Article details: 2018-0084	
Title	**Opioid-related harms and socioeconomic inequalities in Ontario: A descriptive study**
Authors	Zoe F. Cairncross MPH, Jeremy Herring MSc, Trevor van Ingen MPH, Brendan T. Smith PhD, Pamela Leece MD MSc, Brian Schwartz MD MScCH, Karin Hohenadel MSc
Reviewer 1	Dr. Roy Robertson
Institution	University of Edinburgh School of Molecular Genetic and Population Health Sciences, Usher Institute
General comments (author response in bold)	1. This is an important, and topical, area to research as headlines in the USA have reported the "epidemic" of drug deaths due to opiate prescribing. Presumably this paper reports a similar finding although one limitation, which the authors acknowledge, is the difficulty in separating illegal drugs from those prescribed. **We thank the reviewer for these suggestions and hope we have addressed them satisfactorily. We were indeed unable to capture whether the drugs were obtained through prescription or illegally, which would be of great interest to know. Unfortunately, the data that we used does not allow us to differentiate between these variables.** 2. The opioid related harms selected for the data analysis are an interesting selection of harms, presumably, because admin data was available for these indicators. Six indicators of opioid-related harms were evaluated in this study, neonatal abstinence syndrome, opioid poisonings as measured by emergency room visits, hospitalizations, and deaths and non-poisoning opioid-related events, measured by ED visits and hospitalizations. These harms are available from administrative sources and are important ones but, inevitably, others, blood borne virus transmission, septic sequaelae and violence and trauma might have also been interesting. It would be useful to reference additional harms that may be accruing to these cases but are not reported on here. **We have added in our limitations a note that our indicators do not represent a comprehensive list of all opioid-related harms, rather only those that we could capture with the data available to us. We hope that future analyses of opioid-related harms will continue to investigate the broad range of harms associated with opioid use, beyond those traditionally mentioned in research and the media.** 3. In many ways it is not surprising that the primary outcome (association with socioeconomic deprivation) is found. This has been reported extensively over many years. It is, of course, interesting that rates of harms are increasing over the time period studied although this is, again, reported elsewhere. **We would agree that this is not a novel phenomenon and have updated our introductions and implications to better reflect what we are adding to the literature – primarily, trends in the use of less commonly reported indicators (NAS, non-poisoning events) and how they relate with neighborhood SES.** 4. Three things happening in Ontario, increasing harms over time, probably related to increasing prescribing, and a suggestion that there is a shift to less deprived population. In the introduction the plan is to test the shift in morbidity and mortality from poorer to more affluent sectors, but this is not what is reported in the results as far as I can see. No evidence is shown that there has been a shift over time. It may be worth explaining that that wasn't possible or that it wasn't found, therefore not reported. **Though an analysis of trends in SES over time would be interesting, we did not have the data to complete such an analysis and did not want to apply 2015 tax data (that was used**

	to create our income quintiles) to opioid-related harms in 2003. We made substantial revisions to our introduction to better reflect our objectives for the study, and how we completed our analysis. We believe that our use of a cross-sectional analysis is now much clearer to the reader. 5. The authors speculate on the cause of the drop in ED attendances in 2011. Why would the interventions have an effect in 2011 and this not be sustained, did tamper proof oxycodone bottles stop and did methadone prescribing go down? Others have speculated about the variability in heroin purity over time. **This is likely the result of many coinciding changes in prescription drug policy and illegal drug availability, so it is difficult to know exactly what caused these shifts to occur. One hypothesis is as follows: if an individual was experiencing withdrawal or opioid use disorder, they may have had some access to oxycodone through ER at that time. Poisonings may not have increased then because of the availability of pharmaceutical opioids in the community. However, people may have shifted away from going to ER because access to prescription opioids was becoming restricted. Deaths and poisoning events are now increasing because of the toxic supply of non-prescription opioids in the community such as fentanyl or hydromorphone.** 6. The observation that lives and harms could be saved and diverted if socioeconomic gradients were decreased is intuitive but in current political climates is unlikely to happen but should be noted for political observation (see reference). The findings in the attached pre-publication paper infer directly that political and policy changes are connected to increasing harms. It might be interesting to add this to the list of speculative causal factors. **Given the cross-sectional nature of our study, it is difficult to make these speculations. We would hope that in future analyses, long-term trends in the relationship between income and opioid-related harms could be investigated to provide evidence for this hypothesis.**
Reviewer 2	REVIEW withheld
Institution	
General comments (author response in bold)	
Reviewer 3	REVIEW withheld
Institution	
General comments (author response in bold)	