

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Medicine Authentication Technology: A quantitative study of incorrect quarantine, average response times and offline issues in a hospital setting
<b>AUTHORS</b>	Naughton, Bernard

### VERSION 1 – REVIEW

<b>REVIEWER</b>	U. Holzgrabe Institute of Pharmacy, University of Wuerzburg, Germany
<b>REVIEW RETURNED</b>	01-Oct-2018

<b>GENERAL COMMENTS</b>	The study achieves what we are expecting: An offline period is a Problem for digital drug screening and/or medicine authentication with an end-to-end Approach. I think this is not worth to be studied and published. In Addition it would be nice to discuss the Situation in other countries than UK.
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<b>REVIEWER</b>	Abubakr Abdelraouf Alfadl Unaizah College of Pharmacy, Qassim University, Saudi Arabia
<b>REVIEW RETURNED</b>	06-Oct-2018

<b>GENERAL COMMENTS</b>	<p>GENERAL</p> <p>The subject of this paper is a replication of a previous study, but with one alteration (inclusion of an audio alert) with an aim of improving detection rate. I think this is a substantial improvement worth researching but, as such, I'm expecting to see clear explicit paragraphs in the 'Result' and 'Discussion' sections commenting on the effect of the newly included technique. For example, comparing detection rate in the two studies and commenting on whether a significant improvement had been achieved as a result of the new alteration.</p> <p>SPECIFIC</p> <p>Abstract Page 2, 57; add the full term of the abbreviation SF the first time it appears.</p> <p>Results False Quarantine and False Negatives This section presented only the sensitivity (true positive) which is 98.3% <math>\{[(2188 - 37)/2188]*100\}</math>, although it was mentioned that 'the basis and effective diagnostic test relies on its sensitivity and specificity'. This may imply that specificity (true negative) of the detection system is 100%. However, I would prefer the author add the results of both sensitivity and specificity explicitly. In other words, how many of the 96% of the 'Authenticated' detected as</p>
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	<p>such, how many of the 1% of 'Pack Expired' detected as such, and so on.</p> <p>Response Times Page 13, line 11; add the word 'average' before 'response time' because it is the study average response time not actual response time.</p> <p>Workarounds Page 13, line 35; add the full term of the abbreviation SOPS the first time it appears.</p> <p>Page 16, line 7; typing error in the word 'dischargetal'</p>
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<b>REVIEWER</b>	Dr Geetha Mani Karpaga Vinayaga Institute of Medical Sciences and Research Centre, India
<b>REVIEW RETURNED</b>	16-Oct-2018

<b>GENERAL COMMENTS</b>	<p>Substandard and Falsified Medicine Detection in the Hospital Setting: False quarantine, offline incidents and response times</p> <p>Dear Author, Cordial Greetings!!</p> <p>This manuscript focuses on the need of the hour. I would like to point out a few suggestions that could improve the clarity of the article.</p> <ol style="list-style-type: none"> <li>1. In Abstract- The Design section mentions a few results which could be removed. Kindly mention the study design alone.</li> <li>2. Kindly introduce the terms prominently and then you may use the acronyms. For example, though the definition of substandard and falsified medicines have been mentioned in the introduction, the acronym appears later in the page for the first time.</li> <li>3. "Examples of SF medicines" This statement could be reframed. It is rather instances of SF medicines that are more common in LMICs.</li> <li>4. Introduction could be improved by emphasising the burden of the SF medicines through a few more examples.</li> <li>5. Introduction also mentions a lot about the methods in the study which could be replaced under Methods.</li> <li>6. Page 2, Line 28 to 30: statements like "the study generated a wealth of data...." could be rephrased without being opinionated.</li> <li>7. Figure 1 does not give any additional detail. Hence can be removed.</li> <li>8. Most of the content under Results could be added in Discussion section.</li> <li>9. Page 11; Lines 31 to 40 which discusses the sensitivity and specificity could be best placed under Methods after rephrasing.</li> <li>10. Page 14; Line 40- Table number has been mentioned as 3 instead of 4.</li> <li>11. Discussion may be improved by explaining the comparing the reference studies further.</li> </ol> <p>The methodology as we understand is perfect. I would like to suggest minor revisions modifying the write-up so that the flow of information is clear and consistent.</p> <p>Best wishes..</p>
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## VERSION 1 – AUTHOR RESPONSE

