African Americans With Cancer Pain Are More Likely to Receive an Analgesic With Toxic Metabolite Despite Clinical Risks: A Mediation Analysis Study

Salimah H. Meghani, Youjeong Kang, Jesse Chittams, Erin McMenamin, Jun J. Mao, and Jeffrey Fudin

Salimah H. Meghani, Youjeong Kang, and Jesse Chittams, University of Pennsylvania; Erin McMenamin and Jun J. Mao, Perelman Center for Advanced Medicine, University of Pennsylvania, Philadelphia, PA; Jeffrey Fudin, University of Connecticut School of Pharmacy, Storrs, CT; and Jeffrey Fudin, Western New England University College of Pharmacy, Springfield, MA.

Published online ahead of print at www.jco.org on July 21, 2014.

Supported by National Institutes of Health Challenge Grant No. NIH/NINR RC1-NR011591 (S.H.M.).

Presented in part at the 31st Annual Scientific Meeting of the American Pain Society, Honolulu, HI, May 16-19, 2012.

Authors' disclosures of potential conflicts of interest and author contributions are found at the end of this article.

Corresponding author: Salimah H. Meghani, PhD, MBE, RN, FAAN, Department of Biobehavioral Health Sciences, New Courtland Center for Transitions and Health, University of Pennsylvania School of Nursing, 418 Curie Blvd, Room 337, Philadelphia, PA 19104-4217; e-mail: meghanis@nursing.upenn.edu.

© 2014 by American Society of Clinical Oncology

0732-183X/14/3225w-2773w/\$20.00

DOI: 10.1200/JCO.2013.54.7992

ABSTRACT

Purpose

Renal impairment is highly prevalent among patients with cancer, and many patients have undiagnosed chronic kidney disease (CKD) from underlying disease, treatment, or both. African American individuals have disproportionate risk factors (diabetes, hypertension) predisposing them to CKD. We investigated whether African American patients are more likely than white patients to receive morphine with 3- and 6-glucuronide metabolites, which are known to be neurotoxic and accumulate in CKD; whether insurance type mediates the relationship between race and the prescriber's opioid selection; and whether the chosen opioid has a resultant negative effect according to race.

Patients and Methods

Patients (N = 182) were recruited from oncology clinics within the University of Pennsylvania Health System. Inclusion was based on self-identified African American or white race, age older than 18 years, and the presence of cancer-related pain plus a prescription for morphine or oxycodone. Kidney function was estimated using the abbreviated Modification of Diet in Renal Disease formula.

Results

Patients with CKD who received morphine reported a greater severity of analgesic-related adverse effects than patients with CKD who received oxycodone ($P = .010$). Controlling for health insurance type, African American patients had 71% lower odds of receiving a prescription of oxycodone than white patients ($P < .001$). Limiting analysis to those with CKD, the effect of private insurance became insignificant. However, race still remained a significant predictor of the prescribed opioid selection. Race was a strong predictor of adverse effect severity in the presence of CKD, and the type of opioid selection partially mediated this relationship.

Conclusion

Reducing racial disparities in the type of opioid prescription and understanding mechanisms of disproportionate opioid-related adverse effects in African American patients might decrease the clinical disparities in cancer pain outcomes.

J Clin Oncol 32:2773-2779. © 2014 by American Society of Clinical Oncology

INTRODUCTION

Renal impairment is widespread among patients with cancer. Approximately 60% of patients with cancer have a creatinine clearance of less than 90 mL/min, and of these, 20% have a creatinine clearance of less than 60 mL/min.¹⁻³ Although opioids are important front-line treatment for the management of cancer pain, the high prevalence of renal impairment in patients with cancer means that many patients who require opioids might be subjected to opioid toxicities that otherwise are less prevalent in patients with normal kidney function.^{4,5} Disproportionately, African American individuals with cancer may be more likely to have

clinical risk of renal impairment: they are more likely to have comorbid diabetes and/or hypertension, have family history of these comorbidities, and have lower socioeconomic status. Each of these are known clinical risk factors for renal impairment.⁶

