The Contribution of the Emergency Department To Opioid Pain Reliever Misuse And Diversion: A Critical Review

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Abstract: Prescription opioid pain reliever (OPR) misuse and diversion is an important and growing public health problem in the United States that is responsible for significant morbidity and mortality. Emergency physicians are among the top prescribers of OPRs, yet the relative contribution of emergency department (ED) OPR prescriptions to the overall opioid abuse epidemic remains unclear. This study critically reviews seven peer-reviewed studies that specifically identified the ED as a source of OPRs. Of the OPRs prescribed in the ED, approximately 10% are associated with indicators of inappropriate prescribing, and approximately 42% may ultimately be misused; of the OPRs that are diverted, approximately 10% originate from an ED prescription. Among patients who suffer an OPR-related death, approximately 1.8% of the OPR pills given to the decedents will have come from the ED. In addition to the need for more research, the existing literature suggests an urgent need for interventions in the ED to reduce OPR misuse and diversion.

Key Words: opioid-related disorders, opioid analgesics, self medication

INTRODUCTION

The misuse and diversion of opioid pain relievers (OPRs) is a growing public health concern in the United States. Since the late 1990s, aggressive pharmaceutical marketing of OPRs such as oxycodone coupled with increasing national attention to a perceived clinicians’ under-appreciation and under-treatment of pain has resulted in rising rates of OPR prescriptions. Both OPR misuse, characterized by OPR use in greater quantities or for reasons other than originally prescribed, and OPR diversion, defined as redirecting medically prescribed OPRs toward medically unauthorized and illicit uses, emerged as unintended consequences of rising rates of OPR prescriptions, with illicit OPR use increasing at higher rates than licit use between 1999 and 2001. Concomitant with the rise in OPR misuse has been an increase in OPR-related mortality, the majority of which is unintentional.
Between 1999 and 2010, the number of OPR-related deaths increased a staggering 400% among women, and 245% among men. When put in context with other major causes of mortality in the United States, in 2013, deaths from drug overdose (of which more than one-third were caused by OPRs) surpassed motor vehicle collisions as the leading cause of injury-related death among 25 to 64 year olds. U.S. emergency departments (EDs) have played a central role in this new public health epidemic of OPR misuse and diversion. Paradoxically, EDs have historically been identified as a contributor to oligoanalgesia, or under-treatment of pain, which was believed to be partly attributable to the fact that the majority of ED patients present with the complaint of pain. In response to calls for improved patient pain management, rates of OPR prescribing in the ED have steadily risen over the past decade, with a 60% increase in OPR prescribing observed in EDs between 1993 and 2005. In 2009, emergency physicians ranked 3rd among specialists prescribing OPRs to patients aged 20 to 39. This national trend raises the question of what role the ED plays within the epidemic of OPR misuse and diversion, and whether the ED should be targeted as a setting for prevention.

Currently, ED-based OPR misuse and diversion strategies primarily rely on OPR prescribing guidelines and prescription drug monitoring programs, which permit ED physicians to search patients’ prescription histories for evidence of inappropriate OPR use. However, this approach fails to incorporate best practice guidelines, as outlined by the major ED professional organizations, including the American College of Emergency Physicians (ACEP), the American Pain Society, the American Society for Pain Management Nursing, and the Emergency Nurses Association, which highlight the need for adequate pain control regardless of a patient’s prior opioid misuse history and stress the importance of patient education regarding the safety concerns of select analgesics.11 Gaining a more in-depth understanding of the role that the ED plays in OPR misuse and diversion could help inform the development of more focused ED-centered prevention interventions.

This article examines and summarizes the current peer-reviewed medical literature addressing the extent to which OPRs obtained from the ED contribute to OPR misuse and diversion.

METHODS
The PubMed database was searched from 1950 to March 2015 and updated in May 2016 using the MESH search terms “Opioid-related disorder” and “Behavior, Addictive,” combined with the Boolean “OR,” linked by the Boolean “AND” to “Emergency Service, Hospital,” yielding 106 results (Figure 1). A separate search using the MESH term “Prescription Drug Diversion” yielded 85 results. The latter term was also applied to GoogleScholar, yielding 897 results. Abstracts were divided and read among two of the authors (TL or EO). When an abstract was determined to contain content relevant to OPR misuse or diversion, the entire article was reviewed. Citations of pertinent referenced studies were also explored for additional content. Articles were excluded if they did not discuss the source of abused or diverted opioids or if the study methodology did not acknowledge the ED as a potential source of abused or diverted opioids. Two citations were excluded from Figure 1. Search results.
review because they could not be accessed in full form, and one article was excluded because it presented preliminary data that were expanded upon in a subsequent publication, the latter of which was included in this study.

