

**Original Article**

# Patient Patterns and Perspectives on Using Opioid Regimens for Chronic Cancer Pain



Emily M. Wright, BA, Areej El-Jawahri, MD, Jennifer S. Temel, MD, Alaina Carr, BA, Steven A. Safren, PhD, Elyse R. Park, PhD, MPH, William F. Pirl, MD, MPH, Eduardo Bruera, MD, and Lara Traeger, PhD  
*Massachusetts General Hospital Cancer Center (E.M.W., A.E.-J., J.S.T., E.R.P., L.T.), Boston, Massachusetts; Harvard Medical School (A.E.-J., J.S.T., E.R.P., W.F.P., L.T.), Boston, Massachusetts; Department of Psychology (A.C.), University of Colorado Denver, Denver, Colorado; Department of Psychology (S.A.S.), University of Miami, Coral Gables, Florida; Dana-Farber Cancer Institute (W.F.P.), Boston, Massachusetts; and MD Anderson Cancer Center (E.B.), Houston, Texas, USA*

**Abstract**

**Context.** With increasing attention to the undertreatment of cancer pain in parallel with concerns about opioid misuse, little is known about how patients with advanced cancer adhere to opioid regimens for chronic cancer pain.

**Objectives.** We explored patient approaches to managing chronic cancer pain with long-acting opioids.

**Methods.** In a multimethods study at an academic medical center, adult patients with chronic cancer pain ( $n = 17$ ) used electronic pill caps to record adherence to prescribed long-acting opioid regimens. After eight weeks, patients viewed their adherence records and completed a semistructured interview about their opioid use. With a framework approach, we coded interview data ( $Kappa > 0.95$ ) and identified themes in how patients perceived and used opioids to manage cancer pain.

**Results.** Patients (59% female; 94% non-Hispanic white; median age = 65 years) felt grateful about pain benefit from opioids yet concerned about opioid side effects and addiction/tolerance. Main reasons for nonadherence included both intentional decisions (e.g., skipping doses) and unintentional barriers (e.g., missing doses due to inconsistent sleep schedules). Overall, patients set their own opioid adherence goals and developed routines to achieve them. Residual pain varied and was not consistently linked with opioid adherence.

**Conclusion.** Patients commonly felt conflicted about using prescribed long-acting opioids to manage cancer pain due to concurrent perceptions of their risks and benefits, and they set their own parameters for opioid-taking practices. Intentional and unintentional deviations from prescribed opioid schedules highlight the need to enhance adherence communication, education, and counseling, to optimize the use of long-acting opioids as a component of cancer pain management. *J Pain Symptom Manage* 2019;57:1062–1070. © 2019 American Academy of Hospice and Palliative Medicine. Published by Elsevier Inc. All rights reserved.

**Key Words**

*Cancer pain, behavioral medicine, palliative care, qualitative research, medical adherence*

**Introduction**

Cancer pain is one of the most common and distressing problems among patients with advanced cancer.<sup>1</sup> Opioids are a cornerstone of treatment for moderate to severe cancer pain.<sup>2,3</sup> Yet, many patients who are prescribed a long-acting opioid continue to experience bothersome residual or breakthrough pain.<sup>4,5</sup>

For patients with chronic cancer pain, patient-level factors might influence the extent to which patients achieve optimal benefit from long-acting opioids. Based on studies that measured adherence to long-acting opioids by patient self-report or daily data from electronic pill caps, patients may be missing 10–36% of their prescribed daily doses.<sup>6–10</sup> In the U.S., reports of increasing rates of opioid misuse and death in the general population may influence patient

Address correspondence to: Lara Traeger, PhD, Massachusetts General Hospital, One Bowdoin Square, Suite 701, Boston, MA 02114. E-mail: [ltraeger@mgh.harvard.edu](mailto:ltraeger@mgh.harvard.edu)

Accepted for publication: February 21, 2019.

perceptions of using opioids to manage cancer-related pain.<sup>11</sup> Patient concerns about using opioids may impact both opioid adherence and perceived pain control, although findings have been mixed in this regard.<sup>6,9,12–15</sup> Indeed, some qualitative research findings suggest that opioid adherence among patients with cancer involves negotiating perceived risks and benefits.<sup>16–18</sup> However, research to date has not explored in-depth opioid perceptions and daily behaviors when paired with patient's own daily adherence data, specifically for around-the-clock long-acting opioids for chronic cancer pain.

The current multimethods (qualitative and quantitative) study explored patient approaches to using long-acting opioid regimens to manage chronic cancer pain. This work was conducted as part of a larger observational study that electronically captured daily patient data on adherence to a long-acting opioid regimen over eight weeks. To help explain medication-taking behaviors, we selected a consecutive subset of patients who completed the larger study to view their own adherence data and reflect on their opioid attitudes, approaches, and strategies. We anticipated that asking patients to review their own data would facilitate recall and provide richer insight into opioid adherence and pain outcomes. Results were used to help identify potential targets for enhancing pain management.

