Author’s response to reviews

Title: Prescribing errors in electronic prescriptions for outpatients intercepted by pharmacists and the impact of prescribing workload on error rate in a Chinese Tertiary-care Women and Children's Hospital

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Author’s response to reviews:

Response to reviewer 1

Dear Reviewer:

Thank you for your comments concerning our manuscript entitled “Prescribing errors in electronic prescriptions for outpatients intercepted by pharmacists and the impact of prescribing workload on error rate in a Chinese Tertiary-care Women and Children's Hospital (BHSR-D-19-01477)”. Main revisions in the paper and the responds to the reviewer’s comments are listed as follows:

Comment 1:

One of the main features of this study was that the authors explored many potential factors associated with prescription error using logistic regression. Many of the predictors is a multi-level categorial variable. An overall p-value should be obtained from the likelihood ratio test. Alternatively, the r by c chi-square test should give similar results.

Response: Thank you for your advice. The likelihood ratio test was performed by SPSS. The overall p-value of each predictors was added in Table 2. We also added the p-value indicating the goodness of fit of the model (revised version: under the subheading “Analysis of prescribing errors”, page 7, line 12-13).
Comment 2:

Related to comment 1), when writing the results of these regressions (page 7 lines 1-7), it's also useful to also state the comparators. For example, "pediatric patients aged 29 days to 12 years of age were more likely to experience prescribing error", than whom?

Response:

Thank you for your comment. We had revised the expression in the manuscript (revised version: page 7, line16-18).

“Prescribing more drug orders in one prescription was a potential risk factor as error rate tended to rise along with the increasing number of drug orders (between 1 and 5) in each prescription. Pediatric patients aged 29 days to 12 years were more likely to encounter prescribing errors, compared with neonates, adolescents and adults. Physicians prescribing on weekdays (0.39%) were more likely to make prescribing errors than on weekends.”

Comment 3:

Lastly, the study wanted to explore the potential impact of prescribing workload on error rate. This seems to be the emphasis of the paper as it's also in the titled. However, the analysis of prescribing workload on error rate, differed from other analyses as the authors used Spearman correlation. There are two issues, the first is that the sample for analysis is now only the 32 time slots instead of the full dataset of over 150,000 prescriptions. The second issues is that the Spearman correlation is very sensitive to outlier. Particularly the point with the highest error rate is also the estimate with the highest imprecision (from figure3). As the authors have the time of each individual prescription, it could be assigned the prescribing workload for that corresponding period and logistic regression could be used similar to other previous analyses.

Response:

Thank you for your comments. We had included the workload as a predictor in the logistic regression analysis according to your advice. We have calculated the workload at each time-interval and divided the workload into two parts, namely high workload and low workload, in accordance to whether the workload is more than the median value of workload of each time interval. The result also showed there was not association between the workload and prescribing errors (p=0.97, OR 1.00[0.83-1.19]).

We did not discard the scatter plot because it can visually reveal the link of prescribing error rate and prescribing workload. All of the points in the Fig 3 were the average value of 91 days at the same time interval. The calculation was presented below: (revision version: under the subheading “The trend of prescribing workload and error rate over time and the relationship between them”, page 6, line 17-29)
The value of workload was calculated by the formula: Set \( N = \frac{\text{Total number of prescriptions}}{\text{Total number of physicians at one time interval (15mins)}} \), then workload (8:00-8:15) = \[ N_1 (2015-9-1\ 8:00-8:15) + N_2 (2015-9-2\ 8:00-8:15) + \ldots + N_{91} (2015-11-30\ 8:00-8:15) \] / 91 days. The error rate was calculated by formula: Set \( n = \text{Number of prescriptions with errors at one time interval (15mins)} \), \( m = \text{Total number of prescriptions at one time interval (15mins)} \), then error rate (8:00-8:15) = \[ \frac{n_1 (2015-9-1\ 8:00-8:15) + n_2 (2015-9-2\ 8:00-8:15) + \ldots + n_{91} (2015-11-30\ 8:00-8:15)}{m_1 (2015-9-1\ 8:00-8:15) + m_2 (2015-9-2\ 8:00-8:15) + \ldots + m_{91} (2015-11-30\ 8:00-8:15)} \] * 100\%. The workload and error rate of other time interval was calculated by the same formula.

The point with the highest error rate indicated the final time interval of the day shift. The cause of the high error rate we had analyzed in the discussion. (revised version Page 9, lines 12-15: Given the hypotheses that physicians prepared to leave on time to avoid traffic jam in the final hour, relaxing and distraction were considered the key factors leading to poor practice. This result was similar with study by Vik et al. that patients care tended to suffer from errors during the end of both 8-hour and 12-hour shift, compared to beginning of each shift.) Based on the fact that each of point was the average value of 91 days, we did not exclude the highest point from this study.

Comment 4:

The manuscript may also improve if it is review by a native English speaker

Response:

Thank you for your advice. We had invited a native English speaker to revised the manuscript, and all the language revision had been retained in Microsoft Word format.

Response to reviewer 2:

Dear Reviewer:

Thank you for your comments concerning our manuscript entitled “Prescribing errors in electronic prescriptions for outpatients intercepted by pharmacists and the impact of prescribing workload on error rate in a Chinese Tertiary-care Women and Children's Hospital (BHSR-D-19-01477)”. Main revisions in the paper and the responds to the reviewer’s comments are listed as follows:

Comment 1

Under the subheading 'Setting and Study population', page 4, line 11; study method is described as 'This cross-section study' while in page 5, lines 32 and 33; there is a subheading labelled 'Control cohort' under which the study method is described as 'a control cohort'. Please explain.