**RESULTS**

Seven articles were identified as relevant to this literature review, as summarized in Table 1.12–18 The first is a prospective observational single-center study conducted in Colorado between January and March 2013 that identified patients receiving an OPR prescription in the ED and administered these patients questionnaires at baseline, 3 days, and 30-days after ED discharge.12 The mean age of study participants was 36 years. Of the 85 patients sampled, 42% [95% Confidence Interval (CI) 32% to 52%] were classified as having misused their OPR prescription, with the majority of misuse (92% [86% to 98%]) attributed to self-escalation of dose, beyond that prescribed by the ED clinician. Among misusers, 39% [23% to 55%] reported previously using OPRs without a doctor’s prescription and 36% [20% to 52%] reported using OPRs for reasons other than pain (including relaxation, experimentation, and enjoyment); 8 patients reported misuse in both categories described above. Among misusers, oxycodone was the most common discharge prescription (61%), with hydrocodone less frequently prescribed (33%). Among nonmisusers, hydrocodone was more frequently prescribed (57%) than oxycodone (41%). Oxycodone had an odds ratio of 2.7 (1.1 to 6.6) for misuse in this population.

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>No. of Participants</th>
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<tr>
<td>Beaudoin et al.12</td>
<td>Prospective observational single center, Colorado, Jan–Mar 2013</td>
<td>85</td>
<td>Proportion ED OPR misuse: 42% misuse—92% by self-escalation of dose, 39% using without Rx, 36% using for reasons other than pain Most common Rx: Misusers: 61% oxycodone, 33% hydrocodone. Nonmisusers: 57% hydrocodone, 41% oxycodone</td>
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<tr>
<td>Logan et al.13</td>
<td>Retrospective medical claims review (Truven Health MarketScan Research database), Jan–Dec 2009</td>
<td>400,288</td>
<td>Proportion inappropriate OPR prescriptions: 7.7% high daily dose, 2% overlapping opioid prescription, 1% overlapping benzodiazepine prescription, 0.14% LA/ER formulation for acute pain Most common Rx: 61.5% hydrocodone, 20.4% oxycodone, 6.1% tramadol</td>
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<tr>
<td>Inciardi et al.14</td>
<td>Retrospective review of Research Abuse Diversion and Addiction-Related Surveillance System, 2005–2008</td>
<td>9,008 (OTP survey) 4,008 (SKIP survey)</td>
<td>Primary OPR source: Dealer 72%, friends/relatives 44%, doctor 23%, ED 10%, theft 5%, forged Rx 2%, Internet 2%, other 3% Primary OPR source: Dealer 62%, friends/relatives 52%, doctor 41%, ED 9%, theft 15%, forged Rx 6%, Internet 3%, other 3% Most common OPR: 29.4% controlled-release and immediate-release oxycodone, 23.5% hydrocodone, 9% methadone, 4% tramadol</td>
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<tr>
<td>Lev et al.15</td>
<td>Retrospective observational study of San Diego Medical Examiner’s Office reports and PDMP, 2013</td>
<td>186 patients 713 providers</td>
<td>Proportion OPR pills prescribed by specialty in prescription drug–related deaths: PC/IM 69.2%, surgery 16.7%, pain med 9.7%, psychiatry 2.0%, ED/UC 1.8%, dental 0.6% Proportion OPR prescriptions prescribed by specialty in prescription drug–related deaths: PC/IM 68.7%, surgery 10.7%, pain med 8.2%, ED/UC 6.6%, psychiatry 2.9%, dental 2.9% Most common OPR Rx among Rx deaths: 25.5% hydrocodone, 17.2% oxycodone, 7.5% morphine</td>
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<tr>
<td>Porucznik et al.16</td>
<td>Retrospective observational study of Utah Medical Examiner reports and PDMP, 2002–2010</td>
<td>Not given</td>
<td>Average AR of opioid-related death by specialty: Pain med 2.6, PMR 2.1, psych/neuro 2.0, anesthesia 2.0, fam med 1.5, missing 1.3, ED 1.0, podiatry 1.0, IM (ref) 1.0, orthosurg 0.9, dentist 0.6, OB/Gyn 0.4</td>
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<tr>
<td>Inciardi et al.17</td>
<td>Qualitative interviews, Delaware, 2006</td>
<td>43</td>
<td>Mentioned OPR sources: Purchase from elderly and pain patients, ED and other doctor shopping, drug dealers, “script docs,” nurses, open-air drug markets, family, and friends Preferred OPR: Fentanyl patch most desirable, IR oxycodone most available</td>
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<tr>
<td>Rigg et al.18</td>
<td>Qualitative interviews, South Florida, 2008–2010</td>
<td>50</td>
<td>Mentioned OPR sources: prescription from pain clinic (52%), purchase from destitute patients (44%), subsidizing patients’ trips to pain clinic (32%), obtaining pills from a medical insider (38%), stolen prescription pad from ED (1 mention) Preferred OPR: Roxicodone most sold, OxyContin also highly demanded</td>
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ED, emergency department; OPR, opioid pain reliever; Rx, prescription; LA, long-acting; ER, extended release; OTP, opioid addiction treatment program; SKIP, Survey of Key Informants’ Patients Program; PDMP, prescription drug monitoring program; PC, primary care; IM, internal medicine; UC, urgent care; AR, attributable risk; fam med, family medicine; orthosurg, orthopedic surgery; OB/Gyn, obstetrics/gynecology; IR, immediate release.
Factors associated with misuse included chronic pain, disability, preexisting opioid use, oxycodone use, and history of substance abuse within the 12 months prior to the ED encounter.\textsuperscript{12}

