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Adherence to Analgesics for Cancer Pain: A Comparative Study of African Americans and Whites Using an Electronic Monitoring Device

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Abstract: Despite well-documented disparities in cancer pain outcomes among African Americans, surprisingly little research exists on adherence to analgesia for cancer pain in this group. We compared analgesic adherence for cancer-related pain over a 3-month period between African Americans and whites using the Medication Event Monitoring System (MEMS). Patients (N = 207) were recruited from outpatient medical oncology clinics of an academic medical center in Philadelphia (≥18 years of age, diagnosed with solid tumors or multiple myeloma, with cancer-related pain, and at least 1 prescription of oral around-the-clock analgesic). African Americans reported significantly greater cancer pain (*P* < .001), were less likely than whites to have a prescription of long-acting opioids (*P* < .001), and were more likely to have a negative Pain Management Index (*P* < .001). There were considerable differences between African Americans and whites in the overall MEMS dose adherence, ie, percentage of the total number of prescribed doses that were taken (53% vs 74%, *P* < .001). On subanalysis, analgesic adherence rates for African Americans ranged from 34% (for weak opioids) to 63% (for long-acting opioids). Unique predictors of analgesic adherence varied by race; income levels, analgesic side effects, and fear of distracting providers predicted analgesic adherence for African Americans but not for whites.

***Perspective:** Despite evidence of disparities in cancer pain outcomes among African Americans, surprisingly little research exists on African Americans' adherence to analgesia for cancer pain. This prospective study uses objective measures to compare adherence to prescribed pain medications between African American and white patients with cancer pain.*

***Key words:** Cancer pain, African Americans, analgesics, adherence, electronic monitoring.*

The Institute of Medicine report *Relieving Pain in America* finds that one of the most robust findings on differential pain outcomes pertains to African Americans.[16] Previous Institute of Medicine reports,[42] accumulated reviews,[1,8,11,12,26] and a meta-analysis[23] provide a compelling demonstration that African American patients are less likely to receive analgesia for pain in cancer and noncancer settings. There is also strong evidence from studies conducted independently in different geographic regions in the United States that pharmacies in predominantly African American and minority zip codes do not carry the opioids needed to treat moderate to severe pain.[13,30]

Factors at the provider and system levels have been documented in the literature, but surprisingly little is known about adherence to analgesia for cancer pain among African Americans. This issue is important because analgesics remain the predominant and

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consistently reimbursable clinical paradigm for managing cancer pain. Although the National Comprehensive Cancer Network guidelines for adult cancer pain[31] include several complementary and alternative modalities, they are not consistently reimbursed or lack rigorous data on clinical effectiveness for cancer pain.[4,20] Thus, differential analgesic adherence may be conceptualized as an important explanatory variable in cancer pain outcomes.[28]

Most studies on analgesic adherence for cancer pain have been conducted predominantly or exclusively with white samples.[27,28,32,44,48,54,56] The limited studies that exist on African Americans are cross-sectional (eg, computed adherence for the past 24 hours)[39] and are based on self-reported measures of adherence.[2,22,39,51] Studies in noncancer settings comparing self-reported measures of adherence with objective measures such as electronic monitoring have found that subjective adherence measures are not sufficiently accurate and overestimate rates of adherence by 10 to 30%.[3,7,10,14,19,55] Thus, we compared analgesic adherence for cancer pain between African Americans and whites longitudinally using the Medication Event Monitoring System (MEMS; MVW Switzerland Ltd, Sion, Switzerland). The specific aims were to 1) compare adherence to prescribed around-the-clock (ATC) analgesic between African Americans and whites with cancer-related pain over a 3-month period; and 2) identify unique predictors of ATC analgesic adherence for cancer pain for African Americans and whites.

Methods

Design and Study Population

The study was a 3-month observational design with repeated measures at 2 time points, ie, baseline (T1) and 3 months (T2). Patients were recruited from 2 outpatient medical oncology clinics of an academic medical center in Philadelphia between December 2009 and August 2011. Inclusion was based on self-identified African Americans or whites, at least 18 years of age, diagnosed with solid tumors or multiple myeloma, with cancer-related pain, and at least 1 prescription of oral ATC analgesic. Patients were excluded if they were prescribed ATC analgesics using a transdermal system (eg, fentanyl patch) because of limitations of MEMS vials. The study was approved by the institutional review board of the University of Pennsylvania, and all patients provided informed consent.