## Methods

### Participants

Study participants were ambulatory adult patients at the Massachusetts General Hospital Cancer Center who were diagnosed with metastatic cancer (genitourinary, breast, colorectal) or with locally advanced or metastatic cancer (thoracic, sarcoma, noncolorectal gastrointestinal) and who were currently prescribed a long-acting opioid (pill or fentanyl patch) for cancer pain. Patients were excluded if they had impaired cognition or limited English language proficiency to complete study procedures, were not responsible for administering their pain medication, or were determined by their oncology clinician to have physical or mental health symptoms that could interfere with participation.

Participants consented to a prospective study of adherence to a long-acting opioid regimen over eight weeks ( $n = 135$ ). The aim of this study was to prospectively examine patient adherence to a prescribed long-acting opioid for chronic cancer pain and to examine predictors and outcomes of adherence. Midway through this study, procedures were added to invite consecutive patients who completed the parent study to review their eight-week adherence data and complete a semistructured interview. Inclusion and exclusion criteria were not modified. Recruitment for

the semistructured interviews continued until no new themes emerged (data saturation;  $n = 17$ ).

### Procedure

Study procedures were approved by the Dana Farber/Harvard Cancer Center Office for Human Research Studies before initiation. Patients who met eligibility criteria were approached by study staff in person after the patient's oncology clinician had obtained permission from the patient to do so. All patients completed written informed consent with study staff during a regularly scheduled clinic visit.

As part of the larger study, we collected patient self-report survey data and medical record data at study enrollment and at eight-week follow-up. Patients received \$20 for each completed survey. The survey included patient demographics, mood, pain, and quality-of-life questionnaires. Medical record data included clinical history related to cancer and pain. During the eight-week period between the two surveys, patients used a pill bottle fitted with a medical event monitoring system (MEMS; Aardex Ltd, Zug, Switzerland) pill cap to take their long-acting opioid medication (and a second bottle for a short-acting opioid, if prescribed). Patients who were prescribed a fentanyl patch were asked to open and close the MEMS bottle each time they changed their patch, although they did not store the patch inside the bottle. MEMS caps contain a microprocessor that records each date and time when the pill bottle is opened and closed. Patients received instructions on the use of MEMS along with a paper log for when MEMS use was not possible. Study staff also briefly met with patients in person or by phone two to three times during the study to confirm or problem-solve their use of MEMS and to monitor data quality. Electronic health records were reviewed for demographics, cancer diagnosis and treatment history, and pain treatment history.

Patients in the present study also participated in a one-time semistructured interview with study staff, within three weeks after completing their eight-week adherence tracking period. Interviews took place in a private oncology clinic setting. Open-ended questions and follow-up probes were used to elicit 1) initial expectancies and current attitudes about long-acting opioids, 2) current pain level and pain management strategies, and 3) facilitators/barriers to adherence. As part of the interview, patients reviewed their own MEMS adherence data, presented in graphical format (e.g., [Figures 1a–c](#)). The interviewer recorded field notes to capture non-verbal aspects of the encounter. Interviews were audio-recorded and transcribed. Patients received \$20 after the interview. For interview patients in the present study, we report survey, medical record, and adherence data from the larger study

