deviation [SD] 9.73) for Commercial, 81 (SD 13.01) for Medicare Advantage, and 78 (SD 15.53) for Medicaid respondents. Overall, there were 17 of 23 knowledge questions that at least 80% of respondents answered correctly including 13 questions that were answered correctly by at least 90% of respondents. Fewer respondents were aware that opioids can cause serious side effects that can lead to death even when taken as recommended (Commercial: 73%, Medicare: 56%, Medicaid: 63%), the MG should be read at each dispensing (Commercial: 78%, Medicare: 53%, Medicaid: 75%), ER/LA opioid analgesics should not be stored in a medicine cabinet with other medications in the household (Commercial: 77%, Medicare: 79%, Medicaid: 58%), missed doses should be taken as soon as possible (Commercial: 56%, Medicare: 51%, Medicaid: 50%), and ER/LA opioid analgesic pills should not be split or crushed if the respondent is having trouble swallowing their medication (Commercial: 85%, Medicare: 67%, Medicaid: 52%) (Table 4).

Discussion

This study evaluated the use of education tools such as the MG by pharmacists and the PCD by healthcare providers and assessed patient knowledge of the safe use of ER/LA opioid analgesics. Results were obtained from surveying ER/LA opioid analgesic users with Commercial, Medicare Advantage and Medicaid health insurance plans. Although many key messages from the MG and PCD were understood by most respondents, deficits in the knowledge of certain risk messages were more common among Medicare Advantage and/or Medicaid respondents.

Approximately 50% or more of respondents in all groups reported that healthcare providers always or regularly engaged in a variety of counseling behaviors and/or used the PCD. While patients may not be aware that their healthcare providers are using the PCD or that comprehensive screening and discussion may take place with the assistance of other tools or be performed by other members of the healthcare team, promoting improved counseling and use of the PCD by all types of healthcare providers may help to improve patient knowledge in areas where gaps were observed.

Differences in responses across the insurance groups in the survey results for knowledge of certain risk messages may be at least partially explained by differences in the demographic characteristics of the survey respondents that are typical of Commercial versus Medicare Advantage and Medicaid groups, such as age, marital status, income and education level. Areas of action include promoting the use of the PCD across all provider specialties and ensuring that information about potential serious risks associated with opioids, safe storage, and formulation-specific risks is stressed to patients in a way that is understandable to them.

Commercial respondents made up the largest patient subgroup in this study. The HIRD is demographically representative of the Commercial population in the US in terms of gender and age; however, applicability of results to individuals without medical insurance may be limited. This was the fourth and final year that this FDA-mandated post-marketing survey was conducted, and in this year the population was expanded to include Medicare Advantage and Medicaid patients in addition to the Commercial patients to provide a more comprehensive view. While we were able to identify Medicare Advantage patients from their administrative claims in the HIRD and survey them, we did not have access to Medicaid patients and had to depend on their recruitment from a research panel. We were not able to verify the insurance status and ER/LA opioid analgesic use of the Medicaid patients. Based on the small number of Medicare Advantage and Medicaid respondents, it is possible that these respondents may differ from the broader population of individuals with US government sponsored insurance.

While we evaluated respondents' abilities to correctly identify key risk messages from the MG and PCD, we did not measure the extent to which this knowledge is applied. For example, while it is assumed that awareness that ER/LA opioid analgesics should not be used with alcohol translates into actual avoidance of this dangerous behavior, the extent to which this is true is not captured by this assessment.

Further, it is possible that responses to some of the KAS component items are informed by common sense and general awareness of opioid risks promoted by various public health campaigns more than by genuine recollection of the education materials received. Although the knowledge questions were directly related to content in the REMS education tools, patients may receive information about the safe use of their medication from many different sources. As such, observed patient knowledge cannot necessarily be attributed solely to the REMS.

Table 4 Knowledge Assessment Scores and Statements (KAS)

