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Clinical utility and perils of prescription drug monitoring program-based alert systems

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Originally intended to mitigate doctor shopping and diversion of controlled substances in the United States, prescription drug monitoring programs (PDMPs) were not conceived to offer prescribers clinical guidance for treatment decisions. In fact, PDMPs were first introduced as tools to aid law enforcement and regulatory agencies in their drug-related activities.[1]

When granted access, clinicians utilizing these systems are merely presented with the patient's dispensing history for some or all controlled substances obtained from a pharmacy. This information is intended to aid in risk stratification prior to prescribing these medications to deter or prevent occurrence of drug abuse. The clinical utility of PDMPs in predicting patient outcomes has just recently been explored and, given the wide variability in registry design and infrastructure, there is cautious optimism regarding their benefit and performance. Geissert and colleagues constructed a novel prediction model including risk factors ascertained exclusively from an operating PDMP that pose some problematic design features and highlight some perils of such alert systems.[3]

First, the model appears to be built based on a cross-sectional design. Temporality is non-negotiable for predictive modeling and therefore, the outcome must be ascertained after risk factors are computed into the model. The authors do mention that follow-up data could be as small as one week if a patient died from an overdose early January. We raise the possibility that follow-up data could also be twelve months long even if the patient was hospitalized for an overdose in January. We believe the approach used is not only impractical but also potentially biased because utilization data after an overdose may look different from utilization data before an overdose, as do data ascertained during a one-week versus 12-month baseline period. The authors might have been able to combine their 2012/2013 PDMP data and predict outcomes on a rolling basis over a pre-specified follow-up period allowing

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specified proximity between risk factors and overdose. In this design, validation could have been performed through a split-half sample or bootstrapping.

Furthermore, the proposed model has an extremely low positive predictive value (PPV). Even at the highest cutoff of 0.006 reported in Table 2, which captured roughly the upper decile of patients in the registry and only about one third of overdose cases, PPV is only 1.3%, resulting in 98/100 false positives. This is not only impractical for clinicians to act on, it also raises concerns about unintended consequences of mistakenly classifying patients. The “chilling effect” of the opioid abuse epidemic in the United States is steering away some prescribers from offering opioids as treatment option to their patients and an alert system such as the one proposed might compound this problem.[4] Rather than trying to optimize prediction with variables the authors found in the literature, it would be beneficial to explore why the model was not able to capture the majority of cases at this threshold. A clinically meaningful model will likely require the integration of other relevant health information to improve prediction.

Of note, the authors present a “parsimonious” model, which selected variables based on ease of measurement. Retention of variables after employment of formal statistical elimination techniques would assure readers that parsimony has indeed been achieved and follow best practices outlined in the TRIPOD statement for good quality predictive models.[2]

Prediction models can offer significant utility if they achieve a clinically acceptable balance between false positive and false negative cases and predict important clinical endpoints that warrant preventive intervention. Overdoses might not be the end all be all for clinical decision support addressing opioid use. While overdoses are rare and indeed undesirable, there might be other outcomes that could be predicted to avoid the manifestation of opioid use disorder (OUD) in the first place. Prevention of an imminent overdose appears to belong in the hands of addiction specialists and addressed by medication assisted OUD treatment, where PDMP information may need a quite different interpretation than in the routine prescribing of opioids for pain.

Measurement issues will continue to remain an obstacle for researchers in the field, and future efforts should be focused on identifying key markers in patients’ treatment trajectories. Such trajectories may greatly vary by opioid indication, patient comorbidities, age, life experiences or other underexplored factors, emphasizing the need for careful construction of prediction models to mitigate erroneous flagging of patients who are not at risk for OUD and deserve adequate pain management, while missing those with OUD issues.

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