PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Concurrent use of opioids and benzodiazepines/Z-drugs in Alberta, Canada and the risk of hospitalization and death: a case crossover study
AUTHORS	Sharma, Vishal; Simpson, Scot H.; Samanani, Salim; Jess, Ed; Eurich, Dean

VERSION 1 – REVIEW

REVIEWER	Donovan Maust University of Michigan
REVIEW RETURNED	10-Apr-2020

GENERAL COMMENTS	This is a case-crossover study from 2016-2018 in Alberta Canada examining adverse outcomes among those to whom BZD and opioids are co-prescribed. Specifically they consider ED visits, hospitalization, and death—comparison co-Rx to opioids alone (n=1,056,773 total). The OR for hospitalization is 1.13, death 1.90. While I think the topic is important and clinically relevant, I think the authors have perhaps overstated how little is known about the topic and they present a large amount of analyses in a manner that does not make it particularly easy for the reader to absorb it all. Major points: 1. Overall the Introduction covers a lot of ground when I think it should be focused more specifically on opioid-benzo co-prescribing and what is or is not known. Despite what the authors assert, I would argue that a fair amount of attention has focused on bzd-opioid co-prescribing. They should highlight what knowledge gaps the present analysis seeks to fill. 2. In general, perhaps because the authors present so much information and types of stratified analyses, it is somewhat confusing and hard to follow the key results. Furthermore, there are some analytic decisions that are confusing. Why do the authors stratify based on number of unique prescribers or pharmacies? But they do not based on clinical comorbidity, which seems more likely to be associated with adverse outcomes and, for clinicians, would be more helpful. 3. It would help the reader if the two parts of analysis (hospitalization and death) were presented in a more consistent manner, in tables that were more consistent. Abstract - would include the N in design/setting/participants section Introduction:

	- I am not entirely sure it is accurate to say that "concurrent use of opioids and BZDs represents a less highlighted drug use pattern"—analyses of both opioids and BZDs frequently look at co-prescribing of the other medication as an outcome of interest (though perhaps not the primary outcome). - the authors comment that one of the two US studies was of those who were "privately insured" and therefore may not be generalizable. For the non-elderly adult population, in the US (unfortunately) the most common insurance is privately insured—would argue that is the most generalizable group. - it is unclear why the authors chose "dx related to mental health" as an outcome to examine. Compared to those on opioids alone, those co-prescribed would almost certainly have more mental health related visits because the conditions for which they are being prescribed the bzd. Methods: - for the total-days variables on which analysis was stratified, do you only have data going back to start of 2016? So there is a ceiling on the days? Results: - in Table 1, from what period of time are the row characteristics determined? - it seems like days'-supply would be more useful than number of dispensations? Or days supply per person? - in the "opioid only users", why are there any BZRAs? Shouldn't that be zero? - I don't understand why Table 2 includes BZD only when I don't believe that is presented at all in the text? - Table 4: does this account for bzd dose? - codeine seems like an odd reference group for comparison specific opioid type—why not use the most commonly-prescribed opioid? (Though I guess perhaps that could be codeine.) Discussion: - p13 in comparison with Park et al.—"BZDs with increases risk of death, overall and in a dose dependent manner"—do you mean by dose of the BZD? Did you present results looking at BZD dose? - p13: "there could be residual confounding and bias due to the fact that opioid only users could be different than concurrent users in characteristics which our data may not adequately capture"—this is almost certainly true that these groups are different. Most obviously, those on Benzes would likely have more insomnia and a variety of mental health diagnoses that certainly influence hospitalization, also likely influence risk of mortality. I do not think excluding for "malignancy or palliative status" really address this.

REVIEWER	Matthew Hirschtritt, MD, MPH University of California, San Francisco, USA
REVIEW RETURNED	30-Apr-2020

GENERAL COMMENTS	In this retrospective, registry-based study, the authors have examined hospitalizations, emergency department encounters, and all-cause mortality associated with concurrent benzodiazepine and opioid use. The authors have used a case-crossover design to use each case as its own control, which reduces some sources of confounding compared with a conventional cross-sectional design. My suggestions below are intended to help strengthen this report.