The second article examined medical claims data from January 1 to December 31, 2009 obtained through the Truven Health MarketScan Research database, with the objective of quantifying the extent to which ED providers prescribed potentially inappropriate OPRs.\textsuperscript{13} The following indicators were chosen to represent potentially inappropriate OPR prescriptions: overlapping with another OPR prescription by 1 week or more; overlapping with another benzodiazepine prescription; providing a daily dose greater than or equal to 100 morphine milligram equivalents, providing a long-acting/extended release (LA/ER) formulation for acute pain; and overlapping LA/ER OPRs. In total, there were 400,288 patients identified as having received at least one OPR prescription from the ED. Of those, 10.3\% [10.2\% to 10.4\%] of patients received a prescription with at least 1 potentially inappropriate prescribing indicator as follows: 7.7\% [7.6\% to 7.8\%] were prescribed a high daily dose; 2\% [1.96\% to 2.04\%] had an overlapping OPR prescription; 1\% [0.97\% to 1.03\%] had an overlapping benzodiazepine prescription; and 0.14\% [0.13\% to 0.15\%] had been prescribed an LA/ER formulation for acute pain. The majority of opioid prescriptions were for hydrocodone products (61.5\%), with oxycodone (20.4\%) and tramadol (6.1\%) prescribed less frequently. In this study, there were significant differences in prescribing based on patient gender. Relative to men, a larger fraction of women had two (7.3 vs. 6.6, \(P < 0.001\)) or three plus (2.2 vs. 1.7, \(P < 0.001\)) ED opioid prescriptions. A greater proportion of women also had two (0.2 vs. 0.1, \(P < 0.001\)) or three plus (0.0 vs. 0.1, \(P < 0.001\)) ED benzodiazepine prescriptions.\textsuperscript{13}

