

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Awareness, Predictors, and Outcomes of Drug Alerts Among People Who Access Harm Reduction Services in British Columbia, Canada: Findings from a 2021 Cross-Sectional Survey
AUTHORS	Daowd, Kerolos; Ferguson, Max; Liu, Lisa; Loyal, Jackson; Lock, Kurt; Graham, Brittany; Lamb, Jessica; McDougall, Jenny; Buxton, Jane

VERSION 1 – REVIEW

REVIEWER	Purvez, Akhtar Pain & Spine Center of Charlottesville, Interventional Pain Medicine
REVIEW RETURNED	20-Jan-2023

GENERAL COMMENTS	It is a well-designed, well-implemented, and timely study. The conclusions are significant and apply to many other geographical areas
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REVIEWER	vanDraanen, Jenna. University of Washington
REVIEW RETURNED	21-Feb-2023

GENERAL COMMENTS	<p>This study analyzed data from the 2021 BC Harm Reduction Client Survey (HRCS), and examined the characteristics of who reported seeing/hearing drug alerts, where they saw/heard the alerts and if they reported safer use after. Drug alerts are a novel topic and the paper has some interesting findings. However, some revisions could help to enhance the value of this paper.</p> <p>Introduction</p> <ul style="list-style-type: none">- The substantive literature most closely related to the article isn't brought up until the 4th paragraph, the first three can be condensed.- The information presented on drug alerts in the introduction invokes some further questions: How meaningful are drug alerts if there are 160 each year in B.C.? How much do people who use drugs daily change their behavior if they receive alerts every few days? How do people value and use such alerts in a crisis where there is known ongoing high rates of overdose deaths and high rates of contamination of the supply? The implications of these contextual realities should be grappled with in a much more meaningful way in the discussion (and perhaps introduction). <p>Methods</p> <ul style="list-style-type: none">- Could participants have participated more than once, at different sites or even the same site at different times? If so, this should be explicitly acknowledged and added to the limitations.
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	<p>- The question, "Do you take any steps to be safer (get drugs checked/tested, use overdose prevention sites, use with a buddy etc.) when you see an alert about drugs you may use?" seems leading and may bias responses in the positive direction. A more useful question may have been about whether seeing an alert changes behavior and if so, how. This should be addressed in limitations. This question also seems like an important preliminary step in assessing the real-world value of drug alerts though, and may warrant more inclusion in the discussion.</p> <p>Results</p> <p>- I think more attention should be given to the significance of the variables as a whole (not just the significance level of individual response options within the categorical variable). You discuss how frequency of picking up supplies is associated with drug alerts (e.g., "Those who attended more frequently were less likely to report seeing/hearing a drug alert") but seems unsubstantiated without a statistical test, and potentially is overstated given the other p-values in this variable. Just because one response option within the variable is significant doesn't mean that whole variable is. Those p-values only tell you whether each level's mean is significantly different from the reference level's mean. Therefore, they only tell you about the pairwise differences between the levels. To test whether the categorical predictor, as a whole, is significant is equivalent to testing whether there is any heterogeneity in the means of the levels of the predictor. Overall, I am not sure this variable deserves the attention it is given in your paper. Is there a post-estimation test you could conduct to confirm the categorical predictor's significance and adjust your presentation of this finding accordingly?</p> <p>- On the other hand, witnessing an overdose is strongly associated with knowledge of an alert and you may consider giving more weight to this finding in the paper.</p> <p>Discussion</p> <p>- Paragraph 2 of the discussion largely restates the results, and the discussion could benefit from being reorganized to group similar topics together, reduce restating results, and increase the interpretive value of this section. Currently it reads as a cursory explanation of the findings without much content in the way of program/policy implications or future directions. Given space limitations, to include this information, you may need to edit for conciseness throughout the manuscript (which I believe is very possible).</p> <p>- "This may be due to Island Health alerts being more targeted and informed by Vancouver Island Drug Checking (12)." What does this mean? Are you implying communication efforts are greater in this region?</p> <p>- Please explain change blindness</p> <p>- I think the variables that were not statistically significant are among the most interesting, many of the sociodemographic factors that often intersect with health education are not associated with knowledge of alerts in this study, I think this warrants further thought and discussion</p> <p>Conclusions</p> <p>- "Harm reduction is a non-judgemental approach which provides PWUD with resources and support services to provide them with autonomy to make informed decisions about their substance use." It is strange to introduce a definition in the conclusion and this sentence seems unnecessary, consider removing or revising?</p>
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	<p>Minor items:</p> <ul style="list-style-type: none"> - Some phrasing throughout the paper is awkward, you may consider revising, for example: <ul style="list-style-type: none"> o on page 16 “an important consideration” is used twice in the same paragraph o “Although gender was not statistically significant in the bivariable regression, it was included in the model because of the known effects on health outcomes” is worded in a strange way, perhaps you mean because of known gender differences in health outcomes? o “About a third of respondents were ≥50 years old (33.0%) and participants from small urban centers accounted for 29.5%, from medium urban centers for 36.1%, and from large urban centers for 34.4%.” is awkwardly worded, can you rephrase? - “This is elaborated on in the discussion.” Does not need to be stated in the results, it is implied.
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Comment #1: It is a well-designed, well-implemented, and timely study. The conclusions are significant and apply to many other geographical areas.