Total Number of Respondents	Commercial		Medicare Advantage		Medicaid	
	N	(%)	N	(%)	N	(%)
	382	(100)	43	(100)	40	(100)
Knowledge Assessment Score (KAS), mean (SD)	87.4	(9.73)	81.1	(13.01)	77.9	(15.53)
Knowledge Assessment Score (KAS), median		88.2		84.6		80.0
Knowledge Assessment Scores (KAS), n (%)						
≥ 80% correct	325	(85)	26	(60)	21	(53)
<80% correct	57	(15)	17	(40)	19	(48)
RM-1. The patient understands the serious risks associated with the use of their ER/LA opioid analgesic						
a. Taking or using too much ER/LA opioids, also called overdose, may cause life-threatening breathing problems, respiratory depression, or abnormally slow breathing that can lead to death (Correct), n (%)	368	(96)	40	(93)	37	(93)
b. ER/LA opioid analgesics can make you dizzy, lightheaded, or sleepy (Correct), n (%)	340	(89)	35	(81)	34	(85)
c. Constipation is a possible side effect of opioids (Correct), n (%)	361	(95)	35	(81)	34	(85)
d. Opioid can cause serious side effects that can lead to death, even when used as recommended (Correct), n (%)	277	(73)	24	(56)	25	(63)
e. Addiction is a risk associated with use of opioid (Correct), n (%)	357	(93)	36	(84)	37	(93)
f. Death is a risk associated with use of opioid (Correct), n (%)	306	(80)	28	(65)	27	(68)
g. Unintentional overdose is a risk associated with use of opioid (Correct), n (%)	314	(82)	32	(74)	33	(83)
RM-2. The patient knows what to do if they take too much drug						
h. Seek emergency medical help for ER/LA opioid analgesic overdose, even if the respondent feels fine (Correct), n (%)	356	(93)	36	(84)	35	(88)
i. Seek emergency medical help for side effects such as trouble breathing, shortness of breath, fast heartbeat, chest pain, or swelling of their face, tongue, or throat after taking or using ER/LA opioid analgesics (Correct), n (%)	379	(99)	41	(95)	38	(95)
RM-3. The patient understands the need to store the drug in a safe place						
j. Do not store ER/LA opioid analgesics in a medicine cabinet with other medications in the household (Correct), n (%)	295	(77)	34	(79)	23	(58)
k. Do not throw any unused ER/LA opioid analgesic in the trash (Correct), n (%)	352	(92)	41	(95)	29	(73)
l. A child could die if they take or use the respondent's ER/LA opioid analgesics (Correct), n (%)	353	(92)	39	(91)	33	(83)
RM-4. The patient knows they should not share the drug with anyone						
m. Do not give ER/LA opioid analgesics to other people who have the same condition as you (Correct), n (%)	378	(99)	42	(98)	31	(78)
n. Selling or giving away ER/LA opioid analgesics is against the law (Correct), n (%)	379	(99)	40	(93)	36	(90)
RM-5. The patient understands how to use the drug safely	377	(99)	40	(93)	33	(83)
o. It's okay to stop taking or using opioid analgesics without talking to your healthcare provider (Correct), n (%)	377	(99)	40	(93)	33	(83)
p. Talk to a healthcare provider about taking or using more ER/LA opioid analgesics if the current dose does not control the pain (Correct), n (%)	343	(90)	41	(95)	29	(73)
q. It is not okay to drink alcohol while taking or using ER/LA opioid analgesics (Correct), n (%)	369	(97)	38	(88)	37	(93)
r. Read the attached MG every time an ER/LA opioid prescription is filled (Correct), n (%)	299	(78)	23	(53)	30	(75)
s. Inform healthcare provider about all the other medications being used (Correct), n (%)	367	(96)	39	(91)	33	(83)
t. Inform healthcare provider about any history of abuse of street or prescription drugs, alcohol addiction, or mental health problems (Correct), n (%)	350	(92)	36	(84)	33	(83)

(*Continued*)

Table 4 (Continued).

Total Number of Respondents	Commercial		Medicare Advantage		Medicaid	
	N	(%)	N	(%)	N	(%)
	382	(100)	43	(100)	40	(100)
u. Inform healthcare provider about over-the-counter medicines, vitamins, and dietary supplements (Correct), n (%)	342	(90)	38	(88)	35	(88)
v. It is okay to drink caffeine while using ER/LA opioid analgesics (Correct), n (%)	206	(54)	22	(51)	19	(48)
w. If you miss a dose of the ER/LA opioid analgesic, you should take the missed dose as soon as possible (Correct), n (%)	213	(56)	22	(51)	20	(50)
x. ER/LA opioid analgesic pills should not be split or crushed if the respondent is having trouble swallowing their medication (Correct), n (%)[a]	219	(85)	14	(67)	13	(52)
y. Do not take more when it is time for the next dose if a dose of ER/LA opioid analgesics was missed (Correct), n (%)[a]	244	(94)	20	(95)	24	(96)
z. Inform healthcare provider of any fever (Correct), n (%)[b]	63	(82)	12	(80)	3	(75)
aa. Do not use a hot tub or sauna while using ER/LA opioid analgesics if pain persists (Correct), n (%)[b]	61	(79)	12	(80)	1	(25)
bb. Do not cut ER/LA opioid analgesic patches in half to use less medicine (Correct), n (%)[b]	62	(81)	14	(93)	2	(50)

Notes: [a]Survey questions only asked of non-methadone oral drugs only respondents (N = 259, 21, and 25; for Commercial, Medicare, and Medicaid, respectively). [b]Survey questions only asked of patch and non-methadone respondents (N=77, 15, and 4; for Commercial, Medicare, and Medicaid, respectively). Percentages may not sum to 100% due to rounding.

Abbreviations: KAS, knowledge assessment score; SD, standard deviation; ER/LA, extended-release/long-acting; MG, medication guide; PCD, patient counseling document; RM, risk message; N, number.

Conclusion

The ER/LA Opioid REMS appears to be effective in promoting receipt of the MG by patients using ER/LA opioid analgesics, and although respondents demonstrated knowledge of the safe use of ER/LA opioid analgesics with respect to many of the questions associated with key risk messages included in the MG, there were questions where level of knowledge varied. Overall, the PCD was less widely received and used by healthcare providers to educate patients. Additional efforts appear warranted to reinforce knowledge of the core messages of safe use and promote more consistent provider counseling and PCD use across prescribing specialties and patient demographic groups.

Disclosure

JJ Stephenson, CN Holick and S Lanes are employees of HealthCore, which received funding from the REMS Program Companies (RPC) to conduct the study. DB Esposito, VCA Desai and JG Lyons were employees of HealthCore at the time the study was conducted. MS Cepeda is employed by Janssen Research and Development, and GP Wedin is employed by Upsher-Smith Laboratories, LLC. The authors report no other conflicts of interest in this work.

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