### Reviewer 1

1. I agree that for some stakeholders the concept of offline issues is expected. However, many practitioners are unaware of the implications of the EU FMD and professional bodies around Europe have not provided guidance on the penalties regarding failure to authenticate during offline periods. Also unlike other digital solutions which are optional for health care providers, this technology will be mandatory which creates a different kind of tension. The current rhetoric from database providers explains that systems will not 'go down' or experience offline instances. However, the evidence provided in this piece demonstrates that centralised database off-line issues are likely and therefore this evidence will support discussions with database system providers. The author believes that this article has the capacity to raise an important issue, grounded in practice with potential for policy and practice impact. As the evidence is gathered in the UK, and these systems will not be in place until February 2019 in Europe, it was not possible to gather data in any other regions.

### Reviewer 2

1. General: This is an important point that has been raised. The data you have requested has been collected, and has been intentionally left out and will be published in due course in a separate paper. This is because the change in technology and the corresponding results are associated with social science factors which require an in-depth analysis which is better suited to a social science journal.

#### 2. Specific:

Abstract: Page 2, 57: Thank you very much, this amendment has been made.

Results: Incorrect quarantine and false negatives. Your points are entirely relevant and well received.

As I have

mentioned above, the data regarding the detection rate (how many were quarantined) and authentication

rates (how many were scanned) have not been provided as the change is due to a social science phenomenon which would not fit in with this journal in terms of style and word limit. Thank you for taking the

time to perform a calculation. However incorrect quarantine is due to a failure of a staff member to adhere to an

alert and is therefore disconnected from the technology sensitivity itself which is deemed to be 100% as demonstrated through prior technology testing. Therefore a calculation for sensitivity has been intentionally omitted.

Response Times: Good point. Thank you. Throughout this paper 'Response Time' has been changed to

"Average Response Time"

### Reviewer 3:

1. The design describes the percentage of medicines serialised i.e 4%. This is part of the design and not a

result. However, your point is valid and I have therefore made an amendment to make this clearer. I have

also removed the 2,188 number as this is a result and not part of the design.

2. The SF term has been written in full the first time it is mentioned.

3. The word example has been replaced with 'instances'.

4. Considering the focus of the paper is to look at SF medicines in the UK, I have decided to focus on high

income country examples. However, I have provided references for instances of SF medicines in LMIC's and

provided further references to regions and malaria as an example condition affected by SF medicines.

5. The introduction does mention some methods, which is an oversight on my behalf. Thank you for

- highlighting this. The latter end of the introduction has been moved to the methods section.
6. This has been changed from 'A wealth of data' to a 'large data set'. Thank you for highlighting this.
7. This is a valid point. Although it doesn't add much it supports the explanation in the text and in my opinion improves the readability of the paper. I would like to keep it in, but I am fully willing to remove it if the reviewer wishes.
- 8 and 9. A large section of the results has been reworded and moved to the methods section. The results section now only contains results and all discussion or methods content has been removed. Please note that this study not only looked at the new results created by the repeat study but also extracted previously unpublished data from the Naughton et al. study to compare with the repeat study.
10. Thank you for identifying this. The error has now been corrected.
11. A clearer comparison between studies has been added.

Other errors identified by the author since submission

1. P 12 line 31: 'across' replaced with 'a cross'
2. P 12 line 42: The word 'related' has been repeated in error. This has now been removed.
3. P12 line 42: 'understanding of whats happens in practice' replaced with 'Understanding of practice'
4. P16 line 35: The word 'compliance' replaced with 'effectiveness'
5. The term 'False Quarantine' has been replaced with 'Incorrect quarantine' throughout the paper.

