

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	A State-wide Cross Sectional Survey of Emergency Departments' Adoption and Implementation of the Ohio Opioid Prescribing Guidelines and Opioid Prescribing Practices
<b>AUTHORS</b>	Penm, Jonathan; MacKinnon, Neil; Mashni, Rebecca; Lyons, Michael S.; Hooker, Edmond; Winstanley, Erin; Carlton-Ford, Steve; Connelly, Chloe; Tolle, Erica; Boone, Jill; Koechlin, Kathleen; Defiore-Hyrmer, Jolene

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Laxmaiah Manchikanti, MD Pain Management Centers of Paducah (KY) and Marion (IL), United States
<b>REVIEW RETURNED</b>	21-Nov-2017

<b>GENERAL COMMENTS</b>	<p>The authors of this manuscript performed a state-wide survey of emergency departments in Ohio have assessed adoption and implementation of the Ohio opioid prescribing guidelines and opioid prescribing practices. Overall, this is a well-executed manuscript; however, there continues to be some limitations that need to be addressed for the manuscript to improve the guideline utilization in Ohio. This manuscript will be useful for the entire United States, or even globally.</p> <p>The limitations are as follows:</p> <ol style="list-style-type: none"><li>1. The authors start with a statement that drug overdose deaths, largely by opioids, are the leading cause of unintentional death in the United States. This is accurate; however, in the beginning itself, to avoid further confusion, the authors should identify the contributions of prescription opioids, heroin, illicit fentanyl, and methadone. This will clarify the issues. As we all know, prescription opioids are not the only reason for this epidemic. As of now, it appears that heroin and illicit fentanyl are overtaking prescription opioids as the leading cause. Prescription opioids are reducing across the board both with the reduction in the number of prescriptions, as well as the prescribing of smaller dosages, leading to reduced production of opioids.</li><li>2. The authors have \$10 incentive, which appears to be somewhat unusual and a rather ineffective mode of recruiting participants.</li><li>3. It appears that there has been significant improvement; however, it is disappointing that PDMPs have not been utilized by 100% of those surveyed. The goal should be at least 99%.</li><li>4. The authors have not provided information in reference to morphine equivalent dosages of prescriptions. That would better illicit the influence of the entire guideline program and their analysis.</li><li>5. The authors have shown that a number of patients have received repeat scripts. This should be a red flag and should illicit some type</li></ol>
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	<p>of action to avoid repeat visits. In addition, the authors should identify if Ohio has a mechanism to track if patients move from one emergency room to another emergency room. Finally, the authors also should describe the influence of the other border states, specifically Kentucky, West Virginia, and Pennsylvania.</p> <p>6. The education and understanding of the adverse consequences of opioids with the first prescription is the major requirement to reduce the opioid usage. The emergency room is one such place, even though it is not a major contributor. Major contributors are family physicians, surgeons, and dentists. The education must start in all these places, including the emergency rooms. The authors have shown that a significant proportion of patients have not received appropriate education.</p> <p>Consequently, while the manuscript is good and useful, it needs improvements. The manuscript should make appropriate recommendations for improvement in care in the future.</p>
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<b>REVIEWER</b>	Michael A. Grasso, MD, PhD, FACP University of Maryland School of Medicine, Department of Emergency Medicine, 110 S. Paca Street, 6th Floor, Suite 200, Baltimore, MD 21201, USA
<b>REVIEW RETURNED</b>	12-Dec-2017

<b>GENERAL COMMENTS</b>	<p>The authors present the results of a straight-forward survey of ED directors regarding the adoption of opioid prescribing guidelines and the perceived impact of those guidelines. The manuscript is easy to read, and the results are easy to comprehend. The survey approach was appropriate, and resulted in a reasonable 92% response rate. The results of the survey are that a majority of ED have adopted policies based on the Ohio ED Opioid Prescribing Guidelines. A secondary result, although somewhat subjective, is the perception among ED directors that this adoption has changed clinical practice. The discussion included an appropriate review of limitations, causality, and the role of ED practice on opioid misuse.</p>
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<b>REVIEWER</b>	Michael Barnett Harvard Chan School of Public Health, USA
<b>REVIEW RETURNED</b>	20-Dec-2017

