HHS Public Access

Author manuscript

Pain. Author manuscript; available in PMC 2019 April 01.

Published in final edited form as:

Pain. 2018 April ; 159(4): 805–806. doi:10.1097/j.pain.0000000000001156.

Letter to the Editor

Peter Geissert, MPH,

Systems Science, Portland State University, Portland, OR

Sara Hallvik, MPH,

HealthInsight, Portland, OR

Nicole O'Kane, PharmD,

HealthInsight, Portland, OR

Joshua Van Otterloo, MSPH,

Oregon Health Authority, Portland, OR

Lindsey Alley, MS,

HealthInsight, Portland, OR

Jody Carson, RN, MSW,

HealthInsight, Portland, OR

Gillian Leichtling, BA,

HealthInsight, Portland, OR

Christi Hildebran, LMSW,

HealthInsight, Portland, OR

Wayne Wakeland, PhD, and

Systems Science, Portland State University, Portland, OR

Richard A. Deyo, MD, MPH

Family Medicine, Oregon Health & Science University

To the Editor

We thank Dr. Hincapié-Castillo and colleagues for raising several important issues and for prompting further analysis of our data [1].

Although many early prescription drug monitoring programs (PDMPS) were designed to aid law enforcement and regulatory agencies, the orientation varies from state to state. Oregon's PDMP was designed primarily to assist clinicians with decision-making and with public health goals in mind. Access by law enforcement agencies is narrowly limited (requiring a court order). Many state systems provide proactive alerts to clinicians regarding patients with potentially risky or otherwise alarming prescription patterns, with the goal of preventing opioid harms.

Hincapié-Castillo and colleagues are correct in pointing out that, as discussed in the limitations, our predictive model was based on cross-sectional data. For mortality, prescribing data obviously preceded the outcome event. Though it may be tempting to imagine that opioid prescribing stops or is dramatically decreased after hospitalization for an overdose, recent studies document that continued prescribing is the norm [2]. The desirability of using only prescription data *preceding* hospitalization prompted us to conduct a new analysis.

For this purpose, we considered only prescribing data in the 12-month period from October 2012 through September 2013, and opioid overdose mortality or hospitalization occurring in the following 12 month period, from October 2013 through September 2014 (the end of the available dataset). This arrangement emulates a clinician's situation if he or she examines the past year of PDMP data and asks if it predicts an overdose event in the coming year.

Table 1 summarizes the odds ratios for overdose events (death or hospitalization) that emerged from the new model, considering only the same independent variables in our published model 2, and also considering a more complete range. In the latter analysis, the adjusted odds ratio for high-dose opioid prescribing (≥ 90 morphine equivalents/day) increased in both magnitude and statistical significance, though it was eliminated from our earlier model 2. In all the models, odds ratios are strikingly similar, and remain highly statistically significant. As in our original publication, increasing age and use of long-acting opioids were the strongest predictors of opioid-related overdose events. These may be more important to clinicians than to law-enforcement officers. Prediction in the model retaining the high-dose indicator was also very similar to that of the original publication. Using a cutoff of .002, the positive predictive value of the model was .006, suggesting that for every 1000 patients identified as high risk by the model only 6 of them would experience an overdose-related hospitalization or death in the follow-up year. The area under the receiver operating characteristic curve was 0.81, compared with 0.82 in the original publication. Thus, all of our conclusions remain unchanged, and quantitative results are very similar.

We agree that the low positive predictive value severely limits the model's clinical utility and note that the positive predictive value of the model is also a function of the low prior probability of the outcome. In our article we urged caution in the use of such models. We also agree that a clinically meaningful model will likely require integrating other health information to improve prediction. As we noted, "Improvement of the predictive value of such models may require information from sources outside most PDMPs, such as a history of hospitalization for opioid related complications, or other clinical data from electronic health records."

We also agree with Hincapié-Castillo et al regarding the notion that overdoses are not the only important outcomes to consider in designing clinical decision aids. As we noted, increased risk of addiction, misuse, minor overdose, or diversion of medications are other important outcomes, and may be predicted by similar characteristics. Though addiction medicine and medication assisted treatment for opioid use disorders (OUD) play an important role in preventing opioid overdoses, it is important to acknowledge the risk of opioid overdose among patients with no history of OUD. The study findings, particularly the

effects of advancing age and long acting opioids, have clinical implications for routine opioid prescribing and not just for identifying OUD.

We hope these additional analyses and observations will be useful to readers.

Acknowledgments

The authors have no conflicts of interest to disclose. The project was funded through a supplement to National Institute on Drug Abuse Grant # 3R01DA031208-03S1.

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2. Larochelle MR, Liebschutz JM, Zhang F, Ross-Degnan D, Wharam JF. Opioid prescribing after nonfatal overdose and association with repeated overdose. A cohort study. *Ann Intern Med*. 2016; 164:1–9. [PubMed: 26720742]

Table 1

Logistic regression results from the original published article and two models using 12 months of prescribing data to predict opioid-related overdose hospitalization or death in the subsequent 12 months.

	Published aOR (model 2)	aOR in new analysis	aOR including high dose indicator
Age 15–34 y	reference	reference	reference
Age 35–44 y	1.47 **	1.52 **	1.46 **
Age 45–54 y	1.95 ***	2.27 ***	2.14 ***
Age 55–64 y	2.82 ***	3.34 ***	3.12 ***
Age 65–74 y	3.68 ***	4.11 ***	4.10 ***
Age 75+ y	4.99 ***	4.24 ***	4.49 ***
No. of prescribers	1.15 ***	1.14 ***	1.15 ***
No. of pharmacies	1.11 ***	1.11 ***	1.09 ***
Any prescription of ER/LA opioid	4.41 ***	4.04 ***	3.19 ***
Any prescription of benzodiazepine/sedative	2.50 ***	2.06 ***	2.29 ***
Any prescription of carisoprodol	1.63 **	1.79 ***	2.13 **
MMEDD 90 mg	NA	NA	2.37 ***

Note.

**
p<.01,

p<.001;

aOR = adjusted odds ratio; ER/LA = extended release/long acting; MMEDD = morphine milligrams equivalent daily dose; NA = not present in the model as estimated.