The third article\textsuperscript{14} examined the Research Abuse Diversion and Addiction-related Surveillance System (RADARS), a public nonprofit surveillance system designed to collect national data on prescription drug diversion. The objective of the study was to determine the extent to which OPRs are obtained from the internet. Two survey components of RADARS contain information regarding the ED as a potential source of diverted OPRs. One component assesses OPR use from patients in opioid addiction treatment programs throughout the country (OTP survey). From 2005 to 2008, 9008 patients responded to the OTP survey. Of those, 10\% [9.4\% to 10.6\%] reported that the ED was their primary source of OPR prescriptions; more common sources were a drug dealer (78\% [77.1\% to 78.9\%]), friends or relatives (44\% [43.0\% to 45.0\%]), a doctor’s prescription (23\% [22.1\% to 23.9\%]), theft (15\% [14.3\% to 15.6\%]), forged prescription (6\% [5.5\% to 6.5\%]), and Internet (3\% [2.63\% to 3.33\%]). Oxycodone was the most frequently reported OPR of choice (45\%), followed by hydrocodone (20\%) and methadone (12\%). An additional component of RADARS is the Survey of Key Informants’ Patients Program (SKIP), which collects drug use data from patients with a history of recent OPR abuse. From 2005 to 2008, 4008 patients responded to the survey, with 9\% [8.1\% to 9.9\%] of respondents listing the ED as their primary source of OPR prescriptions. A dealer (62\% [60.5\% to 63.5\%]), friends or relatives (52\% [50.5\% to 53.5\%]), and a doctor’s prescription (41\% [39.5\% to 42.5\%]) were more commonly listed sources. The most frequently reported OPR of choice was controlled release and immediate release oxycodone (29.4\%), followed by hydrocodone (23.5\%), methadone (9\%), and morphine (4\%).\textsuperscript{14}

The fourth article\textsuperscript{15} was a retrospective observational study that aimed to characterize the relationship between OPR prescriber specialty and prescription drug-related deaths. The authors examined the 2013 San Diego Medical Examiner’s Office reports and identified 254 patients whose deaths were associated with prescription drugs; of these, 186 patients had corresponding prescription drug monitoring (PDMP) data linking the patients’ prescription histories with a total of 713 providers. The authors found that only 1.8\% of the total OPR pills and 6.6\% of the total OPR prescriptions given to these patients were ordered by the 140 ED or urgent care (UC) physicians identified in the study. Primary care/internal medicine physicians prescribed the greatest proportion of OPR pills (69.2\%) to this population, followed by surgeons (16.7\%), pain medicine specialists (9.7\%), psychiatrists (2.0\%), and finally dentists (0.6\%). Further ED/UC physicians wrote the fewest number of controlled prescriptions per provider (1.6) relative to specialists in primary care/internal medicine (PC/IM), surgery, dentistry, psychiatry, and pain medicine. Hydrocodone was the most frequently prescribed drug (25.5\% of prescriptions) among patients whose deaths were related to medications, followed by oxycodone (17.2\% of prescriptions) and morphine (7.5\% of prescriptions); ED/UC providers were responsible for 1.9\% and 1.6\% of the these pills, respectively.\textsuperscript{15}
The fifth article also focused on the association between OPR provider specialty and opioid-related deaths. The authors calculated the attributable risk (AR) for OPR-related deaths for 12 medical specialties in the years between 2002 and 2010 using the Utah Controlled Substance Database, a type of PDMP, in conjunction with Utah Medical Examiner data. During the 9-year period examined, 0.64% of filled opioid prescriptions resulted in a fatality; of those, 5.7% were related to ED physicians’ prescribing. Family medicine/internal medicine physicians were responsible for the greatest proportion of total OPR prescriptions (34.9%) and prescribed the highest proportion of OPR prescriptions associated with fatalities (39.0%). The AR for ED physicians (1.0) over the 9-year study period was equal to that of IM, but less than that of pain medicine specialists (2.6), physical medicine and rehabilitation physicians (2.1), psychiatrists/neurologists/anesthesiologists (2.0), and family medicine (1.5). During the study period, there was a marked decrease in OPR-related fatalities among all prescribers. The distribution of OPR classes associated with OPR-related deaths was not reported in this study.

The sixth article described qualitative results of an ultra-rapid assessment of prescription drug abuse and diversion in Delaware conducted in 2006. Focus groups and interviews were carried out with prescription drug abusers, dealers, pill brokers, police, and regulatory officials (n = 43). The study population had an even gender split (50/50) and a mean age of 26 years. The majority of participants reported using a variety of recreational drugs in the year prior to the survey, including OPRs (87.5%), benzodiazepine (90.6%), marijuana (87.5%), heroin (84.4%), powder-cocaine (75%), crack cocaine (78.1%), and methamphetamine (40.6%). All of the participants had a history of arrest. The authors note “Occasionally, clinics and hospital emergency rooms were reported as locations for doctor shopping …”; the specific settings of more popular doctor shopping locations were not mentioned. Other common sources of diverted medications described included purchase from elderly and pain patients, drug dealers, “script docs,” and nurses. Among drug abusers, the majority of respondents agreed that the transdermal fentanyl patch was the most desirable OPR, while the most commonly available OPR was immediate-release oxycodone.