<b>GENERAL COMMENTS</b>	<p>In this study, Dr. Penm and colleagues perform a straightforward descriptive analysis of a survey to Ohio hospital ED leadership with an impressive &gt;90% response rate. The study question is reasonable, though fairly narrow: to what extent have hospitals in Ohio adopted practices consistent with Ohio opioid prescribing guidelines? I think this paper provides helpful baseline information that could be helpful for other researchers and state governments looking to understand their EDs' opioid prescribing habits. The paper is fairly simple and straightforward so I don't have much to critique. Here are some things for the authors to consider though:</p> <p>1) The writing is fairly low quality and requires significant editing. The statistic in the introduction of 15,000 opioid overdose deaths is not accurate - 15,000 is the number of *prescription opioid* related overdoses in 2015, which is only about half of the total opioid overdose deaths.</p> <p>2) There is very little detail in how the survey questions were chosen or why, only one sentence in the Methods. It's also unclear how a literature search can validate the design of a survey.</p>
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	<p>3) Some of the major points the authors make don't seem to be very crucial insights for the ED setting. For example, few EDs are going to try to get a pain contract out of patients - they aren't longitudinal providers! It's not really appropriate to expect that so I don't think that is a helpful question. Also a palliative or pain consult for ED opioid users seems like a waste of hospital resources and is rarely a reasonable choice for an ED patient in my clinical experience.</p>
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**VERSION 1 – AUTHOR RESPONSE**

Reviewer(s)' Comments to Author:

Reviewer: 1

Reviewer Name: Laxmaiah Manchikanti, MD

Institution and Country: Pain Management Centers of Paducah (KY) and Marion (IL), United States

Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below

The authors of this manuscript performed a state-wide survey of emergency departments in Ohio have assessed adoption and implementation of the Ohio opioid prescribing guidelines and opioid prescribing practices. Overall, this is a well-executed manuscript; however, there continues to be some limitations that need to be addressed for the manuscript to improve the guideline utilization in Ohio. This manuscript will be useful for the entire United States, or even globally.

Thank you for consideration of our work.

The limitations are as follows:

1. The authors start with a statement that drug overdose deaths, largely by opioids, are the leading cause of unintentional death in the United States. This is accurate; however, in the beginning itself, to avoid further confusion, the authors should identify the contributions of prescription opioids, heroin, illicit fentanyl, and methadone. This will clarify the issues. As we all know, prescription opioids are not the only reason for this epidemic. As of now, it appears that heroin and illicit fentanyl are overtaking prescription opioids as the leading cause. Prescription opioids are reducing across the board both with the reduction in the number of prescriptions, as well as the prescribing of smaller dosages, leading to reduced production of opioids.

To clarify the issue and ensure the readers are aware that prescription opioids are not the only reason for the epidemic, we have added the following to the manuscript:

The number of opioid-related overdose deaths has nearly tripled from 1999-2014 and was mainly associated with prescription opioids and heroin during this time.<sup>1</sup> Opioid-related deaths have continued to rise from 2014-2015<sup>2</sup> Although prescription opioid related deaths still remain a concern, this rise was primarily driven by illicit fentanyl and heroin.<sup>2</sup> Despite reductions in opioid prescribing in some parts of the U.S, the morphine milligram equivalents (MME) dispensed per capita in 2015 remained three times as high as it was in 1999.<sup>3</sup>

2. The authors have \$10 incentive, which appears to be somewhat unusual and a rather ineffective mode of recruiting participants.

To clarify why a \$10 incentive was used, we have added:

Survey distribution followed Dillman's Tailored Design Method, a mixed-mode method including postal mail and e-mail, augmented by telephone interviews to maximize the response rate.<sup>12</sup> Dillman's Tailored Design Method is based on Social Exchange theory, which focuses on establishing trust, increasing benefits and decreasing costs, to improve response rates.<sup>12</sup> One strategy recommend by Dillman is to provide participants with a token of appreciation in advance. This token can be as small as \$2 as it not only increases the benefit, but establishes trust.<sup>12</sup> A \$10 incentive was chosen as it was the smallest amount that could be pre-loaded on a prepaid credit card.