There is limited literature on prescribers' practice of assessing patients' renal function and their awareness of how renal function might be affected by various opioid options. Evidence suggests significant variability in prescribers' assessments of patients' renal function and their choice of opioids.⁵ There is also evidence of systematic variability in prescribers' choices of analgesics according to patient race or ethnicity.⁷⁻¹¹ In a recent meta-analysis¹⁰ that synthesized data on analgesic treatment disparities

for two decades, the authors found that although there were no racial or ethnic disparities in the prescription of nonopioid analgesics across a variety of pain etiologies, there were significant racial or ethnic disparities in the prescription of opioids. African American patients were much more likely than any other racial or ethnic groups in the analysis to experience opioid treatment disparities.¹⁰

Although opioid versus nonopioid analgesics and pain evaluation disparities are clearly described in the literature, prescription patterns specific to particular opioid types are lacking. In the context of opioid treatment, provider variability in assessment of renal function, coupled with factors such as threat of implicit bias in opioid prescription, presence of certain comorbidities, and type of insurance coverage might create a particularly suboptimum cancer pain management scenario for African American individuals.

We investigated patterns of opioid prescription between African American and white patients and studied to what extent race versus insurance type mediates these prescription patterns; importantly, we wanted to discover whether certain prescription patterns occur despite the presence of renal impairment and whether these prescription patterns correlate with reported analgesic adverse effects. Specifically, we investigated the following. (1) Are African Americans more likely than white individuals to receive an analgesic with clinically relevant metabolite (eg, morphine with known toxic metabolites, morphine-3- and 6-glucuronide) and does this occur despite the presence of chronic kidney disease (CKD)? (2) Is the relationship between race and type of opioid prescription mediated by type of insurance and is type of insurance a partial or complete mediator of this relationship? (3) Is the relationship between race and severity of analgesic-related adverse effects mediated by type of opioid and is the type of opioid prescribed a partial or complete mediator of this relationship?

PATIENTS AND METHODS

Design and Study Population

This is a retrospective analysis of a study to understand sources of disparities in cancer pain outcomes and adherence to prescribed analgesia for cancer pain. The parent study was a 3-month observational design with repeated measures at two time points: baseline (T1) and at 3 months (T2). Patients were recruited from two outpatient medical oncology clinics within the University of Pennsylvania Health System. Inclusion for this study was based on self-identified African American and white race, age at least 18 years, diagnosis of solid tumors or multiple myeloma, and cancer-related pain requiring opioid therapy and a prescription of around-the-clock schedule II opioids (such as morphine, oxycodone, and hydromorphone) for cancer pain. The study was approved by the institutional review board of the University of Pennsylvania. All patients provided informed consent.

Measures

Prescribed analgesics. The information regarding prescribed analgesics was gathered from electronic medical record review and triangulated with patient self-report. The prescribed analgesics were coded as morphine, oxycodone, or others. We limited our inclusion of the schedule II opioids to morphine and oxycodone for pragmatic and conceptual reasons. First, most patients in our study were receiving either morphine- or oxycodone-based medications. The others category was small and comprised a heterogeneous opioid mix that might have created noise in the data. More importantly, from a conceptual standpoint, our research question required comparing morphine with a drug that does not accumulate significantly in CKD and had a greater street value than morphine¹² to help answer the prescription bias aim. For purposes of this analysis, we excluded analgesics generally classified as schedule

III opioids such as codeine or hydrocodone combined with acetaminophen, aspirin, or ibuprofen.

Presence of kidney disease. We used the four-variable abbreviated Modification of Diet in Renal Disease (MDRD) study formula to determine the estimated glomerular filtration rate (eGFR), which is based on serum creatinine, sex, age, and ethnicity.¹³ The MDRD, and not the Cockcroft-Gault formula, was chosen because the precision of the latter is limited especially in certain populations, including those older than age 65 and in obese patients.¹⁴ Also, studies confirm better precision of the MDRD (when compared with Cockcroft-Gault) in patients with cancer.¹⁵ The four-variable abbreviated MDRD has shown performance similar to the more precise MDRD7 equation, which is based on additional parameters.¹⁴ Up to seven serum creatinine values between T1 and T2 were extracted from patients' medical records. All eGFR values for a single patient were then averaged to determine CKD status (no CKD = eGFR $\geq$ 90 mL/min/1.73 m²; CKD = eGFR < 89 mL/min/1.73 m²).

