Introduction

Healthcare research is intended to improve patient well-being and, ultimately, people's quality of life. (International Working Party to Promote and Revitalise Academic Medicine. ICRAM [the international campaign to revitalise academic medicine], 2004). One of the most important tools for patients' protection in research is the informed consent process, which aims to make sure that participants are well informed prior to deciding whether or not to participate. (“Alliance for Human Research Protection Mission Statement”, 2014; “Final rule-protection of human subjects; informed consent”, 1981). In the Emergency Department (ED) context, acute disease, lack of time, and stressful environment may be barriers to a proper informed consent process (Spivey, 1989; Salzman, Frascone, Godding, Provo & Gertner, 2006). In 2009, there were 136.1 million ED visits in the US (“National Hospital Ambulatory Medical Care Survey”, 2009), making a proper informed consent process a priority for the research enterprise (Cofield, Conwit, Barsan & Quinn, 2010).

Prior work suggests that the process of educating potential participants can be arduous (Cassileth, Zupkis, Sutton-Smith, March, 1980; Roberts, Prieto-Merino, Shakur, Chalmers, Nicholl, 2011). However, well-informed participants may be more likely to participate (Treschan et al, 2003). Previous work has not specifically evaluated the relationship between research participants' self-assessment of their comprehension of a research study and their willingness to participate in it. Also, although there is a growing consensus that informed consent documents are too long (Beardsley, Jefford, Mileshkin, 2007; Brehaut et al, 2012; Ellenberg, 1997; Terranova et al, 2012), there is a relative dearth of empirical investigation into what current elements in the document are considered to be important by patients (Antoniou et al, 2011). Some information given in informed consent documents might be unnecessary for patients' decisions.

Thus, the relationship between self-perceived comprehension and willingness to participate (WP) remains unclear. If the two are related, it would provide further impetus beyond legal mandates to ensure adequate informed consent and would create a case for innovation. Furthermore, it is unclear which elements of current informed consent documents are considered essential by participants. If these can be identified, they can then be more clearly emphasized and perhaps other sections could be omitted. The goal of this study was to measure hypothetical participants' self-assessed comprehension of an informed consent document and the importance given to each topic. We sought to determine if there was any relationship of these measures to WP in a hypothetical trial.

Methods
Design

We performed a prospective online survey study using a convenience sample, as explained below.

IRB Approval and Informed Consent Process

This study has been approved by the Duke University Institutional Review Board. Every participant could choose between “begin the survey” and “I don’t want to be a part of this study” before the questions were exhibited. In addition, all data were collected anonymously.

Development and Pre-Testing

First, we developed the survey in Qualtrics. After building our tool, we ran a pretest on 15 people for pilot testing.

Recruitment Process and Description of the Sample Having Access to the Questionnaire and Survey Administration

To recruit the participants of our study, we used a website called “Amazon's Mechanical Turk” (MTurk). The logistics of the site is based on “workers” and “requesters”. Workers are paid for performing tasks such as answering surveys. Requesters create these tasks for workers to do. Usually, workers are paid a small amount of money for doing their work (in the order of cents). The payment is only confirmed after the requester “approves” the quality of the work done, to discourage users from giving poor answers. Across different kinds of data collection, Amazon's Mechanical Turk has been shown to provide high quality information in a representative population in a short period of time (Buhrmester, Kwang, Gosling, 2011; Mason & Suri, 2012; Rand, 2011).

We included respondents in the United States who had 90% approval rate on their previous tasks. There was no previous contact with the respondents, nor was there any kind of advertisement. The data was collected in 2012, between June and October and the survey was launched 4 times: the pre-test (15 responses) and 3 more waves (50, 50 and 100 responses, in a chronologic order), summing 216 responses. The respondents received US$0,30 each for their work. This target population allows moderate associations to be found, with correlation coefficients with a power of over 80%. 
Survey

We built a computer-based questionnaire that attempted to reproduce a real ED scenario and informed consent process. The survey had 4 parts: (1) The instructions page, where participants could choose not to participate in the study [1 page], (2) the demographics section [1 page], (3) the “informed consent sections” part [from 1 to 28 pages, according to the participant’s choices - 14 title pages and 14 “topic explanation” pages] and (4) final part, where we measured the importance, comprehension and decision of whether or not to participate in the study [3 pages].