3. It appears that there has been significant improvement; however, it is disappointing that PDMPs have not been utilized by 100% of those surveyed. The goal should be at least 99%.

We agree with the reviewer that PDMPs are a desirable part of ED practice and have acknowledged this in our discussion of the need for ongoing improvements in ED operations and practice as per point 5. .

4. The authors have not provided information in reference to morphine equivalent dosages of prescriptions. That would better illicit the influence of the entire guideline program and their analysis.

We have added into our limitations:

Furthermore, information related to the morphine milligram equivalent per prescription was not obtained, which may provide additional insight into the influence of the guidelines.

5. The authors have shown that a number of patients have received repeat scripts. This should be a red flag and should illicit some type of action to avoid repeat visits. In addition, the authors should identify if Ohio has a mechanism to track if patients move from one emergency room to another emergency room. Finally, the authors also should describe the influence of the other border states, specifically Kentucky, West Virginia, and Pennsylvania.

We have added into our discussion:

Identifying patients that are using EDs for repeat prescriptions is particularly challenging. There is currently no mechanism in Ohio for ED physicians to track patients that move from one ED to another. Although the increased use of Ohio's prescription drug monitoring program could assist with this, it is not mandatory for ED physicians in Ohio to review their records if they prescribe for fewer than seven days.<sup>19</sup> Our results highlight the variability of the program's utilization, with only 12% of respondents stating they used it for more than 95% of their patients prescribed an opioid in the last month. To further complicate the situation, these programs usually do not include information from other states. With neighboring states like West Virginia and Kentucky having the highest and 6th highest rate of opioid-related death rates in the U.S. respectively,<sup>4</sup> tracking patients that move between EDs and states is beyond the current healthcare systems capabilities.

6. The education and understanding of the adverse consequences of opioids with the first prescription is the major requirement to reduce the opioid usage. The emergency room is one such place, even though it is not a major contributor. Major contributors are family physicians, surgeons, and dentists. The education must start in all these places, including the emergency rooms. The authors have shown that a significant proportion of patients have not received appropriate education.

To highlight the variability in ED practices (including education), we have added into our discussion:

Furthermore, similar variability in ED practices were observed, including the use of Ohio's prescription drug monitoring program and education provided to patients. The largest variation in ED practices was observed for opioid prescriptions being provided to patients with chronic pain even though they had previously presented with the same problem or had received an opioid prescription from another provider in the last month. This lack of standardization in the care and information patients receive is concerning and requires additional investigation to identify their cause.

Consequently, while the manuscript is good and useful, it needs improvements. The manuscript should make appropriate recommendations for improvement in care in the future.

We have expanded our discussion of the ways in which this evaluation suggests practice is less than optimal or at least incompletely consistent with current public health recommendations in Ohio. However, we note that the primary intent of this study is to evaluate current practice after issuance of public health recommendations. Thus, formal review of available practice recommendations is outside the scope of this work, and this study provides no evidence to evaluate the effectiveness or feasibility of practice recommendations.

Reviewer: 2

Reviewer Name: Michael A. Grasso, MD, PhD, FACP Institution and Country: University of Maryland School of Medicine, Department of Emergency Medicine, 110 S. Paca Street, 6th Floor, Suite 200, Baltimore, MD 21201, USA Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below

The authors present the results of a straight-forward survey of ED directors regarding the adoption of opioid prescribing guidelines and the perceived impact of those guidelines. The manuscript is easy to read, and the results are easy to comprehend. The survey approach was appropriate, and resulted in a reasonable 92% response rate. The results of the survey are that a majority of ED have adopted policies based on the Ohio ED Opioid Prescribing Guidelines. A secondary result, although somewhat subjective, is the perception among ED directors that this adoption has changed clinical practice. The discussion included an appropriate review of limitations, causality, and the role of ED practice on opioid misuse.

