Author’s response to reviews

Title: Automatically Identifying Social Isolation from Clinical Narratives for Patients with Prostate Cancer

Authors:

Vivienne Zhu (viviennezh@gmail.com)
Leslie Lenert (Lenert@musc.edu)
Brian Bunnell (bunnellb@musc.edu)
Jihad Obeid (jobeid@musc.edu)
Melanie Jefferson (sweatma@musc.edu)
Chanita Hughes-Halbert (hughesha@musc.edu)

Version: 1 Date: 07 Dec 2018

Author’s response to reviews:

Response to reviewer: We appreciate the reviewers’ careful review of our manuscript and thanks the reviewers for their thoughtful and helpful comments and suggestions. We have made several revisions to respond to these comments and these changes enhance the quality of our report. Detailed information on the changes that were made is provided below.

Reviewer 1

[Comment]* One major concern is the evaluation and manual chart review, particularly on the evaluation of 'control' notes. What was the motivation for choosing only 40 notes for this part of the evaluation? Given the obvious prevalence issue of this construct, this sounds like a very (too) small sample. Why was this evaluation not performed on all notes for a random sample of patients instead? That would more likely give a better estimate of potential false negative rates?

[Response] Following reviewer’s comments, we calculated the number of patients’ notes that should be evaluated using estimates from previous research (citation) to determine the sample size. Based on these calculations, we determined that clinical notes from 69 patients needed to be reviewed to determine NLP algorithm performance. We have added text in the manuscript to describe this process. As shown on page 4 (NLP Performance evaluation), we added “Given a sample size of 1,057 patients in the test dataset and 5% prevalence of social isolation in the elderly from other study,22 we estimated a manually review of 69 patients’ notes would reach
95% confidence of the evaluated performance measures. We anticipated that the rate of NLP identified social isolation positives was similar to the training dataset; the domain experts reviewed chart for all the NLP identified social isolation positives. The domain experts also reviewed clinical notes for randomly select NLP identified negatives, with the patient number as 69 minus the number of NLP identified positive patients. Thus, domain experts also reviewed 154 notes for 52 patients in control group. We also updated the performance measure in Figure 2 and in text.

[Comment] The approach to identify terms for the lexicon/terminology seems generally sound, but will inevitably not necessarily capture all potential synonymous variants. Did you consider other approaches to generate potential synonyms, e.g. using data-driven methods such as word embeddings (e.g. similar to Bejan et al.'s study (ref 10))? 

[Response] Generating a lexicon of social isolation is challenging because there are no documented standards and data collection for social isolation in the EHR is still in the early stage. In order to capture all potential synonymous, we tried to include all resources (e.g., standard terminology, questionnaires, thesaurus, and domain expert knowledge) to identify terms for the lexicon/terminology. During this process, we found a big gap of semantics presentation of social isolation between clinical notes and standard terminology/thesaurus. We provided some information about SNOMED in the discussion. From the thesaurus, “social; isolation” has 32 synonyms; among these, some are relevant to clinical documentation of social isolation and are consistent with the terms suggested by the domain experts (“lack of contact”, “lack of communication”, “loneliness”, “isolated”). Some synonyms were very prevalent, but were used to describe other clinical issues (e.g., “detachment” as for retinal detachment, “withdraw” for drug/alcohol withdraw, “distance” for walking distance). In the limitations section, we added “the lexicon in this study may not include all potential synonymous variants. Data-driven methods (e.g., word embedding) are another way to generate synonymous, and we well explore this approached in future studies.

[Comment] Further to this, as is mentioned in the manuscript, the identified concepts were more likely to be found in specific note types and sections - what was the prevalence of the different note types, and the distributions of found concepts in the different types? What was the motivation for including these particular note types in the study (e.g. radiation oncology)?