Beginning in the third page of the survey, each section title (ie. “Why is this study being done”) would appear, who would have to choose among three options: (1)“Skip this information”, (2)“Read more” and (3)”I am ready to decide whether or not to participate”. These sections were based on the 14 required sections of the informed consent document, as described in the DHHS Federal Code, Common Rule (1991). If the “Read more” item was selected, the participant was taken to another screen providing a deeper explanation of the topic. After reading the text about the topic, participants could choose to proceed to the next section or choose the “I am ready to decide whether or not to participate” option. After finishing all sections, the respondents were asked if they would participate in this hypothetical study. Participants were then asked to rate the 14 topics of the informed consent document in terms of Importance on a scale from 0 to 100, with “100” equating to the most important factor. They were then asked to rank the remaining topics in order. After rating the Importance of items, participants were asked to rate their self-perceived degree of Comprehension in similar fashion, where “0” was “I did not understand this topic at all” and “100” was “I understood everything about this topic”. Our predictor variables were based on the choices to skip or read the topics and the importance and comprehension rates. Our outcome variable was WP in the hypothetical study. Confounder variables included demographics.

In order to check if the participants answered all of the questions of our survey, we inserted a random confirmation code in the last page of the survey. The respondents should write this confirmation code on MTurk to prove that they had gone through the entire questionnaire. As every question of our questionnaire was a “Force Response” (which means that participants had to answer to the question before proceeding), we knew that anyone who had the code had been at least to the last question, answering all of the questions that were previously displayed to them.

Response Rates

Given that the questionnaires were answered in an online environment, in which any person could choose to participate, it is not possible to calculate a response rate.
Preventing Multiple Entries from the Same Individual

Multiple entries were prevented by checking the IP addresses from respondents.

Analysis

We had 216 complete questionnaires. Incomplete surveys were not considered in the analysis.

We ran descriptive analysis, including medians, percentages and, since participants could skip some topics of the informed consent, the median number of sections read. Since these were intentional skips by participants, these were considered data points and not incomplete data.

Also, to aid in the understanding of the complex interactions between the variables, a network analysis was conducted. Compared to logistic regression, network analyses provide the final product of all associations combined as opposed to those conditional on other variables’ constants.

Undirected weighted networks graphs were built based on a point-biserial correlation matrix of Importance and Comprehension items correlated with Willingness to Participate (WP). Partial correlations coefficients were estimated through node-wise multiple regression, with graphical least absolute shrinkage and selection operator regularization, or GeLasso (Friedman, Hastie & Tibshirani, 2008). Penalized model selection was made based on extended Bayesian information criterion, EBIC (Chen & Chen, 2008). Those pairwise partial correlations were depicted as edges connecting nodes. Node size varies according to the mean score for each item. Shortest path length (SPL) was extracted as a descriptive metric from the network. SPL is commonly used to indicate what is the level of direct and indirect association between nodes. In our study, the aim of using SPL was to identify which nodes were directly associated with WP. To cross-validate our analysis, we conducted a traditional logistic regression model based on the variables found in the network analysis to compare the direction and size of associations discovered.

Finally, we performed a community structure analysis to identify underlying clusters between informed consent items and evaluated their association with WP. Community structure analyses are applied to complex networks in which groups of variables are densely interconnected among each other, but sparsely connected to the overall network. We used the random walks method incorporated to the Walktrap algorithm, which is suited for weighted networks (Pons & Latapy, 2006). With random starts, a limited (in general three or four) number of steps or "walks" are performed between nodes in a way that they are "trapped" in highly density subgroups. All analysis were conducted with the R Language for Statistical Computing, through the qgraph and igraph packages.

Results
Sample Description

Our sample consisted of 216 participants, mainly young Caucasian males. Full demographic description available on Table 1. One hundred eighty one participants (84%) answered they would be willing to participate in the hypothetical trial, although only 10% read the whole Informed Consent document (Table 1).

Survey Results

The number of participants that read each section of the informed consent document can be seen in table 2, as well as the Importance and Comprehension median for each question.

Looking into Importance and Comprehension scores related to WP in univariate fashion, there was no significant impact when Importance and Comprehension measures were aggregated into a simple additive composite score (p>0.05, Table 2). However, when comparing each question we found that participants who agreed to participate on the hypothetical study rated Q1, Q9, Q10 and Q13 as significantly more Important than other questions (P<0.05). As for Comprehension, those endorsing hypothetical participation reported less comprehension of items Q1, Q3 and Q5 (Figure 1). Also, we found that only 10% of our sample read all of the sections of the informed consent document before rating (median number of sections read was 1; IQR 0 , 5).

Network Analysis

The first graph (Figure 2A) portrays the relationship among the different Importance Scores and WP. WP was directly associated with Q2 and Q3 (negatively) and Q1, Q10, Q13 (positively). Evaluating item-item pattern of association through community analysis showed 3 clustering communities of items (Figure 2A). The first community (yellow), aggregated items related to Research processes, research purpose and involvement of the participant. It involved concepts such as why and how the research is being done, who is responsible for the project and what is involved. The interesting result is that this first community also involved WP, suggesting that participants who chose to participate on the study also had a high chance of endorsing items in this community as being important to their decision. In other words, participants who were willing to participate in our hypothetical study also tend to find items Q1, Q4, Q5 important but find Q2 and Q3 less important. These items compose the core portion of a informed consent that are deemed important for these participants.

