Author's response to reviews

Title: A clinical decision support tool to screen health records for contraindications to stroke thrombolysis-a pilot study

Authors:

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Author's response to reviews: see over
Point-to-Point Response to Reviewers’ Comments

Reviewer: Damian Borbolla

Reviewer's report:
The authors performed the requested modifications.

Response:
We thank the reviewer for kind comment.

Reviewer: Farrant Sakaguchi

Reviewer's report:
I like the paper. I believe it is improved. However, I still feel like further refinement is necessary.

Major Compulsory Revisions:
Comment #1:
I have no single major compulsory revision. I have enough discretionary revisions that I hope that many will be addressed prior to publication.

Minor Essential Revisions:

Comment #2:
I would recommend against the abbreviation on page 4 lines 3-5. The abbreviation for the US Health Information Technology for Economic and Clinical Health Act is "HITECH." If the abbreviation for Information Technology (IT) or Health Information Technology (HIT) is used, it should not break up the name of a specific name or piece of legislation.

Response:
We thank the reviewer for pointing out a shortcoming in our manuscript. The text has been revised as thoughtfully recommended by the reviewer. (Page 4 lines 5)
Comment #3:
Please review the difference between EFFICACY and EFFECTIVENESS trials. http://www.ncbi.nlm.nih.gov/books/NBK44024/ Rather than a trial of the CDS "efficiency" I would consider this an "efficacy" trial. I assume that "efficiency" refers to the speed of the task completion, but I still believe the research methodology should use more established design criteria unless a more compelling argument is made.

Response:
We thank the reviewer for another valid comment on our manuscript. We have revised the term in response to the reviewer’s comment. (Page 2, line 8)

Comment #4:
Abstract: Materials and Methods, Page 2, lines 11-19. Please rewrite, following the reporting guidelines from either CONSORT or STROBE. http://www.equator-network.org/reporting-guidelines/consort/ or http://www.equator-network.org/reporting-guidelines/strobe/ The study design is significantly more clear in the full Methods section, but this deserves better organization. I would recommend identifying A) the study design (e.g. pre-post design vs cross-over design), B) the mock patient case development, C) the study cohort, and D) the task for the study participants.

Response:
The Abstract: Materials and Methods section has been revised as thoughtfully recommended by the reviewer. (Page 2, line 12 to Page 3, line 4)

Revised text in the Abstract: Materials and Methods section:
A CDS tool was developed to rapidly screen health information in seven affiliated hospitals for contraindications to stroke thrombolysis. A fixed-sequence, 2-period crossover study was conducted to test the efficacy of the CDS tool. Four mock patient records derived from the stroke registry that contained a total of nine contraindication items in two or more of the hospitals were used for testing purposes. The test patients were preset and balanced between groups with and without the CDS tool appearing six times in each group before recruiting the participating physicians. Physicians who were responsible for thrombolytic therapy and willing to sign informed consent were
recruited. The participating physicians were asked to check a list of contraindications for two of the patients by using a shared electronic medical record system among the seven hospitals with and without the CDS tool. The test time and missed contraindications were recorded and analyzed statistically.

**Discretionary Revisions:**
I apologize for not identifying these more explicitly before. I like your paper overall, but feel the writing should be significantly strengthened. The grammar is fine, but the flow would benefit from significant refinement. While not all of my recommendations needs to be followed, if I were to have my name on this paper, I would consider the following changes.

**Comment #5:**
Abstract: Background, Page 2, line 4. Recommended changes in CAPS. Start the sentence “THE USE OF intravenous thrombolysis…”

**Response:**
We have revised the sentence according to the reviewer’s suggestion. (Page 2, line 4)

**Comment #6:**

**Response:**
We have revised the sentence according to the reviewer’s recommendation. (Page 2, line 7-9)

**Comment #7:**
Abstract: Conclusions, Page 3, line 13. If you have the space, I would recommend something about the mechanism by with the CDS works. For example, “By extracting or identifying relevant contraindications, the CDS tool may reduce the time needed…”

**Response:**
We have revised the sentence according to the reviewer’s thoughtful recommendation. (Page 3, line 16)

Revised text in the Abstract: Conclusions section:
By screening health records for relevant contraindications, the use of a CDS tool may reduce the time needed to review medical records and reduce the number of missed contraindications for stroke thrombolysis.