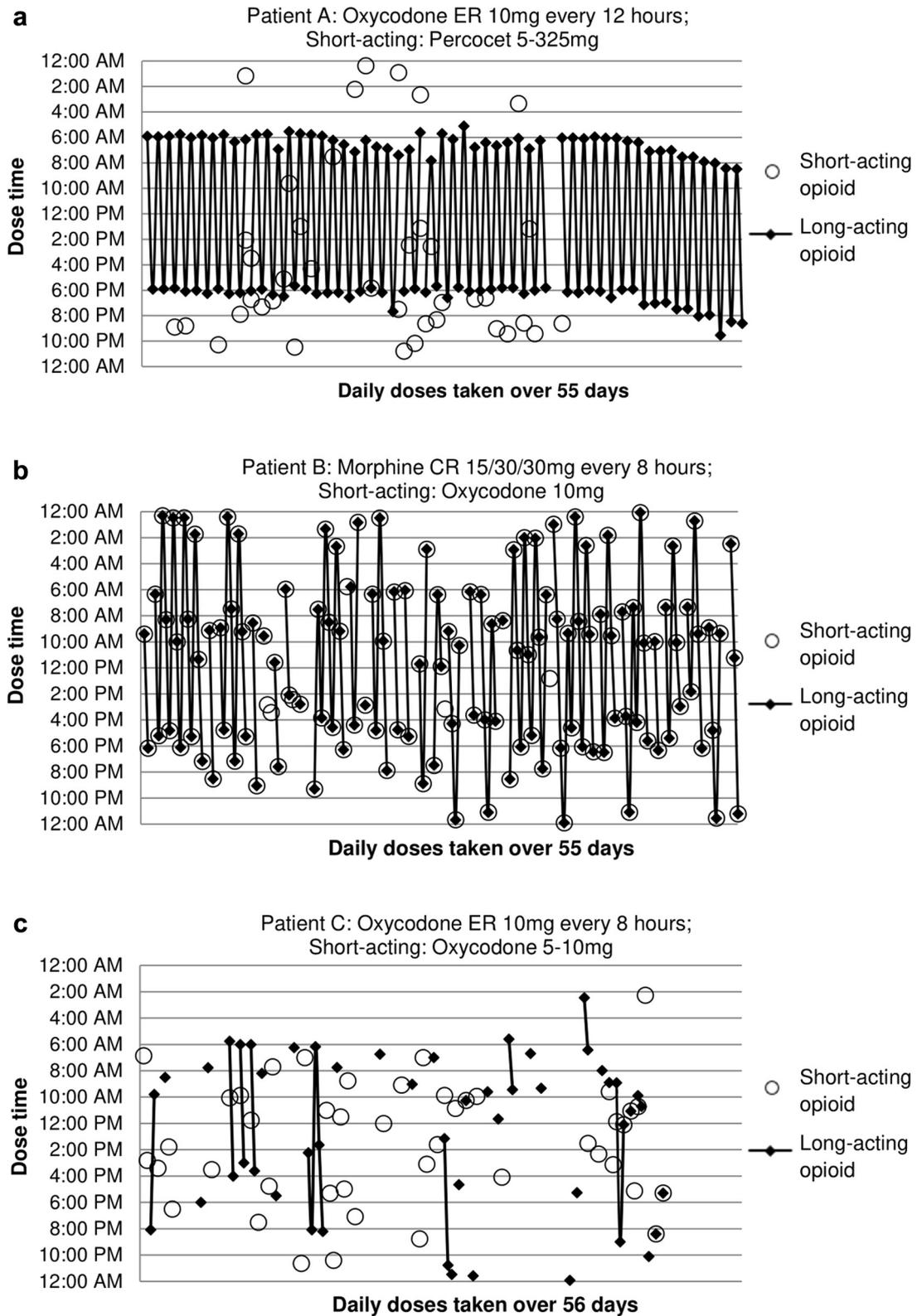


Fig. 1. Example patterns of adherence to long-acting opioids. Opioid adherence patterns for selected patients. Each point indicates a dose taken. Lines connect consecutive doses for the long-acting opioid. Breaks in a line indicate skipped or missed long-acting opioid doses. Percent of long-acting opioid doses taken at all and percent of doses taken within two hours of the prescribed schedule, respectively, are a) 100% and 100%, b) 78.18% and 64.24%, and c) 32.47% and 26.62%.

including patient demographics, cancer diagnosis, long-acting opioid regimen (including morphine equivalent dose),<sup>19</sup> proportion of long-acting opioid taken during the eight-week tracking period, and pain severity (Brief Pain Inventory)<sup>20</sup> at the start of the tracking period.

### Analysis

We used a framework approach to help ensure that results were consistent with the interview data by allowing for continuous comparison of codes and themes as they were developed.<sup>21</sup> The framework approach involves creating and interpreting a thematic framework or a matrix organizing participants' responses by themes and subthemes identified from the data, through familiarization with the raw data; iterative and transparent coding of the data; and sorting and synthesizing of coded data. Our framework was informed in part by prior research results. We first reviewed initial transcripts, used the interview data and interview guide to develop codes, and organized these codes into a structure. Analysis was then applied systematically and iteratively across all transcripts and all sections within transcripts. Two team members independently coded all interview data at the sentence level using NVivo 10. Unexpected and/or discrepant data were examined by the coders and a third team member if necessary, until resolution. New codes were developed and incorporated into the structure as they were identified. Kappa coefficients were calculated to evaluate coding precision (range: 0 to 1 [perfect agreement]). The final Kappa was >0.95, indicating high agreement. Codes were then reviewed by the study team to identify overarching themes. Emerging themes were continually compared back to the raw data. We extracted quotes to exemplify themes.

We also explored whether themes varied by prescribed opioid dose (*high dose*:  $\geq 120$  mg morphine equivalent dose; *low-moderate dose*: <120 mg morphine equivalent dose); time since initial prescription of current long-acting opioid (less than four months; four to less than eight months; eight months or more); or pattern of MEMS adherence data. Notably, there are no established clinical cutoffs to define good or acceptable adherence to opioids. We therefore grouped adherence patterns with respect to the proportion and timing of the prescribed doses that were taken, based on prior research methods<sup>10</sup> and clinical judgment, as illustrated by individual cases in Figure 1. *High adherence* (Figure 1a): >90% of prescribed doses were taken, including >90% within 2 hours (for Q8 and Q12 doses) or 3 hours (for Q72 doses) of the target time. *Variable adherence* (Figure 1b): 50–90% of prescribed doses were taken, including 40–90% within two or three hours of the target time. *Low adherence* (Figure 1c): <50% of prescribed doses were

taken, including <40% within two or three hours of the target time.

