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Title	The impact of emergency department opioid prescribing guidelines on emergency physician behaviour and incidence of overdose in the Saskatoon Health Region: a retrospective pre/post implementation analysis
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Reviewer 1	Stephen DiTommaso
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General comments (author response in bold)	This study is in fact reports two interventions. Firstly, was the behaviour of ER physicians modified after an educational intervention ? (Yes). Secondly, was there a measurable clinical impact following the change in prescribing behaviour of the ER physicians ? (Very difficult to answer). Firstly, I applaud the decreased rate of opioid prescribing in the ER at the Saskatoon Health Region, regardless of impact on the overdose rates. **Thank you for the feedback.** Secondly, I am not discouraged by the negative finding of no change in overdose rates following the educational intervention among the ER physicians. My own analysis of this study agrees closely with the limitations noted by the authors themselves. It seems to me that a determination of the source of prescribed opioids in this catchment area would have been very helpful. I suspect that the ER is the source of only a small fraction of total opioids circulating in the catchment area. Other sources are likely to be specialists (surgeons, pain specialists, and others), family physicians and other primary health care professionals with the power to prescribe opioids, prescribers form nearby cities, as well as illicit suppliers. If the 32 physicians studied by the authors generated only a small percentage of the total quantity of available opioids in the community, then it is unsurprising that the impact of a 31 % decrease of this small fraction of the total amount would not have been measurable in this study. **Thank you, we agree with the above statement and have identified such within our discussion. The ED is unlikely the source of opioids used in overdose and many other sources exist** This study suffers from a lack of a control group, given that it is observational in nature. Could this be partially compensated by comparing overdose rates in southern Saskatchewan with overdose rates in other regions ? For example, if a contemporaneous increase in opioid overdoses had occurred in Manitoba and Alberta, but not in Saskatchewan, this would suggest (but not prove) that the Saskatchewan intervention might have had a clinical impact. **This would be difficult to answer. As people overdosing on opioids varies greatly by region, it would be difficult to use a separate region of the country as a control group given the inherent differences in access to both prescription and illicit opioids. We need only look at the Pacific coastal regions to see higher rates of opioid overdose due to international importation of opioids compared to centrally located provinces. That being said, opioid overdoses in Alberta also outpace Saskatchewan. We feel that Figure 2 demonstrating a general trend in our local opioid overdoses is sufficient to suggest no effect, though we recognize could have theoretically (although unlikely) prevented an unanticipated spike in overdose rates.**

	Also, the frequency of naloxone dispensing over time is not necessarily constant. During the time of this study, so naloxone administration may have become more or less liberal, and therefore is not an entirely reliable proxy for measuring the frequency of overdoses. We have all seen a huge increase of naloxone supply in the community during a similar time period, as pharmacists and physicians encourage drug users to keep naloxone kits on hand. (Even some of my palliative care patients have been given naloxone kits by their pharmacists in the past few years !) **Thank you for the comments. In our health region, naloxone kits were not available out of the ED during this time period and would not have been implicated in any changes of rates. That being said, we recognize that pharmacy restocking of the ED may have been unpredictable and therefore affected the final numbers. This has been added as a limitation. Page 11 of MS Word document.** I add that the population of drug users in a community is heterogenous, so reducing opioid prescribing in the ER will impact different drug users in different ways. **We agree. The population that has adverse effects from opioids includes regular prescription drug use, prescription drug abuse, and illicit drug use.** There are regular users of narcotics, who often use stable quantities on a daily basis. They will simply change the source of their supply when one decreases or disappears. A decrease in the supply of opioids prescribed in the ER will have little effect of these users, as they will switch to other suppliers. In fact, they might increase their risk level as they switch from pharmaceutical grade narcotics to illicit narcotics with a high rate of contamination (fentanyl, etc). **This is frequently a concern surrounding ED opioid prescribing to regular users. Figure 2 at least demonstrates that there wasn't a significant jump in events following the implementation.** There are drug users who are dilettantes or opportunists For example, new or irregular users, for example teenagers with access to the prescribed medications of family members are at very high risk of overdose. Diminishing the quantities of opioids prescribed in an ER might conceivably reduce overdose rates in this sub-population. On the other hand, if the same occasional users resort to illicit drugs, then this is even worse. It is often asserted that receiving a prescription for an opioid increases the risk of drug dependence in a proportionate manner : the greater the number of doses prescribed to a patient, the higher the risk of him or her becoming an opioid abuser. However, this phenomenon takes time. I am not sure that the reduction of prescribed opioids found in this study would have much of an impact on overdoses over such a short time period (one year). **We agree, thank you. The long term impact of reducing opioid prescriptions out of the emergency department will take years to declare themselves. Alternatively, there are also concerns that it will lead to sub-optimal pain management and long term psychological harm.** The previous points only underly the complex nature of drug use and overdose. I therefore believe that this study ahs merit and should be published despite the "negative" finding of no impact on community overdoses.