	1. Please state which opioids and benzodiazepines were included in analyses. 2. What formulations (oral, IV, IM) of benzodiazepines and opioids were considered? 3. Define OME and how it was calculated (it was only spelled out but not defined in the caption for 1 of the figures). 4. Define “health care utilization.” 5. For Table 1, consider presenting pairwise comparisons among the cohorts for each variable. 6. Comment on the higher OR of all-cause hospitalization or ED visits for patients with multiple prescribers and pharmacies in the results and conclusions. 7. How do the authors explain the higher risk of hospitalization or ED visit and mortality in the initial month of concurrent prescription?

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Donovan Maust
Institution and Country: University of Michigan
Please state any competing interests or state ‘None declared’: none declared

Please leave your comments for the authors below
This is a case-crossover study from 2016-2018 in Alberta Canada examining adverse outcomes among those to whom BZD and opioids are co-prescribed. Specifically they consider ED visits, hospitalization, and death—comparison co-Rx to opioids alone (n=1,056,773 total). The OR for hospitalization is 1.13, death 1.90. While I think the topic is important and clinically relevant, I think the authors have perhaps overstated how little is known about the topic and they present a large amount of analyses in a manner that does not make it particularly easy for the reader to absorb it all.
Response:
We have adjusted our manuscript to improve the flow of the document.

Major points:
1. Overall, the Introduction covers a lot of ground when I think it should be focused more specifically on opioid-benzo co-prescribing and what is or is not known. Despite what the authors assert, I would argue that a fair amount of attention has focused on bzd-opioid co-prescribing. They should highlight what knowledge gaps the present analysis seeks to fill.
Response: all recommendations incorporated as described below on page 6.
We have changed the introduction substantially to be more focused on co-prescribing. In the last paragraph of the introduction, we provided more information on the knowledge gaps in Alberta, Canada regarding co-prescribing. As well, we have removed information given in the first paragraph as it did not relate to our study, as Reviewer 1 pointed out.

2. In general, perhaps because the authors present so much information and types of stratified analyses, it is somewhat confusing and hard to follow the key results. Furthermore, there are some analytic decisions that are confusing. Why do the authors stratify based on number of unique

prescribers or pharmacies? But they do not based on clinical comorbidity, which seems more likely to be associated with adverse outcomes and, for clinicians, would be more helpful.
Response:
We stratified by number of unique health providers because this factor is mentioned as a risk for aberrant behaviour by Canadian guidelines and as a risk factor for adverse outcomes by the 2019 Centers for Medicare & Medicaid Services opioid safety measures in the US. Canadian health providers are now required to use prescription drug monitoring tools when assessing patients and the number of unique health providers that a patient has seen is an important consideration. There is a knowledge gap in Alberta, and internationally in general, on how this factor affects adverse outcomes. In terms of stratifying by clinical co-morbidities, this was not the focus of this study as we were following guideline factors associated with risk, and there is good evidence on this already in the literature, especially when it comes to mental health as a co-morbidity. We will address the mental health outcome in the subsequent comment from Reviewer 1.

3. It would help the reader if the two parts of analysis (hospitalization and death) were presented in a more consistent manner, in tables that were more consistent.

Response:
We made Tables 2 and 3 more consistent.

Abstract
- would include the N in design/setting/participants section

Response: page 4 Abstract is amended
Added n=1056773 and 31998 as recommended

Introduction:
- I am not entirely sure it is accurate to say that “concurrent use of opioids and BZDs represents a less highlighted drug use pattern”—analyses of both opioids and BZDs frequently look at co-prescribing of the other medication as an outcome of interest (though perhaps not the primary outcome).
Response:
Reviewer is correct with their statement. We changed the Introduction to address this issue on page 6.

- the authors comment that one of the two US studies was of those who were “privately insured” and therefore may not be generalizable. For the non-elderly adult population, in the US (unfortunately) the most common insurance is privately insured—would argue that is the most generalizable group.
Response: Amended the Introduction according to Reviewer’s comments on page 6.
Reviewer is correct with this reasoning. However, US privately insured population may not be generalizable to Alberta, Canada population. We will change the Introduction to reflect this point: “However, the Canadian studies did not quantify the risk associated with concurrent use and the two US studies used populations limited to US military veterans and those that were privately insured, and may not be generalizable to the Canadian population.”

- it is unclear why the authors chose “dx related to mental health” as an outcome to examine. Compared to those on opioids alone, those co-prescribed would almost certainly have more mental health related visits because the conditions for which they are being prescribed the bzd.