### Results

Of 21 consecutive patients who completed the parent study and were invited to complete the semistructured interview, 17 patients completed the interview. Reasons for noncompletion included hospitalization and/or transition to hospice ( $n = 2$ ) or lack of a scheduled clinic visit ( $n = 2$ ) during the interview time window. Interviews were conducted between December 2016 and July 2017 (average interview duration = 30 minutes [ $SD = 9$ ]). See Table 1 for demographic characteristics. Patients were diagnosed with gastrointestinal (65%), thoracic (18%), gynecologic (12%), or breast cancer (6%). Median time since initial prescription of current long-acting opioid was four months (range: 3–44). Median morphine equivalent dose was 45 mg (range: 30–360). At the start of the eight-week adherence-monitoring period, median scores on average and worst pain in the past 24 hours were 3 (range 0–8) and 4 (range 0–9) out of 10, respectively. During the eight-

Table 1  
Sample Characteristics (N = 17)

Variable	n (%) or Median [Range]
Age (years)	65 [34-76]
Female	10 (59)
Hispanic	1 (6)
Type of cancer	
Gastrointestinal	11 (65)
Thoracic	3 (18)
Gynecologic	2 (12)
Breast	1 (6)
Stage of cancer	
Metastatic	12 (71)
Locally advanced	5 (29)
Prescribed long-acting opioid Medication	
Oxycodone extended-release	11 (65)
Morphine controlled-release	3 (18)
Fentanyl patch	2 (12)
Methadone	1 (6)
Schedule	
Every eight hours (oral)	5 (29)
Every 12 hours (oral)	10 (59)
Every three days (transdermal)	2 (12)
Morphine equivalent dose (mg)	45 [30-360]
Months since initial prescription of current long-acting opioid	4 [3-43]
Method of opioid adherence data collection	
Medical event monitoring system (MEMS)	12 (71)
Paper log	4 (24)
Both MEMS and paper log	1 (6)
Proportion of prescribed long-acting opioid doses taken during eight-week period	94 [34-100]
Pain in the last 24 hours at the start of eight-week period	
Worst	4 [0-9]
Least	1 [0-5]
Average	3 [0-8]
Current	2 [0-5]

Table 2  
Initial Expectancies and Current Attitudes About Long-acting Opioid Regimens

Topics	Themes and Sample Quotes
Initial expectancies	<p><b>Patients' initial expectancies about their long-acting opioid regimen reflected misinformation, concern, or perceived gaps in knowledge.</b></p> <p>Misinformation: <i>I expected that ... the pain will be gone.</i></p> <p>Concern: <i>I thought that ... I was going to be really drugged.</i></p> <p>Gaps in knowledge: <i>I wasn't really sure how it would affect [the pain].</i></p>
Current attitudes	<p><b>Current attitudes about opioid regimens concurrently reflected gratitude, concern, and confusion.</b></p> <p>Gratitude: <i>I'm a huge advocate. Huge. I had grinding pain for two years ... all the time. And I started taking [long-acting opioid] and it was gone and it was like, "Wow."</i></p> <p>Concern: <i>I am still in pain a lot but I get it to tolerable. I just don't want to keep [increasing the dose], getting high, high, high, until I have to.</i></p> <p>Confusion: <i>At some point, they are going to want me to get off this ... I'm not really sure what's going to happen.</i></p>

week period, median proportion of prescribed long-acting opioid doses that patients took was 94% (range 34–100%). Patient approaches to using their long-acting opioid are described below (see Tables 2–4 for illustrative quotes).

#### Initial Expectancies About Long-acting Opioid Regimens

Patients' initial expectancies about their long-acting opioid centered on three concepts: misinformation, concern, or perceived gaps in knowledge (see Table 2). Some patients had anticipated that the regimen would eliminate their pain. Others had feared that the new regimen would be associated with addiction/tolerance or side effects (e.g., feeling "drugged" or "dopey"), with concerns based on social exposure to risks of opioid misuse. Patients who feared addiction commonly denied a medication misuse history; furthermore, they noted that their fear contradicted information from their clinical team (e.g., "[My clinician] told me that the small dose wouldn't addict me" or "[My clinician] said 'With your attitude, I'm not worried about you getting addicted.'"). Finally, some patients denied having expectancies because of insufficient knowledge about opioids. Initial expectancies did not vary by prescribed opioid dose, time since initial prescription, or adherence data pattern as recorded by the MEMS caps during parent study participation.