Analgesic adverse effects. Analgesic adverse effects were captured using the Medication Side-Effects Checklist (MSEC),¹⁶ which elicits information on presence, type, and severity of adverse effects that commonly occur with analgesic use during the past week (scale of zero to 10, from no severity to extreme severity). The reported internal consistency reliability (Cronbach's α coefficient) is more than 0.80.

Pain severity. Pain severity and pain effects were measured using the Brief Pain Inventory.¹⁷ The psychometrics of the Brief Pain Inventory are well established with patients with cancer, including minority patients with cancer. The Cronbach's α coefficient ranges from 0.77 to 0.91.

Health insurance. Health insurance information was self-reported by participants and was cross-referenced with information in patients' medical records. When the two information sources conflicted, the information in the patient records was used. Managed Medicare or Medicaid plans (eg, Bravo, HealthPartners, Keystone Mercy) were classified as Medicare or Medicaid, respectively. Lack of insurance or plans that were not private, Medicare, or Medicaid (such as Veterans Affairs, Consolidated Omnibus Budget Reconciliation Act, or federal insurance) was classified as other. For data analysis, the insurance variable was dichotomized as private and nonprivate insurance.

Statistical Analysis

All data were analyzed using SAS (version 9.3; SAS Institute, Cary, NC). The four steps described by Baron and Kenny¹⁸ were used for establishing mediation. To determine the relationship between race, insurance, and type of opioid selection, the following sequential steps were used.

Step 1 showed that the variable of interest was correlated with the outcome. We used type of opioid prescribed as the criterion variable (Y) in a regression equation and race as a predictor (X). This step established that there is an effect that might be mediated.

Step 2 showed that the variable of interest (X = race) was correlated with the mediator (M = private health insurance). We used having private insurance as the criterion variable in a regression equation and race as a predictor.

Step 3 showed that the mediator affected the outcome variable. We used the type of opioid prescribed as the criterion variable (Y) in a regression equation, and race (X) and type of health insurance (M) as predictors.

Step 4 established that private insurance partially or completely mediated the relation between race and type of opioid prescribed. The effect of race on type of opioid prescribed should be zero after controlling for the mediator to achieve full mediation. The effects in steps 3 and 4 were estimated in the same equation.

A similar set of steps was followed to determine the relationship between race, type of opioid selection, and severity of analgesic adverse effects. The analysis was conducted using the overall sample, and the sample was stratified according to CKD status. We then followed up with the Sobel test¹⁹ to further validate the significance of the indirect effect. Because data were collected at T1 and again at T2, the generalized estimating equations method was used to fit population-averaged models to adjust for the correlated data within patient. For binary outcomes (eg, type of opioid), the population-averaged logistic models were used; for continuous outcomes (eg, adverse effect severity), the population-averaged linear mixed model was used.

Table 1. Characteristics of Study Participants According to Race (N = 182)

Variable	Patient Population						P ^a
	Total (N = 182)		African American (n = 73)		White (n = 109)		
	Freq	%	Freq	%	Freq	%	
Age, years							.253
Mean	55.1		54.0		55.8		
SD	10.1		9.3		10.6		
Sex							.074
Male	92	51	31	42	61	56	
Female	90	49	42	58	48	44	
Marital status							< .001
Married	109	60	24	33	85	78	
Separated/ divorced/ widowed	47	26	33	45	14	13	
Never married	26	14	16	22	10	9	
Education							.079
Elementary	3	2	2	3	1	1	
High school	60	33	27	37	33	30	
College/trade school	89	49	38	52	51	47	
More than college	30	16	6	8	24	22	
Income, \$							< .001
< 30,000	57	31	38	52	19	17	
30,000-50,000	36	20	21	29	15	14	
50,000-70,000	32	18	10	13	22	20	
70,000-90,000	20	11	2	3	18	17	
> 90,000	37	20	2	3	35	32	
Health insurance							< .001
Private	97	54	23	31	74	69	
Medicaid	18	10	16	22	2	2	
Medicare	42	23	21	29	21	19	
Other	24	13	13	18	11	10	

Abbreviation: Freq, frequency.