Study Measures

Index Analgesic

The information regarding prescribed ATC analgesics (index medication) was gathered based on patient self-reports during the baseline T1 interview and triangulated with electronic medical records review. Index analgesics were coded according to the World Health Organization's (WHO) analgesic ladder.[52,53] This includes step 1 (nonopioid analgesics, eg, ibuprofen, acetaminophen, naproxen); step 2 (weak opioids, eg, codeine); and step 3 (strong opioids, eg, morphine, oxycodone, methadone). The step 3 analgesics were further coded according to immediate release and extended or sustained release (long-acting) opioids based on evidence of both differential prescription and use of long-acting opioids by race.[51] We computed the Pain Management Index (PMI) for each patient based on the WHO guidelines for treating cancer pain.[52,53] The PMI measure is based on the most potent analgesic prescribed to a patient relative to the level of his or her reported pain. PMI is calculated by subtracting patient's pain levels ("worst pain" score from the Brief Pain Inventory [BPI] coded as mild, moderate, or severe) from the most potent analgesia prescribed. A negative PMI implies inadequate analgesic prescription relative to the reported pain level.

MEMS Analgesic Adherence

Analgesic adherence was captured using MEMS. MEMS is a medication bottle cap with a microprocessor that records the occurrence and time of bottle opening in real time. The primary measure of ATC analgesic adherence in our study was "dose adherence" (percentage of the total number of prescribed doses that were taken). For example, if a patient took 60 of 80 prescribed doses over the study period, the "dose adherence" measure would be 75%.

Patients were instructed on the correct use of the MEMS bottle during the baseline T1 interview. A follow-up phone call was made to each participant within 7 days of T1 to allow participants to ask any questions they may have about proper usage of the MEMS bottle. Patients were instructed to use the bottle for the duration of the study period and use the bottle only to take the index medication, including any refills for the index medication. They were asked to notify the study staff of any changes in the medication dose or frequency as well as document this information in a medication log, in which they also maintained a record of any instances of bottle opening other than when taking the index medications.

PowerView software (MVW Switzerland Ltd) was used to record and compute MEMS adherence. If a frequency or medication change occurred during the study period, a new medication entry (phase) was created as a denominator, with the previous phase ending at PowerView's default time, 2:59 AM on the day of the change, and the next phase beginning at 3:00 AM. If a dosage change occurred, the average of the 2 (or more) dosages was reported, and no new phase was created. If a patient reported (in writing on the event log or orally with reasonable certainty during the T2 interview) having taken doses that the bottle did not record, the events were added to the MEMS data. For example, added events might occur if a patient took out 2 pills at 1 time and took the second later in the day, or if the patient took out 6 pills for a

3-day trip. Likewise, if a patient reported extra openings for reasons other than taking the medication, the extra openings were excluded from the MEMS adherence calculation. Excluded events included accidental openings and openings only to count pills or refill the bottle.

Also, hospitalization periods were adjusted in the analysis as a nonmonitored period beginning on the calendar day of admission at 3:00 AM and ending on the calendar day after discharge at 2:59 AM. Hospitalization information (including facility name, dates, and primary and secondary diagnoses) was obtained from self-reports between the T1 and T2 dates, self-reports at the T2 interview, and review of patient charts. Hospitalization duration was calculated by subtracting the admission date from the discharge date.

Self-Reported Analgesic Barriers

Barriers Questionnaire II[50] was used at baseline to assess patients' beliefs about management of cancer pain. Barriers Questionnaire II is a 27-item instrument that elicits pain management concerns in 8 domains: 1) fear of addiction, 2) fear of tolerance, 3) fear of side effects, 4) fatalism about cancer pain, 5) desire to be a good patient, 6) fear of distracting the health provider from treating cancer, 7) fear that the analgesics impair the immune system, and 8) concern that analgesics may mask ability to monitor illness symptoms. For each item, the responses range from 0 (do not agree) to 5 (agree very much). The recommended scoring is based on mean scores on the total scale (27 items) and subscales. The internal consistency of the scale is excellent at .89.[50]

Analgesic Side Effects

Analgesic side effects were captured at baseline using the Medication Side-Effects Checklist,[49] which elicits information on the presence, type, and severity of 8 common analgesic side effects during the past week (0–10; no severity to extreme severity). The reported internal consistency reliability (Cronbach α) is greater than .80.

Pain Severity and Pain Impact

Pain severity and pain impact were measured at baseline using the BPI.[9] The tool assesses pain at its worst, least, and average over the past week, and pain currently experienced (pain now) on a 0 to 10 scale (no pain to pain as bad as you can imagine). The psychometrics of the BPI is well established for patients with cancer, including minority patients with cancer. Its Cronbach α ranges from .77 to .91.