The final article was a 4-year qualitative study that described interviews with drug dealers, abusers, and drug diversion investigators (n = 50, male = 36) conducted between 2008 and 2010 in South Florida. The mean age of participants was 33 years. The ED was identified as the venue from which one dealer stole prescription pads. The most commonly employed method, used by 52% of respondents, was frequenting pain management clinics, where patients could easily receive two OPR prescriptions in response to a complaint of pain. One representative participant noted, “I can go and get OxyContin just by complaining about my back, nothing to back it up.” Respondents using this method reported visiting an average of 4 to 5 pain management clinics monthly. Other common methods of obtaining OPRs included buying pills from destitute patients, subsidizing patients’ visits to pain clinics in exchange for the obtained prescriptions, and conniving with medical professionals to steal medications. In this study, Roxicodone was the most frequently sold medication by drug dealers, being generally cheaper than the OxyContin, another highly demanded OPR.

DISCUSSION

Published studies reporting the misuse and diversion of OPRs prescribed in the ED remain limited. In spite of the relative dearth of research in this arena, we found seven studies that specifically identified the ED as a source unique from the broad category of “doctor’s prescription.” Taken together, the studies suggest that, of the OPRs that are prescribed in the ED, approximately 10% are associated with indicators of inappropriate prescribing, and approximately 42% may ultimately be misused. However, despite the potential for misuse, Lev et al.’s work estimates that only 1.8% of patients who suffer an opioid-related death will have received their OPR prescription from the ED. Of the opioids that are diverted, approximately 10% originate from an ED prescription. If Beaudoin et al’s estimate of OPR misuse is representative, almost 1 million [0.53 million to 1.4 million] of the 6.3 million OPRs prescribed in the ED upon discharge each year can be considered to have been used for reasons other than pain. Although this estimate comes from a single-site study with a small sample size, it is consistent with national reports of the 12 million Americans who used OPRs nonmedically in 2010, representing 16% of the population aged 18 to 64 in 2010. Similarly, the reliance of about 10% of opioid abusers on an OPR prescription from the ED points to a systematic problem that is amenable to change.

Although the ED appears to play a lesser role than dealers or pain management clinics as the source of misused OPRs, the ED is uniquely a
location that can implement interventions to reduce the burden of OPR misuse.

Although the source of misused drugs is not well established, there is evidence that OPR misuse typically occurs through one of two pathways: initial legal use by patients suffering from pain and diversion of OPRs through illegal activities such as selling prescriptions to drug dealers.\(^\text{21}\) The former pathway represents an opportunity for ED physicians to use OPRs to control patients’ pain while also employing effective measures to prevent misuse, abuse, and overdose. Prescription drug monitoring programs (PDMP) offer one opportunity for ED physicians to identify patients with a history of inappropriate OPR use.\(^\text{22}\) However, a recent assessment of the effect of PDMPs suggested that these programs may not change the number of prescriptions that ED physicians write for controlled substances, despite their effect of making ED physicians feel more confident in their prescribing decisions and erroneously perceive that their prescribing habits are altered in response to PDMP data.\(^\text{23}\) These results point to an important limitation of PDMPs, namely that they do not address the potential for OPR misuse among patients who do not have a history of high OPR consumption.