*P values were based on *t* tests for continuous variables and χ^2 for categorical variables.**Table 2.** Clinical Variables of Study Participants According to Race

Variable	Patient Population						P*
	Total (N = 182)		African American (n = 73)		White (n = 109)		
	Freq	%	Freq	%	Freq	%	
Pain worst (0-10)							< .001
Mean	6.8		7.6		6.2		
SD	2.3		2.0		2.5		
Pain least (0-10)							< .001
Mean	3.3		4.1		2.7		
SD	2.0		2.0		1.8		
Pain average (0-10)							< .001
Mean	4.7		5.4		4.2		
SD	2.0		1.9		2.0		
Pain interference (0-10)							.048
Mean	35.4		38.3		33.5		
SD	16.0		16.5		15.4		
Severity of analgesic adverse effects							.047
Mean	25.6		28.3		23.8		
SD	14.7		17.5		12.4		
eGFR, mL/min/ 1.73 m ² †							.054
≥ 90	100	55	46	63	54	49	
60-89	53	29	14	19	39	36	
< 60	29	16	13	18	16	15	
Type of opioid prescribed							< .001
Oxycodone	128	70	39	53	89	82	
Morphine	54	30	34	47	20	18	

Abbreviations: CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; Freq, frequency.

*P values are based on *t* tests for continuous variables and χ^2 for categorical variables.†CKD was estimated using eGFR: no CKD = eGFR ≥ 90 mL/min/1.73 m²; CKD = eGFR < 89 mL/min/1.73 m².

RESULTS

The sample size was 182 at T1 (African American, *n* = 73; white, *n* = 109) and 150 at T2 (African American, *n* = 62; white, *n* = 88). Participants in both groups identified themselves as non-Hispanic. The 18% attrition was not associated with race (*P* = .466) or patients' general health status (*P* = .640). Relevant demographic and clinical data are presented in Tables 1 and 2, respectively. There was no difference between African American and white patients regarding age (*P* = .253). However, African American patients belonged to a lower income bracket (*P* < .001) and were less likely to carry private health insurance when compared with white patients (*P* < .001). In terms of prescriber opioid selection, overall, African American patients were less likely to be prescribed oxycodone preparations than white patients (53% *v* 82%, respectively) and more likely to be prescribed morphine preparations than white patients (47% *v* 18%; *P* < .001). This prescription pattern persisted in the presence of CKD (Fig 1). There was no difference between African American and white patients in renal status measured according to the eGFR (*P* = .054).

African American patients reported significantly greater cancer pain worst score (*P* < .001), pain least score (*P* < .001), and more

severe analgesic adverse effects (*P* = .047) than white patients. In general, patients with CKD who were taking morphine reported a greater severity of analgesic adverse effects than patients with CKD who were taking oxycodone (Fig 2). Interestingly, although there was no racial difference in the reported severity of adverse effects in the absence of CKD (African American patients' MSEC score, 25.2 *v* 24.7 for white patients; *P* = .841), African American patients reported significantly greater severity of adverse effects than white patients in the presence of CKD (MSEC score, 32.0 *v* 23.0; *P* = .014).

Mediation Analysis

For the mediation analysis aim, the subsample of patients receiving morphine or oxycodone were included.

Race, Insurance, and Type of Opioid Prescription

Self-identified race was strongly associated with type of opioid prescription (Baron and Kenny¹⁸, step 1). African American patients were significantly more likely to be prescribed morphine, and

Fig 1. Percentage of opioid prescription according to race and chronic kidney disease (CKD) status.

white patients were significantly more likely to be prescribed oxycodone ($P < .001$; Fig 3A). Race was also associated with the conceptualized mediator, private health insurance (Baron and Kenny¹⁸, step 2). African American patients were significantly less likely than white patients to have private health insurance. Specifically, African American patients had 79% lower odds of having private insurance than white patients (odds ratio, 0.21; 95% CI, 0.12 to 0.37; $P < .001$).