Intentional versus Unintentional Nonadherence

Morisky Medication Adherence Scale (MMAS),[29] a structured, 4-item, self-reporting measure, was used at baseline to distinguish between both intentional (active) and unintentional (passive) dimensions of nonadherence. Statements corresponding to unintentional nonadherence include "I sometimes forget to take my pain medicine" and "I am sometimes careless about taking my pain medicine." Statements that correspond to intentional nonadherence include "When I feel better I sometimes stop taking my pain medicine" and "If I feel worse when I take the pain medicine, sometimes I stop taking it." The participants were asked to indicate the extent to which they agree with each statement on the MMAS 4-point scale. The scores for each of the 4 items are aggregated to give a score ranging from 0 to 4; higher scores indicate higher levels of reported nonadherence.[29] MAMS has established concurrent and predictive validity, and its Cronbach α in different studies has ranged from .61 to .86.

Demographic and Illness Variables

Self-reported demographic data were gathered on age, gender, self-identified race and ethnicity, marital status, education, income, and type of health insurance. Illness-related variables collected from patients' medical records included type of cancer, stage of cancer, time since cancer diagnosis, past history of drug or substance abuse, comorbidities, and history of depression.

Statistical Analysis

All data were analyzed using SAS version 9.3.[41] A prediction model was constructed using a backward elimination method considering all variables that were significant at the bivariate level ($P < .2$) as potential predictors. The backward elimination method involved starting with all candidate variables in the model, then deleting the variable (if any) that improves the model the most by being deleted, and repeating this process until no further improvement is possible (ie, all remaining variables in the model are significant at the $\alpha = .05$ level).

Separate models were run for African Americans and whites to understand unique predictors of analgesic adherence. The rationale for running separate models by race rather than an overall model of adherence was to identify potential intervention targets that may be unique to each subgroup.

To assess potential bias caused by confounding, we generated a series of bivariate analyses with adherence as the outcome and several key variables obtained at the initial visit as potential predictors. All variables that were found to be statistically significant at the .2 level were then considered as covariates in the final analysis. Once the multivariable model was derived, each of the original variables was re-entered into the model, 1 variable at a time, by testing the most significant to least significant variable to allow a previously insignificant variable to become significant in the final model and retaining any variable that yielded a P value <.05.

Furthermore, to assess for potential bias because patients were lost to follow-up at month 3, we created a binary (yes/no) indicator variable for retention. We then ran a series of bivariate analyses considering several key variables obtained at the initial visit as potential predictors of retention status. We found no statistically

significant predictors of dropout, which supports the statistical missing at random data assumption, suggesting no significant bias as a result of retention.

Sensitivity Analysis for the Observer Effect

A critique of MEMS monitoring is that because of the awareness of being observed, MEMS monitoring may lead some individuals to modify aspects of their medication-taking behavior.[45,46] To account for this potential source of bias, we created 2 separate variables to determine the internal consistency between the "dose adherence" outcomes containing data from all the days monitored to the outcome containing data with the first 30 days of observation removed. The Spearman correlation between adherence scores for all days monitored and the adherence scores with the first 30 days excluded was .97 ($P < .001$) for African Americans and .95 ($P < .001$) for whites.

Because all Spearman correlations were significantly large, there was strong internal consistency between total adherence scores and the total adherence scores with the first 30 days of observations removed. Similar trends in parameter estimates were observed when the outcome with the first 30 days removed was used, with little difference in the available data between all monitored data and the data with 30 days of observations removed. Based on this, the outcome containing the adherence scores for all days monitored was chosen for the final analysis.

Results

A participant and recruitment flowchart is presented in Fig 1. Adherence data using MEMS were available for 207 patients (non-Hispanic whites = 121; non-Hispanic African Americans = 86). There was no differential attrition from T1 to T2 based on key variables such as race ($P = .496$) or participants' general health status ($P = .612$). The mean age of the group was 54 years (SD = 11). There were significant differences between African Americans and whites based on education, income, type of health insurance, and presence of metastasis (Table 1). However, there were no significant differences between the groups based on age, gender, type of cancer, time since cancer diagnosis, comorbidity burden, and past history of substance or alcohol abuse (Table 1).

Pain and Analgesic Prescription

Compared with whites, African Americans reported significantly greater cancer pain, including higher BPI "worst pain" scores ($P < .001$); higher "least pain" scores, indicating lower pain relief ($P < .001$); and negative PMI, indicating inadequate analgesic prescription given the pain levels ($P < .001$) (Table 2). There were no differences in African Americans and whites in analgesic prescription according to the WHO analgesic step. However, within WHO step 3 analgesics, African Americans were less likely to be prescribed long-acting opioids for pain relief ($P < .001$). There was a significant difference between groups on Morisky nonadherence items. More specially, a larger percentage of African Americans reported being forgetful (41% vs 27%, $P = .043$) and intentionally stopping pain medicine when feeling better (58% vs 40%; $P = .009$).