The second community (red) involved five items and was related to Compensation and burden of participating on the research such as costs, confidentiality and dropping out. It is
noteworthy that, two items in this community (Q10 and Q13) importance was directly associated to endorsing WP.

The third community (blue) referred to Benefits and risks to being part of the study. This community had no direct association with WP, but has been associated, however, with elements from the other communities. Q14, for instance, was highly connected to both Q13 which is directly associated with WP. So it seems that Risks and Benefits are not primarily important to endorse WP, however, they are relevant to attribute importance to other portions of the informed consent.

The second figure (Figure 2B) shows the network relationships between Comprehension Scores and WP. In this network analysis, WP was directly associated with Comprehension of Q1, Q3 (negatively), and Q14 (positively). In terms of communities, the Comprehension network showed only two patterns of variables with the same type of information. WP was part of community (yellow) treating Research processes added by benefits and compensation. So comprehending what is being done and also what the participant will gain by taking part on the study was relevant for endorsing WP. Interestingly enough, items related to purpose (Q1), methods (Q2) and responsible (Q3) for the study had a negative association, suggesting that content on these items might be critical to decision making. The second community (blue) had items regarding comprehending the impact of the research on the participants, meaning how long the research would take, confidentiality benefits and risks and costs/compensation. This community had no direct univariate predictors of WP, meaning that comprehension of these items was secondary to choosing to participate in relation to the first community. Weights of both networks’ edges are displayed in Table 3, resulting from a glLasso correlation matrix which penalized the associations providing conditional associations between items.

Complementarily, a standard logistic regression model was built based on the variables found to be directly associated with WP in the network analysis (Table 3). For each point attributed to the Importance, we observed an increased chance of endorsing WP of 2% for Q1 and Q13, and a lesser chance of participating in the study of 2% for items Q2 and Q3. For Comprehension, a lesser risk of 3% for endorsing WP was observed for each point in Q3, and an increased chance of 2% was observed for each point of Q14. All OR values were parallel to the network paths weights in terms of direction of the association.

**Discussion**

To the best of our knowledge, our study is the first to evaluate the relationship between participants’ self-perceived comprehension of an informed consent document and their willingness to participate in a hypothetical trial. Also, we believe this is the first study to
assess the degree of importance attributed to each part of the informed consent and to relate these values to willingness to participate. Our results showed that both the Comprehension and Importance composite additive scores were not associated with a higher likelihood to participate in the hypothetical trial. Nevertheless, self-perceived comprehension of and importance given to specific topics were shown to have a direct relation to willingness to participate. In simple survey results, participants found the topic of risk, compensation and what was involved in the study the most important and found how many people were involved in the study the least important.

The value of network analysis is that complex patterns of association can be discovered that are missed by traditional logistic regression. By using network analysis we take into account all other correlations/associations in the network. This means that the associations found here (being in the same community) are associations conditional on all others in the network. Our network analysis demonstrated that participants who were willing to participate in our hypothetical study also tended to rate items related to the research process (what was involved, their physician within the study, risks and benefits of study) as important to their decision, as well as have a higher self-perceived level of comprehension of these factors. No other community included willingness to participate. In the network analysis, we found some associations that the traditional logistic regression deemed not significant because of its conditional characteristic. This indicates that a more complex analysis of associations identifies different items of importance that simpler, univariate analyses miss. Similar to the aggregate Comprehension Score, our network analysis showed no communal relationships between self-perceived comprehension of specific items and WP.

Only 10% of our sample actually read the entire informed consent document. This phenomena may be considered both a cause and an effect of factors that affect research participation. First, it may be considered as supporting evidence for prior authors who have suggested that the informed consent document is too long (“Federal Register”, 2011). Documents that are too long may prevent actual comprehension of research study information. This might also suggest low engagement of our participants in our hypothetical trial informed consent construct. However, prior studies using observation of actual research participants similarly found a significant rate of incomplete reading of the informed consent document (Baren et al, 2010) suggesting that this may indeed be typical of participant engagement in the informed consent process.

The fact that only 10% of our sample actually read all the sections, but most participants still consider themselves to have knowledge about the research topics leads to 2 scenarios. First, it is possible that participants indeed already know everything they need to know about research participation, declining new information. If this was truly the case, then it is possible that informed consent documents could be shortened without undue ethical risk. However it is possible that participants are mistaken in their level of comprehension, being at risk of missing out on important aspects of the informed consent process. Plus, if WP is
determined mainly by inherently factors outside the informed consent document (such as a general mistrust in research), participants may be less likely to read the whole informed consent document. Both scenarios suggest that informed consent documents, as they currently exist, do not serve the information needs of potential participants. One final possibility is that the artifact of our experimental design led patients to not be fully engaged in the process.

