Text

Description automatically generated

**Joint Supervisor Feedback on Draft Dissertation.**

Please use the structure below to compile a **single** piece of feedback from all supervisors who were able to comment on the dissertation draft. We have asked students to add page and line numbers to their work so, as if providing reviewer comments to a peer-reviewed journal article, you may refer to these when providing feedback. If the student has not provided this, you can ask them to do so for the purposes of providing feedback. Once all feedback has been compiled into this **single** document, please share with the student ***within five days*** of receiving the draft, to give them enough time to amend before submission.

**Student name: Fan Zhang**

**Overall:**

* The report examines four outcomes and the associated risk ratios for individuals exposed to opioids only and to both opioids and cocaine (C&O). However, several points are missing, and some definitions may not be accurately described. These issues are highlighted in the sections below.
* As a general observation, the tone and level of formality vary between sections, with some written in a formal style and others more informally.
* When introducing an abbreviation (e.g., cocaine and opioids; C&O), it should be used consistently thereafter. In the report, some abbreviations are redefined multiple times, even within the same section.
* Whenever an estimated quantity is reported (e.g., IRR), it would be useful to also present the associated confidence interval (CI). This helps the reader immediately understand whether the effect is statistically significant.
* The report does not currently include a discussion of study limitations, which is an essential component.
* More effort could be put towards explaining clearly the definition of the cohort, with more details. In multiple places you describe the study population as individuals “who were receiving OAT” (e.g. line 78, line 84, line 110, line 377). Remember that the study population was people who had received OAT within the preceding two years. This doesn’t necessarily mean they were receiving OAT during your period of follow-up.
* The tables reported throughout seem like code output, and the labels seem to be the covariates names form the code, which is not clear to the reader.
* Lines 91-93: Suggest rewrite the paragraph and go back to your original research question for conclusion - and say whether the evidence supports (or not) that C&O dependence cause more drug related harm.
* All conclusions should clearly relate to your specific research question(s). You should not be making conclusions about questions that you did not explore. For example, PLS, lines 94-96: these are not questions that were investigated in these analyses.
* See the ILOs for the Dissertation Unit. ILO #4 is “Demonstrate critical thinking by summarising the research in the context of existing literature, discussing key limitations and strengths of the work.” Additionally, see page 11 of the Dissertation Handbook “you should explain how your project and the results from it fit into the context of what is already known on the subject. In doing this, you should reference work already carried out in this area.” Your draft does not yet do this.
* Carefully check your Author Contributions statement for accuracy – be careful not to claim that you completed any tasks that your supervisors completed (e.g. defining the study cohort).

**Plain Language Summary:**

* The report states that the study examined patterns of C&O dependence. It is unclear what is meant by this – does it refer to trends over time (e.g., increases or decreases in prevalence), event rates among individuals exposed to different drugs, or something else?
* Carefully review the cohort definition. The report describes it as individuals who received OAT, but not all individuals necessarily received OAT during 2015–2022. The prevalence report may provide useful guidance on defining such concepts more precisely.
* Be cautious in how OAT is described, as it could cause confusion. OAT is a substitution therapy, not a treatment in the traditional sense of the term.
* The study uses four outcomes, two of which are overdose-related (DRD: fatal overdose; NFOD: non-fatal overdose). When using the term “overdose” in the report, specify which type you are referring to for clarity.
* Some terms are vague or may not accurately convey the intended meaning. For example, the phrase “solving accommodation” is unclear—what exactly is meant by “solving” in this context?

**Abstract:**

* Some arguments lack supporting references. For example, the statement “concurrent cocaine and opioid (C&O) dependence is increasingly prevalent among socially vulnerable groups” requires evidence or citations to substantiate it.
* The meaning of “patterns of C&O dependence” is unclear, and it is not evident from the report how this was examined.
* When describing significant or non-significant differences, it would be helpful to report the associated measures (e.g., IRR with corresponding confidence intervals).
* Terms such as “strongly dependent” or “strongly linked” imply a high level of certainty, which may not be warranted, particularly given the study’s limitations. Consider using more cautious language when appropriate.
* Line 117, it would be better to state clearly what the comparison is against to, i.e. “significantly higher NFOD rates” compared with…?
* Lines 117-118 “particularly among males aged 15-34” would appear to imply an interaction between C&O and age group, but I don’t think you fitted one.
* We would recommend including numerical results for all 4 outcomes, regardless of statistical “significance”.
* Line 126 ‘but to lower CVD mortality compared with opioid-only’: Better to focus on whether evidence in support of increased risk or doesn’t suggest there is an increased risk.
* Lines 126-128: Again, you should only make conclusions relating to your specific research question(s).