#### Current Attitudes About Long-acting Opioid Regimens

In comparison to initial expectancies, current attitudes about opioid regimens concurrently reflected gratitude, concern, and confusion (see Table 2). Gratitude was grounded in experiences with prior pain medication trials that failed to adequately control pain. Patients felt relief from severe or frightening pain and more ability to engage in ordinary daily activities. However, patients expressed this gratitude in concert with concerns about prolonged or unnecessary use (e.g., risk of prolonged cognitive side effects or development of tolerance). Patients also wondered how long they might need to continue taking the opioid in context of their advanced cancer prognosis. Several patients hoped they might be able to stop using the opioid at some point, in parallel with their hope or anticipation of cancer treatment response. As with initial expectancies, current attitudes did not vary by prescribed opioid dose, time since initial prescription, or adherence patterns as recorded by the MEMS caps.

#### Pain Outcomes and Pain Management Behaviors

Patients often endorsed residual or breakthrough pain, including patients with a high prescribed opioid dose and those with a low or moderate dose (see Table 3). They sought behavioral patterns to explain

Table 3  
Pain Outcomes and Pain Management Behaviors

Topics	Themes and Sample Quotes
Pain outcomes	<p><b>Patients often endorsed residual or breakthrough pain and sought behavioral patterns to explain it or found it to be distressingly unpredictable.</b></p> <p><i>I kind of wish ... I could just take the things on a certain schedule and be done with it. But I'm constantly dealing with pain management ... do I have it, do I not have it, am I on time? It's been very unpredictable.</i></p>
Pain management behaviors	<p><b>Pain management involved daily pain monitoring and negotiation between pain relief versus pain management beliefs.</b></p> <p><i>Rather than waiting for the pain, I'm trying to take [short-acting opioid] an hour ahead [of long-acting opioid] and skip the pain entirely.</i></p> <p><i>I'd rather have a little bit of pain, as long as I can function ... than deal with the side effects of the medication.</i></p> <p><i>At some point, I want to decide whether I want to float along all day and have the troughs of [pain] be minor, or to actually be [alert] all day and have more awful troughs.</i></p>

Table 4  
Long-acting Opioid Adherence and Facilitators and Barriers to Adherence

Topics	Themes and Sample Quotes
Adherence	<p><b>Concerns about opioids generated underlying unease but did not consistently interfere with adherence.</b>  <i>The longer I'm on [opioids], the more anxious I am to get off them.</i>  <i>I got frustrated with how I was feeling and I stopped taking ... all of the opioids.</i></p> <p><b>Patients largely felt compelled to adhere to their long-acting opioid regimens because of trust in their clinician, motivation to 'follow the rules', desire to stay active and avoid pain, and concern about discontinuing their opioid.</b>  <i>Trust: I'll do it until the doctors tell me don't do it anymore.</i>  <i>Motivation to "follow the rules": I'm just good at taking [opioids] because that's what I'm supposed to do.</i>  <i>Desire to avoid pain: [I take it] because I like having no pain. I've been to that pain place. It's not a good place to be. So, I'm not going back.</i>  <i>Concern about discontinuing opioid: A couple of times I was tempted [to cut back on opioids], but I'm like, "is it safe to just stop taking it?"</i></p> <p><b>However, patients also commonly expressed little concern about skipping or delaying a long-acting opioid dose.</b>  <i>Well, if I need to sleep, I need to sleep. So, I just sleep [and skip or delay a dose]. I don't beat myself up about it anymore.</i></p>
Practical facilitators to adherence	<p><b>Patients developed self-management routines to maintain their desired level of adherence.</b>  <i>I had [opioid] in the pill boxes so I always knew whether I had taken it with 100% certainty because it was either in there or it wasn't. I wouldn't remember to do it. So, I asked [my wife] to help me.</i></p>
Practical barriers to adherence	<p><b>Practical barriers to adherence primarily included a lack of daily anchors to which patients could link their medication taking times or disruptions in sleep/awake schedules.</b>  <i>The mid-day [dose] is sometimes problematic .... If I fall asleep at 2 PM and I wake up and it's 5 PM, I've missed my [dose]. I've sometimes fallen asleep prior to [taking my opioid at night]. So, I might wake up at 3 or 4 AM and if I've got pain, I'll take it then, but if I'm still not in pain, I'll just wait until the morning dose.</i></p>

it (e.g., linking it to recent physical overexertion or to an intentional or unintentional delay in last opioid dose) or found it to be distressingly unpredictable. Others noted that even under optimal conditions, the opioid dose did not last the prescribed amount of time.

Given insufficient opioid coverage and pain unpredictability, pain management involved daily pain monitoring and negotiation between pain relief versus pain management beliefs (see Table 3). To 'stay on top of the pain,' some patients took their short-acting opioid at the first sign of pain, whereas others delayed until pain reached a certain threshold. Other patients took their short-acting opioid just before, or at the same time as, the long-acting opioid to help ward off pain (e.g., Figure 1b). Perceptions of short-acting opioids varied, with some patients perceiving that short-acting doses were more effective, less harmful or more judicious relative to round-the-clock doses. Consequently, some patients took their short-acting opioid in place of their long-acting opioid at times and one patient did this daily (Figure 1c). Pain outcomes and pain management behaviors did not vary by time since initial prescription or adherence patterns as recorded by the MEMS caps.