Response: amended Methods and Results section according to Reviewer comments.
In the Canadian and US guidelines, health providers are cautioned against prescribing opioids in patients with mental health disorders because of the risk of adverse effects. This is why we specifically considered this outcome. However, the point the Reviewer makes is correct, in that the BZD group would have more hospital events due to their underlying condition. We will remove this as an outcome and consider only the opioid toxicity related events. The Results section was also amended to include only the opioid toxicity result.
Page 8 Methods: "The secondary outcome was incident hospitalization or ED visit due to ICD-10 diagnoses related to opioid toxicity (ICD10 F04-F99, T400-T404, T406) between Jan 1, 2016 and Dec 31, 2018 as this endpoint maybe more specific to the population using BZD and opioids12."
Page 11 Results: "In the secondary analysis, the estimated risk of hospitalization or ED visit was also higher in concurrent patients when compared to opioid only patients for admissions related to opioid toxicity (OR 1.8; P<0.001)."

Methods:
- for the total-days variables on which analysis was stratified, do you only have data going back to start of 2016? So there is a ceiling on the days?

Response:
Correct, our data for analysis only goes back to 2016. As such a patient could have almost 1000 days of overlap in prescribing of opioids and BZDs. Although a ceiling may exist, we do not feel this is a major limitation given patients could have upwards of 3 years of co-prescription use.

Results:
- in Table 1, from what period of time are the row characteristics determined?
Response:
All characteristics are from 2016-2018 except Elixhauser score, which is from 2012-2016 as we had access to Physician Claims data. Table 1 on page 16 was amended to reflect this information:
"**Determined using Physician Claims data from 2012-2016"

- it seems like days'-supply would be more useful than number of dispensations? Or days supply per person?
Response:
We did consider days' supply as a characteristic for analysis. However, both the College of Physicians and Surgeons of Alberta and Alberta College of Pharmacy both have Standards of Practice that recommend strongly against days' supply > 30 days. Therefore, we considered number of dispensations in our analysis. Indeed, the vast majority of dispenses in this jurisdiction are 7 day supplies of medications for opioids.

- in the "opioid only users", why are there any BZRAs? Shouldn't that be zero?
- I don't understand why Table 2 includes BZD only when I don't believe that is presented at all in the text?
Response:
"Opioid only users" refers to opioid-only use during the study windows in the case crossover analyses. If patients had BZRA use outside of the study windows, then this was captured in our summary statistics in Table 1. The Exposure section in Methods (page 8) was amended to reflect this as follows: "In our case crossover analyses, "none", "opioid only", "BZD only" and "concurrent" refer to drug use during the study windows".
A footnote was added to Table 1 (page 16) to clarify the Reviewer's point: "If patients had BZRA use

outside of the study windows, then this was captured in our summary statistics".
Table 2 contained "BZD only" group because we thought readers maybe interested in that sub-group. We identified "BZD only" as an exposure group through our process of identifying "concurrent use" as the main exposure group. However, concurrent use is our focus in this study. We believe this information is important for the reader. Moreover, as noted below, the BZD alone group also addresses potential confounding in the analysis as is outlined below. As a result, for the time being, we will leave the "BZD only" group in the table, but we are happy to remove this at the discretion of the editor.

- Table 4: does this account for bzd dose?
Response:
Bzd dose (DDD) was not included in this analysis. From Canadian and US guidelines on opioid use, any BZD use is not recommended for co-prescribing with opioids, irrespective of dose.

- codeine seems like an odd reference group for comparison specific opioid type—why not use the most commonly-prescribed opioid? (Though I guess perhaps that could be codeine.)

Response:
Codeine is the most commonly prescribed and considered a "safe" opioid to use by many clinicians although it is well known issues exist with codeine use as well. This is why we thought that readers would be interested in this comparison.

Discussion:
- p13 in comparison with Park et al.—"BZDs with increases risk of death, overall and in a dose dependent manner"—do you mean by dose of the BZD? Did you present results looking at BZD dose?
Response:
We mean in an opioid dose dependent manner. Table 4 in the Park study stratified their estimates using opioid dose. We will use "opioid dose dependent" in the Discussion section to clarify your point which now reads: "Although both of our studies associated concurrent use of opioids and BZDs with increased risk of death, overall and in an opioid-dose dependent manner, the Park et al risk estimates were much higher than ours, almost double."