Response:

Thank you for your comment. ‘Control cohort’ was a wrong expression and what we actually meant was ‘control group’. This was a cross-section study, and we selected the normal prescriptions without errors as control group during the same study period. We had revised the manuscript in page 5, lines 25-28.
Comment 2
Page 6, lines 16 - 19; under subheading 'The trend of prescribing workload and error rate over time and the link between error rate and prescribing workload' it is mentioned that 'We performed time series analysis of prescribing workload as well as error rate during a day shift'. Please elaborate on this analysis ensuring assumptions were met.
Response:
Thank you for your comment. We had elaborated the analysis as follow(Page 6 lines 19-29):

‘The value of workload was calculated by the formula: Set N= Total number of prescriptions / Total number of physicians, at one time interval (15mins), then workload (8:00-8:15) = [N1 (2015-9-1 8:00-8:15) + N2 (2015-9-2 8:00-8:15) + …… + N91 (2015-11-30 8:00-8:15)] / 91 days. The error rate was calculated by formula: Set n=Number of prescriptions with errors at one time interval (15mins), m=Total number of prescriptions at one time interval (15mins), then error rate (8:00-8:15) = [n1 (2015-9-1 8:00-8:15) + n2 (2015-9-2 8:00-8:15) + ……+ n91 (2015-11-30 8:00-8:15)] / [m1 (2015-9-1 8:00-8:15) + m2 (2015-9-2 8:00-8:15) +……+ m91 (2015-11-30 8:00-8:15)] * 100%. The workload and error rate of other time interval was calculated by the same method.

Comment 3
Page 7, lines 2 and 3; it is mentioned 'Polypharmacy was a potential risk factor as we observed that error rate rose with the increase number of drug orders (between 1 and 5) of each prescription.' However, this is not one of the factors specified by authors to be studied as factors were clearly listed in the 'Methods' section under subheading 'Subgroup analysis of errors' lines 39 and 40 as 'The subgroup analysis of prescribing errors was conducted according to number of drug orders, age group of patients, seniority of physicians, specialty of physicians and work day.', and the number of drug orders explained in page 5, lines 41 - 43 as 'Number of drug orders indicated the number of orders at each prescription, not the total drugs a patient was taking at the time.' So, it is not clear why polypharmacy was mentioned here.
Response:
Thank you for your comment. ‘Polypharmacy’ in our study indicated multiple drug orders in one prescription, accordingly corresponding to the factor of number of drug orders. This study was conducted at outpatient setting which differed from many other studies conducted at inpatient setting and we had adopted the phrase of ‘polypharmacy’ by mistake. We used the phrase ‘multiple drugs in one prescription’, replacing ‘polypharmacy’ in the manuscript (Page 7, lines 14 and 16).

Comment 4
The relation between error rate and prescribing workload of physician
Page 7, line 12; it is mentioned 'As to the trend of error rate over time', but I think it is not possible to assume trend based on Figure 3 as it represents a snapshot for only one working day. Please, clarify. Response :
Thank you for your comment. The value of the dot in Figure 3 was the average value of each corresponding time interval of 91 days (study period).
Give the value of workload and error rate at time interval 8:00-8:15 as example, the value of workload was calculated by formula:
Set N= Total number of prescriptions / Total number of physicians, at one time interval (15mins)
Workload (8:00-8:15) = [N1 (2015-9-1 8:00-8:15) + N2 (2015-9-2 8:00-8:15) + …… + N91(2015-11-30 8:00-8:15)] / 91 days.

The error rate was calculated by formula:

Set n=Number of prescriptions with errors at one time interval (15mins)
m=Total number of prescriptions at one time interval (15mins)
Error rate (8:00-8:15) = [n1 (2015-9-1 8:00-8:15) + n2 (2015-9-2 8:00-8:15) +……+ n91 (2015-11-30 8:00-8:15)] / [m1 (2015-9-1 8:00-8:15) + m2 (2015-9-2 8:00-8:15) +……+ m91 (2015-11-30 8:00-8:15)] * 100%

The value of workload and error rate at other time interval was also calculated by the same formula.

Therefore, the Figure 3 presented the trend of workload and error rate over time during one working day. We had added the specific calculation in the manuscript (Page 6, lines 17-29).

Comment 5
Page 9, line 21; it is not clear how authors reached to a conclusion that 'No patient harm due to medication error was received'. This is because according to the system explained in the study, nothing explaining if a patient harm occurred due to a medication error, how this will be documented and reported.

Response:
Thank you for your advice. Our service provided a telephone number to public for consultation, such as the usage of the medications or the method to deal with suspected ADRs. There might be some circumstances as follow when no patient harm was received by telephone: a) No error occurred. b) Error occurred, but no harm happened. c) Error and harm occurred, but not severely, therefore the patient did not care about it. d) Severe harm happened, but patients were unable to give feedback to our service by telephone.

Because the possibility of circumstances of b), c), and d) cannot be ruled out, we deleted the sentence ‘No patient harm……prior to the drug being dispensed.’, avoiding being misunderstood, although it may reflect the importance of intervention by pharmacists to some extent.