#### Long-acting Opioid Adherence

Opioid concerns generated unease but were not consistently related to poorer adherence (see Table 4). Patients largely felt compelled to adhere to their regimens. Some patients were motivated by trust in their prescribing clinician or importance of following clinical advisement. Notably, patients who showed near-perfect adherence, as recorded by their MEMS caps (e.g., Figure 1a), primarily expressed

taking their medication as "the right thing to do" or due to being a "rules follower." Others described being intrinsically motivated by the wish to stay active and avoid disruptive pain. Still others were concerned about health risks of discontinuing their opioid.

On the other hand, when patients were shown their own adherence data, they commonly expressed little concern about skipping or delaying a dose (e.g., "it's not an exact science," "I don't beat myself up about it anymore")—especially if it did not lead to intolerable pain (e.g., Figure 1b). Some patients intentionally skipped or delayed doses or took a lower dose than prescribed to minimize how much medication they took. Still others experimented with discontinuing their medication or chose not to follow a prescribed opioid dose increase despite residual pain. These approaches reflected an underlying belief that it was best to take as little opioid as needed to achieve an acceptable level of pain. Approaches also reflected that patients commonly treated long-acting opioid adherence as a dynamic or adaptive process. Study data did not show long-acting opioid overuse. Adherence did not vary by prescribed opioid dose or time since initial prescription.

#### Facilitators and Barriers to Adherence

Patients developed self-management routines to maintain their desired level of adherence (see Table 4). Routines involved combinations of strategies such as pill boxes, medication logs, phone alarms, mobile applications, or family support. These routines offered reassurance that patients were taking the medication as planned, particularly in the context of memory impairment or high pill burden.

Despite routines, patients continued to face practical adherence challenges (see Table 4). Viewing their own MEMS data facilitated patient realization or recall of adherence deviations. Barriers to adherence primarily included a lack of consistent daily anchors to which patients could link their medication-taking times. Patients on eight-hour dosing schedules had difficulties taking their mid-day dose on time if they did not have a consistent daytime schedule (e.g., Figure 1b). Disruptions in sleep/awake schedules interfered with morning and evening doses. Patients who frequently took their long-acting opioid early and/or late attributed this exclusively to sleep issues. When patients slept through their usual dose time, they would need to navigate whether to skip the dose, take it on a delayed schedule, and/or revise the time of their next dose. However, only one patient acknowledged that without shifting their subsequent schedule, a late dose would make the next dose early. Two patients encountered pharmacy delays in filling their opioid prescription. Facilitators and barriers to adherence did not vary by prescribed opioid dose or time since initial prescription.

## Discussion

Results highlight the internal conflict that patients with advanced cancer experience in taking long-acting opioids. Patients experienced a complex mix of gratitude, concern, and confusion about using their long-acting opioid to manage cancer pain, leading to an underlying unease. Consequently, despite the need to manage severe or frightening levels of pain, patients commonly perceived that the optimal approach would be to take the minimum amount of opioid needed to achieve acceptable pain control. Moreover, for this sample of patients with advanced disease, the hope to eventually taper off opioids meshed with the hope of cancer treatment response. Tailored adherence communication, education, and counseling may play a critical role in improving current pain management outcomes, as described below.

Despite their long-acting opioid regimen, patients commonly experienced residual or breakthrough pain. These findings are consistent with prior studies of patients with cancer-related pain on diverse analgesics.<sup>9,16,17</sup> Attributing pain to controllable reasons allowed patients in the present study to reduce their pain distress. However, for some patients, the dose did not last the prescribed amount of time or pain felt unpredictable, requiring patients to monitor and manage pain throughout the day. Results suggest that patients may find it difficult to link variations in pain to variations in long-acting opioid adherence. In the absence of accepted cutoffs for opioid adherence, patients may benefit from explicit clinician

communication about adherence recommendations including assessment, problem-solving, and guidance on the use of short-acting opioids. Clinicians may be able to titrate long-acting opioids more effectively when patients monitor pain in the context of consistent long-acting opioid use.

