Author's response to reviews

Title: Clinical coding of paediatric adverse drug reactions: a retrospective review of patient records

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Clinical coding of paediatric adverse drug reactions: a retrospective review of patient records

Responses to Reviewer’s Comments

Dr Brvar

I have read this paper with much interest. The manuscript is interesting and well written. However, the methodology of the study should be better explained.

Thank you for your comments. They have highlighted that parts of the report were unclear and we have attempted to rectify this. We have provided a more detailed explanation of the study methodology and have addressed your detailed comments below.

How were the patients with ADR identified / selected?

Patients who had experienced an ADR were identified in a preceding prospective study in which all unplanned admissions were reviewed shortly after admission. We have provided additional detail which relates to the methodology of that study (Lines 50-59). We have also provided a reference for readers who may be interested in the methods and findings of that study.

Were they identified via reviewing ICD codes or abstracts?

Patients who had experienced an ADR were not identified via a review of ICD codes or abstracts (see response above for more detail). Conversely, ICD codes and abstracts were reviewed after the patients who had experienced an ADR had been identified and subsequently discharged. The aim was to determine whether ICD codes could have been used to identify those patients in the absence of a prospective study.

Were admission abstracts of patients without ADR’s ICD codes also examined?

We examined the admission abstracts of all patients deemed to have experienced an ADR in the prospective study. We determined whether ‘ICD 10 ADR codes’ and/or ‘ICD 10 sign and symptom’ codes had been used to summarise their admission. We did not examine the abstracts of patients who had not been identified as having an ADR in the prospective study. We have updated the manuscript to describe this more clearly (Lines 74-88).

The prospectively of the study should be better explained, perhaps with a flow chart.

We have updated the manuscript to better describe the link between the primary prospective study and the retrospective study which this paper reports (Lines 46-88). We have also updated the title of the paper to reflect this.

The explanation of proper ADR coding would be also very useful.

We have added some additional explanation about which ICD-10 codes we considered to be ‘ADR codes’ (Lines 78-88). We have also provided some additional detail about one type of ADR code (external cause codes) in Table 1 whilst acknowledging in the narrative that these
were not the only relevant ADR codes that we looked for in the admissions abstracts. In addition, we have provided a Supplementary Table (Additional File 1) which contains our detailed findings which relate to other codes which may be relevant to ADR detection (discussed Lines 149-155).

Professor Hohl

Major Compulsory Revisions:

1. The case-finding method for this study is prospective, based on the quoted primary study. However throughout the manuscript I was confused as to whether it was prospective or established via “audit” (usually retrospective) or review of electronic records (usually retrospective. Please clarify throughout.

   Many thanks for highlighting that the description of the methodology was unclear in parts. Patients who had experienced an ADR were identified in a preceding prospective study in which all unplanned admissions were reviewed shortly after admission. We have provided additional detail which relates to the methodology of that study (Lines 50-59). We have updated the manuscript to better describe the link between the primary prospective study and the retrospective study which this paper reports (Lines 46-88). We have also updated the title of the paper to reflect this.

2. More detail is required to assess how complete the code set was for ADRs. If your code set was very restrictive, you may have found low sensitivity as a result. Please report the number of codes or code categories you used, and provide access to the code set. This limitation should be discussed in the Discussion section.

   We have added some additional explanation about which ICD-10 codes we considered to be ‘ADR codes’ (Lines 78-88). We have also provided some additional detail about one type of ADR code (external cause codes) in Table 1 whilst acknowledging in the narrative that these were not the only relevant ADR codes that we looked for in the admissions abstracts. We looked for codes containing the term ‘drug-induced’ and for external cause codes (adverse effects in therapeutic use).

Minor Revisions:

3. Abstract, line 14: Data...are (not “is”).

   Thanks. This has been updated.

4. Methods: Lines 46-51: I am confused as to the design of the primary study based on this paragraph. The use of the word “prospective” and “audit” is confusing. This needs clarification.

   We have provided additional detail which relates to the methodology of the prospective study (Lines 50-59). The use of the word ‘audit’ relates to the wording of the opinion received from the Research Ethics Committee Review – this has been separated into a single paragraph and moved to the end of the methods section to reduce confusion.
5. Methods: Lines 64-72: Did you account for variation in the certainty of the medication-related cause in the code set you used? There are many ICD-10 codes that refer to syndromes that may be medication-related without referring specifically to the agent (e.g., agranulocytosis). Without making the code set you used available, and providing more details it is difficult for the reader to determine whether you found low sensitivity because the code set was too restrictive, or because ADRs were not coded as ADRs. The following references below may be useful in this regard.1-3

You make an excellent point that there are some diagnosis codes that are likely to relate to a drug-induced event. We agree that these could provide an additional means of ADR detection in addition to the ‘external cause’ and ‘drug-induced’ codes. This concept led us to record what we termed ‘ICD-10 sign and symptom’ codes for each admission abstract in the study. We hoped to identify codes which were consistently used to record certain ADRs. However, we found a lack of consistency. So that the reader can gain more insight into these findings, we have added Supplementary Table 1 (Additional File 1) and we have also added a discussion of these data (Lines 149-155).

5. Results: Line 77. I would refrain from the use of the word “correctly”. The ADRs may have been accurately coded with regard to the syndromes or diagnoses that they caused, but external cause codes were omitted. These cases were simply "not coded as ADRs".

We accept that the use of the word ‘correctly’ does not accurately describe the scenario. We have removed all instances of ‘correctly.’ We have strengthened our description of ‘ICD ADR codes’ and ‘ICD sign and symptom codes’ (Lines 78-88). These definitions have been used consistently to report the results and subsequently in the discussion.

6. Discussion: Line 113-119. This is an interesting finding and worth highlighting. Another thought is that in oncology there is generally better documentation of ADRs within clinical records, leading coders (if they are not physicians) to code ADRs more precisely. Please discuss who codes within your institution. Also, it is known that pharmacists identify a greater proportion of ADRs than physicians. Were oncology patients more likely to see pharmacists in the primary study?

Yes, ADRs are much more consistently and clearly documented in oncology and that is due, in part, to the use of a standard proforma (Line 136-139). Detail of who undertakes coding at our institution has been added, they are a non-clinical team (Lines 78 & 139). Detail about the make-up of the research study team and the case-load assigned to each have been added to the methods section (Lines 54-56). Overall, a similar number of each patient type was seen by each member of the multidisciplinary team.

7. Discussion: The following points should be touched upon:

a. A mention of the restrictiveness of your code set should be provided. In comparison to other studies how many codes did you search with?

We examined the admission abstracts for patients known to have experienced an ADR. We looked for codes containing the term ‘drug-induced’ and for external cause codes (adverse effects in therapeutic use) – these we termed ‘ICD ADR codes’ but we also looked for ‘sign and symptom codes’. We hope that the additional information provided in the narrative (Lines 78 – 88 and Supplementary Table 1, Additional File 1) will provide the reader with a
better understanding of which codes we considered and of how restrictive (or not) these were.

b. Please provide a brief discussion of the limitation of the gold standard determination in the primary study (e.g., lack of pharmacist use, lack of taking medication histories in all pts, etc.) This is important, because if you did not identify all ADR cases in your primary study, your estimate of sensitivity may be falsely high.

We have provided additional detail which relates to the methodology of the prospective study inclusive of the make-up of the research team (Lines 50-61). A discussion of the limitations of the primary study has been added (Lines 124-134).

8. For reference number 3 the journal is incorrect.

Thanks – we have updated this.