Comment #8:
Background, Page 4. Starting with the HITECH act does not seem to fit in with the rest of the paper. I would recommend starting with your second paragraph. (page 4, line 11).

Response:
The first paragraph has been deleted as thoughtfully recommended by the reviewer. (Page 4, line 3)

Comment #9:
Background, Page 4. I still do not understand the relevance of the HITECH act with regards to your intervention. Your tool would not be relevant to Meaningful Use, even if it were available in the US. Meaningful Use has not yet shown any improvements in the delivery of care to date. Thus, I would remove the first sentence (page 4, line 3-5). I would move the last sentence in the paragraph (Strong evidence supports…) to be the first, and I would change the next sentence to: A systematic review of the literature shows that most studies report that health IT interventions...

Response:
The first sentence has been deleted. The first paragraph has been revised as thoughtfully recommended by the reviewer. (Page 4, line 3-6)

Comment #10:
Background. I do not have specific recommendations for the order, but feel that much of the literature cited in the Discussion would work better in the Background and would create a more compelling argument for the need for your CDS tool.
Response:
We thank the reviewer for this comment. Since we have described the complicate decision making process and risk of serious complications of stroke thrombolysis in the “Introduction” section, the need of a useful tool to support clinical decision making may be evident. It may be appropriate to use the literature in the “Discussion” section.

Comment #11:
Methods: Page 6, line 13-16. The following sentence should be used as a closing sentence in the background or else as the first sentence in this paragraph. Suggested minor changes in CAPS. (The CCHS iStroke was developed to allow for rapid screening of THE relevant medical history for stroke thrombolysis among all ELECTRONIC CCHS hospital RECORDS to support clinical decision making.)

Response:
We have revised the sentence according to the reviewer’s suggestion. (Page 6, line 12-14)

Comment #12:
Methods, CCHS iStroke: Page 6. There should be 1 sentence indicating the total number of contraindications for tPA according to the guidelines, and the number or percentage or significance of those contraindications identified by iStroke.

Response:
We thank the reviewer for this valid comment. A sentence has been added in response to the reviewer’s thoughtful comment. (Page 6, line 8-9)

Text added in the Methods CCHS iStroke section:
In a total of 26 contraindications, 17 (65%) are regarding information that can be extracted from medical records reported before the stroke.

Comment #13:
Methods, CCHS iStroke: Page 7, lines 5-7. I would recommend moving the sentence “The treating physician…” down to line 13, just before the last sentence. This way,
the flow is more logical, describing the application and database, then how it is used.

**Response:**
We have revised the paragraph according to the reviewer’s suggestion. (Page 7, line 2-12)

The revised paragraph:

The app also synchronously accesses the shared EMR of the seven hospitals for contraindications, laboratory results, and brain imaging results that were generated in the last 24 hours (Figure 1). The app includes forms for National Institute of Health Stroke Scale score assessment, treating criteria assessment, physician visit time record, informed consent, tPA dose calculator, relevant laboratory results, computed tomography images of the brain, and a visual aid for risk communication (Figure 2). The result of contraindication item search is presented below the checkboxes of the item when the physician assesses for treating criteria (Figure 2). The treating physician could further confirm this information with the patient and/or family member(s) or by checking the EMR to be able to make a clinical decision for thrombolysis more rapidly and accurately.

**Comment #14:**
Methods, Test use of the CCHS iStroke: Page 7, line 17. I would recommend changing the subsection heading to “EVALUATION of the CCHS iStroke.”

**Response:**
The sentence has been revised according to the reviewer’s suggestion. (Page 7, line 16)

**Comment #15:**
Methods, Page 8, line 1-3. I would recommend changing the sentence to something like the following (recommended changes in CAPS). “To limit the situational variables and increase the significance, four mock patient records WERE GENERATED. THESE RECORDS WERE DERIVED from the stroke registry that contained records from two or more CCHS hospitals.”