Given patient ambivalence about using opioids and, in some cases, inconsistent pain benefit from opioids, patients in the present study established their own opioid taking goals and routines. These results elucidate prior evidence that patients commonly do not take long-acting opioids at the prescribed time intervals<sup>22</sup> and that adherence may vary on a daily basis and over time.<sup>23</sup> For patients in the present study who had near-perfect adherence, following the prescribed dose schedule was described by patients as part of their character. In comparison, other patients treated adherence as a dynamic or adaptive process rather than a firm schedule. They were motivated to take opioids because of pain benefit and might describe themselves as adherent yet still made sporadic efforts to minimize opioid use by skipping, lowering, or delaying doses or taking a short-acting opioid dose instead. Thus, adherence as a personalized target may help to explain why factors such as perceived pain benefit or concerns about opioids have inconsistently predicted analgesic adherence in prior research.<sup>9,12,13,16,17,24–26</sup>

Results have important implications for opioid adherence counseling. Patients may benefit from explicit information about opioid addiction/tolerance, with attention to media reports of opioid misuse and to clinical implications of gaps in daily opioid coverage. However, adherence interventions may be most effective if they further address not only opioid concerns but also ways in which individual patients act (or do not act) on them. Patients had been taking their long-acting opioid for a few months to a few years at the time of study participation, underscoring that clinical attention to adherence should be ongoing.

Although patients developed adherence routines, they still faced practical adherence challenges. Most were related to cancer and treatment sequelae. Changes in sleep and activity patterns are common in advanced cancer, and in the present study, they commonly interfered with opioid adherence. When patients missed a dose because of waking up late, sleeping mid-day, or falling asleep early, they made subsequent decisions about opioid taking based on heuristics such as current level of pain or proximity to the next scheduled dose time. Patients also might delay or skip a dose when “bargaining” between pain and cognitive side effects, as described in prior work.<sup>17</sup> These findings have important implications for pain management interventions. Existing trials of educational interventions for patients with cancer pain have shown inconsistent benefits for reducing cancer pain, and few trials measured adherence or self-

efficacy outcomes.<sup>27</sup> Patients need targeted assistance to problem-solving strategies for managing pain when sleep issues or other factors preclude consistent opioid taking or when patients choose to forego their opioid dose because of other priorities. Patients and their clinicians may generate tailored guidelines to help patients make pain management decisions between clinic visits.

A key strength of the present study was the use of each patient's adherence data during the study interview. Notably, patients rarely identified specific deviations from prescribed regimens unless prompted by the data. Moreover, when deviations were identified, patients rarely expressed concern about them especially if patients could not clearly link them to pain escalation. On the other hand, being able to attribute breakthrough pain to a controllable reason might reduce pain distress without leading a patient to improve adherence. Results emphasize the potential benefits of integrating daily adherence data as points of discussion and feedback in existing interventions that are designed to enhance cancer pain management.<sup>27</sup> Findings emphasize that viewing adherence data may help patients and clinicians to more effectively identify and address individual patients' adherence gaps and opportunities for enhancing pain management.

Current results should be interpreted in the context of important limitations. For one, the study design precluded drawing conclusions about causality between opioid adherence and pain outcomes beyond study patient perspectives. More work is needed to understand complex longitudinal relationships between adherence and pain control. Second, the study was conducted at an academic medical center with primarily non-Hispanic white patients and almost two-thirds with gastrointestinal cancer. Study data also did not show long-acting opioid overuse. Therefore, insights of patients outside of these demographics may not be represented by the concerns of the current sample. Finally, patient descriptions of their opioid taking may have been affected by social desirability factors; however, as described previously, we enhanced recall of actual adherence patterns by pairing patient insights with their own adherence data.

In sum, results provide in-depth insight into the patient experience of using opioids to manage chronic cancer pain. Patients may feel uneasy about using long-acting opioids to manage cancer pain in the long term and may set their own adherence goals and routines. Intentional adherence lapses or deviations may relate to concerns about opioid risks and unclear links between adherence and pain control. Unintentional deviations commonly stemmed from practical barriers related to cancer and treatment sequelae. Findings highlight the need to enhance patient adherence communication, education, and

counseling within the oncology setting, to optimize the use of long-acting opioids as a component of chronic cancer pain management.

### **Disclosures and Acknowledgments**

Dr. Safren receives royalties from Oxford University Press, Guilford Publications, and Humana Press for authorship on books. All other authors have no conflicts of interest to disclose. This work was supported by the American Cancer Society (MRSO PCSM 14-017-01 to L. T.) with additional author time supported by the National Institutes of Health (K24 MH094214 to S. A. S.; K24 CA181253 to J. S. T.). The funding sources were not involved in study design, collection, analysis or interpretation of data, or writing of the report. The authors thank our participants for sharing their knowledge.