MEMS Analgesic Adherence

Patients' adherence was monitored for an average of 88 days (standard deviation [SD] = 17) using MEMS. There

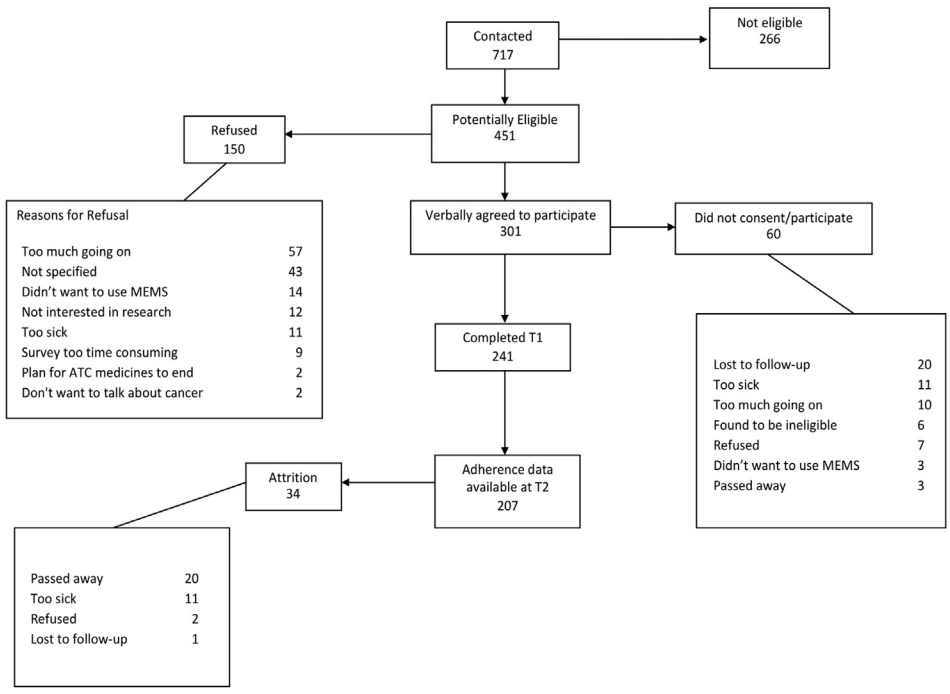

Figure 1. Participant and recruitment flowchart.

Table 1. Demographic and Illness Characteristics

Variable	*Total (N = 207)*	*Whites (n = 121)*	*African Americans (n = 86)*	P *Values**
Age, y, mean (SD)	54 (11)	54 (12)	53 (10)	.392
Time since cancer diagnosis, mo, mean (SD)	37 (35)	36 (35)	38 (36)	.784
Charlson Comorbidity Index, mean (SD)	4 (3)	4 (2)	4 (3)	.260
Gender				
Male	90 (43)	59 (49)	31 (36)	.069
Female	117 (57)	62 (51)	55 (64)	
Marital status				<.001
Married	110 (53)	84 (69)	26 (30)	
Separated/divorced/widowed	56 (27)	19 (16)	37 (43)	
Never married	41 (20)	18 (15)	23 (27)	
Education				.016
Elementary	3 (1)	1 (1)	2 (2)	
High school	70 (34)	35 (29)	35 (41)	
College/trade school	101 (49)	58 (48)	43 (50)	
More than college	33 (16)	27 (22)	6 (7)	
Income (US$)				<.001
<30,000	73 (35)	24 (20)	49 (57)	
30,000–50,000	36 (17)	15 (12)	21 (24)	
50,000–70,000	37 (18)	26 (21)	11 (13)	
70,000–90,000	24 (12)	21 (17)	3 (3)	
>90,000	37 (18)	35 (29)	2 (2)	
Health insurance				<.001
Private	107 (52)	81 (68)	26 (30)	
Medicaid	27 (13)	5 (4)	22 (26)	
Medicare	41 (20)	21 (18)	20 (23)	
Multiple	25 (12)	12 (10)	13 (15)	
Other	6 (3)	1 (1)	5 (6)	
Cancer type				.907
Lung	32 (15)	21 (17)	11 (13)	
Breast	38 (18)	21 (17)	17 (20)	
Gastrointestinal	31 (15)	19 (16)	12 (14)	
Genitourinary/reproductive	25 (12)	15 (12)	10 (12)	
Multiple myeloma	34 (16)	17 (14)	17 (20)	
Other solid tumors	47 (23)	28 (23)	19 (22)	
Presence of metastasis				.008
Yes	148 (72)	95 (78)	53 (62)	
No	59 (28)	26 (22)	33 (38)	
History of substance abuse				.131
Yes	35 (17)	16 (13)	19 (22)	
No	172 (83)	105 (87)	67 (78)	
History of alcohol abuse				.636
Yes	20 (10)	13 (11)	7 (8)	
No	187 (90)	108 (89)	79 (92)	
History of depression				.236
Yes	87 (42)	55 (45)	32 (37)	
No	120 (58)	66 (55)	54 (63)	