**Response:**
We have revised the sentence according to the reviewer’s suggestion. (Page 7, line 18
to Page 8, line 2)

**Comment #16:**
Methods, Page 8, line 3-4. I would recommend moving this sentence “Table 1 shows…” down to line 11 before the sentence “The four cases…”

**Response:**
The paragraph has been revised according to the reviewer’s suggestion. (Page 8, line 9-12)

**Comment #17:**
Methods, Page 8, line 11. I would recommend a sentence something like, “Of the 13 total contraindications for tPA, iStroke helps to identify 10 that can be extracted from the EHR…”

**Response:**
We have revised the sentence according to the reviewer’s suggestion. (Page 8, line 10-12)

The revised text:
*Of the 17 total contraindications for stroke thrombolysis that can be extracted from the EMR, the four cases had six different and a total of nine contraindications.*

**Comment #18:**
Methods, Page 8, lines 11-12. I would recommend rewriting something like, “The four cases had A TOTAL OF NINE CONTRAINDICATIONS, SIX OF WHICH WERE UNIQUE.”

**Response:**
We thank the reviewer for this commend. However, the total number of contraindication was 9 was because that 1 contraindication was shared by 3 cases and 1 by 2 cases. We think that our original description may be appropriate.

**Comment #19:**
Methods, Page 8, Lines 12-13. I would recommend moving the sentence “Case 3 had a record…” to line 16, after describing Case 2 and prior to discussing Case 4.

Response:
We have revised the paragraph according to the reviewer’s suggestion. (Page 8, line 15-16)

Comment #20:
Methods, Page 8, line 18. I would recommend starting a new paragraph after “…a known history of diabetes and stroke.” I would begin it something like, “A pilot study using a pre-post (vs crossover) design was used to study the efficacy of the CDS tool.”

Response:
A sentence has been added according to the reviewer’s suggestion. (Page 9, line 1-2)

The text added:
A pilot study using a fixed-sequence, 2-period crossover design was conducted to study the efficacy of the CDS tool.

Comment #21:
Methods, Page 8, line 19, I would recommend changing the sentence to something like, “…with the CDS tool SO THAT EACH MOCK PATIENT APPEARED SIX TIMES IN EACH GROUP.

Response:
We have revised the sentence according to the reviewer’s suggestion. (Page 9, line 2-4)

Comment #22:
Methods, Page 9, Line 1. I would recommend changing the sentence to something like, “…during off-duty hours WERE RECRUITED AND INFORMED CONSENT WAS OBTAINED.”

Response:
The sentence has been revised according to the reviewer’s suggestion. (Page 9, line 4-7)

**Comment #23:**
Methods, Page 9, line 3. If you identify that the number of participants was limited to 12, please explain the rationale – e.g. power calculation. If this was not predefined in the study protocol, then eliminate that sentence.

**Response:**
We thank the reviewer for this commend. The sentence has been revised to avoid ambiguity. (Page 9, line 7-8)

The total number of participating physicians was set at 12 because each mock patient appeared six times in both groups with and without the CDS tool.

**Comment #24:**
Methods, Page 9, Line 4. Recommend creating a new paragraph here and rewriting the sentence to something like, “EACH PARTICIPANT WAS PRESENTED WITH A SET OF STROKE TEST CASES. EACH CASE BEGAN WITH THE SCENARIO OF THE PATIENT ARRIVING AT CCH WITHIN 1 HOUR OF THE STROKE ONSET.”

**Response:**
The sentence has been revised according to the reviewer’s suggestion. (Page 9, line 10-11)

**Comment #25:**

**Response:**
The sentence has been revised according to the reviewer’s suggestion. (Page 9, line 13-17)
Comment #26:
Methods, Page 9, line 12. Be cautious of identifying control groups here… Due to your study design, there is not really a “control group” but rather a “Control Series” or “set of control cases.”

Response:
We have revised the sentence according to the reviewer’s suggestion. (Page 9, line 17-18)

Comment #27:
Methods: Analysis, Page 9. There really should be some power analysis – how many subjects or the magnitude of the difference that you are looking as you go into the study.

Response:
We thank the reviewer for this comment. Because this is a pilot study of a newly developed application of IT, it may not be feasible to estimate the difference. Therefore \textit{a priori} power analysis may not be appropriate. A power analysis based on the results of this study may be helpful for future study in the real world practice. On the other hand, the usefulness of \textit{post-hoc} power analysis is controversial. [1, 2]

References:

Comment #28:
Results, Page 10. I recommend describing the cases/scenarios prior to describing the participant recruitment. This would follow your Methods section closer. As such, I would suggest starting the paragraph with line 10-11.

Response:
We have revised the paragraph according to the reviewer’s suggestion. (Page 10, line 11-12)
Comment #29:
Results, Page 11, Lines 1-4. The description of the two physicians belongs with the results of the individual participants rather than collapsing the results into “with vs without CDS.” I would recommend moving the sentence “Notably, two physicians…” to Page 10, line 17.