**Introduction:**

* Lines 137-143 include statements without evidence/references. Is it true that polydrug use among people receiving OAT “is the reason” for high DRD rates?
* Line 144 (reference (1)): This reference does not support the sentence. The reference supports statement that drug related deaths have increased in Scotland and constitute a public health emergency.
* Lines 145-148 are also lacking referencing. How do you know that C&O dependence has risen? The cited reference (4) does not seem to say anything about C&O dependence.
* Lines 153-161: Is this relevant to your research questions?
* Lines 173-175: This is an intro not a conclusion and so better to raise hypotheses and research questions you are going to test.
* Rather than finishing this section with a “conclusion”, it would be very informative to clearly state your aims.

**Methods:**

* The data for this study were provided by PHS through SHIELD, and this should be explicitly acknowledged.
* Line 188-189 ‘the Scottish National Prescription Information System (PIS)’: Just ‘Prescribing Information System’.
* Line 193 ‘a unique patient identifier (IAIN)’: This is the SHIeLD pseudonymised index number that we added. It isn’t part of PIS. Maybe rephrase to ‘unique identifier’. In general, there is no need to discuss the labels used in coding.
* The covariates used should be clearly defined:
* How is accommodation status determined – based on every SDMD/DAISy record (e.g. time-varying), the most recent record, or other?
* How is the NHS Board of residence defined – this is derived from the most recent OAT prescription, correct?
* Why are financial years mentioned if they are not used in the analysis.
* The study cohort is a subset of individuals with at least one OAT and one SDMD/DAISy record. This cohort was created and provided by the team; it should be clearly stated that it was not constructed by the author of this report.
* Line 198: It is not necessary “at the time of the visit”. The SDMD definition: for illicit drugs is “ILLICIT DRUGS PROFILE (**PAST MONTH**)” and for prescribed is “PRESCRIPTION DRUGS PROFILE - Give details of **current prescription** related to treatment of addiction”. The DAISy definition: for illicit drugs either “in the last month” or “previous to the last month” and for prescribed is “receipt of a prescription, within the last month, related to treatment of their addiction”.
  + We suggest either to simplify the wording by avoiding the time reference or state it in a way that would reflect the definitions.
* It would be helpful to include the definitions of all codes in Supplementary Materials (e.g. line 204 T code definitions, lines 207-209 codes definitions, similarly for cardiovascular mortality codes).
* Line 201 ‘the national hospitalisation database’: Scottish Morbidity Records Acute hospital inpatient and daycase database (SMR01).
* Lines 201-205: Can you give any motivation for only including opioid, heroin and methadone drug-related poisoning NFOD events rather than all NFOD events? Would it be more appropriate to refer to this by a more specific name rather than NFOD, due to this restriction? Also, you need to be clearer throughout that you’re talking about NFODs resulting in hospital admission, which is a measurable but small minority of NFODs - most aren’t admitted and are treated at scene or discharged from emergency dept.
* Line 206 ‘Scottish National Death Registry’: Scottish Morbidity Records death registration database (SMR99) - a subset of National Records of Scotland’s death registration database, held by PHS. Also clarify if you used confirmed DRDs via the supplementary NRS datafile, or just identified via ICD10 codes.
* Lines 218-219: “Follow-up began at the date of the first OAT prescription within the study period”. Follow-up should begin at the start of the study period for anyone who received OAT during the two years prior.
* Lines 223-224: You describe that 12292/53100 (23%) of individuals didn’t have an SDMD/DAISy record. Can you explain what that means?
* Lines 222-235 and Figure 1 would be better placed in the Results section.
* Lines 229-235 appear to be repetition of information already provided directly above.
* Lines 232-233: Why were people excluded if they had no OAT prescription during 2015-2022? If people were included in the 2015 analysis if they received any OAT prescription during the two years prior, then data from 2013 onwards was used.
* Lines 240-242: Does record of cocaine on SDMD/DAISy imply “C&O dependence” or does it only imply use of cocaine (rather than necessarily “dependence” on it). It could be misleading to term this as dependence when we’ve coded ALL cocaine use to this category. It could be chronic overuse/dependence but could also just be occasional/non-dependent use.
* Line 246: “covariates… included” would imply that there were also other covariates that are not mentioned here. You should list all covariates.
* Line 249 ‘accommodation status’: Can’t have missing as separate group - better just two levels; Homeless / Other?
* Lines 267-268: Can you explain what the purpose was of adjusting for these covariates?
* Lines 270-271: Including an interaction between age and sex does not assess “potential effect modification”. (This would require fitting models with interactions between the exposure variable and age and/or sex.)
* Line 273: I would advise against use of a binary cutoff for “statistical significance” based on p-values.
* The final paragraph of the Study Design section is repeated and should be revised to remove duplication.
* The statement “Covariates were measured at the annual observation period level” is unclear and requires further explanation.
* The final paragraph of the Statistical Analysis section, which attempts to define interaction terms, is somewhat confusing and should be clarified.