NOTE. Values are n (%) unless otherwise indicated.
**P* values are based on t-tests for continuous variables and χ^2 for categorical variables.

was no difference between African Americans and whites in the number and frequency of medication changes during the index period (Table 2). However, there were considerable differences between African Americans and whites in the overall analgesic adherence (53% vs 74%, $P < .001$) as well as adherence according to the WHO analgesic step (Table 2). On subanalysis, analgesic adherence rates for African Americans ranged from 34% for weak opioids to 63% for long-acting opioids. For whites, adherence ranged from 55% for weak opioids to 78% for long-acting opioids (Fig 2).

Unique Predictors of MEMS Analgesic Adherence

Tables 3 and 4 present the findings of the unique predictors of overall adherence (dose adherence) for African Americans and whites, respectively.

African Americans

Income level was the strongest predictor of analgesic adherence for cancer pain among African Americans (Table 3). Compared with those who reported a

Table 2. Analgesic Prescription and Pain Management Variables

Variable	Total (N = 207)	Whites (n = 121)	African Americans (n = 86)	P Values*
Index analgesic, n (%)				.111
WHO step 1	19 (9.2)	7 (5.8)	12 (14.0)	
WHO step 2	22 (10.6)	12 (9.9)	10 (11.6)	
WHO step 3	166 (80.2)	102 (84.3)	64 (74.4)	
Negative PMI, n (%)				<.001
Yes	18 (8.7)	5 (4.13)	13 (15.1)	
No	189 (91.3)	116 (95.9)	73 (84.9)	
Prescription of long-acting opioids, n (%)				<.001
Yes	117 (56.5)	82 (67.8)	35 (40.7)	
No	90 (43.5)	39 (32.2)	51 (59.3)	
MMAS unintentional; forgetfulness, n (%)				.043
Yes	68 (32.9)	33 (27.3)	35 (40.7)	
No	139 (67.1)	88 (72.7)	51 (59.3)	
MMAS unintentional; carelessness, n (%)				.839
Yes	35 (16.9)	21 (17.4)	14 (16.3)	
No	172 (83.1)	100 (82.6)	72 (83.7)	
MMAS intentional; stop when feel better, n (%)				.009
Yes	98 (47.3)	48 (39.7)	50 (58.1)	
No	109 (52.7)	73 (60.3)	36 (41.9)	
MMAS intentional; stop when feel worse, n (%)				.739
Yes	34 (16.4)	19 (15.7)	15 (17.4)	
No	173 (83.6)	102 (84.3)	71 (82.6)	
Worst pain (BPI, 0–10)	6.4 (3)	5.9 (3)	7.0 (2)	<.001
Least pain (BPI, 0–10)	3.3 (2)	2.8 (2)	4.0 (2)	<.001
Average pain (BPI, 0–10)	4.7 (2)	4.1 (2)	5.3 (2)	<.001
Pain interference (BPI, 0–70)	35.2 (16)	33.6 (15)	37.6 (16)	.086
Severity of side effects (MSEC, 0–80)	25.2 (15)	23.8 (13)	27.1 (17)	.130
Barriers Questionnaire (BQ-II, 0–135)	66.8 (20)	64.5 (19)	70.0 (21)	.052
Number of index medication changes during the study period	.05 (.24)	.06 (.23)	.05 (.26)	.744
Number of medication frequency changes during the study period	.14 (.40)	.18 (.46)	.09 (.29)	.094
Total number of analgesics prescribed (excluding coanalgesics)	2.1 (.80)	2.1 (.79)	2.0 (.82)	.711
Total number coanalgesics prescribed	.24 (.50)	.24 (.51)	.23 (.47)	.920
% overall adherence	65.1 (34.5)	73.7 (31.5)	52.8 (34.9)	<.001
Number of MEMS days monitored	87.6 (16.7)	86.8 (15.5)	88.4 (17.9)	.486
% adherence by WHO step				
WHO step 1	50.6 (33.5)	59.5 (37.5)	45.4 (31.5)	.391
WHO step 2	45.2 (31.8)	54.9 (28.6)	33.6 (33.0)	.121
WHO step 3	69.3 (33.7)	76.9 (30.7)	57.3 (35.1)	.000
% adherence by long-acting opioids only	73.6 (31.0)	78.1 (29.2)	62.9 (32.9)	.015