Response:
The paragraph has been revised according to the reviewer’s suggestion. (Page 11, line 3-6)

Comment #30:
Results, Page 11, lines 7-10. I would recommend the following changes, “The time WAS 14.6+/-7.4 MINUTES IN THE CONTROL GROUP AND WAS ONLY 7.3+/-5.2 MINUTES IN THE ISTROKE GROUP (P=0.010). THE TOTAL NUMBER OF MISSED CONTRAINDICATIONS WAS 23 IN THE CONTROL GROUP AND WAS ONLY SEVEN IN THE ISTROKE GROUP…

Response:
The paragraph has been revised according to the reviewer’s suggestion. (Page 11, line 13-16)

Comment #31:
Discussion, Page 11, lines 17-19, Page 12, Lines 1-4. Please see how to use this more in the Background. In the discussion it would be nice to see more about how your CDS tool fits into the literature, not just describing the literature (which is more of a Background thing). Certainly referencing this literature briefly is useful in the discussion, but please spend more time discussing your results and less describing the literature.

Response:
We thank the reviewer for this comment. Since we have described the complicate decision making process and risk of serious complications of stroke thrombolysis in the “Introduction” section, the need of a useful tool to support clinical decision making may be evident. It may be appropriate to use the literature in the “Discussion”
Comment #32:
Discussion, Page 12, Lines 7-19, Page 13, Lines 1-2. Please see how to use this more in the Background. In the discussion it would be nice to see more about how your CDS tool fits into the literature, not just describing the literature (which is more of a Background thing). Certainly referencing this literature briefly is useful in the discussion, but please spend more time discussing your results and less describing the literature.

Response:
We thank the reviewer for this comment. Since we have described the complicated decision making process and risk of serious complications of stroke thrombolysis in the “Introduction” section, the need of a useful tool to support clinical decision making may be evident. It may be appropriate to use the literature in the “Discussion” section.

Comment #33:
Discussion, Page 13, Line 2 – if you do not move the Background material, then the paragraphs describing your study “In our study…” should be the beginning of a new paragraph.

Response:
The paragraph has been revised according to the reviewer’s suggestion. (Page 13, line 10)

Comment #34:
Discussion, Page 13, Lines 9-13. Please see how to use this more in the Background. In the discussion it would be nice to see more about how your CDS tool fits into the literature, not just describing the literature (which is more of a Background thing). Certainly referencing this literature briefly is useful in the discussion, but please spend more time discussing your results and less describing the literature.

Response:
We thank the reviewer for this comment. Since we have described the complicated
decision making process and risk of serious complications of stroke thrombolysis in the “Introduction” section, the need of a useful tool to support clinical decision making may be evident. It may be appropriate to use the literature in the “Discussion” section.

Comment #35:
Discussion, Page 14, Line 2. “Efficiency.” As described above, I believe you are referring to the real-world “effectiveness” instead of the pilot-testing “efficacy.”

Response:
We have revised the sentence according to the reviewer’s suggestion. (Page 14, line 8)

Comment #36:
Discussion, Page 14, Lines 7-12. These sentences would fit better in the Methods section describing the iStroke application.

Response:
We thank the reviewer for this comment. Since we have described how the iStroke app works in the “Methods” section, the sentences may be appropriate in the “Discussion” section.

Comment #37:
It would be interesting in the discussion to mention the number of days saved or the financial benefit gained between the difference of 7.3 minutes saved in reviewing the chart. Also I am curious whether a chart review would still be required as some contraindications are not captured by your CDS tool.

Response:
The CDS tool extracts all medical records that are related to stroke thrombolysis. The CDS tool can also capture lab test results that are required for decision making. However, the treating physician is encouraged to further confirm the information provided by the CDS tool.

Comment #38:
Conclusion, Page 14, line 19. “Efficiency.” As described above, I believe you are referring to trial “efficacy.”

**Response:**
The sentence has been revised according to the reviewer’s suggestion. (Page 15, line 7)

**Comment #39:**
Conclusion, Page 15, line 3. “Efficiency.” As described above, I believe you referring to real-world “effectiveness.”

**Response:**
The sentence has been revised according to the reviewer’s suggestion. (Page 15, line 10)

Thank you again for your insightful comments and help.