Many thanks for the positive input

Reviewer: 2

Comment #2: This study analyzed data from the 2021 BC Harm Reduction Client Survey (HRCS), and examined the characteristics of who reported seeing/hearing drug alerts, where they saw/heard the alerts and if they reported safer use after. Drug alerts are a novel topic and the paper has some interesting findings. However, some revisions could help to enhance the value of this paper.

Many thanks for the positive input and pleased the reviewer felt our findings were interesting. Below we have numbered and responded to the reviewer’s comments.

Introduction

Comment #3: The substantive literature most closely related to the article isn’t brought up until the 4th paragraph, the first three can be condensed.

Thank you for this input. The authors have removed text from the first three paragraphs (>60 words) but feel the Canadian/BC context is important for readers from other countries who may be unaware of the changes in toxic drug supply and provides relevance for the drug alerts.

Comment #4: The information presented on drug alerts in the introduction invokes some further questions: How meaningful are drug alerts if there are 160 each year in B.C.? How much do people who use drugs daily change their behavior if they receive alerts every few days? How do people value and use such alerts in a crisis where there is known ongoing high rates of overdose deaths and high rates of contamination of the supply? The implications of these contextual realities should be grappled with in a much more meaningful way in the discussion (and perhaps introduction).

Thank you for this feedback. The authors agree these are very important points some of which would be best explored by qualitative enquiry. The aim of our study was to determine the characteristics of who saw/heard drug alerts and people’s response to the alerts i.e. changing substance use practices/safer use. We identified and discussed that the commonest

source of alert information is hearing from friends/peer networks and thus the importance of peers having accurate information to disseminate.

We have added a couple of sentences in response to the reviewer's comments to provide additional context and clarification in the discussion highlighted in yellow below. This is an important consideration when disseminating drug alerts to ensure that individuals receive the message in a timely and accessible manner. It also highlights the need for clear and correct information to be made available to ensure messaging by word of mouth is accurate.

We have also added the sentence "The implications of our findings and contextual realities should be further explored using qualitative methods."

In response to the reviewers concerns about the number of alerts (160/year) we have explained that many alerts are disseminated to a specific geographic area not to the province as a whole. In 2020, there were 160 drug alerts issued in B.C., a few alerts were province wide but most were disseminated to a specific region or town, with more than half implicating fentanyl as a concern (10).

Methods

Comment #5: Could participants have participated more than once, at different sites or even the same site at different times? If so, this should be explicitly acknowledged and added to the limitations.

Thank you for this question. The survey informs potential participants that they may only respond to the survey once. Most sites complete data collection during a period of a few weeks so those enrolling participants and those participating are likely to remember if they previously answered the survey. With only 17 sites participating across the vast geography of BC, most PWUD would attend only one of these sites. To clarify this we added a statement in data source "participants are informed that they may only complete the survey once."

Comment #6: The question, "Do you take any steps to be safer (get drugs checked/tested, use overdose prevention sites, use with a buddy etc.) when you see an alert about drugs you may use?" seems leading and may bias responses in the positive direction. A more useful question may have been about whether seeing an alert changes behavior and if so, how. This should be addressed in limitations. This question also seems like an important preliminary step in assessing the real-world value of drug alerts though, and may warrant more inclusion in the discussion.