NOTE. Values are mean (SD) unless otherwise indicated.
Abbreviations: MSEC, Medication Side-Effects Checklist; BQ, Barriers Questionnaire.
*P values are based on t-tests for continuous variables and χ^2 for categorical variables.

household income of more than $50,000 a year, those between $10,000 and $50,000 a year had a 25.89% lower percentage of adherence (P = .002) and those with less than $10,000 a year had a 41.83% lower percentage of dose adherence (P < .001). Also, clinical variables were significant in explaining nonadherence in African Americans. For instance, for each unit increase in the severity of analgesic side effects, the percentage of dose adherence decreased by 1.39 (P < .001). Similarly, for each unit increase in concern about distracting the doctor from curing the disease, the percentage of dose adherence decreased by 7.44 (P = .002). The Morisky subscale of intentional nonadherence was also a strong predictor of dose adherence for African Americans. Those who reported intentional nonadherence (ie, stopping analgesics when feeling better) had a −22.17% lower percentage of dose adherence (P < .001). On the other hand, the number of analgesic side effects reported and the number of analgesics prescribed were associated positively with dose adherence. This model was statistically significant and explained 44% of the variance for dose adherence for African Americans.

Whites

The intentional nonadherence subscale (ie, stopping prescribed analgesics when feeling better or worse) was the strongest predictor of dose adherence for whites (Table 4). Those who reported stopping analgesics when feeling better had a 23.67% lower percentage of dose adherence (P < .001). Similarly, those who reported

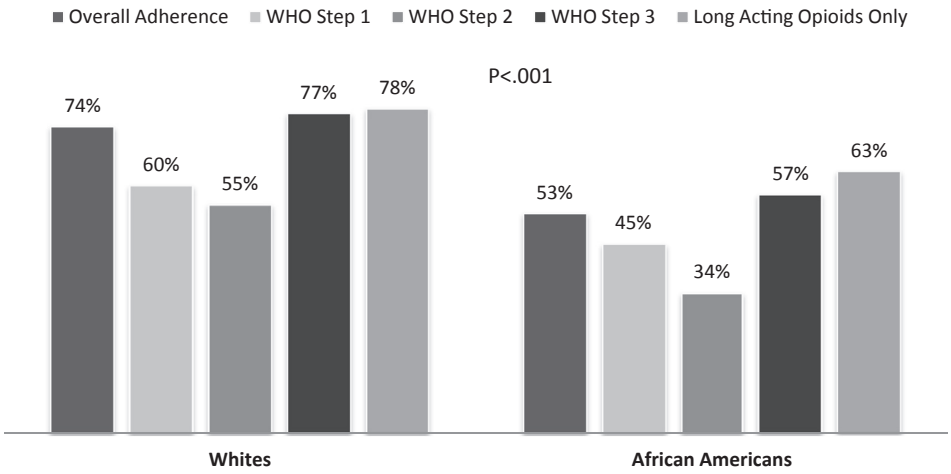

Figure 2. MEMS dose adherence by race and type of analgesic.

stopping analgesics when feeling worse had an 18.56% lower percentage of dose adherence ($P = .010$). Clinical variables such as length of pain due to cancer and pain levels also predicted dose adherence for whites. For every unit increase in time since cancer diagnosis (in months), dose adherence increased by .16% ($P = .026$), whereas for every unit increase in "least pain" (higher scores indicate lower pain relief), dose adherence decreased by 2.88% ($P = .041$). This model was statistically significant and explained 30% of the variance for dose adherence for whites.

Discussion

"Drugs don't work in patients who don't take them" (C. Everett Koop).[36] By the same token, not taking medication is a behavioral representation of what may be right or wrong for the patient in a medication treatment setting. We found that analgesic adherence was low for both whites and African Americans but it was considerably lower for African Americans.

Most existing interventions to improve cancer pain outcomes are conceived within a psychoeducational paradigm that focuses on knowledge transfer to address attitudes and barriers to opioid use.[17,40,43] A systematic review of the effectiveness of such interventions for cancer pain management found that although the interventions improved knowledge about cancer pain management in most of the studies (73%), most did not improve reported adherence to analgesics.[35] These findings were confirmed in another meta-analysis[5] that found no benefit of educational interventions on analgesic adherence or pain-related interference. This indicates that the knowledge path to improving analgesic adherence or cancer pain outcomes may be inadequate.

Consistently, we found that most common analgesic-related fears (including addiction concerns) did not explain objective analgesic adherence for cancer pain for African Americans or whites. Most of the identified predictors of objective adherence may be thought of as circumstantial or experiential, likely based on patients' previous clinical experience of cancer pain management or clinician–patient interaction. Furthermore, African Americans had more of such barriers (eg, need for more information about pain medications, fear of distracting or annoying clinicians, and concern for side effects) than whites.