The adoption of OPR prescribing guidelines is another intervention that has the potential to positively influence ED physicians’ prescribing patterns. These guidelines may be hospital initiated, or in the case of Washington, Ohio, and New York City, may reflect larger scale initiatives to guide OPR prescribing from the ED, with common recommendations including limiting long-acting OPR prescriptions, prescribing no more than a short course of OPRs when OPRs are clinically indicated, consulting a PDMP prior to prescribing, and preventing routine prescribing of lost or stolen OPR prescriptions.\(^\text{24–26}\) Such guidelines have the potential to help ED physicians by guiding them to make decisions that will improve patient safety while also relieving some of the pressures to inappropriately prescribe OPRs in response to patients’ demands.\(^\text{27,28}\)

A recent qualitative study of 61 emergency physicians attending the October 2012 ACEP scientific assembly (Denver, CO) examined the use of hospital-based OPR prescribing guidelines.\(^\text{29}\) In general, most physicians favored guidelines, but there was some opposition, especially from those classified as liberal prescribers, who preferred to “err on the side of treating.” The study concluded that most of the ED physicians in their sample ultimately made prescription decisions independent of OPR prescribing guidelines, which they instead used as a tool to explain their OPR prescribing decisions to patients.\(^\text{29}\)

An important intervention that continues to hold the promise of reducing OPR misuse and diversion is targeted patient education about the appropriate and safe use of OPRs. Prior research has demonstrated that patients are more likely to understand how to correctly take their medications if provided with written instructions in addition to verbal explanation prior to discharge, with individually tailored instructions recommended as a particularly effective strategy.\(^\text{30,31}\) Further, a recent randomized control trial by McCarthy et al.\(^\text{32}\) involving 210 patients (median age 43 years) at an urban academic ED demonstrated that implementing a targeted educational intervention to patients discharged from the ED with OPRs improved patients’ understanding of their medication’s side effects and resulted in fewer reports of driving within 6 h of taking the medication. Currently, however, there is no systematic protocol enabling physicians to educate patients about whether to use OPRs and, when used, how to safely use, store, and dispose of them. The absence of a patient education protocol is a particular shortcoming given the evidence that many patients engage in misuse and self-escalation of OPR dose.\(^\text{12}\)

Developing an education protocol through the platform of mobile-health technology can fill the gap in patient education while not interrupting the workflow of the ED; computer-based technologies have been used successfully to address other injury prevention topics in ED settings.\(^\text{33,34}\) In the case of OPRs, patient decisions aids can help patients make informed decisions about how to manage their pain.\(^\text{32}\) An example of an approach combining the benefits of computer technology and decision aids is developing a patient education tool to be used on a tablet prior to the prescribing clinician’s interaction combined with a smartphone application that delivers tailored education and reminder text messages on OPR safe use, storage, and disposal for those discharged with an OPR. Additional research characterizing the misuse and diversion of opioids received through the ED is needed to better understand the problem and to help inform the development of interventions to combat it.

This study is limited by having employed only two search engines that, while representing the majority of journals publishing relevant work, may have led to some studies being missed. Secondly, with so few quantitative studies, it is difficult to draw firm conclusions about the role of ED prescribing in the OPR misuse and diversion epidemic. Moreover, the majority of existing data do not consistently capture the type of medical provider or
setting from which these medications are obtained. Despite these limitations, it is clear that the ED plays an important role in OPR misuse and diversion.

CONCLUSIONS
The existing data suggest that the ED is an important contributor to both OPR misuse and diversion. A significant fraction of ED patients engage in OPR misuse, with hydrocodone and oxycodone preparations being the most commonly misused. As such, the ED is an important setting for providers to educate patients about the risks of OPR use. State and hospital-based OPR prescribing guidelines may help ED physicians make pain management decisions and may support them in explaining their decisions to patients. Additional research is needed to further investigate the effectiveness of interventions such as patient education protocols in reducing the ED’s contribution to the OPR epidemic.

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AUTHOR CONTRIBUTIONS
Tatyana Lyapustina was responsible for study concept and design; acquisition of the data; analysis and interpretation of the data; drafting of the manuscript; critical revision of the manuscript for important intellectual content; and statistical expertise. Renan Castillo was responsible for study concept and design; critical revision of the manuscript for important intellectual content; administrative, technical, or material support; and study supervision. Elise Omaki was responsible for acquisition of the data; critical revision of the manuscript for important intellectual content; and administrative, technical, or material support. Wendy Shields, Eileen McDonald, Richard Rothman, and Andrea Gie- len were responsible for critical revision of the manuscript for important intellectual content.

CONFLICT OF INTEREST
TL, RC, EO, WS, EM, RR, and AG report no conflict of interest.

REFERENCES