Controlling for private insurance, the association between race and type of opioid prescribed (morphine *vs* oxycodone) diminished only slightly and was still highly significant ($P < .0007$; Baron and Kenny¹⁸, steps 3 and 4). Notably, after controlling for health insurance status, African American patients had 71% lower odds of receiving a prescription of oxycodone than white patients (adjusted odds ratio, 0.29; 95% CI, 0.14 to 0.60; $P < .001$; Fig 3B). A significant Sobel test ($z = 2.310$; $P = .021$) further established the evidence that health insurance status partially mediated the observed differences in type of opioid prescribed to African American patients.

Limiting the analysis to those with renal impairment, the effect of private insurance on type of opioid prescription became insignificant (Figs 3C and 3D). However, race still remained a significant independent predictor of the type of opioid being prescribed for cancer pain, even in the presence of CKD (Fig 3D).

Fig 2. Average severity of analgesic adverse effects according to type of opioid and presence of chronic kidney disease (CKD).

Fig 3. Race, insurance, and type of opioid prescription. AOR, adjusted odds ratio; OR, odds ratio.

Race, Type of Opioid Prescription, and Severity of Analgesic Adverse Effects

Self-identified race was strongly associated with severity of analgesic adverse effects (Baron and Kenny¹⁸, step 1), with African American patients more likely to report more severe adverse effects ($P = .015$; Fig 4A). Furthermore, race was a significant predictor of type of opioid prescribed (Baron and Kenny¹⁸, step 2). However, race was no longer a significant predictor of severity of adverse effects after adjusting for type of opioid prescribed ($P = .085$), whereas type of opioid prescribed remained a significant predictor of adverse effect severity after adjusting for race ($P = .037$; Baron and Kenny¹⁸, steps 3 and 4; Fig 4B). A significant Sobel test ($z = -2.426$; $P = .015$) further established the evidence that type of opioid fully mediated the relationship between race and severity of adverse effects.

Our mediation analysis was repeated, limiting the analysis to those with presence of renal impairment. The African American-white disparity in severity of adverse effects increased in the subgroup with renal impairment (Figs 4A and 4B *vs* Figs 4C and 4D). The average of adverse effect severity for African American patients with renal impairment was 8.40 (95% CI, 1.91 to 14.90) points greater than for white patients with renal impairment ($P = .012$). In the mediation analysis, the effect of opioid selection on adverse effects severity became insignificant statistically but remained clinically meaningful (Fig

Fig 4. Race, type of opioid prescription, and analgesic adverse effects. OR, odds ratio.

4D). However, race remained strongly associated with severity of analgesic adverse effects.

DISCUSSION

In this study, we investigated the role of race and type of opioid selection on reported analgesic adverse effects. The findings indicate that type of opioid prescription is only partially mediated by insurance type, and race remains a strong predictor of the type of opioid selection after controlling for insurance type. This suggests that factors other than insurance/copayment structures might relate to clinical disparities in opioid prescription for cancer pain.

Clinicians' decision about opioid selection might be on the basis of perceived greater abuse potential, diversion, or street value of certain opioids. The main problem with implicit or unconscious bias is that it frequently escapes recognition²⁰; in addition, there is little correlation between explicit (what we know of ourselves) and implicit bias.²¹ Social cognition research suggests that everyday clinical realities such as time constraints, stressful high-volume patient loads, and fear of regulatory agencies might further provoke racial stereotyping.²² An alternative explanation might be prescriber assumption that African American patients live in neighborhoods where pharmacies do not

carry adequate supplies of certain opioids.^{23,24} Although the problem of implicit bias is complex, the literature suggests that simple interventions focused on heightening clinicians' awareness about their blind spots, increasing awareness of stereotypes on clinical judgments, and promoting egalitarian commitment to equity might ameliorate disparities in clinical outcomes.²⁰