Similar findings were supported in a previous study of adherence to analgesia for cancer pain (using subjective measures of adherence and African American patients only).[39] The investigators found that addiction concerns were not correlated with adherence for WHO step 2 or step 3 analgesics; pain intensity, side effects, and fear of distracting clinicians were associated with analgesic adherence in African Americans with cancer pain.

Similarly, in our study, an increase in the severity of side effects was associated with lower adherence to analgesia for African Americans but not for whites. Moreover, more adherent African Americans reported a greater number of analgesic side effects at baseline, suggesting disparities in analgesic management of adverse effects in African Americans. The higher burden of side effects in African Americans may also be related to the choice of analgesics in African Americans. A recent study[25] found that after controlling for the type of health insurance, African Americans with cancer pain had 71% lower odds of receiving a prescription of oxycodone than white patients ($P < .001$) and they were more likely to be prescribed morphine even in the presence of renal insufficiency. The investigators further reported that the type of analgesics prescribed partially mediated the reported adverse analgesic effects.[25]

In whites, lower pain relief (higher "least pain" scores) predicted lower adherence to analgesia, whereas time since cancer diagnosis, possibly indicating disease severity, predicted greater analgesic adherence. Consistently, in a previous analysis to understand trade-offs that African Americans and whites use in making cancer pain decisions, we found that African Americans were more likely to make decisions on analgesic use based on side effects, whereas whites were more likely to make decisions on analgesic use based on the amount of relief expected from using pain medications.[24]

Table 3. Unique Predictors of Analgesic Adherence for African Americans

Variable	β Coefficients*	Standard Error	P Value
Household income (US$)			
<10,000	−41.828	9.207	<.001
10,000–50,000	−25.894	8.188	.002
>50,000 (reference)	—	—	—
Feel the need to receive further information about pain medication			
Yes	25.629	9.381	.008
No (reference)	—	—	—
Intentional nonadherence ("When I feel better I sometimes stop taking my pain medicine")			
Yes	−22.174	6.131	<.001
No (reference)	—	—	—
Total number of analgesics prescribed (excluding coanalgesics)	10.720	3.836	.007
Number of analgesic side effects	9.812	2.675	<.001
Fear that if doctors have to deal with pain they will not concentrate on curing the disease (0 = do not agree at all, 5 = agree very much)	−7.440	2.256	.002
Fear that doctors might find it annoying to be told about pain (0 = do not agree at all, 5 = agree very much)	5.911	2.394	.016
Severity of analgesic side effects	−1.389	.406	<.001

NOTE. Model: ($F(9,76) = 6.65$, $P < .001$, $R^2 = .441$).
*The β coefficients from the final prediction model represent slope coefficients for the continuous predictors and the difference from the reference category for the categorical predictors. A large value implies a large effect size.

Another important finding of this study is the strong negative linear relationship in the levels of income and adherence to analgesia for cancer pain among African Americans. Studies in nonpain settings have found that higher out-of-pocket cost and household income less than $20,000 are associated with medication nonadherence behaviors, including decreasing the dose or frequency of medications, failing to refill, or extending time between the refills.[15,37,38,47] In the setting in which patients refill their pain medications, they may save pain medications until they cannot stand pain or hoard pain medications for when pain is severe, a behavior termed medication triaging.[21] Although studies of medication triaging in the context of pain are limited, there is some evidence that patients may be nonadherent to pain medications to be able to afford medications for other chronic conditions such as diabetes.[18] Thus, low-income patients may compromise on taking pain medications to be able to afford medications considered as more important or lifesaving or even resort to less expensive but also less potent over-the-counter alternative therapies.[18,21]

The fact that African Americans with lower incomes were less adherent brings to the forefront the importance of discussing cost and ability to pay when writing an analgesic prescription. In the current clinical scenario, management of multiple conditions and symptoms occurs in isolation and by multiple health care providers, resulting in accumulated cost and complexity for the patients. In a national study, most patients (two-thirds) with chronic illnesses reporting underuse of medications because of cost-related concerns never discussed these concerns with their clinicians.[38] Of those reporting cost-related nonadherence, the clinicians never asked them about their ability to pay for medications or the patients did not believe that clinicians could help.[38] Clinicians may take a more proactive role in assessing cost-related issues potentially contributing to analgesic nonadherence and provide assistance such as reviewing overall medication regimens, simplifying regimens, changing medications to less expensive alternatives when clinically appropriate, or providing information about programs that may assist with prescription medication cost.