- p13: "there could be residual confounding and bias due to the fact that opioid only users could be different than concurrent users in characteristics which our data may not adequately capture"—this is almost certainly true that these groups are different. Most obviously, those on Benzes would likely have more insomnia and a variety of mental health diagnoses that certainly influence hospitalization, also likely influence risk of mortality. I do not think excluding for "malignancy or palliative status" really address this.
Response: amended according to Reviewer's comments
The Reviewer's point regarding our sensitivity analysis is correct. The sensitivity analysis was not intended to address residual confounding, but simply to exclude cancer and palliative patients. However, it is also for this reason the "BZD only group" was included in the analysis as the "BZD only group" would be more similar from a BZD utilization point of view within the concurrent group and therefore reduce the confounding effects as the reviewer suggested. Indeed, the "BZD only" group was consistently and substantially lower with respect to risk compared to the concurrent group. As the 'reason' why a BZD user would be similar between the "BZD only" and the "concurrent" group, it is unlikely that confounding is driving the concurrent results and it is the co-prescribing of these drugs that is more likely the causal association. As the data shows, the risk is substantially lower compared to the BZD alone group; suggesting that it is in fact the combination with the opioids that are driving the results. We will amend the Discussion section to reflect the Reviewer's comment by removing the

statement “We conducted a sensitivity analysis that excluded patients diagnosed with a malignancy or palliative status to explore these issues and our original risk estimates were preserved”.

Reviewer: 2
Reviewer Name: Matthew Hirschtritt, MD, MPH
Institution and Country: University of California, San Francisco, USA
Please state any competing interests or state ‘None declared’: None declared

Please leave your comments for the authors below
In this retrospective, registry-based study, the authors have examined hospitalizations, emergency department encounters, and all-cause mortality associated with concurrent benzodiazepine and opioid use. The authors have used a case-crossover design to use each case as its own control, which reduces some sources of confounding compared with a conventional cross-sectional design. My suggestions below are intended to help strengthen this report.

Thank you for your feedback on our manuscript. We have amended our manuscript to reflect the comments from Reviewer 2 as follows.

1. Please state which opioids and benzodiazepines were included in analyses.
Response: We will amend the Methods-Exposure section (page 8) to reflect this information as follows:
“We identified opioid and BZD prescriptions using Anatomical Therapeutic Chemical codes25 and included all Health Canada approved26 opioid and benzodiazepine/Z-drug formulations which are monitored in the Alberta Triplicate Prescription Program27”
We will also add an eAppendix to list the ATC codes used in the analysis.

2. What formulations (oral, IV, IM) of benzodiazepines and opioids were considered?
Response: We used Anatomical Therapeutic Chemical codes to identify opioid use, regardless of route of administration. We will amend Methods-Exposure on page 8 to include this information. The Methods section now reads “We identified opioid and BZD prescriptions using Anatomical Therapeutic Chemical codes25 and included all Health Canada approved26 opioid and benzodiazepine/Z-drug formulations which are monitored in the Alberta Triplicate Prescription Program27”

3. Define OME and how it was calculated (it was only spelled out but not defined in the caption for 1 of the figures).
Response: We will amend the Methods Design and Statistical Analyses section on page 9 to reflect the Reviewer’s comments and add this information. The methods section now reads:
“Opioid doses were standardized into oral morphine equivalents (OME) using conversion factors outlined by the Triplicate Prescription Program29 in Alberta, Canada.”

4. Define “health care utilization.”
Response:
We added this definition to Design and Statistical Analyses section on page 8-9 as follows: “Health care utilization28 was defined by number of unique providers visited and number of opioid prescriptions dispensed”

5. For Table 1, consider presenting pairwise comparisons among the cohorts for each variable.
Response:
Pairwise comparisons were added to Table 1 between “concurrent users” and “opioid only users” as suggested

6. Comment on the higher OR of all-cause hospitalization or ED visits for patients with multiple prescribers and pharmacies in the results and conclusions.
Response:
We added this information to Results and Conclusions in the context of higher healthcare utilization.
The Results- Hospitalizations or ED visits section on page 10 now reads: “and those visiting >5 health providers (13.0% vs. 16.5%; OR 1.67; P<0.001) had the highest risk associated with concurrent use and hospitalizations or ED visits”
The Interpretation section in the Abstract on page 4 now reads: “Concurrent use of opioids and BZDs further contributes to the risk of hospitalization/ED visits and mortality in Alberta, Canada over opioid use alone, with higher opioid doses, older age and increased number of unique health providers carrying higher risks.”