	Replication I don't believe that the precise nature of the educational intervention is really needed in this report. Physicians are notorious for resisting educational interventions, and changing physician behaviour is a vast subject. The ER physicians in this study did respond with significant behaviour change. This doesn't mean that another group of physicians will respond to the same intervention in a similar manner. Nor does it mean that the ER physicians in this study will maintain their improved prescribing habits over time. Other critics might expect a more complete description of the educational intervention, but I do not. Clinical comments What is the "correct" amount of opioid analgesics which should be prescribed in an ER ? Reducing quantities is an attractive concept, but opioids remain a useful class of medications. It is hard to say whether the ER physicians in this study still have room for improvement, or whether further reductions in opioid prescribing could in fact be harmful to patients in need of pain relief. **Agreed. This is often a difficult part of these studies as there is no definition of the "right" amount of opioids that a given patient needs, and over what period of time they need it. It is impossible to deem prescriptions as "appropriate" or "inappropriate", and there is always a concern that further reductions in opioid prescribing will adversely affect the "appropriate" prescriptions.** I don't know why the authors referred to the SHR Public Health Observatory (PHO) Sentinel Opioid Overdose Surveillance Group, which only began collecting data prospectively after termination of this study. **Within the methods section, we clarify that while the prospective collection only began after the study, a retrospective analysis of ED data was collected back to Jan 2016. Page 7 of MS Word document.** It would have been interesting to evaluate if the ER physicians in this study compensated the reduced opioid prescribing with an increase if the prescribing of other analgesics. Although I agree that opioids are the most dangerous analgesics, there is evidence that alternatives such as gabapentin and pregabalin can also lead to problematic overuse and serious morbidities in the community. I would be disappointed if diminished opioid prescribing had led to increased use of other dangerous medications. **Thank you for the feedback. I agree that this is a concern. We initially pulled data on gabapentin and pregabalin, however prescription numbers were so small (0-2 prescriptions per physician) in both the pre and post intervals that it was impossible to draw any meaningful conclusions from the information. In our experience ED physicians generally avoid prescribing neuropathic medications.** Conclusions 1) I am concerned that readers will misinterpret this study, and conclude that reducing opioid prescribing is useless. A greater emphasis should be made on the

	importance of continuing a restrictive opioid prescribing policy. **We agree it would be concerning if people took this intervention as useless. We worked within our interpretation and conclusion sections to emphasize the reduction in opioids prescribed. Additionally, we have emphasized that a short-term impact on overdoses was not seen, though long term effects may still occur. Page 9-10 of MS Word document.** 2) I am concerned that non-ER physicians will not read this study. In fact, all clinicians should be aware of the impressive reductions in opioid prescribing that this group of ER physicians achieved. **Thank you! We agree that all physicians should look at the effect of a department policy and consider implementing it within their own clinics and departments. This could lead to further research on the implications and effect of restrictive opioid prescribing on both addictions, but also chronic pain populations.** 3) Although I elaborated on the possible reasons that ER opioid prescribing had little impact on community overdose rates, the authors should not feel compelled to expand on this discussion in their paper. **We appreciate the insight provided by Dr. DiTommaso on the complicated nature of opioid misuse and community overdose rates, and how a reduction of opioids from a single source is unlikely to have an immediate impact. Thank you.**
Reviewer 2	Maryna Yaskina
Institution	Women and Children's Health Research Institute, University of Alberta, Edmonton, Alta.
General comments (author response in bold)	I think this is a carefully carried study and very well written paper, such a pleasure to read. It is useful to see the detailed description of data collection and analysis. I have 3 very minor comments: 1. In the analysis you have included the data from 32 ED physician prescribers since they held positions in ED at least from November 1, 2015 to April 30, 2017. It will be useful to see how many physicians were excluded from the analysis in each time period. **Thank you for the feedback, we have included this within the "participants" section. As noted in the manuscript now, 34 physicians worked in the region across the time period, with 2 physicians being excluded for not working in both the pre and post periods. Page 5 of MS Word document.** 2. Since the study examines the short-term effect of the guideline change, I would stress it in the sentence on page 14 last paragraph. I would change "Finally, our study failed to demonstrate meaningful impact on reducing opioid-related overdoses in the community" to "Finally, our study failed to demonstrate meaningful short-term impact on reducing opioid-related overdoses in the community". **Thank you. We have adjusted the interpretation to emphasize the short-term follow up done within this study. Page 10-11 of MS Word document.** 3. Figures and tables are not displayed properly, I am not sure whose fault is it. **I believe there were issues (mainly with figure 2) during the upload process. We have worked to rectify this problem.**