[Response] We were not sure which kind of note has most prevalent information of social isolation. Instead of studying one specific note type as in previous studies, we extracted all the notes for this cohort at the beginning, and that sample included 49 note types (e.g., provider notes, nurse notes, etc.). Developing NLP component against all the note types would not be efficient; therefore, we analyzed frequencies to determine the most common types of notes that
were available in the EHR and selected most prevalent types of notes. The notes we included in our analysis covered 95% of the notes that are available in the EHR. In data source, we added in text: “Instead of using all kinds of notes (49 note types) existing for this cohort, we selected most prevalent note types and all of them together covered 95% of note sample.” In results, we added a Figure for distributions of founded concepts in the different note type as well as provider types.

[Comment] The background is concise and well motivated, but there is a lack of definitions and/or discussions about the key concept (social isolation) - this would be important to include to better understand the subsequent methodological work. For instance, the concept of 'social support' is used sometimes as an important variable/concept which probably is synonymous to 'social isolation', some more discussion on the nomenclature and definitions (e.g. from the clinical/epidemiological perspective) would be important to include.

[Response]: As suggested, we now include a definition of social isolation from previous research that examined this construct in population-based samples of adults. As shown in the Background, we now indicate that “Social isolation refers to the extent to which individuals perceive that the quality and quantity of their social relationships are insufficient to meet their social needs). Indicators of social isolation include having limited contact with members of one’s social network, lack of social support, and feeling lonely. Consistent with this, social isolation instruments used in population-based samples ask individuals to self-report the extent to which they lack companionship, feel left out, and feel isolated from others”

[Comment]* Other relevant studies that might be of interest, where identification of social risk factors using NLP including social support have been included:

[Response] we added these two papers in the discussion section.

[Comment] data size: there are mismatching numbers provided about the training data set size: '55,516 clinical notes from 3,138 patients' (Abstract) vs. '3,138 patients (75%) as a training dataset with 150,990 notes to develop the lexicon and NLP pipelines' (Data source) - which number is correct?

[Response] Corrected in abstract: '55,516' to ‘150,990’

[Comment] Chart review: in the section 'Development of NLP algorithm to identify social isolation' it is stated that 'These chart review evaluations were done independently by a domain expert who was blinded to the I2E query development', while in the section 'NLP algorithm
performance' it is stated that two domain experts performed the review. Please explain, and also clarify if this was a blind double-review (if so, what was the agreement?) or if each chart was reviewed only by one domain expert (if so, why?)

[Response] During the NLP algorithm development process, one domain expert reviewed the NLP results generated from the training data set, this process guided the NLP developer to iteratively refine the lexicon and algorithms. After the lexicon and algorithms were finalized, we applied them to the test dataset to evaluate the NLP performance. During evaluation process, two domain experts performed manual review (blinded-double review).

[Comment] * Table 1: very interesting with these examples and prevalence numbers. What was the motivation for not conflating at least capitalized versions of the same concept to one frequency count (e.g. 'social isolation' and 'Social isolation')?

[Response] We intended to report the morphologic and synonymous variations to demonstrate the characteristics of clinical notes; these variations are different from standard clinical terminology.

[Comment] * Resulting NLP approach: will any of this be made available to the research community (e.g. resulting terminology, queries/rules)? What was the motivation for choosing this particular (commercial) NLP system? Did you consider comparing results with other (open source) systems?

[Response] Yes, all resulting terminology, queries/rules are available to the research community by request. We always appreciate collaborative work; making developed NLP components available to other researchers is one of our goals. In fact, we already have provided I2E queries for our fall risk screening project to another medical center, and we are willing to do the same for this project. Our NLP projects always study critical health care issues. Our institution encourages us to utilize highly adopted and evaluated NLP software; Linguamatics I2E is the best NLP commercial software in the market for health care with customers from hospitals, pharmaceutics, and institutions.

[Comment] * Typos (might have missed some here, please ensure a thorough read-through and proof-read before submission)*

[Response] Typographical errors in the text have been corrected.
Reviewer 2

Background

[Comment] * There is lack of definition of social isolation, which is the key concept of this manuscript.