We also found that type of prescribed opioid mediates the relation between race and analgesic adverse effects; however, race becomes a significant independent predictor of analgesic adverse effect severity in the presence of CKD ($\beta = 8.40$; $P = .011$). The issue of analgesic adverse effects is a critical one, which often relates to nonadherence of analgesia, poor pain control, and diminished function in patients with cancer, especially African American patients.²⁵⁻²⁹ A larger sample would permit a more nuanced analysis for opioid analgesic selection, perhaps using multiple relevant clinical monitors, including analysis of serum for medication levels, pharmacogenetic monitoring, and drug-drug or disease-drug confounds that could improve or worsen tolerability and/or toxicities for either group. Larger systematic studies might also consider the polymorphic differences in type and allele frequencies of cytochrome P 2D6 hepatic enzyme activity in white and African American patients,^{30,31} which might compromise effective pharmacotherapy because of drug clearance or risk of concentration-dependent toxicities.

The high prevalence of renal impairment in patients with cancer, which has been demonstrated in a number of recent studies,¹⁻³ means that many patients have undiagnosed CKD and certain segments might have unequal risks related to unique drug selection. Providers must appreciate that certain opioids have toxic metabolites, which might proportionately translate to the risk for adverse clinical outcomes.³² Also, knowledge of serum creatinine levels alone does not accurately predict kidney dysfunction in comparison with creatinine clearance.⁴ Approximately 60% of patients with cancer have creatinine clearance of less than 90 mL/min; however, only 10% would show increased serum creatinine levels.³ A comparative study of nephrology versus palliative care physicians found that a keen understanding of opioid pharmacology is too often lacking in prescribing clinicians. The considerable variability in prescribing practices and possible knowledge deficits of clinically relevant metabolites, coupled with implicit bias, might disproportionately affect certain subsegments.

Some findings of our study are limited. First, the relatively small sample size came from two oncology clinics of an academic medical center. Despite the small sample size, most findings were highly significant, which indicates a clinical phenomenon of sizeable effect that would allow detection in a relatively small sample.

It is important to clarify that all data collection for our study was completed by August 2011. In August 2010, Purdue Pharma introduced an abuse-deterrent reformulation of oxycodone with a controlled-release delivery that makes it difficult to abuse the product by snorting or intravenous injection. The new abuse-deterrent labeling has only recently been approved (April 2013) by the US Food and Drug Administration.³³ Although some of the formal epidemiologic studies suggest a decline in the abuse of the reformulated oxycodone, other studies do not support such a finding.³⁴ Despite a period of overlap between our data collection and the early phase of the release of the reformulated version, postmarketing surveillance studies show that there was only a 5.1% decrease in all oxycodone prescriptions 1 year after introduction.³⁵ At the same time, street values for immediate-

release (IR) oxycodone formulations increased by 15%.³⁵ On the basis of this balance, and that the reformulated oxycodone was not separated from oxycodone IR in our analysis, it is likely that any opioid-prescribing patterns based on implicit bias among clinicians did not change during the study period.

Also, we did not stratify our analysis according to IR versus extended release (ER) preparations for any opioids studied. Generic ER morphine is available from several pharmaceutical companies and is relatively inexpensive. ER oxycodone is only available by brand name and is comparatively expensive. Although such analysis is warranted in larger studies, we are confident that this categorization will not change our findings because we combined IR and ER preparations as oxycodone. If African American patients were equally likely to receive oxycodone in any preparation in the setting of CKD, it would have been evident in our classification, but this was not the case (Fig 1).

Because the original study aimed at understanding adherence to around-the-clock opioid medication, we limited our analysis to one index medication. Also, we focused our analysis on schedule II analgesics. Some patients might have been prescribed additional analgesics. Studies with larger samples might be able to account for all opioids received.

We did not directly investigate serum morphine-3- or 6-glucuronide concentrations or actual glomerular filtration rate, a gold standard method (such as 51 chrome–ethylenediaminetetraacetic acid).¹ Nevertheless, we used an eGFR determined by using a method that has been found to be reliable in several studies.

In conclusion, this study generated important preliminary hypotheses to investigate sources of disparities in cancer pain manage-

ment outcomes. Reducing racial disparities in the type of opioid prescription and understanding mechanisms of disproportionate opioid-related adverse effects in African American patients might decrease cancer pain–related clinical disparities.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Although all authors completed the disclosure declaration, the following author(s) and/or an author's immediate family member(s) indicated a financial or other interest that is relevant to the subject matter under consideration in this article. Certain relationships marked with a "U" are those for which no compensation was received; those relationships marked with a "C" were compensated. For a detailed description of the disclosure categories, or for more information about ASCO's conflict of interest policy, please refer to the Author Disclosure Declaration and the Disclosures of Potential Conflicts of Interest section in Information for Contributors.