#### VERSION 2 – REVIEW

<b>REVIEWER</b>	Abubakr Abdelraouf Alfadl Unaizah College of Pharmacy, Qassim University, Saudi Arabia
<b>REVIEW RETURNED</b>	05-Nov-2018

<b>GENERAL COMMENTS</b>	<p><b>GENERAL</b> The manuscript was improved and clarity enhanced with most of points being satisfactorily addressed.</p> <p><b>SPECIFIC</b> Method Objectives better to be rephrased as follow:</p> <ul style="list-style-type: none"> <li>• To establish MA technology offline frequency in the repeat study (i.e. how often the system failed to connect to the medicines verification database), and compare with the published results in Naughton et al., 2016,</li> <li>• To identify the frequency of false incorrect quarantine in the repeat study, and compare with the published results in Naughton et al., 2016,</li> <li>• To identify MA average response times in the repeat study (i.e. how long it took for the technology to communicate with the database and return a response) and compare this to the published results in Naughton et al., 2016,</li> <li>• To observe workarounds associated with the MA approach in the repeat study, and compare with the published results in Naughton et al., 2016.</li> </ul> <p>Discussion I think Standard Operating Procedures is abbreviated as (SOPs) not (SOPS's) or (SOP's).</p>
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<b>REVIEWER</b>	Geetha Mani Karpaga Vinayaga Institute of Medical Sciences and Research Centre, Tamil Nadu, India
<b>REVIEW RETURNED</b>	18-Nov-2018

<b>GENERAL COMMENTS</b>	<p>Dear Author, Cordial Greetings!!</p> <p>The changes done by the authors have improved the quality and readability of the manuscript. However I would like to suggest the following changes.</p> <ol style="list-style-type: none"> <li>1. The title seems so long, hence could be shortened to be more specific.</li> <li>2. Page 3- Lines 33-51: Under Strengths and Limitations, repeated use of the term "This study" could be avoided.</li> <li>3. Page 4- Line 9: "There" to be replaced with "The".</li> <li>4. This study according to the authors is a replication of a previous study by the same authors with only one addition- the audio alert. Hence this added tool could be mentioned in the objective to explain the purpose of the study.</li> <li>5. The number of objectives could be reduced to two. The objectives could be made more specific.</li> <li>6. Page 10- Lines 8-13: These sentences do not serve the purpose of the study and hence may be removed.</li> <li>7. Kindly introduce the terms before you use acronyms (as in UK)</li> <li>8. The standard of language of the content under "Introduction" and "Methodology" could be improved to make it more concise and comprehensive.</li> </ol> <p>Thank you. Best wishes..</p>
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## VERSION 2 – AUTHOR RESPONSE

Firstly, I would like to thank the reviewers for the time they have taken to review this paper for a second time. I am pleased with how the paper has evolved and I have valued their input. Please find below my response to the suggestions, all of which I have endeavoured to incorporate.

Reviewer 1:

-Method: Thank you for your suggestion regarding the objectives, I have amended them as per your request. I believe that your approach improves the readability. For clarification, false quarantine, and offline issues were recorded in the 2016 study data but were not published as part of the Naughton et al., 2016 paper. However, response times were. I have made it clear which objectives compares to published data and which objectives compare to previously gathered but unpublished data. I have also made it clear that workarounds were only examined in the repeat study. According to the other reviewer's comments, I have amalgamated objective one and two to reduce repetition.

- The abbreviation SOP has been corrected throughout this paper, as per your instructions.

Reviewer 2:

1. I have reviewed the title and made it more succinct without removing the descriptive study terms required by the journal.

2. The language within the Study Strengths and Limitations section has been diversified to remove repetition of the phrase "this study"

3. Page 4 line 9 - This typo has been amended - Thank you

4. We have mentioned the audio alert in the objectives and added the following line to the discussion 'Although the addition of the audio alert did not appear to affect the technical parameters measured in this paper i.e. technology response times, false quarantine or offline instances. Further, research is required to understand the effect of this user instigated alteration on overall technology use and compliance'

5. I have grouped objective one and two and I have also clarified the objectives also which has reduced the objectives from four to three.

6. These sentences have now been removed

7. The abbreviated terms have been introduced in full before being abbreviated.

8. The language in the introduction, methodology and throughout the paper has been improved to make it more concise and comprehensive.

Thank you again for your contribution to this paper,

#### **VERSION 3 – REVIEW**

<b>REVIEWER</b>	Abubakr Abdelraouf Alfadl Unaizah College of Pharmacy, Qassim University, Saudi Arabia
<b>REVIEW RETURNED</b>	06-Dec-2018
<b>GENERAL COMMENTS</b>	I think all concerns were satisfactorily addressed.