[Response] As described in the response to Reviewer 1, we now provide a definition of social isolation in the Background. Social isolation refers to the extent to which individuals perceive that the quality and quantity of their social relationships are insufficient to meet their social needs (Hawkley and Cacioppo, 2010). Indicators of social isolation include having limited contact with members of one’s social network, lack of social support, and feeling lonely (Cornwall and Waite, 2009). Consistent with this, social isolation instruments used in population-based samples ask individuals to self-report the extent to which they lack companionship, feel left out, and feel isolated from others (Hughes et al., 2004).

[Comment]* The sample of this study was prostate cancer patients. Although the authors mentioned that the that the study sample from a large study, there is still lack of explanation for why using this particular population to explore "social isolation". For example, is "social isolation" is a particular issue from this population or is there any gender or cancer diagnosis consideration regarding social isolation?

[Response]: We now provide our rationale for examining social isolation among prostate cancer patient. As shown under Data Source, we now indicate that “Prostate cancer is one of the leading causes of cancer among men in the United States that disproportionately affects African American men in terms of morbidity and mortality; therefore, this is an important patient population to study with respect to social determinants that increase risk for morbidity and mortality. Previous research has shown that greater social constraints (e.g., strained relationships with family members and friends) is associated with psychological distress among men who have been diagnosed with prostate cancer).” Additional information on our rationale for examining social isolation among prostate cancer patients is also provided under the Background. Specifically, we now indicate that “Recently, Ettridge and colleagues found that prostate cancer patients experience social isolation because of treatment-related side effects (e.g., incontinence). However, studies have not examined the extent to which social isolation is discussed and documented in the electronic health records (EHR) among prostate cancer patients despite recommendations from the National Academy of Medicine to document this issue in electronic clinical notes (EHR).”
Social isolation could be generally categorized as "subjective" social isolation and "objective" social isolation. It was not clear whether the authors wanted to address both types of social isolation or the particular one in this study.

In clinical notes, “social isolation” is usually documented by providers when their patients expressed social isolation. We did not explicitly distinguish if “social isolation” documented in clinical notes is “subjective” or “objective” since we lack of details for such a categorization. In our discussion section, we included some informative data from the literature regarding the prevalence of ‘subjective social isolation and ’objective social isolation’, that supported our study findings.

Method

Under "NLP software" section, it seemed like that the authors tried to use an exemplar to show the usefulness of I2 E. But please indicate that the concept of fall risk is very different from the concept of social isolation.

Although the concept of fall risk screening is very different from the concept of social isolation, our experience with I2E ensures the development of accurate NLP algorithms identifying social isolation from clinical notes.”

Under "Data source" section, the authors stated that "This study was conducted as part of a transdisciplinary center in precision medicine and minority men's health……". Please describe what "minority” men meant. Was any specific ethnicity or race included in the study?

We now provide information about racial disparities in prostate cancer outcomes under Data Source. We have also clarified that our sample was racially diverse and included African American and white prostate cancer patients (see Data Source).

Under "Development of the lexicon for social isolation" section, domain experts' knowledge was added to generate the social isolation terms. Please describe the background and knowledge expertise of those domain experts and why the authors considered that they were domain experts.

We have two behavioral science researchers to help us for the lexicon development. We listed their background in the following sentence and added the researchers’ initials in the text. “The initial list of terms was provided by behavioral science researchers (CHH and MJ) who have extensive expertise in examining health care quality and racial disparities in clinical outcomes.”
Comment: "Live alone" was excluded in the lexicon; however, it could be part of objective social isolation. It was not clear what "WILL SEND CITATION" was indicated in the content. Based on the reference, Hughes et al's reference (titled "A short scale for measuring loneliness in large surveys: Results from two population-based studies"), the scales included in this article were measuring loneliness but not social isolation; but the manuscript content stated they were "Social Isolation Scale", which cannot be found in Hughes' article. Social isolation and loneliness are related but they are still different concepts.