Thank you for the review of our submission.

Reviewer: 3

Reviewer Name: Michael Barnett  
Institution and Country: Harvard Chan School of Public Health, USA Please state any competing interests or state 'None declared': None

In this study, Dr. Penm and colleagues perform a straightforward descriptive analysis of a survey to Ohio hospital ED leadership with an impressive >90% response rate. The study question is reasonable, though fairly narrow: to what extent have hospitals in Ohio adopted practices consistent with Ohio opioid prescribing guidelines? I think this paper provides helpful baseline information that could be helpful for other researchers and state governments looking to understand their EDs' opioid prescribing habits. The paper is fairly simple and straightforward so I don't have much to critique. Here are some things for the authors to consider though:

1) The writing is fairly low quality and requires significant editing. The statistic in the introduction of 15,000 opioid overdose deaths is not accurate - 15,000 is the number of \*prescription opioid\* related overdoses in 2015, which is only about half of the total opioid overdose deaths.

The introduction has been modified as suggested by reviewer 1. The 15,000 number referred to has been deleted. We have generally reviewed the manuscript for writing quality and clarity as requested, though reviewer 2 was complimentary in this regard.

The number of opioid-related overdose deaths has nearly tripled from 1999-2014 and was mainly associated with prescription opioids and heroin during this time.<sup>1</sup> Opioid-related deaths have continued to rise from 2014-2015<sup>2</sup> Although prescription opioid related deaths still remain a concern, this rise was primarily driven by illicit fentanyl and heroin.<sup>2</sup> Despite reductions in opioid prescribing in some parts of the U.S, the morphine milligram equivalents (MME) dispensed per capita in 2015 remained three times as high as it was in 1999.<sup>3</sup>

2) There is very little detail in how the survey questions were chosen or why, only one sentence in the Methods. It's also unclear how a literature search can validate the design of a survey.

Thank you for this comment.

We have added some additional detail into the survey design into the Methods:  
The survey instrument included primarily closed-ended questions using a Likert-scale to evaluate the implementation of the guidelines and local opioid policies. Questions were chosen to correspond with each recommendation in the guideline. Additional questions focused on the respondents' demographic details, strategies used to implement the guidelines and the perceived benefits of the guidelines.

We have also removed face validity from the literature search description. The literature search was only used to ensure content validity.

A literature review and input from ODH also ensured content validity of the survey

3) Some of the major points the authors make don't seem to be very crucial insights for the ED setting. For example, few EDs are going to try to get a pain contract out of patients - they aren't longitudinal providers! It's not really appropriate to expect that so I don't think that is a helpful question. Also a palliative or pain consult for ED opioid users seems like a waste of hospital resources and is rarely a reasonable choice for an ED patient in my clinical experience.

Although we respect and even agree with these comments, we also note that this study in no way endeavours to evaluate the quality of the Ohio guideline or generate evidence for development of new practice recommendations. Rather this was an evaluation of the implementation of the Ohio guideline as it was originally constructed. We have however amended the text to note that one possible reason for incomplete implementation could be that practitioners disagree with the guideline or elements within it. We have furthermore highlighted these specific elements as examples of areas where emergency providers might have objection.

Such prescribing variability may highlight that these specific guideline recommendations may not be practical or that respondents generally do not agree with them. A revision of these statements and guidance on which clinical scenario they apply to may ensure the guidelines support best practices.

## VERSION 2 – REVIEW

<b>REVIEWER</b>	Laxmaiah Manchikant, MD Medical Director, Pain Management Center of Paducah, Clinical Professor, Anesthesiology and Perioperative Medicine, University of Louisville, Kentucky , Professor of Anesthesiology-Research,
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	Department of Anesthesiology, School of Medicine, LSU Health Sciences Center
<b>REVIEW RETURNED</b>	10-Jan-2018