7. How do the authors explain the higher risk of hospitalization or ED visit and mortality in the initial month of concurrent prescription?
Response: This may be due to the fact that highly susceptible patients will experience an adverse outcome early in concurrent use. The Discussion (page 13, second paragraph) was revised to address this point as follows: “Both of our estimates associate a higher risk during the first few days of concurrent use as more susceptible patients may experience adverse outcomes earlier in concurrent use, thus signaling that even short periods of concurrent use carry risks.”

VERSION 2 – REVIEW

REVIEWER	Donovan Maust University of Michigan
REVIEW RETURNED	07-Jul-2020

GENERAL COMMENTS	Thank you for your responses. I still think there is some lack of precision in describing how the cohort was defined and what exact time period is being used to derive characteristics that are being presented. - Perhaps part of the problem is that the cohort is described in several sections in the methods--the "identification of Patients and Outcomes", "Exposure", and "Design and Statistical Analyses". - the cohort is anyone with an opioid at any time during the time period? This is why "BZD only" label for a group is confusing--if membership in the cohort is defined by also having opioid use, then no one should be BZD only. Or maybe they got one opioid at some time Jan 2016-Dec 2018, but then is the BZD only referring to the risk or control window? The risk window? The "opioid only", "BZD only", and "concurrent" groups in Table 2--if the cohort by definition is opioid users, it is confusing who the BZD only group is.

	- furthermore, on p. 10 you write "'opioid only' and 'BZD only' use refer to drug use during the study windows"--is this during risk or control window? "Study window" is confusing, given there are several windows described. - Table 1 column headers--concurrent and opioid-only are defined by index time? Perhaps add a footnote or clarify in title. - Lingering confusion re: time frame for characteristics in Table 1. Elixhauser has been clarified, but what about "cumulative concurrency"? this is slightly confusing b/c it is obviously not limited to risk or control intervals. Characteristics for model in Table 2--are these defined in 12mo pre-index and 12-mo pre-control? Or are index and control characteristics from the exact same 12 mo period?

REVIEWER	Matthew Hirschtritt University of California, San Francisco; USA
REVIEW RETURNED	07-Jul-2020

GENERAL COMMENTS	The authors have addressed my concerns.

VERSION 2 – AUTHOR RESPONSE

Reviewer Name: Donovan Maust
Institution and Country: University of Michigan
Competing interests: none declared

Please leave your comments for the authors below. Thanks for the feedback. We will try to incorporate all suggestions as identified by the Reviewer. Our responses are in red.

C1.) Thank you for your responses. I still think there is some lack of precision in describing how the cohort was defined and what exact time period is being used to derive characteristics that are being presented.
R1.) Time period for identifying opioid cohort using opioid dispensation records from PIN and time period for outcomes:
• Hospitalization or ED visit cohort and outcome: Jan 1st, 2016 – Dec 31st, 2018
• Death cohort and outcome: Jan 1st, 2016- Dec 31st, 2017
Table 1 now specifies that the summary statistics were derived using period 2016-2018, except for Elixhauser, which was 2012-2016.

C2.) - Perhaps part of the problem is that the cohort is described in several sections in the methods--the "identification of Patients and Outcomes", "Exposure", and "Design and Statistical Analyses".
R2.) “The Identification of Patients and Outcomes” section specifies the above-mentioned dates for cohort definition and outcomes definition. We also added wording to provide clarity on this issue:
“Two distinct analysis cohorts were generated corresponding to two different study periods.”
“Exposure” section: we see that there could be confusion regarding time period here. We changed some wording to make things clearer:
“The exposure of interest was whether an opioid patient also used a BZD concurrently during the two study periods.”
“Design and Statistical Analyses” section: we do see the confusion about time periods. We amended to indicate time period for the characteristics:
“We first conducted a descriptive analysis of our study population and performed pairwise comparisons between “opioid only users” and “concurrent users” using t-tests and chi2 tests of independence using data from 2016-2018.”

We also added a visual in the eAppendix as eFigure 1 to help explain time periods. See below for figure.