Response: We agree that “social isolation” and “loneliness” are related, but different concepts in standard terminology. However, previous studies have also indicated loneliness is highly similar to social isolation (Hawkely and Cacioppo, Ann Behav Med., 2010) because being isolated from one’s social network and being socially disconnected are the defining features of loneliness (Hughes et al., 2008). Further, indicators of social isolation include feeling lonely and not belonging (Cornwell and Waite, Journal of Gerontology: Social Sciences, 2009). The scale developed by Hughes et al. (2004) measure the extent to which individuals lack companionship, feel left out, or feel isolated from others. We have clarified that we used components from validated instruments such as the Loneliness Scale to generate our lexicon.

Comment: Under "Development of NLP algorithm ....." section, one domain expert was used to chart review. Potentially, it could have a bias by using one domain expert which could be a limitation of this study design.

Response: During the NLP algorithm development process, one domain expert reviewed the NLP results generated from the training data set; this process guided the NLP developer to iteratively refine the lexicon and algorithms. After the lexicon and algorithms were finalized, we applied them to the test dataset to evaluate the NLP performance. During the evaluation process, two domain experts performed manual review (blinded-double review).

Results

Comment: Under "NLP algorithm performance .....", two domain expects were used to validate the results. However, the report of the inter-rater/coder reliability (IRR) was not showed or used.

Response: We added the following text to report IRR as: "Among 194 notes, the two reviewers agreed 36 positives and 153 negatives. The rater agreement is 97.4%.”
It would be clear to give one or two examples to explain why the term "all family" is usually a pre-negation in clinical context.

We added this example in the text as: “(e.g., “all family have drink history” doesn’t necessary mean that the patient has drink history unless supportive information has been identified)

"Nurse practitioner" was showed as one of the most common author types but not "nurse" who may also document patient’s social isolation. I was wondering whether nursing notes were used in this study. Besides, please add the n and % for each author type.

We did not include nursing notes; however, our data about provider type showed that nurse practitioner is one of the common author types in the selected note types.

"identified having social isolation by NLP were more likely to be White and Medicare/Medicaid patients" may be misleading description because the White and Medicare/Medicaid patients were the majority of the sample. Therefore, for the group which was identified as no social isolation, the patients were also likely be White and Medicare/Medicaid.

We re-organized the table, and it still showed that the rate of NLP identified patients was slightly higher in White and Medicare/Medicaid patients; we acknowledge in text as “However, the statistical significance of these observation is undetermined due to small number of NLP identified social isolation positives.”

Under "NLP algorithm performance", two domain experts were used to review the notes but there was no IRR to show the consistency between these two experts.

We added in text to report IRR as: "Among 194 notes, the two reviewers agreed 36 positives and 153 negatives. The rater agreement is 97.4%.”

Based on Table 2, this statement, "African Americans have a slightly lower prevalence of social isolation compared to whites." may be a misleading statement because the number of African Americans was lower than white in the sample. Therefore, the audience also see the same thing in the group identified without social isolation.
We re-organized Table 2 which still shows that Whites have slightly higher rate of NLP identified social isolation than African Americans (1.4% vs. 1.1%).

There was no discussion regarding the finding of the study specifically for prostate cancer patients, which is the sample of the study.

We added in text: “Our study found that prostate cancer patients with evidence of social isolation had similar demographic, social, and economic characteristics leading to multiple risk factors for mortality. Thus, providing sufficient social support to those patients, in addition to medical treatment, is important to improve their quality of life and survival rate.”

The authors mentioned that the social exclusion and social outcast, two SNOMED-CT terms, were not found in clinical notes. However, there was no further discussion regarding this finding. It is suggested to the authors to discuss the possibility of these two terms are not commonly used in clinical settings or between/among providers. The clinical notes are used by the healthcare providers; if providers do not use the social exclusion and social outcast in their work or communicated with others, these two terms may not be showed in the clinical notes.