<b>GENERAL COMMENTS</b>	<p><b>COMMENTS TO AUTHORS:</b> The authors have made significant changes based on reviewer comments. However, multiple issues still remain.</p> <p>1. The authors are still confusing in some of the statements. For example, in the first paragraph, their revised sentence states that, "morphine milligram equivalence (MME) dispensed per capita in 2015 remained 3 times as high as it was in 1999." This is confusing. I believe the authors actually mean that despite overall reductions in opioid prescribing, 3 times the amount of opioids were prescribed in 2015 compared with 1999.</p> <p>However, the data shows that average daily MME per prescription was lower, at least from 2006 to 2015 from the reference the authors have quoted in the manuscript (reference 3).</p> <p>Essentially, they are converting this to per capita, which means that if in 1999 a person received 200 mg, the same person in 2015 received 600 mg. Milligram equivalence dispensed in per capita might be confusing since it essentially refers to per capita prescription opioid sales rather than opioids dispensed per person.</p> <p>2. The last sentence in the first paragraph in the Background states that it is now widely acknowledged that the rise of opioid prescribing is a contributing factor to the opioid epidemic. However, the authors should expand on it based on the latest data. Provisional data from the US Centers for Disease Control and Prevention (CDC) indicated drug overdose deaths increased again from 2015 to 2016 by more than 20% from 52,898 deaths in the year ending in January 2016 to 64,079 deaths in the year ending in January 2017. The total increase was 11,172; however, increases were greatest for overdose-related deaths to the category which included illicitly manufactured fentanyl (i.e., synthetic opioids excluding methadone), which more than doubled, thus accounting for more than 20,000 overdose deaths in 2016 vs. less than 10,000 deaths in 2015. As Dowell et al stated in their JAMA opinion piece, the difference is enough to account for nearly all the increase in drug overdose deaths from 2015 to 2016. Consequently, the tables are turning. The authors should acknowledge that instead of focusing on old data.</p> <p>The authors should also look at the admissions to drug treatment programs, which have shown significant numbers of patients with heroin, as well as fentanyl addiction. This indicates the reductions in opioid abuse disorders related to prescription opioids.</p> <p>3. In the Discussion, the authors state that there are many difficulties utilizing PDMP to obtain the data from Kentucky and West Virginia. This may not be totally accurate as there is provision to obtain PDMPs from neighboring states, or any state.</p> <p>If the above issues are revised, the article may be valuable to the readership, public in general, and policymakers.</p>
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**VERSION 2 – AUTHOR RESPONSE**

Reviewer: 1  
Reviewer Name: Laxmaiah Manchikant, MD

Institution and Country: Medical Director, Pain Management Center of Paducah, Clinical Professor, Anesthesiology and Perioperative Medicine, University of Louisville, Kentucky; Professor of Anesthesiology-Research, Department of Anesthesiology, School of Medicine, LSU Health Sciences Center Please state any competing interests or state 'None declared': none declared

Please leave your comments for the authors below COMMENTS TO AUTHORS:

The authors have made significant changes based on reviewer comments. However, multiple issues still remain.

1. The authors are still confusing in some of the statements. For example, in the first paragraph, their revised sentence states that, "morphine milligram equivalence (MME) dispensed per capita in 2015 remained 3 times as high as it was in 1999." This is confusing. I believe the authors actually mean that despite overall reductions in opioid prescribing, 3 times the amount of opioids were prescribed in 2015 compared with 1999.

However, the data shows that average daily MME per prescription was lower, at least from 2006 to 2015 from the reference the authors have quoted in the manuscript (reference 3).

Essentially, they are converting this to per capita, which means that if in 1999 a person received 200 mg, the same person in 2015 received 600 mg. Milligram equivalence dispensed in per capita might be confusing since it essentially refers to per capita prescription opioid sales rather than opioids dispensed per person.

We agree that it is confusing when going between per capita, MME, prescriptions and sales. Just for clarification, Guy and colleagues (2017, MMWR) found that in 1999 the MME per capita was 180 and in 2015 the per capita MME was 640; the former being 3 times higher.