C3.) - the cohort is anyone with an opioid at any time during the time period? This is why "BZD only" label for a group is confusing--if membership in the cohort is defined by also having opioid use, then no one should be BZD only. Or maybe they got one opioid at some time Jan 2016-Dec 2018, but then is the BZD only referring to the risk or control window ? The risk window? The "opioid only", "BZD only", and "concurrent" groups in Table 2--if the cohort by definition is opioid users, it is confusing who the BZD only group is.
R3. Thank you for the comments. The reviewer is correct. There are two different opioid cohorts as defined in the "Identification of Patients and Outcomes" section. Hospitalization/ED are anyone with an opioid during 2016-2018 while deaths are 2016-2017.
In the "Exposure" section, we defined each day during 2016-2018 with one of the 4 exposure categories: none, opioid only, BZD only, and concurrent. Everyone in our cohort received an opioid at some point during 2016-2018, however, depending on their drug use pattern, each subject may or may not have received a BZD as well, either concurrently with the opioid or not. Also in this section, we specified that each day of follow up was categorized as one of the four groups and that this categorization is directly translated to the case crossover study periods; "BZD only" does not refer to people that were "BZD only", rather, it refers to exposure group "BZD only" in the case crossover study windows in which the patient received only a BZD in either the control and risk window
Table 2 comment: "opioid only", "BZD only", "none" and "concurrent" are exposure categories experienced by the study subjects during the risk and control windows (and not groups of patients) and these exposure categories are contrasted in the conditional logistic regression. We specified this point in "Design and Statistical Analyses" section, last paragraph (page 9).
In Tables 2 and 3, we added the heading: "Analysis group based on exposure category" to provide clarity on this issue you raise.
eFigure 1 was added to clarify. See below.

C4.) - furthermore, on p. 10 you write "'opioid only' and 'BZD only' use refer to drug use during the study windows"--is this during risk or control window? "Study window" is confusing, given there are several windows described.
R4. "study windows" refers to both control and risk windows. The exposure category in the risk window is contrasted with the exposure category in the control window. We see the confusion you highlight and changed the wording to "risk and control periods".

C5.)- Table 1 column headers--concurrent and opioid-only are defined by index time? Perhaps add a footnote or clarify in title.
R5.) Title clarified as suggested

6.)- Lingering confusion re: time frame for characteristics in Table 1. Elixhauser has been clarified, but what about "cumulative concurrency"? this is slightly confusing b/c it is obviously not limited to risk or control intervals. Characteristics for model in Table 2--are these defined in 12mo pre-index and 12-mo pre-control? Or are index and control characteristics from the exact same 12 mo period?
R6.) Reviewer is correct
Table 1: "Cumulative concurrency" characteristic/summary statistics, like all except Elixhauser, is from 2016-2018. It is not limited to the risk/control periods, rather, are summary stats derived from the data. We amended the Table 1 title to read "Table 1. Characteristics and summary statistics of opioid users with incident hospitalizations/emergency department visits using data from 2016-2018."
Table 2: The characteristics are based on data within 12 months prior to index outcome.
Also, in the "Design and Statistical Analyses" section, we added the following to clarify this point:
"The analyses were stratified into the following sub-groups using data within the year prior to the

outcome: sex, age at admission or death, total days of cumulative concurrency prior to event, total days of previous opioid use, health care utilization, opioid molecule and dose (OME)."
We have also included an eFigure 1 (referenced in Methods) to visually depict study design and time periods:
eFigure 1. Schematic of case crossover design. Each patient's exposure category (opioid only, BZD only, concurrent, none) was coded in both the risk and control periods. These exposures were contrasted using conditional logistic regression.

Note:
1. Hospital admission or emergency department visit between Jan 1 2016 to Dec 31, 2018; Death between Jan 1, 2016 and Dec 31, 2017
2. Exposure categories measured in each of risk and control periods: 1) BZD only, 2) opioid only, 3) concurrent BZD and opioid, and 4) none
3. Characteristics include cumulative days of concurrent use, total days of opioid use, number of opioid dispensations, and health care utilization

VERSION 3 – REVIEW

REVIEWER	Donovan Maust University of Michigan
REVIEW RETURNED	23-Oct-2020

GENERAL COMMENTS	Thank you for the additional clarifications.