We noted that only one section was rated as particularly low in importance to participants. We thus could not readily identify sections that could be omitted from standard informed consent documents. Our data do seem to support the notion that different respondents valued different topics. Thus, an interactive or adaptable informed consent document might be needed to meet the needs of a diverse population.

A study performed by Marco (2005), attempted to assess the difference in participation rates between groups that received a verbal informed consent, a limited informed consent document and a detailed informed consent document with signature. However, this study did not evaluate the degree of understanding of the informed consent. Prior studies have also sought to determine the reasons why patients choose to participate or to decline research participation. One such study conducted in Australia (Park, White & Bates, 2012), assessed how many people out of their sample would be willing to participate in a HCV vaccine trial and the reasons for this decision. However, these studies did not evaluate participants understanding of consent document information.

This study is about one element of the informed consent process in an emergency medical setting. However, we recruited the participants in an online environment. To minimize this fact, we attempted to create a scenario that would be as similar as possible to an emergency department setting. Nevertheless, we acknowledge that the hypothetical nature of our survey is a significant limitation to our findings. The hypothetical nature of the study may also explain respondent behavior with regard to reading sections of the informed consent document. Respondents are probably more likely to read more sections in an actual research scenario. Second, we only studied the consent document element of the informed consent process. It is recognized that this is not the entirety of the informed consent process, but we focused on it because it is the most consistent, reproducible part of the experience. A consent process varies based on many factors, not least of which are who conducts the discussion and the context and environment in which it occurs. Providing the text from a prior research consent document allowed for a uniform stimulus to provide to our subjects. This allowed us to reduce variation in an effort to identify any signal in the relationship between self-assessed comprehension, importance, and willingness to participate.

We did not include an objective assessment of participant comprehension of informed consent document details. This was in keeping with prior research on this topic, suggesting that promoting self-assessed comprehension is a valid ethical goal (Joffe, Cook, Cleary, Clark & Weeks, 2001a, 2001b). Nonetheless, it is possible that there is a disconnect between self-assessed comprehension and actual comprehension. There are arguments
about whether or not self-assessed comprehension is a valid goal of the informed consent process; these are beyond the scope of the current paper. Future study should investigate whether our findings hold up for measured comprehension as opposed to perceived comprehension. Finally, it is important to note that in our sample only 5% of the participants were African-American, which is not representative of most US emergency departments.

**Conclusion**

In conclusion, we observed that higher levels of self-assessed comprehension is not associated with increased WP in a hypothetical trial. Also, we conclude that potential research participants do not read all the items in an informed consent document and that certain sections are considered to be more important than others, for instance “what’s involved”, “compensation” and “risks” sections.

**Best Practice**

As there is still not an ideal Informed Consent document, it is of the utmost importance that researchers consider the recognized flaws and ethical questions in the process (as potential participants not reading the informed consent document, possible mismatch between self-assessed understanding and technically correct understanding, etc) when enrolling participants.

**Educational Implications**

It is our understanding that the Informed Consent process is complex, and involves more than the consent document, such as the environment of the decision and the relationship between the healthcare provider and the potential participant. Thus, in light of our and other concordant work, it is important that the professionals involved in the informed consent process are educated on the potential participants view of the informed consent documents, and keep in mind the possibility that the trial participants may not read the document and give different importance to part of the document, in order to allow a safer and more thoughtful decision.

**Research Agenda**

We believe that future research should focus on new ways to make the informed consent process more ethical and effective, involving the patient in the decision making process. This should make possible a better relationship between the research team and participants, by showing participants that there is important and new information to be understood in the
informed consent process. This could make participants safer (receiving all the information necessary to make his or her decision), and possibly improve trial participation rates.

Figure Legends:

Figure 1 = Figure 1. Profile of importance and comprehension among those who would participate and those who would not participate in the hypothetical trial. Median and Quantiles of Importance and Comprehension ratings according to Willingness to Participate groups. Participants endorsing Willingness to Participate significantly rated items Q1, Q9, Q10, Q13 and Q14 as more Important (P<0.05) and less comprehension of items Q1, Q3 and Q5 according to rank position differences.

Figure 2A = Figure 2. (A) Importance and (B) comprehension communities networks and the association with Willingness to Participate (WP) in the study. The thickness of the connecting bar between the variables corresponds to the magnitude of their correlation (green bars mean a positive correlation, while red bars indicate a negative correlation).

Figure 2B = Figure 2. (A) Importance and (B) comprehension communities networks and the association with Willingness to Participate (WP) in the study. The thickness of the connecting bar between the variables corresponds to the magnitude of their correlation (green bars mean a positive correlation, while red bars indicate a negative correlation).

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