I understand the reviewer wants us to make this article as clear as possible. We have rewritten the first paragraph in light of comment 1 and 2. The revised paragraph now states:

"Drug overdoses are the leading cause of unintentional death in the United States (U.S.), driven largely by opioids (66%), both prescription and illicit.<sup>1,2</sup> In total, 40% of opioid related deaths are due to a prescription opioid, with the remainder primarily driven by heroin and illicitly manufactured fentanyl (IMF).<sup>3</sup> Although heroin and IMF related deaths are the primary cause of opioid-related deaths in the U.S, there are significant geographic variations in opioid prescribing practices and involvement of specific opioid compounds in overdose deaths.<sup>2,4</sup> Reducing unnecessary exposure to prescription opioids may prevent the development of opioid use disorder that is later supplemented or replaced by illicit opioids.<sup>5</sup> This has led to the implementation of multiple strategies aimed at improving opioid prescribing around the U.S.<sup>2,6</sup> Such strategies appear to be improving the situations in some states, as the rate of overdose deaths involving a prescription (age-adjusted) have steadied from 2011-2015<sup>5</sup> and the annual opioid prescribing rate has decreased from 2012 to 2015.<sup>4</sup> "

2. The last sentence in the first paragraph in the Background states that it is now widely acknowledged that the rise of opioid prescribing is a contributing factor to the opioid epidemic. However, the authors should expand on it based on the latest data. Provisional data from the US Centers for Disease Control and Prevention (CDC) indicated drug overdose deaths increased again from 2015 to 2016 by more than 20% from 52,898 deaths in the year ending in January 2016 to 64,079 deaths in the year ending in January 2017. The total increase was 11,172; however, increases were greatest for overdose-related deaths to the category which included illicitly manufactured fentanyl (i.e., synthetic opioids excluding methadone), which more than doubled, thus accounting for more than 20,000 overdose deaths in 2016 vs. less than 10,000 deaths in 2015. As Dowell et al stated in their JAMA opinion piece, the difference is enough to account for nearly all the increase in drug overdose deaths from 2015 to 2016. Consequently, the tables are turning. The authors should acknowledge that instead of focusing on old data.

Guy et al. (2017) found significant geographic variations across the U.S. in opioid prescribing patterns. Increasingly, overdose deaths are in fact poly-drug deaths including prescription drugs. We have updated the first paragraph to incorporate this new data. Please see our response in comment 1.

The authors should also look at the admissions to drug treatment programs, which have shown significant numbers of patients with heroin, as well as fentanyl addiction. This indicates the reductions in opioid abuse disorders related to prescription opioids.

Although we agree with this statement, we wanted the focus of our introduction to be on prescription opioids. Further, it is estimated that only 10% of patients with substance use disorders receive care from speciality addiction treatment programs. As such, we acknowledge this issue by stating that:

“Although heroin and IMF related deaths are the primary cause of opioid-related deaths in the U.S, there are significant geographic variations in opioid prescribing practices and involvement of specific opioid compounds in overdose deaths”

3. In the Discussion, the authors state that there are many difficulties utilizing PDMP to obtain the data from Kentucky and West Virginia. This may not be totally accurate as there is provision to obtain PDMPs from neighboring states, or any state.

Ohio’s PDMP uses PMP InterConnect which provides access to more than 40 states’ PDMPs. We have removed the above sentence and stated that:

“Without mandatory use of prescription drug monitoring programs in EDs, which may be administratively cumbersome, tracking patients that move between EDs is beyond the current healthcare systems capabilities.”

If the above issues are revised, the article may be valuable to the readership, public in general, and policymakers.

**VERSION 3 – REVIEW**

<b>REVIEWER</b>	Laxmaiah Manchikant, MD Medical Director, Pain Management Center of Paducah, Clinical Professor, Anesthesiology and Perioperative Medicine, University of Louisville, Kentucky, Professor of Anesthesiology-Research, Department of Anesthesiology, School of Medicine, LSU Health Sciences Center, USA
<b>REVIEW RETURNED</b>	21-Mar-2018
<b>GENERAL COMMENTS</b>	The authors have made appropriate changes. Now the manuscript is easy to follow with appropriate information. I would like to thank the authors for going the extra mile in preparing this manuscript.