Consistent with the study by Rhee et al,[39] overuse of analgesia among African Americans is not supported in our study. Unlike adherence for some other chronic conditions for which there is more agreement on adherence cutoff rates, there is no agreement about which cutoff is

Table 4. Unique Predictors of Analgesic Adherence for Whites

Variable	β Coefficients*	Standard Error	P Value
Intentional nonadherence ("When I feel better I sometimes stop taking my pain medicine")			
Yes	−23.672	5.315	<.001
No (reference)	—	—	—
Intentional nonadherence ("If I feel worse when I take the pain medicine, sometimes I stop taking it")			
Yes	−18.557	7.054	.010
No (reference)	—	—	—
Least pain in last week (0 = no pain, 10 = pain as bad as you can imagine)	−2.876	1.394	.041
Length of time since the diagnosis of cancer (mo)	.160	.071	.026

NOTE. Model: ($F(4,116) = 12.34$, $P < .001$, $R^2 = .299$).
*The β coefficients from the final prediction model represent slope coefficients for the continuous predictors and the difference from the reference category for the categorical predictors. A large value implies a large effect size.

valid for analgesic use for cancer pain.[34] Previous non-U.S. studies have used cutoffs of 70%[32] to 100%.[33,34] However, regardless of the cutoff used, the analgesic adherence rates of 34 to 63% in African Americans are considerably lower. Similar lower analgesic adherence rates for cancer pain in African Americans were also identified in another study (46%),[39] even using subjective measures that typically overestimate adherence. These findings should be a cause for concern for the goal of achieving equity in clinical cancer pain outcomes.

Strengths and Limitations

This is the first study to our knowledge that has compared adherence to analgesia for cancer pain and its unique predictors between African Americans and whites using objective measures of adherence over time. However, some findings of our study are limited. First, we limited objective monitoring of analgesics to 1 ATC analgesic. Because we used a MEMS vial for electronic monitoring, it was not feasible to monitor ATC prescription in a patch form. However, we have no reason to believe that analgesics in a patch form would be prescribed disproportionately to African Americans, an assumption that is needed to nullify our findings of differential prescription of long-acting opioids by race.

Furthermore, although MEMS allows for long-term assessment of adherence and detailed information about patterns of prescription use, it does not guarantee ingestion of medication. Vial opening other than for medication taking, medication changes within the study period, and medication holidays (eg, secondary to hospitalization) may result in inaccuracies in adherence measurement. We minimized this potential source of bias by accounting for cap openings other than for medication taking (eg, for refills), a change in frequency and dose of analgesics during the study period, or medication holidays caused by hospitalizations (see the Study Measures section). Despite these limitations, studies in the noncancer pain setting comparing MEMS with a variety of subjective measures have concluded that MEMS is one of the more accurate adherence measurement approaches.[6]

Our study is limited in that there were unmeasured cancer (cancer treatment, medications other than analgesics and coanalgesics, cancer treatment-related side effects, cancer-related functional impairments) and psychiatric variables (cancer-related anxiety, cancer treatment-related posttraumatic symptoms) that may confound the findings. Furthermore, we included history of depression from patients' medical records and did not use self-reported measures of depression. Also, to create predictive models, we used self-reported data from baseline. Since our main goal was to assess patients' adherence behaviors, we believed that multiple contacts by the study staff would create an observational effect resulting in alteration of patients' behavior. It is conceivable that some of the predictors of interest changed over the 3-month course of the study. Although we computed PMI for adequacy of analgesic prescription given patients' levels of pain, we did not compare doses of analgesics between African Americans and whites. Despite these limitations, our findings add to a scarce body of literature to understand differences in analgesic adherence and provide preliminary understanding of the sources of those differences as a way to explain the widely observed clinical disparities in cancer pain outcomes.

Conclusions

Our salient findings indicate that 1) there are significant disparities between African Americans and whites in the treatment of cancer pain and adherence to analgesia captured using MEMS over a 3-month period; 2) analgesic-related beliefs commonly implicated in analgesic- and opioid-related nonadherence (eg, addiction concerns) do not explain objective analgesic taking in both groups; 3) clinical pain management variables explain objective analgesic adherence in this sample of African Americans and whites; 4) the unique predictors of analgesic adherence vary by race; especially socioeconomic variables, fear of distracting providers, and analgesic side effects predict analgesic adherence for African Americans but not for whites; 5) these additional variables may explain differential analgesic adherence and consequent disparities in cancer pain outcomes in African Americans. The greater burden of unmet cancer pain management needs in African Americans deserves correspondingly greater attention and perhaps greater intensity of interventions with this group; however, most of the existing interventions have been both conceptualized and investigated predominantly with white patients.

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