**Results (including tables/figures):**

* When reporting estimates, it is helpful to always include the associated confidence intervals (CIs).
* In several instances, findings are reported without the corresponding IRR (and CI) – for example, line 341: “and those who were homeless or had missing accommodation data.”
* Lines 278-280: You describe this twice. Either here or in the methods but not in both places.
* Line 289 ‘were classified as opioid-only’: Its not (necessarily) opioid only - just not O&C.
* Lines 324-325: The cocaine use you identified is probably indicative of wider illicit drug use and higher overdose risk, while absence of cocaine use may indicate adherence to OAT and lower overdose risk.
* Lines 329-330: Is there an age and gender difference between C&O and O groups that might explain differences in Cardiovascular mortality?
* Interpretation here should be that no evidence of an increase - not evidence of a decrease
* In line 346, you refer to a change in the direction of association; however, this is not the case – in both instances, the mean IRR is less than one.
* Tables 3 and 4 are presented in an unusual format, appearing as unprocessed code output. Typically, results are presented horizontally for each covariate (e.g., unadjusted and adjusted IRRs for age displayed side-by-side in the same table, rather than in separate tables).
* Reference levels for each covariate should be stated clearly within the table itself, not only in the caption.
* Event rates for each covariate level and outcome should also be reported, with associated CIs. See the relevant tables in McAuley et al. (2023) for examples.
* Findings for each outcome are usually presented in separate tables (e.g., one table per outcome).
* Tables in the main results section should generally include only findings from the best-fitting model. Additional tables can be placed in the supplementary material.
* Figure 2: age at what time point?
* Table 2 was not referred to in the text. Consider also if rates per follow-up period (person-years at risk) may be more informative than percentages here.
* Lines 307-308: Consider whether you can quantify any such change (with an estimate and 95% confidence interval) or test for a change (reporting a p-value).
* Lines 315-330: I would recommend avoiding making comparative statements (C&O vs O) in this subsection: these comparative statements are better placed in the “Regression analyses” section, where quantitative results are included. Additionally, we cannot say e.g. “has always been significantly higher” (lines 324-325) or “has always been relatively high” (line 330) since you only studied the years 2015-2022.
* Line 336, line 345, line 352, e.g. “C&O dependence had…rates”. Please rephrase more clearly (e.g. people with… experienced higher drug-related death rates than…).
* It would be very helpful to show regression results in a table, rather than only presenting “significant” results.
* Line 366 ‘C&O dependence had lower CVD mortality rates than opioid-only dependence ’: Too strong. Maybe something like ‘There appears to be a lower risk of CVD mortality in people with C&O exposure…’. Can you expand analysis here and show which factors are key confounders - and also show differences in terms of age/ homelessness and other factors between C&O and O groups

**Discussion:**

* As noted above, your Discussion section should cover how your project and the results from it fit into the context of what is already known on the subject.
* Line 385 ‘In contrast, C&O dependence is associated with a lower cardiovascular mortality rate (CVD)’: Too strong. Go back to your main research questions. You found differences in NFOD but no support or evidence for higher risk in CVD/ ACM or DRD.
* Line 386: Again, I would avoid focus on “statistical significance”. Additionally it is not helpful to refer to “our prior knowledge”. Can you find and discuss any relevant literature instead?
* Lines 379-389: Both of these findings are contrary to our prior expectations. I’d be looking for a bit more awareness of this and discussion of what other aspects of the data or study design might have produced these results (e.g. discussing limitations).
* Lines 393-398: See our earlier comments about how conclusions must clearly relate to your specific research question(s). This isnt your main question.
* The discussion section seems to be missing strengths and limitations section. The analysis was based on several assumptions (e.g. how we defines the exposure, homelessness, missing OAT prescriptions among those in prison) which should be discussed.

**Supplementary Material:**

* No Sup provided.