### **References**

1. van den Beuken-van Everdingen MHJ, Hochstenbach LMJ, Joosten AJ, Tjan-Heijnen VCG, Janssen DJA. Update on prevalence of pain in patients with cancer: systematic review and meta-analysis. *J Pain Symptom Manage* 2016;51:1070–1090.
2. World Health Organization. *Cancer pain relief*, 2nd edition. Geneva: WHO, 1996.
3. Caraceni A, Hanks G, Kaasa S, et al. Use of opioid analgesics in the treatment of cancer pain: evidence-based recommendations from the EAPC. *Lancet Oncol* 2012;13:e58–e68.
4. Breivik H, Cherny N, Collett B, et al. Cancer-related pain: a pan-European survey of prevalence, treatment, and patient attitudes. *Ann Oncol* 2009;20:1420–1433.
5. Kroenke K, Theobald D, Wu J, et al. The association of Depression and pain with health-related quality of life, Disability, and health care Use in cancer patients. *J Pain Symptom Manage* 2010;40:327–341.
6. Liang S-Y, Yates P, Edwards H, Tsay S-L. Factors influencing opioid-taking self-efficacy and analgesic adherence in Taiwanese outpatients with cancer. *Psychooncology* 2008;17:1100–1107.
7. Yoong J, Traeger LN, Gallagher ER, et al. A Pilot study to Investigate adherence to long-acting opioids among patients with advanced Lung cancer. *J Palliat Med* 2013;16:391–396.
8. Miaskowski C, Dodd MJ, West C, et al. Lack of adherence with the analgesic regimen: a Significant barrier to effective cancer pain management. *J Clin Oncol* 2001;19:4275–4279.
9. Meghani SH, Thompson AML, Chittams J, Bruner DW, Riegel B. Adherence to analgesics for cancer pain: a comparative study of African Americans and whites using an electronic monitoring device. *J Pain* 2015;16:825–835.
10. Oldenmenger WH, Echteld MA, de Wit R, et al. Analgesic adherence measurement in cancer patients: comparison between electronic monitoring and diary. *J Pain Symptom Manage* 2007;34:639–646.
11. Nguyen LMT, Rhondali W, De la Cruz M, et al. Frequency and predictors of patient deviation from prescribed opioids and barriers to opioid pain management in patients with advanced cancer. *J Pain Symptom Manage* 2013;45:506–515.

12. Rhee YO, Kim E, Kim B. Assessment of pain and analgesic Use in African American cancer patients: factors related to adherence to analgesics. *J Immigrant Minor Health* 2012;14:1045–1051.
13. Gunnarsdottir S, Donovan HS, Serlin RC, Voge C, Ward S. Patient-related barriers to pain management: the barriers questionnaire II (BQ-II). *Pain* 2002;99:385–396.
14. Jacobsen R, Liubarskiene Z, Moldrup C, et al. Barriers to cancer pain management: a review of empirical research. *Medicina (Kaunas)* 2009;45:427–433.
15. Dart RC, Surratt HL, Cicero TJ, et al. Trends in opioid analgesic abuse and mortality in the United States. *N Engl J Med* 2015;372:241–248.
16. Manzano A, Ziegler L, Bennett M. Exploring interference from analgesia in patients with cancer pain: a longitudinal qualitative study. *J Clin Nurs* 2013;23:1877–1888.
17. Torresan MM, Garrino L, Borraccino A, et al. Adherence to treatment in patient with severe cancer pain: a qualitative enquiry through illness narratives. *Eur J Oncol Nurs* 2015;19:397–404.
18. Schumacher KL, Koresawa S, West C, et al. Qualitative research Contribution to a Randomized clinical trial. *Res Nurs Health* 2005;28:268–280.
19. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain - United States, 2016. *MMWR Recomm Rep* 2016;65:1–49.
20. Cleeland CS, Ryan KM. Pain assessment: global use of the Brief pain Inventory. *Ann Acad Med Singapore* 1994;23:129–138.
21. Ritchie J, Lewis J. *Qualitative research practice: A guide for social science students and researchers*. Washington DC: Sage Publications, 2003.
22. Oldenmenger WH, Sillevs Smitt PAE, de Raaf PJ, van der Rijt CCD. Adherence to analgesics in oncology outpatients: focus on taking analgesics on time. *Pain Pract* 2017;17:616–624.
23. Meghani SH, Knafl GJ. Patterns of analgesic adherence predict health care utilization among outpatients with cancer pain. *Patient Prefer Adherence* 2016;10:81–98.
24. Jacobsen R, Samsanaviciene J, Liubarskiene Z, Sciupokas A. Barriers to pain management among Lithuanian cancer patients. *Pain Pract* 2010;10:145–157.
25. Valeberg BT, Miaskowski C, Hanestad BR, et al. Prevalence rates for and predictors of self-reported adherence of oncology outpatients with analgesic medications. *Clin J Pain* 2008;24:627–636.
26. Lai Y-H, Keefe FJ, Sun W-Z, et al. Relationship between pain-specific beliefs and adherence to analgesic regimens in Taiwanese cancer patients: a preliminary study. *J Pain Symptom Manage* 2002;24:415–423.
27. Oldenmenger WH, Geerling JI, Mostovaya I, et al. A systematic review of the effectiveness of patient-based educational interventions to improve cancer-related pain. *Cancer Treat Rev* 2018;63:96–103.