The authors agree the question may be seen as leading. We wanted to ensure this was answered in a way we could quantitatively analyse with a simple yes/no response. Open ended questions or 'no response' to a list of responses may miss those who do not answer but do take measures to be safer. About a third (32.6%) reported not taking measures to be safer. Assistance to answer the survey was often provided by peers therefore we hope this would minimise social desirability bias. We have added mention of social desirability bias in the limitations/discussion: "The survey also relied on individuals' reporting and recollection of their behaviours which introduces recall bias and there is potential for social desirability for example when asked if they had seen an alert did they take steps to be safer."

Results

Comment #7: I think more attention should be given to the significance of the variables as a whole (not just the significance level of individual response options within the categorical variable). You discuss how frequency of picking up supplies is associated with drug alerts (e.g., "Those who attended more frequently were less likely to report seeing/hearing a drug alert") but seems unsubstantiated without a statistical test, and potentially is overstated given the other p-values in this variable. Just because one response option within the variable is significant doesn't mean that whole variable is. Those p-values only tell you whether each level's mean is significantly different from the

reference level's mean. Therefore, they only tell you about the pairwise differences between the levels. To test whether the categorical predictor, as a whole, is significant is equivalent to testing whether there is any heterogeneity in the means of the levels of the predictor. Overall, I am not sure this variable deserves the attention it is given in your paper. Is there a post-estimation test you could conduct to confirm the categorical predictor's significance and adjust your presentation of this finding accordingly?

Thank you, we appreciate the comment. We have revised the statement in the result section

Interestingly, the adjusted odds of participants who picked up harm reduction supplies more frequently (every day or a few times per week) seeing/hearing a drug alert was not significantly different from those who had not picked up supplies in the past 6 months.

We have removed the discussion about change blindness but added further text about alert fatigue and desensitization which we feel may be more relevant to the readers.

Although posted drugs alerts are usually removed after two weeks, a person who attends the harm reduction supply site frequently will have been exposed to the same alerts on multiple occasions. Therefore there may be 'alert fatigue', a phenomenon described in healthcare when frequent alerts may desensitize people, and as a result they may ignore or fail to respond appropriately to such warnings (28). Alert fatigue has also been reported in the context of drug alerts (29); therefore ways of minimizing alert fatigue should be further explored.

Comment #8: On the other hand, witnessing an overdose is strongly associated with knowledge of an alert and you may consider giving more weight to this finding in the paper.

We thank the reviewer for this comment. We have added more detail and reference regarding witnessing an overdose.

Individuals who witnessed an opioid-related overdose in the past 6 months had more than two and a half times the odds of reporting seeing/hearing a drug alert compared to participants who did not witness an opioid-related overdose. Those who witnessed an overdose have previously been found to change harm reduction behaviours; in a cohort study in B.C., witnessing an overdose was found to be positively associated with using drug checking services (31). Therefore those who witness an overdose may be more sensitized to information surrounding drug alerts; however, due to the cross-sectional nature of our study, we are unable to determine causality.

We found experiencing an overdose was not associated with seeing/hearing a drug alert and added some text into the discussion

In contrast, we found no association with experiencing an overdose in the past 6 months and seeing/hearing a drug alert. This is consistent with previous studies which have identified that people often underestimate their own risk of an overdose. For example, despite a high level of fentanyl risk knowledge most did not translate this knowledge into a personal risk of having an overdose (32) and people who used opioids and injected more frequently and those who were older were less likely to perceive themselves as being at risk of an overdose (33).

Discussion

Comment #9: Paragraph 2 of the discussion largely restates the results, and the discussion could benefit from being reorganized to group similar topics together, reduce restating results, and increase the interpretive value of this section. Currently it reads as a cursory explanation of the findings without much content in the way of program/policy implications or future directions. Given space limitations, to

include this information, you may need to edit for conciseness throughout the manuscript (which I believe is very possible).

Thank you for this input. We have reorganized the discussion to improve the flow and avoid repetition.

We include suggestions for policy and further research e.g. explore and enhance methods of disseminating accurate information through peer networks, increasing access to drug checking and standardization of the alerting process, explore ways of minimizing alert fatigue and using qualitative methods to explore the quantitative findings.