We added in text: ““social exclusion” and “social outcast” were not found in clinical notes, the plausible explanation is that these two standard SNOMED terms are not commonly used in clinical settings or between/among providers and thus they are not showed in the clinical notes.“

Social support related terms (e.g., lack of social support, limited social support) were included as part of lexicon of social isolation. However, social support and social isolation are different concepts; it could be the reason that social support is listed as another standard concept in SNOMED CT.

We agree that social support and social isolation are different, but related concepts in SNOMED. According to the IOM report (Capturing Social and Behavioral Domains and Measures in Electronic Health Records: Phase 2), “The quantity and quality of an individual’s social relationships can be conceived of in several important ways. The first one is social integration or isolation, or the degree to which a person has social ties or relationships with other individuals, groups, or organizations.” The second way in which social relationships can be understood is the level of social support, which refers to the actual aspect or perceived support or a benefit that a person derives from such relationships.” In a study contacted by Greenwald, Jeffrey L, et all, “poor social support” and “social isolation” are associated with each other and
social support has been used as an indicator of social isolation in previous research (Cornwall and Waite, 2009). Thus, including “lack of social support” and “limited social support” may more completely identify social isolation from clinical notes. However, we acknowledge that including social support in the lexicon may be a potential limitation. We added the following in limitation as “Although “lack of social support” and “social isolation” are associated with each other and impact patients’ outcome together,23-24 “lack of social support” may be a separate social factors.”

[Comment] * Due to the lexicon mixed with social support terms, the authors may need to further discuss it. By presenting that this term is suggested by the domain experts may not be sufficient also could bring an issue of whether the experts understand the difference between social support and social isolation.

[Response]: We added following text in the discussion section: ”Instead, the most prevalent term we found through our NLP analysis, “lack of social support” is not a specific component of the instruments that are used to measure social isolation by self-report; however, lack of social support has been used as an indication of social isolation in previous research (Cornwell and Waite, 2009).”

Limitations

[Comment] * Limitations of this study were addressed properly. Another important limitation which is suggested to consider is that using clinical notes to detect or describe patients’ social isolation has its limitation due to social isolation is subjective; therefore, the clinical notes which are used by the providers may not include all the social isolation information from the patients. The clinical notes capture the most information about providers' observations regarding the patient and some patients' chief complaints. Therefore, to understand whether a patient experiences social isolation, we still need to conduct a comprehensive assessment.

[Response] We modified the last limitation as follows: ”Finally, we developed a highly accurate NLP approach to extract social isolation from clinical notes; however, the clinical notes capture the most information about providers' observations regarding the patient and some patients' chief complaints. Therefore, we remain cautious about claiming an NLP determinant for prevalence of social isolation (1.2%) in patients with prostate cancer, due to the lack of confirmation from other measures. To understand whether a patient experience social isolation, a comprehensive assessment is warranted.”
Moreover, the lexicon in this study may not be completed and also mix with "social support" terms which is different from social isolation.

We added this limitation in the text as: “Second, the lexicon in this study may not be completed and also included "social support" related terms.”

Conclusion

Based on the concern related to including social support related terms in the lexicon of social isolation, there may be a question of whether the NLP algorithms in this study really can accurately identify the patient experienced social isolation.

According to the IOM report (Capturing Social and Behavioral Domains and Measures in Electronic Health Records: Phase 2), “The quantity and quality of an individual’s social relationships can be conceived of in several important ways. The first one is social integration or isolation, or the degree to which a person has social ties or relationships with other individuals, groups, or organizations.” “The second way in which social relationships can be understood is the level of social support, which refers to the actual aspect or perceived support or a benefit that a person derives from such relationships.” “Social isolation” and “lack of social support” are related with each other; especially, “lack if social support” is one of the indicator of “social isolation” in previous study (Cornwell and Waite, 2009). Thus, including “lack of social support” and “limited social support” may be a more accurate way to identify socially isolated patients from clinical notes. We acknowledge that including social support in the lexicon as a limitation. We added text in limitation as “Although “lack of social support” and “social isolation” are associated with each other and impact patients’ outcome together,23-24 “lack of social support” may be a separate social factors.”