Employment or Leadership Position: None **Consultant or Advisory Role:** None **Stock Ownership:** None **Honoraria:** Jeffrey Fudin, Purdue Pharma **Research Funding:** None **Expert Testimony:** None **Patents, Royalties, and Licenses:** None **Other Remuneration:** None

AUTHOR CONTRIBUTIONS

Conception and design: Salimah H. Meghani

Collection and assembly of data: Salimah H. Meghani

Data analysis and interpretation: Salimah H. Meghani, Youjeong Kang, Jesse Chittams, Erin McMenamin, Jun J. Mao, Jeffrey Fudin

Manuscript writing: All authors

Final approval of manuscript: All authors

REFERENCES

- Launay-Vacher V: Epidemiology of chronic kidney disease in cancer patients: Lessons from the IRMA study group. *Semin Nephrol* 30:548-556, 2010
- Janus N, Launay-Vacher V, Byloos E, et al: Cancer and renal insufficiency results of the BIRMA study. *Br J Cancer* 103:1815-1821, 2010
- Launay-Vacher V, Oudard S, Janus N, et al: Prevalence of renal insufficiency in cancer patients and implications for anticancer drug management: The renal insufficiency and anticancer medications (IRMA) study. *Cancer* 110:1376-1384, 2007
- Aapro M, Launay-Vacher V: Importance of monitoring renal function in patients with cancer. *Cancer Treat Rev* 38:235-240, 2012
- Droney J, Levy J, Quigley C: Prescribing opioids in renal failure. *J Opioid Manag* 3:309-316, 2007
- Lipworth L, Mumma MT, Cavanaugh KL, et al: Incidence and predictors of end stage renal disease among low-income blacks and whites. *PLoS One* 7:e48407, 2012
- Anderson KO, Green CR, Payne R: Racial and ethnic disparities in pain: Causes and consequences of unequal care. *J Pain* 10:1187-1204, 2009
- Cintron A, Morrison RS: Pain and ethnicity in the United States: A systematic review. *J Palliat Med* 9:1454-1473, 2006
- Green CR, Anderson KO, Baker TA, et al: The unequal burden of pain: Confronting racial and ethnic disparities in pain. *Pain Med* 4:277-294, 2003
- Meghani SH, Byun E, Gallagher RM: Time to take stock: A meta-analysis and systematic review of analgesic treatment disparities for pain in the United States. *Pain Med* Feb 13:150-174, 2012
- Meghani SH, Polomano RC, Tait RC, et al: Advancing a national agenda to eliminate disparities in pain care: Directions for health policy, education, practice, and research. *Pain Med* 13:5-28, 2012
- Street Rx. Street Prices for Prescription Drugs 2013. <http://streetrx.com>
- National Kidney Foundation. Calculators for Health Care Professionals: GFR Calculators. http://www.kidney.org/professionals/kdoqi/gfr_calculator.cfm
- Pöge U, Gerhardt T, Palmedo H, et al: MDRD equations for estimation of GFR in renal transplant recipients. *Am J Transplant* 5:1306-1311, 2005
- Kleber M, Cybulla M, Bauchmüller K, et al: Monitoring of renal function in cancer patients: An ongoing challenge for clinical practice. *Ann Oncol* 18:950-958, 2007
- Ward SE, Carlson-Dakes K, Hughes SH, et al: The impact on quality of life of patient-related barriers to pain management. *Res Nurs Health* 21:405-413, 1998
- Cleeland CS, Ryan KM: Pain assessment: Global use of the Brief Pain Inventory. *Ann Acad Med Singapore* 23:129-138, 1994
- Baron RM, Kenny DA: The moderator-mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. *J Pers Soc Psychol* 51:1173-1182, 1986
- Preacher KJ, Hayes AF: SPSS and SAS procedures for estimating indirect effects in simple mediation models. *Behav Res Methods* 717-731, 2004
- Burgess DJ, van Ryn M, Crowley-Matoka M, et al: Understanding the provider contribution to race/ethnicity disparities in pain treatment: Insights from dual process models of stereotyping. *Pain Med* 7:119-134, 2006
- Green AR, Carney DR, Pallin DJ, et al: Implicit bias among physicians and its prediction of thrombolysis decisions for black and white patients. *J Gen Intern Med* 22:1231-1238, 2007
- Meghani SH: Corporatization of pain medicine: Implications for widening pain care disparities. *Pain Med* 12:634-644, 2011
- Green CR, Ndao-Brumblay SK, West B, et al: Differences in prescription opioid analgesic availability: Comparing minority and white pharmacies across Michigan. *J Pain* 6:689-699, 2005
- Morrison RS, Nadeau S, Natale DK, et al: "We don't carry that": Failure of pharmacies in predominantly nonwhite neighborhoods to stock opioid analgesics. *N Engl J Med* 342:1023-1026, 2000
- Meghani S, Hanlon A, Robinson A, et al: Pain treatment outcomes among African-Americans and whites: Evidence of age-race disparities. *Gerontologist* 52:62, 2012
- Meghani SH, Chittams J, Hanlon AL, et al: Measuring preferences for analgesic treatment for cancer pain: How do African-Americans and whites perform on choice-based conjoint (CBC) analysis experiments? *BMC Med Inform Decis Mak* 13:118, 2013
- Meghani SH, Hanlon A, Bruner D, et al: Do subjective measures of adherence predict actual analgesic taking behavior for cancer pain? *J Pain* 12:S20, 2011
- Meghani SH, Hanlon A, Robinson A, et al: Unique clusters and correlates of preference for