We expanded on witnessing an overdose and experiencing an overdose as per response #8 above and the final sentence in our conclusion states: "Further research is needed to ensure alerts are reaching the appropriate audiences and identify how to better communicate to younger PWUD."

We have included 5 new references in order to improve the interpretation of the finding.

Comment #10 " This may be due to Island Health alerts being more targeted and informed by Vancouver island Drug Checking (12)" What does this mean? Are you implying communication efforts are greater in this region?

Thank you for this comment. Following discussions with the medical health officers in the various health authorities we have added further context in the discussion regarding how the alerts are determined to explain why it is hard to compare between the health authorities and have removed the actual alert numbers as these may be confusing. We have amended text in the discussion:

Compared to participants from Interior Health, those from Island Health had significantly higher odds of reporting seeing/hearing a drug alert. "The decision to issue a drug alert is generally based on a number of factors including drug toxicity deaths (7), emergency health service calls, drug checking (11, 12) and community input. However, the availability of these factors may vary by region and therefore make it difficult to directly compare health regions."

Comment #11: Please explain change blindness

Please see response to comment #9 - we have removed discussion of change blindness and focussed on alert fatigue which may be more relevant to the reader.

Comment #12: I think the variables that were not statistically significant are among the most interesting, many of the sociodemographic factors that often intersect with health education are not associated with the knowledge of alerts in this study, I think this warrants further thought and discussion.

Thank you for this comment regarding sociodemographic factors which may intersect with health education not being associated with knowledge of alerts. Unfortunately questions which could elucidate this more clearly were not asked e.g. past employment or past housing; parents' employment or educational level or highest level of education achieved by the participant. In addition, data relating to Indigeneity from the survey are shared with First Nations Health Authority and Metis Nation BC, for them to analyse and interpret the data. Thus the authors do not feel it appropriate to include a discussion about sociodemographic factors and have added no text.

Conclusions

Comment #13: "Harm reduction is a non-judgemental approach which provides PWUD with resources and support services to provide them with autonomy to make informed decisions about

their substance use.” It is strange to introduce a definition in the conclusion and this sentence seems unnecessary, consider removing or revising.

We thank the reviewer for this comment and have removed the sentence.

Minor items:

Some phrasing throughout the paper is awkward, you may consider revising, for example:

Comment #14: on page 16 “an important consideration “ is used twice in the same paragraph

We thank the reviewer and have removed one of the “an important consideration”

Comment #15: “Although gender was not statistically significant in the bivariable regression, it was included in the model because of the known effects on health outcomes” is worded in a strange way, perhaps you mean because of known gender differences in health outcomes?

We thank the reviewer and have changed the wording to make it clearer that inclusion is for conceptual not statistical reasons: Age category and gender were included despite not being selected for using backwards selection because of their conceptual relevance and known differences in health outcomes.

Comment #16: “About a third of respondents were ≥50 years old (33%) and participants from small urban centres accounted for 29.5%, from medium urban centres 36.1% and from large urban centres 34.4%” is awkwardly worded, can you rephrase?

We thank the reviewer and agree the sentence was awkward. We have revised the main points exactly 33% were aged ≥50 years and there was a fairly even distribution of the three categories of urbanicity of participants. A third of respondents were ≥50 years old and the distribution across urbanicity categories of the site where they participated in the survey were fairly even (29.5% from small urban centers; 36.1% from medium urban centers and 34.4% from large urban centers).

Comment #17: “This is elaborated on in the discussion” Does not need to be stated in the results, it is implied.

We thank the reviewer and have removed this sentence

18 - Error identified and corrected by the authors

The authors identified an error in figure 2 – there were 55 participants who provided no response to question 24 (previously we stated 57). This number and percentage has been corrected in figure 2, and percentage updated in abstract; it was correct in the full manuscript text.

VERSION 2 – REVIEW

REVIEWER	vanDraanen, Jenna University of Washington
REVIEW RETURNED	24-Apr-2023
GENERAL COMMENTS	The comments have been addressed in the revised version, for the most part, and this is a nice paper. The only comment that was not fully addressed was comment #7 asking the authors for post-estimation tests to confirm categorical predictor significance. Instead the authors opted to remove the text in question.