analgesic treatment for cancer pain. *Pain* 7:119-134, 2013

29. Rhee YO, Kim E, Kim B: Assessment of pain and analgesic use in African American cancer patients: Factors related to adherence to analgesics. *J Immigr Minor Health* 14:1045-1051, 2012

30. Gaedigk A, Bradford LD, Marcucci KA, et al: Unique CYP2D6 activity distribution and genotype-phenotype discordance in black Americans. *Clin Pharmacol Ther* 72:76-89, 2002

31. Teh LK, Bertilsson L. Pharmacogenomics of CYP2D6: molecular genetics, interethnic differences and

clinical importance. *Drug Metab Pharmacokinet* 27: 55-67, 2012

32. Gretton SK, Ross JR, Rutter D, et al: Plasma morphine and metabolite concentrations are associated with clinical effects of morphine in cancer patients. *J Pain Symptom Manage* 45:670-680, 2013

33. U.S. Food and Drug Administration. FDA News Release. FDA approves abuse-deterrent labeling for reformulated OxyContin. <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm348252.htm>

34. Throckmorton DC: Abuse-deterrent properties of Purdue's reformulated OxyContin (oxycodone hydrochloride) extended-release tablets. Center for Drug Evaluation and Research, DHHS [Memo]. http://www.accessdata.fda.gov/drugsatfda_docs/nda/2013/022272Orig1s014_ODMemo.pdf

35. Coplan P: FDA's Abuse Deterrence Guidance: Food and Drug Law Institute Conference on Controlled Substances Regulation. Food and Drug Law Institute. <http://www.fdli.org/docs/default-document-library/coplan—oxycontin-reformulation—v2.pdf?sfvrsn=0>

ASCO Quality Care Symposium

Join us for the third annual ASCO Quality Care Symposium, which will take place October 17 and 18, 2014, at the Boston Marriott Copley Place, Boston, MA. The meeting will bring together leaders in the expanding fields of health services research and quality initiatives. The Symposium is a unique, comprehensive forum for disseminating information on the improvement of the quality of patient and survivor care through value-based decision making, enhanced research design and methodology, and the innovation of data infrastructure for quality evaluation/improvement.

For additional details, visit quality.asco.org.

Join us for one or more of ASCO's meetings to interact with oncology experts, network with colleagues, and earn CME credit.